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[Continued on next page]

(54) Title: ORGANIC COMPOSITIONS TO TREAT BETA-CATENIN-RELATED DISEASES

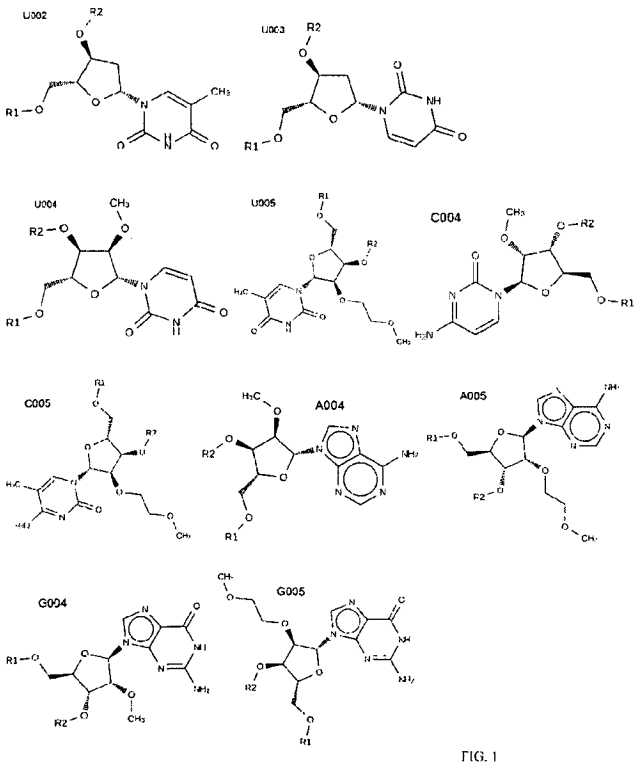


FIG. 1

(57) Abstract: The present disclosure relates to RNAi agents useful in methods of treating Beta-Catenin-related diseases such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to Beta-Catenin.

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ORGANIC COMPOSITIONS TO TREAT BETA-CATENIN-RELATED DISEASES

BACKGROUND OF THE INVENTION

[001] Signaling by the Wnt family of secreted glycolipoproteins is one of the fundamental mechanisms that direct cell proliferation, cell polarity, and cell fate determination during embryonic development and tissue homeostasis. As a result, mutations in the Wnt pathway are often linked to human birth defects, cancer, and other diseases. A critical Wnt pathway is the canonical Wnt signaling pathway.

[002] The transcriptional co-activator Beta-Catenin is the molecular node in this pathway. In the absence of Wnt, cytoplasmic Beta-catenin protein is constantly degraded by the action of the Axin complex, which is composed of the scaffolding protein Axin, the tumor suppressor *adenomatous polyposis coli* gene product (APC), casein kinase 1 (CK1), and glycogen synthase kinase 3 (GSK3). CK1 and GSK3 sequentially phosphorylate the amino terminal region of Beta-catenin, resulting in Beta-catenin recognition by Beta-Trcp, an E3 ubiquitin ligase subunit, and subsequent Beta-catenin ubiquitination and proteasomal degradation.

[003] This continual elimination of Beta-catenin prevents Beta-catenin from reaching the nucleus, and Wnt target genes are thereby repressed by the DNA-bound T cell factor/lymphoid enhancer factor (TCF/LEF) family of proteins. The Wnt/Beta-catenin pathway is activated when a Wnt ligand binds to the seven-pass transmembrane Frizzled (Fz or Fzd) receptor and its coreceptor, low-density lipoprotein receptor-related protein 6 (LRP6), or its close relative LRP5. The formation of a likely Wnt-Fz-LRP6 complex, together with the recruitment of the scaffolding protein Dishevelled (Dvl), results in LRP6 phosphorylation and activation and the recruitment of the Axin complex to the receptors. These events lead to inhibition of Axin-mediated Beta-catenin phosphorylation and thereby to the stabilization of Beta-catenin, which accumulates, travels to the nucleus to form complexes with TCF/LEF and activates Wnt target gene expression.

[004] Given the critical roles of Wnt/Beta-catenin signaling in development and homeostasis, it is no surprise that mutations of the Wnt pathway components are associated with many disorders and diseases. McDonald et al. 2009 Dev. Cell 17: 9-26. Association of deregulated Wnt/Beta-catenin signaling with cancer has been well documented, particularly with colorectal cancer. Polakis 2007. Curr. Opin. Genet. Dev. 17: 45-51. Constitutively activated Beta-catenin signaling, due to APC deficiency or Beta-catenin mutations that prevent its degradation, leads to excessive stem cell renewal/proliferation that predisposes cells to tumorigenesis. Indeed, APC deletion or Beta-catenin activation in stem cells is essential for intestinal neoplasia. Fuchs 2009 Cell 137: 811-819.

[005] Mutations in Beta-Catenin, alterations of levels and cellular compartmentalization of Beta-Catenin, and other aberrations of the Wnt/Beta-Catenin pathway are thus involved directly or indirectly with many diseases. In some Beta-Catenin-related cancers, Beta-Catenin is required for

tumor growth but is not amplified, over-expressed or mis-localized.

[006] There exists the need for treatments related to Beta-Catenin-related diseases.

BRIEF SUMMARY OF THE INVENTION

[007] The present disclosure provides RNAi (RNA interference) agents to Beta-Catenin, for inhibition of the target gene Beta-Catenin, which are useful in the treatment of Beta-Catenin-related diseases, such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases. The present disclosure also encompasses a method of treating a human subject having a pathological state mediated at least in part by Beta-Catenin expression, the method comprising the step of administering to the subject a therapeutically effect amount of a RNAi agent to Beta-Catenin.

[008] The present disclosure provides specific RNAi agents and methods that are useful in reducing Beta-Catenin levels in a subject, e.g., a mammal, such as a human. The present disclosure specifically provides double-stranded RNAi agents comprising at least 15 or more contiguous nucleotides of Beta-Catenin. In particular, the present disclosure provides agents comprising a sense strand and an anti-sense strand, wherein the sense strand and/or the anti-sense strand comprise sequences of 15 or more contiguous nucleotides differing by 0, 1, 2 or 3 from those of the RNAi agents provided, e.g., in Table 1 or elsewhere herein, and modified and unmodified variants thereof. Unmodified sequences are sometimes referred to as "generic". The present disclosure also provides agents comprising a sense strand and an anti-sense strand, wherein the sense strand and/or the anti-sense strand comprise sequences of 19 or more contiguous nucleotides differing by 0, 1, 2 or 3 from those of the RNAi agents provided, e.g., in Table 1 or elsewhere herein, and modified and unmodified variants thereof. The sense strand and anti-sense strand can be contiguous, or covalently bound, e.g., via a loop or linker. The RNAi agents particularly can in one embodiment comprise less than about 30 nucleotides per strand, e.g., such as 17 to 23 nucleotides, 18 to 22 nucleotides, 17 to 23 nucleotides, and/or 19 to 21 nucleotides, and/or 19 to 30 nucleotides, and/or such as those provided, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 or elsewhere herein.

[009] The double-stranded RNAi agents can have 0, 1 or 2 blunt ends, and/or overhangs of 1, 2, 3 or 4 nucleotides (i.e., 1 to 4 nt) from one or both 3' and/or 5' ends. The double-stranded RNAi agents can also optionally comprise one or two 3' caps and/or one or more modified nucleotides. Modified variants of sequences as provided herein include those that are otherwise identical but contain substitutions of a naturally-occurring nucleotide for a corresponding modified nucleotide.

[0010] Further, the RNAi agent can either contain only naturally-occurring ribonucleotide subunits, or one or more modifications to the sugar, phosphate or base of one or more of the replacement nucleotide subunits, whether they comprise ribonucleotide subunits or deoxyribonucleotide subunits. In one embodiment, modified variants of the disclosed RNAi agents have a thymidine (as RNA, or, preferably, DNA) replacing a uridine. In one embodiment, modified variants of the disclosed RNAi agents include RNAi agents with the same sequence (e.g., the same sequence of bases), but with one or more modifications to one or more of the sugar, phosphate or base of one or more of the nucleotide subunits. In one embodiment, the modifications improve efficacy, stability (e.g., against nucleases in blood serum and/or intestinal fluid), and/or reduce immunogenicity of the RNAi agent. One aspect of the present disclosure relates to a double-stranded oligonucleotide comprising at least one non-natural nucleobase. In certain embodiments, the non-natural nucleobase is difluorotolyl, nitroindolyl, nitropyrrolyl, or nitroimidazolyl. In a particular embodiment, the non-natural nucleobase is difluorotolyl. In certain embodiments, only one of the two oligonucleotide strands contains a non-natural nucleobase. In certain embodiments, both of the oligonucleotide strands contain a non-natural nucleobase.

[0011] The RNAi agent(s) can optionally be attached to a ligand selected to improve one or more characteristics, e.g., stability, distribution and/or cellular uptake of the agent, e.g. cholesterol or a derivative thereof. The RNAi agent(s) can be isolated or part of a pharmaceutical composition used for the methods described herein. The pharmaceutical compositions can optionally comprise two or more RNAi agents, each one directed to the same or a different segment the Beta-Catenin mRNA. Optionally, the pharmaceutical compositions can further comprise or be used in conjunction with any known treatment for any Beta-Catenin-related disease.

[0012] The present disclosure further provides methods for reducing the level of Beta-Catenin mRNA in a cell, particularly in the case of a disease characterized by over-expression or hyper-activity of Beta-Catenin. Such methods comprise the step of administering one or more of the RNAi agents of the present disclosure to a cell, as further described below. The present methods utilize the cellular mechanisms involved in RNA interference to selectively degrade the target RNA in a cell and are comprised of the step of contacting a cell with one of the RNAi agents of the present disclosure. The present disclosure also encompasses a method of treating a human subject having a pathological state mediated at least in part by Beta-Catenin expression, over-expression, hyper-activity or improper cellular compartmentalization, the method comprising the step of administering to the subject a therapeutically effect amount of a RNAi agent to Beta-Catenin. Additional methods involve a pathological state wherein disease progression (e.g., tumor growth) requires Beta-Catenin, although Beta-Catenin is not amplified, over-expressed or mis-localized. Such methods can be performed directly on a cell or can be performed on a mammalian subject by administering to a cell or a subject one or more of the RNAi agents/pharmaceutical compositions of the present disclosure.

Reduction of target Beta-Catenin RNA in a cell results in a reduction in the amount of encoded Beta-Catenin protein produced. In an organism, this can result in restoration of balance in the Wnt/Beta-Catenin pathway, and/or prevention of Beta-Catenin accumulation, and/or restoration of proper cell compartmentalization of Beta-Catenin, and/or a reduction in Beta-Catenin activity and/or expression, and/or prevention of Beta-Catenin-mediated activation of Wnt-related genes such as the proto-oncogene c-myc, and/or amelioration, treatment and/or prevention of a Beta-Catenin-related disease. In some Beta-Catenin-related cancers, Beta-Catenin is required for tumor growth but is not amplified, over-expressed or mis-localized. A reduction in Beta-Catenin expression, level or activity should thus limit tumor growth.

[0013] The methods and compositions of the present disclosure, e.g., the methods and Beta-Catenin RNAi agent compositions, can be used with any dosage and/or formulation described herein, as well as with any route of administration described herein.

[0014] The details of one or more embodiments of the present disclosure are set forth in the accompanying drawings and the description below. Elements of the various embodiments (e.g., sequences, modifications, endcaps, combinations of RNAi agents, ligands, additional treatments or methods which can be used, etc.) which are not mutually-exclusive can be combined with each other. Combinations which are mutually exclusive include, for example, the fact that a RNAi agent comprising two strands cannot by definition have both two blunt ends and two overhangs. Furthermore, any RNAi agent sequence can be combined with any set of modifications or endcaps disclosed herein, provided the elements of the combination are not mututally exclusive. Any combination of modifications, 5' end caps, and/or 3' end caps can be used with any RNAi agent sequence disclosed herein. Any RNAi agent can be combined with any other RNAi agent or other treatment composition or method. Other features, objects, and advantages of the present disclosure will be apparent from this description, the drawings, and from the claims.

BRIEF DESCRIPTION OF THE FIGURES

[0015] Figure 1 illustrates various modified nucleotides: U002, U003, U004, U005, C004, C005, A004, A005, G005, and G004, which can be used in the RNAi agents disclosed herein. U002 indicates a 2'- deoxy-thymidine which is DNA. U003 indicates 2'-deoxy uridine. U004 indicates a nucleotide with a U base with a 2'-O-methyl modification. U005 indicates a U base with a 2'-O-methoxyethyl (MOE) modification. C004 indicates a C base with a 2'-O-methyl modification. C005 indicates a C base with 2'-O-methoxyethyl modification. A004 indicates an A base with a 2'-O-methyl modification. A005 indicates an A base with 2'-O-methoxyethyl modification. G005 indicates a G base with a 2'O-methyl modification. G004 indicates a G base with a 2'O-methyl modification. Polynucleotide sequences written with the symbols U002, U003, U004, etc. are sometimes prefaced by "X" (indicating the start of the sequence), and sometimes have a "p"

between the bases, indicating the phosphodiester bond between nucleosides.

DETAILED DESCRIPTION OF THE INVENTION

[0016] The present disclosure encompasses RNAi agents to Beta-Catenin, for inhibition of the target gene Beta-Catenin, which are useful in treatment of Beta-Catenin-related diseases (e.g., diseases associated with mutations in and/or altered expression, compartmentalization, level and/or activity of Beta-Catenin, and/or diseases treatable by modulating the expression, level and/or activity of Beta-Catenin), such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases. In some Beta-Catenin-related cancers, Beta-Catenin is required for tumor growth but is not amplified, over-expressed or mis-localized. A reduction in Beta-Catenin expression, level or activity should thus limit tumor growth. The present disclosure also encompasses a method of treating a human subject having a pathological state mediated at least in part by Beta-Catenin expression, the method comprising the step of administering to the subject a therapeutically effect amount of a RNAi agent to Beta-Catenin.

[0017] **Various embodiments of the present disclosure include:**

[0018] **RNAi agent comprising an anti-sense strand of a RNAi agent described herein.**

[0019] In one embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin (or any set of overlapping RNAi agents specific to Beta-Catenin) provided, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a sense and an anti-sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sense strand of a RNAi agent from any sequence provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the first strand, and the second strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the second strand of any RNAi agent provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second

strand, wherein the sequence of the first strand comprises the sequence of the first strand of any RNAi agent provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the sequence of the first strand of any RNAi agent provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequences of the first and/or second strands comprise the sequences of the first and/or second strand of any RNAi agent provided herein. In another embodiment, the present disclosure relates to a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequences of the first and/or second strand are the sequences of the first and/or second strand of any RNAi agent provided herein. In these various embodiments, the RNAi agent is for inhibition of the target gene Beta-Catenin.

[0020] Particular duplexes include the unmodified and example modified sequences listed in Table 1. In addition to the described example modifications, other modified variants can be made using the nucleotide sequences provided.

[0021] TABLE 1. SEQ ID NOs. for RNAi Agents to Beta-Catenin

[0022] Provided in Table 1 are the nickname of various Beta-Catenin RNAi duplexes; the unmodified sense and anti-sense sequences and SEQ ID NOs; an example modified sense and antisense sequence and SEQ ID NOs; and the position of the RNAi agent within the Beta-Catenin gene.

	UNMODIFIED SEQUENCE		EXAMPLE MODIFIED SEQUENCE		
DUPLEX	Sense SEQ ID NO:	Anti-sense SEQ ID NO:	Sense SEQ ID NO:	Anti-sense SEQ NO:	Position
AD-18892	4112	4771	1	660	2500
AD-18893	4113	4772	2	661	1659
AD-18894	4114	4773	3	662	3038
AD-18895	4115	4774	4	663	2096
AD-18896	4116	4775	5	664	265
AD-18897	4117	4776	6	665	1797
AD-18898	4118	4777	7	666	2587
AD-18899	4119	4778	8	667	1541
AD-18900	4120	4779	9	668	2391
AD-18901	4121	4780	10	669	954
AD-18902	4122	4781	11	670	2908
AD-18903	4123	4782	12	671	3104
AD-18904	4124	4783	13	672	1665
AD-18905	4125	4784	14	673	2594

AD-18906	4126	4785	15	674	3147
AD-18907	4127	4786	16	675	2592
AD-18908	4128	4787	17	676	2507
AD-18909	4129	4788	18	677	2325
AD-18910	4130	4789	19	678	2326
AD-18911	4131	4790	20	679	577
AD-18912	4132	4791	21	680	2116
AD-18913	4133	4792	22	681	2708
AD-18914	4134	4793	23	682	2912
AD-18915	4135	4794	24	683	2704
AD-18916	4136	4795	25	684	3146
AD-18917	4137	4796	26	685	1542
AD-18918	4138	4797	27	686	621
AD-18919	4139	4798	28	687	2505
AD-18920	4140	4799	29	688	2590
AD-18921	4141	4800	30	689	3099
AD-18922	4142	4801	31	690	2591
AD-18923	4143	4802	32	691	2112
AD-18925	4144	4803	33	692	366
AD-18926	4145	4804	34	693	2479
AD-18927	4146	4805	35	694	1502
AD-18928	4147	4806	36	695	2073
AD-18929	4148	4807	37	696	2702
AD-18930	4149	4808	38	697	1774
AD-18931	4150	4809	39	698	708
AD-18932	4151	4810	40	699	1667
AD-18933	4152	4811	41	700	2629
AD-18934	4153	4812	42	701	2114
AD-18935	4154	4813	43	702	2706
AD-18936	4155	4814	44	703	2899
AD-18937	4156	4815	45	704	1639
AD-18938	4157	4816	46	705	1638
AD-18939	4158	4817	47	706	2906
AD-18940	4159	4818	48	707	3145
AD-18941	4160	4819	49	708	2390
AD-18942	4161	4820	50	709	2707
AD-18943	4162	4821	51	710	1668
AD-18944	4163	4822	52	711	2506
AD-18945	4164	4823	53	712	1286
AD-18946	4165	4824	54	713	1660
AD-18947	4166	4825	55	714	2328
AD-18948	4167	4826	56	715	1776
AD-18949	4168	4827	57	716	619

AD-18950	4169	4828	58	717	807
AD-18951	4170	4829	59	718	2417
AD-18952	4171	4830	60	719	3165
AD-18953	4172	4831	61	720	266
AD-18954	4173	4832	62	721	618
AD-18955	4174	4833	63	722	2113
AD-18956	4175	4834	64	723	3040
AD-18957	4176	4835	65	724	3166
AD-18958	4177	4836	66	725	3041
AD-18959	4178	4837	67	726	582
AD-18960	4179	4838	68	727	3220
AD-18961	4180	4839	69	728	2125
AD-18962	4181	4840	70	729	2101
AD-18963	4182	4841	71	730	1773
AD-18964	4183	4842	72	731	2588
AD-18965	4184	4843	73	732	2598
AD-18966	4185	4844	74	733	2907
AD-18967	4186	4845	75	734	2508
AD-18968	4187	4846	76	735	3102
AD-18969	4188	4847	77	736	3042
AD-18970	4189	4848	78	737	2499
AD-18971	4190	4849	79	738	2124
AD-18972	4191	4850	80	739	3105
AD-18973	4192	4851	81	740	2119
AD-18974	4193	4852	82	741	641
AD-18975	4194	4853	83	742	2584
AD-18976	4195	4854	84	743	2105
AD-18977	4196	4855	85	744	1069
AD-18978	4197	4856	86	745	2330
AD-18979	4198	4857	87	746	2388
AD-18980	4199	4858	88	747	3224
AD-18981	4200	4859	89	748	3098
AD-18982	4201	4860	90	749	2049
AD-18983	4202	4861	91	750	1796
AD-18984	4203	4862	92	751	2127
AD-18985	4204	4863	93	752	3029
AD-18986	4205	4864	94	753	2596
AD-18987	4206	4865	95	754	3221
AD-18988	4207	4866	96	755	3159
AD-18989	4208	4867	97	756	2583
AD-18990	4209	4868	98	757	1655
AD-18991	4210	4869	99	758	874
AD-18992	4211	4870	100	759	3028

AD-18993	4212	4871	101	760	3037
AD-18994	4213	4872	102	761	1504
AD-18995	4214	4873	103	762	3095
AD-18996	4215	4874	104	763	2703
AD-18997	4216	4875	105	764	3154
AD-18998	4217	4876	106	765	3094
AD-18999	4218	4877	107	766	2599
AD-19000	4219	4878	108	767	643
AD-19001	4220	4879	109	768	2389
AD-19002	4221	4880	110	769	1669
AD-19003	4222	4881	111	770	2106
AD-19004	4223	4882	112	771	3170
AD-19005	4224	4883	113	772	3103
AD-19006	4225	4884	114	773	642
AD-19007	4226	4885	115	774	3230
AD-19008	4227	4886	116	775	3222
AD-19009	4228	4887	117	776	2905
AD-19010	4229	4888	118	777	2904
AD-19011	4230	4889	119	778	579
AD-19012	4231	4890	120	779	3171
AD-19042	4232	4891	121	780	2504
AD-19043	4233	4892	122	781	3039
AD-19044	4234	4893	123	782	3034
AD-19045	4235	4894	124	783	1505
AD-19046	4236	4895	125	784	1288
AD-19047	4237	4896	126	785	2123
AD-19048	4238	4897	127	786	620
AD-19049	4239	4898	128	787	3164
AD-19050	4240	4899	129	788	3101
AD-19051	4241	4900	130	789	2329
AD-19052	4242	4901	131	790	2115
AD-19053	4243	4902	132	791	2627
AD-19054	4244	4903	133	792	2902
AD-19055	4245	4904	134	793	262
AD-19056	4246	4905	135	794	1406
AD-19057	4247	4906	136	795	2497
AD-19058	4248	4907	137	796	3043
AD-19059	4249	4908	138	797	2589
AD-19060	4250	4909	139	798	2586
AD-19061	4251	4910	140	799	1658
AD-19062	4252	4911	141	800	2050
AD-19063	4253	4912	142	801	2385
AD-19064	4254	4913	143	802	1637

AD-19065	4255	4914	144	803	707
AD-19066	4256	4915	145	804	2597
AD-19067	4257	4916	146	805	3161
AD-19068	4258	4917	147	806	875
AD-19069	4259	4918	148	807	3044
AD-19070	4260	4919	149	808	617
AD-19071	4261	4920	150	809	2498
AD-19072	4262	4921	151	810	367
AD-19073	4263	4922	152	811	2545
AD-19074	4264	4923	153	812	1544
AD-19075	4265	4924	154	813	3148
AD-19076	4266	4925	155	814	2909
AD-19077	4267	4926	156	815	2509
AD-19078	4268	4927	157	816	1775
AD-19079	4269	4928	158	817	1407
AD-19080	4270	4929	159	818	2327
AD-19081	4271	4930	160	819	3031
AD-19082	4272	4931	161	820	1661
AD-19083	4273	4932	162	821	3162
AD-19738	4274	4933	163	822	1906
AD-19739	4275	4934	164	823	825
AD-19740	4276	4935	165	824	1838
AD-19741	4277	4936	166	825	1714
AD-19742	4278	4937	167	826	1859
AD-19743	4279	4938	168	827	324
AD-19744	4280	4939	169	828	535
AD-19745	4281	4940	170	829	822
AD-19746	4282	4941	171	830	826
AD-19747	4283	4942	172	831	851
AD-19748	4284	4943	173	832	1313
AD-19749	4285	4944	174	833	1860
AD-19750	4286	4945	175	834	2016
AD-19751	4287	4946	176	835	1868
AD-19752	4288	4947	177	836	1869
AD-19753	4289	4948	178	837	1876
AD-19754	4290	4949	179	838	1908
AD-19755	4291	4950	180	839	2192
AD-19756	4292	4951	181	840	520
AD-19757	4293	4952	182	841	524
AD-19758	4294	4953	183	842	623
AD-19759	4295	4954	184	843	916
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AD-19765	4300	4959	189	848	637
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AD-19767	4302	4961	191	850	1028
AD-19768	4303	4962	192	851	1314
AD-20124	4304	4963	193	852	2012
AD-25889	4305	4964	194	853	2632
AD-25890	4306	4965	195	854	2637
AD-25891	4307	4966	196	855	2648
AD-25892	4308	4967	197	856	2649
AD-25893	4309	4968	198	857	2663
AD-25894	4310	4969	199	858	2664
AD-25895	4311	4970	200	859	2694
AD-25896	4312	4971	201	860	2695
AD-25897	4313	4972	202	861	2697
AD-25898	4314	4973	203	862	2698
AD-25899	4315	4974	204	863	2699
AD-25900	4316	4975	205	864	2751
AD-25901	4317	4976	206	865	2752
AD-25902	4318	4977	207	866	2753
AD-25903	4319	4978	208	867	2832
AD-25904	4320	4979	209	868	2833
AD-25905	4321	4980	210	869	2837
AD-25906	4322	4981	211	870	2843
AD-25907	4323	4982	212	871	2844
AD-25908	4324	4983	213	872	2845
AD-25909	4325	4984	214	873	2846
AD-25910	4326	4985	215	874	2859
AD-25911	4327	4986	216	875	2913
AD-25912	4328	4987	217	876	2914
AD-25913	4329	4988	218	877	2938
AD-25914	4330	4989	219	878	2940
AD-25915	4331	4990	220	879	2941
AD-25916	4332	4991	221	880	2942
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AD-25918	4334	4993	223	882	2992
AD-25919	4335	4994	224	883	2997
AD-25920	4336	4995	225	884	2998
AD-25921	4337	4996	226	885	3077
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AD-25923	4339	4998	228	887	3080
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AD-25928	4344	5003	233	892	3123
AD-25929	4345	5004	234	893	3124
AD-25930	4346	5005	235	894	3125
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AD-25932	4348	5007	237	896	3133
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AD-25934	4350	5009	239	898	3168
AD-25935	4351	5010	240	899	3169
AD-25936	4352	5011	241	900	3172
AD-25937	4353	5012	242	901	3192
AD-25938	4354	5013	243	902	2665
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AD-25940	4356	5015	245	904	2683
AD-25941	4357	5016	246	905	2684
AD-25942	4358	5017	247	906	2685
AD-25943	4359	5018	248	907	2686
AD-25944	4360	5019	249	908	2687
AD-25945	4361	5020	250	909	2696
AD-25946	4362	5021	251	910	2709
AD-25947	4363	5022	252	911	2710
AD-25948	4364	5023	253	912	2711
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AD-25950	4366	5025	255	914	2713
AD-25951	4367	5026	256	915	2714
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AD-25953	4369	5028	258	917	2835
AD-25954	4370	5029	259	918	2836
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AD-25956	4372	5031	261	920	2847
AD-25957	4373	5032	262	921	2848
AD-25958	4374	5033	263	922	2871
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AD-25960	4376	5035	265	924	2996
AD-25961	4377	5036	266	925	3079
AD-25962	4378	5037	267	926	3084
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AD-26017	4381	5040	270	929	3152
AD-26018	4382	5041	271	930	3170
AD-26019	4383	5042	272	931	3171

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AD-26022	4386	5045	275	934	207
AD-26023	4387	5046	276	935	208
AD-26024	4388	5047	277	936	215
AD-26025	4389	5048	278	937	216
AD-26026	4390	5049	279	938	217
AD-26027	4391	5050	280	939	221
AD-26028	4392	5051	281	940	222
AD-26029	4393	5052	282	941	225
AD-26030	4394	5053	283	942	230
AD-26031	4395	5054	284	943	231
AD-26032	4396	5055	285	944	232
AD-26033	4397	5056	286	945	235
AD-26034	4398	5057	287	946	236
AD-26035	4399	5058	288	947	251
AD-26036	4400	5059	289	948	252
AD-26037	4401	5060	290	949	257
AD-26038	4402	5061	291	950	262
AD-26039	4403	5062	292	951	268
AD-26040	4404	5063	293	952	269
AD-26041	4405	5064	294	953	270
AD-26042	4406	5065	295	954	273
AD-26043	4407	5066	296	955	285
AD-26044	4408	5067	297	956	291
AD-26045	4409	5068	298	957	295
AD-26046	4410	5069	299	958	305
AD-26047	4411	5070	300	959	307
AD-26048	4412	5071	301	960	111
AD-26049	4413	5072	302	961	316
AD-26050	4414	5073	303	962	317
AD-26051	4415	5074	304	963	331
AD-26052	4416	5075	305	964	338
AD-26053	4417	5076	306	965	339
AD-26054	4418	5077	307	966	353
AD-26055	4419	5078	308	967	354
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AD-26057	4421	5080	310	969	1216
AD-26058	4422	5081	311	970	383
AD-26059	4423	5082	312	971	397
AD-26060	4424	5083	313	972	402
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AD-26068	4432	5091	321	980	1232
AD-26069	4433	5092	322	981	1233
AD-26070	4434	5093	323	982	460
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AD-26074	4438	5097	327	986	481
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AD-26084	4448	5107	337	996	559
AD-26085	4449	5108	338	997	562
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AD-26087	4451	5110	340	999	581
AD-26088	4452	5111	341	1000	584
AD-26089	4453	5112	342	1001	591
AD-26090	4454	5113	343	1002	595
AD-26091	4455	5114	344	1003	604
AD-26092	4456	5115	345	1004	611
AD-26093	4457	5116	346	1005	612
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AD-26095	4459	5118	348	1007	623
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AD-26099	4463	5122	352	1011	649
AD-26100	4464	5123	353	1012	652
AD-26101	4465	5124	354	1013	658
AD-26102	4466	5125	355	1014	662
AD-26103	4467	5126	356	1015	666
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AD-26105	4469	5128	358	1017	670

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AD-26107	4471	5130	360	1019	682
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AD-26110	4474	5133	363	1022	707
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AD-26123	4477	5136	366	1025	722
AD-26124	4478	5137	367	1026	723
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AD-26127	4481	5140	370	1029	731
AD-26128	4482	5141	371	1030	732
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AD-26130	4484	5143	373	1032	755
AD-26131	4485	5144	374	1033	756
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AD-26135	4489	5148	378	1037	1551
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AD-26137	4491	5150	380	1039	778
AD-26138	4492	5151	381	1040	785
AD-26139	4493	5152	382	1041	788
AD-26140	4494	5153	383	1042	789
AD-26141	4495	5154	384	1043	1624
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AD-26144	4498	5157	387	1046	812
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AD-26149	4503	5162	392	1051	842
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AD-26151	4505	5164	394	1053	851
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AD-26155	4509	5168	398	1057	866
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AD-26168	4522	5181	411	1070	976
AD-26169	4523	5182	412	1071	977
AD-26170	4524	5183	413	1072	978
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AD-26172	4526	5185	415	1074	986
AD-26173	4527	5186	416	1075	997
AD-26174	4528	5187	417	1076	998
AD-26175	4529	5188	418	1077	1848
AD-26176	4530	5189	419	1078	1849
AD-26177	4531	5190	420	1079	1005
AD-26178	4532	5191	421	1080	1008
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AD-26184	4538	5197	427	1086	1927
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AD-26186	4540	5199	429	1088	1022
AD-26187	4541	5200	430	1089	1032
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AD-26217	4571	5230	460	1119	1226
AD-26218	4572	5231	461	1120	1227
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AD-26652	4574	5233	463	1122	1229
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AD-26661	4583	5242	472	1131	1291
AD-26662	4584	5243	473	1132	1292
AD-26663	4585	5244	474	1133	1337
AD-26664	4586	5245	475	1134	1338
AD-26665	4587	5246	476	1135	1346
AD-26666	4588	5247	477	1136	1347
AD-26667	4589	5248	478	1137	1366
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AD-26669	4591	5250	480	1139	1375
AD-26670	4592	5251	481	1140	1381
AD-26671	4593	5252	482	1141	1384
AD-26672	4594	5253	483	1142	1396
AD-26673	4595	5254	484	1143	1397
AD-26674	4596	5255	485	1144	1410
AD-26675	4597	5256	486	1145	1411
AD-26676	4598	5257	487	1146	1414

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AD-26681	4603	5262	492	1151	1430
AD-26682	4604	5263	493	1152	1432
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AD-26684	4606	5265	495	1154	1447
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AD-26693	4615	5274	504	1163	2441
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AD-26700	4622	5281	511	1170	1522
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AD-26702	4624	5283	513	1172	1526
AD-26703	4625	5284	514	1173	1527
AD-26704	4626	5285	515	1174	1539
AD-26705	4627	5286	516	1175	1540
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AD-26707	4629	5288	518	1177	1546
AD-26708	4630	5289	519	1178	1547
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AD-26714	4636	5295	525	1184	1629
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AD-26724	4646	5305	535	1194	1717
AD-26725	4647	5306	536	1195	1723
AD-26726	4648	5307	537	1196	1729
AD-26727	4649	5308	538	1197	1735
AD-26728	4650	5309	539	1198	1736
AD-26729	4651	5310	540	1199	1737
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AD-26731	4653	5312	542	1201	1744
AD-26732	4654	5313	543	1202	1754
AD-26733	4655	5314	544	1203	1770
AD-26734	4656	5315	545	1204	1771
AD-26735	4657	5316	546	1205	1772
AD-26736	4658	5317	547	1206	1778
AD-26737	4659	5318	548	1207	1783
AD-26738	4660	5319	549	1208	1787
AD-26739	4661	5320	550	1209	1792
AD-26740	4662	5321	551	1210	1798
AD-26741	4663	5322	552	1211	1861
AD-26742	4664	5323	553	1212	1866
AD-26743	4665	5324	554	1213	1870
AD-26744	4666	5325	555	1214	1873
AD-26745	4667	5326	556	1215	1882
AD-26746	4668	5327	557	1216	1888
AD-26747	4669	5328	558	1217	1889
AD-26748	4670	5329	559	1218	1928
AD-26749	4671	5330	560	1219	1929
AD-26750	4672	5331	561	1220	1930
AD-26751	4673	5332	562	1221	1955
AD-26752	4674	5333	563	1222	1956
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AD-26754	4676	5335	565	1224	2002
AD-26755	4677	5336	566	1225	2007
AD-26756	4678	5337	567	1226	2013
AD-26757	4679	5338	568	1227	2014
AD-26758	4680	5339	569	1228	2038
AD-26759	4681	5340	570	1229	2042
AD-26760	4682	5341	571	1230	2046
AD-26761	4683	5342	572	1231	2047
AD-26762	4684	5343	573	1232	2059

AD-26763	4685	5344	574	1233	2060
AD-26764	4686	5345	575	1234	2061
AD-26765	4687	5346	576	1235	2062
AD-26766	4688	5347	577	1236	2063
AD-26767	4689	5348	578	1237	2070
AD-26768	4690	5349	579	1238	2071
AD-26769	4691	5350	580	1239	2076
AD-26770	4692	5351	581	1240	2079
AD-26771	4693	5352	582	1241	2083
AD-26772	4694	5353	583	1242	2110
AD-26773	4695	5354	584	1243	2128
AD-26774	4696	5355	585	1244	2178
AD-26775	4697	5356	586	1245	2179
AD-26776	4698	5357	587	1246	2182
AD-26777	4699	5358	588	1247	2189
AD-26778	4700	5359	589	1248	2193
AD-26779	4701	5360	590	1249	2194
AD-26780	4702	5361	591	1250	2197
AD-26781	4703	5362	592	1251	2234
AD-26782	4704	5363	593	1252	2235
AD-26783	4705	5364	594	1253	2254
AD-26784	4706	5365	595	1254	2257
AD-26785	4707	5366	596	1255	2262
AD-26786	4708	5367	597	1256	2265
AD-26787	4709	5368	598	1257	2272
AD-26788	4710	5369	599	1258	2278
AD-26789	4711	5370	600	1259	2298
AD-26790	4712	5371	601	1260	2303
AD-26791	4713	5372	602	1261	2365
AD-26792	4714	5373	603	1262	2375
AD-26793	4715	5374	604	1263	2376
AD-26794	4716	5375	605	1264	2386
AD-26795	4717	5376	606	1265	2393
AD-26796	4718	5377	607	1266	2397
AD-26797	4719	5378	608	1267	2398
AD-26798	4720	5379	609	1268	2402
AD-26799	4721	5380	610	1269	2406
AD-26800	4722	5381	611	1270	2407
AD-26801	4723	5382	612	1271	2420
AD-26802	4724	5383	613	1272	2421
AD-26803	4725	5384	614	1273	2422
AD-26804	4726	5385	615	1274	2431
AD-26805	4727	5386	616	1275	2436

AD-26806	4728	5387	617	1276	2451
AD-26807	4729	5388	618	1277	2454
AD-26808	4730	5389	619	1278	675
AD-26809	4731	5390	620	1279	676
AD-26810	4732	5391	621	1280	679
AD-26811	4733	5392	622	1281	2458
AD-26812	4734	5393	623	1282	2461
AD-26813	4735	5394	624	1283	2466
AD-26814	4736	5395	625	1284	2493
AD-26815	4737	5396	626	1285	2494
AD-26816	4738	5397	627	1286	2503
AD-26817	4739	5398	628	1287	2515
AD-26818	4740	5399	629	1288	2542
AD-26819	4741	5400	630	1289	2580
AD-26820	4742	5401	631	1290	2581
AD-26821	4743	5402	632	1291	2595
AD-26822	4744	5403	633	1292	2601
AD-26823	4745	5404	634	1293	2605
AD-26824	4746	5405	635	1294	2606
AD-26825	4747	5406	636	1295	2607
AD-26826	4748	5407	637	1296	878
AD-26900	4749	5408	638	1297	2745
AD-26901	4750	5409	639	1298	2872
AD-26902	4751	5410	640	1299	2915
AD-26903	4752	5411	641	1300	2916
AD-26904	4753	5412	642	1301	2918
AD-26905	4754	5413	643	1302	2919
AD-26906	4755	5414	644	1303	2939
AD-26907	4756	5415	645	1304	2978
AD-26908	4757	5416	646	1305	2979
AD-26909	4758	5417	647	1306	2980
AD-26910	4759	5418	648	1307	2981
AD-26911	4760	5419	649	1308	2983
AD-26912	4761	5420	650	1309	2984
AD-26913	4762	5421	651	1310	2986
AD-26914	4763	5422	652	1311	3081
AD-26915	4764	5423	653	1312	3082
AD-26916	4765	5424	654	1313	2917
AD-26917	4766	5425	655	1314	2994
AD-26918	4767	5426	656	1315	2995
AD-26919	4768	5427	657	1316	3134
AD-26920	4769	5428	658	1317	1535
AD-26921	4770	5429	659	1318	1801

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SET1 1249	6091	6112	6199	6367	1231
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SET1 1249	6091	6112	6157	6325	1231
SET1 1249	6091	6112	6178	6346	1231
SET1 1250	6092	6113	6200	6368	1232
SET1 1250	6092	6113	6221	6389	1232
SET1 1250	6092	6113	6158	6326	1232
SET1 1250	6092	6113	6179	6347	1232
SET1 1450	6093	6114	6195	6363	1432
SET1 1450	6093	6114	6216	6384	1432
SET1 1450	6093	6114	6153	6321	1432
SET1 1450	6093	6114	6174	6342	1432
SET1 1545	6094	6115	6202	6370	1527
SET1 1545	6094	6115	6223	6391	1527
SET1 1545	6094	6115	6160	6328	1527
SET1 1545	6094	6115	6181	6349	1527
SET1 1755	6095	6116	6203	6371	1737
SET1 1755	6095	6116	6224	6392	1737
SET1 1755	6095	6116	6161	6329	1737
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SET1 1814	6096	6117	6213	6381	1796
SET1 1814	6096	6117	6150	6318	1796
SET1 1814	6096	6117	6171	6339	1796
SET1 1816	6097	6118	6187	6355	1798
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SET1 1816	6097	6118	6145	6313	1798
SET1 1816	6097	6118	6166	6334	1798
SET1 1974	6098	6119	6188	6356	1956
SET1 1974	6098	6119	6209	6377	1956
SET1 1974	6098	6119	6146	6314	1956
SET1 1974	6098	6119	6167	6335	1956
SET1 2202	6099	6120	6201	6369	2184
SET1 2202	6099	6120	6222	6390	2184
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SET1 2202	6099	6120	6180	6348	2184
SET1 2425	6100	6121	6189	6357	2407
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SET1 2425	6100	6121	6147	6315	2407

SET1 2425	6100	6121	6168	6336	2407
SET1 254	6101	6122	6183	6351	236
SET1 254	6101	6122	6204	6372	236
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SET1 254	6101	6122	6162	6330	236
SET1 3146	6102	6123	6190	6358	3128
SET1 3146	6102	6123	6211	6379	3128
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SET1 3146	6102	6123	6169	6337	3128
SET1 3169	6103	6124	6196	6364	3151
SET1 3169	6103	6124	6217	6385	3151
SET1 3169	6103	6124	6154	6322	3151
SET1 3169	6103	6124	6175	6343	3151
SET1 3196	6104	6125	6194	6362	3178
SET1 3196	6104	6125	6215	6383	3178
SET1 3196	6104	6125	6152	6320	3178
SET1 3196	6104	6125	6173	6341	3178
SET1 3477	6105	6126	6197	6365	3459
SET1 3477	6105	6126	6218	6386	3459
SET1 3477	6105	6126	6155	6323	3459
SET1 3477	6105	6126	6176	6344	3459
SET1 703	6106	6127	6184	6352	685
SET1 703	6106	6127	6205	6373	685
SET1 703	6106	6127	6142	6310	685
SET1 703	6106	6127	6163	6331	685
SET1 709	6107	6128	6185	6353	691
SET1 709	6107	6128	6206	6374	691
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SET1 709	6107	6128	6164	6332	691
SET1 865	6108	6129	6198	6366	847
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SET1 865	6108	6129	6177	6345	847
SET1 889	6109	6130	6191	6359	871
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SET1 889	6109	6130	6170	6338	871
SET1 895	6110	6131	6186	6354	877
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SET1 895	6110	6131	6144	6312	877
SET1 895	6110	6131	6165	6333	877
SET1 1245	6090	6111	6235	6403	1227
SET1 1245	6090	6111	6256	6424	1227

SET1 1245	6090	6111	6277	6445	1227
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SET1 1249	6091	6112	6241	6409	1231
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SET1 1249	6091	6112	6283	6451	1231
SET1 1249	6091	6112	6304	6472	1231
SET1 1250	6092	6113	6242	6410	1232
SET1 1250	6092	6113	6263	6431	1232
SET1 1250	6092	6113	6284	6452	1232
SET1 1250	6092	6113	6305	6473	1232
SET1 1450	6093	6114	6237	6405	1432
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SET1 1814	6096	6117	6255	6423	1796
SET1 1814	6096	6117	6276	6444	1796
SET1 1814	6096	6117	6297	6465	1796
SET1 1816	6097	6118	6229	6397	1798
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SET1 1816	6097	6118	6271	6439	1798
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SET1 1974	6098	6119	6230	6398	1956
SET1 1974	6098	6119	6251	6419	1956
SET1 1974	6098	6119	6272	6440	1956
SET1 1974	6098	6119	6293	6461	1956
SET1 2202	6099	6120	6243	6411	2184
SET1 2202	6099	6120	6264	6432	2184
SET1 2202	6099	6120	6285	6453	2184
SET1 2202	6099	6120	6306	6474	2184
SET1 2425	6100	6121	6231	6399	2407
SET1 2425	6100	6121	6252	6420	2407
SET1 2425	6100	6121	6273	6441	2407
SET1 2425	6100	6121	6294	6462	2407
SET1 254	6101	6122	6225	6393	236

SET1 254	6101	6122	6246	6414	236
SET1 254	6101	6122	6267	6435	236
SET1 254	6101	6122	6288	6456	236
SET1 3146	6102	6123	6232	6400	3128
SET1 3146	6102	6123	6253	6421	3128
SET1 3146	6102	6123	6274	6442	3128
SET1 3146	6102	6123	6295	6463	3128
SET1 3169	6103	6124	6238	6406	3151
SET1 3169	6103	6124	6259	6427	3151
SET1 3169	6103	6124	6280	6448	3151
SET1 3169	6103	6124	6301	6469	3151
SET1 3196	6104	6125	6236	6404	3178
SET1 3196	6104	6125	6257	6425	3178
SET1 3196	6104	6125	6278	6446	3178
SET1 3196	6104	6125	6299	6467	3178
SET1 3477	6105	6126	6239	6407	3459
SET1 3477	6105	6126	6260	6428	3459
SET1 3477	6105	6126	6281	6449	3459
SET1 3477	6105	6126	6302	6470	3459
SET1 703	6106	6127	6226	6394	685
SET1 703	6106	6127	6247	6415	685
SET1 703	6106	6127	6268	6436	685
SET1 703	6106	6127	6289	6457	685
SET1 709	6107	6128	6227	6395	691
SET1 709	6107	6128	6248	6416	691
SET1 709	6107	6128	6269	6437	691
SET1 709	6107	6128	6290	6458	691
SET1 865	6108	6129	6240	6408	847
SET1 865	6108	6129	6261	6429	847
SET1 865	6108	6129	6282	6450	847
SET1 865	6108	6129	6303	6471	847
SET1 889	6109	6130	6233	6401	871
SET1 889	6109	6130	6254	6422	871
SET1 889	6109	6130	6275	6443	871
SET1 889	6109	6130	6296	6464	871
SET1 895	6110	6131	6228	6396	877
SET1 895	6110	6131	6249	6417	877
SET1 895	6110	6131	6270	6438	877
SET1 895	6110	6131	6291	6459	877

[0023] Various Embodiments of the Present Disclosure

[0024] Various RNAi agents to Beta-Catenin are disclosed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[0025] Tables 1, 2 and 3 provide the sequence, SEQ ID NOs and positions of various RNAi agents to Beta-Catenin, including both unmodified sequences and example modified sequences. The sequences in Table 2 are not modified.

[0026] Table 3 provides the sequences and SEQ ID NOs for example modified sequences of the sense and anti-sense strands of various RNAi agents to Beta-Catenin. The present disclosure also encompasses unmodified versions of these sequences, and different versions comprising other modifications or patterns of modification (but the same sequence of bases).

[0027] In the sequences in Table 3, lower-case letters (e.g., c, u) indicate modified nucleotides while upper case letters (e.g., C, U, A, G) indicate unmodified nucleotides. In Table 3, example modified versions of each of the sequences are shown. However, the present disclosure encompasses unmodified versions of these sequences and other versions which comprise additional or alternative modifications. Thus, for example, AD-18892 can optionally have the unmodified (or "generic") sequence UGGUGCUGACUAUCCAGUU (SEQ ID NO: 429) in the sense strand and AACUGGAUAGUCAGCACCA (SEQ ID NO: 430) in the anti-sense strand. The present disclosure also encompasses alternative modified versions of the duplex comprising UGGUGCUGACUAUCCAGUU (SEQ ID NO: 429) in the sense strand and AACUGGAUAGUCAGCACCA (SEQ ID NO: 430) in the anti-sense strand.

[0028] In the sequences in Tables 1, 2, 3, 4, 5, 6, 7 and 8, the modified and unmodified sequences can optionally comprise the sequence "dTdT", "dTsdT" or "UU" at the 3' end. Thus, for example, AD-18892 can optionally have the modified sequence uGGuGcuGAcuAuccAGuudTdT (SEQ ID NO: 6136) or uGGuGcuGAcuAuccAGuudTsdT (SEQ ID NO: 6137) in the sense strand; and AACUGGAuAGUcAGcACcAdTdT (SEQ ID NO: 6138) or AACUGGAuAGUcAGcACcAdTsdT (SEQ ID NO: 6139) in the anti-sense strand. As noted in Table 3, below, dT is 2'-deoxy-thymidine-5'-phosphate and sdT is 2'-deoxy Thymidine 5'-phosphorothioate. In the disclosed sequences, terminal dinucleotide "UU" is 2'-OMe-U 2'-OMe-U, and neither the terminal TT nor the terminal UU are in the inverted/reverse orientation. In various embodiments UU as standard RNA can also be used.

[0029] The terminal dithymidine (or TT or dTdT or sdTsdT or UU or the like) is not part of the Beta-Catenin target sequence, but is a modified variant of the dithymidine dinucleotide commonly placed as an overhang to protect the ends of siRNAs from nucleases (see, for example, Elbashir et al. 2001 Nature 411: 494-498; Elbashir et al. 2001 EMBO J. 20: 6877-6888; and Kraynack et al. 2006 RNA 12:163-176). A terminal dinucleotide is known from these references to enhance nuclease resistance but not contribute to target recognition. On any modified or unmodified sequence, a 3' end cap, as is known in the art, can be used instead of a terminal dinucleotide to stabilize the end from nuclease degradation provided that the 3' end cap is able to both stablize the RNAi agent (e.g., against nucleases) and not interfere excessively with siRNA activity.

[0030] Table 4 provides sets of overlapping RNAi agents to Beta-Catenin.

[0031] Activity levels of various Beta-Catenin RNAi agents are provided in Tables 5 to 9.

[0032] **RNAi agent comprising an anti-sense strand of a RNAi agent described herein**

[0033] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent for inhibition of the target gene Beta-Catenin comprising an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to Beta-Catenin selected from those anti-sense strands in the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[0034] In one embodiment, the composition comprises a RNAi agent for inhibition of the target gene Beta-Catenin comprising a sense and an anti-sense strand, wherein the sequence of the sense strand and the sequence of the anti-sense strand are the sequences of the sense and anti-sense strand, respectively, of any RNAi agent provided herein. In one embodiment, the composition comprises a RNAi agent for inhibition of the target gene Beta-Catenin comprising a sense and an anti-sense strand, wherein the sequence of the antisense strand is the sequence of anti-sense strand of any RNAi agent provided herein. In one embodiment, the composition comprises a RNAi agent for inhibition of the target gene Beta-Catenin comprising a sense and an anti-sense strand, wherein the sequence of the sense strand and the sequence of the anti-sense strand are the sequences of the sense and anti-sense strand, respectively, of any RNAi agent provided herein, further comprising an additional about 6 to 20 nucleotides on one or both strands (e.g., about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 nt). In one embodiment, the composition comprises a RNAi agent for inhibition of the target gene Beta-Catenin comprising a sense and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of any RNAi agent provided herein, further comprising an additional about 6 to 20 nucleotides on one or both strands (e.g., about 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 nt). In these various embodiments, the RNAi agent is for inhibition of the target gene Beta-Catenin.

[0035] Various specific embodiments of these embodiments are described below.

[0036] In one embodiment, the composition further comprises a second RNAi agent to Beta-Catenin. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated), or combined within the same pharmaceutical composition.

[0037] In one embodiment, the antisense strand is about 30 or fewer nt in length.

[0038] In one embodiment, the sense strand and the antisense strand form a duplex region of about 15 to about 30 nucleotide pairs in length.

[0039] In one embodiment, the antisense strand is about 15 to about 36 nt in length, about 17 to

about 30 nt in length, about 17 to 23 nt in length, about 19 to about 49 nt in length, or about 19 to about 23 nt in length. In one embodiment, the antisense strand has at least the length selected from about 15 nt, about 16 nt, about 17 nt, about 18 nt, about 19 nt, about 20 nt, about 21 nt, about 22 nt, about 23 nt, about 24 nt, about 25 nt, about 26 nt, about 27 nt, about 28 nt, about 29 nt and about 30 nt.

[0040] In one embodiment, the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment, e.g., blood serum or intestinal lavage fluid.

[0041] In one embodiment, the RNAi agent comprises at least one sugar backbone modification (e.g., phosphorothioate linkage) and/or at least one 2'-modified nucleotide. In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0042] In one embodiment, the RNAi agent comprises: at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[0043] In one embodiment, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA). In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0044] In one embodiment, the RNAi agent comprises a blunt end.

[0045] In one embodiment, the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[0046] In one embodiment, the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[0047] In one embodiment, the RNAi agent is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[0048] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-

Catenin gene by at least about 60% at a concentration of 10 nM in HeLa cells *in vitro*.

[0049] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 70% at a concentration of 10 nM in HeLa cells *in vitro*.

[0050] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 80% at a concentration of 10 nM in HeLa cells *in vitro*.

[0051] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 90% at a concentration of 10 nM in HeLa cells *in vitro*.

[0052] In one embodiment, the RNAi has an EC50 of no more than about 0.1 nM.

[0053] In one embodiment, the RNAi has an EC50 of no more than about 0.01 nM.

[0054] In one embodiment, the RNAi has an EC50 of no more than about 0.001 nM.

[0055] A RNAi agent comprising a first and a second strand

[0056] In one particular specific embodiment, the present disclosure relates to a composition comprising a RNAi agent for inhibition of the target gene Beta-Catenin comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides, each differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In these various embodiments, the RNAi agent is for inhibition of the target gene Beta-Catenin.

[0057] Various specific embodiments of this embodiment are described below.

[0058] In one embodiment, the composition further comprises a second RNAi agent to Beta-Catenin. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated), or combined within the same pharmaceutical composition.

[0059] In one embodiment, the antisense strand is about 30 or fewer nt in length.

[0060] In one embodiment, the sense strand and the antisense strand form a duplex region of about 15 to about 30 nt pairs in length.

[0061] In one embodiment, the antisense strand is about 15 to about 36 nt in length, including about 17 to about 23 nt in length, and including about 19 to about 23 nt in length. In one embodiment, the antisense strand has at least the length selected from about 15 nt, about 16 nt, about 17 nt, about 18 nt, about 19 nt, about 20 nt, about 21 nt, about 22 nt, about 23 nt, about 24 nt, about 25 nt, about 26 nt, about 27 nt, about 28 nt, about 29 nt and about 30 nt.

[0062] In one embodiment, the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment, e.g., blood serum or intestinal lavage fluid.

[0063] In one embodiment, the RNAi agent comprises at least one sugar backbone modification (e.g., phosphorothioate linkage) and/or at least one 2'-modified nucleotide. In one embodiment, all the pyrimidines are 2' O-methyl-modified nucleotides.

[0064] In one embodiment, the RNAi agent comprises: at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[0065] In one embodiment, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[0066] In one embodiment, the RNAi agent comprises a blunt end.

[0067] In one embodiment, the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[0068] In one embodiment, the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[0069] In one embodiment, the RNAi agent is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[0070] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 60% at a concentration of 10 nM in HeLa cells *in vitro*.

[0071] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 70% at a concentration of 10 nM in HeLa cells *in vitro*.

[0072] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 80% at a concentration of 10 nM in HeLa cells *in vitro*.

[0073] In one embodiment, the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 90% at a concentration of 10 nM in HeLa cells *in vitro*.

[0074] In one embodiment, the RNAi has an EC50 of no more than about 0.1 nM.

[0075] In one embodiment, the RNAi has an EC50 of no more than about 0.01 nM.

[0076] In one embodiment, the RNAi has an EC50 of no more than about 0.001 nM.

[0077] **A method of treatment using a RNAi agent described herein**

[0078] In one particular specific embodiment, the present disclosure relates to a method of treating a Beta-Catenin-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising any one or more of the RNAi agents disclosed herein. In one embodiment of this method, the RNAi agent comprises at least an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a sense and an anti-sense strand, wherein the sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sense strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand comprises the sequence of the first strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand is the sequence of the first strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In these various embodiments, the RNAi agent is for the inhibition of the target gene Beta-Catenin.

[0079] Various particular specific embodiments of these embodiments are described below.

[0080] In one embodiment, the Beta-Catenin-related disease is adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and/or impaired wound healing, and/or similar and related diseases.

[0081] In one embodiment, the Beta-Catenin-related disease is cancer.

[0082] In one embodiment, the method further comprises the administration of an additional treatment. In one embodiment, the additional treatment is a therapeutically effective amount of a composition.

[0083] In one embodiment, the additional treatment is a method (or procedure).

[0084] In one embodiment, the additional treatment and the RNAi agent can be administered in any order, or can be administered simultaneously.

[0085] In one embodiment, the method further comprises the step of administering an additional treatment for adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and/or impaired wound healing, and/or similar and related diseases.

[0086] In one embodiment, the composition comprises a second RNAi agent to Beta-Catenin. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated), or combined within the same pharmaceutical composition.

[0087] In one embodiment, the method further comprises the step of administering an additional RNAi agent which comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[0088] **Inhibiting the expression of Beta-Catenin, using a RNAi agent**

[0089] In one particular specific embodiment, the present disclosure relates to a method of inhibiting the expression of the Beta-Catenin gene in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising any one or more of the RNAi agents of the present disclosure. In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent

comprises a first and a second strand, wherein the sequence of the first strand comprises sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand is sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[0090] Various embodiments of this aspect of these embodiments are described below.

[0091] In one embodiment, the individual is afflicted with or susceptible to a Beta-Catenin-related disease.

[0092] In one embodiment, the Beta-Catenin-related disease is adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and/or impaired wound healing, and/or similar and related diseases.

[0093] In one embodiment, the Beta-Catenin-related disease is cancer.

[0094] In one embodiment, the method further comprises the administration of an additional treatment. In one embodiment, the additional treatment is a therapeutically effective amount of a composition.

[0095] In one embodiment, the additional treatment is a method (or procedure).

[0096] In one embodiment, the additional treatment and the RNAi agent can be administered in any order or can be administered simultaneously.

[0097] In one embodiment, the method further comprises the step of administering an additional treatment for adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and/or impaired wound healing, and/or similar and related diseases.

[0098] In one embodiment, the composition comprises a second RNAi agent to Beta-Catenin. In various embodiments, the second RNAi agent is physically separate from the first, or the two are physically connected (e.g., covalently linked or otherwise conjugated), or combined within the same pharmaceutical composition.

[0099] In one embodiment, the method further comprises the step of administering an additional RNAi agent which comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3

nucleotides from the antisense strand of a RNAi agent to Beta-Catenin selected from the specific duplexes provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[00100] Pharmaceutical formulations of a RNAi agent to Beta-Catenin

[00101] In one particular specific embodiment, the present disclosure relates to a composition comprising any one or more of the RNAi agents of the present disclosure. In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand comprises the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand is the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation.

[00102] In one embodiment, the present disclosure pertains to the use of a RNAi agent in the manufacture of a medicament for treatment of a Beta-Catenin-related disease, wherein the RNAi agent is any RNAi disclosed herein. In one embodiment, the RNAi agent comprises a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the RNAi agent comprises at least an anti-sense strand, and/or comprises a sense and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the

sequence of the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand comprises the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation. In one embodiment, the RNAi agent comprises a first and a second strand, wherein the sequence of the first strand is the sequence of the first strand of a RNAi agent to Beta-Catenin selected from those specific duplex provided herein and as listed, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, wherein the composition is in a pharmaceutically effective formulation.

[00103] Specific Embodiments of RNAi Agents to Beta-Catenin comprising mismatches from the disclosed sequences

[00104] Various specific embodiments of a RNAi agent to Beta-Catenin are disclosed herein. The present disclosure encompasses the example modified sequences provided in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and the corresponding unmodified sequences and other modified sequences (e.g., modified and unmodified variants). Specific embodiments of the present disclosure include RNAi agents which comprise sequences differing by 0, 1, 2, or 3 nt (nucleotides) or bp [basepair(s)] (e.g., with 0, 1, 2 or 3 mismatches) from any of the RNAi agents listed in Table 1, and modified and unmodified variants thereof. As described in additional detail below, a mismatch is defined herein as a difference between the base sequence (e.g., A instead of G) or length when two sequences are maximally aligned and compared. In addition, as described in more detail below, an "unmodified variant" is a variant in which the base sequence is identical, but none of the bases are modified; this includes, for example, the corresponding portion of the wild-type Beta-Catenin mRNA or gene. A "modified variant" contains one or more modifications (or one or more fewer or different modifications) to a nucleotide, sugar, phosphate or backbone, and/or addition of one or more moieties; but without a change, substitution, addition, or deletion to the base sequence. A particular sequence and its modified or unmodified variants have 0 mismatches among them.

[00105] In one particular embodiment, the present disclosure comprises a RNAi agent comprising a anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand of: any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00106] In another particular embodiment, the RNAi agent comprises a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sense strand of any of the

RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00107] Definitions

[00108] For convenience, the meaning of certain terms and phrases used in the specification, examples, and appended claims, are provided below. If there is an apparent discrepancy between the usage of a term in other parts of this specification and its definition provided in this section, the definition in this section shall prevail.

[00109] Other embodiments

[00110] Various particular specific embodiments of this disclosure are described below.

[00111] In one embodiment, the disclosure pertains to a composition according to any of the disclosed embodiments, for use in a method of treating a Beta-Catenin-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to the disclosure.

[00112] Various particular specific embodiments of this embodiment are described below.

[00113] In one embodiment, the disclosure pertains to the composition according to any of the above embodiments, for use in a method of inhibiting the expression of Beta-Catenin in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to any of the disclosed embodiments.

[00114] One embodiment of the disclosure is the use of a composition according to any of the above embodiments, in the manufacture of a medicament for treatment of an Beta-Catenin-related disease.

[00115] In one embodiment, the Beta-Catenin-related disease is selected from cancer, viral disease or autoimmune disease.

[00116] In one embodiment, the disclosure pertains to the composition of any of the above embodiments, for use in the treatment of an Beta-Catenin-related disease.

[00117] In one embodiment, the Beta-Catenin-related disease is selected from cancer, viral disease or autoimmune disease.

[00118] In one embodiment, the disclosure relates to a method of inhibiting the expression of Beta-Catenin in an cell, comprising the step of introducing into the cell a composition comprising an RNAi agent comprising an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of an RNAi agent to Beta-Catenin selected from the Beta-Catenin siRNAs disclosed herein.

[00119] In one embodiment, the disclosure relates to a method of inhibiting the expression of Beta-Catenin in an cell, comprising the step of introducing into the cell a composition comprising an

RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand, and the sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the sense strand of an RNAi agent to Beta-Catenin selected from the Beta-Catenin siRNAs disclosed herein.

[00120] Beta-Catenin

[00121] By "Beta-Catenin" is meant the gene, mRNA, and/or protein, or any nucleic acid encoding the protein, also designated cadherin-associated protein beta 1; CTNNB1; CTNNB; CTNNB; CTNB1; FLJ25606; OMIM: 116806; MGI: 88276 HomoloGene: 1434; OTTHUMP00000209288; DKFZp686D02253; HGNC: 2514; Entrez Gene: 1499; Ensembl: ENSG00000168036; UniProtKB: P35222; GC03P040551; GC03P041054; or GC03P041201. See: Kraus et al. 1994. Genomics 23: 272–4.

[00122] Beta-Catenin is involved in the regulation of cell adhesion and in signal transduction through the Wnt pathway. It is part of a complex of proteins that constitute adherens junctions (AJs). AJs are necessary for the creation and maintenance of epithelial cell layers and regulate cell growth and adhesion between cells. Beta-Catenin also anchors the actin cytoskeleton and may be responsible for transmitting the contact inhibition signal that causes cells to stop dividing once the epithelial sheet is complete.

[00123] When Beta-Catenin was sequenced, it was found to be a member of the armadillo family of proteins. These proteins have multiple copies of the so-called armadillo repeat domain, which is specialized for protein-protein binding. When Beta-Catenin is not associated with cadherins and alpha-catenin, it can interact with other proteins such as ICAT and APC.

[00124] Beta-Catenin is also involved in the Wnt pathway. When Wnt is not present, GSK-3 (a kinase) constitutively phosphorylates the Beta-Catenin protein. Beta-Catenin is associated with axin (scaffolding protein) complexed with GSK-3 and APC (adenomatosis polyposis coli). The creation of this complex increases the phosphorylation of Beta-Catenin by facilitating the activity of GSK-3. When Beta-Catenin is phosphorylated, it is degraded and thus does not significantly accumulate in the cell. When Wnt binds to frizzled (Fz), its receptor, dishevelled (Dsh), is recruited to the membrane. GSK-3 is inhibited by the activation of Dsh by Fz. Because of this, Beta-Catenin is permitted to accumulate in the cytosol and can be translocated to the nucleus, where it performs several functions. It can act in conjunction with TCF / LEF transcription factors to activate target genes involved in different processes, including proliferation, survival and matrix remodeling.

[00125] Beta-Catenin interacts with many other proteins, including: cadherins, transcription factors, axin, galectin-3, beta-galactoside-binding protein, GSK-3, protein kinase A, Androgen receptor, APC, AXIN1, CBY1, CDH1, CDH2, CDH3, CDK5R1, CHUK, CTNNA1, CTNND1,

EGFR, FHL2, HER2/neu, HNF4A, IKK2, LEF1, MAGI1, MUC1, NF5A1, PCAF, PHF17, Plakoglobin, PTPN14, PTPRF, PRPRK, PSEN1, RuvB-like 1, SMAD7, SLC913R1, SMARCA4, USP9X, and VE-cadherin.

[00126] Beta-Catenin is associated with several diseases. Beta-Catenin itself can act as an oncogene. In adenomatous polyposis of the colon, the APC gene, whose product binds Beta-Catenin, is mutated. As described in more detail below, mutations in, over-expression of, and/or abnormal cellular compartmentalization (e.g., aberrant accumulation in the cytoplasm and/or nucleus) of Beta-Catenin are associated with various diseases, including: adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, pilomatrixoma, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, anaplastic thyroid carcinoma, and uterine carcinosarcoma. See: Thompson et al. 2007 Hepatology 45: 1298–305; Wang et al. 2008 Cancer Epidemiol. Biomarkers Prev. 17: 2101–8; Saldanha et al. Br. J. Dermatol. 151: 157–64.

[00127] Nuclear and cytosolic accumulation (e.g., improper cellular compartmentalization) is enriched in basal-like breast cancer and are associated with poor outcome. Beta-Catenin accumulation is more often observed in basal-like in situ carcinomas than in other sub-types, suggesting that activation of this pathway might be an early event in basal-like tumor development. Khramtsov et al. 2010 Am. J. Pathol. 176: 2911-2920.

[00128] Sequences and structure of Beta-Catenin

[00129] Three human transcript variants encoding the same protein have been found for this gene: NP_001091679.1; NP_001091680.1; and NP_001895.1. The amino acid and nucleotide sequences of human Beta-Catenin are provided in LOCUS NM_001098209 (ACCESSION NM_001098209 XM_001133660 XM_001133664 XM_001133673 XM_001133675; VERSION NM_001098209.1 GI:148233337); LOCUS NM_001098210 (ACCESSION NM_001098210; VERSION NM_001098210.1 GI:148227671); and LOCUS NM_001904 (ACCESSION NM_001904 XM_942045 XM_945648 XM_945650 XM_945651 XM_945652 XM_945653 XM_945654 XM_945655 XM_945657; VERSION NM_001904.3 GI:148228165).

[00130] The mouse (*Mus musculus*) sequence of Beta-Catenin is available as Q02248 (CTNB1_MOUSE); MGI:88276; NP_031640.1 GI:6671684; NM 007614.3. The rat (*Rattus norvegicus*) sequence is available as Q9WU82 (CTNB1_RAT); Li et al. 2002 Gene 283: 255-62.

[00131] A RNAi agent specific to Beta-Catenin can be designed such that the sequence thereof completely matches that of the mRNA corresponding to the human Beta-Catenin gene and the homologous gene from a test animal. Thus, the exact same RNAi agent can be used in both test animals (e.g., rat, mouse, cynomolgus monkey, etc.) and humans. The sequences for the various Beta-Catenin genes have been determined in many species, including humans, mice and rats (as

described above).

[00132] The Beta-Catenin sequence in cynomolgus monkey (*Macaca fascicularis*, or "cyno") has been determined.

[00133] The alignment of the cyno and human (NM_001098210.1) Beta-Catenin mRNA sequences is shown below.

```
Human       AGGATACAGCGGCTTCTGCGCGACTTATAAGAGCTCCTTGTGCGGCGCCATTTTAAGCCT 60
Cyno        -------------------------------------------CGCCATTTTAAGCCT 15
                                                       ***************

Human       CTCGGTCTGTGGCAGCAGCGTTGGCCCGGCCCCGGGAGCGGAGAGCGAGGGGAGGCGGAG 120
Cyno        CTTGGTCTGTGGCAGCCGTGTTGGCCCGGCCCCGAGAGCGGAGAGCGAGGGGAGGCGGAG 75
            ** ************* * *************** ************************

Human       ACGGAGGAAGGTCTGAGGAGCAGCTTCAGTCCCCGCCGAGCCGCCACCGCAGGTCGAGGA 180
Cyno        ACGGAGGAAGGTCCGAGGAGCAGCTTCAGTCCTCGCCGAGCCGCCACCGCAGGTCGAGGA 135
            ************* ****************** ***************************

Human       CGGTCGGACTCCCGCGGCGGGAGGAGCCTGTTCCCCTGAGGGTATTTGAAGTATACCATA 240
Cyno        CGGTCGGACTCCCGCGACGGGAGGAGCCTGTTCCCCTGAGGGTATTTGAAGTATACCATA 195
            **************** ******************************************

Human       CAACTGTTTTGAAAATCCAGCGTGGACAATGGCTACTCAAGCTGATTTGATGGAGTTGGA 300
Cyno        CAACTGTTTTGAAAATCCAGCGTGGACAATGGCTACTCAAGCTGATTTGATGGAGTTGGA 255
            ************************************************************

Human       CATGGCCATGGAACCAGACAGAAAAGCGGCTGTTAGTCACTGGCAGCAACAGTCTTACCT 360
Cyno        CATGGCCATGGAACCAGACAGAAAAGCGGCTGTTAGTCACTGGCAGCAACAGTCTTACCT 315
            ************************************************************

Human       GGACTCTGGAATCCATTCTGGTGCCACTACCACAGCTCCTTCTCTGAGTGGTAAAGGCAA 420
Cyno        GGACTCTGGAATCCATTCTGGTGCCACTACCACAGCTCCTTCTCTGAGTGGTAAAGGCAA 375
            ************************************************************

Human       TCCTGAGGAAGAGGATGTGGATACCTCCCAAGTCCTGTATGAGTGGGAACAGGGATTTTC 480
Cyno        TCCTGAGGAAGAGGATGTGGATACCTCCCAAGTCCTGTATGAGTGGGAACAGGGATTTTC 435
            ************************************************************

Human       TCAGTCCTTCACTCAAGAACAAGTAGCTGATATTGATGGACAGTATGCAATGACTCGAGC 540
Cyno        TCAGTCCTTCACTCAAGAACAAGTAGCTGATATTGATGGACAGTATGCAATGACTCGAGC 495
            ************************************************************

Human       TCAGAGGGTACGAGCTGCTATGTTCCCTGAGACATTAGATGAGGGCATGCAGATCCCATC 600
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Cyno        TCAGAGGGTACGAGCTGCTATGTTCCCTGAGACATTAGATGAGGGCATGCAGATCCCATC 555
            ************************************************************

Human       TACACAGTTTGATGCTGCTCATCCCACTAATGTCCAGCGTTTGGCTGAACCATCACAGAT 660
Cyno        TACACAGTTTGATGCTGCTCATCCCACTAATGTCCAGCGTTTGGCTGAACCATCACAGAT 615
            ************************************************************

Human       GCTGAAACATGCAGTTGTAAACTTGATTAACTATCAAGATGATGCAGAACTTGCCACACG 720
Cyno        GCTGAAACATGCAGTTGTAAACTTGATTAACTATCAAGATGATGCAGAACTTGCCACACG 675
            ************************************************************

Human       TGCAATCCCTGAACTGACAAAACTGCTAAATGACGAGGACCAGGTGGTGGTTAATAAGGC 780
Cyno        TGCAATCCCTGAACTGACAAAACTGCTAAATGATGAGGACCAGGTGGTGGTTAATAAGGC 735
            ********************************* ************************

Human       TGCAGTTATGGTCCATCAGCTTTCTAAAAAGGAAGCTTCCAGACACGCTATCATGCGTTC 840
Cyno        TGCAGTTATGGTCCATCAGCTTTCTAAAAAGGAAGCTTCCAGACACGCTATCATGCGTTC 795
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Human       TCCTCAGATGGTGTCTGCTATTGTACGTACCATGCAGAATACAAATGATGTAGAAACAGC 900
Cyno        TCCTCAGATGGTGTCTGCTATTGTACGTACCATGCAGAATACAAATGATGTAGAAACAGC 855
            ************************************************************

Human       TCGTTGTACCGCTGGGACCTTGCATAACCTTTCCCATCATCGTGAGGGCTTACTGGCCAT 960
Cyno        TCGTTGTACCGCTGGGACCTTGCATAACCTTTCCCATCATCGGGAGGGCTTGTTGGCCAT 915
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Human       CTTTAAGTCTGGAGGCATTCCTGCCCTGGTGAAAATGCTTGGTTCACCAGTGGATTCTGT 1020
Cyno        CTTTAAGTCTGGAGGCATTCCTGCCCTGGTGAAAATGCTTGGTTCACCAGTGGATTCTGT 975
            ************************************************************

Human       GTTGTTTTATGCCATTACAACTCTCCACAACCTTTTATTACATCAAGAAGGAGCTAAAAT 1080
Cyno        GTTGTTTTATGCCATTACAACTCTCCACAACCTTTTATTACATCAAGAAGGAGCTAAAAT 1035
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Human       GGCAGTGCGTTTAGCTGGTGGGCTGCAGAAAATGGTTGCCTTGCTCAACAAAACAAATGT 1140
Cyno        GGCAGTGCGTTTAGCTGGCGGGCTACAGAAAATGGTTGCCTTGCTCAACAAAACAAACGT 1095
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Human       TAAATTCTTGGCTATTACGACAGACTGCCTTCAAATTTTAGCTTATGGCAACCAAGAAAG 1200
Cyno        TAAATTCTTGGCTATTACGACAGACTGCCTTCAGATTTTAGCATATGGCAACCAAGAAAG 1155
            ********************************** ******** *****************

Human       CAAGCTCATCATACTGGCTAGTGGTGGACCCCAAGCTTTAGTAAATATAATGAGGACCTA 1260
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Cyno        CAAGCTGATCATACTGGCTAGTGGTGGACCCCAAGCTTTAGTAAATATAATGAGGACCTA 1215
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Human       TACTTACGAAAAACTACTGTGGACCACAAGCAGAGTGCTGAAGGTGCTATCTGTCTGCTC 1320
Cyno        TACTTATGAGAAACTACTGTGGACCACAAGCAGAGTGCTGAAGGTGCTATCCGTCTGCTC 1275
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Human       TAGTAATAAGCCGGCTATTGTAGAAGCTGGTGGAATGCAAGCTTTAGGACTTCACCTGAC 1380
Cyno        TAGTAATAAGCCAGCTATTGTAGAAGCTGGTGGAATGCAAGCTTTAGGACTTCACCTGAC 1335
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Human       AGATCCAAGTCAACGTCTTGTTCAGAACTGTCTTTGGACTCTCAGGAATCTTTCAGATGC 1440
Cyno        AGATCCAAGTCAACGTCTTGTTCAGAACTGTCTTTGGACTCTCAGGAATCTTTCAGATGC 1395
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Human       TGCAACTAAACAGGAAGGGATGGAAGGTCTCCTTGGGACTCTTGTTCAGCTTCTGGGTTC 1500
Cyno        TGCAACTAAACAGGAAGGGATGGAAGGTCTCCTTGGGACTCTTGTTCAGCTTCTGGGTTC 1455
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Human       AGATGATATAAATGTGGTCACCTGTGCAGCTGGAATTCTTTCTAACCTCACTTGCAATAA 1560
Cyno        AGATGATATAAATGTGGTCACCTGTGCAGCTGGAATTCTTTCTAACCTCACTTGCAATAA 1515
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Human       TTATAAGAACAAGATGATGGTCTGCCAAGTGGGTGGTATAGAGGCTCTTGTGCGTACTGT 1620
Cyno        TTATAAGAATAAGATGATGGTCTGCCAAGTGGGTGGTATAGAGGCTCTTGTGCGTACTGT 1575
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Human       CCTTCGGGCTGGTGACAGGGAAGACATCACTGAGCCTGCCATCTGTGCTCTTCGTCATCT 1680
Cyno        CCTTCGGGCTGGTGACAGGGAAGACATCACTGAGCCTGCCATCTGTGCTCTTCGTCATCT 1635
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Human       GACCAGCCGACACCAAGAAGCAGAGATGGCCCAGAATGCAGTTCGCCTTCACTATGGACT 1740
Cyno        GACCAGCCGACACCAAGAAGCAGAGATGGCCCAGAATGCAGTTCGCCTTCACTATGGACT 1695
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Human       ACCAGTTGTGGTTAAGCTCTTACACCCACCATCCCACTGGCCTCTGATAAAGGCTACTGT 1800
Cyno        ACCAGTTGTGGTTAAGCTCTTACACCCACCATCCCACTGGCCTCTGATAAAGGCTACTGT 1755
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Human       TGGATTGATTCGAAATCTTGCCCTTTGTCCCGCAAATCATGCACCTTTGCGTGAGCAGGG 1860
Cyno        TGGATTGATTCGAAATCTTGCCCTTTGTCCAGCAAATCATGCACCTTTGCGTGAGCAGGG 1815
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Human       TGCCATTCCACGACTAGTTCAGTTGCTTGTTCGTGCACATCAGGATACCCAGCGCCGTAC 1920
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Cyno        TGCCATTCCACGACTAGTTCAGTTGCTTGTTCGTGCACATCAGGATACCCAGCGCCGTAC 1875
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Human       GTCCATGGGTGGGACACAGCAGCAATTTGTGGAGGGGGTCCGCATGGAAGAAATAGTTGA 1980
Cyno        GTCCATGGGTGGGACACAGCAGCAATTTGTGGAGGGGGTCCGCATGGAAGAAATAGTTGA 1935
            ************************************************************

Human       AGGTTGTACCGGAGCCCTTCACATCCTAGCTCGGGATGTTCACAACCGAATTGTTATCAG 2040
Cyno        AGGTTGTACTGGAGCCCTTCACATCCTAGCTCGGGATGTTCACAACCGAATTGTAATCAG 1995
            ********* ************************************************ ******

Human       AGGACTAAATACCATTCCATTGTTTGTGCAGCTGCTTTATTCTCCCATTGAAAACATCCA 2100
Cyno        AGGACTAAATACCATTCCATTGTTTGTGCAGCTGCTTTATTCTCCCATTGAAAACATCCA 2055
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Human       AAGAGTAGCTGCAGGGGTCCTCTGTGAACTTGCTCAGGACAAGGAAGCTGCAGAAGCTAT 2160
Cyno        AAGAGTAGCTGCAGGGGTCCTCTGTGAACTTGCTCAGGACAAGGAAGCTGCAGAAGCGAT 2115
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Human       TGAAGCTGAGGGAGCCACAGCTCCTCTGACAGAGTTACTTCACTCTAGGAATGAAGGTGT 2220
Cyno        TGAAGCTGAGGGAGCCACAGCTCCTCTGACAGAGTTACTTCACTCTAGGAATGAAGGTGT 2175
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Human       GGCGACATATGCAGCTGCTGTTTTGTTCCGAATGTCTGAGGACAAGCCACAAGATTACAA 2280
Cyno        GGCGACGTATGCAGCTGCTGTTTTGTTCCGAATGTCTGAGGACAAGCCACAAGATTACAA 2235
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Human       GAAACGGCTTTCAGTTGAGCTGACCAGCTCTCTCTTCAGAACAGAGCCAATGGCTTGGAA 2340
Cyno        GAAACGGCTTTCAGTTGAGCTGACCAGCTCTCTCTTCAGAACGGAGCCAATGGCTTGGAA 2295
            ****************************************** ****************

Human       TGAGACTGCTGATCTTGGACTTGATATTGGTGCCCAGGGAGAACCCCTTGGATATCGCCA 2400
Cyno        TGAGACTGCGGATCTTGGACTTGATATTGGTGCCCAGGGAGAACCCCTTGGATATCGCCA 2355
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Human       GGATGATCCTAGCTATCGTTCTTTTCACTCTGGTGGATATGGCCAGGATGCCTTGGGTAT 2460
Cyno        GGATGATCCTAGCTATCGTTCTTTTCACTCTGGTGGATATGGCCAGGATGCCTTGGGTAT 2415
            ************************************************************

Human       GGACCCCATGATGGAACATGAGATGGGTGGCCACCACCCTGGTGCTGACTATCCAGTTGA 2520
Cyno        GGACCCCATGATGGAACATGAGATGGGTGGCCACCACCCTGGTGCTGACTATCCAGTTGA 2475
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Human       TGGGCTGCCAGATCTGGGGCATGCCCAGGACCTCATGGATGGGCTGCCTCCAGGTGACAG 2580
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Cyno        TGGGCTGCCAGATCTGGGACATGCCCAGGACCTCATGGATGGGCTGCCTCCAGGTGATAG 2535
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Human       CAATCAGCTGGCCTGGTTTGATACTGACCTGTAAATCATCCTTTAG-------------- 2626
Cyno        CAATCAGCTGGCCTGGTTTGATACTGACCTGTAAATCATCCTTTAGCTGTATTGTCTGAA 2595
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Human       ------------------------------------------------------------
Cyno        CTTGCATTGTGATTGGCCTGTAGAGTTGCTGAGAGGGCTCGAGGGGTGGGCTGGTATCTC 2655


Human       ------------------------------------------------------------
Cyno        AGAAAGTGCCTGACACACTAACCAAGCTGAGTTTCCTATGGGAACAATTGAAGTAAACTT 2715


Human       -------------------------GAGTAACAATACAAATGGATTTTGGGAGTGACTCA 2661
Cyno        TTTGTTCTGGTCCTTTTTGGTCGAGGAGTAACAATACAAATGGATTTTGGGAGTGACTCA 2775
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Human       AGAAGTGAAGAATGCACAAGAATGGATCACAAGATGGAATTTATCAAACCCTAGCCTTGC 2721
Cyno        AGAAGTGAAGAATGCACAAGAATGGATCACAAGATGGAATTTATCAAACCCTAGCCTTGC 2835
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Human       TTGTTAAATTTTTTTTTTTTTTTTTTAAGAATATCTGTAATGGTACTGACTTTGCTTGC 2781
Cyno        TTGTTAAATTTTTTTTTTTTTTTTTTAAGAATATCTGTAATGGTACTGACTTTGCTTGC 2895
            ************************************************************

Human       TTTGAAGTAGCTCTTTTTTTTTTTTTTTTTTTTTTTTGCAGTAACTGTTTTTTAAGTCT 2841
Cyno        TTTGAAGTAGCTCTTTTTTTTTTTTTTTTTTTTTTTTGCAGTAACTGTTTTTTAAGTCT 2955
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Human       CTCGTAGTGTTAAGTTATAGTGAATACTGCTACAGCAATTTCTAATTTTTAAGAATTGAG 2901
Cyno        CTCGTAGTGTTAAGTTATAGTGAATACTGCTACAGCAATTTCTAATTTTTAAGAATTGAG 3015
            ************************************************************

Human       TAATGGTGTAGAACACTAATTCATAATCACTCTAATTAATTGTAATCTGAATAAAGTGTA 2961
Cyno        TAATGGTGTAGAACACTAATTCATAATCACTCTAAT-AATTGTAATCTGAATAAAGTGTA 3074
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Human       ACAATTGTGTAGCCTTTTTGTATAAAATAGACAAATAGAAAATGGTCCAATTAGTTTCCT 3021
Cyno        ACA-TTGTGTAGCCTTTTTGTATAAAATAGACAAATAGAAAATGGTCCAATTAGTTTCCT 3133
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Human       TTTTAATATGCTTAAAATAAGCAGGTGGATCTATTTCATGTTTTTGATCAAAAACT--AT 3079
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Cyno        TTTTAATATGCTTAAAATAAGCAGGTGGATCTATTTCATGTTTTTGATCAAAAACTTTAT 3193
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Human       TTGGGATATGTATGGGTAGGGTAAATCAGTAAGAGGTGTTATTTGGAACCTTGTTTTGGA 3139
Cyno        TTGGGATATGTATGGGTAGGGTAAATCAGTAAGAGGTGTTATTTGGAACCTTGTTTTGGA 3253
            ************************************************************

Human       CAGTTTACCAGTTGCCTTTTATCCCAAAGTTGTTGTAACCTGCTGTGATACGATGCTTCA 3199
Cyno        CAGTTTACCAGTTGCCTTTTATCCCAAAGTTGTTGTAACCTGCTGTGATACAATGCTTCA 3313
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Human       AGAGAAAATGCGGTTATAAAAAATGGTTCAGAATTAAACTTTTAATTCATTCGATTG 3256
Cyno        AGAGAAAATGCGGTTATAAAAAATGGTTCAGAA---------------------- 3346
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Human         (SEQ ID NO: 4112)
Cyno          (SEQ ID NO: 4113)
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[00134] The start (ATG) and stop (TGA) of the cyno and human sequences are in bold, underlined. Nucleotides matching between the human and cyno sequences are marked with an asterick (*). Whether or not a given sequence (e.g., a first or second strand of a siRNA or duplex) matches the sense or anti-sense strand of the Beta-Catenin sequence can be readily determined by comparison of the sequences above (SEQ ID NOs: 4112 and 4113).

[00135] **Additional embodiments of a RNAi agent to Beta-Catenin**

[00136] The present disclosure encompasses various embodiments of RNAi agents to Beta-Catenin.

[00137] In one embodiment, the Beta-Catenin RNAi agent of the present disclosure comprises a sequence which is identical in the human, rat and cyno Beta-Catenin mRNAs. This sequence identity facilitates animal testing prior to human testing. In another embodiment, the Beta-Catenin RNAi agent comprises a sequence which is identical in the human, mouse and cyno Beta-Catenin mRNAs. In another embodiment, the Beta-Catenin RNAi agent comprises a sequence which is identical in the human and mouse Beta-Catenin mRNAs. In another embodiment, the Beta-Catenin RNAi agent comprises a sequence which is identical in the human and rat cyno Beta-Catenin mRNAs. In another embodiment, the Beta-Catenin RNAi agent comprises a sequence which is identical in the human, mouse and rat Beta-Catenin mRNAs. In another embodiment, the Beta-Catenin RNAi agent comprises a sequence which is identical in the human, rat and cyno Beta-Catenin mRNAs.

[00138] In one embodiment, the Beta-Catenin RNAi agent comprises a sequence which does not

match that of any other mRNA. In one embodiment, the Beta-Catenin RNAi agent comprises a sequence which differs from all other known non-Beta-Catenin mRNAs by at least 0, 1, 2 or 3 nucleotides. In various embodiments, the Beta-Catenin RNAi agent does knock-down any other gene by more than 5, 10, 15, 20, 25, 30, or 40%. The ability of the Beta-Catenin RNAi agent to knock down other genes can be tested in vitro, or by using arrays of various genes.

[00139] Various mutations in Beta-Catenin are known; many of these are involved in Beta-Catenin-related diseases. These include mutations of the residues at 33, 37, 41 and 45, but disease-associated mutations have also been found at positions 8, 11, 13, 21, 24, 25, 28, 29, 32, 34, 39, 47, 48 and 55. In various embodiments of the present disclosure, RNAi agents can be devised to preferentially target the mutated (rather than wildtype) form of Beta-Catenin.

[00140] In other embodiments, the RNAi agents of the present disclosure bind to the 5' or 3' UTR [untranslated region(s)].

[00141] The efficacy of a RNAi agent in reducing the level of Beta-Catenin can be measured directly, e.g., measuring the levels of Beta-Catenin mRNA abundance or levels or cellular distribution of the protein itself. For example, the accumulation of Beta-Catenin in the cytoplasm and/or nucleus is associated with various disease states. After administration of a RNAi agent, cells and tissues can be tested for the accumulation of Beta-Catenin in the cytoplasm and nucleus. Alternatively, the efficacy of the RNAi can be measured indirectly by measuring the level of any one or more of the known activities of Beta-Catenin. For example, localization of Beta-Catenin to the nucleus can lead to transcription of various genes, including c-myc. After administration of a RNAi agent to Beta-Catenin, the expression of c-myc or other genes activated by Beta-Catenin can be measured.

[00142] In one embodiment, the Beta-Catenin RNAi agent of the present disclosure is administered to a patient in need thereof (e.g., a patient suffering from, suspected of having, or predisposed for, adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases).

[00143] The patient can also be administered more than one RNAi agent specific to Beta-Catenin. In one embodiment, the Beta-Catenin RNAi agent(s) of the present disclosure can optionally be administered along with one or more additional pharmaceutical agent appropriate for that disease. In one embodiment, the Beta-Catenin RNAi agent(s) of the present disclosure can be optionally administered along with any other appropriate additional treatment, wherein the additional treatment can be a composition or a method.

[00144] Various disease states are associated with mutations in Beta-Catenin (such as those listed above), which result in over-expression, hyper-activity and/or improper cellular compartmentalization of Beta-Catenin. Mutations in components other than Beta-Catenin can also activate the Wnt signaling pathway. For example, APC (adenomatous polyposis coli) normally controls Beta-Catenin activity. APC normally builds a complex with glycogen synthase kinase 3-beta (GSK-3beta) and axin. This complex binds Beta-Catenin in the cytoplasm. With the help of casein kinase (CK1), which carries out an initial phosphyrlation of Beta-Catenin, GSK-3beta is able to phosphorylate Beta-Catenin a second time. This targets Beta-Catenin for ubiquitination and degradation by cellular proteosomes and prevents translocation of Beta-Catenin to the nucleus. APC mutations thus can result in constitutive activation of the Wnt signaling pathway. RNAi agents to Beta-Catenin can thuse be administered to patients with disease strates associated not only with mutations in Beta-Catenin but also in related mutations in other components (such as APC) of the Wnt signaling pathway.

[00145] In the case of adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases, the RNAi agent(s) and additional disease treatment(s) can be administered in any order, simultaneously or sequentially, or in one or multiple doses over time.

[00146] In the treatment of these Beta-Catenin-related diseases, the RNAi agent(s) and additional disease treatment(s) can be administered in any order, simultaneously or sequentially, or in multiple doses over time. Administration of the RNAi agent and the additional treatment can be, for example, simultaneous, concurrent, separate or sequential.

[00147] Simultaneous administration may, e.g., take place in the form of one fixed combination with two or more active ingredients, or by simultaneously administering two or more active ingredients that are formulated independently. Sequential use (administration) preferably means administration of one (or more) components of a combination at one time point, other components at a different time point, that is, in a chronically staggered manner, preferably such that the combination shows more efficiency than the single compounds administered independently (especially showing synergism). Separate use (administration) preferably means administration of the components of the combination independently of each other at different time points, preferably meaning that the components (a) and (b) are administered such that no overlap of significant measurable blood levels of both compounds are present in an overlapping manner (at the same time).

[00148] Also combinations of two or more of sequential, separate and simultaneous administration are possible, preferably such that the combination component-drugs show a joint therapeutic effect that exceeds the effect found when the combination component-drugs are used independently at time intervals so large that no mutual effect on their therapeutic efficiency can be found, a synergistic effect being especially preferred.

[00149] The term "delay of progression" as used herein means administration of the combination to patients being in a pre-stage or in an early phase, of the first manifestation or a relapse of the disease to be treated, in which patients, e.g., a pre-form of the corresponding disease is diagnosed or which patients are in a condition, e.g., during a medical treatment or a condition resulting from an accident, under which it is likely that a corresponding disease will develop.

[00150] "Jointly therapeutically active" or "joint therapeutic effect" means that the compounds may be given separately (in a chronically staggered manner, especially a sequence-specific manner) in such time intervals that they preferably, in the warm-blooded animal, especially human, to be treated, still show a (preferably synergistic) interaction (joint therapeutic effect). Whether this is the case, can inter alia be determined by following the blood levels, showing that both compounds are present in the blood of the human to be treated at least during certain time intervals.

[00151] Additional Definitions

[00152] For convenience, the meaning of certain terms and phrases used in the specification, examples, and appended claims, are provided below. If there is an apparent discrepancy between the usage of a term in other parts of this specification and its definition provided in this document, the definition in this document shall prevail.

[00153] As used throughout this disclosure, articles such as “a” and “an” refer to one or more than one (at least one) of the grammatical object of the article.

[00154] RNAi Agents to Beta-Catenin

[00155] In one embodiment, the present disclosure pertains to a Beta-Catenin RNAi agent or other anti-sense nucleic acid complementary to a mRNA encoding the Beta-Catenin gene (or portion thereof), or a recombinant expression vector encoding encoding at least one strand of the siRNA (RNAi agent) or a composition comprising the antisense nucleic acid that can function as an RNAi agent as defined below.

[00156] As used herein, an "anti-sense" nucleic acid comprises a nucleotide sequence complementary to a "sense" nucleic acid encoding the Beta-Catenin protein (e.g., complementary to the coding strand of a double-stranded DNA, complementary to an mRNA or complementary to the coding strand of a Beta-Catenin gene).

[00157] As used herein, the term "RNAi agent to Beta-Catenin," "RNAi agent specific to Beta-Catenin," "iRNA agent to Beta-Catenin," "siRNA to Beta-Catenin", "Beta-Catenin siRNA" and the like refer to a siRNA (short inhibitory RNA), shRNA (short or small hairpin RNA), iRNA (interference RNA) agent, RNAi (RNA interference) agent, dsRNA (double-stranded RNA), microRNA, and the like, and refer to a composition which specifically targets, is specific to, and/or binds to a mRNA corresponding to the Beta-Catenin gene. As used herein, the term "antisense nucleic acid" or "composition comprising an anti-sense nucleic acid" and the like is broadly meant to encompass any composition comprising at least one nucleic acid strand which is anti-sense to its target; this includes, but is not limited to, any siRNA, shRNA, iRHA, dsRNA, microRNA, antisense oligonucleotide, and any other composition comprising an anti-sense nucleic acid.

[00158] As used herein, the terms "iRNA" and "RNAi" refers to an agent that contains RNA (or a derivative thereof), and which mediates the targeted cleavage of another RNA transcript via an RNA-induced silencing complex (RISC) pathway. In one embodiment, the RNAi agent is an oligonucleotide composition that activates the RISC complex/pathway. In another embodiment, the RNAi agent comprises an anti-sense strand sequence (anti-sense oligonucleotide). RNAi agents include, for example, siRNAs, dsRNAs and shRNAs. The RNAi agents can be wholly RNA, or can comprise a backbone or individual nucleotides which are not RNA, such as LNA, GNA, TNA, boranophosphate RNA, FANA, etc. Individual nucleotides can be replaced by DNA (e.g., the terminal UU, TT, or the like) or individual nucleotides at the 5' end or internally. However, in no case does the disclosure contemplate the RNAi agent comprising two strands which are completely DNA (e.g., a double-stranded DNA).

[00159] In one embodiment, the RNAi comprises a single strand. This single-stranded RNAi agent oligonucleotide or polynucleotide can comprise the sense or antisense strand, as described by Sioud 2005 J. Mol. Biol. 348:1079-1090, and references therein. Thus the disclosure encompasses RNAi agents with a single strand comprising either the sense or antisense strand of an RNAi agent described herein.

[00160] The RNAi agent(s) of the present disclosure target (e.g., bind to, anneal to, etc.) the Beta-Catenin mRNA. The use of the RNAi agent specific to Beta-Catenin results in a decrease of Beta-Catenin activity, level and/or expression, e.g., a "knock-down" or "knock-out" of the target gene or target sequence. Particularly, in one embodiment, in the case of a disease state characterized by over-expression or hyper-activity of Beta-Catenin, administration of a RNAi agent to Beta-Catenin knocks down the Beta-Catenin target enough to restore a normal level of Beta-Catenin activity.

[00161] In one embodiment, the RNAi comprises a single strand (such as an shRNA, as described herein). In other embodiments, the RNAi agent comprises a single strand because the sense and anti-sense strands are contiguous, connected by a loop, or otherwise linked.

[00162] In various embodiments, one or both strands are nicked.

[00163] In one embodiment, a single-stranded RNAi agent oligonucleotide or polynucleotide can comprise the sense and/or antisense strand. See, e.g., Sioud 2005 J. Mol. Biol. 348:1079-1090, and references cited therein. Thus the present disclosure encompasses RNAi agents with a single strand comprising either the sense or antisense strand of a RNAi agent described herein.

[00164] RNAi agents that are particularly useful for this disclosure include those which can bind specifically to a region of the Beta-Catenin mRNA, and have one or more of the following qualities: binding in the coding segment of Beta-Catenin; binding at or near the junction of the 5' untranslated region and the start of the coding segment; binding at or near the translational start site of the mRNA; binding in the third exon of the Beta-Catenin gene; binding at or near junctions of exons and introns; little or no binding to the mRNAs of other genes (little or no "off-target effects"); binding to the Beta-Catenin mRNA in or near a region or regions that is not double-stranded or a stem region, e.g., in a loop or single-stranded portion; eliciting little or no immunogenicity; binding in a segment of the Beta-Catenin mRNA sequence which is conserved among various animal species (including human, mouse, rat, cynomolgus monkey, etc.), as the presence of a conserved sequence facilitates testing using various laboratory animals; binding to double-stranded region(s) of the mRNA; binding to an AT-rich region (e.g., at least about 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, or 60% AT-rich); and/or lacking particular sequences known or suspected to decrease siRNA activity, e.g., the presence of a GG sequence at the 5' end, which may decrease separation of the double-stranded portion of the RNAi agent. In various embodiments, the RNAi agent specific to Beta-Catenin can be a double-stranded RNA having any one or more of these qualities.

[00165] The term "double-stranded RNA" or "dsRNA," as used herein, refers to a RNAi agent comprising a first and a second strand; e.g., a composition that includes an RNA molecule or complex of molecules having a hybridized duplex region (i.e., a region where the nucleotide bases from the first strand and the second strand are paired) that comprises two anti-parallel and substantially complementary nucleic acid strands, which will be referred to as having "sense" and "anti-sense" orientations with respect to a target RNA. The anti-sense strand, with respect to the mRNA target, is also called the "guide" strand, and the sense strand is also called the "passenger" strand. The passenger strand can include at least one or more of the following: one or more extra nucleotides (e.g., a bulge or 1 nt loop) compared to the other strand, a nick, a gap, etc., compared to the other strand. In various embodiments, the RNAi agent comprises a first strand and a second strand. In various embodiments, the first strand is the sense strand and the second strand is the anti-sense strand. In other embodiments, the first strand is the anti-sense strand and the second strand is the sense strand.

[00166] The duplex region can be of any length that permits specific degradation of a desired target RNA through a RISC pathway, but will typically range from 9 to 36 base pairs ("bp") in

length, e.g., 15-30 base pairs in length. Considering a duplex between 9 and 36 base pairs, the duplex can be any length in this range, for example, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 base pairs (bp) and any sub-range therebetween, including, but not limited to 15-30 base pairs, 15-26 base pairs, 15-23 base pairs, 15-22 base pairs, 15-21 base pairs, 15-20 base pairs, 15-19 base pairs, 15-18 base pairs, 15-17 base pairs, 18-30 base pairs, 18-26 base pairs, 18-23 base pairs, 18-22 base pairs, 18-21 base pairs, 18-20 base pairs, 19-30 base pairs, 19-26 base pairs, 19-23 base pairs, 19-22 base pairs, 19-21 base pairs, 19-20 base pairs, 19 base pairs, 20-30 base pairs, 20-26 base pairs, 20-25 base pairs, 20-24 base pairs, 20-23 base pairs, 20-22 base pairs, 20-21 base pairs, 20 basepairs, 21-30 base pairs, 21-26 base pairs, 21-25 base pairs, 21-24 base pairs, 21-23 base pairs, 21-22 base pairs, 21 base pairs, 22 base pairs, or 23 base pairs. dsRNAs generated in the cell by processing with Dicer and similar enzymes are generally in the range of 19-22 base pairs in length. One strand of the duplex region of a dsRNA comprises a sequence that is substantially complementary to a region of a target RNA. The two strands forming the duplex structure can be from a single RNA molecule having at least one self-complementary duplex region, or can be formed from two or more separate RNA molecules that hybridize to form the duplex. Where the duplex region is formed from two strands of a single molecule, the molecule can have a duplex region separated by a single-stranded chain of nucleotides (herein referred to as a "hairpin loop", e.g., such as found in a shRNA construct) between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure. The hairpin loop can comprise at least one unpaired nucleotide; in some embodiments the hairpin loop can comprise at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 23 or more unpaired nucleotides. Where the two substantially complementary strands of a dsRNA are comprised by separate RNA molecules, those molecules need not, but can be covalently connected. Where the two strands are connected covalently by a hairpin loop, the construct is generally referred to herein and in the art as a "shRNA." Where the two strands are connected covalently by means other than a hairpin loop, the connecting structure is referred to as a "linker."

[00167] The terms "RNAi agent" and "siRNA" are also used herein to refer to a dsRNA as described above, useful for RNA interference.

[00168] In various embodiments of the present disclosure, the composition pertains to RNAi agents to Beta-Catenin comprising a sense strand comprising at least 15 contiguous nt with 0, 1, 2 or 3 mismatches from the sense strand, and/or an anti-sense strand comprising at least 15 contiguous nt with 0, 1, 2, or 3 mismatches from the anti-sense strand of any RNAi agent disclosed herein, particularly in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00169] RNAi Agents to Beta-Catenin comprising mismatches from the disclosed sequences

[00170] Various specific embodiments of a RNAi agent to Beta-Catenin are disclosed herein; example sequences are provided in Tables 1, 2 and 3. Specific embodiments of the present disclosure include RNAi agents which comprise sequences differing by 0, 1, 2, or 3 nt (nucleotides) or bp [basepair(s)] (e.g., with 0, 1, 2 or 3 mismatches) from any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00171] A mismatch is defined herein as a difference between the base sequence or length when two sequences are maximally aligned and compared. A mismatch is defined as a position wherein the base of one sequence does not match the base of the other sequence. Thus, a mismatch is counted, for example, if a position in one sequence has a particular base (e.g., A), and the corresponding position on the other sequence has a different base (e.g., G). Substitution of A, for example, with T, C, G or U would constitute a mismatch. Substitution of G with T, A, C or U would also constitute a mismatch. Substitution of C with T, G, A or U would also constitute a mismatch. Substitution of U with A, C or G would constitute a mismatch. Note, however, that on a given strand, a U can be replaced by T (either as RNA or, preferably, DNA, e.g., 2'-deoxy-thymidine); the replacement of a U with a T is not a mismatch, as either U or A can pair with A on the opposite strand. The RNAi agent can thus comprise some DNA bases, e.g., T, or a terminal TT or UU.

[00172] A mismatch is also counted, e.g., if a position in one sequence has a base (e.g., A), and the corresponding position on the other sequence has no base (e.g., that position is an abasic nucleotide, which comprises a phosphate-sugar backbone but no base). A single-stranded nick in either sequence (or in the sense or anti-sense strand) is not counted as mismatch. Thus, as a non-limiting example, no mismatch would be counted if one sequence comprises the sequence AG, but the other sequence comprises the sequence AG with a single-stranded nick between the A and the G. If one sequence comprises a C, and the other sequence comprises a modified C (e.g., 2'-modification) at the same position, no mismatch would be counted.

[00173] In addition, no mismatches are counted if modifications are made to the sugar, phosphate, or backbone of the RNAi agent without modifying the base. Thus, a sequence of UGGUGCUGACUAUCCAGUU (SEQ ID NO: 429) as an RNA and the same sequence as a PNA (peptide nucleic acid) have 0 mismatches from each other.

[00174] It is also noted that the sequences of the RNAi agents in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 include sequences which comprise modifications, as detailed in Table 3. For example, one modified variant of the RNAi agent AD-18892 comprises strands of the sequences uGGuGcuGAcuAuccAGuudTdT (SEQ ID NO: 6132) and AACUGGAuAGUcAGcACcAdTdT (SEQ ID NO: 660). It is noted that dTdT (2'-deoxy-thymidine-5'-phosphate and 2'-deoxy-thymidine-5'-phosphate), or in some cases, TT or UU, is added as a cap or extension to both 3'-ends, but this cap or extension is not included in the calculation of the total number of mismatches.

In addition, the sequence uGGuGcuGAcuAuccAGuu (SEQ ID NO: 1) comprises modifications from the corresponding portion of the Beta-Catenin gene, or UGGUGCUGACUAUCCAGUU (SEQ ID NO: 4771). In this case, lowercase "c" represents 2'-O-methylcytidine-5'-phosphate, and lowercase "u" represents 2'-O-methyluridine-5'-phosphate. Uppercase "A", "C", "G" and "U" represent the un-modified adenosine-5'-phosphate, cytidine-5'-phosphate, guanosine-5'-phosphate, and uridine-5'-phosphate, respectively. The substitution of modified c for unmodified C does not count as a mismatch in numbering the 0, 1, 2, or 3 mismatches between sequences. This is true of all sequences in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. Thus, an equal number of mismatches would be calculated (a) between a test sequence and a modified sequence (e.g., that of AD-18892 or any other sequence in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9), and (b) between the same test sequence and the corresponding unmodified sequence from the Beta-Catenin gene (e.g., the portion of the Beta-Catenin gene corresponding to AD-18892 or any other sequence in Table 1), and (c) between a modified sequence and a differently modified sequence which have the same base sequence.

[00175] In one particular embodiment, the present disclosure comprises a RNAi agent comprising a anti-sense strand comprising at least 15 or 19 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand of: any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00176] It is noted that the present disclosure pertains to "modified and unmodified variants" of the disclosed sequences.

[00177] An "unmodified variant" (also known as a "generic") of a particular sequence is the corresponding portion of Beta-Catenin without any modifications. For example, a modified variant (or "generic") of AD-18892 comprises a strand of the sequence uGGuGcuGAcuAuccAGuudTdT (SEQ ID NO: 6132); the corresponding "unmodified variant" is the corresponding portion of the wild-type Beta-Catenin sequence without modifications or terminal dTdT, namely, UGGUGCUGACUAUCCAGUU (SEQ ID NO: 6140), as described above. The "unmodified variants" of the sequences of Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 have the identical sequence, without base modifications or terminal dTdT. A given sequence and an "unmodified variant" of it differ by 0 nt (and have no mismatches).

[00178] A "modified variant" of a particular sequence comprises one or more (or one or more fewer) modifications to the backbone, sugar, phosphate or base, but do not have any base substitutions (e.g., G for C, or A for G); thus a given sequence and a modified variant thereof differ by 0 nt (and have no mismatches). A modified variant of the sequence of uGGuGcuGAcuAuccAGuu (SEQ ID NO: 1) is, as a non-limiting example, UGGuGcuGAcUAuccAGuu (SEQ ID NO: 6089). As another example, a given sequence [e.g., uGGuGcuGAcuAuccAGuu (SEQ ID NO: 1)] as a RNA and the same sequence as a PNA are modified variants of each other and differ by 0 nt (and have no mismatches). Similarly, the same

sequence (with no base substitutions) as a locked nucleic acid (LNA), Morpholino, threose nucleic acid (TNA), or glycol nucleic acid (GNA) or FANA would be a modified variant which has 0 mismatches.

[00179] As detailed below, substituting a single nucleotide at a given position with a modified version of the same nucleotide would produce a modified variant (with 0 mismatches).

[00180] In another particular embodiment, the RNAi agent comprises a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sense strand of any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00181] RNAi agents to Beta-Catenin of the present disclosure can be used in RNA interference.

[00182] **Modifications of RNAi Agent Sequences**

[00183] The present disclosure encompasses both unmodified sequences and example modified sequences, such as those disclosed in Tables 1, 2 and 3.

[00184] The present disclosure further encompasses any other modification of a disclosed sequence (e.g., a modified variant).

[00185] For example, the disclosure encompasses a RNAi agent with a substitution of a single nucleotide at a given position with a modified version of the same nucleotide. Thus a nucleotide (A, G, C or U) can be replaced by the corresponding 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5- oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3) w, or 2,6-diaminopurine.

[00186] Additional modified variants include the addition of any other moiety (e.g., a radiolabel or other tag or conjugate) to the RNAi agent; provided that the base sequence is identical, the addition of other moieties produces a "modified variant" (with no mismatches).

[00187] Various sets of modifications can be used. These include the following formats, which are used in various screens disclosed herein.

A22 a All UA as 2'-OMe-U A and all CA as 2'-OMe-C A
S26 a All U as 2'-OMe-U and all C as 2'-OMe-C
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A25S27

A25 a wt RNA
S27 a wt RNA
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A48S26

A48 a All UA as 2'-OMe-U A and all CA as 2'-OMe-C A, first 5'-N is DNA
S26 a All U as 2'-OMe-U and all C as 2'-OMe-C
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A51S26

A51 a All U as 2'-OMe-U and all C as 2'-OMe-C, except pos. 1, 2 and 14
S26 a All U as 2'-OMe-U and all C as 2'-OMe-C
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A52S36

A52 a 2'-OMe-N at pos. 3, 7, 10 and 13, 2'-MOE-N at pos. 18 and 19
S36 a 2'-OMe-N at pos. 4, 8, 12 and 15, 2'-MOE-N at pos. 1, 2, 18 and 19
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A53S37

A53 a 2'-MOE-N at pos. 3, 7, 10, 13, 18 and 19
S37 a 2'-MOE-N at pos. 1, 2, 4, 8, 12, 15, 18 and 19
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A54S36

A54 a 2'-OMe-N at pos. 3, 7, 10 and 13, 2'-MOE-N at pos. 18 and 19, DNA at pos. 1
S36 a 2'-OMe-N at pos. 4, 8, 12 and 15, 2'-MOE-N at pos. 1, 2, 18 and 19
All 3' overhangs as 2'-OMe-U 2'-OMe-U

A55S36

A55 a 2'-OMe-N at pos. 3, 7, 10 and 13, 2'-MOE-N at pos. 18 and 19,

2'-F-N at pos. 1
S36 a 2'-OMe-N at pos. 4, 8, 12 and 15, 2'-MOE-N at pos. 1, 2, 18 and 19
All 3' overhangs as 2'-OMe-U 2'-OMe-U

[00188] In addition to these modifications and patterns (e.g, formats) for modifications, other modifications or sets of modifications of the sequences provided can be generated using common knowledge of nucleic acid modification.

[00189] RNA Interference

[00190] RNA interference (RNAi) is a post-transcriptional, targeted gene-silencing technique that uses double-stranded RNA (dsRNA) to degrade messenger RNA (mRNA) containing the same sequence as the dsRNA. The process of RNAi occurs when ribonuclease III (Dicer) cleaves the longer dsRNA into shorter fragments called siRNAs. siRNAs (small interfering RNAs) produced by Dicer are typically about 21 to 23 nucleotides long and comprise about 19 base pair duplexes (though artificial siRNAs or RNAi agents can be shorter, and/or blunt-ended, and/or comprises one or more endcaps). The smaller RNA segments then mediate the degradation of the target mRNA. Dicer has also been implicated in the excision of 21- and 22-nucleotide small temporal RNAs (stRNAs) from precursor RNA of conserved structure that are implicated in translational control. Hutvagner et al. 2001 Science 293: 834. The RNAi response also features an endonuclease complex, commonly referred to as an RNA-induced silencing complex (RISC), which mediates cleavage of single-stranded mRNA complementary to the anti-sense strand of the RNAi agent. Cleavage of the target RNA takes place in the middle of the region complementary to the anti-sense strand of the siRNA duplex.

[00191] In one aspect, an RNA interference agent includes a single-stranded RNA that interacts with a target RNA sequence to direct the cleavage of the target RNA. Without wishing to be bound by theory, long double-stranded RNA introduced into plants and invertebrate cells is broken down into siRNA by a Type III endonuclease known as Dicer. Sharp et al. 2001 Genes Dev. 15:485. Dicer, a ribonuclease-III-like enzyme, processes the dsRNA into 19-23 base pair short interfering RNAs with characteristic two base 3' overhangs. Bernstein et al. 2001 Nature 409:363. The siRNAs are then incorporated into an RNA-induced silencing complex (RISC) where one or more helicases unwind the siRNA duplex, enabling one of the now-unpaired siRNA strands to act as a "guide" strand to guide target recognition. Nykanen et al. 2001 Cell 107:309. Upon binding of the anti-sense guide strand to the appropriate target mRNA, one or more endonucleases within the RISC cleaves the target to induce silencing. Elbashir et al. 2001 Genes Dev. 15:188. Thus, in one aspect the present disclosure relates to a single-stranded RNA that promotes the formation of a RISC complex to effect silencing of the target gene.

[00192] RNA interference has also been studied in a variety of systems. Work in *Drosophila* embryonic lysates (Elbashir et al. 2001 EMBO J. 20: 6877 and Tuschl et al. International PCT Publication No. WO 01/75164) has revealed certain requirements for siRNA length, structure, chemical composition, and sequence that are essential to mediate efficient RNAi activity in a variety of systems, including especially mammals. These studies have shown that 21-nucleotide siRNA duplexes are most active when containing 3'-terminal dinucleotide overhangs. Substitution of the 3'-terminal siRNA overhang nucleotides with 2'-deoxy nucleotides (2'-H) was tolerated. In addition, a 5'-phosphate on the target-complementary strand of a siRNA duplex is usually required for siRNA activity. Most importantly for therapeutic uses, siRNA duplexes shorter than 50 bp or so do not activate the interferon response in mammalian cells. See., e.g., Tuschl et al., WO 01/752164.

[00193] Others have reported on various RNAi and gene-silencing systems. For example, Churikov et al. International PCT Publication No. WO 01/42443 describe certain methods for modifying genetic characteristics of an organism using certain dsRNAs. Reed et al. International PCT Publication No. WO 01/68836 describe certain methods for gene silencing in plants. Honer et al. International PCT Publication No. WO 01/70944 describe certain methods of drug screening using transgenic nematodes as Parkinson's Disease models using certain dsRNAs. Arndt et al. International PCT Publication No. WO 01/92513 describe certain methods for mediating gene suppression by using factors that enhance RNAi. Tuschl et al. International PCT Publication No. WO 02/44321 describe certain synthetic siRNA constructs. Pachuk et al. International PCT Publication No. WO 00/63364, and Satishchandran et al. International PCT Publication No. WO 01/04313 describe certain methods and compositions for inhibiting the function of certain polynucleotide sequences using certain long (over 250 bp), vector expressed dsRNAs. Kreutzer et al. International PCT Publications Nos. WO 02/055692, WO 02/055693, and EP 1144623 B1 describes certain methods for inhibiting gene expression using dsRNA. Graham et al. International PCT Publications Nos. WO 99/49029 and WO 01/70949, and AU 4037501 describe certain vector expressed siRNA molecules. Fire et al. U.S. Pat. No. 6,506,559 describe certain methods for inhibiting gene expression *in vitro* using certain long dsRNA (299 bp-1033 bp) constructs that mediate RNAi. Martinez et al. 2002 Cell, 110, 563-574 describe certain single-stranded siRNA constructs, including certain 5'-phosphorylated single-stranded siRNAs that mediate RNA interference in HeLa cells. Harborth et al. 2003 Anti-sense & Nucleic Acid Drug Development 13: 83-105 describe certain chemically and structurally modified siRNA molecules. Chiu and Rana 2003 RNA 9: 1034-1048 describe certain chemically and structurally modified siRNA molecules. Woolf et al. International PCT Publication Nos. WO 03/064626 and WO 03/064625 describe certain chemically modified dsRNA constructs.

[00194] Kits for RNAi synthesis are commercially available, e.g., from New England Biolabs and Ambion.

[00195] The RNAi agent(s) of the present disclosure target (e.g., bind to, anneal to, etc.) the Beta-Catenin mRNA. The use of the RNAi agent to Beta-Catenin results in a decrease of Beta-Catenin activity, level and/or expression, e.g., a "knock-down" or "knock-out" of the target gene or target sequence. Particularly, in one embodiment, in the case of a disease state characterized by over-expression or hyper-activity or improper cellular compartmentalization of Beta-Catenin, administration of a RNAi agent to Beta-Catenin knocks down the Beta-Catenin target enough to restore a normal level of Beta-Catenin activity.

[00196] A suitable RNAi agent can be selected by any process known in the art or conceivable by one of ordinary skill in the art. For example, the selection criteria can include one or more of the following steps: initial analysis of the Beta-Catenin gene sequence and design of RNAi agents; this design can take into consideration sequence similarity across species (human, cynomolgus, mouse, etc.) and dissimilarity to other (non-Beta-Catenin) genes; screening of RNAi agents *in vitro* (e.g., at 10 nM in HeLa cells); determination of EC50 in HeLa cells; determination of viability of cells treated with RNAi agents, including insensitive cells which do not require Beta-Catenin for survival (e.g., NCI-H28 or RKO), or sensitive cells, which do require Beta-Catenin for survival (e.g., LoVo, DLD-1, LS411N, or SW403); testing with human PBMC (peripheral blood mononuclear cells), e.g., to test levels of TNF-alpha to estimate immunogenicity, wherein immunostimulatory sequences are less desired; testing in human whole blood assay, wherein fresh human blood is treated with an RNAi agent and cytokine/chemokine levels are determined [e.g., TNF-alpha (tumor necrosis factor-alpha) and/or MCP1 (monocyte chemotactic protein 1)], wherein Immunostimulatory sequences are less desired; determination of gene knockdown *in vivo* using Hep3B subcutaneous tumors in test animals; Beta-Catenin target gene modulation analysis, e.g., using a pharmacodynamic (PD) marker, for example, other components of the Wnt/Beta-Catenin pathway, wherein Beta-Catenin knockdown leads to a dose-dependent reduction of abundance of those components; and optimization of specific modifications of the RNAi agents.

[00197] The dsRNA molecules (RNAi agents) described herein are thus useful in RNA interference of the Beta-Catenin gene.

[00198] Features of a RNAi Agent: Sense strand, Anti-Sense Strand and (Optional) Overhangs

[00199] In various embodiments, the RNAi agents comprise a first strand and a second strand, e.g., a sense strand and an anti-sense strand. Optionally, one or both ends of the duplex contain unpaired nucleotides referred to herein as "overhangs".

[00200] The term "anti-sense strand" refers to the strand of a RNAi agent which includes a region that is substantially complementary to a target sequence. As used herein, the term "region of complementarity" refers to the region on the anti-sense strand that is substantially complementary to

a sequence, for example a target sequence, as defined herein. Where the region of complementarity is not fully complementary to the target sequence, the mismatches may be in the internal or terminal regions of the molecule. Generally, the most tolerated mismatches are in the terminal regions, e.g., within 5, 4, 3, or 2 nucleotides of the 5' and/or 3' terminus.

[00201] The term "sense strand," as used herein, refers to the strand of a RNAi agent that includes a region that is substantially complementary to a region of the anti-sense strand as that term is defined herein.

[00202] The sequence of a gene may vary from individual to individual, especially at wobble positions within the coding segment, or in the untranslated region; individuals may also differ from each other in coding sequence, resulting in additional differences in mRNA. The sequence of the sense and anti-sense strands of the RNAi agent can thus be designed to correspond to that of an individual patient, if and where needed. RNAi agents can also be modified in sequence to reduce immunogenicity, binding to undesired mRNAs (e.g., "off-target effects") or to increase stability in the blood. These sequence variants are independent of chemical modification of the bases or 5' or 3' or other end-caps of the RNAi agents. In the case of Beta-Catenin, three human transcripts have been published: NP_001091679.1; NP_001091680.1; and NP_001895.1. Variants between these can be used to design RNAi agents to Beta-Catenin.

[00203] The RNAi agents can comprise overhang(s), blunt end(s) and/or endcap(s). The RNAi agents can have overhangs of 0, 1, or 2 overhangs; in the case of 0 nt overhangs, they are blunt-ended. A RNAi agent can have 0, 1 or 2 blunt ends. In a "blunt-ended RNAi agent" both strands terminate in a base-pair; thus a blunt-ended molecule lacks either 3' or 5' single-stranded nucleotide overhangs.

[00204] As used herein, the term "overhang" or "nucleotide overhang" refer to at least one unpaired nucleotide that protrudes from end of at least one of the two strands of the duplex structure of a RNAi agent. For example, when a 3'-end of one strand of a dsRNA extends beyond the 5'-end of the other strand, or vice versa, there is an overhang. A dsRNA can comprise an overhang of at least one nucleotide; alternatively the overhang can comprise at least two nucleotides, at least three nucleotides, at least four nucleotides, at least five nucleotides or more. An overhang can comprise or consist of a nucleotide/nucleoside analog, including a deoxynucleotide/nucleoside. The overhang(s) may be on the sense strand, the anti-sense strand or any combination thereof. Furthermore, the nucleotide(s) of an overhang can be present on the 5' end, 3' end or both ends of either an anti-sense or sense strand of a dsRNA.

[00205] The RNAi agent can also optionally comprise a cap. The term "Cap" and the like include a chemical moiety attached to the end of a double-stranded nucleotide duplex, but is used herein to exclude a chemical moiety that is a nucleotide or nucleoside. A "3' Cap" is attached at the 3' end of a nucleotide or oligonucleotide and protects the molecule, e.g., from nucleases, such as

those in blood serum or intestinal fluid. A useful 3' cap will increase stability (e.g., reduce degradation, for example, by nucleases) and also still allow RNAi activity. Various 3' end caps are as disclosed in, for example, WO 2005/021749 and WO 2007/128477; and U.S. Patent Nos. 8,084,600 and 8,097,716. A "5' cap" is attached at the 5' end of a nucleotide or oligonucleotide. A cap should not interfere (or unduly interfere) with RNAi activity.

[00206] The present disclosure thus contemplates a RNAi agent specific to Beta-Catenin comprising an anti-sense strand. In a more specific embodiment, the present disclosure contemplates a RNAi agent specific to Beta-Catenin comprising a first and a second strand, e.g., a sense strand and an anti-sense strand (which may optionally be contiguous or connected via a linker or loop), or an anti-sense strand and a sense strand (which may optionally be contiguous or connected via a linker or loop), which together comprise a double-stranded or complementary region, and can also optionally comprise one or two overhangs, and/or one or two caps, and/or modifications of the sugar, phosphate or base, and/or additional moieties. The RNAi agent is used to induce RNA interference of the Beta-Catenin gene.

[00207] Target and Complementary Sequences

[00208] The RNAi agents of the present disclosure target (e.g., specifically bind to, anneal to, etc.) the mRNA encoding the gene Beta-Catenin. The use of the RNAi agent specific to Beta-Catenin results in a decrease of Beta-Catenin activity, level and/or expression and/or cellular distribution/compartmentalization, e.g., a "knock-down" or "knock-out" of the target gene or target sequence. Particularly in one embodiment, in the case of a disease state characterized by over-expression or hyper-activity of Beta-Catenin, administration of a RNAi agent to Beta-Catenin knocks down the Beta-Catenin gene enough to restore a normal level, abundance or cellular distribution of Beta-Catenin activity.

[00209] As used herein, "target sequence" or "target gene" refer to a contiguous portion of the nucleotide sequence of an mRNA molecule formed during the transcription of a gene, e.g., a Beta-Catenin gene, including mRNA that is a product of RNA processing of a primary transcription product. The target portion of the sequence will be at least long enough to serve as a substrate for iRNA-directed cleavage at or near that portion. For example, the target sequence will generally be from 9-36 nucleotides (nt) in length, e.g., 15-30 nucleotides in length, including all sub-ranges therebetween. As non-limiting examples, the target sequence can be from 15-30 nucleotides, 15-26 nucleotides, 15-23 nucleotides, 15-22 nucleotides, 15-21 nucleotides, 15-20 nucleotides, 15-19 nucleotides, 15-18 nucleotides, 15-17 nucleotides, 18-30 nucleotides, 18-26 nucleotides, 18-23 nucleotides, 18-22 nucleotides, 18-21 nucleotides, 18-20 nucleotides, 19-30 nucleotides, 19-26 nucleotides, 19-23 nucleotides, 19-22 nucleotides, 19-21 nucleotides, 19-20 nucleotides, 19 nucleotides, 20-30 nucleotides, 20-26 nucleotides, 20-25 nucleotides, 20-24 nucleotides, 20-23

nucleotides, 20-22 nucleotides, 20-21 nucleotides, 20 nucleotides, 21-30 nucleotides, 21-26 nucleotides, 21-25 nucleotides, 21-24 nucleotides, 21-23 nucleotides, or 21-22 nucleotides, 21 nucleotides, 22 nucleotides, or 23 nucleotides. The sense and anti-sense strands of the RNAi comprise a sequence complementary to that of the target nucleic acid, Beta-Catenin.

[00210] As used herein, the term "strand comprising a sequence" refers to an oligonucleotide comprising a chain of nucleotides that is described by the sequence referred to using the standard nucleotide nomenclature.

[00211] As used herein, and unless otherwise indicated, the term "complementary" refers to the ability of an oligonucleotide or polynucleotide comprising a first nucleotide sequence to hybridize and form a duplex structure under certain conditions with an oligonucleotide or polynucleotide comprising a second nucleotide sequence. Such conditions can, for example, be stringent, e.g., 400 mM NaCl, 40 mM PIPES pH 6.4, 1 mM EDTA, 50°C or 70°C for 12-16 hours followed by washing. Other conditions, such as physiologically relevant conditions as may be encountered inside an organism, can apply. The skilled person will be able to determine the set of conditions most appropriate for a test of complementarity of two sequences in accordance with the ultimate application of the hybridized nucleotides.

[00212] Complementary sequences within a RNAi agent, e.g., within a dsRNA as described herein, include base-paired oligonucleotides or polynucleotides comprising a first nucleotide sequence to an oligonucleotide or polynucleotide comprising a second nucleotide sequence over the entire length of one or both nucleotide sequences. Such sequences can be referred to as "fully complementary" with respect to each other herein. However, where a first sequence is referred to as "substantially complementary" with respect to a second sequence herein, the two sequences can be fully complementary, or they may form one or more, but generally not more than 5, 4, 3 or 2 mismatched base pairs upon hybridization for a duplex up to 30 base pairs, while retaining the ability to hybridize under the conditions most relevant to their ultimate application, e.g., inhibition of gene expression via a RISC pathway. However, where two oligonucleotides are designed to form, upon hybridization, one or more single-stranded overhangs, such overhangs shall not be regarded as mismatches with regard to the determination of complementarity. For example, a dsRNA comprising one oligonucleotide 21 nucleotides in length and another oligonucleotide 23 nucleotides in length, wherein the longer oligonucleotide comprises a sequence of 21 nucleotides that is fully complementary to the shorter oligonucleotide, may yet be referred to as "fully complementary" for the purposes described herein. The term "overhang" describes an unpaired nucleotide at the 3' or 5' end of a double-stranded nucleotide duplex, as described above. In one embodiment, the overhang is 1 to 4 nt long and is on the 3' end.

[00213] "Complementary" sequences, as used herein, may also include, or be formed entirely from, non-Watson-Crick base pairs and/or base pairs formed from non-natural and modified

nucleotides, in as far as the above requirements with respect to their ability to hybridize are fulfilled. Such non-Watson-Crick base pairs includes, but are not limited to, G:U Wobble or Hoogstein base pairing.

[00214] The terms "complementary," "fully complementary" and "substantially complementary" herein may furthermore be used with respect to the base matching between the sense strand and the anti-sense strand of a dsRNA, or between the anti-sense strand of a RNAi agent and a target sequence, as will be understood from the context of their use. The RNAi agent of the present disclosure can comprise a sequence which is complementary to the sequence of a target sequence (DNA) which is disclosed herein. For example, if the target sequence disclosed is DNA, the RNAi agent can comprise a strand which is complementary to it (anti-parallel and having a sequence of bases which hydrogen bonds to the sequence of the target) and which is, for example, RNA, or RNA with a small number of DNA substitutions, or an alternative backbone such as FANA, PNA, GNA, TNA, boranophosphate or LNA, or RNA with a small number of substitutions which are FANA, PNA, GNA, TNA, boranophosphate or LNA, etc.

[00215] As used herein, a polynucleotide that is "substantially complementary to at least part of" a messenger RNA (mRNA) refers to a polynucleotide that is substantially complementary to a contiguous portion of the mRNA of interest (e.g., an mRNA encoding Beta-Catenin). For example, a polynucleotide is complementary to at least a part of a Beta-Catenin mRNA if the sequence is substantially complementary to a non-interrupted portion of an mRNA encoding Beta-Catenin.

[00216] Thus, the RNAi agent of the present disclosure is complimentary or substantially complimentary to a target sequence in the mRNA corresponding to the target gene Beta-Catenin and is double-stranded, comprising a sense and an anti-sense strand (which can be contiguous, linked via a loop, or otherwise joined), where the double-stranded region an be 9 to 36 bp long (particularly for example, 19 to 22 or 19 to 23 bp long), and can furthermore optionally comprise a 3' or 5' overhang, and the RNAi agent can furthermore comprise a 3' cap. The RNAi agent mediates RNA interference, down-regulating or inhibiting the level, expression and/or activity of Beta-Catenin, and/or establishing or re-establishing an approximately normal level of Beta-Catenin and/or Beta-Catenin activity, or other biological function related to Beta-Catenin.

[00217] **Double-stranded RNA**

[00218] The term "double-stranded RNA" or "dsRNA," as used herein, refers to an RNAi agent comprising a first and a second strand; e.g., a composition that includes an RNA molecule or complex of molecules having a hybridized duplex region that comprises two anti-parallel and substantially complementary nucleic acid strands, which will be referred to as having "sense" and "antisense" orientations with respect to a target RNA. The antisense strand, with respect to the mRNA target, is also called the "guide" strand, and the sense strand is also called the "passenger"

strand. The passenger strand can include at least one or more of the following: one or more extra nucleotides (e.g., a bulge or 1 nt loop) compared to the other strand, a nick, a gap, etc., compared to the other strand. In various embodiments, the first strand is the sense strand and the second strand is the anti-sense strand. In other embodiments, the first strand is the anti-sense strand, and the second strand is the sense strand.

[00219] The duplex region can be of any length that permits specific degradation of a desired target RNA through a RISC pathway, but will typically range from 9 to 36 base pairs ("bp") in length, e.g., 15-30 base pairs in length. Considering a duplex between 9 and 36 base pairs, the duplex can be any length in this range, for example, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, or 36 bp and any sub-range therebetween, including, but not limited to 15-30 base pairs, 15-26 bp, 15-23 bp, 15-22 bp, 15-21 bp, 15-20 bp, 15-19 bp, 15-18 bp, 15-17 bp, 18-30 bp, 18-26 bp, 18-23 bp, 18-22 bp, 18-21 bp, 18-20 bp, 19-30 bp, 19-26 bp, 19-23 bp, 19-22 bp, 19-21 bp, 19-20 bp, 19 bp, 20-30 bp, 20-26 bp, 20-25 bp, 20-24 bp, 20-23 bp, 20-22 bp, 20-21 bp, 20 bp, 21-30 bp, 21-26 bp, 21-25 bp, 21-24 bp, 21-23 bp, 21-22 bp, 21 bp, 22 bp, or 23 bp. The dsRNAs generated in the cell by processing with Dicer and similar enzymes are generally in the range of about 19 to about 22 base pairs in length. One strand of the duplex region of a dsRNA comprises a sequence that is substantially complementary to a region of a target RNA. The two strands forming the duplex structure can be from a single RNA molecule having at least one self-complementary duplex region, or can be formed from two or more separate RNA molecules that hybridize to form the duplex. Where the duplex region is formed from two self-complementary regions of a single molecule, the molecule can have a duplex region separated by a single stranded chain of nucleotides (herein referred to as a "hairpin loop", e.g., such as found in an shRNA construct) between the 3'-end of one strand and the 5'-end of the respective other strand forming the duplex structure. The hairpin loop can comprise at least one unpaired nucleotide; in some embodiments the hairpin loop can comprise at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 20, at least 23 or more unpaired nucleotides. Where the two substantially complementary strands of a dsRNA are comprised by separate RNA molecules, those molecules need not, but can be covalently connected. Where the two strands are connected covalently by a hairpin loop, the construct is generally referred to herein and in the art as a "shRNA". Where the two strands are connected covalently by means other than a hairpin loop, the connecting structure is referred to as a "linker." The term "siRNA" is also used herein to refer to a dsRNA as described above.

[00220] RNAi Agents Lowering or Normalizing Beta-Catenin Level, Expression, Cellular Distribution, And/Or Activity

[00221] Example RNAi agents for targeting Beta-Catenin include those which bind to a mRNA

corresponding to the Beta-Catenin gene provided herein. Example RNAi agents to Beta-Catenin are provided in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[00222] Any method known in the art can be use to measure changes in Beta-Catenin activity, level, cellular distribution (e.g., localization to the membrane but not the cytoplasm or nucleus) and/or expression induced by a Beta-Catenin RNAi agent. Measurements can be performed at multiple timepoints, prior to, during and after administration of the RNAi agent, to determine the effect of the RNAi agent.

[00223] The RNAi agents of the present disclosure silence, inhibit the expression of, down-regulate the expression of, and/or suppress the expression of the Beta-Catenin gene, such that an approximately normal level of Beta-Catenin activity, expression and/or level and/or distribution in various cellular compartments is achieved.

[00224] In addition, in various embodiments, depending on the disease condition and biological context, it is acceptable to use the RNAi agents of the present disclosure to establish a level of Beta-Catenin expression, activity and/or level which is below the normal level, or above the normal level.

[00225] Types of RNAi Agents and Modification Thereof

[00226] The use of RNAi agents or compositions comprising an anti-sense nucleic acid to down-modulate the expression of a particular protein in a cell is well known in the art. A RNAi agent comprises a sequence complementary to, and is capable of hydrogen binding to, the coding strand of another nucleic acid (e.g., an mRNA). Thus, in various embodiments, the RNAi agents of the present disclosure encompass any RNAi agents which target (e.g., are complementary to, capable of specific hydrogen binding to, etc.) any sequences presented herein, e.g., in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[00227] Anti-sense sequences complementary to an mRNA can be complementary to the coding region, the 5' or 3' untranslated region of the mRNA, and/or a region bridging the coding and untranslated regions, and/or portions thereof. Furthermore, a RNAi agent can be complementary to a regulatory region of the gene encoding the mRNA, for instance a transcription or translation initiation sequence or regulatory element. Particularly, a RNAi agent or any portion thereof can be complementary to a region preceding or spanning the initiation codon on the coding strand or in the 3' untranslated region of an mRNA.

[00228] RNAi agent molecules can be designed according to the rules of Watson and Crick base pairing. The RNAi agent can be complementary to the entire coding region of Beta-Catenin mRNA, but more particularly is an oligonucleotide which is anti-sense to only a portion of the coding or non-coding region of Beta-Catenin mRNA. For example, the anti-sense oligonucleotide can be complementary to the region surrounding the translation start site of Beta-Catenin mRNA. An anti-sense oligonucleotide can be, for example, about 5, 10, 15, 19, 20, 21, 22, 23, 24, 25, 30, 35, 40, 45

or 50 nucleotides in length.

[00229] RNAi agent may have modifications internally, and/or at one or both ends. The modifications at the ends can help stabilize the RNAi agent, protecting it from degradation by nucleases in the blood.

[00230] The RNAi agents can also optionally be designed to anneal to known or predicted exposed and/or single-stranded regions of the mRNA (e.g., loops).

[00231] A RNAi agent can be constructed using chemical synthesis and enzymatic ligation reactions using procedures known in the art. For example, a RNAi agent can be chemically synthesized using naturally-occurring nucleotides or variously modified nucleotides designed to decrease off-target effects, and/or increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the anti-sense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides can be used.

[00232] "G," "C," "A," "T" and "U" each generally stand for a nucleotide that contains guanine, cytosine, adenine, thymidine and uracil as a base, respectively. However, the term "ribonucleotide" or "nucleotide" can also refer to a modified nucleotide or a surrogate replacement moiety. The skilled person is well aware that guanine, cytosine, adenine, and uracil may be replaced by other moieties without substantially altering the base pairing properties of an oligonucleotide comprising a nucleotide bearing such replacement moiety. For example, without limitation, a nucleotide comprising inosine as its base may base pair with nucleotides containing adenine, cytosine, or uracil. Hence, nucleotides containing uracil, guanine, or adenine may be replaced in the nucleotide sequences of dsRNA featured in the present disclosure by a nucleotide containing, for example, inosine. In another example, adenine and cytosine anywhere in the oligonucleotide can be replaced with guanine and uracil, respectively to form G-U Wobble base pairing with the target mRNA. Sequences containing such replacement moieties are suitable for the compositions and methods featured in the present disclosure.

[00233] The skilled artisan will recognize that the term "RNA molecule" or "ribonucleic acid molecule" encompasses not only RNA molecules as expressed or found in nature (i.e., are naturally occurring), but also non-naturally-occurring analogs and derivatives of RNA comprising one or more ribonucleotide/ribonucleoside analogs or derivatives as described herein or as known in the art. Strictly speaking, a "ribonucleoside" includes a nucleoside base and a ribose sugar, and a "ribonucleotide" is a ribonucleoside with one, two or three phosphate moieties. However, the terms "ribonucleoside" and "ribonucleotide" can be considered to be equivalent as used herein. The RNA can be modified in the nucleobase structure or in the ribose-phosphate backbone structure, e.g., as described herein below. However, the molecules comprising ribonucleoside analogs or derivatives must retain the ability to form a duplex. As non-limiting examples, an RNA molecule can also include at least one modified ribonucleoside, including but not limited to a 2'-O-methyl modified

nucleotide, a nucleoside comprising a 5' phosphorothioate group, a terminal nucleoside linked to a cholesteryl derivative or dodecanoic acid bisdecylamide group, a locked nucleoside, an abasic nucleoside, a 2'-deoxy-2'-fluoro modified nucleoside, a 2'-amino-modified nucleoside, 2'-alkyl-modified nucleoside, morpholino nucleoside, an unlocked ribonucleotide (e.g., an acyclic nucleotide monomer, as described in WO 2008/147824), a phosphoramidate or a non-natural base comprising nucleoside, or any combination thereof. Alternatively, an RNA molecule can comprise at least two modified ribonucleosides, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 9, at least 10, at least 15, at least 20 or more, up to the entire length of the dsRNA molecule. The modifications need not be the same for each of such a plurality of modified ribonucleosides in an RNA molecule. In one embodiment, modified RNAs contemplated for use in methods and compositions described herein are peptide nucleic acids (PNAs) that have the ability to form the required duplex structure and that permit or mediate the specific degradation of a target RNA via a RISC pathway. In some cases, a RNA molecule can include a terminal dinucleotide (e.g., TT) which is DNA, and/or a small number of internal (e.g., base-pairing) DNA bases (e.g., fewer than the number of RNA bases), for example, a T substituting a U.

[00234] Examples of modified nucleotides which can be used to generate the RNAi agent include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N6-adenine, 7-methylguanine, 5-methylaminomethyluracil, 5-methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5- oxyacetic acid methylester, uracil-5-oxyacetic acid (v), 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, (acp3) w, and 2,6-diaminopurine.

[00235] A "modified variant" of a sequence disclosed herein includes any variant comprising the same sequence, but with a modification in the base, sugar, phosphate or backbone (but not a base substitution, e.g., A for G, or C for U). Thus, a modified variant can comprise any modified nucleotide described above (e.g., 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine, 4-acetylcytosine, 5-(carboxyhydroxylmethyl) uracil, etc.). When a base is replaced by a corresponding modified base (e.g., A for modified A), these modified nucleotides do not constitute a mismatch or base difference. Thus a given sequence with a U at a particular position and a modified variant comprising a 5-fluorouracil, 5-bromouracil, 5-chlorouracil, or 5-iodouracil at the same sequence would differ by 0 nt (or have no mismatches); however, a given

sequence with a C at a particular position and a different sequence with a 5-fluorouracil (wherein the two sequences are otherwise identical) would differ by 1 nt (1 mismatch).

[00236] In one embodiment, the present disclosure encompasses any modified variant of any RNAi agent disclosed herein. The modified variant contains the same sequence, but can be modified to contain modifications in the phosphate, sugar, base, nucleotide, etc. For example, the modified variant can contain one or more of the modified nucleotides listed herein, for example a C replaced by a 2'-modified C (such sequences would differ by 0 mismatches).

[00237] In one aspect, a modified ribonucleoside includes a deoxyribonucleoside. In such an instance, a RNAi agent can comprise one or more deoxynucleosides, including, for example, a deoxynucleoside overhang(s), or one or more deoxynucleosides within the double-stranded portion of a dsRNA. However, it is self-evident that under no circumstances is a double-stranded DNA molecule encompassed by the term "RNAi agent."

[00238] Replacing the 3'-terminal nucleotide overhanging segments of a 21-mer RNAi agent duplex having two-nucleotide 3'-overhangs with deoxyribonucleotides does not have an adverse effect on RNAi activity. Replacing up to four nucleotides on each end of the RNAi agent with deoxyribonucleotides has been well tolerated, whereas complete substitution with deoxyribonucleotides results in no RNAi activity. International PCT Publication No. WO 00/44914, and Beach et al. International PCT Publication No. WO 01/68836 preliminarily suggest that siRNA may include modifications to either the phosphate-sugar backbone or the nucleoside to include at least one of a nitrogen or sulfur heteroatom. Kreutzer et al. Canadian Patent Application No. 2,359,180, also describe certain chemical modifications for use in dsRNA constructs in order to counteract activation of double-stranded RNA-dependent protein kinase PKR, specifically 2'-amino or 2'-O-methyl nucleotides, and nucleotides containing a 2'-O or 4'-C methylene bridge. Additional 3'-terminal nucleotide overhangs include dT (deoxythimidine), 2'-O,4'-C-ethylene thymidine (eT), and 2-hydroxyethyl phosphate (hp).

[00239] Parrish et al. 2000 Molecular Cell 6: 1077-1087 tested certain chemical modifications targeting the unc-22 gene in C. elegans using long (>25 nt) siRNA transcripts. The authors describe the introduction of thiophosphate residues into these siRNA transcripts by incorporating thiophosphate nucleotide analogs with T7 and T3 RNA polymerase and observed that RNAs with two phosphorothioate modified bases also had substantial decreases in effectiveness as RNAi. Further, Parrish et al. reported that phosphorothioate modification of more than two residues greatly destabilized the RNAs *in vitro* such that interference activities could not be assayed. Id. at 1081. The authors also tested certain modifications at the 2'-position of the nucleotide sugar in the long siRNA transcripts and found that substituting deoxynucleotides for ribonucleotides produced a substantial decrease in interference activity, especially in the case of Uridine to Thymidine and/or Cytidine to deoxy-Cytidine substitutions. Id. In addition, the authors tested certain base modifications, including

substituting, in sense and anti-sense strands of the siRNA, 4-thiouracil, 5-bromouracil, 5-iodouracil, and 3-(aminoallyl) uracil for uracil, and inosine for guanosine. Whereas 4-thiouracil and 5-bromouracil substitution appeared to be tolerated, Parrish reported that inosine produced a substantial decrease in interference activity when incorporated in either strand. Parrish also reported that incorporation of 5-iodouracil and 3-(aminoallyl) uracil in the anti-sense strand resulted in a substantial decrease in RNAi activity as well.

[00240] Those skilled in the art will appreciate that it is possible to synthesize and modify the siRNA as desired, using any conventional method known in the art (see Henschel et al. 2004 DEQOR: a web-based tool for the design and quality control of siRNAs. Nucleic Acids Research 32 (Web Server Issue) : W113-W120). Further, it will be apparent to those skilled in the art that there are a variety of regulatory sequences (for example, constitutive or inducible promoters, tissue-specific promoters or functional fragments thereof, etc.) which are useful for the anti-sense oligonucleotide, siRNA, or shRNA expression construct/vector.

[00241] There are several examples in the art describing sugar, base, phosphate and backbone modifications that can be introduced into nucleic acid molecules with significant enhancement in their nuclease stability and efficacy. For example, oligonucleotides are modified to enhance stability and/or enhance biological activity by modification with nuclease resistant groups, for example, 2'-amino, 2'-C-allyl, 2'-flouro, 2'-O-methyl, 2'-O-allyl, 2'-H, nucleotide base modifications (for a review see Usman and Cedergren 1992 TIBS. 17: 34; Usman et al. 1994 Nucleic Acids Symp. Ser. 31: 163; Burgin et al. 1996 Biochemistry 35: 14090). Sugar modification of nucleic acid molecules are extensively described in the art.

[00242] Additional modifications and conjugations of RNAi agents have been described. Soutschek et al. 2004 Nature 432: 173-178 presented conjugation of cholesterol to the 3'-end of the sense strand of a RNAi agent by means of a pyrrolidine linker, thereby generating a covalent and irreversible conjugate. Chemical modifications (including conjugation with other molecules) of siRNA may also be made to improve the *in vivo* pharmacokinetic retention time and efficiency.

[00243] In various embodiments of the present disclosure, the RNAi agent to Beta-Catenin comprises at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[00244] In various embodiments of the present disclosure, the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and

2'-O-N-methylacetamido (2'-O-NMA).

[00245] In another embodiment, the RNAi comprises a gap or missing base. For example, the phosphate-sugar backbone may be present, but the base missing.

[00246] In another embodiment, the RNAi agent has a single-stranded nick (e.g., a break or missing bond in the backbone). In various embodiments, a single-stranded nick can be in either the sense or anti-sense strand, or both.

[00247] This nick can be, for example, in the sense strand, producing a small internally segmented interfering RNA, or sisiRNA, which may have less off-target effects than the corresponding RNAi agent without a nick.

[00248] The anti-sense nucleic acid or RNAi agent can also have an alternative backbone such as locked nucleic acid (LNA), Morpholino, peptidic nucleic acid (PNA), threose nucleic acid (TNA), or glycol nucleic acid (GNA), FANA, boranophosphate RNA, or be primarily RNA with a few nucleotides which are substituted by DNA, LNA, PNA, TNA, GNA, FANA, boranophosphate, or the like, and/or it can be labeled (e.g., radiolabeled or otherwise tagged).

[00249] One or both strands can comprise an alternative backbone

[00250] In yet another embodiment, the RNAi agent employed by the methods of the present disclosure can include an α-anomeric nucleic acid molecule. An α-anomeric nucleic acid molecule forms specific double-stranded hybrids with complementary RNA in which, contrary to the usual β-units, the strands run parallel to each other. Gaultier et al. 1987 Nucleic Acids. Res. 15: 6625-6641. The RNAi agent can also comprise a 2'-o-methylribonucleotide (Inoue et al. 1987 Nucleic Acids Res. 15: 6131-6148) or a chimeric RNA-DNA analogue (Inoue et al. 1987 FEBS Lett. 215: 327-330).

[00251] Alternatively, gene expression can be inhibited by targeting nucleotide sequences complementary to the regulatory region of Beta-Catenin (e.g., the promoter and/or enhancers) to form triple helical structures that prevent transcription of the Beta-Catenin gene. See generally, Helene 1991 Anticancer Drug Des. 6(6) : 569-84; Helene et al. 1992 Ann. N.Y. Acad. Sci. 660: 27-36; and Maher 1992, Bioassays 14(12) : 807-15.

[00252] Production of RNAi Agents

[00253] The RNAi agent can be produced biologically within a cell using an expression vector into which a nucleic acid has been subcloned in an anti-sense orientation (i.e., RNA transcribed from the inserted nucleic acid will be in an anti-sense orientation to a target nucleic acid of interest). The RNAi agent can also be produced biologically using an expression vector into which a nucleic acid has been subcloned as an shRNA construct (eg., RNA transcribed from the inserted nucleic acid will have a first region in an anti-sense orientation to a target nucleic acid of interest, a second region that comprises a loop or hinge, and a third region in a sense orientation to the target nucleic acid of

interest, wherein the first and third regions of the transcript preferably hydribize to each other, thereby forming a stem-and-loop structure.

[00254] Methods of producing RNAi agents are well-known in the art and available to persons of ordinary skill in the art.

[00255] Kits for synthesis of RNAi are commercially available from, e.g., New England Biolabs and Ambion.

[00256] Delivery of RNAi Agents

[00257] RNAi agents of the present disclosure can be delivered or introduced (e.g., to a cell *in vitro*, to a test animal, or to a human) by any means known in the art.

[00258] The RNAi agents of the present disclosure are typically administered to a subject or generated in situ such that they hybridize with cellular mRNA and/or genomic DNA encoding Beta-Catenin, and inhibit expression by inhibiting transcription and/or translation. An example of a route of administration of RNAi agents includes direct injection at a tissue site. Alternatively, RNAi agents can be modified to target selected cells and then administered systemically. For example, for systemic administration, anti-sense molecules can be modified such that they specifically bind to receptors or antigens expressed on a selected cell surface, e.g., by linking the anti-sense nucleic acid molecules to peptides or antibodies which bind to cell surface receptors or antigens. The anti-sense nucleic acid molecules can also be delivered to cells using vectors well known in the art and described in, for example, US20070111230. To achieve sufficient intracellular concentrations of the anti-sense molecules, vector constructs in which the anti-sense nucleic acid molecule is placed under the control of a strong pol II or pol III promoter are preferred.

[00259] "Introducing into a cell," when referring to a RNAi agent, means facilitating or effecting uptake or absorption into the cell, as is understood by those skilled in the art. Absorption or uptake of a RNAi agent can occur through unaided diffusive or active cellular processes, or by auxiliary agents or devices. The meaning of this term is not limited to cells *in vitro*; a RNAi agent may also be "introduced into a cell," wherein the cell is part of a living organism. In such an instance, introduction into the cell will include the delivery to the organism. For example, for *in vivo* delivery, a RNAi agent can be injected into a tissue site or administered systemically. *In vivo* delivery can also be by a beta-glucan delivery system, such as those described in U.S. Patent Nos. 5,032,401 and 5,607,677, and U.S. Publication No. 2005/0281781. *In vitro* introduction into a cell includes methods known in the art such as electroporation and lipofection. Further approaches are described herein below or known in the art.

[00260] Delivery of RNAi agent to tissue is a problem both because the material must reach the target organ and must also enter the cytoplasm of target cells. RNA cannot penetrate cellular membranes, so systemic delivery of naked RNAi agent is unlikely to be successful. RNA is quickly

degraded by RNAse activity in serum. For these reasons, other mechanisms to deliver RNAi agent to target cells has been devised. Methods known in the art include but are not limited to: viral delivery (retrovirus, adenovirus, lentivirus, baculovirus, AAV); liposomes (Lipofectamine, cationic DOTAP, neutral DOPC) or nanoparticles (cationic polymer, PEI), bacterial delivery (tkRNAi), electroporation, and also chemical modification (LNA) of siRNA to improve stability. Xia et al. 2002 Nat. Biotechnol. 20 and Devroe et al. 2002. BMC Biotechnol. 2 1: 15, disclose incorporation of siRNA into a viral vector. Porphysomes can also be used to deliver RNAi agents. Lovell et al. 2001 Nature Mater. 10: 324-32; and WO 2011/044671. Other systems for delivery of RNAi agents are contemplated and the RNAi agents of the present disclosure can be delivered by various methods yet to be found and/or approved by the FDA or other regulatory authorities. RNAi agents of the present disclosure can delivered in a suitable pharmaceutical composition. Several of these are described in greater detail, below.

[00261] Pharmaceutical Compositions of RNAi Agents

[00262] As used here, a "pharmaceutical composition" comprises a pharmaceutically effective amount of one or more Beta-Catenin RNAi agent, a pharmaceutically acceptable carrier, and, optionally, an additional disease treatment which works synergistically with the RNAi agent. The additional disease treatment can be additional RNAi agent(s) to Beta-Catenin, and/or additional RNAi agent(s) to another gene. As used herein, "pharmacologically effective amount," "therapeutically effective amount" or simply "effective amount" refers to that amount of a RNAi agent effective to produce the intended pharmacological, therapeutic or preventive result. For example, if a given clinical treatment is considered effective when there is at least a 10% reduction in a measurable parameter associated with a disease or disorder, a therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 10% reduction in that parameter. In this embodiment, a therapeutically effective amount of a RNAi agent targeting Beta-Catenin can reduce Beta-Catenin protein levels by at least 10%. In additional embodiments, a given clinical treatment is considered effective where there is at least a 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95% reduction in a measurable parameter associated with a disease or disorder, and the therapeutically effective amount of a drug for the treatment of that disease or disorder is the amount necessary to effect at least a 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, or 95% reduction, respectively, in that parameter.

[00263] The term "pharmaceutically acceptable carrier" refers to a carrier for administration of a therapeutic agent. Such carriers include, but are not limited to, saline, buffered saline, dextrose, water, glycerol, ethanol, and combinations thereof. The term specifically excludes cell culture medium. For drugs administered orally, pharmaceutically acceptable carriers include, but are not limited to pharmaceutically acceptable excipients such as inert diluents, disintegrating agents,

binding agents, lubricating agents, sweetening agents, flavoring agents, coloring agents and preservatives. Suitable inert diluents include sodium and calcium carbonate, sodium and calcium phosphate, and lactose, while corn starch and alginic acid are suitable disintegrating agents. Binding agents may include starch and gelatin, while the lubricating agent, if present, will generally be magnesium stearate, stearic acid or talc. If desired, the tablets may be coated with a material such as glyceryl monostearate or glyceryl distearate, to delay absorption in the gastrointestinal tract. Agents included in drug formulations are described further herein.

[00264] The pharmaceutical compositions comprising a Beta-Catenin RNAi agent can be in solid form, for example, powders, granules, tablets, pills, gelcaps, gelatin capsules, liposomes, suppositories, chewable forms, or patches. The pharmaceutical compositions comprising a Beta-Catenin RNAi agent can also be presented in liquid form, for example, solutions, emulsions, suspensions, elixirs, or syrups. Appropriate liquid supports can be, for example, water, organic solvents such as polyol, such as glycerol or glycols, including propylene glycol and polyethylene glycol, or ethanol, Cremophor EL, or mixtures thereof, in varying proportions, in water. The compositions can comprise nano-sized amorphous or crystalline granules coated with albumin or a surfactant.

[00265] Appropriate supports can include, for example, antibacterial and antifungal agents, buffering agents, calcium phosphate, cellulose, methyl cellulose, chlorobutanol, cocoa butter, colorings, dextrin, emulsifiers, enteric coatings, flavorings, gelatin, isotonic agents, lecithin, magnesium stearate, perfuming agents, polyalcohols such as mannitol, injectable organic esters such as ethyl oleate, paraben, phenol sorbic acid, polyethylene glycol, polyvinylpyrrolidine, phosphate buffered saline (PBS), preserving agents, propylene glycol, sodium carboxymethylcellulose, sodium chloride, sorbitol, various sugars (including, but not limited to, sucrose, fructose, galactose, lactose and trehalose), starch, suppository wax, talc, vegetable oils, such as olive oil and corn oil, vitamins, wax, and/or wetting agents. For Beta-Catenin RNAi agents, a preferred support comprises dextran and water, e.g. 5% dextrose in water (D5W).

[00266] The biologically inert portion of the pharmaceutical composition can optionally be erodible, allowing timed release of the RNAi agent.

[00267] The pharmaceutical composition can comprise additional components which aid in delivery, stability, efficacy, or reduction of immunogenicity.

[00268] Additional Components of a Pharmaceutical Composition Comprising a RNAi Agent to Beta-Catenin

[00269] Additional components of a pharmaceutical composition comprising a RNAi Agent to Beta-Catenin can be added to aid in delivery, stability, efficacy, or reduction of immunogenicity.

[00270] Liposomes have been used previously for drug delivery (e.g., delivery of a

chemotherapeutic). Liposomes (e.g., cationic liposomes) are described in PCT publications WO02/100435A1, WO03/015757A1, and WO04029213A2; U.S. Pat. Nos. 5,962,016; 5,030,453; and 6,680,068; and U.S. Patent Application 2004/0208921. A process of making liposomes is also described in WO04/002453A1. Furthermore, neutral lipids have been incorporated into cationic liposomes (e.g., Farhood et al. 1995).

[00271] Cationic liposomes have been used to deliver RNAi agent to various cell types (Sioud and Sorensen 2003; U.S. Patent Application 2004/0204377; Duxbury et al., 2004; Donze and Picard, 2002).

[00272] Use of neutral liposomes disclosed in Miller et al. 1998, and U.S. Patent Application 2003/0012812.

[00273] As used herein, the term "SNALP" refers to a stable nucleic acid-lipid particle. A SNALP represents a vesicle of lipids coating a reduced aqueous interior comprising a nucleic acid such as an iRNA or a plasmid from which an iRNA is transcribed. SNALPs are described, e.g., in U.S. Patent Application Publication Nos. 20060240093, 20070135372, and in International Application No. WO 2009082817.

[00274] Chemical transfection using lipid-based, amine-based and polymer-based techniques, is disclosed in products from Ambion Inc., Austin, Tex.; and Novagen, EMD Biosciences, Inc, an Affiliate of Merck KGaA, Darmstadt, Germany); Ovcharenko D (2003) "Efficient delivery of siRNAs to human primary cells." Ambion TechNotes 10 (5) : 15-16). Additionally, Song et al. (Nat Med. published online (Fete 1 0, 2003) doi: 10.1038/nm828) and others [Caplen et al. 2001 Proc. Natl. Acad. Sci. (USA), 98: 9742-9747; and McCaffrey et al. Nature 414: 34-39] disclose that liver cells can be efficiently transfected by injection of the siRNA into a mammal's circulatory system.

[00275] A variety of molecules have been used for cell-specific RNAi agent delivery. For example, the nucleic acid-condensing property of protamine has been combined with specific antibodies to deliver siRNAs. Song et al. 2005 Nat Biotech. 23: 709-717. The self-assembly PEGylated polycation polyethylenimine (PEI) has also been used to condense and protect siRNAs. Schiffelers et al. 2004 Nucl. Acids Res. 32: el49, 141-1 10.

[00276] The siRNA-containing nanoparticles were then successfully delivered to integrin-overexpressing tumor neovasculature. Hu-Lieskovan et al. 2005 Cancer Res. 65: 8984-8992.

[00277] The RNAi agents of the present disclosure can be delivered via, for example, Lipid nanoparticles (LNP); neutral liposomes (NL); polymer nanoparticles; double-stranded RNA binding motifs (dsRBMs); or via modification of the RNAi agent (e.g., covalent attachment to the dsRNA).

[00278] Lipid nanoparticles (LNP) are self-assembling cationic lipid based systems. These can comprise, for example, a neutral lipid (the liposome base); a cationic lipid (for siRNA loading); cholesterol (for stabilizing the liposomes); and PEG-lipid (for stabilizing the formulation, charge shielding and extended circulation in the bloodstream).

[00279] The cationic lipid can comprise, for example, a headgroup, a linker, a tail and a cholesterol tail. The LNP can have, for example, good tumor delivery, extended circulation in the blood, small particles (e.g., less than 100 nm), and stability in the tumor microenvironment (which has low pH and is hypoxic).

[00280] Neutral liposomes (NL) are non-cationic lipid based particles.

[00281] Polymer nanoparticles are self-assembling polymer-based particles.

[00282] Double-stranded RNA binding motifs (dsRBMs) are self-assembling RNA binding proteins, which will need modifications.

[00283] In various embodiments of the present disclosure, the RNAi agent to Beta-Catenin is ligated to one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and transferrin.

[00284] The RNAi agents of the present disclosure can be prepared in a pharmaceutical composition comprising various components appropriate for the particular method of administration of the RNAi agent.

[00285] **Administration of a Pharmaceutical Composition Comprising a RNAi agent**

[00286] The pharmaceutical composition comprising a Beta-Catenin can be administered by buccal, inhalation (including insufflation and deep inhalation), nasal, oral, parenteral, implant, injection or infusion via epidural, intra-arterial, intra-articular, intra-capsular, intra-cardiac, intra-cerebroventricular, intracranial, intradermal, intramuscular, intra-orbital, ocular, intraperitoneal, intra-spinal, intrasternal, intrathecal, intravenous, subarachnoid, sub-capsular, subcutaneous, sub-cuticular, transendothelial, transtracheal, transvascular, rectal, sublingual, topical, and/or vaginal routes. This may be by injection, infusion, dermal patch, or any other method known in the art. The formulation can be powdered, nebulized, aerosolized, granulized or otherwise appropriately prepared for delivery. The administration, if liquid, may be slow or via bolus, though, under some circumstances known in the art, bolus injections may lead to loss of material through the kidneys.

[00287] The pharmaceutical compositions comprising a Beta-Catenin RNAi agent can be administered with medical devices known in the art. For example, in a particular embodiment, a RNAi agent can be administered with a needle-less hypodermic injection device, such as the devices disclosed in U.S. Patent Nos. 5,399,163, 5,383,851, 5,312,335, 5,064,413, 4,941,880, 4,790,824, or 4,596,556. Examples of well-known implants and modules useful in the present disclosure include:

U.S. Patent No. 4,487,603, which discloses an implantable micro-infusion pump for dispensing medication at a controlled rate; U.S. Patent No. 4.,486,194, which discloses a therapeutic device for administering medications through the skin; U.S. Patent No. 4,447,233, which discloses a medication infusion pump for delivering medication at a precise infusion rate; U.S. Patent No. 4,447,224, which discloses a variable flow implantable infusion apparatus for continuous drug delivery; U.S. Patent No. 4,439,196, which discloses an osmotic drug delivery system having multi-chamber compartments; and U.S. Patent No. 4,475,196, which discloses an osmotic drug delivery system. Many other such implants, delivery systems, and modules are known to those skilled in the art.

[00288] In certain embodiments, the pharmaceutical compositions comprising a RNAi agent can be formulated to ensure proper distribution *in vivo*. Administration of a RNAi agent to Beta-Catenin can be systemic (whole-body) or, particularly, targeted to tissues or organs that express (or over-express or demonstrate a hyper-activity of) Beta-Catenin. Methods for targeting these particular tissues or organs are described herein, and/or are known in the art. For example, they can be formulated in liposomes. For methods of manufacturing liposomes, see, e.g., U.S. Patents 4,522,811; 5,374,548; and 5,399,331. The liposomes may comprise one or more moieties which are selectively transported into specific cells or organs, thus enhance targeted drug delivery (see, e.g., V.V. Ranade (1989) J. Clin. Pharmacol. 29: 685).

[00289] Example targeting moieties include folate or biotin (see, e.g., U.S. Patent 5,416,016 to Low et al.); mannosides (Umezawa et al., (1988) Biochem. Biophys. Res. Commun. 153: 1038); antibodies (P.G. Bloeman et al. (1995) FEBS Lett. 357: 140; M. Owais et al. (1995) Antimicrob. Agents Chemother. 39: 180); surfactant protein A receptor (Briscoe et al. (1995) Am. J. Physiol. 1233: 134), different species of which may comprise the formulations of the present disclosures, as well as components of the invented molecules; p120 (Schreier et al. (1994) J. Biol. Chem. 269: 9090); see also K. Keinanen; M.L. Laukkanen (1994) FEBS Lett. 346: 123; J.J. Killion; I.J. Fidler (1994) Immunomethods 4: 273.

[00290] The present disclosure thus encompasses pharmaceutical compositions comprising one or more RNAi agents to Beta-Catenin, which can optionally comprise various modifications and/or additional components, for use in treatment of Beta-Catenin-related diseases.

[00291] Measuring the effect of a RNAi agent on Beta-Catenin activity, level, expression or compartmentalization

[00292] Any method known in the art can be used to measure changes in Beta-Catenin activity, level, cellular distribution, and/or expression induced or altered by Beta-Catenin RNAi agent. Measurements can be performed at multiple timepoints, prior to, during and after administration of the RNAi agent, to determine the effect of the RNAi agent.

[00293] The terms "silence," "inhibit the expression of," "down-regulate the expression of," "suppress the expression of," and the like, in so far as they refer to a Beta-Catenin gene, herein refer to the at least partial suppression of the expression of a Beta-Catenin gene, as manifested by a reduction of the amount of Beta-Catenin mRNA which may be isolated from or detected in a first cell or group of cells in which a Beta-Catenin gene is transcribed and which has or have been treated such that the expression of a Beta-Catenin gene is inhibited, as compared to a second cell or group of cells substantially identical to the first cell or group of cells but which has or have not been so treated (control cells). The degree of inhibition is usually expressed in terms of

$$\frac{(\text{mRNA in control cells}) - (\text{mRNA in treated cells})}{(\text{mRNA in control cells})} \bullet 100\% \qquad \text{Equation 1}$$

[00294] Alternatively, the degree of inhibition may be given in terms of a reduction of a parameter that is functionally linked to Beta-Catenin gene expression, e.g., the amount of protein encoded by a Beta-Catenin gene, etc. In principle, Beta-Catenin gene silencing may be determined in any cell expressing Beta-Catenin, either constitutively or by genomic engineering, and by any appropriate assay. However, when a reference or control is needed in order to determine whether a given RNAi agent inhibits the expression of the Beta-Catenin gene by a certain degree and therefore is encompassed by the instant disclosure, the assays provided in the Examples below shall serve as such reference.

[00295] For example, in certain instances, expression of a Beta-Catenin gene is suppressed by at least about 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, or 50% by administration of a RNAi agent featured in the present disclosure. In some embodiments, a Beta-Catenin gene is suppressed by at least about 60%, 70%, or 80% by administration of a RNAi agent featured in the present disclosure. In some embodiments, a Beta-Catenin gene is suppressed by at least about 85%, 90%, or 95% or more by administration of a RNAi agent, as described herein.

[00296] The ability of a RNAi agent to suppress Beta-Catenin can be first tested *in vitro* (e.g., using test cells such as HeLa cells).

[00297] RNAi agents which can suppress Beta-Catenin *in vitro* can then be tested for immunostimulation using, for example, a PBMC (peripheral blood mononuclear cell) assay. RNAi agents can also be tested in animal tests. Test and control animals include those which over-express or under-express Beta-Catenin, as described in, for example, Chenn et al. 2003 Cer. Cortex 13: 599-606. RNAi agents which suppress or alter the level, activity and/or expression of Beta-Catenin can be used in medicaments to treat various Beta-Catenin-related diseases.

[00298] By "lower" in the context of Beta-Catenin or a symptom of a Beta-Catenin-related disease is meant a statistically significant decrease in such level. The decrease can be, for example, at least 10%, at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, or more. If, for a particular disease, or for an individual

suffering from a particular disease, the levels or expression of Beta-Catenin are elevated, treatment with a Beta-Catenin RNAi agent of the present disclosure can particularly reduce the level or expression of Beta-Catenin to a level considered in the literature as within the range of normal for an individual without such disorder.

[00299] The level or expression of Beta-Catenin can be measured by evaluation of mRNA (e.g., via Northern blots or PCR), or protein (e.g., Western blots). The effect of a RNAi agent on Beta-Catenin expression can be determined by measuring Beta-Catenin gene transcription rates (e.g., via Northern blots; or reverse transcriptase polymerase chain reaction or real-time polymerase chain reaction). Direct measurements can be made of levels of Beta-Catenin (which is expressed by the cell surface), e.g. by Western blots of tissues in which Beta-Catenin is expressed. The presence of Beta-Catenin in various cellular compartments (membrane, cytoplasm, and nucleus) can also be determined.

[00300] As used herein, "down-regulates" refers to any statistically significant decrease in a biological activity and/or expression of Beta-Catenin, including full blocking of the activity (i.e., complete inhibition) and/or expression. For example, "down-regulation" can refer to a decrease of at least about 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 % in Beta-Catenin level, activity and/or expression.

[00301] As used herein, the term "inhibit" or "inhibiting" Beta-Catenin refers to any statistically significant decrease in biological level, activity and/or expression of Beta-Catenin, including full blocking of the activity and/or expression. For example, "inhibition" can refer to a decrease of at least about 10, 20, 30, 40, 50, 60, 70, 80, 90 or 100 % in Beta-Catenin level, activity and/or expression. As used herein, the term "inhibit" similarly refers to a significant decrease in level, activity and/or expression, while referring to any other biological agent or composition.

[00302] By "level", it is meant that the Beta-Catenin RNAi agent can alter the level of Beta-Catenin, e.g., the level of Beta-Catenin mRNA or the level of Beta-Catenin protein, or the level of activity of Beta-Catenin.

[00303] Some diseases, such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases, are characterized by excessive and/or mutated Beta-Catenin activity, and/or unusual Beta-Catenin distribution within the cell. Thus, in various embodiments, administration of a RNAi agent to Beta-Catenin particularly establishes or re-establishes a normal or approximately normal level of Beta-Catenin activity, expression, distribution, and/or level.

[00304] By "normal" or "approximately normal" in terms of level, expression and/or activity, is meant at least: about 50%, about 60%, about 70%, about 80%, about 90%, and/or about 100%; and/or no more than: about 100%, about 120%, about 130%, about 140%, or about 150% of the level, expression or activity of Beta-Catenin in a healthy cellular compartment, cell, tissue, or organ. In one embodiment, administration of the appropriate amount of the appropriate Beta-Catenin RNAi agent restores Beta-Catenin level, activity and/or expression levels to about 50% to about 150%, more particularly about 60% to about 140%, more particularly to about 70% to about 130%, more particularly to about 80% to about 120%, more particularly to about 90% to about 110%, and most particularly to about 100% of that of a healthy cell, tissue or organ. Administration of a Beta-Catenin RNAi to a patient with a Beta-Catenin-related disease thus particularly restores the level, activity, and/or expression of Beta-Catenin to an approximately normal level, as determined by direct measurements of Beta-Catenin mRNA or protein levels, or indirect determinations, such as analyses of histological samples or levels of tissue samples. The RNAi agents of the present disclosure can also achieve a normal or approximately normal level of distribution of Beta-Catenin within the cell (e.g., in the membrane but not in the cytoplasm or nucleus).

[00305] In some Beta-Catenin-related cancers, Beta-Catenin is required for tumor growth but is not amplified, over-expressed or mis-localized. A reduction in Beta-Catenin expression, level or activity should thus limit tumor growth. The disclosure thus encompasses methods wherein Beta-Catenin expression, level or activity is reduced to an expression, level or activity which is lower than normal.

[00306] In addition, in various embodiments, depending on the disease condition and biological context, it is acceptable to use the RNAi agents of the present disclosure to establish a level of Beta-Catenin expression, activity and/or level which is below the normal level, or above the normal level.

[00307] **Beta-Catenin-Related Diseases**

[00308] The present disclosure encompasses RNAi agents to Beta-Catenin and administration of the RNAi agents to humans and non-human animals to treat various Beta-Catenin-related diseases.

[00309] By "Beta-Catenin-related disease" is meant any disease related to a mutation and/or dysfunction in the level, expression, cellular location, and/or activity of Beta-Catenin, and/or any disease which can be treated, prevented and/or ameliorated by modulating the level, expression, cellular location, and/or activity of Beta-Catenin. In some cases, the "Beta-Catenin-related disease" includes cancers wherein Beta-Catenin is required for tumor growth but is not amplified, over-expressed or mis-localized. A reduction in Beta-Catenin expression, level or activity should thus limit tumor growth. In various embodiments of the present disclosure, a Beta-Catenin-related disease can be treated and/or ameliorated by a RNAi agent to Beta-Catenin.

[00310] Beta-Catenin-related diseases are often associated with aberrations in the canonical

Wnt/Beta-Catenin pathway. Wnt signaling is involved in virtually every aspect of embryonic development and also controls homeostatic self-renewal in a number of adult tissues. Germline mutations in the Wnt pathway cause several hereditary diseases, and somatic mutations are associated with cancer of the intestine and a variety of other tissues. In the Wnt pathway, when Wnt receptor complexes are not bound by ligand, the serine/threonine kinases, CK1 and GSK3α/β, phosphorylate Beta-Catenin. Phosphorylated Beta-Catenin is recognized by the F box / WD repeat protein β-TrCP, a component of a dedicated E3 ubiquitin ligase complex. Following ubiquitination, Beta-Catenin is targeted for rapid destruction by the proteosome. In the nucleus, the binding of Groucho to TCF (T cell factor) inhibits the transcription of Wnt target genes, including proto-oncogene c-myc. However, Beta-Catenin accumulation in the nucleus can lead to activation of these Wnt target genes. For example, once bound by Wnt, the Frizzled (Fz)/LRP co-receptor complex activates the canonical signaling pathway. Fz interacts with Dsh, a cytoplasmic protein that functions upstream of Beta-Catenin and the kinase GSK3β. Wnt signaling controls phosphorylation of LRP by GSK3β and casein kinase I-γ (CK1γ), thus regulating the docking of Axin. The recruitment of Axin away from the destruction complex leads to the stabilization of beta-catenin in the cytoplasm. Once in the nucleus, Beta-Catenin displaces Groucho from TCF/LEF to promote the transcription of Wnt target genes, including c-myc. Moon et al. 2002 science 296: 1644-1646; Nelson et al. 2004 Science 303: 1483-1487; and Clevers 2006 Cell 127: 469-480; and references cited therein.

[00311] Beta-Catenin-related diseases are thus often associated with a mutated form of the protein, and/or an elevated level of mutant or wild-type Beta-Catenin, and/or presence of Beta-Catenin in cytoplasm and/or nucleus. In normal gastric mucosa, Beta-Catenin is localized to the cell membrane. Clements et al. 2002 Cancer Res. 62: 3503-6. As noted above, in the absence of growth or differentiation signals, cytoplasmic Beta-Catenin is rapidly turned over, under the control of the APC (adenomatous polyposis coli) protein and GSK-3β. Beta-Catenin accumulates in the cytoplasm in some cancer cells, chronic wounds and other diseased cells and tissues. Nuclear translocation can also occur. Beta-Catenin accumulation can result in interaction with the T-cell factor 4 or lymphoid-enhancer factor family of transcriptional activators, and can result in the activation of some developmentally-related genes and/or proto-oncogenes, including c-myc. Behrens et al. 1996 Nature 382: 638-642; and He et al. 1998 Science 281: 1509-1512.

[00312] As noted above, Beta-Catenin turnover occurs in the proteosome, where Beta-Catenin is degraded after targeted phosphorylation of highly-conserved Ser and Thr residues (Ser33, Ser37, Thr41, and Ser45) and ubiquitination in the NH_2 terminus. Mutations in these Ser and Thr residues result in accumulated Beta-Catenin and are associated with various cancers. A Ser37 to Phe37 mutation, at a mutational hotspot, is associated with Beta-Catenin accumulation and increased half-

life in the SK23 mel (melanoma) cell line. Rubinfeld et al. 1997 Science 275: 1790-1792. A Ser45 to Tyr45 mutation in the 624 mel cell line also increased the half-life of Beta-Catenin. Rubinfeld et al. 1997. Other deletions and mutations of these residues resulting in Beta-Catenin accumulation are described in Funayama et al. 1995 J. Cell Biol. 128: 959; Munemitsu et al. 1996 Mol. Cell. Biol. 16: 4088; Yost et al. 1996 Genes Dev. 10: 1443; and Ha et al. 2002 Acta Derm. Venereol. 82: 428-431. Altered phosphorylation of Beta-Catenin is also associated with breast cancer. Sommers et al. 1994 Cancer Res. 54: 3544-3552.

[00313] Beta-Catenin mutations outside the four Ser and Thr residues have also been associated with disease states. A nearby mutation of Aspartic acid 32 to Tyr was detected in a prostate cancer cell line. Voeller et al. 1998 Cancer Res. 58: 2520-2523. The 321-bp deletion from +82 to +402 was found in the HSC-39 gastric cancer cell line, Kawanishi et al. 1995 Mol. Cell. Biol. 15: 1175-1181. Other mutations at positions 32, 33, 34, 37 and 41 have been associated with pilomatrixomas (skin tumors of unknown origin and aetiology). Chan et al. 1999 Nature Genet. 21: 410-413. Additional mutations associated with gastric cancer were found at positions 8, 11, 13, 21, 24, 25, 28, 29, 32, 37, 39, 47, 48 and 55. Clements et al. 2002 Cancer Res. 62: 3503-3506. Various mutations in colorectal tumors are described in Miyaki et al. 1999 Cancer Res. 59: 4506-4509. All in all, mutations of Beta-Catenin at positions 8, 11, 13, 21, 24, 25, 28, 29, 32, 33, 34, 37, 39, 41, 45, 47, 48 and 55 have been associated with various cancers and other disease states.

[00314] In addition, a 321-bp deletion from +82 to +402 occurs in HSC-39 gastric cancer cell line, Kawanishi et al. 1995 Mol. Cell. Biol. 15: 1175-1181. Additional Beta-Catenin mutations (inside and outside the region of the four Ser and Thr residues) have been associated with medulloblastoma, endometroid ovarian carcinoma, uterine endometrial carcinoma, hepatocellular carcinoma, and prostatic adenocarcinoma. Zurawel et al. 1998 Cancer Res. 58: 896-899; Palacios et al. 1998 Cancer Res. 58: 1344-1347; Fukuchi et al. 1998 Cancer Res. 58: 3526-3528; Miyoshi et al. 1998 Cancer Res. 58: 2524-2527; Voeller et al. 1998 Cancer Res. 2520-2523; and Iwao et al. 1998 Cancer Res. 58: 1021-1026; and Garcia-Rostan et al. 1999 Cancer Res. 59: 1811-1815.

[00315] Alterations in the genetic or biochemical context can also alter Beta-Catenin level or activity. Excess intracellular Beta-Catenin is expressed in colon and other cancer cells with a defective APC. Munemitsu et al. 1995 Proc. Natl. Acad. Sci. USA 92:3046. A reduced cell-cell adhesion is caused by tyrosine-phosphorylation of Beta-Catenin with v-src gene transfection. Behrens et al. 1993 J. Cell Biol. 120: 757-766; Hamaguchi et al. 1993 EMBO J. 12:307-314; Matsuyoshi et al. 1992 J. Cell Biol. 118: 703-714.

[00316] In addition, the term "Beta-Catenin-related disease" includes those diseases in which Beta-Catenin (in normal form, mutant form, and/or in an elevated level of normal or mutant form and/or altered localization within the cell) directly or indirectly causes an increase in expression, level or activity of a factor involved in a disease state; for example, nuclear beta-catenin activates

production of c-myc, which is involved in several diseases. In addition, "Beta-Catenin-related disease" includes those diseases related to aberrations in the Wnt/Beta-Catenin pathway. For example, abnormalities of the Wnt/Beta-Catenin pathway are associated with various cancers, osteoporosis, ageing, oligodontia, and degenerative diseases. Clevers et al. 2006 Cell 127: 469-480; Moon et al. 2004 Nat. Rev. Genet. 5: 691-701; He et al. 2004 Develop. 131: 1663-1677; Logan et al. 2004 Ann. Rev. Cell. Dev. Biol. 20: 781-810. In addition, Wilms tumors (a pediatric kidney cancer) are sometimes associated with mutations in the WTX gene, a tumor suppressor gene which has recently been discovered to be involved in the Wnt/Beta-Catenin pathway. Huang et al. 2008. Curr. Opin. Cell Biol. 20: 119-125.

[00317] In particular, the term "Beta-Catenin-related disease" includes adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing. See: Delektorskaya et al. 2008. Bull. Exp. Biol. Med. 146: 616-619; Li et al. 2005 World J. Gastroent. 11: 2117-23; Liu et al. 2010 J. Dental Res. 89: 318-330; Noda et al. 1009 Br. J. Cancer 100: 1647-1658; Saegusa et al. 2009 Am. J. Pathol. 174: 2107-2115; Saldanha et al. Br. J. Dermatol. 151: 157–64; Stojadinovic et al. Am. J. Pathol. 167: 59-69; Thompson et al. 2007 Hepatology 45: 1298–305; Wang et al. 2008 Cancer Epidemiol. Biomarkers Prev. 17: 2101–8.

[00318] RNAi agents to Beta-Catenin can be used to treat Beta-Catenin-related diseases, particularly those diseases associated with altered expression, activity, compartmentalization, and/or levels of Beta-Catenin, or wherein Beta-Catenin is required for disease progression (e.g., tumor growth).

[00319] RNAi Agents to Beta-Catenin for Treatment of Beta-Catenin-Related Diseases

[00320] The RNAi agents to Beta-Catenin described herein can be formulated into pharmaceutical compositions which can be administered to humans or non-human animals. These compositions can comprise one or more RNAi agents, and, optionally, additional treatments useful for treating Beta-Catenin-related diseases. They can be administered as part of an early/preventative treatment, and can be administered in a therapeutically-effective dosage. The pharmaceutical composition can comprise a pharmaceutical carrier and can be administered by any method known in the art. These various aspects of the present disclosure are described in additional detail below.

[00321] RNAi agents to Beta-Catenin can be administered to humans and non-human animals for treatment of Beta-Catenin-related diseases.

[00322] In one embodiment of the present disclosure, the compositions comprising a Beta-

Catenin RNAi agent can be administered to non-human animals. For example, the compositions can be given to chickens, turkeys, livestock animals (such as sheep, pigs, horses, cattle, etc.), companion animals (e.g., cats and dogs) and can have efficacy in treatment of adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing and similar and related diseases. In each case, the RNAi agent to Beta-Catenin would be selected to match the sequence of the Beta-Catenin of the genome of the animal, and to, particularly, contain at least 1 nt mismatch from all other genes in that animal's genome. The RNAi agents of the present disclosure can thus be used in treatment of Beta-Catenin-related diseases in humans and non-human animals.

[00323] As used herein in the context of Beta-Catenin expression, the terms "treat," "treatment," and the like, refer to relief from or alleviation of pathological processes mediated by Beta-Catenin expression. In the context of the present disclosure insofar as it relates to any of the other conditions recited herein below (other than pathological processes mediated by Beta-Catenin expression), the terms "treat," "treatment," and the like mean to relieve or alleviate at least one symptom associated with such condition, or to slow or reverse the progression or anticipated progression of such condition.

[00324] By "treatment" is also meant prophylaxis, therapy, cure, or any other change in a patient's condition indicating improvement or absence of degradation of physical condition. By "treatment" is meant treatment of Beta-Catenin-related disease (e.g., adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases), or any appropriate treatment of any other ailment the patient has. As used herein, the terms "treatment" and "treat" refer to both prophylactic or preventative treatment and curative or disease-modifying treatment, including treatment of patients at risk of contracting a disease or suspected of having a disease, as well as patients already ill or diagnosed as suffering from a condition. The terms "treatment" and "treat" also refer to the maintenance and/or promotion of health in an individual not suffering from a disease but who may be susceptible to developing an unhealthy condition. In one embodiment, "treatment" does not encompass prevention of a disease state. Thus, the present disclosure is useful for suppressing expression of the Beta-Catenin gene and/or treating a Beta-Catenin-related disease in an individual afflicted by a Beta-Catenin-related

disease, or an individual susceptible to a Beta-Catenin-related disease. An individual "afflicted" by a Beta-Catenin-related disease has demonstrated detectable symptoms characteristics of the disease, or had otherwise been shown clinically to have been exposed to or to carry Beta-Catenin-related disease pathogens or markers. As non-limiting examples, an individual afflicted by a Beta-Catenin-related disease can show outward symptoms; or can show no outward symptoms but can be shown with a clinical test to carry protein markers associated with a Beta-Catenin-related disease, or proteins or genetic material associated with a pathogen in the blood.

[00325] Treatment of some Beta-Catenin-related diseases may be more efficacious if administered early rather than later. Thus, in one particular embodiment, the RNAi agent to Beta-Catenin is administered early, prior to disease manifestation, and/or as a preventative agent, rather than administered after disease establishment.

[00326] Additional treatments used in addition to or in conjunction with RNAi agents to Beta-Catenin

[00327] Treatments of Beta-Catenin-related diseases can thus comprises various treatments, comprising a Beta Beta-Catenin RNAi agent, and optionally further comprising an additional treatment, which can be a method (or procedure), and/or an additional composition (e.g., an agent or additional RNAi agent).

[00328] Beta-Catenin-related diseases include adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases. The use of known treatments for any of these diseases is within the capabilities of one of ordinary skill in the art. Any such additional treatment can be used in conjunction with a RNAi agent to Beta-Catenin.

[00329] These additional treatments, which can be administered prior to, simultaneously, or after administration of the RNAi agent(s) to Beta-Catenin, include: 5-fluoro-29-deoxyuridine, 7-hydroxystaurosporine, a goserlin implant, antibiotic, bevacizumab, bicalutamide, bleomycin, camptothecin, carboplatin, cetuximab, cisplatin, colcemid, Cycloheximide, cyclophosphamide, cytarabine, cytosine arabinoside (Ara-C), dacarbazine, docetaxel, doxorubicin, edelfosine, ehlorambucil, epipodophyllotoxin, epirubicin, erlotinib, estramustine, etoposide, fenretinide, finasteride, flavopiridol, fludarabine, fluorouracil, gefitinib, gemeitabine, goserelin, hexamethylmelamine, hydroxyurea, ifosfamide, irinotecan, L-asparaginase, leuprolide, meiphalan, mercaptopurine, methotrexate, mitixantrone, mitomycin, mitoxantrone, nitrogen mustard, octreotide, paclitaxel, pirubicin, Puromycin, sargramostim, staurosporine, steroids, tamoxifen, Taxol, tegafur,

teniposide, topotecan, trastuzumab, UFT, 1-Hydroxy-2-imidazol-1-yl-phosphonoethyl) phosphonic acid monohydrate (sold under the tradename Zometa® by Novartis), 2-chloro-N-[4-chloro-3-(2-pyridinyl)phenyl]-4-(methylsulfonyl)- benzamide (also known as GDC-0449, and described in PCT Publication No. WO 06/028958), GDC 0941 (PCT Publication Nos. WO 09/036082 and WO 09/055730), BEZ 235 or NVP-BEZ 235 (PCT Publication No. WO 06/122806), ABT-263 (PCT Publication No. WO 09/155386), 5-azacitidine (sold under the tradename Vidaza®), decitabine (sold under the tradename Dacogen®), 6-thioguanine (sold under the tradename Purinethol®), pemetrexed (sold under the tradename Alimta®), Afutuzumab (available from Roche®), pegfilgrastim (sold under the tradename Neulasta® by Amgen), lenalidomide (also known as CC-5013 sold under the tradename Revlimid®), thalidomide (sold under the tradename Thalomid®), Alemtuzumab (sold under the tradename Campath®), Alitretinoin (sold under the tradename Panretin®), tretinoin (all-*trans* retinoic acid, also known as ATRA sold under the tradename Vesanoid®), Isotretinoin, bexarotene (sold under the tradename Targretin®), Alvocidib (US Patent No. 5621002), Amifostine (sold under the tradename Ethyol®), leucovorin, aminoglutethimide (sold under the tradename Cytadren®), Anagrelide (sold under the tradename Agrylin®), *Anti-nausea drugs*, Arsenic trioxide (sold under the tradename Trisenox®), asparaginase (also known as L-asparaginase, Erwinia L-asparaginase sold under the tradenames Elspar® and Kidrolase®), axitinib, bacillus calmette-guerin (sold under the tradenames theraCys® and TICE® BCG), denileukin diftitox (sold under the tradename Ontak®), Bortezomib (sold under the tradename Velcade®), Brivanib Alaninate ((*S*)-((*R*)-1-(4-(4-Fluoro-2-methyl-1*H*-indol-5-yloxy)-5-methylpyrrolo[2,1-*f*][1,2,4]triazin-6-yloxy)propan-2-yl)2-aminopropanoate, also known as BMS-582664), Cabazitaxel (1-hydroxy-7β,10β-dimethoxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl-4-acetate-2-benzoate-13-[(2R,3S)-3-{[(tert-butoxy)carbonyl]amino}-2-hydroxy-3-phenylpropanoate), larotaxel ((2α,3ξ,4α,5β,7α,10β,13α)-4,10-bis(acetyloxy)-13-({(2*R*,3*S*)-3- [(*tert*-butoxycarbonyl) amino]-2-hydroxy-3-phenylpropanoyl}oxy)-1- hydroxy-9-oxo-5,20-epoxy-7,19-cyclotax-11-en-2-yl benzoate), Capecitabine (sold under the trademark Xeloda® by Roche), Casopitant (sold under the tradenames Rezonic® and Zunrisa® by GlaxoSmithKline), Cervarix® sold by GlaxoSmithKline, Gardasil® sold by Merck, cladribine (also known as 2-chlorodeoxyadenosine (2-CdA) sold under the tradename Leustatin™), Claribine (2-chlorodeoxyadenosine sold under the tradename leustatin®), Dacetuzumab (also known as SGN-40 or huS2C6, available from Seattle Genetics, Inc), Darbepoetin alfa (sold under the tradename Aranesp® by Amgen), daunorubicin, decitabine (sold under the tradename Dacogen®), Deferasinox (sold under the tradename Exjade® by Novartis), Denosumab (sold under the tradename Prolia® by Amgen), Dulanermin (also known as AMG-951, available from Amgen/Genentech), Elotuzumab (HuLuc63, CAS No. 915296-00-3), Eltrombopag (sold under the tradenames Promacta® and Revolade® by GlaxoSmithKline), etoposide (also known as VP-16 and Etoposide phosphate sold under the tradenames Toposar®, VePesid® and

Etopophos®), teniposide (also known as VM-26 sold under the tradename Vumon®), Exemestane (sold under the trademark Aromasin® by Pfizer), letrozole (sold under the tradename Femara® by Novartis), anastrozole (sold under the tradename Arimidex®), Figitumumab (also known as CP-751,871, available from ACC Corp), robatumumab (CAS No. 934235-44-6), Filgrastim (sold under the tradename Neupogen® by Amgen), floxuridine (sold under the tradename FUDR®), Fluoxymesterone (sold under the tradename Halotestin®), Fulvestrant (sold under the tradename Faslodex®), Gefitnib (sold under the tradename Iressa®), N-[4-[(3-Chloro-4-fluorophenyl)amino]-7-[[(3"S")-tetrahydro-3-furanyl]oxy]-6-quinazolinyl]-4(dimethylamino)-2-butenamide sold under the tradename Tovok® by Boehringer Ingelheim), Gemtuzumab ozogamicin (sold under the tradename Mylotarg® by Pfizer/Wyeth), Hydrocortisone (also known as cortisone, hydrocortisone sodium succinate, hydrocortisone sodium phosphate, and sold under the tradenames Ala-Cort®, Hydrocortisone Phosphate, Solu-Cortef®, Hydrocort Acetate® and Lanacort®), dexamethazone ((8*S*,9*R*,10*S*,11*S*,13*S*,14*S*,16*R*,17*R*)-9-fluoro-11,17-dihydroxy-17-(2-hydroxyacetyl)-10,13,16-trimethyl-6,7,8,9,10,11,12,13,14,15,16,17-dodecahydro-3*H*-cyclopenta[*a*]phenanthren-3-one), prednisolone (sold under the tradenames Delta-Cortel®, Orapred®, Pediapred® and Prelone®), prednisone (sold under the tradenames Deltasone®, Liquid Red®, Meticorten® and Orasone®), methylprednisolone (also known as 6-Methylprednisolone, Methylprednisolone Acetate, Methylprednisolone Sodium Succinate sold under the tradenames Duralone®, Medralone®, Medrol®, M-Prednisol® and Solu-Medrol®), Ibritumomab tiuxetan (sold under the tradename Zevalin®), idarubicin (sold under the tradenames Idamycin®, Idamycin PFS®), Inotuzumab ozogamicin (also referred to as CMC-544 and WAY-207294, available from Hangzhou Sage Chemical Co., Ltd.), interleukin-2 (also known as aldesleukin and IL-2 sold under the tradename Proleukin®), interleukin-11 (also known as oprevelkin sold under the tradename Neumega®), alpha interferon alfa (also known as IFN-alpha sold under the tradenames Intron® A, and Roferon-A®), Irinotecan (sold under the trademark Camptosar® by Pfizer), topotecan hydrochloride (sold under the tradename Hycamtin® by GlaxoSmithKline), Ixabepilone (sold under the tradename Lxempra® by Bristol-Myers Squibb), lapatinib or lapatinib ditosylate (sold under the trademark Tykerb® by GlaxoSmithKline), Leuprolide or leuprolide acetate (sold under the tradenames Viadure® by Bayer AG, Eligard® by Sanofi-Aventis and Lupron® by Abbott Lab), Linifanib (N-[4-(3-amino-1H-indazol-4-yl)phenyl]-N'-(2-fluoro-5-methylphenyl)urea, also known as ABT 869, available from Genentech), sunitinib malate (sold under the tradename Sutent® by Pfizer), bosutinib (4-[(2,4-dichloro-5-methoxyphenyl)amino]-6-methoxy-7-[3-(4-methylpiperazin-1-yl)propoxy]quinoline-3-carbonitrile, also known as SKI-606, and described in US Patent No. 6,780,996), dasatinib (sold under the tradename Sprycel® by Bristol-Myers Squibb), armala (also known as pazopanib sold under the tradename Votrient® by GlaxoSmithKline), imatinib and imatinib mesylate (sold under the tradenames Gilvec® and Gleevec® by Novartis), megestrol (also known as megestrol acetate

sold under the tradename Megace®), motesanib (N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]-3-pyridinecarboxamide, and described in PCT Publication No. WO 02/066470), pasireotide (also known as SOM230, and described in PCT Publication No. WO 02/010192), sorafenib (sold under the tradename Nexavar®), nelarabine ((2*R*,3*S*,4*R*,5*R*)-2-(2-amino-6-methoxy-purin-9-yl)-5-(hydroxymethyl)oxolane-3,4-diol sold under the tradenames Arranon® and Atriance® by GlaxoSmithKline), neratinib (also known as HKI-272, (2*E*)-N-[4-[[3-chloro-4-[(pyridin-2-yl)methoxy]phenyl]amino]-3-cyano-7-ethoxyquinolin-6-yl]-4-(dimethylamino)but-2-enamide, and described PCT Publication No. WO 05/028443), nilotinib hydrochloride (sold under the tradename Tasigna® by Novartis), Nilutamide (sold under the tradenames Nilandron® and Anandron®), bicalutamide (sold under tradename Casodex®), flutamide (sold under the tradename Fulexin™), *N*-methyl-2-[[3-[(*E*)-2-pyridin-2-ylethenyl]-1*H*-indazol-6-yl]sulfanyl]benzamide, also known as AG013736, and described in PCT Publication No. WO 01/002369, octreotide (also known as octreotide acetate sold under the tradenames Sandostatin® and Sandostatin LAR®), Odanacatib (also know as MK-0822, *N*-(1-cyanocyclopropyl)-4-fluoro-N^2-{(1*S*)-2,2,2-trifluoro-1-[4'-(methylsulfonyl)biphenyl-4-yl]ethyl}-L-leucinamide, available from Lanzhou Chon Chemicals, ACC Corp., and ChemieTek, and described in PCT Publication no. WO 03/075836), oprelvekin (sold under the tradename Neumega® by Pfizer/Wyeth), oxaliplatin (sold under the tradename Eloxatin® ay Sanofi-Aventis and described in US Patent No. 4,169,846), Palifermin (sold under the tradename Kepivance® by Amgen), Pamidronate (sold under the tradename Aredia®), zoledronic acid (sold under the tradename Zometa®), panitumumab (sold under the tradename Vectibix® by Amgen), pentostatin (sold under the tradename Nipent®), Pertuzumab (sold under the trademark Omnitarg®, by Genentech), Raloxifene (sold under the tradename Evista®), Rituximab (sold under the trademarks Riuxan® and MabThera® by Genentech/Roche), Romiplostim (sold under the tradename Nplate® by Amgen), tamoxifen (sold under the tradename Novaldex®), Tanespimycin (17-allylamino-17-demethoxygeldanamycin, also known as KOS-953 and 17-AAG, available from SIGMA, and described in US Patent No. 4,261,989), Temozolomide (sold under the tradenames Temodar® and Temodal® by Schering-Plough/Merck), dactinomycin (also known as actinomycin-D and sold under the tradename Cosmegen®), melphalan (also known as L-PAM, L-sarcolysin, and phenylalanine mustard sold under the tradename Alkeran®), altretamine (also known as hexamethylmelamine (HMM) sold under the tradename Hexalen®), carmustine (sold under the tradename BiCNU®), bendamustine (sold under the tradename Treanda®), busulfan (sold under the tradenames Busulfex® and Myleran®), carboplatin (sold under the tradename Paraplatin®), lomustine (also known as CCNU sold under the tradename CeeNU®), cisplatin (also known as CDDP sold under the tradenames Platinol® and Platinol®-AQ), chlorambucil (sold under the tradename Leukeran®), cyclophosphamide (sold under the tradenames Cytoxan® and Neosar®), dacarbazine (also known as DTIC, DIC and imidazole carboxamide sold under the tradename DTIC-

Dome®), altretamine (also known as hexamethylmelamine (HMM) sold under the tradename Hexalen®), ifosfamide (sold under the tradename Ifex®), procarbazine (sold under the tradename Matulane®), mechlorethamine (also known as nitrogen mustard, mustine and mechloroethamine hydrochloride sold under the tradename Mustargen®), streptozocin (sold under the tradename Zanosar®), thiotepa (also known as thiophosphoamide, TESPA and TSPA sold under the tradename Thioplex®, Temsirolimus (sold under the tradename Torisel® by Pfizer), ridaforolimus (formally known as deferolimus, (1*R*,2*R*,4*S*)-4-[(2*R*)-2 [(1*R*,9*S*,12*S*,15*R*,16*E*,18*R*,19*R*,21*R*, 23*S*,24*E*,26*E*,28*Z*,30*S*,32*S*,35*R*)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxa-4-azatricyclo[30.3.1.$0^{4,9}$] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383), everolimus (sold under the tradename Afinitor® by Novartis), Toremifene (sold under the tradename Fareston®), tositumomab (sold under the trademarks Bexxar® by GlaxoSmithKline), ofatumumab (sold under the trademark Arzerra® by GlaxoSmithKline), Tremelimumab (IgG2 monoclonal antibody available from Pfizer, formerly known as ticilimumab, CP-675,206), ipilimumab (CTLA-4 antibody, also known as MDX-010, CAS No. 477202-00-9), vinblastine (also known as vinblastine sulfate, vincaleukoblastine and VLB sold under the tradenames Alkaban-AQ® and Velban®), vincristine (also known as vincristine sulfate, LCR, and VCR sold under the tradenames Oncovin® and Vincasar Pfs®), vinorelbine (sold under the tradename Navelbine®), Voninostat (sold under the tradename Zolinza® by Merck), Xaliproden (also known as SR57746, 1-[2-(2-naphthyl)ethyl]-4-[3-(trifluoromethyl)phenyl]-1,2,3,6-tetrahydropyridine, and described in US Patent No. 5,266,573), XL-518 (also known as GDC-0973, Cas No. 1029872-29-4, available from ACC Corp.); Selumetinib (5-[(4-bromo-2-chlorophenyl)amino]-4-fluoro-N-(2-hydroxyethoxy)-1-methyl-1H-benzimidazole-6-carboxamide, also known as AZD6244 or ARRY 142886, described in PCT Publication No. WO2003077914); 2-[(2-chloro-4-iodophenyl)amino]-N-(cyclopropylmethoxy)-3,4-difluoro-benzamide (also known as CI-1040 or PD184352 and described in PCT Publication No. WO2000035436); N-[(2R)-2,3-dihydroxypropoxy]-3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]- benzamide (also known as PD0325901 and described in PCT Publication No. WO2002006213); 2,3-bis[amino[(2-aminophenyl)thio]methylene]-butanedinitrile (also known as U0126 and described in US Patent No. 2,779,780); N-[3,4-difluoro-2-[(2-fluoro-4-iodophenyl)amino]-6-methoxyphenyl]-1-[(2R)-2,3-dihydroxypropyl]- cyclopropanesulfonamide (also known as RDEA119 or BAY869766 and described in PCT Publication No. WO2007014011); (3S,4R,5Z,8S,9S,11E)-14-(ethylamino)-8,9,16-trihydroxy-3,4-dimethyl-3,4,9, 19-tetrahydro-1H-2-benzoxacyclotetradecine-1,7(8H)-dione] (also known as E6201 and described in PCT Publication No. WO2003076424); 2'-Amino-3'-methoxyflavone (also known as PD98059 available from Biaffin GmbH & Co., KG, Germany); AS-703026 (CAS No. 1204531-26-9); AZD-8330 (also known as ARRY-424704 or ARRY-704, CAS

No. 1204531-17-8); ARRY-438162 (CAS No. 1073666-70-2); GSK-1120212 (CAS No. 1204531-25-8); RO-4987665 (CAS No. 1204531-24-7); and TAK-733; Antiresorptive agents, Bisphosphonates, Bone anabolic agents, Calcitonin, Calcium, Calcium salts, Estrogen analogs, Raloxifene, RANKL inhibitors, Sodium fluoride, Strontium ranelate, Teriparatide, and Vitamin D.

[00330] The dosages of the additional treatments and RNAi agents can be easily determined by one of ordinary skill in the art, and as described herein.

[00331] **Dosages and Effective Amounts of RNAi Agents**

[00332] The RNAi agents of the present disclosure are administered in a dosage of a therapeutically effective amount to a patient in need thereof.

[00333] An "effective amount" or a "therapeutically effective amount" is an amount that treats a disease or medical condition of an individual, or, more generally, provides a nutritional, physiological or medical benefit to an individual. As used herein, the phrases "therapeutically effective amount" and "prophylactically effective amount" refer to an amount that provides a therapeutic benefit in the treatment, prevention, or management of pathological processes mediated by Beta-Catenin expression or an overt symptom of pathological processes mediated by Beta-Catenin expression. The specific amount that is therapeutically effective can be readily determined by an ordinary medical practitioner, and may vary depending on factors known in the art, such as, for example, the type of pathological processes mediated by Beta-Catenin expression, the patient's history and age, the stage of pathological processes mediated by Beta-Catenin expression, and the administration of other agents that inhibit pathological processes mediated by Beta-Catenin expression.

[00334] In various embodiments of the present disclosure, the patient is at least about 1, 3, 6, or 9 months, or 1, 5, 10, 20, 30, 40, 50, 55, 60, 65, 70, or 75 years of age. In various embodiments of the present disclosure, the patient is no more than about 1, 3, 6, or 9 months, or 1, 5, 10, 20, 30, 40, 50, 55, 60, 65, 70, 75, 80, 90, or 100 years of age. In various embodiments the patient has a body weight of at least about 5, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380 or 400 lbs. In various embodiments of the present disclosure, the patient has a body weight of no more than about 5, 10, 15, 20, 30, 40, 50, 60, 70, 80, 90, 100, 120, 140, 160, 180, 200, 220, 240, 260, 280, 300, 320, 340, 360, 380 or 400 lbs.

[00335] In various embodiments of the present disclosure, the dosage [measuring only the active ingredient(s)] can be at least about 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 ng, 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 micrograms, 1, 5, 10, 25, 50, 100, 200, 250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 mg. In various embodiments of the present disclosure, the dosage can be no more than about 10, 25, 50, 100, 200,

250, 300, 250, 400, 450, 500, 550, 600, 650, 700, 750, 800, 850, 900, 950 or 1000 mg. In various embodiments of the present disclosure, the dosage can be administered at least more than once a day, daily, more than once a weekly, weekly, bi-weekly, monthly, and/or every 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 or 12 months, or a combination thereof.

[00336] In various embodiments of the present disclosure, the dosage is correlated to the body weight or body surface area of the individual. The actual dosage level can be varied to obtain an amount of active agent which is effective for a particular patient, composition and mode of administration, without being toxic to the patient. The selected dose will depend on a variety of pharmacokinetic factors, including the activity of the particular RNAi agent employed, the route of administration, the rate of excretion of the RNAi agent, the duration of the treatment, other drugs, compounds and/or materials used in combination with the RNAi agent, the age, sex, weight, condition, general health and prior medical history of the patient, and like factors well known in the medical arts. A physician or veterinarian having ordinary skill in the art can readily determine the effective amount of the RNAi agent required. A suitable dose will be that amount which is the lowest dose effective to produce a therapeutic effect, or a dose low enough to produce a therapeutic effect without causing side effects.

[00337] In addition to a therapeutically-effective dosage of one or more RNAi agents to Beta-Catenin, the pharmaceutical compositions of the present disclosure can comprise or be used in conjunction with an additional disease treatment which works synergistically with the RNAi agent. For example, the pharmaceutical composition can comprise an additional antagonist to Beta-Catenin.

[00338] Additional Embodiments of RNAi Agents to Beta-Catenin

[00339] In a particular embodiment, the present disclosure encompasses a composition comprising one or more Beta-Catenin RNAi agents. In one embodiment, the present disclosure comprises a RNAi agent comprising a sense strand and an anti-sense strand. In one embodiment, the anti-sense strand consists of, consists essentially of, or comprises the sequence of the anti-sense strand of, a RNAi agent listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the anti-sense strand consists of, consists essentially of, or comprises a sequence of at least 15 contiguous nt with 0, 1, 2, or 3 mismatches from that of, the anti-sense strand of any RNAi agent listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9. In one embodiment, the anti-sense strand consists of the sequence of the anti-sense strand of a RNAi agent listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and further comprises 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides. In one embodiment, the anti-sense strand consists of a sequence with 0, 1, 2, or 3 mismatches from that of the anti-sense strand of a RNAi agent listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and further comprises 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 nucleotides.

[00340] In various embodiments of the present disclosure, the composition of the claimed disclosure has the proviso that it does not comprise any particular individual RNAi agent listed in Tables 1, 2 or 3. In various embodiments of the present disclosure, the RNAi agent to Beta-Catenin has the proviso that it does not have the sequence of any Beta-Catenin RNAi agent disclosed in the patent or scientific literature, e.g., WO 2006/086772, US 2007 0207974, US 2007 0042381, US 2005 0255487, US 2007/0275914, US 2007 0039072, US 2006 0193870, or US 2008 0113351.

Additional embodiments of RNAi agents

[00341] In another particular embodiment, the RNAi agent comprises any of the RNAi agents listed in Table 1, and modified and unmodified variants thereof.

[00342] In another particular embodiment, the RNAi agent comprises the sense strand of any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00343] In another particular embodiment, the RNAi agent comprises the anti-sense strand of any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00344] In another particular embodiment, the RNAi agent comprises a sense strand with a sequence consisting of that of the sense strand of any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 and modified and unmodified variants thereof.

[00345] In another particular embodiment, the RNAi agent comprises an anti-sense strand with a sequence consisting of that of the anti-sense strand any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00346] In another particular embodiment, the RNAi agent comprises a sense stand with a sequence consisting of that of the sense strand and/or an anti-sense strand with a sequence consisting of that of the anti-sense strand of any RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9.

[00347] In another particular embodiment, the RNAi agent has a sequence consisting of that of any of the RNAi agents listed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00348] Embodiments comprising one or more efficacious RNAi agents to Beta-Catenin

[00349] In various embodiments of the present disclosure, the present disclosure comprises a RNAi agent demonstrating at least about 40, 50, 60, 70, 80, 90 or 95% knockdown (no more than about 60, 50, 40, 30, 20, 10, or 5% residual gene activity, respectively) of the Beta-Catenin gene at an *in vitro* concentration of 10 or 0.1 nM in HeLa cells.

[00350] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of a Fold-Change at 10 nM at 24 hr of ≤ 0.05, ≤ 0.10, ≤ 0.20, ≤ 0.30, $\leq$

0.40 (indicating a Beta-Catenin gene knock-down of at least 95, 90, 80, 70, or 60%, respectively, at a concentration of 10 nM at 24 hrs in HeLa cells). RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00351] Embodiments comprising one or more efficacious RNAi agents to Beta-Catenin

[00352] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of a Fold-Change at 0.1 nM at 120 hr of ≤ 0.30, ≤ 0.20, or ≤ 0.10 (indicating a Beta-Catenin gene knock-down of at least 70, 80, or 90%, respectively, at a concentration of 0.1 nM at 120 hrs in HeLa cells). RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00353] Various embodiments comprising one or more RNAi agents to Beta-Catenin with low EC50

[00354] In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of mediating 50% gene knockdown (EC50) of Beta-Catenin at a low concentration in HeLa cells. For many of the RNAi agents listed herein, an estimated EC50 was calculated. Cells were treated at 10nM, 1nM, 0.1nM, 0.01nM, and 0.001nM of RNAi agent, and the data fit to a curve. The indicated EC50 is an estimated EC50 calculated from available data that is expected to give 50% gene knock-down of Beta-Catenin in HeLa cells. In various embodiments of the present disclosure, the composition comprises one or more RNAi agents capable of mediating 50% gene knockdown (EC50) at 100, 75, 50, 25, 10, 5, 2.5, 1, 0.75, 0.5, 0.25, 0.2, 0.12, 0.1, 0.09, 0.08, 0.07, 0.06, 0.05, 0.04, 0.03, or 0.02 nM or less in HeLa cells. RNAi agents capable of these levels of activity are disclosed in the Tables herein.

[00355] Specific embodiments of RNAi agents to Beta-Catenin

[00356] In one embodiment, the present disclosure pertains to: a composition comprising any one or more of: a RNAi agent comprising a sense strand and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the anti-sense strand of: any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 and modified or unmodified variants thereof.

[00357] In one embodiment, the composition comprises any one or more of: a RNAi agent comprising a sense strand and an anti-sense strand, wherein the anti-sense strand comprises at least 15 contiguous nucleotides differing by 0 nucleotides from the anti-sense strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00358] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified

variants thereof.

[00359] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising an anti-sense strand comprising the sequence of the anti-sense strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00360] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprises an anti-sense strand consisting of the sequence of the anti-sense strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00361] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the second of the first strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00362] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first and a second strand, wherein the sequences of the first and the second strand are the sequences of the first and second strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00363] In one embodiment, the present disclosure pertains to a composition comprising any one or more of: a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the second of the first strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof, wherein the first and/or second strand further comprise up to about 20 additional nucleotides.

[00364] **Additional embodiments of specific RNAi agents to Beta-Catenin**

[00365] In one embodiment, the present disclosure comprises a RNAi agent comprising a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, or modified or unmodified variants thereof.

[00366] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[00367] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26104, or modified or unmodified variants thereof.

[00368] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26063, or modified or unmodified variants thereof.

[00369] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26082, or modified or unmodified variants thereof.

[00370] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26034, or modified or unmodified variants thereof.

[00371] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26091, or modified or unmodified variants thereof.

[00372] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26047, or modified or unmodified variants thereof.

[00373] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26651, or modified or unmodified variants thereof.

[00374] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26696, or modified or unmodified variants thereof.

[00375] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26109, or modified or unmodified variants thereof.

[00376] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25941, or modified or unmodified variants thereof.

[00377] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26028, or modified or unmodified variants thereof.

[00378] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26652, or modified or unmodified variants thereof.

[00379] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26742, or modified or unmodified variants thereof.

[00380] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26921, or modified or unmodified variants thereof.

[00381] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18893, or modified or unmodified variants thereof.

[00382] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18983, or modified or unmodified variants thereof.

[00383] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25950, or modified or unmodified variants thereof.

[00384] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25951, or modified or unmodified variants thereof.

[00385] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26042, or modified or unmodified variants thereof.

[00386] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26043, or modified or unmodified variants thereof.

[00387] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26673, or modified or unmodified variants thereof.

[00388] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26704, or modified or unmodified variants thereof.

[00389] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26068, or modified or unmodified variants thereof.

[00390] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26183, or modified or unmodified variants thereof.

[00391] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26700, or modified or unmodified variants thereof.

[00392] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26701, or modified or unmodified variants thereof.

[00393] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25942, or modified or unmodified variants thereof.

[00394] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26076, or modified or unmodified variants thereof.

[00395] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26031, or modified or unmodified variants thereof.

[00396] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26210, or modified or unmodified variants thereof.

[00397] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26664, or modified or unmodified variants thereof.

[00398] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26691, or modified or unmodified variants thereof.

[00399] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26740, or modified or unmodified variants thereof.

[00400] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19765, or modified or unmodified variants thereof.

[00401] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26158, or modified or unmodified variants thereof.

[00402] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26180, or modified or unmodified variants thereof.

[00403] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26078, or modified or unmodified variants thereof.

[00404] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25894, or modified or unmodified variants thereof.

[00405] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25964, or modified or unmodified variants thereof.

[00406] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26156, or modified or unmodified variants thereof.

[00407] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26670, or modified or unmodified variants thereof.

[00408] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26743, or modified or unmodified variants thereof.

[00409] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25890, or modified or unmodified variants thereof.

[00410] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26044, or modified or unmodified variants thereof.

[00411] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26685, or modified or unmodified variants thereof.

[00412] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26731, or modified or unmodified variants thereof.

[00413] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26800, or modified or unmodified variants thereof.

[00414] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26066, or modified or unmodified variants thereof.

[00415] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26682, or modified or unmodified variants thereof.

[00416] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26684, or modified or unmodified variants thereof.

[00417] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26757, or modified or unmodified variants thereof.

[00418] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26788, or modified or unmodified variants thereof.

[00419] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18963, or modified or unmodified variants thereof.

[00420] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19076, or modified or unmodified variants thereof.

[00421] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25943, or modified or unmodified variants thereof.

[00422] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26052, or modified or unmodified variants thereof.

[00423] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26665, or modified or unmodified variants thereof.

[00424] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26746, or modified or unmodified variants thereof.

[00425] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18974, or modified or unmodified variants thereof.

[00426] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25938, or modified or unmodified variants thereof.

[00427] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25944, or modified or unmodified variants thereof.

[00428] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26178, or modified or unmodified variants thereof.

[00429] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26669, or modified or unmodified variants thereof.

[00430] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26730, or modified or unmodified variants thereof.

[00431] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26825, or modified or unmodified variants thereof.

[00432] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25956, or modified or unmodified variants thereof.

[00433] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26822, or modified or unmodified variants thereof.

[00434] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26108, or modified or unmodified variants thereof.

[00435] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26752, or modified or unmodified variants thereof.

[00436] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26779, or modified or unmodified variants thereof.

[00437] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25891, or modified or unmodified variants thereof.

[00438] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26101, or modified or unmodified variants thereof.

[00439] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26181, or modified or unmodified variants thereof.

[00440] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26218, or modified or unmodified variants thereof.

[00441] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26660, or modified or unmodified variants thereof.

[00442] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18966, or modified or unmodified variants thereof.

[00443] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19074, or modified or unmodified variants thereof.

[00444] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26179, or modified or unmodified variants thereof.

[00445] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26722, or modified or unmodified variants thereof.

[00446] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26768, or modified or unmodified variants thereof.

[00447] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26920, or modified or unmodified variants thereof.

[00448] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26020, or modified or unmodified variants thereof.

[00449] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26713, or modified or unmodified variants thereof.

[00450] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26727, or modified or unmodified variants thereof.

[00451] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26808, or modified or unmodified variants thereof.

[00452] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25958, or modified or unmodified variants thereof.

[00453] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26105, or modified or unmodified variants thereof.

[00454] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26674, or modified or unmodified variants thereof.

[00455] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26781, or modified or unmodified variants thereof.

[00456] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26801, or modified or unmodified variants thereof.

[00457] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26813, or modified or unmodified variants thereof.

[00458] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26816, or modified or unmodified variants thereof.

[00459] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25945, or modified or unmodified variants thereof.

[00460] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26203, or modified or unmodified variants thereof.

[00461] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26021, or modified or unmodified variants thereof.

[00462] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26040, or modified or unmodified variants thereof.

[00463] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26069, or modified or unmodified variants thereof.

[00464] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26134, or modified or unmodified variants thereof.

[00465] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26702, or modified or unmodified variants thereof.

[00466] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18933, or modified or unmodified variants thereof.

[00467] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26690, or modified or unmodified variants thereof.

[00468] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26698, or modified or unmodified variants thereof.

[00469] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25910, or modified or unmodified variants thereof.

[00470] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26747, or modified or unmodified variants thereof.

[00471] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26810, or modified or unmodified variants thereof.

[00472] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26083, or modified or unmodified variants thereof.

[00473] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26061, or modified or unmodified variants thereof.

[00474] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26904, or modified or unmodified variants thereof.

[00475] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18903, or modified or unmodified variants thereof.

[00476] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18980, or modified or unmodified variants thereof.

[00477] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26202, or modified or unmodified variants thereof.

[00478] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26679, or modified or unmodified variants thereof.

[00479] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26719, or modified or unmodified variants thereof.

[00480] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26758, or modified or unmodified variants thereof.

[00481] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26783, or modified or unmodified variants thereof.

[00482] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26902, or modified or unmodified variants thereof.

[00483] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18892, or modified or unmodified variants thereof.

[00484] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18897, or modified or unmodified variants thereof.

[00485] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25902, or modified or unmodified variants thereof.

[00486] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26705, or modified or unmodified variants thereof.

[00487] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26782, or modified or unmodified variants thereof.

[00488] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19082, or modified or unmodified variants thereof.

[00489] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26176, or modified or unmodified variants thereof.

[00490] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26196, or modified or unmodified variants thereof.

[00491] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26199, or modified or unmodified variants thereof.

[00492] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26678, or modified or unmodified variants thereof.

[00493] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26683, or modified or unmodified variants thereof.

[00494] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26729, or modified or unmodified variants thereof.

[00495] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26804, or modified or unmodified variants thereof.

[00496] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26900, or modified or unmodified variants thereof.

[00497] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25914, or modified or unmodified variants thereof.

[00498] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26060, or modified or unmodified variants thereof.

[00499] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26763, or modified or unmodified variants thereof.

[00500] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18902, or modified or unmodified variants thereof.

[00501] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18914, or modified or unmodified variants thereof.

[00502] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26100, or modified or unmodified variants thereof.

[00503] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26128, or modified or unmodified variants thereof.

[00504] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26193, or modified or unmodified variants thereof.

[00505] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26765, or modified or unmodified variants thereof.

[00506] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25960, or modified or unmodified variants thereof.

[00507] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26018, or modified or unmodified variants thereof.

[00508] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25893, or modified or unmodified variants thereof.

[00509] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26823, or modified or unmodified variants thereof.

[00510] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25940, or modified or unmodified variants thereof.

[00511] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26190, or modified or unmodified variants thereof.

[00512] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26675, or modified or unmodified variants thereof.

[00513] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26797, or modified or unmodified variants thereof.

[00514] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26916, or modified or unmodified variants thereof.

[00515] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26755, or modified or unmodified variants thereof.

[00516] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26901, or modified or unmodified variants thereof.

[00517] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19004, or modified or unmodified variants thereof.

[00518] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19009, or modified or unmodified variants thereof.

[00519] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26148, or modified or unmodified variants thereof.

[00520] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26186, or modified or unmodified variants thereof.

[00521] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26737, or modified or unmodified variants thereof.

[00522] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25955, or modified or unmodified variants thereof.

[00523] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26029, or modified or unmodified variants thereof.

[00524] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26131, or modified or unmodified variants thereof.

[00525] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18894, or modified or unmodified variants thereof.

[00526] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18939, or modified or unmodified variants thereof.

[00527] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26654, or modified or unmodified variants thereof.

[00528] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18929, or modified or unmodified variants thereof.

[00529] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26135, or modified or unmodified variants thereof.

[00530] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26774, or modified or unmodified variants thereof.

[00531] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26780, or modified or unmodified variants thereof.

[00532] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26819, or modified or unmodified variants thereof.

[00533] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26918, or modified or unmodified variants thereof.

[00534] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19050, or modified or unmodified variants thereof.

[00535] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18994, or modified or unmodified variants thereof.

[00536] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26769, or modified or unmodified variants thereof.

[00537] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26666, or modified or unmodified variants thereof.

[00538] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26784, or modified or unmodified variants thereof.

[00539] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18969, or modified or unmodified variants thereof.

[00540] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18986, or modified or unmodified variants thereof.

[00541] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25929, or modified or unmodified variants thereof.

[00542] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25932, or modified or unmodified variants thereof.

[00543] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26095, or modified or unmodified variants thereof.

[00544] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26908, or modified or unmodified variants thereof.

[00545] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26071, or modified or unmodified variants thereof.

[00546] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26912, or modified or unmodified variants thereof.

[00547] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19054, or modified or unmodified variants thereof.

[00548] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25918, or modified or unmodified variants thereof.

[00549] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26903, or modified or unmodified variants thereof.

[00550] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25931, or modified or unmodified variants thereof.

[00551] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26146, or modified or unmodified variants thereof.

[00552] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26200, or modified or unmodified variants thereof.

[00553] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26917, or modified or unmodified variants thereof.

[00554] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26794, or modified or unmodified variants thereof.

[00555] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26910, or modified or unmodified variants thereof.

[00556] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25939, or modified or unmodified variants thereof.

[00557] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26032, or modified or unmodified variants thereof.

[00558] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26776, or modified or unmodified variants thereof.

[00559] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26806, or modified or unmodified variants thereof.

[00560] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26748, or modified or unmodified variants thereof.

[00561] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26725, or modified or unmodified variants thereof.

[00562] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18958, or modified or unmodified variants thereof.

[00563] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26672, or modified or unmodified variants thereof.

[00564] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26905, or modified or unmodified variants thereof.

[00565] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19056, or modified or unmodified variants thereof.

[00566] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19762, or modified or unmodified variants thereof.

[00567] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26919, or modified or unmodified variants thereof.

[00568] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18946, or modified or unmodified variants thereof.

[00569] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19066, or modified or unmodified variants thereof.

[00570] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19746, or modified or unmodified variants thereof.

[00571] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26057, or modified or unmodified variants thereof.

[00572] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26073, or modified or unmodified variants thereof.

[00573] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26689, or modified or unmodified variants thereof.

[00574] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19008, or modified or unmodified variants thereof.

[00575] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26026, or modified or unmodified variants thereof.

[00576] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26761, or modified or unmodified variants thereof.

[00577] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19752, or modified or unmodified variants thereof.

[00578] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18981, or modified or unmodified variants thereof.

[00579] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18927, or modified or unmodified variants thereof.

[00580] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19753, or modified or unmodified variants thereof.

[00581] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25907, or modified or unmodified variants thereof.

[00582] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26671, or modified or unmodified variants thereof.

[00583] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19080, or modified or unmodified variants thereof.

[00584] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26075, or modified or unmodified variants thereof.

[00585] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26681, or modified or unmodified variants thereof.

[00586] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18976, or modified or unmodified variants thereof.

[00587] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25900, or modified or unmodified variants thereof.

[00588] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26126, or modified or unmodified variants thereof.

[00589] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26688, or modified or unmodified variants thereof.

[00590] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25912, or modified or unmodified variants thereof.

[00591] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25930, or modified or unmodified variants thereof.

[00592] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18995, or modified or unmodified variants thereof.

[00593] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26802, or modified or unmodified variants thereof.

[00594] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25892, or modified or unmodified variants thereof.

[00595] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25947, or modified or unmodified variants thereof.

[00596] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26088, or modified or unmodified variants thereof.

[00597] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26098, or modified or unmodified variants thereof.

[00598] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26778, or modified or unmodified variants thereof.

[00599] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26215, or modified or unmodified variants thereof.

[00600] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26739, or modified or unmodified variants thereof.

[00601] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18950, or modified or unmodified variants thereof.

[00602] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25949, or modified or unmodified variants thereof.

[00603] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26141, or modified or unmodified variants thereof.

[00604] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18961, or modified or unmodified variants thereof.

[00605] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25957, or modified or unmodified variants thereof.

[00606] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26826, or modified or unmodified variants thereof.

[00607] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25963, or modified or unmodified variants thereof.

[00608] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26019, or modified or unmodified variants thereof.

[00609] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26035, or modified or unmodified variants thereof.

[00610] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25946, or modified or unmodified variants thereof.

[00611] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26714, or modified or unmodified variants thereof.

[00612] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26022, or modified or unmodified variants thereof.

[00613] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26096, or modified or unmodified variants thereof.

[00614] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26132, or modified or unmodified variants thereof.

[00615] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26062, or modified or unmodified variants thereof.

[00616] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18991, or modified or unmodified variants thereof.

[00617] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26164, or modified or unmodified variants thereof.

[00618] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26209, or modified or unmodified variants thereof.

[00619] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25895, or modified or unmodified variants thereof.

[00620] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25933, or modified or unmodified variants thereof.

[00621] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26017, or modified or unmodified variants thereof.

[00622] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19749, or modified or unmodified variants thereof.

[00623] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26653, or modified or unmodified variants thereof.

[00624] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26759, or modified or unmodified variants thereof.

[00625] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25924, or modified or unmodified variants thereof.

[00626] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26153, or modified or unmodified variants thereof.

[00627] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25953, or modified or unmodified variants thereof.

[00628] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26764, or modified or unmodified variants thereof.

[00629] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26790, or modified or unmodified variants thereof.

[00630] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-20124, or modified or unmodified variants thereof.

[00631] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25919, or modified or unmodified variants thereof.

[00632] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18913, or modified or unmodified variants thereof.

[00633] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26211, or modified or unmodified variants thereof.

[00634] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18936, or modified or unmodified variants thereof.

[00635] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25898, or modified or unmodified variants thereof.

[00636] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26741, or modified or unmodified variants thereof.

[00637] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19043, or modified or unmodified variants thereof.

[00638] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26079, or modified or unmodified variants thereof.

[00639] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19000, or modified or unmodified variants thereof.

[00640] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25911, or modified or unmodified variants thereof.

[00641] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26786, or modified or unmodified variants thereof.

[00642] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19069, or modified or unmodified variants thereof.

[00643] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26037, or modified or unmodified variants thereof.

[00644] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26723, or modified or unmodified variants thereof.

[00645] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19067, or modified or unmodified variants thereof.

[00646] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25928, or modified or unmodified variants thereof.

[00647] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26677, or modified or unmodified variants thereof.

[00648] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19006, or modified or unmodified variants thereof.

[00649] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19758, or modified or unmodified variants thereof.

[00650] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26913, or modified or unmodified variants thereof.

[00651] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25917, or modified or unmodified variants thereof.

[00652] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26189, or modified or unmodified variants thereof.

[00653] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26787, or modified or unmodified variants thereof.

[00654] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26707, or modified or unmodified variants thereof.

[00655] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26094, or modified or unmodified variants thereof.

[00656] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26097, or modified or unmodified variants thereof.

[00657] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26699, or modified or unmodified variants thereof.

[00658] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26756, or modified or unmodified variants thereof.

[00659] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26720, or modified or unmodified variants thereof.

[00660] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25926, or modified or unmodified variants thereof.

[00661] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26212, or modified or unmodified variants thereof.

[00662] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26687, or modified or unmodified variants thereof.

[00663] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26753, or modified or unmodified variants thereof.

[00664] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18982, or modified or unmodified variants thereof.

[00665] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18908, or modified or unmodified variants thereof.

[00666] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18968, or modified or unmodified variants thereof.

[00667] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25948, or modified or unmodified variants thereof.

[00668] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26188, or modified or unmodified variants thereof.

[00669] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26708, or modified or unmodified variants thereof.

[00670] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25961, or modified or unmodified variants thereof.

[00671] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26803, or modified or unmodified variants thereof.

[00672] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19741, or modified or unmodified variants thereof.

[00673] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26056, or modified or unmodified variants thereof.

[00674] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25959, or modified or unmodified variants thereof.

[00675] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26059, or modified or unmodified variants thereof.

[00676] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26102, or modified or unmodified variants thereof.

[00677] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26106, or modified or unmodified variants thereof.

[00678] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26744, or modified or unmodified variants thereof.

[00679] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26099, or modified or unmodified variants thereof.

[00680] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26170, or modified or unmodified variants thereof.

[00681] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19012, or modified or unmodified variants thereof.

[00682] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26198, or modified or unmodified variants thereof.

[00683] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26766, or modified or unmodified variants thereof.

[00684] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18951, or modified or unmodified variants thereof.

[00685] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18975, or modified or unmodified variants thereof.

[00686] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26749, or modified or unmodified variants thereof.

[00687] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18911, or modified or unmodified variants thereof.

[00688] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26906, or modified or unmodified variants thereof.

[00689] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-19747, or modified or unmodified variants thereof.

[00690] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18960, or modified or unmodified variants thereof.

[00691] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-25909, or modified or unmodified variants thereof.

[00692] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26184, or modified or unmodified variants thereof.

[00693] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26077, or modified or unmodified variants thereof.

[00694] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26680, or modified or unmodified variants thereof.

[00695] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26085, or modified or unmodified variants thereof.

[00696] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18926, or modified or unmodified variants thereof.

[00697] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18945, or modified or unmodified variants thereof.

[00698] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26703, or modified or unmodified variants thereof.

[00699] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26911, or modified or unmodified variants thereof.

[00700] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26661, or modified or unmodified variants thereof.

[00701] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-18905, or modified or unmodified variants thereof.

[00702] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: AD-26142, or modified or unmodified variants thereof.

[00703] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Setl_1245, or modified or unmodified variants thereof.

[00704] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Setl_1249, or modified or unmodified variants thereof.

[00705] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1250, or modified or unmodified variants thereof.

[00706] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1450, or modified or unmodified variants thereof.

[00707] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1545, or modified or unmodified variants thereof.

[00708] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1755, or modified or unmodified variants thereof.

[00709] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1814, or modified or unmodified variants thereof.

[00710] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1816, or modified or unmodified variants thereof.

[00711] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_1974, or modified or unmodified variants thereof.

[00712] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_2202, or modified or unmodified variants thereof.

[00713] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_2425, or modified or unmodified variants thereof.

[00714] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_254, or modified or unmodified variants thereof.

[00715] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_3146, or modified or unmodified variants thereof.

[00716] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_3169, or modified or unmodified variants thereof.

[00717] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_3196, or modified or unmodified variants thereof.

[00718] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_3477, or modified or unmodified variants thereof.

[00719] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_703, or modified or unmodified variants thereof.

[00720] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_709, or modified or unmodified variants thereof.

[00721] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_865, or modified or unmodified variants thereof.

[00722] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_889, or modified or unmodified variants thereof.

[00723] A RNAi agent comprising: a first strand and a second strand, wherein the first strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the first strand of: Set1_895, or modified or unmodified variants thereof.

[00724] In various embodiments, the first and second strand can be either the sense and anti-sense strand, or the anti-sense and sense strand.

[00725] **Additional embodiments of specific RNAi agents to Beta-Catenin**

[00726] In one embodiment, the present disclosure comprises a RNAi agent comprising an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of any RNAi in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, and modified and unmodified variants thereof.

[00727] Thus, in various embodiments, the present disclosure pertains to a composition comprising any one or more of the following:

[00728] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26104, or modified or unmodified variants thereof.

[00729] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26063, or modified or unmodified variants thereof.

[00730] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26082, or modified or unmodified variants thereof.

[00731] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26034, or modified or unmodified variants thereof.

[00732] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26091, or modified or unmodified variants thereof.

[00733] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26047, or modified or unmodified variants thereof.

[00734] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26651, or modified or unmodified variants thereof.

[00735] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26696, or modified or unmodified variants thereof.

[00736] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26109, or modified or unmodified variants thereof.

[00737] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25941, or modified or unmodified variants thereof.

[00738] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26028, or modified or unmodified variants thereof.

[00739] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26652, or modified or unmodified variants thereof.

[00740] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26742, or modified or unmodified variants thereof.

[00741] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26921, or modified or unmodified variants thereof.

[00742] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18893, or modified or unmodified variants thereof.

[00743] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18983, or modified or unmodified variants thereof.

[00744] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25950, or modified or unmodified variants thereof.

[00745] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25951, or modified or unmodified variants thereof.

[00746] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26042, or modified or unmodified variants thereof.

[00747] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26043, or modified or unmodified variants thereof.

[00748] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26673, or modified or unmodified variants thereof.

[00749] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26704, or modified or unmodified variants thereof.

[00750] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26068, or modified or unmodified variants thereof.

[00751] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26183, or modified or unmodified variants thereof.

[00752] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26700, or modified or unmodified variants thereof.

[00753] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26701, or modified or unmodified variants thereof.

[00754] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25942, or modified or unmodified variants thereof.

[00755] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26076, or modified or unmodified variants thereof.

[00756] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26031, or modified or unmodified variants thereof.

[00757] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26210, or modified or unmodified variants thereof.

[00758] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26664, or modified or unmodified variants thereof.

[00759] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26691, or modified or unmodified variants thereof.

[00760] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26740, or modified or unmodified variants thereof.

[00761] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19765, or modified or unmodified variants thereof.

[00762] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26158, or modified or unmodified variants thereof.

[00763] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26180, or modified or unmodified variants thereof.

[00764] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26078, or modified or unmodified variants thereof.

[00765] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25894, or modified or unmodified variants thereof.

[00766] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25964, or modified or unmodified variants thereof.

[00767] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26156, or modified or unmodified variants thereof.

[00768] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26670, or modified or unmodified variants thereof.

[00769] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26743, or modified or unmodified variants thereof.

[00770] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25890, or modified or unmodified variants thereof.

[00771] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26044, or modified or unmodified variants thereof.

[00772] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26685, or modified or unmodified variants thereof.

[00773] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26731, or modified or unmodified variants thereof.

[00774] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26800, or modified or unmodified variants thereof.

[00775] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26066, or modified or unmodified variants thereof.

[00776] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26682, or modified or unmodified variants thereof.

[00777] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26684, or modified or unmodified variants thereof.

[00778] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26757, or modified or unmodified variants thereof.

[00779] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26788, or modified or unmodified variants thereof.

[00780] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18963, or modified or unmodified variants thereof.

[00781] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19076, or modified or unmodified variants thereof.

[00782] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25943, or modified or unmodified variants thereof.

[00783] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26052, or modified or unmodified variants thereof.

[00784] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26665, or modified or unmodified variants thereof.

[00785] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26746, or modified or unmodified variants thereof.

[00786] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18974, or modified or unmodified variants thereof.

[00787] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25938, or modified or unmodified variants thereof.

[00788] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25944, or modified or unmodified variants thereof.

[00789] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26178, or modified or unmodified variants thereof.

[00790] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26669, or modified or unmodified variants thereof.

[00791] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26730, or modified or unmodified variants thereof.

[00792] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26825, or modified or unmodified variants thereof.

[00793] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25956, or modified or unmodified variants thereof.

[00794] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26822, or modified or unmodified variants thereof.

[00795] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26108, or modified or unmodified variants thereof.

[00796] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26752, or modified or unmodified variants thereof.

[00797] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26779, or modified or unmodified variants thereof.

[00798] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25891, or modified or unmodified variants thereof.

[00799] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26101, or modified or unmodified variants thereof.

[00800] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26181, or modified or unmodified variants thereof.

[00801] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26218, or modified or unmodified variants thereof.

[00802] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26660, or modified or unmodified variants thereof.

[00803] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18966, or modified or unmodified variants thereof.

[00804] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19074, or modified or unmodified variants thereof.

[00805] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26179, or modified or unmodified variants thereof.

[00806] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26722, or modified or unmodified variants thereof.

[00807] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26768, or modified or unmodified variants thereof.

[00808] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26920, or modified or unmodified variants thereof.

[00809] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26020, or modified or unmodified variants thereof.

[00810] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26713, or modified or unmodified variants thereof.

[00811] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26727, or modified or unmodified variants thereof.

[00812] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26808, or modified or unmodified variants thereof.

[00813] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25958, or modified or unmodified variants thereof.

[00814] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26105, or modified or unmodified variants thereof.

[00815] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26674, or modified or unmodified variants thereof.

[00816] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26781, or modified or unmodified variants thereof.

[00817] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26801, or modified or unmodified variants thereof.

[00818] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26813, or modified or unmodified variants thereof.

[00819] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26816, or modified or unmodified variants thereof.

[00820] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25945, or modified or unmodified variants thereof.

[00821] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26203, or modified or unmodified variants thereof.

[00822] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26021, or modified or unmodified variants thereof.

[00823] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26040, or modified or unmodified variants thereof.

[00824] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26069, or modified or unmodified variants thereof.

[00825] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26134, or modified or unmodified variants thereof.

[00826] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26702, or modified or unmodified variants thereof.

[00827] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18933, or modified or unmodified variants thereof.

[00828] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26690, or modified or unmodified variants thereof.

[00829] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26698, or modified or unmodified variants thereof.

[00830] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25910, or modified or unmodified variants thereof.

[00831] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26747, or modified or unmodified variants thereof.

[00832] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26810, or modified or unmodified variants thereof.

[00833] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26083, or modified or unmodified variants thereof.

[00834] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26061, or modified or unmodified variants thereof.

[00835] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26904, or modified or unmodified variants thereof.

[00836] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18903, or modified or unmodified variants thereof.

[00837] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18980, or modified or unmodified variants thereof.

[00838] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26202, or modified or unmodified variants thereof.

[00839] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26679, or modified or unmodified variants thereof.

[00840] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26719, or modified or unmodified variants thereof.

[00841] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26758, or modified or unmodified variants thereof.

[00842] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26783, or modified or unmodified variants thereof.

[00843] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26902, or modified or unmodified variants thereof.

[00844] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18892, or modified or unmodified variants thereof.

[00845] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18897, or modified or unmodified variants thereof.

[00846] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25902, or modified or unmodified variants thereof.

[00847] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26705, or modified or unmodified variants thereof.

[00848] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26782, or modified or unmodified variants thereof.

[00849] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19082, or modified or unmodified variants thereof.

[00850] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26176, or modified or unmodified variants thereof.

[00851] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26196, or modified or unmodified variants thereof.

[00852] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26199, or modified or unmodified variants thereof.

[00853] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26678, or modified or unmodified variants thereof.

[00854] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26683, or modified or unmodified variants thereof.

[00855] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26729, or modified or unmodified variants thereof.

[00856] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26804, or modified or unmodified variants thereof.

[00857] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26900, or modified or unmodified variants thereof.

[00858] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25914, or modified or unmodified variants thereof.

[00859] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26060, or modified or unmodified variants thereof.

[00860] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26763, or modified or unmodified variants thereof.

[00861] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18902, or modified or unmodified variants thereof.

[00862] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18914, or modified or unmodified variants thereof.

[00863] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26100, or modified or unmodified variants thereof.

[00864] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26128, or modified or unmodified variants thereof.

[00865] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26193, or modified or unmodified variants thereof.

[00866] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26765, or modified or unmodified variants thereof.

[00867] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25960, or modified or unmodified variants thereof.

[00868] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26018, or modified or unmodified variants thereof.

[00869] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25893, or modified or unmodified variants thereof.

[00870] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26823, or modified or unmodified variants thereof.

[00871] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25940, or modified or unmodified variants thereof.

[00872] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26190, or modified or unmodified variants thereof.

[00873] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26675, or modified or unmodified variants thereof.

[00874] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26797, or modified or unmodified variants thereof.

[00875] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26916, or modified or unmodified variants thereof.

[00876] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26755, or modified or unmodified variants thereof.

[00877] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26901, or modified or unmodified variants thereof.

[00878] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19004, or modified or unmodified variants thereof.

[00879] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19009, or modified or unmodified variants thereof.

[00880] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26148, or modified or unmodified variants thereof.

[00881] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26186, or modified or unmodified variants thereof.

[00882] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26737, or modified or unmodified variants thereof.

[00883] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25955, or modified or unmodified variants thereof.

[00884] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26029, or modified or unmodified variants thereof.

[00885] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26131, or modified or unmodified variants thereof.

[00886] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18894, or modified or unmodified variants thereof.

[00887] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18939, or modified or unmodified variants thereof.

[00888] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26654, or modified or unmodified variants thereof.

[00889] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18929, or modified or unmodified variants thereof.

[00890] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26135, or modified or unmodified variants thereof.

[00891] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26774, or modified or unmodified variants thereof.

[00892] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26780, or modified or unmodified variants thereof.

[00893] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26819, or modified or unmodified variants thereof.

[00894] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26918, or modified or unmodified variants thereof.

[00895] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19050, or modified or unmodified variants thereof.

[00896] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18994, or modified or unmodified variants thereof.

[00897] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26769, or modified or unmodified variants thereof.

[00898] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26666, or modified or unmodified variants thereof.

[00899] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26784, or modified or unmodified variants thereof.

[00900] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18969, or modified or unmodified variants thereof.

[00901] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18986, or modified or unmodified variants thereof.

[00902] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25929, or modified or unmodified variants thereof.

[00903] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25932, or modified or unmodified variants thereof.

[00904] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26095, or modified or unmodified variants thereof.

[00905] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26908, or modified or unmodified variants thereof.

[00906] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26071, or modified or unmodified variants thereof.

[00907] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26912, or modified or unmodified variants thereof.

[00908] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19054, or modified or unmodified variants thereof.

[00909] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25918, or modified or unmodified variants thereof.

[00910] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26903, or modified or unmodified variants thereof.

[00911] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25931, or modified or unmodified variants thereof.

[00912] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26146, or modified or unmodified variants thereof.

[00913] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26200, or modified or unmodified variants thereof.

[00914] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26917, or modified or unmodified variants thereof.

[00915] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26794, or modified or unmodified variants thereof.

[00916] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26910, or modified or unmodified variants thereof.

[00917] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25939, or modified or unmodified variants thereof.

[00918] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26032, or modified or unmodified variants thereof.

[00919] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26776, or modified or unmodified variants thereof.

[00920] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26806, or modified or unmodified variants thereof.

[00921] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26748, or modified or unmodified variants thereof.

[00922] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26725, or modified or unmodified variants thereof.

[00923] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18958, or modified or unmodified variants thereof.

[00924] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26672, or modified or unmodified variants thereof.

[00925] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26905, or modified or unmodified variants thereof.

[00926] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19056, or modified or unmodified variants thereof.

[00927] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19762, or modified or unmodified variants thereof.

[00928] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26919, or modified or unmodified variants thereof.

[00929] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18946, or modified or unmodified variants thereof.

[00930] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19066, or modified or unmodified variants thereof.

[00931] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19746, or modified or unmodified variants thereof.

[00932] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26057, or modified or unmodified variants thereof.

[00933] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26073, or modified or unmodified variants thereof.

[00934] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26689, or modified or unmodified variants thereof.

[00935] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19008, or modified or unmodified variants thereof.

[00936] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26026, or modified or unmodified variants thereof.

[00937] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26761, or modified or unmodified variants thereof.

[00938] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19752, or modified or unmodified variants thereof.

[00939] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18981, or modified or unmodified variants thereof.

[00940] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18927, or modified or unmodified variants thereof.

[00941] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19753, or modified or unmodified variants thereof.

[00942] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25907, or modified or unmodified variants thereof.

[00943] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26671, or modified or unmodified variants thereof.

[00944] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19080, or modified or unmodified variants thereof.

[00945] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26075, or modified or unmodified variants thereof.

[00946] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26681, or modified or unmodified variants thereof.

[00947] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18976, or modified or unmodified variants thereof.

[00948] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25900, or modified or unmodified variants thereof.

[00949] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26126, or modified or unmodified variants thereof.

[00950] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26688, or modified or unmodified variants thereof.

[00951] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25912, or modified or unmodified variants thereof.

[00952] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25930, or modified or unmodified variants thereof.

[00953] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18995, or modified or unmodified variants thereof.

[00954] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26802, or modified or unmodified variants thereof.

[00955] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25892, or modified or unmodified variants thereof.

[00956] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25947, or modified or unmodified variants thereof.

[00957] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26088, or modified or unmodified variants thereof.

[00958] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26098, or modified or unmodified variants thereof.

[00959] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26778, or modified or unmodified variants thereof.

[00960] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26215, or modified or unmodified variants thereof.

[00961] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26739, or modified or unmodified variants thereof.

[00962] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18950, or modified or unmodified variants thereof.

[00963] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25949, or modified or unmodified variants thereof.

[00964] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26141, or modified or unmodified variants thereof.

[00965] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18961, or modified or unmodified variants thereof.

[00966] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25957, or modified or unmodified variants thereof.

[00967] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26826, or modified or unmodified variants thereof.

[00968] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25963, or modified or unmodified variants thereof.

[00969] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26019, or modified or unmodified variants thereof.

[00970] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26035, or modified or unmodified variants thereof.

[00971] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25946, or modified or unmodified variants thereof.

[00972] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26714, or modified or unmodified variants thereof.

[00973] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26022, or modified or unmodified variants thereof.

[00974] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26096, or modified or unmodified variants thereof.

[00975] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26132, or modified or unmodified variants thereof.

[00976] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26062, or modified or unmodified variants thereof.

[00977] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18991, or modified or unmodified variants thereof.

[00978] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26164, or modified or unmodified variants thereof.

[00979] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26209, or modified or unmodified variants thereof.

[00980] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25895, or modified or unmodified variants thereof.

[00981] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25933, or modified or unmodified variants thereof.

[00982] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26017, or modified or unmodified variants thereof.

[00983] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19749, or modified or unmodified variants thereof.

[00984] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26653, or modified or unmodified variants thereof.

[00985] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26759, or modified or unmodified variants thereof.

[00986] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25924, or modified or unmodified variants thereof.

[00987] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26153, or modified or unmodified variants thereof.

[00988] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25953, or modified or unmodified variants thereof.

[00989] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26764, or modified or unmodified variants thereof.

[00990] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26790, or modified or unmodified variants thereof.

[00991] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-20124, or modified or unmodified variants thereof.

[00992] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25919, or modified or unmodified variants thereof.

[00993] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18913, or modified or unmodified variants thereof.

[00994] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26211, or modified or unmodified variants thereof.

[00995] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18936, or modified or unmodified variants thereof.

[00996] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25898, or modified or unmodified variants thereof.

[00997] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26741, or modified or unmodified variants thereof.

[00998] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19043, or modified or unmodified variants thereof.

[00999] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26079, or modified or unmodified variants thereof.

[001000] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19000, or modified or unmodified variants thereof.

[001001] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25911, or modified or unmodified variants thereof.

[001002] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26786, or modified or unmodified variants thereof.

[001003] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19069, or modified or unmodified variants thereof.

[001004] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26037, or modified or unmodified variants thereof.

[001005] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26723, or modified or unmodified variants thereof.

[001006] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19067, or modified or unmodified variants thereof.

[001007] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25928, or modified or unmodified variants thereof.

[001008] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26677, or modified or unmodified variants thereof.

[001009] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19006, or modified or unmodified variants thereof.

[001010] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19758, or modified or unmodified variants thereof.

[001011] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26913, or modified or unmodified variants thereof.

[001012] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25917, or modified or unmodified variants thereof.

[001013] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26189, or modified or unmodified variants thereof.

[001014] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26787, or modified or unmodified variants thereof.

[001015] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26707, or modified or unmodified variants thereof.

[001016] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26094, or modified or unmodified variants thereof.

[001017] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26097, or modified or unmodified variants thereof.

[001018] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26699, or modified or unmodified variants thereof.

[001019] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26756, or modified or unmodified variants thereof.

[001020] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26720, or modified or unmodified variants thereof.

[001021] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25926, or modified or unmodified variants thereof.

[001022] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26212, or modified or unmodified variants thereof.

[001023] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26687, or modified or unmodified variants thereof.

[001024] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26753, or modified or unmodified variants thereof.

[001025] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18982, or modified or unmodified variants thereof.

[001026] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18908, or modified or unmodified variants thereof.

[001027] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18968, or modified or unmodified variants thereof.

[001028] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25948, or modified or unmodified variants thereof.

[001029] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26188, or modified or unmodified variants thereof.

[001030] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26708, or modified or unmodified variants thereof.

[001031] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25961, or modified or unmodified variants thereof.

[001032] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26803, or modified or unmodified variants thereof.

[001033] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19741, or modified or unmodified variants thereof.

[001034] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26056, or modified or unmodified variants thereof.

[001035] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25959, or modified or unmodified variants thereof.

[001036] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26059, or modified or unmodified variants thereof.

[001037] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26102, or modified or unmodified variants thereof.

[001038] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26106, or modified or unmodified variants thereof.

[001039] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26744, or modified or unmodified variants thereof.

[001040] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26099, or modified or unmodified variants thereof.

[001041] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26170, or modified or unmodified variants thereof.

[001042] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19012, or modified or unmodified variants thereof.

[001043] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26198, or modified or unmodified variants thereof.

[001044] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26766, or modified or unmodified variants thereof.

[001045] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18951, or modified or unmodified variants thereof.

[001046] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18975, or modified or unmodified variants thereof.

[001047] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26749, or modified or unmodified variants thereof.

[001048] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18911, or modified or unmodified variants thereof.

[001049] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26906, or modified or unmodified variants thereof.

[001050] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-19747, or modified or unmodified variants thereof.

[001051] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18960, or modified or unmodified variants thereof.

[001052] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-25909, or modified or unmodified variants thereof.

[001053] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26184, or modified or unmodified variants thereof.

[001054] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26077, or modified or unmodified variants thereof.

[001055] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26680, or modified or unmodified variants thereof.

[001056] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26085, or modified or unmodified variants thereof.

[001057] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18926, or modified or unmodified variants thereof.

[001058] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18945, or modified or unmodified variants thereof.

[001059] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26703, or modified or unmodified variants thereof.

[001060] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26911, or modified or unmodified variants thereof.

[001061] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26661, or modified or unmodified variants thereof.

[001062] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-18905, or modified or unmodified variants thereof.

[001063] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of AD-26142, or modified or unmodified variants thereof.

[001064] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1245, or modified or unmodified variants thereof.

[001065] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1249, or modified or unmodified variants thereof.

[001066] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1250, or modified or unmodified variants thereof.

[001067] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1450, or modified or unmodified variants thereof.

[001068] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1545, or modified or unmodified variants thereof.

[001069] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1755, or modified or unmodified variants thereof.

[001070] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1814, or modified or unmodified variants thereof.

[001071] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1816, or modified or unmodified variants thereof.

[001072] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_1974, or modified or unmodified variants thereof.

[001073] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_2202, or modified or unmodified variants thereof.

[001074] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_2425, or modified or unmodified variants thereof.

[001075] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_254, or modified or unmodified variants thereof.

[001076] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_3146, or modified or unmodified variants thereof.

[001077] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_3169, or modified or unmodified variants thereof.

[001078] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_3196, or modified or unmodified variants thereof.

[001079] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_3477, or modified or unmodified variants thereof.

[001080] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_703, or modified or unmodified variants thereof.

[001081] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_709, or modified or unmodified variants thereof.

[001082] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_865, or modified or unmodified variants thereof.

[001083] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_889, or modified or unmodified variants thereof.

[001084] A RNAi agent comprising: an anti-sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the anti-sense strand, and/or a sense strand comprising at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nt from the sequence of the sense strand, of Set1_895, or modified or unmodified variants thereof.

Additional embodiments encompassing specific RNAi agents to Beta-Catenin

[001085] In various embodiments, the present disclosure pertains to a composition comprising one or more of the following:

[001] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26104.

[002] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26063.

[003] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26082.

[004] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26034.

[005] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26091.

[006] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26047.

[007] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26651.

[008] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26696.

[009] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26109.

[0010] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25941.

[0011] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26028.

[0012] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26652.

[0013] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26742.

[0014] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26921.

[0015] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18893.

[0016] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18983.

[0017] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25950.

[0018] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25951.

[0019] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26042.

[0020] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26043.

[0021] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26673.

[0022] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26704.

[0023] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26068.

[0024] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26183.

[0025] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26700.

[0026] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26701.

[0027] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25942.

[0028] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26076.

[0029] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26031.

[0030] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26210.

[0031] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26664.

[0032] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26691.

[0033] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26740.

[0034] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19765.

[0035] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26158.

[0036] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26180.

[0037] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26078.

[0038] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25894.

[0039] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25964.

[0040] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26156.

[0041] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26670.

[0042] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26743.

[0043] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25890.

[0044] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26044.

[0045] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26685.

[0046] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26731.

[0047] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26800.

[0048] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26066.

[0049] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26682.

[0050] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26684.

[0051] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26757.

[0052] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26788.

[0053] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18963.

[0054] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19076.

[0055] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25943.

[0056] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26052.

[0057] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26665.

[0058] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26746.

[0059] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18974.

[0060] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25938.

[0061] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25944.

[0062] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26178.

[0063] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26669.

[0064] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26730.

[0065] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26825.

[0066] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25956.

[0067] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26822.

[0068] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26108.

[0069] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26752.

[0070] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26779.

[0071] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25891.

[0072] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26101.

[0073] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26181.

[0074] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26218.

[0075] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26660.

[0076] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18966.

[0077] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19074.

[0078] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26179.

[0079] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26722.

[0080] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26768.

[0081] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26920.

[0082] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26020.

[0083] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26713.

[0084] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26727.

[0085] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26808.

[0086] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25958.

[0087] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26105.

[0088] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26674.

[0089] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26781.

[0090] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26801.

[0091] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26813.

[0092] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26816.

[0093] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25945.

[0094] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26203.

[0095] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26021.

[0096] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26040.

[0097] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26069.

[0098] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26134.

[0099] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26702.

[00100] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18933.

[00101] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26690.

[00102] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26698.

[00103] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25910.

[00104] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26747.

[00105] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26810.

[00106] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26083.

[00107] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26061.

[00108] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26904.

[00109] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18903.

[00110] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18980.

[00111] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26202.

[00112] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26679.

[00113] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26719.

[00114] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26758.

[00115] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26783.

[00116] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26902.

[00117] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18892.

[00118] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18897.

[00119] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25902.

[00120] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26705.

[00121] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26782.

[00122] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19082.

[00123] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26176.

[00124] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26196.

[00125] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26199.

[00126] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26678.

[00127] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26683.

[00128] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26729.

[00129] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26804.

[00130] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26900.

[00131] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25914.

[00132] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26060.

[00133] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26763.

[00134] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18902.

[00135] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18914.

[00136] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26100.

[00137] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26128.

[00138] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26193.

[00139] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26765.

[00140] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25960.

[00141] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26018.

[00142] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25893.

[00143] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26823.

[00144] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25940.

[00145] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26190.

[00146] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26675.

[00147] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26797.

[00148] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26916.

[00149] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26755.

[00150] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26901.

[00151] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19004.

[00152] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19009.

[00153] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26148.

[00154] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26186.

[00155] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26737.

[00156] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25955.

[00157] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26029.

[00158] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26131.

[00159] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18894.

[00160] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18939.

[00161] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26654.

[00162] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18929.

[00163] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26135.

[00164] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26774.

[00165] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26780.

[00166] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26819.

[00167] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26918.

[00168] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19050.

[00169] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18994.

[00170] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26769.

[00171] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26666.

[00172] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26784.

[00173] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18969.

[00174] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18986.

[00175] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25929.

[00176] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25932.

[00177] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26095.

[00178] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26908.

[00179] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26071.

[00180] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26912.

[00181] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19054.

[00182] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25918.

[00183] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26903.

[00184] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25931.

[00185] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26146.

[00186] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26200.

[00187] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26917.

[00188] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26794.

[00189] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26910.

[00190] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25939.

[00191] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26032.

[00192] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26776.

[00193] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26806.

[00194] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26748.

[00195] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26725.

[00196] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18958.

[00197] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26672.

[00198] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26905.

[00199] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19056.

[00200] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19762.

[00201] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26919.

[00202] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18946.

[00203] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19066.

[00204] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19746.

[00205] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26057.

[00206] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26073.

[00207] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26689.

[00208] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19008.

[00209] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26026.

[00210] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26761.

[00211] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19752.

[00212] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18981.

[00213] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18927.

[00214] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19753.

[00215] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25907.

[00216] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26671.

[00217] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19080.

[00218] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26075.

[00219] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26681.

[00220] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18976.

[00221] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25900.

[00222] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26126.

[00223] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26688.

[00224] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25912.

[00225] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25930.

[00226] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18995.

[00227] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26802.

[00228] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25892.

[00229] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25947.

[00230] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26088.

[00231] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26098.

[00232] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26778.

[00233] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26215.

[00234] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26739.

[00235] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18950.

[00236] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25949.

[00237] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26141.

[00238] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18961.

[00239] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25957.

[00240] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26826.

[00241] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25963.

[00242] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26019.

[00243] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26035.

[00244] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25946.

[00245] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26714.

[00246] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26022.

[00247] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26096.

[00248] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26132.

[00249] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26062.

[00250] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18991.

[00251] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26164.

[00252] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26209.

[00253] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25895.

[00254] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25933.

[00255] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26017.

[00256] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19749.

[00257] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26653.

[00258] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26759.

[00259] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25924.

[00260] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26153.

[00261] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25953.

[00262] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26764.

[00263] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26790.

[00264] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-20124.

[00265] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25919.

[00266] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18913.

[00267] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26211.

[00268] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18936.

[00269] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25898.

[00270] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26741.

[00271] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19043.

[00272] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26079.

[00273] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19000.

[00274] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25911.

[00275] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26786.

[00276] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19069.

[00277] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26037.

[00278] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26723.

[00279] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19067.

[00280] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25928.

[00281] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26677.

[00282] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19006.

[00283] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19758.

[00284] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26913.

[00285] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25917.

[00286] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26189.

[00287] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26787.

[00288] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26707.

[00289] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26094.

[00290] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26097.

[00291] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26699.

[00292] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26756.

[00293] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26720.

[00294] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25926.

[00295] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26212.

[00296] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26687.

[00297] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26753.

[00298] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18982.

[00299] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18908.

[00300] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18968.

[00301] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25948.

[00302] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26188.

[00303] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26708.

[00304] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25961.

[00305] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26803.

[00306] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19741.

[00307] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26056.

[00308] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25959.

[00309] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26059.

[00310] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26102.

[00311] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26106.

[00312] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26744.

[00313] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26099.

[00314] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26170.

[00315] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19012.

[00316] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26198.

[00317] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26766.

[00318] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18951.

[00319] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18975.

[00320] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26749.

[00321] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18911.

[00322] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26906.

[00323] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-19747.

[00324] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18960.

[00325] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-25909.

[00326] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26184.

[00327] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26077.

[00328] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26680.

[00329] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26085.

[00330] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18926.

[00331] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18945.

[00332] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26703.

[00333] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26911.

[00334] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26661.

[00335] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-18905.

[00336] A RNAi agent comprising a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of AD-26142.

[00337] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1245.

[00338] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1249.

[00339] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1250.

[00340] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1450.

[00341] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1545.

[00342] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1755.

[00343] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1814.

[00344] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1816.

[00345] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_1974.

[00346] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_2202.

[00347] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_2425.

[00348] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the

sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_254.

[00349] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_3146.

[00350] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_3169.

[00351] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_3196.

[00352] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_3477.

[00353] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_703.

[00354] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_709.

[00355] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_865.

[00356] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_889.

[00357] A RNAi agent comprising: a sense strand and an anti-sense strand, wherein the sequence of the anti-sense strand is the sequence of the anti-sense strand of Set1_895.

Additional embodiments encompassing specific RNAi agents to Beta-Catenin

[001086] In various embodiments, the present disclosure pertains to a composition comprising one or more of the following:

[00358] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26104, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00359] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26063, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00360] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26082, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00361] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26034, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00362] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26091, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00363] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26047, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00364] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26651, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00365] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26696, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00366] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26109, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00367] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25941, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00368] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26028, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00369] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26652, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00370] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26742, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00371] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26921, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00372] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18893, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00373] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18983, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00374] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-25950, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00375] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25951, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00376] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26042, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00377] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26043, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00378] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26673, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00379] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26704, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00380] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26068, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00381] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26183, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00382] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26700, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00383] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26701, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00384] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25942, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00385] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26076, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00386] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26031, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00387] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26210, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00388] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26664, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00389] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26691, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00390] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26740, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00391] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19765, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00392] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26158, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00393] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26180, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00394] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26078, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00395] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25894, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00396] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25964, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00397] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26156, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00398] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26670, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00399] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26743, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00400] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25890, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00401] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26044, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00402] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26685, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00403] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26731, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00404] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26800, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00405] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26066, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00406] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26682, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00407] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26684, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00408] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26757, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00409] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26788, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00410] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-18963, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00411] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19076, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00412] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25943, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00413] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26052, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00414] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26665, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00415] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26746, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00416] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18974, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00417] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25938, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00418] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25944, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00419] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26178, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00420] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26669, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00421] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26730, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00422] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26825, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00423] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25956, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00424] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26822, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00425] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26108, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00426] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26752, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00427] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26779, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00428] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25891, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00429] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26101, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00430] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26181, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00431] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26218, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00432] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26660, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00433] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18966, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00434] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-19074, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00435] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26179, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00436] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26722, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00437] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26768, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00438] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26920, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00439] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26020, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00440] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26713, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00441] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26727, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00442] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26808, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00443] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25958, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00444] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26105, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00445] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26674, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00446] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26781, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00447] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26801, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00448] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26813, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00449] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26816, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00450] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25945, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00451] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26203, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00452] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26021, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00453] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26040, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00454] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26069, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00455] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26134, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00456] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26702, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00457] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18933, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00458] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26690, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00459] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26698, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00460] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25910, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00461] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26747, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00462] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26810, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00463] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26083, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00464] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26061, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00465] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26904, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00466] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18903, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00467] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18980, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00468] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26202, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00469] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26679, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00470] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26719, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00471] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26758, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00472] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26783, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00473] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26902, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00474] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18892, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00475] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18897, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00476] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25902, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00477] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26705, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00478] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26782, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00479] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19082, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00480] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26176, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00481] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26196, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00482] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26199, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00483] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26678, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00484] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26683, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00485] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26729, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00486] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26804, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00487] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26900, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00488] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25914, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00489] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26060, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00490] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26763, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00491] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18902, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00492] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18914, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00493] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26100, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00494] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26128, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00495] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26193, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00496] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26765, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00497] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25960, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00498] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26018, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00499] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25893, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00500] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26823, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00501] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25940, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00502] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26190, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00503] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26675, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00504] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26797, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00505] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26916, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00506] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26755, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00507] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26901, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00508] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19004, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00509] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19009, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00510] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26148, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00511] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26186, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00512] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26737, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00513] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25955, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00514] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26029, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00515] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26131, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00516] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18894, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00517] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18939, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00518] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26654, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00519] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18929, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00520] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26135, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00521] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26774, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00522] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26780, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00523] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26819, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00524] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26918, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00525] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19050, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00526] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18994, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00527] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26769, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00528] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26666, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00529] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26784, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00530] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-18969, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00531] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18986, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00532] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25929, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00533] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25932, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00534] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26095, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00535] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26908, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00536] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26071, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00537] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26912, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00538] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19054, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00539] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25918, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00540] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26903, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00541] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25931, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00542] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26146, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00543] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26200, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00544] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26917, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00545] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26794, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00546] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26910, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00547] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25939, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00548] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26032, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00549] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26776, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00550] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26806, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00551] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26748, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00552] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26725, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00553] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18958, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00554] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26672, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00555] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26905, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00556] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19056, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00557] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19762, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00558] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26919, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00559] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18946, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00560] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19066, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00561] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19746, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00562] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26057, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00563] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26073, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00564] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26689, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00565] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19008, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00566] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26026, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00567] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26761, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00568] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19752, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00569] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18981, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00570] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18927, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00571] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19753, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00572] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25907, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00573] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26671, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00574] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19080, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00575] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26075, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00576] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26681, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00577] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18976, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00578] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-25900, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00579] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26126, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00580] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26688, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00581] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25912, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00582] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25930, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00583] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18995, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00584] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26802, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00585] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25892, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00586] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25947, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00587] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26088, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00588] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26098, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00589] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26778, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00590] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26215, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00591] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26739, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00592] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18950, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00593] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25949, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00594] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26141, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00595] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18961, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00596] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25957, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00597] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26826, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00598] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25963, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00599] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26019, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00600] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26035, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00601] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25946, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00602] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26714, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00603] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26022, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00604] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26096, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00605] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26132, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00606] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26062, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00607] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18991, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00608] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26164, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00609] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26209, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00610] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25895, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00611] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25933, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00612] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26017, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00613] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19749, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00614] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26653, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00615] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26759, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00616] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25924, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00617] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26153, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00618] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25953, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00619] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26764, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00620] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26790, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00621] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-20124, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00622] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25919, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00623] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18913, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00624] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26211, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00625] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18936, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00626] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-25898, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00627] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26741, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00628] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19043, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00629] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26079, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00630] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19000, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00631] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25911, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00632] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26786, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00633] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19069, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00634] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26037, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00635] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26723, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00636] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19067, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00637] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25928, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00638] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26677, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00639] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19006, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00640] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19758, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00641] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26913, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00642] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25917, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00643] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26189, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00644] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26787, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00645] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26707, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00646] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26094, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00647] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26097, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00648] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26699, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00649] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26756, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00650] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26720, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00651] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25926, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00652] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26212, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00653] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26687, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00654] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26753, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00655] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18982, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00656] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18908, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00657] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18968, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00658] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25948, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00659] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26188, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00660] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26708, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00661] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25961, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00662] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26803, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00663] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19741, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00664] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26056, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00665] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25959, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00666] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26059, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00667] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26102, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00668] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26106, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00669] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26744, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00670] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26099, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00671] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26170, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00672] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19012, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00673] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26198, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00674] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26766, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00675] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18951, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00676] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18975, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00677] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26749, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00678] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18911, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00679] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26906, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00680] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-19747, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00681] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18960, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00682] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-25909, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00683] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26184, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00684] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26077, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00685] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26680, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00686] A RNAi agent comprising a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of AD-26085, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00687] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18926, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00688] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18945, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00689] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26703, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00690] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26911, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00691] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26661, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00692] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-18905, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00693] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of AD-26142, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00694] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1245, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00695] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1249, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00696] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1250, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00697] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1450, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00698] A RNAi agent comprising: a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of Set1_1545, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00699] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1755, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00700] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1814, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00701] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1816, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00702] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_1974, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00703] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_2202, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00704] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_2425, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00705] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_254, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00706] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_3146, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00707] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_3169, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00708] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_3196, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00709] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_3477, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00710] A RNAi agent comprising: a first strand and a second strand, wherein the sequence

of the first or second strand is the sequence of the first or second strand of Set1_703, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00711] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_709, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00712] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_865, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00713] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_889, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00714] A RNAi agent comprising: a first strand and a second strand, wherein the sequence of the first or second strand is the sequence of the first or second strand of Set1_895, and wherein the first and/or second strand further comprises up to about 20 additional nucleotides.

[00715] **Additional embodiments of specific RNAi agents to Beta-Catenin.**

[00716] In various embodiments, the present disclosure pertains to:

[00717] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6096 and/or 6117, or modified or unmodified variants thereof.

[00718] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6097 and/or 6118, or modified or unmodified variants thereof.

[00719] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6098 and/or 6119, or modified or unmodified variants thereof.

[00720] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6100 and/or 6121, or modified or unmodified variants thereof.

[00721] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6101 and/or 6122, or modified or unmodified variants thereof.

[00722] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6103 and/or 6124, or modified or unmodified variants thereof.

[00723] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6105 and/or 6126, or modified or unmodified variants thereof.

[00724] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6106 and/or 6127, or modified or unmodified variants thereof.

[00725] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, is or consists of the sequence of SEQ ID NOs: 6107 and/or 6128, or modified or unmodified variants thereof.

[00726] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6096 and/or 6117, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00727] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6097 and/or 6118, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00728] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6098 and/or 6119, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00729] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6100 and/or 6121, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00730] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6101 and/or 6122, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00731] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6103 and/or 6124, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00732] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs:

6105 and/or 6126, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00733] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6106 and/or 6127, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00734] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise the sequence of SEQ ID NOs: 6107 and/or 6128, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00735] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6096 and/or 6117, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00736] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6097 and/or 6118, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00737] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6098 and/or 6119, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00738] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6100 and/or 6121, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00739] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6101 and/or 6122, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00740] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6103 and/or 6124, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00741] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides

of the sequence of SEQ ID NOs: 6105 and/or 6126, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00742] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6106 and/or 6127, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00743] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides of the sequence of SEQ ID NOs: 6107 and/or 6128, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00744] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6096 and/or 6117, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00745] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6097 and/or 6118, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00746] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6098 and/or 6119, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00747] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6100 and/or 6121, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00748] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6101 and/or 6122, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00749] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6103 and/or 6124, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00750] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6105 and/or 6126, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00751] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6106 and/or 6127, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00752] A RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand and/or the second strand, respectively, comprise at least 15 contiguous nucleotides differing by 0, 1, 2 or 3 nucleotides from the sequence of SEQ ID NOs: 6107 and/or 6128, wherein the first and second strand are each no more than about 30 nucleotides in length, or unmodified variants thereof.

[00753] In various embodiments, the first and second strand can be either the sense and anti-sense strand, or the anti-sense and sense strand.

[00754] Additional embodiments of specific RNAi agents to Beta-Catenin, further comprising additional nt.

[00755] In various embodiments of the present disclosure, the RNAi agent comprises an anti-sense strand consisting of a sequence of at least 15 contiguous nucleotides with 0, 1, 2, or 3 mismatches from that of the anti-sense strand of any RNAi agent from Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9, or modified or unmodified variants thereof, wherein the anti-sense strand optionally further comprises 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 or more nt (or any range thereof, e.g., 0-1, 1-2, 1-3, 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, 1-10, 2-3, 2-4, or 2-5 nt, etc.)

[00756] Additional embodiments comprising overlapping groups of RNAi agents to Beta-Catenin

[00757] In various embodiments of the present disclosure, the present disclosure relates to groups of RNAi agents with overlapping sequences. Thus, the present disclosure encompasses groups of RNAi agents wherein each RNAi agent in the group overlaps with each other RNAi agent in the same group by at least 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or more nucleotides. In one embodiment, the overlap is at least 12 nt. Groups of sequences that overlap are shown in Table 4.

[00758] Table 4 shows, for example, that AD-26022 and AD-26204 share the common technical feature of the sequence of CCUGUUCCCCUG (SEQ ID NO: 1319) in the sense strand, and the sequence of CAGGGGAACAGG (SEQ ID NO: 2714) in the anti-sense strand. Note of course that only a 12-nt portion of the overlap is shown; many groups of RNAi agents will overlap by more than 12 nt. The position within the gene is also indicated.

[00759] The present disclosure thus encompasses various embodiments comprising groups of overlapping RNAi agents, for example (1) RNAi agents comprising the sequences of AD-26022 and AD-26204; (2) RNAi agents consisting of the sequences of AD-26022 and AD-26204; (3) RNAi agents comprising a sense strand and/or a anti-sense strand comprising a sequence of AD-26022 and AD-26204; (4) RNAi agents comprising a sense strand and/or a anti-sense strand comprising 15 contiguous nt with 0 to 3 mismatches from a sequence of AD-26022 and AD-26204; (5) RNAi agents comprising a sense strand comprising 15 contiguous nt with 0 to 3 mismatches from a sequence of AD-26022 and AD-26204; (6) RNAi agents comprising an anti-sense strand comprising 15 contiguous nt with 0 to 3 mismatches from a sequence of AD-26022 and AD-26204; etc. and similar embodiments reflecting all the overlapping groups of RNAi agents.

[00760] Thus, in various embodiments, the RNAi agents of the present disclosure comprise a sense strand and an anti-sense (which may optionally be covalently linked, linked via a loop or linker, or contiguous), wherein the sense and/or anti-sense strand consist of, consist essentially of, or comprise sequences of at least 15 contiguous nt with 0, 1, 2, or 3 nt or bp mismatches of, the sense and/or anti-sense strand, respectively, of any one or more of the RNAi agents disclosed in Tables 1, 2, 3, 4, 5, 6, 7, 8 and/or 9 (or any member of a group of overlapping RNAi agents from Table 4), optionally further comprising 0-10 nt or bp.

[00761] Additional Definitions

[00762] The articles "a" and "an" as used herein and in the claims refer to one or more than one (at least one) of the grammatical object of the article.

[00763] The terms "RNAi agent," "RNAi agents", "RNAi agent(s)" and the like all refer without limitation to one or more RNAi agents of the present disclosure.

[00764] The designations of particular example duplexes of RNAi agents to Beta-Catenin disclosed herein on occasion have the suffix "b" followed by a number. This indicates a batch

number. Thus, the suffix "b1" indicates "batch 1." Thus, a RNAi duplex designated, for example, "AD-18892-b1" is specifically from batch 1 and has the same sequence as any RNAi agent designated "AD-18892".

[00765] Unless defined otherwise, the technical and scientific terms used herein have the same meaning as that usually understood by a specialist familiar with the field to which the present disclosure belongs.

[00766] Unless indicated otherwise, all methods, steps, techniques and manipulations that are not specifically described in detail can be performed and have been performed in a manner known per se, as will be clear to the skilled person. Reference is for example again made to the standard handbooks and the general background art mentioned herein and to the further references cited therein.

[00767] Claims to the present disclosure are non-limiting and are provided below.

[00768] Although particular embodiments and claims have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, or the scope of subject matter of claims of any corresponding future application. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the present disclosure without departing from the spirit and scope of the present disclosure as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims. Redrafting of claim scope in later-filed corresponding applications may be due to limitations by the patent laws of various countries and should not be interpreted as giving up subject matter of the claims.

[00769] Various additional formulations and obvious variants of the described RNAi agents to Beta-Catenin can be devised by those of ordinary skill in the art. Non-limiting example RNAi agents to Beta-Catenin are described in the Examples below, which do not limit the scope of the present disclosure as described in the claims.

[00770] EXAMPLE 1

[00771] Bioinformatics and Beta-Catenin RNAi Agent (siRNA) sequences

[00772] Bioinformatics

[00773] Transcripts

[00774] RNAi agent design is carried out to identify RNAi agents targeting the human Beta-Catenin gene (CTNNB1). The design uses the CTNNB1 transcript NM_001098210.1 from the NCBI (National Center for Biotechnology Information) Refseq collection. All RNAi agent duplexes are designed with 100% identity to all three human CTNNB1 transcripts (NM_001098210.1, NM_001098209.1, and NM_001904.3).

[00775] siRNA Design and Specificity Prediction

[00776] The predicted specificity of all possible 19-mers is predicted from each sequence. The CTNNB1 RNAi agents are used in a comprehensive search against the human transcriptome (defined as the set of NM_ and XM_ records within the human NCBI Refseq set) using the FASTA algorithm. The perl script 'parseFasta.pl' is then used to parse the alignments and generate a score based on the position and number of mismatches between the siRNA and any potential 'off-target' transcript. The off-target score is weighted to emphasize differences in the 'seed' region of siRNAs, in positions 2-9 from the 5' end of the molecule. Each oligo-transcript pair from the FASTA search is given a mismatch score by summing the individual mismatch scores; mismatches in the position 2-9 are counted as 2.8, mismatches in the cleavage site positions 10-11 are counted as 1.2, and mismatches in region 12-19 counted as 1.0. An additional off-target prediction is carried out by comparing the frequency of heptamers and octomers derived from 3 distinct, seed-derived hexamers of each oligo. The hexamers from positions 2-7 relative to the 5' start is used to create 2 heptamers and one octomer. The 'heptamer1' is created by adding a 3' A to the hexamer; the heptamer2 is created by adding a 5' A to the hexamer; the octomer is created by adding an A to both 5' and 3' ends of the hexamer. The frequency of octomers and heptamers in the human 3'UTRome (defined as the subsequence of the transcriptome from NCBI's Refseq database where the end of the coding region, the 'CDS', is clearly defined) is pre-calculated. The octomer frequency is normalized to the heptamer frequency using the median value from the range of octomer frequencies. A 'mirSeedScore' is then calculated by calculating the sum of ((3 X normalized octomer count) + (2 X heptamer2 count) + (1 X heptamer1 count)).

[00777] Both RNAi agent strands are assigned to a category of specificity according to the calculated scores: a score above 3 qualifies as highly specific, equal to 3 as specific and between 2.2 and 2.8 as moderately specific. RNAi agents are sorted by the specificity of the anti-sense strand. Oligonucleotides with perfect matches to known human microRNA seed regions are excluded.

TABLE 2. RNAi Agents to Beta-Catenin: Unmodified Sequences

DUPLEX	SENSE SEQUENCE	SENSE SEQ ID NO:	ANTI-SENSE SEQUENCE	Anti-sense SEQ ID NO:	POSITION
AD-18892	UGGUGCUGACUAUCCAGUU	4771	AACUGGAUAGUCAGCACCA	5430	2500
AD-18893	CCAUCUGUGCUCUUCGUCA	4772	UGACGAAGAGCACAGAUGG	5431	1659
AD-18894	AUAAGCAGGUGGAUCUAUU	4773	AAUAGAUCCACCUGCUUAU	5432	3038
AD-18895	AUCCAAAGAGUAGCUGCAG	4774	CUGCAGCUACUCUUUGGAU	5433	2096
AD-18896	GACAAUGGCUACUCAAGCU	4775	AGCUUGAGUAGCCAUUGUC	5434	265
AD-18897	CUGUUGGAUUGAUUCGAAA	4776	UUUCGAAUCAAUCCAACAG	5435	1797
AD-18898	GCUGGCCUGGUUUGAUACU	4777	AGUAUCAAACCAGGCCAGC	5436	2587
AD-18899	UCUAACCUCACUUGCAAUA	4778	UAUUGCAAGUGAGGUUAGA	5437	1541
AD-18900	GAUAUCGCCAGGAUGAUCC	4779	GGAUCAUCCUGGCGAUAUC	5438	2391
AD-18901	UGGCCAUCUUUAAGUCUGG	4780	CCAGACUUAAAGAUGGCCA	5439	954
AD-18902	UGUAGAACACUAAUUCAUA	4781	UAUGAAUUAGUGUUCUACA	5440	2908
AD-18903	AUCAGUAAGAGGUGUUAUU	4782	AAUAACACCUCUUACUGAU	5441	3104
AD-18904	GUGCUCUUCGUCAUCUGAC	4783	GUCAGAUGACGAAGAGCAC	5442	1665
AD-18905	UGGUUUGAUACUGACCUGU	4784	ACAGGUCAGUAUCAAACCA	5443	2594
AD-18906	CCAGUUGCCUUUUAUCCCA	4785	UGGGAUAAAAGGCAACUGG	5444	3147
AD-18907	CCUGGUUUGAUACUGACCU	4786	AGGUCAGUAUCAAACCAGG	5445	2592
AD-18908	GACUAUCCAGUUGAUGGGC	4787	GCCCAUCAACUGGAUAGUC	5446	2507
AD-18909	AGCCAAUGGCUUGGAAUGA	4788	UCAUUCCAAGCCAUUGGCU	5447	2325
AD-18910	GCCAAUGGCUUGGAAUGAG	4789	CUCAUUCCAAGCCAUUGGC	5448	2326
AD-18911	AGAUGAGGGCAUGCAGAUC	4790	GAUCUGCAUGCCCUCAUCU	5449	577
AD-18912	GGUCCUCUGUGAACUUGCU	4791	AGCAAGUUCACAGAGGACC	5450	2116
AD-18913	AACCCUAGCCUUGCUUGUU	4792	AACAAGCAAGGCUAGGGUU	5451	2708
AD-18914	GAACACUAAUUCAUAAUCA	4793	UGAUUAUGAAUUAGUGUUC	5452	2912
AD-18915	AUCAAACCCUAGCCUUGCU	4794	AGCAAGGCUAGGGUUUGAU	5453	2704
AD-18916	ACCAGUUGCCUUUUAUCCC	4795	GGGAUAAAAGGCAACUGGU	5454	3146
AD-18917	CUAACCUCACUUGCAAUAA	4796	UUAUUGCAAGUGAGGUUAG	5455	1542
AD-18918	AUCCCACUAAUGUCCAGCG	4797	CGCUGGACAUUAGUGGGAU	5456	621
AD-18919	CUGACUAUCCAGUUGAUGG	4798	CCAUCAACUGGAUAGUCAG	5457	2505
AD-18920	GGCCUGGUUUGAUACUGAC	4799	GUCAGUAUCAAACCAGGCC	5458	2590
AD-18921	GGUAAAUCAGUAAGAGGUG	4800	CACCUCUUACUGAUUUACC	5459	3099
AD-18922	GCCUGGUUUGAUACUGACC	4801	GGUCAGUAUCAAACCAGGC	5460	2591
AD-18923	CAGGGGUCCUCUGUGAACU	4802	AGUUCACAGAGGACCCCUG	5461	2112
AD-18925	CUGGAAUCCAUUCUGGUGC	4803	GCACCAGAAUGGAUUCCAG	5462	366
AD-18926	UGAGAUGGGUGGCCACCAC	4804	GUGGUGGCCACCCAUCUCA	5463	2479
AD-18927	GAUGAUAUAAAUGUGGUCA	4805	UGACCACAUUUAUAUCAUC	5464	1502
AD-18928	UGCUUUAUUCUCCCAUUGA	4806	UCAAUGGGAGAAUAAAGCA	5465	2073
AD-18929	UUAUCAAACCCUAGCCUUG	4807	CAAGGCUAGGGUUUGAUAA	5466	2702

AD-18930	CCACUGGCCUCUGAUAAAG	4808	CUUUAUCAGAGGCCAGUGG	5467	1774
AD-18931	AACUUGCCACACGUGCAAU	4809	AUUGCACGUGUGGCAAGUU	5468	708
AD-18932	GCUCUUCGUCAUCUGACCA	4810	UGGUCAGAUGACGAAGAGC	5469	1667
AD-18933	GUAACAAUACAAAUGGAUU	4811	AAUCCAUUUGUAUUGUUAC	5470	2629
AD-18934	GGGGUCCUCUGUGAACUUG	4812	CAAGUUCACAGAGGACCCC	5471	2114
AD-18935	CAAACCCUAGCCUUGCUUG	4813	CAAGCAAGGCUAGGGUUUG	5472	2706
AD-18936	GAGUAAUGGUGUAGAACAC	4814	GUGUUCUACACCAUUACUC	5473	2899
AD-18937	GGAAGACAUCACUGAGCCU	4815	AGGCUCAGUGAUGUCUUCC	5474	1639
AD-18938	GGGAAGACAUCACUGAGCC	4816	GGCUCAGUGAUGUCUUCCC	5475	1638
AD-18939	GGUGUAGAACACUAAUUCA	4817	UGAAUUAGUGUUCUACACC	5476	2906
AD-18940	UACCAGUUGCCUUUUAUCC	4818	GGAUAAAAGGCAACUGGUA	5477	3145
AD-18941	GGAUAUCGCCAGGAUGAUC	4819	GAUCAUCCUGGCGAUAUCC	5478	2390
AD-18942	AAACCCUAGCCUUGCUUGU	4820	ACAAGCAAGGCUAGGGUUU	5479	2707
AD-18943	CUCUUCGUCAUCUGACCAG	4821	CUGGUCAGAUGACGAAGAG	5480	1668
AD-18944	UGACUAUCCAGUUGAUGGG	4822	CCCAUCAACUGGAUAGUCA	5481	2506
AD-18945	ACAAGCAGAGUGCUGAAGG	4823	CCUUCAGCACUCUGCUUGU	5482	1286
AD-18946	CAUCUGUGCUCUUCGUCAU	4824	AUGACGAAGAGCACAGAUG	5483	1660
AD-18947	CAAUGGCUUGGAAUGAGAC	4825	GUCUCAUUCCAAGCCAUUG	5484	2328
AD-18948	ACUGGCCUCUGAUAAAGGC	4826	GCCUUUAUCAGAGGCCAGU	5485	1776
AD-18949	UCAUCCCACUAAUGUCCAG	4827	CUGGACAUUAGUGGGAUGA	5486	619
AD-18950	AAAAGGAAGCUUCCAGACA	4828	UGUCUGGAAGCUUCCUUUU	5487	807
AD-18951	CGUUCUUUUCACUCUGGUG	4829	CACCAGAGUGAAAAGAACG	5488	2417
AD-18952	AAAGUUGUUGUAACCUGCU	4830	AGCAGGUUACAACAACUUU	5489	3165
AD-18953	ACAAUGGCUACUCAAGCUG	4831	CAGCUUGAGUAGCCAUUGU	5490	266
AD-18954	CUCAUCCCACUAAUGUCCA	4832	UGGACAUUAGUGGGAUGAG	5491	618
AD-18955	AGGGGUCCUCUGUGAACUU	4833	AAGUUCACAGAGGACCCCU	5492	2113
AD-18956	AAGCAGGUGGAUCUAUUUC	4834	GAAAUAGAUCCACCUGCUU	5493	3040
AD-18957	AAGUUGUUGUAACCUGCUG	4835	CAGCAGGUUACAACAACUU	5494	3166
AD-18958	AGCAGGUGGAUCUAUUUCA	4836	UGAAAUAGAUCCACCUGCU	5495	3041
AD-18959	AGGGCAUGCAGAUCCCAUC	4837	GAUGGGAUCUGCAUGCCCU	5496	582
AD-18960	AAAUGGUUCAGAAUUAAAC	4838	GUUUAAUUCUGAACCAUUU	5497	3220
AD-18961	UGAACUUGCUCAGGACAAG	4839	CUUGUCCUGAGCAAGUUCA	5498	2125
AD-18962	AAGAGUAGCUGCAGGGGUC	4840	GACCCCUGCAGCUACUCUU	5499	2101
AD-18963	CCCACUGGCCUCUGAUAAA	4841	UUUAUCAGAGGCCAGUGGG	5500	1773
AD-18964	CUGGCCUGGUUUGAUACUG	4842	CAGUAUCAAACCAGGCCAG	5501	2588
AD-18965	UUGAUACUGACCUGUAAAU	4843	AUUUACAGGUCAGUAUCAA	5502	2598
AD-18966	GUGUAGAACACUAAUUCAU	4844	AUGAAUUAGUGUUCUACAC	5503	2907
AD-18967	ACUAUCCAGUUGAUGGGCU	4845	AGCCCAUCAACUGGAUAGU	5504	2508
AD-18968	AAAUCAGUAAGAGGUGUUA	4846	UAACACCUCUUACUGAUUU	5505	3102
AD-18969	GCAGGUGGAUCUAUUUCAU	4847	AUGAAAUAGAUCCACCUGC	5506	3042
AD-18970	CUGGUGCUGACUAUCCAGU	4848	ACUGGAUAGUCAGCACCAG	5507	2499
AD-18971	GUGAACUUGCUCAGGACAA	4849	UUGUCCUGAGCAAGUUCAC	5508	2124
AD-18972	UCAGUAAGAGGUGUUAUUU	4850	AAAUAACACCUCUUACUGA	5509	3105

AD-18973	CCUCUGUGAACUUGCUCAG	4851	CUGAGCAAGUUCACAGAGG	5510	2119
AD-18974	UUGGCUGAACCAUCACAGA	4852	UCUGUGAUGGUUCAGCCAA	5511	641
AD-18975	UCAGCUGGCCUGGUUUGAU	4853	AUCAAACCAGGCCAGCUGA	5512	2584
AD-18976	GUAGCUGCAGGGGUCCUCU	4854	AGAGGACCCCUGCAGCUAC	5513	2105
AD-18977	AGGAGCUAAAAUGGCAGUG	4855	CACUGCCAUUUUAGCUCCU	5514	1069
AD-18978	AUGGCUUGGAAUGAGACUG	4856	CAGUCUCAUUCCAAGCCAU	5515	2330
AD-18979	UUGGAUAUCGCCAGGAUGA	4857	UCAUCCUGGCGAUAUCCAA	5516	2388
AD-18980	GGUUCAGAAUUAAACUUUU	4858	AAAAGUUUAAUUCUGAACC	5517	3224
AD-18981	GGGUAAAUCAGUAAGAGGU	4859	ACCUCUUACUGAUUUACCC	5518	3098
AD-18982	AUACCAUUCCAUUGUUUGU	4860	ACAAACAAUGGAAUGGUAU	5519	2049
AD-18983	ACUGUUGGAUUGAUUCGAA	4861	UUCGAAUCAAUCCAACAGU	5520	1796
AD-18984	AACUUGCUCAGGACAAGGA	4862	UCCUUGUCCUGAGCAAGUU	5521	2127
AD-18985	AUGCUUAAAAUAAGCAGGU	4863	ACCUGCUUAUUUUAAGCAU	5522	3029
AD-18986	GUUUGAUACUGACCUGUAA	4864	UUACAGGUCAGUAUCAAAC	5523	2596
AD-18987	AAUGGUUCAGAAUUAAACU	4865	AGUUUAAUUCUGAACCAUU	5524	3221
AD-18988	UAUCCCAAAGUUGUUGUAA	4866	UUACAACAACUUUGGGAUA	5525	3159
AD-18989	AUCAGCUGGCCUGGUUUGA	4867	UCAAACCAGGCCAGCUGAU	5526	2583
AD-18990	CCUGCCAUCUGUGCUCUUC	4868	GAAGAGCACAGAUGGCAGG	5527	1655
AD-18991	GCAGAAUACAAAUGAUGUA	4869	UACAUCAUUUGUAUUCUGC	5528	874
AD-18992	UAUGCUUAAAAUAAGCAGG	4870	CCUGCUUAUUUUAAGCAUA	5529	3028
AD-18993	AAUAAGCAGGUGGAUCUAU	4871	AUAGAUCCACCUGCUUAUU	5530	3037
AD-18994	UGAUAUAAAUGUGGUCACC	4872	GGUGACCACAUUUAUAUCA	5531	1504
AD-18995	GUAGGGUAAAUCAGUAAGA	4873	UCUUACUGAUUUACCCUAC	5532	3095
AD-18996	UAUCAAACCCUAGCCUUGC	4874	GCAAGGCUAGGGUUUGAUA	5533	2703
AD-18997	CCUUUUAUCCCAAAGUUGU	4875	ACAACUUUGGGAUAAAAGG	5534	3154
AD-18998	GGUAGGGUAAAUCAGUAAG	4876	CUUACUGAUUUACCCUACC	5535	3094
AD-18999	UGAUACUGACCUGUAAAUC	4877	GAUUUACAGGUCAGUAUCA	5536	2599
AD-19000	GGCUGAACCAUCACAGAUG	4878	CAUCUGUGAUGGUUCAGCC	5537	643
AD-19001	UGGAUAUCGCCAGGAUGAU	4879	AUCAUCCUGGCGAUAUCCA	5538	2389
AD-19002	UCUUCGUCAUCUGACCAGC	4880	GCUGGUCAGAUGACGAAGA	5539	1669
AD-19003	UAGCUGCAGGGGUCCUCUG	4881	CAGAGGACCCCUGCAGCUA	5540	2106
AD-19004	UGUUGUAACCUGCUGUGAU	4882	AUCACAGCAGGUUACAACA	5541	3170
AD-19005	AAUCAGUAAGAGGUGUUAU	4883	AUAACACCUCUUACUGAUU	5542	3103
AD-19006	UGGCUGAACCAUCACAGAU	4884	AUCUGUGAUGGUUCAGCCA	5543	642
AD-19007	GAAUUAAACUUUUAAUUCA	4885	UGAAUUAAAAGUUUAAUUC	5544	3230
AD-19008	AUGGUUCAGAAUUAAACUU	4886	AAGUUUAAUUCUGAACCAU	5545	3222
AD-19009	UGGUGUAGAACACUAAUUC	4887	GAAUUAGUGUUCUACACCA	5546	2905
AD-19010	AUGGUGUAGAACACUAAUU	4888	AAUUAGUGUUCUACACCAU	5547	2904
AD-19011	AUGAGGGCAUGCAGAUCCC	4889	GGGAUCUGCAUGCCCUCAU	5548	579
AD-19012	GUUGUAACCUGCUGUGAUA	4890	UAUCACAGCAGGUUACAAC	5549	3171
AD-19042	GCUGACUAUCCAGUUGAUG	4891	CAUCAACUGGAUAGUCAGC	5550	2504
AD-19043	UAAGCAGGUGGAUCUAUUU	4892	AAAUAGAUCCACCUGCUUA	5551	3039
AD-19044	UAAAAUAAGCAGGUGGAUC	4893	GAUCCACCUGCUUAUUUUA	5552	3034

AD-19045	GAUAUAAAUGUGGUCACCU	4894	AGGUGACCACAUUUAUAUC	5553	1505
AD-19046	AAGCAGAGUGCUGAAGGUG	4895	CACCUUCAGCACUCUGCUU	5554	1288
AD-19047	UGUGAACUUGCUCAGGACA	4896	UGUCCUGAGCAAGUUCACA	5555	2123
AD-19048	CAUCCCACUAAUGUCCAGC	4897	GCUGGACAUUAGUGGGAUG	5556	620
AD-19049	CAAAGUUGUUGUAACCUGC	4898	GCAGGUUACAACAACUUUG	5557	3164
AD-19050	UAAAUCAGUAAGAGGUGUU	4899	AACACCUCUUACUGAUUUA	5558	3101
AD-19051	AAUGGCUUGGAAUGAGACU	4900	AGUCUCAUUCCAAGCCAUU	5559	2329
AD-19052	GGGUCCUCUGUGAACUUGC	4901	GCAAGUUCACAGAGGACCC	5560	2115
AD-19053	GAGUAACAAUACAAAUGGA	4902	UCCAUUUGUAUUGUUACUC	5561	2627
AD-19054	UAAUGGUGUAGAACACUAA	4903	UUAGUGUUCUACACCAUUA	5562	2902
AD-19055	GUGGACAAUGGCUACUCAA	4904	UUGAGUAGCCAUUGUCCAC	5563	262
AD-19056	AACUGUCUUUGGACUCUCA	4905	UGAGAGUCCAAAGACAGUU	5564	1406
AD-19057	CCCUGGUGCUGACUAUCCA	4906	UGGAUAGUCAGCACCAGGG	5565	2497
AD-19058	CAGGUGGAUCUAUUUCAUG	4907	CAUGAAAUAGAUCCACCUG	5566	3043
AD-19059	UGGCCUGGUUUGAUACUGA	4908	UCAGUAUCAAACCAGGCCA	5567	2589
AD-19060	AGCUGGCCUGGUUUGAUAC	4909	GUAUCAAACCAGGCCAGCU	5568	2586
AD-19061	GCCAUCUGUGCUCUUCGUC	4910	GACGAAGAGCACAGAUGGC	5569	1658
AD-19062	UACCAUUCCAUUGUUUGUG	4911	CACAAACAAUGGAAUGGUA	5570	2050
AD-19063	CCCUUGGAUAUCGCCAGGA	4912	UCCUGGCGAUAUCCAAGGG	5571	2385
AD-19064	AGGGAAGACAUCACUGAGC	4913	GCUCAGUGAUGUCUUCCCU	5572	1637
AD-19065	GAACUUGCCACACGUGCAA	4914	UUGCACGUGUGGCAAGUUC	5573	707
AD-19066	UUUGAUACUGACCUGUAAA	4915	UUUACAGGUCAGUAUCAAA	5574	2597
AD-19067	UCCCAAAGUUGUUGUAACC	4916	GGUUACAACAACUUUGGGA	5575	3161
AD-19068	CAGAAUACAAAUGAUGUAG	4917	CUACAUCAUUUGUAUUCUG	5576	875
AD-19069	AGGUGGAUCUAUUUCAUGU	4918	ACAUGAAAUAGAUCCACCU	5577	3044
AD-19070	GCUCAUCCCACUAAUGUCC	4919	GGACAUUAGUGGGAUGAGC	5578	617
AD-19071	CCUGGUGCUGACUAUCCAG	4920	CUGGAUAGUCAGCACCAGG	5579	2498
AD-19072	UGGAAUCCAUUCUGGUGCC	4921	GGCACCAGAAUGGAUUCCA	5580	367
AD-19073	CCAGGACCUCAUGGAUGGG	4922	CCCAUCCAUGAGGUCCUGG	5581	2545
AD-19074	AACCUCACUUGCAAUAAUU	4923	AAUUAUUGCAAGUGAGGUU	5582	1544
AD-19075	CAGUUGCCUUUUAUCCCAA	4924	UUGGGAUAAAAGGCAACUG	5583	3148
AD-19076	GUAGAACACUAAUUCAUAA	4925	UUAUGAAUUAGUGUUCUAC	5584	2909
AD-19077	CUAUCCAGUUGAUGGGCUG	4926	CAGCCCAUCAACUGGAUAG	5585	2509
AD-19078	CACUGGCCUCUGAUAAAGG	4927	CCUUUAUCAGAGGCCAGUG	5586	1775
AD-19079	ACUGUCUUUGGACUCUCAG	4928	CUGAGAGUCCAAAGACAGU	5587	1407
AD-19080	CCAAUGGCUUGGAAUGAGA	4929	UCUCAUUCCAAGCCAUUGG	5588	2327
AD-19081	GCUUAAAAUAAGCAGGUGG	4930	CCACCUGCUUAUUUUAAGC	5589	3031
AD-19082	AUCUGUGCUCUUCGUCAUC	4931	GAUGACGAAGAGCACAGAU	5590	1661
AD-19083	CCCAAAGUUGUUGUAACCU	4932	AGGUUACAACAACUUUGGG	5591	3162
AD-19738	UACCCAGCGCCGUACGUCC	4933	GGACGUACGGCGCUGGGUA	5592	1906
AD-19739	ACGCUAUCAUGCGUUCUCC	4934	GGAGAACGCAUGAUAGCGU	5593	825
AD-19740	CAUGCACCUUUGCGUGAGC	4935	GCUCACGCAAAGGUGCAUG	5594	1838
AD-19741	GAAUGCAGUUCGCCUUCAC	4936	GUGAAGGCGAACUGCAUUC	5595	1714

AD-19742	GGUGCCAUUCCACGACUAG	4937	CUAGUCGUGGAAUGGCACC	5596	1859
AD-19743	AAGCGGCUGUUAGUCACUG	4938	CAGUGACUAACAGCCGCUU	5597	324
AD-19744	UCGAGCUCAGAGGGUACGA	4939	UCGUACCCUCUGAGCUCGA	5598	535
AD-19745	GACACGCUAUCAUGCGUUC	4940	GAACGCAUGAUAGCGUGUC	5599	822
AD-19746	CGCUAUCAUGCGUUCUCCU	4941	AGGAGAACGCAUGAUAGCG	5600	826
AD-19747	GUGUCUGCUAUUGUACGUA	4942	UACGUACAAUAGCAGACAC	5601	851
AD-19748	GUCUGCUCUAGUAAUAAGC	4943	GCUUAUUACUAGAGCAGAC	5602	1313
AD-19749	GUGCCAUUCCACGACUAGU	4944	ACUAGUCGUGGAAUGGCAC	5603	1860
AD-19750	AUGUUCACAACCGAAUUGU	4945	ACAAUUCGGUUGUGAACAU	5604	2016
AD-19751	CCACGACUAGUUCAGUUGC	4946	GCAACUGAACUAGUCGUGG	5605	1868
AD-19752	CACGACUAGUUCAGUUGCU	4947	AGCAACUGAACUAGUCGUG	5606	1869
AD-19753	AGUUCAGUUGCUUGUUCGU	4948	ACGAACAAGCAACUGAACU	5607	1876
AD-19754	CCCAGCGCCGUACGUCCAU	4949	AUGGACGUACGGCGCUGGG	5608	1908
AD-19755	GAGUUACUUCACUCUAGGA	4950	UCCUAGAGUGAAGUAACUC	5609	2192
AD-19756	ACAGUAUGCAAUGACUCGA	4951	UCGAGUCAUUGCAUACUGU	5610	520
AD-19757	UAUGCAAUGACUCGAGCUC	4952	GAGCUCGAGUCAUUGCAUA	5611	524
AD-19758	CCCACUAAUGUCCAGCGUU	4953	AACGCUGGACAUUAGUGGG	5612	623
AD-19759	GACCUUGCAUAACCUUUCC	4954	GGAAAGGUUAUGCAAGGUC	5613	916
AD-19760	UAUUACGACAGACUGCCUU	4955	AAGGCAGUCUGUCGUAAUA	5614	1153
AD-19761	AUCUGACCAGCCGACACCA	4956	UGGUGUCGGCUGGUCAGAU	5615	1677
AD-19762	CAUUCCACGACUAGUUCAG	4957	CUGAACUAGUCGUGGAAUG	5616	1864
AD-19763	GUUUUGAAAAUCCAGCGUG	4958	CACGCUGGAUUUUCAAAAC	5617	246
AD-19765	GCGUUUGGCUGAACCAUCA	4959	UGAUGGUUCAGCCAAACGC	5618	637
AD-19766	ACACGCUAUCAUGCGUUCU	4960	AGAACGCAUGAUAGCGUGU	5619	823
AD-19767	UAUGCCAUUACAACUCUCC	4961	GGAGAGUUGUAAUGGCAUA	5620	1028
AD-19768	UCUGCUCUAGUAAUAAGCC	4962	GGCUUAUUACUAGAGCAGA	5621	1314
AD-20124	CGGGAUGUUCACAACCGAA	4963	UUCGGUUGUGAACAUCCCG	5622	2012
AD-25889	ACAAUACAAAUGGAUUUUG	4964	CAAAAUCCAUUUGUAUUGU	5623	2632
AD-25890	ACAAAUGGAUUUUGGGAGU	4965	ACUCCCAAAAUCCAUUUGU	5624	2637
AD-25891	UUGGGAGUGACUCAAGAAG	4966	CUUCUUGAGUCACUCCCAA	5625	2648
AD-25892	UGGGAGUGACUCAAGAAGU	4967	ACUUCUUGAGUCACUCCCA	5626	2649
AD-25893	GAAGUGAAGAAUGCACAAG	4968	CUUGUGCAUUCUUCACUUC	5627	2663
AD-25894	AAGUGAAGAAUGCACAAGA	4969	UCUUGUGCAUUCUUCACUU	5628	2664
AD-25895	GAUGGAAUUUAUCAAACCC	4970	GGGUUUGAUAAAUUCCAUC	5629	2694
AD-25896	AUGGAAUUUAUCAAACCCU	4971	AGGGUUUGAUAAAUUCCAU	5630	2695
AD-25897	GGAAUUUAUCAAACCCUAG	4972	CUAGGGUUUGAUAAAUUCC	5631	2697
AD-25898	GAAUUUAUCAAACCCUAGC	4973	GCUAGGGUUUGAUAAAUUC	5632	2698
AD-25899	AAUUUAUCAAACCCUAGCC	4974	GGCUAGGGUUUGAUAAAUU	5633	2699
AD-25900	GAAUAUCUGUAAUGGUACU	4975	AGUACCAUUACAGAUAUUC	5634	2751
AD-25901	AAUAUCUGUAAUGGUACUG	4976	CAGUACCAUUACAGAUAUU	5635	2752
AD-25902	AUAUCUGUAAUGGUACUGA	4977	UCAGUACCAUUACAGAUAU	5636	2753
AD-25903	UUUUAAGUCUCUCGUAGUG	4978	CACUACGAGAGACUUAAAA	5637	2832
AD-25904	UUUAAGUCUCUCGUAGUGU	4979	ACACUACGAGAGACUUAAA	5638	2833

AD-25905	AGUCUCUCGUAGUGUUAAG	4980	CUUAACACUACGAGAGACU	5639	2837
AD-25906	UCGUAGUGUUAAGUUAUAG	4981	CUAUAACUUAACACUACGA	5640	2843
AD-25907	CGUAGUGUUAAGUUAUAGU	4982	ACUAUAACUUAACACUACG	5641	2844
AD-25908	GUAGUGUUAAGUUAUAGUG	4983	CACUAUAACUUAACACUAC	5642	2845
AD-25909	UAGUGUUAAGUUAUAGUGA	4984	UCACUAUAACUUAACACUA	5643	2846
AD-25910	UAGUGAAUACUGCUACAGC	4985	GCUGUAGCAGUAUUCACUA	5644	2859
AD-25911	AACACUAAUUCAUAAUCAC	4986	GUGAUUAUGAAUUAGUGUU	5645	2913
AD-25912	ACACUAAUUCAUAAUCACU	4987	AGUGAUUAUGAAUUAGUGU	5646	2914
AD-25913	UAAUUGUAAUCUGAAUAAA	4988	UUUAUUCAGAUUACAAUUA	5647	2938
AD-25914	AUUGUAAUCUGAAUAAAGU	4989	ACUUUAUUCAGAUUACAAU	5648	2940
AD-25915	UUGUAAUCUGAAUAAAGUG	4990	CACUUUAUUCAGAUUACAA	5649	2941
AD-25916	UGUAAUCUGAAUAAAGUGU	4991	ACACUUUAUUCAGAUUACA	5650	2942
AD-25917	GACAAAUAGAAAAUGGUCC	4992	GGACCAUUUUCUAUUUGUC	5651	2991
AD-25918	ACAAAUAGAAAAUGGUCCA	4993	UGGACCAUUUUCUAUUUGU	5652	2992
AD-25919	UAGAAAAUGGUCCAAUUAG	4994	CUAAUUGGACCAUUUUCUA	5653	2997
AD-25920	AGAAAAUGGUCCAAUUAGU	4995	ACUAAUUGGACCAUUUUCU	5654	2998
AD-25921	UAUUUGGGAUAUGUAUGGG	4996	CCCAUACAUAUCCCAAAUA	5655	3077
AD-25922	AUUUGGGAUAUGUAUGGGU	4997	ACCCAUACAUAUCCCAAAU	5656	3078
AD-25923	UUGGGAUAUGUAUGGGUAG	4998	CUACCCAUACAUAUCCCAA	5657	3080
AD-25924	GGAUAUGUAUGGGUAGGGU	4999	ACCCUACCCAUACAUAUCC	5658	3083
AD-25925	AAGAGGUGUUAUUUGGAAC	5000	GUUCCAAAUAACACCUCUU	5659	3110
AD-25926	AGAGGUGUUAUUUGGAACC	5001	GGUUCCAAAUAACACCUCU	5660	3111
AD-25927	GAGGUGUUAUUUGGAACCU	5002	AGGUUCCAAAUAACACCUC	5661	3112
AD-25928	UGGAACCUUGUUUUGGACA	5003	UGUCCAAAACAAGGUUCCA	5662	3123
AD-25929	GGAACCUUGUUUUGGACAG	5004	CUGUCCAAAACAAGGUUCC	5663	3124
AD-25930	GAACCUUGUUUUGGACAGU	5005	ACUGUCCAAAACAAGGUUC	5664	3125
AD-25931	GUUUUGGACAGUUUACCAG	5006	CUGGUAAACUGUCCAAAAC	5665	3132
AD-25932	UUUUGGACAGUUUACCAGU	5007	ACUGGUAAACUGUCCAAAA	5666	3133
AD-25933	UUGGACAGUUUACCAGUUG	5008	CAACUGGUAAACUGUCCAA	5667	3135
AD-25934	GUUGUUGUAACCUGCUGUG	5009	CACAGCAGGUUACAACAAC	5668	3168
AD-25935	UUGUUGUAACCUGCUGUGA	5010	UCACAGCAGGUUACAACAA	5669	3169
AD-25936	UUGUAACCUGCUGUGAUAC	5011	GUAUCACAGCAGGUUACAA	5670	3172
AD-25937	AUGCUUCAAGAGAAAAUGC	5012	GCAUUUUCUCUUGAAGCAU	5671	3192
AD-25938	AGUGAAGAAUGCACAAGAA	5013	UUCUUGUGCAUUCUUCACU	5672	2665
AD-25939	AAUGGAUCACAAGAUGGAA	5014	UUCCAUCUUGUGAUCCAUU	5673	2682
AD-25940	AUGGAUCACAAGAUGGAAU	5015	AUUCCAUCUUGUGAUCCAU	5674	2683
AD-25941	UGGAUCACAAGAUGGAAUU	5016	AAUUCCAUCUUGUGAUCCA	5675	2684
AD-25942	GGAUCACAAGAUGGAAUUU	5017	AAAUUCCAUCUUGUGAUCC	5676	2685
AD-25943	GAUCACAAGAUGGAAUUUA	5018	UAAAUUCCAUCUUGUGAUC	5677	2686
AD-25944	AUCACAAGAUGGAAUUUAU	5019	AUAAAUUCCAUCUUGUGAU	5678	2687
AD-25945	UGGAAUUUAUCAAACCCUA	5020	UAGGGUUUGAUAAAUUCCA	5679	2696
AD-25946	ACCCUAGCCUUGCUUGUUA	5021	UAACAAGCAAGGCUAGGGU	5680	2709
AD-25947	CCCUAGCCUUGCUUGUUAA	5022	UUAACAAGCAAGGCUAGGG	5681	2710

AD-25948	CCUAGCCUUGCUUGUUAAA	5023	UUUAACAAGCAAGGCUAGG	5682	2711
AD-25949	CUAGCCUUGCUUGUUAAAU	5024	AUUUAACAAGCAAGGCUAG	5683	2712
AD-25950	UAGCCUUGCUUGUUAAAUU	5025	AAUUUAACAAGCAAGGCUA	5684	2713
AD-25951	AGCCUUGCUUGUUAAAUUU	5026	AAAUUUAACAAGCAAGGCU	5685	2714
AD-25952	UUAAGUCUCUCGUAGUGUU	5027	AACACUACGAGAGACUUAA	5686	2834
AD-25953	UAAGUCUCUCGUAGUGUUA	5028	UAACACUACGAGAGACUUA	5687	2835
AD-25954	AAGUCUCUCGUAGUGUUAA	5029	UUAACACUACGAGAGACUU	5688	2836
AD-25955	CUCGUAGUGUUAAGUUAUA	5030	UAUAACUUAACACUACGAG	5689	2842
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AD-25957	GUGUUAAGUUAUAGUGAAU	5032	AUUCACUAUAACUUAACAC	5691	2848
AD-25958	CUACAGCAAUUUCUAAUUU	5033	AAAUUAGAAAUUGCUGUAG	5692	2871
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AD-25960	AUAGAAAAUGGUCCAAUUA	5035	UAAUUGGACCAUUUUCUAU	5694	2996
AD-25961	UUUGGGAUAUGUAUGGGUA	5036	UACCCAUACAUAUCCCAAA	5695	3079
AD-25962	GAUAUGUAUGGGUAGGGUA	5037	UACCCUACCCAUACAUAUC	5696	3084
AD-25963	UGGGUAGGGUAAAUCAGUA	5038	UACUGAUUUACCCUACCCA	5697	3092
AD-25964	UAAGAGGUGUUAUUUGGAA	5039	UUCCAAAUAACACCUCUUA	5698	3109
AD-26017	UGCCUUUUAUCCCAAAGUU	5040	AACUUUGGGAUAAAAGGCA	5699	3152
AD-26018	UGUUGUAACCUGCUGUGAU	5041	AUCACAGCAGGUUACAACA	5700	3170
AD-26019	GUUGUAACCUGCUGUGAUA	5042	UAUCACAGCAGGUUACAAC	5701	3171
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AD-26021	AAGAGAAAAUGCGGUUAUA	5044	UAUAACCGCAUUUUCUCUU	5703	3199
AD-26022	CCUGUUCCCCUGAGGGUAU	5045	AUACCCUCAGGGGAACAGG	5704	207
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AD-26024	CCUGAGGGUAUUUGAAGUA	5047	UACUUCAAAUACCCUCAGG	5706	215
AD-26025	CUGAGGGUAUUUGAAGUAU	5048	AUACUUCAAAUACCCUCAG	5707	216
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AD-26027	GGUAUUUGAAGUAUACCAU	5050	AUGGUAUACUUCAAAUACC	5709	221
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AD-26030	AGUAUACCAUACAACUGUU	5053	AACAGUUGUAUGGUAUACU	5712	230
AD-26031	GUAUACCAUACAACUGUUU	5054	AAACAGUUGUAUGGUAUAC	5713	231
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AD-26033	ACCAUACAACUGUUUUGAA	5056	UUCAAAACAGUUGUAUGGU	5715	235
AD-26034	CCAUACAACUGUUUUGAAA	5057	UUUCAAAACAGUUGUAUGG	5716	236
AD-26035	GAAAAUCCAGCGUGGACAA	5058	UUGUCCACGCUGGAUUUUC	5717	251
AD-26036	AAAAUCCAGCGUGGACAAU	5059	AUUGUCCACGCUGGAUUUU	5718	252
AD-26037	CCAGCGUGGACAAUGGCUA	5060	UAGCCAUUGUCCACGCUGG	5719	257
AD-26038	GUGGACAAUGGCUACUCAA	5061	UUGAGUAGCCAUUGUCCAC	5720	262
AD-26039	AAUGGCUACUCAAGCUGAU	5062	AUCAGCUUGAGUAGCCAUU	5721	268
AD-26040	AUGGCUACUCAAGCUGAUU	5063	AAUCAGCUUGAGUAGCCAU	5722	269
AD-26041	UGGCUACUCAAGCUGAUUU	5064	AAAUCAGCUUGAGUAGCCA	5723	270
AD-26042	CUACUCAAGCUGAUUUGAU	5065	AUCAAAUCAGCUUGAGUAG	5724	273

AD-26043	AUUUGAUGGAGUUGGACAU	5066	AUGUCCAACUCCAUCAAAU	5725	285
AD-26044	UGGAGUUGGACAUGGCCAU	5067	AUGGCCAUGUCCAACUCCA	5726	291
AD-26045	GUUGGACAUGGCCAUGGAA	5068	UUCCAUGGCCAUGUCCAAC	5727	295
AD-26046	GCCAUGGAACCAGACAGAA	5069	UUCUGUCUGGUUCCAUGGC	5728	305
AD-26047	CAUGGAACCAGACAGAAAA	5070	UUUUCUGUCUGGUUCCAUG	5729	307
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AD-26049	AGACAGAAAAGCGGCUGUU	5072	AACAGCCGCUUUUCUGUCU	5731	316
AD-26050	GACAGAAAAGCGGCUGUUA	5073	UAACAGCCGCUUUUCUGUC	5732	317
AD-26051	UGUUAGUCACUGGCAGCAA	5074	UUGCUGCCAGUGACUAACA	5733	331
AD-26052	CACUGGCAGCAACAGUCUU	5075	AAGACUGUUGCUGCCAGUG	5734	338
AD-26053	ACUGGCAGCAACAGUCUUA	5076	UAAGACUGUUGCUGCCAGU	5735	339
AD-26054	UCUUACCUGGACUCUGGAA	5077	UUCCAGAGUCCAGGUAAGA	5736	353
AD-26055	CUUACCUGGACUCUGGAAU	5078	AUUCCAGAGUCCAGGUAAG	5737	354
AD-26056	CCUGGACUCUGGAAUCCAU	5079	AUGGAUUCCAGAGUCCAGG	5738	358
AD-26057	GGCUAGUGGUGGACCCCAA	5080	UUGGGGUCCACCACUAGCC	5739	1216
AD-26058	GCCACUACCACAGCUCCUU	5081	AAGGAGCUGUGGUAGUGGC	5740	383
AD-26059	UCCUUCUCUGAGUGGUAAA	5082	UUUACCACUCAGAGAAGGA	5741	397
AD-26060	CUCUGAGUGGUAAAGGCAA	5083	UUGCCUUUACCACUCAGAG	5742	402
AD-26061	UAAAGGCAAUCCUGAGGAA	5084	UUCCUCAGGAUUGCCUUUA	5743	412
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AD-26065	UACCUCCCAAGUCCUGUAU	5088	AUACAGGACUUGGGAGGUA	5747	442
AD-26066	AGUCCUGUAUGAGUGGGAA	5089	UUCCCACUCAUACAGGACU	5748	451
AD-26067	UAUGAGUGGGAACAGGGAU	5090	AUCCCUGUUCCCACUCAUA	5749	458
AD-26068	CAAGCUUUAGUAAAUAUAA	5091	UUAUAUUUACUAAAGCUUG	5750	1232
AD-26069	AAGCUUUAGUAAAUAUAAU	5092	AUUAUAUUUACUAAAGCUU	5751	1233
AD-26070	UGAGUGGGAACAGGGAUUU	5093	AAAUCCCUGUUCCCACUCA	5752	460
AD-26071	GAGUGGGAACAGGGAUUUU	5094	AAAAUCCCUGUUCCCACUC	5753	461
AD-26072	AGGGAUUUUCUCAGUCCUU	5095	AAGGACUGAGAAAAUCCCU	5754	471
AD-26073	UUCUCAGUCCUUCACUCAA	5096	UUGAGUGAAGGACUGAGAA	5755	478
AD-26074	UCAGUCCUUCACUCAAGAA	5097	UUCUUGAGUGAAGGACUGA	5756	481
AD-26075	CUUCACUCAAGAACAAGUA	5098	UACUUGUUCUUGAGUGAAG	5757	487
AD-26076	UCAAGAACAAGUAGCUGAU	5099	AUCAGCUACUUGUUCUUGA	5758	493
AD-26077	CUGAUAUUGAUGGACAGUA	5100	UACUGUCCAUCAAUAUCAG	5759	507
AD-26078	AUUGAUGGACAGUAUGCAA	5101	UUGCAUACUGUCCAUCAAU	5760	512
AD-26079	GACUCGAGCUCAGAGGGUA	5102	UACCCUCUGAGCUCGAGUC	5761	532
AD-26080	CAGAGGGUACGAGCUGCUA	5103	UAGCAGCUCGUACCCUCUG	5762	542
AD-26081	AGAGGGUACGAGCUGCUAU	5104	AUAGCAGCUCGUACCCUCU	5763	543
AD-26082	GGGUACGAGCUGCUAUGUU	5105	AACAUAGCAGCUCGUACCC	5764	546
AD-26083	CUAUGUUCCCUGAGACAUU	5106	AAUGUCUCAGGGAACAUAG	5765	558
AD-26084	UAUGUUCCCUGAGACAUUA	5107	UAAUGUCUCAGGGAACAUA	5766	559
AD-26085	GUUCCCUGAGACAUUAGAU	5108	AUCUAAUGUCUCAGGGAAC	5767	562

AD-26086	UAGAUGAGGGCAUGCAGAU	5109	AUCUGCAUGCCCUCAUCUA	5768	576
AD-26087	GAGGGCAUGCAGAUCCCAU	5110	AUGGGAUCUGCAUGCCCUC	5769	581
AD-26088	GGCAUGCAGAUCCCAUCUA	5111	UAGAUGGGAUCUGCAUGCC	5770	584
AD-26089	AGAUCCCAUCUACACAGUU	5112	AACUGUGUAGAUGGGAUCU	5771	591
AD-26090	CCCAUCUACACAGUUUGAU	5113	AUCAAACUGUGUAGAUGGG	5772	595
AD-26091	ACAGUUUGAUGCUGCUCAU	5114	AUGAGCAGCAUCAAACUGU	5773	604
AD-26092	GAUGCUGCUCAUCCCACUA	5115	UAGUGGGAUGAGCAGCAUC	5774	611
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AD-26094	UGCUGCUCAUCCCACUAAU	5117	AUUAGUGGGAUGAGCAGCA	5776	613
AD-26095	CCCACUAAUGUCCAGCGUU	5118	AACGCUGGACAUUAGUGGG	5777	623
AD-26096	CAGCGUUUGGCUGAACCAU	5119	AUGGUUCAGCCAAACGCUG	5778	635
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AD-26099	ACCAUCACAGAUGCUGAAA	5122	UUUCAGCAUCUGUGAUGGU	5781	649
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AD-26104	AUGCAGUUGUAAACUUGAU	5127	AUCAAGUUUACAACUGCAU	5786	669
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AD-26111	AACUUGCCACACGUGCAAU	5134	AUUGCACGUGUGGCAAGUU	5793	708
AD-26112	CACACGUGCAAUCCCUGAA	5135	UUCAGGGAUUGCACGUGUG	5794	715
AD-26123	GCAAUCCCUGAACUGACAA	5136	UUGUCAGUUCAGGGAUUGC	5795	722
AD-26124	CAAUCCCUGAACUGACAAA	5137	UUUGUCAGUUCAGGGAUUG	5796	723
AD-26125	AAUCCCUGAACUGACAAAA	5138	UUUUGUCAGUUCAGGGAUU	5797	724
AD-26126	UGAACUGACAAAACUGCUA	5139	UAGCAGUUUUGUCAGUUCA	5798	730
AD-26127	GAACUGACAAAACUGCUAA	5140	UUAGCAGUUUUGUCAGUUC	5799	731
AD-26128	AACUGACAAAACUGCUAAA	5141	UUUAGCAGUUUUGUCAGUU	5800	732
AD-26129	ACUGACAAAACUGCUAAAU	5142	AUUUAGCAGUUUUGUCAGU	5801	733
AD-26130	GAGGACCAGGUGGUGGUUA	5143	UAACCACCACCUGGUCCUC	5802	755
AD-26131	AGGACCAGGUGGUGGUUAA	5144	UUAACCACCACCUGGUCCU	5803	756
AD-26132	GGACCAGGUGGUGGUUAAU	5145	AUUAACCACCACCUGGUCC	5804	757
AD-26133	GACCAGGUGGUGGUUAAUA	5146	UAUUAACCACCACCUGGUC	5805	758
AD-26134	UCACUUGCAAUAAUUAUAA	5147	UUAUAAUUAUUGCAAGUGA	5806	1548
AD-26135	CUUGCAAUAAUUAUAAGAA	5148	UUCUUAUAAUUAUUGCAAG	5807	1551
AD-26136	ACCAGGUGGUGGUUAAUAA	5149	UUAUUAACCACCACCUGGU	5808	759
AD-26137	GGCUGCAGUUAUGGUCCAU	5150	AUGGACCAUAACUGCAGCC	5809	778
AD-26138	GUUAUGGUCCAUCAGCUUU	5151	AAAGCUGAUGGACCAUAAC	5810	785

AD-26139	AUGGUCCAUCAGCUUUCUA	5152	UAGAAAGCUGAUGGACCAU	5811	788
AD-26140	UGGUCCAUCAGCUUUCUAA	5153	UUAGAAAGCUGAUGGACCA	5812	789
AD-26141	UCGGGCUGGUGACAGGGAA	5154	UUCCCUGUCACCAGCCCGA	5813	1624
AD-26142	GGUCCAUCAGCUUUCUAAA	5155	UUUAGAAAGCUGAUGGACC	5814	790
AD-26143	GUCCAUCAGCUUUCUAAAA	5156	UUUUAGAAAGCUGAUGGAC	5815	791
AD-26144	GAAGCUUCCAGACACGCUA	5157	UAGCGUGUCUGGAAGCUUC	5816	812
AD-26145	AAGCUUCCAGACACGCUAU	5158	AUAGCGUGUCUGGAAGCUU	5817	813
AD-26146	CUUCCAGACACGCUAUCAU	5159	AUGAUAGCGUGUCUGGAAG	5818	816
AD-26147	AGACACGCUAUCAUGCGUU	5160	AACGCAUGAUAGCGUGUCU	5819	821
AD-26148	UCAUGCGUUCUCCUCAGAU	5161	AUCUGAGGAGAACGCAUGA	5820	831
AD-26149	CCUCAGAUGGUGUCUGCUA	5162	UAGCAGACACCAUCUGAGG	5821	842
AD-26150	CUCAGAUGGUGUCUGCUAU	5163	AUAGCAGACACCAUCUGAG	5822	843
AD-26151	GUGUCUGCUAUUGUACGUA	5164	UACGUACAAUAGCAGACAC	5823	851
AD-26152	CUGCUAUUGUACGUACCAU	5165	AUGGUACGUACAAUAGCAG	5824	855
AD-26153	UUGUACGUACCAUGCAGAA	5166	UUCUGCAUGGUACGUACAA	5825	861
AD-26154	UGUACGUACCAUGCAGAAU	5167	AUUCUGCAUGGUACGUACA	5826	862
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AD-26156	CAUGCAGAAUACAAAUGAU	5169	AUCAUUUGUAUUCUGCAUG	5828	871
AD-26157	GCAGAAUACAAAUGAUGUA	5170	UACAUCAUUUGUAUUCUGC	5829	874
AD-26158	GAAUACAAAUGAUGUAGAA	5171	UUCUACAUCAUUUGUAUUC	5830	877
AD-26159	GAUGUAGAAACAGCUCGUU	5172	AACGAGCUGUUUCUACAUC	5831	887
AD-26160	GUUGUACCGCUGGGACCUU	5173	AAGGUCCCAGCGGUACAAC	5832	903
AD-26161	UACCGCUGGGACCUUGCAU	5174	AUGCAAGGUCCCAGCGGUA	5833	907
AD-26162	CCGCUGGGACCUUGCAUAA	5175	UUAUGCAAGGUCCCAGCGG	5834	909
AD-26163	UGGGACCUUGCAUAACCUU	5176	AAGGUUAUGCAAGGUCCCA	5835	913
AD-26164	GGGACCUUGCAUAACCUUU	5177	AAAGGUUAUGCAAGGUCCC	5836	914
AD-26165	CUUGCAUAACCUUUCCCAU	5178	AUGGGAAAGGUUAUGCAAG	5837	919
AD-26166	UCUUUAAGUCUGGAGGCAU	5179	AUGCCUCCAGACUUAAAGA	5838	960
AD-26167	GCAUUCCUGCCCUGGUGAA	5180	UUCACCAGGGCAGGAAUGC	5839	975
AD-26168	CAUUCCUGCCCUGGUGAAA	5181	UUUCACCAGGGCAGGAAUG	5840	976
AD-26169	AUUCCUGCCCUGGUGAAAA	5182	UUUUCACCAGGGCAGGAAU	5841	977
AD-26170	UUCCUGCCCUGGUGAAAAU	5183	AUUUUCACCAGGGCAGGAA	5842	978
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AD-26172	CUGGUGAAAAUGCUUGGUU	5185	AACCAAGCAUUUUCACCAG	5844	986
AD-26173	GCUUGGUUCACCAGUGGAU	5186	AUCCACUGGUGAACCAAGC	5845	997
AD-26174	CUUGGUUCACCAGUGGAUU	5187	AAUCCACUGGUGAACCAAG	5846	998
AD-26175	UGCGUGAGCAGGGUGCCAU	5188	AUGGCACCCUGCUCACGCA	5847	1848
AD-26176	GCGUGAGCAGGGUGCCAUU	5189	AAUGGCACCCUGCUCACGC	5848	1849
AD-26177	CACCAGUGGAUUCUGUGUU	5190	AACACAGAAUCCACUGGUG	5849	1005
AD-26178	CAGUGGAUUCUGUGUUGUU	5191	AACAACACAGAAUCCACUG	5850	1008
AD-26179	AGUGGAUUCUGUGUUGUUU	5192	AAACAACACAGAAUCCACU	5851	1009
AD-26180	GUGGAUUCUGUGUUGUUUU	5193	AAAACAACACAGAAUCCAC	5852	1010
AD-26181	UGGAUUCUGUGUUGUUUUA	5194	UAAAACAACACAGAAUCCA	5853	1011

AD-26182	GGAUUCUGUGUUGUUUUAU	5195	AUAAAACAACACAGAAUCC	5854	1012
AD-26183	UGUGUUGUUUUAUGCCAUU	5196	AAUGGCAUAAAACAACACA	5855	1018
AD-26184	GGGUGGGACACAGCAGCAA	5197	UUGCUGCUGUGUCCCACCC	5856	1927
AD-26185	GUGUUGUUUUAUGCCAUUA	5198	UAAUGGCAUAAAACAACAC	5857	1019
AD-26186	UUGUUUUAUGCCAUUACAA	5199	UUGUAAUGGCAUAAAACAA	5858	1022
AD-26187	CCAUUACAACUCUCCACAA	5200	UUGUGGAGAGUUGUAAUGG	5859	1032
AD-26188	UACAACUCUCCACAACCUU	5201	AAGGUUGUGGAGAGUUGUA	5860	1036
AD-26189	ACAACUCUCCACAACCUUU	5202	AAAGGUUGUGGAGAGUUGU	5861	1037
AD-26190	CAACUCUCCACAACCUUUU	5203	AAAAGGUUGUGGAGAGUUG	5862	1038
AD-26191	AACUCUCCACAACCUUUUA	5204	UAAAAGGUUGUGGAGAGUU	5863	1039
AD-26192	ACUCUCCACAACCUUUUAU	5205	AUAAAAGGUUGUGGAGAGU	5864	1040
AD-26193	CUCUCCACAACCUUUUAUU	5206	AAUAAAAGGUUGUGGAGAG	5865	1041
AD-26194	UCUCCACAACCUUUUAUUA	5207	UAAUAAAAGGUUGUGGAGA	5866	1042
AD-26195	CAACCUUUUAUUACAUCAA	5208	UUGAUGUAAUAAAAGGUUG	5867	1048
AD-26196	CCUUUUAUUACAUCAAGAA	5209	UUCUUGAUGUAAUAAAAGG	5868	1051
AD-26197	UUACAUCAAGAAGGAGCUA	5210	UAGCUCCUUCUUGAUGUAA	5869	1058
AD-26198	UACAUCAAGAAGGAGCUAA	5211	UUAGCUCCUUCUUGAUGUA	5870	1059
AD-26199	CAUCAAGAAGGAGCUAAAA	5212	UUUUAGCUCCUUCUUGAUG	5871	1061
AD-26200	AUCAAGAAGGAGCUAAAAU	5213	AUUUUAGCUCCUUCUUGAU	5872	1062
AD-26201	GCUAAAAUGGCAGUGCGUU	5214	AACGCACUGCCAUUUUAGC	5873	1073
AD-26202	UAAAAUGGCAGUGCGUUUA	5215	UAAACGCACUGCCAUUUUA	5874	1075
AD-26203	AAAUGGUUGCCUUGCUCAA	5216	UUGAGCAAGGCAACCAUUU	5875	1110
AD-26204	GCCUGUUCCCCUGAGGGUA	5217	UACCCUCAGGGGAACAGGC	5876	206
AD-26205	UGGUUGCCUUGCUCAACAA	5218	UUGUUGAGCAAGGCAACCA	5877	1113
AD-26206	GGUUGCCUUGCUCAACAAA	5219	UUUGUUGAGCAAGGCAACC	5878	1114
AD-26207	GUUGCCUUGCUCAACAAAA	5220	UUUUGUUGAGCAAGGCAAC	5879	1115
AD-26208	GCCUUGCUCAACAAAACAA	5221	UUGUUUUGUUGAGCAAGGC	5880	1118
AD-26209	CCUUGCUCAACAAAACAAA	5222	UUUGUUUUGUUGAGCAAGG	5881	1119
AD-26210	GUUAAAUUCUUGGCUAUUA	5223	UAAUAGCCAAGAAUUUAAC	5882	1139
AD-26211	UAUUACGACAGACUGCCUU	5224	AAGGCAGUCUGUCGUAAUA	5883	1153
AD-26212	AUGGCAACCAAGAAAGCAA	5225	UUGCUUUCUUGGUUGCCAU	5884	1185
AD-26213	AGUGGUGGACCCCAAGCUU	5226	AAGCUUGGGGUCCACCACU	5885	1220
AD-26214	GUGGUGGACCCCAAGCUUU	5227	AAAGCUUGGGGUCCACCAC	5886	1221
AD-26215	UGGUGGACCCCAAGCUUUA	5228	UAAAGCUUGGGGUCCACCA	5887	1222
AD-26216	UGGACCCCAAGCUUUAGUA	5229	UACUAAAGCUUGGGGUCCA	5888	1225
AD-26217	GGACCCCAAGCUUUAGUAA	5230	UUACUAAAGCUUGGGGUCC	5889	1226
AD-26218	GACCCCAAGCUUUAGUAAA	5231	UUUACUAAAGCUUGGGGUC	5890	1227
AD-26651	ACCCCAAGCUUUAGUAAAU	5232	AUUUACUAAAGCUUGGGGU	5891	1228
AD-26652	CCCCAAGCUUUAGUAAAUA	5233	UAUUUACUAAAGCUUGGGG	5892	1229
AD-26653	CCCAAGCUUUAGUAAAUAU	5234	AUAUUUACUAAAGCUUGGG	5893	1230
AD-26654	CCAAGCUUUAGUAAAUAUA	5235	UAUAUUUACUAAAGCUUGG	5894	1231
AD-26655	UAAAUAUAAUGAGGACCUA	5236	UAGGUCCUCAUUAUAUUUA	5895	1242
AD-26656	AAAUAUAAUGAGGACCUAU	5237	AUAGGUCCUCAUUAUAUUU	5896	1243

AD-26657	AAUAUAAUGAGGACCUAUA	5238	UAUAGGUCCUCAUUAUAUU	5897	1244
AD-26658	AUAAUGAGGACCUAUACUU	5239	AAGUAUAGGUCCUCAUUAU	5898	1247
AD-26659	AAACUACUGUGGACCACAA	5240	UUGUGGUCCACAGUAGUUU	5899	1271
AD-26660	CCACAAGCAGAGUGCUGAA	5241	UUCAGCACUCUGCUUGUGG	5900	1284
AD-26661	CAGAGUGCUGAAGGUGCUA	5242	UAGCACCUUCAGCACUCUG	5901	1291
AD-26662	AGAGUGCUGAAGGUGCUAU	5243	AUAGCACCUUCAGCACUCU	5902	1292
AD-26663	AUUGUAGAAGCUGGUGGAA	5244	UUCCACCAGCUUCUACAAU	5903	1337
AD-26664	UUGUAGAAGCUGGUGGAAU	5245	AUUCCACCAGCUUCUACAA	5904	1338
AD-26665	GCUGGUGGAAUGCAAGCUU	5246	AAGCUUGCAUUCCACCAGC	5905	1346
AD-26666	CUGGUGGAAUGCAAGCUUU	5247	AAAGCUUGCAUUCCACCAG	5906	1347
AD-26667	AGGACUUCACCUGACAGAU	5248	AUCUGUCAGGUGAAGUCCU	5907	1366
AD-26668	CUUCACCUGACAGAUCCAA	5249	UUGGAUCUGUCAGGUGAAG	5908	1370
AD-26669	CCUGACAGAUCCAAGUCAA	5250	UUGACUUGGAUCUGUCAGG	5909	1375
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AD-26671	UCCAAGUCAACGUCUUGUU	5252	AACAAGACGUUGACUUGGA	5911	1384
AD-26672	UCUUGUUCAGAACUGUCUU	5253	AAGACAGUUCUGAACAAGA	5912	1396
AD-26673	CUUGUUCAGAACUGUCUUU	5254	AAAGACAGUUCUGAACAAG	5913	1397
AD-26674	GUCUUUGGACUCUCAGGAA	5255	UUCCUGAGAGUCCAAAGAC	5914	1410
AD-26675	UCUUUGGACUCUCAGGAAU	5256	AUUCCUGAGAGUCCAAAGA	5915	1411
AD-26676	UUGGACUCUCAGGAAUCUU	5257	AAGAUUCCUGAGAGUCCAA	5916	1414
AD-26677	UGCCCAGGGAGAACCCCUU	5258	AAGGGGUUCUCCCUGGGCA	5917	2371
AD-26678	UGGACUCUCAGGAAUCUUU	5259	AAAGAUUCCUGAGAGUCCA	5918	1415
AD-26679	UCUCAGGAAUCUUUCAGAU	5260	AUCUGAAAGAUUCCUGAGA	5919	1420
AD-26680	AAUCUUUCAGAUGCUGCAA	5261	UUGCAGCAUCUGAAAGAUU	5920	1427
AD-26681	CUUUCAGAUGCUGCAACUA	5262	UAGUUGCAGCAUCUGAAAG	5921	1430
AD-26682	UUCAGAUGCUGCAACUAAA	5263	UUUAGUUGCAGCAUCUGAA	5922	1432
AD-26683	UGCUGCAACUAAACAGGAA	5264	UUCCUGUUUAGUUGCAGCA	5923	1438
AD-26684	UAAACAGGAAGGGAUGGAA	5265	UUCCAUCCCUUCCUGUUUA	5924	1447
AD-26685	AGGGAUGGAAGGUCUCCUU	5266	AAGGAGACCUUCCAUCCCU	5925	1456
AD-26686	AGGUCUCCUUGGGACUCUU	5267	AAGAGUCCCAAGGAGACCU	5926	1465
AD-26687	UCUCCUUGGGACUCUUGUU	5268	AACAAGAGUCCCAAGGAGA	5927	1468
AD-26688	UGGGACUCUUGUUCAGCUU	5269	AAGCUGAACAAGAGUCCCA	5928	1474
AD-26689	CUUGUUCAGCUUCUGGGUU	5270	AACCCAGAAGCUGAACAAG	5929	1481
AD-26690	UCAGCUUCUGGGUUCAGAU	5271	AUCUGAACCCAGAAGCUGA	5930	1486
AD-26691	GCUUCUGGGUUCAGAUGAU	5272	AUCAUCUGAACCCAGAAGC	5931	1489
AD-26692	CUUCUGGGUUCAGAUGAUA	5273	UAUCAUCUGAACCCAGAAG	5932	1490
AD-26693	GGCCAGGAUGCCUUGGGUA	5274	UACCCAAGGCAUCCUGGCC	5933	2441
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AD-26695	CUGGGUUCAGAUGAUAUAA	5276	UUAUAUCAUCUGAACCCAG	5935	1493
AD-26696	UGGGUUCAGAUGAUAUAAA	5277	UUUAUAUCAUCUGAACCCA	5936	1494
AD-26697	GUCACCUGUGCAGCUGGAA	5278	UUCCAGCUGCACAGGUGAC	5937	1517
AD-26698	UCACCUGUGCAGCUGGAAU	5279	AUUCCAGCUGCACAGGUGA	5938	1518
AD-26699	CACCUGUGCAGCUGGAAUU	5280	AAUUCCAGCUGCACAGGUG	5939	1519

AD-26700	CUGUGCAGCUGGAAUUCUU	5281	AAGAAUUCCAGCUGCACAG	5940	1522
AD-26701	UGUGCAGCUGGAAUUCUUU	5282	AAAGAAUUCCAGCUGCACA	5941	1523
AD-26702	GCAGCUGGAAUUCUUUCUA	5283	UAGAAAGAAUUCCAGCUGC	5942	1526
AD-26703	CAGCUGGAAUUCUUUCUAA	5284	UUAGAAAGAAUUCCAGCUG	5943	1527
AD-26704	UUUCUAACCUCACUUGCAA	5285	UUGCAAGUGAGGUUAGAAA	5944	1539
AD-26705	UUCUAACCUCACUUGCAAU	5286	AUUGCAAGUGAGGUUAGAA	5945	1540
AD-26706	ACCUCACUUGCAAUAAUUA	5287	UAAUUAUUGCAAGUGAGGU	5946	1545
AD-26707	CCUCACUUGCAAUAAUUAU	5288	AUAAUUAUUGCAAGUGAGG	5947	1546
AD-26708	CUCACUUGCAAUAAUUAUA	5289	UAUAAUUAUUGCAAGUGAG	5948	1547
AD-26709	GUCUGCCAAGUGGGUGGUA	5290	UACCACCCACUUGGCAGAC	5949	1580
AD-26710	UCUGCCAAGUGGGUGGUAU	5291	AUACCACCCACUUGGCAGA	5950	1581
AD-26711	GGGUGGUAUAGAGGCUCUU	5292	AAGAGCCUCUAUACCACCC	5951	1591
AD-26712	AUAGAGGCUCUUGUGCGUA	5293	UACGCACAAGAGCCUCUAU	5952	1598
AD-26713	UCUUGUGCGUACUGUCCUU	5294	AAGGACAGUACGCACAAGA	5953	1606
AD-26714	CUGGUGACAGGGAAGACAU	5295	AUGUCUUCCCUGUCACCAG	5954	1629
AD-26715	ACAUCACUGAGCCUGCCAU	5296	AUGGCAGGCUCAGUGAUGU	5955	1644
AD-26716	GCCUGCCAUCUGUGCUCUU	5297	AAGAGCACAGAUGGCAGGC	5956	1654
AD-26717	UCUGACCAGCCGACACCAA	5298	UUGGUGUCGGCUGGUCAGA	5957	1678
AD-26718	GACCAGCCGACACCAAGAA	5299	UUCUUGGUGUCGGCUGGUC	5958	1681
AD-26719	GACACCAAGAAGCAGAGAU	5300	AUCUCUGCUUCUUGGUGUC	5959	1689
AD-26720	AGCAGAGAUGGCCCAGAAU	5301	AUUCUGGGCCAUCUCUGCU	5960	1699
AD-26721	GAUGGCCCAGAAUGCAGUU	5302	AACUGCAUUCUGGGCCAUC	5961	1705
AD-26722	CCAGAAUGCAGUUCGCCUU	5303	AAGGCGAACUGCAUUCUGG	5962	1711
AD-26723	AUGCAGUUCGCCUUCACUA	5304	UAGUGAAGGCGAACUGCAU	5963	1716
AD-26724	UGCAGUUCGCCUUCACUAU	5305	AUAGUGAAGGCGAACUGCA	5964	1717
AD-26725	UCGCCUUCACUAUGGACUA	5306	UAGUCCAUAGUGAAGGCGA	5965	1723
AD-26726	UCACUAUGGACUACCAGUU	5307	AACUGGUAGUCCAUAGUGA	5966	1729
AD-26727	UGGACUACCAGUUGUGGUU	5308	AACCACAACUGGUAGUCCA	5967	1735
AD-26728	GGACUACCAGUUGUGGUUA	5309	UAACCACAACUGGUAGUCC	5968	1736
AD-26729	GACUACCAGUUGUGGUUAA	5310	UUAACCACAACUGGUAGUC	5969	1737
AD-26730	CAGUUGUGGUUAAGCUCUU	5311	AAGAGCUUAACCACAACUG	5970	1743
AD-26731	AGUUGUGGUUAAGCUCUUA	5312	UAAGAGCUUAACCACAACU	5971	1744
AD-26732	AAGCUCUUACACCCACCAU	5313	AUGGUGGGUGUAAGAGCUU	5972	1754
AD-26733	CAUCCCACUGGCCUCUGAU	5314	AUCAGAGGCCAGUGGGAUG	5973	1770
AD-26734	AUCCCACUGGCCUCUGAUA	5315	UAUCAGAGGCCAGUGGGAU	5974	1771
AD-26735	UCCCACUGGCCUCUGAUAA	5316	UUAUCAGAGGCCAGUGGGA	5975	1772
AD-26736	UGGCCUCUGAUAAAGGCUA	5317	UAGCCUUUAUCAGAGGCCA	5976	1778
AD-26737	UCUGAUAAAGGCUACUGUU	5318	AACAGUAGCCUUUAUCAGA	5977	1783
AD-26738	AUAAAGGCUACUGUUGGAU	5319	AUCCAACAGUAGCCUUUAU	5978	1787
AD-26739	GGCUACUGUUGGAUUGAUU	5320	AAUCAAUCCAACAGUAGCC	5979	1792
AD-26740	UGUUGGAUUGAUUCGAAAU	5321	AUUUCGAAUCAAUCCAACA	5980	1798
AD-26741	UGCCAUUCCACGACUAGUU	5322	AACUAGUCGUGGAAUGGCA	5981	1861
AD-26742	UUCCACGACUAGUUCAGUU	5323	AACUGAACUAGUCGUGGAA	5982	1866

AD-26743	ACGACUAGUUCAGUUGCUU	5324	AAGCAACUGAACUAGUCGU	5983	1870
AD-26744	ACUAGUUCAGUUGCUUGUU	5325	AACAAGCAACUGAACUAGU	5984	1873
AD-26745	GUUGCUUGUUCGUGCACAU	5326	AUGUGCACGAACAAGCAAC	5985	1882
AD-26746	UGUUCGUGCACAUCAGGAU	5327	AUCCUGAUGUGCACGAACA	5986	1888
AD-26747	GUUCGUGCACAUCAGGAUA	5328	UAUCCUGAUGUGCACGAAC	5987	1889
AD-26748	GGUGGGACACAGCAGCAAU	5329	AUUGCUGCUGUGUCCCACC	5988	1928
AD-26749	GUGGGACACAGCAGCAAUU	5330	AAUUGCUGCUGUGUCCCAC	5989	1929
AD-26750	UGGGACACAGCAGCAAUUU	5331	AAAUUGCUGCUGUGUCCCA	5990	1930
AD-26751	GGGGUCCGCAUGGAAGAAA	5332	UUUCUUCCAUGCGGACCCC	5991	1955
AD-26752	GGGUCCGCAUGGAAGAAAU	5333	AUUUCUUCCAUGCGGACCC	5992	1956
AD-26753	UCACAUCCUAGCUCGGGAU	5334	AUCCCGAGCUAGGAUGUGA	5993	1999
AD-26754	CAUCCUAGCUCGGGAUGUU	5335	AACAUCCCGAGCUAGGAUG	5994	2002
AD-26755	UAGCUCGGGAUGUUCACAA	5336	UUGUGAACAUCCCGAGCUA	5995	2007
AD-26756	GGGAUGUUCACAACCGAAU	5337	AUUCGGUUGUGAACAUCCC	5996	2013
AD-26757	GGAUGUUCACAACCGAAUU	5338	AAUUCGGUUGUGAACAUCC	5997	2014
AD-26758	CAGAGGACUAAAAUACCAUU	5339	AAUGGUAUUUAGUCCUCUG	5998	2038
AD-26759	GGACUAAAAUACCAUUCCAU	5340	AUGGAAUGGUAUUUAGUCC	5999	2042
AD-26760	UAAAUACCAUUCCAUUGUU	5341	AACAAUGGAAUGGUAUUUA	6000	2046
AD-26761	AAAUACCAUUCCAUUGUUU	5342	AAACAAUGGAAUGGUAUUU	6001	2047
AD-26762	AUUGUUUGUGCAGCUGCUU	5343	AAGCAGCUGCACAAACAAU	6002	2059
AD-26763	UUGUUUGUGCAGCUGCUUU	5344	AAAGCAGCUGCACAAACAA	6003	2060
AD-26764	UGUUUGUGCAGCUGCUUUA	5345	UAAAGCAGCUGCACAAACA	6004	2061
AD-26765	GUUUGUGCAGCUGCUUUAU	5346	AUAAAGCAGCUGCACAAAC	6005	2062
AD-26766	UUUGUGCAGCUGCUUUAUU	5347	AAUAAAGCAGCUGCACAAA	6006	2063
AD-26767	AGCUGCUUUAUUCUCCCAU	5348	AUGGGAGAAUAAAGCAGCU	6007	2070
AD-26768	GCUGCUUUAUUCUCCCAUU	5349	AAUGGGAGAAUAAAGCAGC	6008	2071
AD-26769	UUUAUUCUCCCAUUGAAAA	5350	UUUUCAAUGGGAGAAUAAA	6009	2076
AD-26770	AUUCUCCCAUUGAAAACAU	5351	AUGUUUUCAAUGGGAGAAU	6010	2079
AD-26771	UCCCAUUGAAAACAUCCAA	5352	UUGGAUGUUUUCAAUGGGA	6011	2083
AD-26772	UGCAGGGGUCCUCUGUGAA	5353	UUCACAGAGGACCCCUGCA	6012	2110
AD-26773	ACUUGCUCAGGACAAGGAA	5354	UUCCUUGUCCUGAGCAAGU	6013	2128
AD-26774	CAGCUCCUCUGACAGAGUU	5355	AACUCUGUCAGAGGAGCUG	6014	2178
AD-26775	AGCUCCUCUGACAGAGUUA	5356	UAACUCUGUCAGAGGAGCU	6015	2179
AD-26776	UCCUCUGACAGAGUUACUU	5357	AAGUAACUCUGUCAGAGGA	6016	2182
AD-26777	ACAGAGUUACUUCACUCUA	5358	UAGAGUGAAGUAACUCUGU	6017	2189
AD-26778	AGUUACUUCACUCUAGGAA	5359	UUCCUAGAGUGAAGUAACU	6018	2193
AD-26779	GUUACUUCACUCUAGGAAU	5360	AUUCCUAGAGUGAAGUAAC	6019	2194
AD-26780	ACUUCACUCUAGGAAUGAA	5361	UUCAUUCCUAGAGUGAAGU	6020	2197
AD-26781	GCUGCUGUUUUGUUCCGAA	5362	UUCGGAACAAAACAGCAGC	6021	2234
AD-26782	CUGCUGUUUUGUUCCGAAU	5363	AUUCGGAACAAAACAGCAG	6022	2235
AD-26783	GUCUGAGGACAAGCCACAA	5364	UUGUGGCUUGUCCUCAGAC	6023	2254
AD-26784	UGAGGACAAGCCACAAGAU	5365	AUCUUGUGGCUUGUCCUCA	6024	2257
AD-26785	ACAAGCCACAAGAUUACAA	5366	UUGUAAUCUUGUGGCUUGU	6025	2262

AD-26786	AGCCACAAGAUUACAAGAA	5367	UUCUUGUAAUCUUGUGGCU	6026	2265
AD-26787	AGAUUACAAGAAACGGCUU	5368	AAGCCGUUUCUUGUAAUCU	6027	2272
AD-26788	CAAGAAACGGCUUUCAGUU	5369	AACUGAAAGCCGUUUCUUG	6028	2278
AD-26789	AGCUGACCAGCUCUCUCUU	5370	AAGAGAGAGCUGGUCAGCU	6029	2298
AD-26790	ACCAGCUCUCUCUUCAGAA	5371	UUCUGAAGAGAGAGCUGGU	6030	2303
AD-26791	UAUUGGUGCCCAGGGAGAA	5372	UUCUCCCUGGGCACCAAUA	6031	2365
AD-26792	CAGGGAGAACCCCUUGGAU	5373	AUCCAAGGGGUUCUCCCUG	6032	2375
AD-26793	AGGGAGAACCCCUUGGAUA	5374	UAUCCAAGGGGUUCUCCCU	6033	2376
AD-26794	CCUUGGAUAUCGCCAGGAU	5375	AUCCUGGCGAUAUCCAAGG	6034	2386
AD-26795	UAUCGCCAGGAUGAUCCUA	5376	UAGGAUCAUCCUGGCGAUA	6035	2393
AD-26796	GCCAGGAUGAUCCUAGCUA	5377	UAGCUAGGAUCAUCCUGGC	6036	2397
AD-26797	CCAGGAUGAUCCUAGCUAU	5378	AUAGCUAGGAUCAUCCUGG	6037	2398
AD-26798	GAUGAUCCUAGCUAUCGUU	5379	AACGAUAGCUAGGAUCAUC	6038	2402
AD-26799	AUCCUAGCUAUCGUUCUUU	5380	AAAGAACGAUAGCUAGGAU	6039	2406
AD-26800	UCCUAGCUAUCGUUCUUUU	5381	AAAAGAACGAUAGCUAGGA	6040	2407
AD-26801	UCUUUUCACUCUGGUGGAU	5382	AUCCACCAGAGUGAAAAGA	6041	2420
AD-26802	CUUUUCACUCUGGUGGAUA	5383	UAUCCACCAGAGUGAAAAG	6042	2421
AD-26803	UUUUCACUCUGGUGGAUAU	5384	AUAUCCACCAGAGUGAAAA	6043	2422
AD-26804	UGGUGGAUAUGGCCAGGAU	5385	AUCCUGGCCAUAUCCACCA	6044	2431
AD-26805	GAUAUGGCCAGGAUGCCUU	5386	AAGGCAUCCUGGCCAUAUC	6045	2436
AD-26806	CCUUGGGUAUGGACCCCAU	5387	AUGGGGUCCAUACCCAAGG	6046	2451
AD-26807	UGGGUAUGGACCCCAUGAU	5388	AUCAUGGGGUCCAUACCCA	6047	2454
AD-26808	UUGUAAACUUGAUUAACUA	5389	UAGUUAAUCAAGUUUACAA	6048	675
AD-26809	UGUAAACUUGAUUAACUAU	5390	AUAGUUAAUCAAGUUUACA	6049	676
AD-26810	AAACUUGAUUAACUAUCAA	5391	UUGAUAGUUAAUCAAGUUU	6050	679
AD-26811	UAUGGACCCCAUGAUGGAA	5392	UUCCAUCAUGGGGUCCAUA	6051	2458
AD-26812	GGACCCCAUGAUGGAACAU	5393	AUGUUCCAUCAUGGGGUCC	6052	2461
AD-26813	CCAUGAUGGAACAUGAGAU	5394	AUCUCAUGUUCCAUCAUGG	6053	2466
AD-26814	ACCACCCUGGUGCUGACUA	5395	UAGUCAGCACCAGGGUGGU	6054	2493
AD-26815	CCACCCUGGUGCUGACUAU	5396	AUAGUCAGCACCAGGGUGG	6055	2494
AD-26816	UGCUGACUAUCCAGUUGAU	5397	AUCAACUGGAUAGUCAGCA	6056	2503
AD-26817	AGUUGAUGGGCUGCCAGAU	5398	AUCUGGCAGCCCAUCAACU	6057	2515
AD-26818	UGCCCAGGACCUCAUGGAU	5399	AUCCAUGAGGUCCUGGGCA	6058	2542
AD-26819	GCAAUCAGCUGGCCUGGUU	5400	AACCAGGCCAGCUGAUUGC	6059	2580
AD-26820	CAAUCAGCUGGCCUGGUUU	5401	AAACCAGGCCAGCUGAUUG	6060	2581
AD-26821	GGUUUGAUACUGACCUGUA	5402	UACAGGUCAGUAUCAAACC	6061	2595
AD-26822	AUACUGACCUGUAAAUCAU	5403	AUGAUUUACAGGUCAGUAU	6062	2601
AD-26823	UGACCUGUAAAUCAUCCUU	5404	AAGGAUGAUUUACAGGUCA	6063	2605
AD-26824	GACCUGUAAAUCAUCCUUU	5405	AAAGGAUGAUUUACAGGUC	6064	2606
AD-26825	ACCUGUAAAUCAUCCUUUA	5406	UAAAGGAUGAUUUACAGGU	6065	2607
AD-26826	AAUACAAAUGAUGUAGAAA	5407	UUUCUACAUCAUUUGUAUU	6066	878
AD-26900	UUUUAAGAAUAUCUGUAAU	5408	AUUACAGAUAUUCUUAAAA	6067	2745
AD-26901	UACAGCAAUUUCUAAUUUU	5409	AAAAUUAGAAAUUGCUGUA	6068	2872

AD-26902	CACUAAUUCAUAAUCACUC	5410	GAGUGAUUAUGAAUUAGUG	6069	2915
AD-26903	ACUAAUUCAUAAUCACUCU	5411	AGAGUGAUUAUGAAUUAGU	6070	2916
AD-26904	UAAUUCAUAAUCACUCUAA	5412	UUAGAGUGAUUAUGAAUUA	6071	2918
AD-26905	AAUUCAUAAUCACUCUAAU	5413	AUUAGAGUGAUUAUGAAUU	6072	2919
AD-26906	AAUUGUAAUCUGAAUAAAG	5414	CUUUAUUCAGAUUACAAUU	6073	2939
AD-26907	UUUGUAUAAAAUAGACAAA	5415	UUUGUCUAUUUUAUACAAA	6074	2978
AD-26908	UUGUAUAAAAUAGACAAAU	5416	AUUUGUCUAUUUUAUACAA	6075	2979
AD-26909	UGUAUAAAAUAGACAAAUA	5417	UAUUUGUCUAUUUUAUACA	6076	2980
AD-26910	GUAUAAAAUAGACAAAUAG	5418	CUAUUUGUCUAUUUUAUAC	6077	2981
AD-26911	AUAAAAUAGACAAAUAGAA	5419	UUCUAUUUGUCUAUUUUAU	6078	2983
AD-26912	UAAAAUAGACAAAUAGAAA	5420	UUUCUAUUUGUCUAUUUUA	6079	2984
AD-26913	AAAUAGACAAAUAGAAAAU	5421	AUUUUCUAUUUGUCUAUUU	6080	2986
AD-26914	UGGGAUAUGUAUGGGUAGG	5422	CCUACCCAUACAUAUCCCA	6081	3081
AD-26915	GGGAUAUGUAUGGGUAGGG	5423	CCCUACCCAUACAUAUCCC	6082	3082
AD-26916	CUAAUUCAUAAUCACUCUA	5424	UAGAGUGAUUAUGAAUUAG	6083	2917
AD-26917	AAAUAGAAAAUGGUCCAAU	5425	AUUGGACCAUUUUCUAUUU	6084	2994
AD-26918	AAUAGAAAAUGGUCCAAUU	5426	AAUUGGACCAUUUUCUAUU	6085	2995
AD-26919	UUUGGACAGUUUACCAGUU	5427	AACUGGUAAACUGUCCAAA	6086	3134
AD-26920	AUUCUUUCUAACCUCACUU	5428	AAGUGAGGUUAGAAAGAAU	6087	1535
AD-26921	UGGAUUGAUUCGAAAUCUU	5429	AAGAUUUCGAAUCAAUCCA	6088	1801
SET1_1245	GACCCCAAGCUUUAGUAAA	6090	UUUACUAAAGCUUGGGGUC	6111	1227
SET1_1249	CCAAGCUUUAGUAAAUAUA	6091	UAUAUUUACUAAAGCUUGG	6112	1231
SET1_1250	CAAGCUUUAGUAAAUAUAA	6092	UUAUAUUUACUAAAGCUUG	6113	1232
SET1_1450	UUCAGAUGCUGCAACUAAA	6093	UUUAGUUGCAGCAUCUGAA	6114	1432
SET1_1545	CAGCUGGAAUUCUUUCUAA	6094	UUAGAAAGAAUUCCAGCUG	6115	1527
SET1_1755	GACUACCAGUUGUGGUUAA	6095	UUAACCACAACUGGUAGUC	6116	1737
SET1_1814	ACUGUUGGAUUGAUUCGAA	6096	UUCGAAUCAAUCCAACAGU	6117	1796
SET1_1816	UGUUGGAUUGAUUCGAAAU	6097	AUUUCGAAUCAAUCCAACA	6118	1798
SET1_1974	GGGUCCGCAUGGAAGAAAU	6098	AUUUCUUCCAUGCGGACCC	6119	1956
SET1_2202	CUCUGACAGAGUUACUUCA	6099	UGAAGUAACUCUGUCAGAG	6120	2184
SET1_2425	UCCUAGCUAUCGUUCUUUU	6100	AAAAGAACGAUAGCUAGGA	6121	2407
SET1_254	CCAUACAACUGUUUUGAAA	6101	UUUCAAAACAGUUGUAUGG	6122	236
SET1_3146	AAGUGAAGAAUGCACAAGA	6102	UCUUGUGCAUUCUUCACUU	6123	3128
SET1_3169	AUCACAAGAUGGAAUUUAU	6103	AUAAAUUCCAUCUUGUGAU	6124	3151
SET1_3196	AGCCUUGCUUGUUAAAUUU	6104	AAAUUUAACAAGCAAGGCU	6125	3178
SET1_3477	AAUAGAAAAUGGUCCAAUU	6105	AAUUGGACCAUUUUCUAUU	6126	3459
SET1_703	GAUUAACUAUCAAGAUGAU	6106	AUCAUCUUGAUAGUUAAUC	6127	685
SET1_709	CUAUCAAGAUGAUGCAGAA	6107	UUCUGCAUCAUCUUGAUAG	6128	691
SET1_865	GAUGGUGUCUGCUAUUGUA	6108	UACAAUAGCAGACACCAUC	6129	847
SET1_889	CAUGCAGAAUACAAAUGAU	6109	AUCAUUUGUAUUCUGCAUG	6130	871
SET1_895	GAAUACAAAUGAUGUAGAA	6110	UUCUACAUCAUUUGUAUUC	6131	877

[00778] Modified sequences are listed in Table 3; the specific modifications are disclosed

herein. The sequences in Table 2 correspond to portions of the wild-type Beta-Catenin gene without modifications or dTdT extensions. The positions are also provided. In the sequences in these tables, lower-case letters (e.g., c, u) indicate modified nucleotides while upper case letters (e.g., C, U, A, G) indicate unmodified nucleotides. In Table 3, modified versions of the sequences are shown. However, the present disclosure encompasses unmodified versions of these sequences and other versions which comprise additional or alternative modifications. Thus, for example, AD-18892 can optionally have the unmodified sequence uGGuGcuGAcuAuccAGuu (SEQ ID NO: 429) in the sense strand and AACUGGAuAGUcAGcACcA (SEQ ID NO: 430) in the anti-sense strand. The present disclosure also encompasses alternative modified versions of the duplex comprising uGGuGcuGAcuAuccAGuu (SEQ ID NO: 429) in the sense strand and AACUGGAuAGUcAGcACcA (SEQ ID NO: 430) in the anti-sense strand.

[00779] In the sequences in Tables 1, 2 and 3, the modified and unmodified sequences can optionally comprise the sequence "dTsdT" or "UU" at the 3' end. In the sequences disclosed herein, the TT and UU dinucleotides were not in the inverted/reverse orientation and "UU" is 2'-OMe-U 2'-OMe-U.

[00780] Thus, for example, AD-18892 can optionally have the modified sequence uGGuGcuGAcuAuccAGuudTdT (SEQ ID NO: 6132) or uGGuGcuGAcuAuccAGuudTsdT (SEQ ID NO: 6133) in the sense strand; and AACUGGAuAGUcAGcACcAdTdT (SEQ ID NO: 6134) or AACUGGAuAGUcAGcACcAdTsdT (SEQ ID NO: 6135) in the anti-sense strand. As noted in Table 3, below, dT is 2'-deoxy-thymidine-5'-phosphate and sdT is 2'-deoxy Thymidine 5'-phosphorothioate.

[00781] In several sequences in this Table, the nickname "Set1_#" can be preceded by the prefix "hsCTNNB1_". Thus "Set1_254" is also designated "hsCTNNB1_Set1_254". The number is derived from one type of calculation of the position on the gene. Thus, the designations Set1_1245, Set1_1249, Set1_1250, Set1_1450, Set1_1545, Set1_1755, Set1_1814, Set1_1816, Set1_1974, Set1_2202, Set1_2425, Set1_254, Set1_3146, Set1_3169, Set1_3196, Set1_3477, Set1_703, Set1_709, Set1_865, Set1_889, Set1_895 indicate duplexes (or modified variants thereof) which correspond to one type of calculation of the positions 1245, 1249, 1250, 1450, 1545, 1755, 1814, 1816, 1974, 2202, 2425, 254, 3146, 3169, 3196, 3477, 703, 709, 865, 889, 895, respectively. However, these positions were calculated using different parameters than other sequences in this Table, resulting in a 18 nt shift. Thus, "Set1_254" pertains to a sequence which corresponds to position 236. Also note that the underscore (_) is sometimes replaced by a space ( ); thus, for example, "Set1_3169" is the same as "Set1 3169"; and "hsCTNNB1_Set2_254_A48_S26" is the same as "hsCTNNB1 Set2 254 A48 S26".

[00782] In addition, additional suffices can be appended to the nickname to designate different variants which have the same sequence (e.g., the same sequence of nucleotides), but different

modifications. Thus, assorted variants of duplexes within "hsCTNNB1_Set1_1245" include, inter alia: hsCTNNB1_Set1_254_A22_S26; hsCTNNB1_Set1_254_A25_S27; hsCTNNB1_Set1_254_A_LO_V1_S26; hsCTNNB1_Set1_254_A_LO_V2_S_LO_V1; hsCTNNB1_Set2_254_A_LO_V3_S_LO_V2; hsCTNNB1_Set2_254_A_LO_V4_S_LO_V1; hsCTNNB1_Set2_254_A_LO_V5_S_LO_V1; and hsCTNNB1_Set2_254_A48_S26.

TABLE 3. Beta-Catenin RNAi agents: Example Modified Sequences

Duplex	Sense Sequence	Sense SEQ ID NO:	Anti-sense Sequence	Anti-sense SEQ ID NO:	Position
AD-18892	uGGuGcuGAcuAuccAGuu	1	AACUGGAuAGUcAGcACcA	660	2500
AD-18893	ccAucuGuGcucuucGucA	2	UGACGAAGAGcAcAGAUGG	661	1659
AD-18894	AuAAGcAGGuGGAucuAuu	3	AAuAGAUCcACCUGCUuAU	662	3038
AD-18895	AuccAAAGAGuAGcuGcAG	4	CUGcAGCuACUCUUUGGAU	663	2096
AD-18896	GAcAAuGGcuAcucAAGcu	5	AGCUUGAGuAGCcAUUGUC	664	265
AD-18897	cuGuuGGAuuGAuucGAAA	6	UUUCGAAUcAAUCcAAcAG	665	1797
AD-18898	GcuGGccuGGuuuGAuAcu	7	AGuAUcAAACcAGGCcAGC	666	2587
AD-18899	ucuAAccucAcuuGcAAuA	8	uAUUGcAAGUGAGGUuAGA	667	1541
AD-18900	GAuAucGccAGGAuGAucc	9	GGAUcAUCCUGGCGAuAUC	668	2391
AD-18901	uGGccAucuuuAAGucuGG	10	CcAGACUuAAAGAUGGCcA	669	954
AD-18902	uGuAGAAcAcuAAuucAuA	11	uAUGAAUuAGUGUUCuAcA	670	2908
AD-18903	AucAGuAAGAGGuGuuAuu	12	AAuAAcACCUCUuACUGAU	671	3104
AD-18904	GuGcucuucGucAucuGAc	13	GUcAGAUGACGAAGAGcAC	672	1665
AD-18905	uGGuuuGAuAcuGAccuGu	14	AcAGGUcAGuAUcAAACcA	673	2594
AD-18906	ccAGuuGccuuuuAucccA	15	UGGGAuAAAAGGcAACUGG	674	3147
AD-18907	ccuGGuuuGAuAcuGAccu	16	AGGUcAGuAUcAAACcAGG	675	2592
AD-18908	GAcuAuccAGuuGAuGGGc	17	GCCcAUcAACUGGAuAGUC	676	2507
AD-18909	AGccAAuGGcuuGGAAuGA	18	UcAUUCcAAGCcAUUGGCU	677	2325
AD-18910	GccAAuGGcuuGGAAuGAG	19	CUcAUUCcAAGCcAUUGGC	678	2326
AD-18911	AGAuGAGGGcAuGcAGAuc	20	GAUCUGcAUGCCCUcAUCU	679	577
AD-18912	GGuccucuGuGAAcuuGcu	21	AGcAAGUUcAcAGAGGACC	680	2116
AD-18913	AAcccuAGccuuGcuuGuu	22	AAcAAGcAAGGCuAGGGUU	681	2708
AD-18914	GAAcAcuAAuucAuAAucA	23	UGAUuAUGAAUuAGUGUUC	682	2912
AD-18915	AucAAAcccuAGccuuGcu	24	AGcAAGGCuAGGGUUUGAU	683	2704
AD-18916	AccAGuuGccuuuuAuccc	25	GGGAuAAAAGGcAACUGGU	684	3146
AD-18917	cuAAccucAcuuGcAAuAA	26	UuAUUGcAAGUGAGGUuAG	685	1542
AD-18918	AucccAcuAAuGuccAGcG	27	CGCUGGAcAUuAGUGGGAU	686	621
AD-18919	cuGAcuAuccAGuuGAuGG	28	CcAUcAACUGGAuAGUcAG	687	2505
AD-18920	GGccuGGuuuGAuAcuGAc	29	GUcAGuAUcAAACcAGGCC	688	2590
AD-18921	GGuAAAucAGuAAGAGGuG	30	cACCUCUuACUGAUUuACC	689	3099
AD-18922	GccuGGuuuGAuAcuGAcc	31	GGUcAGuAUcAAACcAGGC	690	2591
AD-18923	cAGGGGuccucuGuGAAcu	32	AGUUcAcAGAGGACCCCUG	691	2112

AD-18925	cuGGAAuccAuucuGGuGc	33	GcACcAGAAUGGAUUCcAG	692	366
AD-18926	uGAGAuGGGuGGccAccAc	34	GUGGUGGCcACCcAUCUcA	693	2479
AD-18927	GAuGAuAuAAAuGuGGucA	35	UGACcAcAUUuAuAUcAUC	694	1502
AD-18928	uGcuuuAuucucccAuuGA	36	UcAAUGGGAGAAuAAAGcA	695	2073
AD-18929	uuAucAAAcccuAGccuuG	37	cAAGGCuAGGGUUUGAuAA	696	2702
AD-18930	ccAcuGGccucuGAuAAAG	38	CUUuAUcAGAGGCcAGUGG	697	1774
AD-18931	AAcuuGccAcAcGuGcAAu	39	AUUGcACGUGUGGcAAGUU	698	708
AD-18932	GcucuucGucAucuGAccA	40	UGGUcAGAUGACGAAGAGC	699	1667
AD-18933	GuAAcAAuAcAAAuGGAuu	41	AAUCcAUUUGuAUUGUuAC	700	2629
AD-18934	GGGGuccucuGuGAAcuuG	42	cAAGUUcAcAGAGGACCCC	701	2114
AD-18935	cAAAcccuAGccuuGcuuG	43	cAAGcAAGGCuAGGGUUUG	702	2706
AD-18936	GAGuAAuGGuGuAGAAcAc	44	GUGUUCuAcACcAUuACUC	703	2899
AD-18937	GGAAGAcAucAcuGAGccu	45	AGGCUcAGUGAUGUCUUCC	704	1639
AD-18938	GGGAAGAcAucAcuGAGcc	46	GGCUcAGUGAUGUCUUCCC	705	1638
AD-18939	GGuGuAGAAcAcuAAuucA	47	UGAAUuAGUGUUCuAcACC	706	2906
AD-18940	uAccAGuuGccuuuuAucc	48	GGAuAAAAGGcAACUGGuA	707	3145
AD-18941	GGAuAucGccAGGAuGAuc	49	GAUcAUCCUGGCGAuAUCC	708	2390
AD-18942	AAAcccuAGccuuGcuuGu	50	AcAAGcAAGGCuAGGGUUU	709	2707
AD-18943	cucuucGucAucuGAccAG	51	CUGGUcAGAUGACGAAGAG	710	1668
AD-18944	uGAcuAuccAGuuGAuGGG	52	CCcAUcAACUGGAuAGUcA	711	2506
AD-18945	AcAAGcAGAGuGcuGAAGG	53	CCUUcAGcACUCUGCUUGU	712	1286
AD-18946	cAucuGuGcucuucGucAu	54	AUGACGAAGAGcAcAGAUG	713	1660
AD-18947	cAAuGGcuuGGAAuGAGAc	55	GUCUcAUUCcAAGCcAUUG	714	2328
AD-18948	AcuGGccucuGAuAAAGGc	56	GCCUUuAUcAGAGGCcAGU	715	1776
AD-18949	ucAucccAcuAAuGuccAG	57	CUGGAcAUuAGUGGGAUGA	716	619
AD-18950	AAAAGGAAGcuuccAGAcA	58	UGUCUGGAAGCUUCCUUUU	717	807
AD-18951	cGuucuuuucAcucuGGuG	59	cACcAGAGUGAAAAGAACG	718	2417
AD-18952	AAAGuuGuuGuAAccuGcu	60	AGcAGGUuAcAAcAACUUU	719	3165
AD-18953	AcAAuGGcuAcucAAGcuG	61	cAGCUUGAGuAGCcAUUGU	720	266
AD-18954	cucAucccAcuAAuGuccA	62	UGGAcAUuAGUGGGAUGAG	721	618
AD-18955	AGGGGuccucuGuGAAcuu	63	AAGUUcAcAGAGGACCCCU	722	2113
AD-18956	AAGcAGGuGGAucuAuuuc	64	GAAAuAGAUCcACCUGCUU	723	3040
AD-18957	AAGuuGuuGuAAccuGcuG	65	cAGcAGGUuAcAAcAACUU	724	3166
AD-18958	AGcAGGuGGAucuAuuucA	66	UGAAAuAGAUCcACCUGCU	725	3041
AD-18959	AGGGcAuGcAGAucccAuc	67	GAUGGGAUCUGcAUGCCCU	726	582
AD-18960	AAAuGGuucAGAAuuAAAc	68	GUUuAAUUCUGAACcAUUU	727	3220
AD-18961	uGAAcuuGcucAGGAcAAG	69	CUUGUCCUGAGcAAGUUcA	728	2125
AD-18962	AAGAGuAGcuGcAGGGGuc	70	GACCCCUGcAGCuACUCUU	729	2101
AD-18963	cccAcuGGccucuGAuAAA	71	UUuAUcAGAGGCcAGUGGG	730	1773
AD-18964	cuGGccuGGuuuGAuAcuG	72	cAGuAUcAAACcAGGCcAG	731	2588
AD-18965	uuGAuAcuGAccuGuAAAu	73	AUUuAcAGGUcAGuAUcAA	732	2598
AD-18966	GuGuAGAAcAcuAAuucAu	74	AUGAAUuAGUGUUCuAcAC	733	2907
AD-18967	AcuAuccAGuuGAuGGGcu	75	AGCCcAUcAACUGGAuAGU	734	2508

AD-18968	AAAucAGuAAGAGGuGuuA	76	uAAcACCUCUuACUGAUUU	735	3102
AD-18969	GcAGGuGGAucuAuuucAu	77	AUGAAAuAGAUCcACCUGC	736	3042
AD-18970	cuGGuGcuGAcuAuccAGu	78	ACUGGAuAGUcAGcACcAG	737	2499
AD-18971	GuGAAcuuGcucAGGAcAA	79	UUGUCCUGAGcAAGUUcAC	738	2124
AD-18972	ucAGuAAGAGGuGuuAuuu	80	AAAuAAcACCUCUuACUGA	739	3105
AD-18973	ccucuGuGAAcuuGcucAG	81	CUGAGcAAGUUcAcAGAGG	740	2119
AD-18974	uuGGcuGAAccAucAcAGA	82	UCUGUGAUGGUUcAGCcAA	741	641
AD-18975	ucAGcuGGccuGGuuuGAu	83	AUcAAACcAGGCcAGCUGA	742	2584
AD-18976	GuAGcuGcAGGGGuccucu	84	AGAGGACCCCUGcAGCuAC	743	2105
AD-18977	AGGAGcuAAAAuGGcAGuG	85	cACUGCcAUUUuAGCUCCU	744	1069
AD-18978	AuGGcuuGGAAuGAGAcuG	86	cAGUCUcAUUCcAAGCcAU	745	2330
AD-18979	uuGGAuAucGccAGGAuGA	87	UcAUCCUGGCGAuAUCcAA	746	2388
AD-18980	GGuucAGAAuuAAAcuuuu	88	AAAAGUUuAAUUCUGAACC	747	3224
AD-18981	GGGuAAAucAGuAAGAGGu	89	ACCUCUuACUGAUUuACCC	748	3098
AD-18982	AuAccAuuccAuuGuuuGu	90	AcAAAcAAUGGAAUGGuAU	749	2049
AD-18983	AcuGuuGGAuuGAuucGAA	91	UUCGAAUcAAUCcAAcAGU	750	1796
AD-18984	AAcuuGcucAGGAcAAGGA	92	UCCUUGUCCUGAGcAAGUU	751	2127
AD-18985	AuGcuuAAAAuAAGcAGGu	93	ACCUGCUuAUUUuAAGcAU	752	3029
AD-18986	GuuuGAuAcuGAccuGuAA	94	UuAcAGGUcAGuAUcAAAC	753	2596
AD-18987	AAuGGuucAGAAuuAAAcu	95	AGUUuAAUUCUGAACcAUU	754	3221
AD-18988	uAucccAAAGuuGuuGuAA	96	UuAcAAcAACUUUGGGAuA	755	3159
AD-18989	AucAGcuGGccuGGuuuGA	97	UcAAACcAGGCcAGCUGAU	756	2583
AD-18990	ccuGccAucuGuGcucuuc	98	GAAGAGcAcAGAUGGcAGG	757	1655
AD-18991	GcAGAAuAcAAAuGAuGuA	99	uAcAUcAUUUGuAUUCUGC	758	874
AD-18992	uAuGcuuAAAAuAAGcAGG	100	CCUGCUuAUUUuAAGcAuA	759	3028
AD-18993	AAuAAGcAGGuGGAucuAu	101	AuAGAUCcACCUGCUuAUU	760	3037
AD-18994	uGAuAuAAAuGuGGucAcc	102	GGUGACcAcAUUuAuAUcA	761	1504
AD-18995	GuAGGGuAAAucAGuAAGA	103	UCUuACUGAUUuACCCuAC	762	3095
AD-18996	uAucAAAcccuAGccuuGc	104	GcAAGGCuAGGGUUUGAuA	763	2703
AD-18997	ccuuuuAucccAAAGuuGu	105	AcAACUUUGGGAuAAAAGG	764	3154
AD-18998	GGuAGGGuAAAucAGuAAG	106	CUuACUGAUUuACCCuACC	765	3094
AD-18999	uGAuAcuGAccuGuAAAuc	107	GAUUuAcAGGUcAGuAUcA	766	2599
AD-19000	GGcuGAAccAucAcAGAuG	108	cAUCUGUGAUGGUUcAGCC	767	643
AD-19001	uGGAuAucGccAGGAuGAu	109	AUcAUCCUGGCGAuAUCcA	768	2389
AD-19002	ucuucGucAucuGAccAGc	110	GCUGGUcAGAUGACGAAGA	769	1669
AD-19003	uAGcuGcAGGGGuccucuG	111	cAGAGGACCCCUGcAGCuA	770	2106
AD-19004	uGuuGuAAccuGcuGuGAu	112	AUcAcAGcAGGUuAcAAcA	771	3170
AD-19005	AAucAGuAAGAGGuGuuAu	113	AuAAcACCUCUuACUGAUU	772	3103
AD-19006	uGGcuGAAccAucAcAGAu	114	AUCUGUGAUGGUUcAGCcA	773	642
AD-19007	GAAuuAAAcuuuuAAuucA	115	UGAAUuAAAAGUUuAAUUC	774	3230
AD-19008	AuGGuucAGAAuuAAAcuu	116	AAGUUuAAUUCUGAACcAU	775	3222
AD-19009	uGGuGuAGAAcAcuAAuuc	117	GAAUuAGUGUUCuAcACcA	776	2905
AD-19010	AuGGuGuAGAAcAcuAAuu	118	AAUuAGUGUUCuAcACcAU	777	2904

AD-19011	AuGAGGGcAuGcAGAuccc	119	GGGAUCUGcAUGCCCUcAU	778	579
AD-19012	GuuGuAAccuGcuGuGAuA	120	uAUcAcAGcAGGUuAcAAC	779	3171
AD-19042	GcuGAcuAuccAGuuGAuG	121	cAUcAACUGGAuAGUcAGC	780	2504
AD-19043	uAAGcAGGuGGAucuAuuu	122	AAAuAGAUCcACCUGCUuA	781	3039
AD-19044	uAAAAuAAGcAGGuGGAuc	123	GAUCcACCUGCUuAUUUuA	782	3034
AD-19045	GAuAuAAAuGuGGucAccu	124	AGGUGACcAcAUUuAuAUC	783	1505
AD-19046	AAGcAGAGuGcuGAAGGuG	125	cACCUUcAGcACUCUGCUU	784	1288
AD-19047	uGuGAAcuuGcucAGGAcA	126	UGUCCUGAGcAAGUUcAcA	785	2123
AD-19048	cAucccAcuAAuGuccAGc	127	GCUGGAcAUuAGUGGGAUG	786	620
AD-19049	cAAAGuuGuuGuAAccuGc	128	GcAGGUuAcAAcAACUUUG	787	3164
AD-19050	uAAAucAGuAAGAGGuGuu	129	AAcACCUCUuACUGAUUuA	788	3101
AD-19051	AAuGGcuuGGAAuGAGAcu	130	AGUCUcAUUCcAAGCcAUU	789	2329
AD-19052	GGGuccucuGuGAAcuuGc	131	GcAAGUUcAcAGAGGACCC	790	2115
AD-19053	GAGuAAcAAuAcAAAuGGA	132	UCcAUUUGuAUUGUuACUC	791	2627
AD-19054	uAAuGGuGuAGAAcAcuAA	133	UuAGUGUUCuAcACcAUuA	792	2902
AD-19055	GuGGAcAAuGGcuAcucAA	134	UUGAGuAGCcAUUGUCcAC	793	262
AD-19056	AAcuGucuuuGGAcucucA	135	UGAGAGUCcAAAGAcAGUU	794	1406
AD-19057	cccuGGuGcuGAcuAuccA	136	UGGAuAGUcAGcACcAGGG	795	2497
AD-19058	cAGGuGGAucuAuuucAuG	137	cAUGAAAuAGAUCcACCUG	796	3043
AD-19059	uGGccuGGuuuGAuAcuGA	138	UcAGuAUcAAACcAGGCcA	797	2589
AD-19060	AGcuGGccuGGuuuGAuAc	139	GuAUcAAACcAGGCcAGCU	798	2586
AD-19061	GccAucuGuGcucuucGuc	140	GACGAAGAGcAcAGAUGGC	799	1658
AD-19062	uAccAuuccAuuGuuuGuG	141	cAcAAAcAAUGGAAUGGuA	800	2050
AD-19063	cccuuGGAuAucGccAGGA	142	UCCUGGCGAuAUCcAAGGG	801	2385
AD-19064	AGGGAAGAcAucAcuGAGc	143	GCUcAGUGAUGUCUUCCCU	802	1637
AD-19065	GAAcuuGccAcAcGuGcAA	144	UUGcACGUGUGGcAAGUUC	803	707
AD-19066	uuuGAuAcuGAccuGuAAA	145	UUuAcAGGUcAGuAUcAAA	804	2597
AD-19067	ucccAAAGuuGuuGuAAcc	146	GGUuAcAAcAACUUUGGGA	805	3161
AD-19068	cAGAAuAcAAAuGAuGuAG	147	CuAcAUcAUUUGuAUUCUG	806	875
AD-19069	AGGuGGAucuAuuucAuGu	148	AcAUGAAAuAGAUCcACCU	807	3044
AD-19070	GcucAucccAcuAAuGucc	149	GGAcAUuAGUGGGAUGAGC	808	617
AD-19071	ccuGGuGcuGAcuAuccAG	150	CUGGAuAGUcAGcACcAGG	809	2498
AD-19072	uGGAAuccAuucuGGuGcc	151	GGcACcAGAAUGGAUUCcA	810	367
AD-19073	ccAGGAccucAuGGAuGGG	152	CCcAUCcAUGAGGUCCUGG	811	2545
AD-19074	AAccucAcuuGcAAuAAuu	153	AAUuAUUGcAAGUGAGGUU	812	1544
AD-19075	cAGuuGccuuuuAucccAA	154	UUGGGAuAAAAGGcAACUG	813	3148
AD-19076	GuAGAAcAcuAAuucAuAA	155	UuAUGAAUuAGUGUUCuAC	814	2909
AD-19077	cuAuccAGuuGAuGGGcuG	156	cAGCCcAUcAACUGGAuAG	815	2509
AD-19078	cAcuGGccucuGAuAAAGG	157	CCUUuAUcAGAGGCcAGUG	816	1775
AD-19079	AcuGucuuuGGAcucucAG	158	CUGAGAGUCcAAAGAcAGU	817	1407
AD-19080	ccAAuGGcuuGGAAuGAGA	159	UCUcAUUCcAAGCcAUUGG	818	2327
AD-19081	GcuuAAAAuAAGcAGGuGG	160	CcACCUGCUuAUUUuAAGC	819	3031
AD-19082	AucuGuGcucuucGucAuc	161	GAUGACGAAGAGcAcAGAU	820	1661

AD-19083	cccAAAGuuGuuGuAAccu	162	AGGUuAcAAcAACUUUGGG	821	3162
AD-19738	uAcccAGcGccGuAcGucc	163	GGACGuACGGCGCUGGGuA	822	1906
AD-19739	AcGcuAucAuGcGuucucc	164	GGAGAACGcAUGAuAGCGU	823	825
AD-19740	cAuGcAccuuuGcGuGAGc	165	GCUcACGcAAAGGUGcAUG	824	1838
AD-19741	GAAuGcAGuucGccuucAc	166	GUGAAGGCGAACUGcAUUC	825	1714
AD-19742	GGuGccAuuccAcGAcuAG	167	CuAGUCGUGGAAUGGcACC	826	1859
AD-19743	AAGcGGcuGuuAGucAcuG	168	cAGUGACuAAcAGCCGCUU	827	324
AD-19744	ucGAGcucAGAGGGuAcGA	169	UCGuACCCUCUGAGCUCGA	828	535
AD-19745	GAcAcGcuAucAuGcGuuc	170	GAACGcAUGAuAGCGUGUC	829	822
AD-19746	cGcuAucAuGcGuucuccu	171	AGGAGAACGcAUGAuAGCG	830	826
AD-19747	GuGucuGcuAuuGuAcGuA	172	uACGuAcAAuAGcAGAcAC	831	851
AD-19748	GucuGcucuAGuAAuAAGc	173	GCUuAUuACuAGAGcAGAC	832	1313
AD-19749	GuGccAuuccAcGAcuAGu	174	ACuAGUCGUGGAAUGGcAC	833	1860
AD-19750	AuGuucAcAAccGAAuuGu	175	AcAAUUCGGUUGUGAAcAU	834	2016
AD-19751	ccAcGAcuAGuucAGuuGc	176	GcAACUGAACuAGUCGUGG	835	1868
AD-19752	cAcGAcuAGuucAGuuGcu	177	AGcAACUGAACuAGUCGUG	836	1869
AD-19753	AGuucAGuuGcuuGuucGu	178	ACGAAcAAGcAACUGAACU	837	1876
AD-19754	cccAGcGccGuAcGuccAu	179	AUGGACGuACGGCGCUGGG	838	1908
AD-19755	GAGuuAcuucAcucuAGGA	180	UCCuAGAGUGAAGuAACUC	839	2192
AD-19756	AcAGuAuGcAAuGAcucGA	181	UCGAGUcAUUGcAuACUGU	840	520
AD-19757	uAuGcAAuGAcucGAGcuc	182	GAGCUCGAGUcAUUGcAuA	841	524
AD-19758	cccAcuAAuGuccAGcGuu	183	AACGCUGGAcAUuAGUGGG	842	623
AD-19759	GAccuuGcAuAAccuuucc	184	GGAAAGGUuAUGcAAGGUC	843	916
AD-19760	uAuuAcGAcAGAcuGccuu	185	AAGGcAGUCUGUCGuAAuA	844	1153
AD-19761	AucuGAccAGccGAcAccA	186	UGGUGUCGGCUGGUcAGAU	845	1677
AD-19762	cAuuccAcGAcuAGuucAG	187	CUGAACuAGUCGUGGAAUG	846	1864
AD-19763	GuuuuGAAAAuccAGcGuG	188	cACGCUGGAUUUUcAAAAC	847	246
AD-19765	GcGuuuGGcuGAAccAucA	189	UGAUGGUUcAGCcAAACGC	848	637
AD-19766	AcAcGcuAucAuGcGuucu	190	AGAACGcAUGAuAGCGUGU	849	823
AD-19767	uAuGccAuuAcAAcucucc	191	GGAGAGUUGuAAUGGcAuA	850	1028
AD-19768	ucuGcucuAGuAAuAAGcc	192	GGCUuAUuACuAGAGcAGA	851	1314
AD-20124	cGGGAuGuucAcAAccGAA	193	UUCGGUUGUGAAcAUCCCG	852	2012
AD-25889	AcAAuAcAAAuGGAuuuuG	194	cAAAAUCcAUUUGuAUUGU	853	2632
AD-25890	AcAAAuGGAuuuuGGGAGu	195	ACUCCcAAAAUCcAUUUGU	854	2637
AD-25891	uuGGGAGuGAcucAAGAAG	196	CUUCUUGAGUcACUCCcAA	855	2648
AD-25892	uGGGAGuGAcucAAGAAGu	197	ACUUCUUGAGUcACUCCcA	856	2649
AD-25893	GAAGuGAAGAAuGcAcAAG	198	CUUGUGcAUUCUUcACUUC	857	2663
AD-25894	AAGuGAAGAAuGcAcAAGA	199	UCUUGUGcAUUCUUcACUU	858	2664
AD-25895	GAuGGAAuuuAucAAAccc	200	GGGUUUGAuAAAUUCcAUC	859	2694
AD-25896	AuGGAAuuuAucAAAcccu	201	AGGGUUUGAuAAAUUCcAU	860	2695
AD-25897	GGAAuuuAucAAAcccuAG	202	CuAGGGUUUGAuAAAUUCC	861	2697
AD-25898	GAAuuuAucAAAcccuAGc	203	GCuAGGGUUUGAuAAAUUC	862	2698
AD-25899	AAuuuAucAAAcccuAGcc	204	GGCuAGGGUUUGAuAAAUU	863	2699

AD-25900	GAAuAucuGuAAuGGuAcu	205	AGuACcAUuAcAGAuAUUC	864	2751
AD-25901	AAuAucuGuAAuGGuAcuG	206	cAGuACcAUuAcAGAuAUU	865	2752
AD-25902	AuAucuGuAAuGGuAcuGA	207	UcAGuACcAUuAcAGAuAU	866	2753
AD-25903	uuuuAAGucucucGuAGuG	208	cACuACGAGAGACUuAAAA	867	2832
AD-25904	uuuAAGucucucGuAGuGu	209	AcACuACGAGAGACUuAAA	868	2833
AD-25905	AGucucucGuAGuGuuAAG	210	CUuAAcACuACGAGAGACU	869	2837
AD-25906	ucGuAGuGuuAAGuuAuAG	211	CuAuAACUuAAcACuACGA	870	2843
AD-25907	cGuAGuGuuAAGuuAuAGu	212	ACuAuAACUuAAcACuACG	871	2844
AD-25908	GuAGuGuuAAGuuAuAGuG	213	cACuAuAACUuAAcACuAC	872	2845
AD-25909	uAGuGuuAAGuuAuAGuGA	214	UcACuAuAACUuAAcACuA	873	2846
AD-25910	uAGuGAAuAcuGcuAcAGc	215	GCUGuAGcAGuAUUcACuA	874	2859
AD-25911	AAcAcuAAuucAuAAucAc	216	GUGAUuAUGAAUuAGUGUU	875	2913
AD-25912	AcAcuAAuucAuAAucAcu	217	AGUGAUuAUGAAUuAGUGU	876	2914
AD-25913	uAAuuGuAAucuGAAuAAA	218	UUuAUUcAGAUuAcAAUuA	877	2938
AD-25914	AuuGuAAucuGAAuAAAGu	219	ACUUuAUUcAGAUuAcAAU	878	2940
AD-25915	uuGuAAucuGAAuAAAGuG	220	cACUUuAUUcAGAUuAcAA	879	2941
AD-25916	uGuAAucuGAAuAAAGuGu	221	AcACUUuAUUcAGAUuAcA	880	2942
AD-25917	GAcAAAuAGAAAAuGGucc	222	GGACcAUUUUCuAUUUGUC	881	2991
AD-25918	AcAAAuAGAAAAuGGuccA	223	UGGACcAUUUUCuAUUUGU	882	2992
AD-25919	uAGAAAAuGGuccAAuuAG	224	CuAAUUGGACcAUUUUCuA	883	2997
AD-25920	AGAAAAuGGuccAAuuAGu	225	ACuAAUUGGACcAUUUUCU	884	2998
AD-25921	uAuuuGGGAuAuGuAuGGG	226	CCcAuAcAuAUCCcAAAuA	885	3077
AD-25922	AuuuGGGAuAuGuAuGGGu	227	ACCcAuAcAuAUCCcAAAU	886	3078
AD-25923	uuGGGAuAuGuAuGGGuAG	228	CuACCcAuAcAuAUCCcAA	887	3080
AD-25924	GGAuAuGuAuGGGuAGGGu	229	ACCCuACCcAuAcAuAUCC	888	3083
AD-25925	AAGAGGuGuuAuuuGGAAc	230	GUUCcAAAuAAcACCUCUU	889	3110
AD-25926	AGAGGuGuuAuuuGGAAcc	231	GGUUCcAAAuAAcACCUCU	890	3111
AD-25927	GAGGuGuuAuuuGGAAccu	232	AGGUUCcAAAuAAcACCUC	891	3112
AD-25928	uGGAAccuuGuuuuGGAcA	233	UGUCcAAAAcAAGGUUCcA	892	3123
AD-25929	GGAAccuuGuuuuGGAcAG	234	CUGUCcAAAAcAAGGUUCC	893	3124
AD-25930	GAAccuuGuuuuGGAcAGu	235	ACUGUCcAAAAcAAGGUUC	894	3125
AD-25931	GuuuuGGAcAGuuuAccAG	236	CUGGuAAACUGUCcAAAAC	895	3132
AD-25932	uuuuGGAcAGuuuAccAGu	237	ACUGGuAAACUGUCcAAAA	896	3133
AD-25933	uuGGAcAGuuuAccAGuuG	238	cAACUGGuAAACUGUCcAA	897	3135
AD-25934	GuuGuuGuAAccuGcuGuG	239	cAcAGcAGGUuAcAAcAAC	898	3168
AD-25935	uuGuuGuAAccuGcuGuGA	240	UcAcAGcAGGUuAcAAcAA	899	3169
AD-25936	uuGuAAccuGcuGuGAuAc	241	GuAUcAcAGcAGGUuAcAA	900	3172
AD-25937	AuGcuucAAGAGAAAAuGc	242	GcAUUUUCUCUUGAAGcAU	901	3192
AD-25938	AGuGAAGAAuGcAcAAGAA	243	UUCUUGUGcAUUCUUcACU	902	2665
AD-25939	AAuGGAucAcAAGAuGGAA	244	UUCcAUCUUGUGAUCcAUU	903	2682
AD-25940	AuGGAucAcAAGAuGGAAu	245	AUUCcAUCUUGUGAUCcAU	904	2683
AD-25941	uGGAucAcAAGAuGGAAuu	246	AAUUCcAUCUUGUGAUCcA	905	2684
AD-25942	GGAucAcAAGAuGGAAuuu	247	AAAUUCcAUCUUGUGAUCC	906	2685

AD-25943	GAucAcAAGAuGGAAuuuA	248	uAAAUUCcAUCUUGUGAUC	907	2686
AD-25944	AucAcAAGAuGGAAuuuAu	249	AuAAAUUCcAUCUUGUGAU	908	2687
AD-25945	uGGAAuuuAucAAAcccuA	250	uAGGGUUUGAuAAAUUCcA	909	2696
AD-25946	AcccuAGccuuGcuuGuuA	251	uAAcAAGcAAGGCuAGGGU	910	2709
AD-25947	cccuAGccuuGcuuGuuAA	252	UuAAcAAGcAAGGCuAGGG	911	2710
AD-25948	ccuAGccuuGcuuGuuAAA	253	UUuAAcAAGcAAGGCuAGG	912	2711
AD-25949	cuAGccuuGcuuGuuAAAu	254	AUUuAAcAAGcAAGGCuAG	913	2712
AD-25950	uAGccuuGcuuGuuAAAuu	255	AAUUuAAcAAGcAAGGCuA	914	2713
AD-25951	AGccuuGcuuGuuAAAuuu	256	AAAUUuAAcAAGcAAGGCU	915	2714
AD-25952	uuAAGucucucGuAGuGuu	257	AAcACuACGAGAGACUuAA	916	2834
AD-25953	uAAGucucucGuAGuGuuA	258	uAAcACuACGAGAGACUuA	917	2835
AD-25954	AAGucucucGuAGuGuuAA	259	UuAAcACuACGAGAGACUU	918	2836
AD-25955	cucGuAGuGuuAAGuuAuA	260	uAuAACUuAAcACuACGAG	919	2842
AD-25956	AGuGuuAAGuuAuAGuGAA	261	UUcACuAuAACUuAAcACU	920	2847
AD-25957	GuGuuAAGuuAuAGuGAAu	262	AUUcACuAuAACUuAAcAC	921	2848
AD-25958	cuAcAGcAAuuucuAAuuu	263	AAAUuAGAAAUUGCUGuAG	922	2871
AD-25959	cAAAuAGAAAAuGGuccAA	264	UUGGACcAUUUUCuAUUUG	923	2993
AD-25960	AuAGAAAAuGGuccAAuuA	265	uAAUUGGACcAUUUUCuAU	924	2996
AD-25961	uuuGGGAuAuGuAuGGGuA	266	uACCcAuAcAuAUCCcAAA	925	3079
AD-25962	GAuAuGuAuGGGuAGGGuA	267	uACCCuACCcAuAcAuAUC	926	3084
AD-25963	uGGGuAGGGuAAAucAGuA	268	uACUGAUUuACCCuACCcA	927	3092
AD-25964	uAAGAGGuGuuAuuuGGAA	269	UUCcAAAuAAcACCUCUuA	928	3109
AD-26017	uGccuuuuAucccAAAGuu	270	AACUUUGGGAuAAAAGGcA	929	3152
AD-26018	uGuuGuAAccuGcuGuGAu	271	AUcAcAGcAGGUuAcAAcA	930	3170
AD-26019	GuuGuAAccuGcuGuGAuA	272	uAUcAcAGcAGGUuAcAAC	931	3171
AD-26020	cAAGAGAAAAuGcGGuuAu	273	AuAACCGcAUUUUCUCUUG	932	3198
AD-26021	AAGAGAAAAuGcGGuuAuA	274	uAuAACCGcAUUUUCUCUU	933	3199
AD-26022	ccuGuuccccuGAGGGuAu	275	AuACCCUcAGGGGAAcAGG	934	207
AD-26023	cuGuuccccuGAGGGuAuu	276	AAuACCCUcAGGGGAAcAG	935	208
AD-26024	ccuGAGGGuAuuuGAAGuA	277	uACUUcAAAuACCCUcAGG	936	215
AD-26025	cuGAGGGuAuuuGAAGuAu	278	AuACUUcAAAuACCCUcAG	937	216
AD-26026	uGAGGGuAuuuGAAGuAuA	279	uAuACUUcAAAuACCCUcA	938	217
AD-26027	GGuAuuuGAAGuAuAccAu	280	AUGGuAuACUUcAAAuACC	939	221
AD-26028	GuAuuuGAAGuAuAccAuA	281	uAUGGuAuACUUcAAAuAC	940	222
AD-26029	uuuGAAGuAuAccAuAcAA	282	UUGuAUGGuAuACUUcAAA	941	225
AD-26030	AGuAuAccAuAcAAcuGuu	283	AAcAGUUGuAUGGuAuACU	942	230
AD-26031	GuAuAccAuAcAAcuGuuu	284	AAAcAGUUGuAUGGuAuAC	943	231
AD-26032	uAuAccAuAcAAcuGuuuu	285	AAAAcAGUUGuAUGGuAuA	944	232
AD-26033	AccAuAcAAcuGuuuuGAA	286	UUcAAAAcAGUUGuAUGGU	945	235
AD-26034	ccAuAcAAcuGuuuuGAAA	287	UUUcAAAAcAGUUGuAUGG	946	236
AD-26035	GAAAAuccAGcGuGGAcAA	288	UUGUCcACGCUGGAUUUUC	947	251
AD-26036	AAAAuccAGcGuGGAcAAu	289	AUUGUCcACGCUGGAUUUU	948	252
AD-26037	ccAGcGuGGAcAAuGGcuA	290	uAGCcAUUGUCcACGCUGG	949	257

AD-26038	GuGGAcAAuGGcuAcucAA	291	UUGAGuAGCcAUUGUCcAC	950	262
AD-26039	AAuGGcuAcucAAGcuGAu	292	AUcAGCUUGAGuAGCcAUU	951	268
AD-26040	AuGGcuAcucAAGcuGAuu	293	AAUcAGCUUGAGuAGCcAU	952	269
AD-26041	uGGcuAcucAAGcuGAuuu	294	AAAUcAGCUUGAGuAGCcA	953	270
AD-26042	cuAcucAAGcuGAuuuGAu	295	AUcAAAUcAGCUUGAGuAG	954	273
AD-26043	AuuuGAuGGAGuuGGAcAu	296	AUGUCcAACUCcAUcAAAU	955	285
AD-26044	uGGAGuuGGAcAuGGccAu	297	AUGGCcAUGUCcAACUCcA	956	291
AD-26045	GuuGGAcAuGGccAuGGAA	298	UUCcAUGGCcAUGUCcAAC	957	295
AD-26046	GccAuGGAAccAGAcAGAA	299	UUCUGUCUGGUUCcAUGGC	958	305
AD-26047	cAuGGAAccAGAcAGAAAA	300	UUUUCUGUCUGGUUCcAUG	959	307
AD-26048	GGAGGcGGAGAcGGAGGAA	301	UUCCUCCGUCUCCGCCUCC	960	111
AD-26049	AGAcAGAAAAGcGGcuGuu	302	AAcAGCCGCUUUUCUGUCU	961	316
AD-26050	GAcAGAAAAGcGGcuGuuA	303	uAAcAGCCGCUUUUCUGUC	962	317
AD-26051	uGuuAGucAcuGGcAGcAA	304	UUGCUGCcAGUGACuAAcA	963	331
AD-26052	cAcuGGcAGcAAcAGucuu	305	AAGACUGUUGCUGCcAGUG	964	338
AD-26053	AcuGGcAGcAAcAGucuuA	306	uAAGACUGUUGCUGCcAGU	965	339
AD-26054	ucuuAccuGGAcucuGGAA	307	UUCcAGAGUCcAGGuAAGA	966	353
AD-26055	cuuAccuGGAcucuGGAAu	308	AUUCcAGAGUCcAGGuAAG	967	354
AD-26056	ccuGGAcucuGGAAuccAu	309	AUGGAUUCcAGAGUCcAGG	968	358
AD-26057	GGcuAGuGGuGGAccccAA	310	UUGGGGUCcACcACuAGCC	969	1216
AD-26058	GccAcuAccAcAGcuccuu	311	AAGGAGCUGUGGuAGUGGC	970	383
AD-26059	uccuucucuGAGuGGuAAA	312	UUuACcACUcAGAGAAGGA	971	397
AD-26060	cucuGAGuGGuAAAGGcAA	313	UUGCCUUuACcACUcAGAG	972	402
AD-26061	uAAAGGcAAuccuGAGGAA	314	UUCCUcAGGAUUGCCUUuA	973	412
AD-26062	cAAuccuGAGGAAGAGGAu	315	AUCCUCUUCCUcAGGAUUG	974	418
AD-26063	uGAGGAAGAGGAuGuGGAu	316	AUCcAcAUCCUCUUCCUcA	975	424
AD-26064	AuAccucccAAGuccuGuA	317	uAcAGGACUUGGGAGGuAU	976	441
AD-26065	uAccucccAAGuccuGuAu	318	AuAcAGGACUUGGGAGGuA	977	442
AD-26066	AGuccuGuAuGAGuGGGAA	319	UUCCcACUcAuAcAGGACU	978	451
AD-26067	uAuGAGuGGGAAcAGGGAu	320	AUCCCUGUUCCcACUcAuA	979	458
AD-26068	cAAGcuuuAGuAAAuAuAA	321	UuAuAUUuACuAAAGCUUG	980	1232
AD-26069	AAGcuuuAGuAAAuAuAAu	322	AUuAuAUUuACuAAAGCUU	981	1233
AD-26070	uGAGuGGGAAcAGGGAuuu	323	AAAUCCCUGUUCCcACUcA	982	460
AD-26071	GAGuGGGAAcAGGGAuuuu	324	AAAAUCCCUGUUCCcACUC	983	461
AD-26072	AGGGAuuuucucAGuccuu	325	AAGGACUGAGAAAAUCCCU	984	471
AD-26073	uucucAGuccuucAcucAA	326	UUGAGUGAAGGACUGAGAA	985	478
AD-26074	ucAGuccuucAcucAAGAA	327	UUCUUGAGUGAAGGACUGA	986	481
AD-26075	cuucAcucAAGAAcAAGuA	328	uACUUGUUCUUGAGUGAAG	987	487
AD-26076	ucAAGAAcAAGuAGcuGAu	329	AUcAGCuACUUGUUCUUGA	988	493
AD-26077	cuGAuAuuGAuGGAcAGuA	330	uACUGUCcAUcAAuAUcAG	989	507
AD-26078	AuuGAuGGAcAGuAuGcAA	331	UUGcAuACUGUCcAUcAAU	990	512
AD-26079	GAcucGAGcucAGAGGGuA	332	uACCCUCUGAGCUCGAGUC	991	532
AD-26080	cAGAGGGuAcGAGcuGcuA	333	uAGcAGCUCGuACCCUCUG	992	542

AD-26081	AGAGGGuAcGAGcuGcuAu	334	AuAGcAGCUCGuACCCUCU	993	543
AD-26082	GGGuAcGAGcuGcuAuGuu	335	AAcAuAGcAGCUCGuACCC	994	546
AD-26083	cuAuGuucccuGAGAcAuu	336	AAUGUCUcAGGGAAcAuAG	995	558
AD-26084	uAuGuucccuGAGAcAuuA	337	uAAUGUCUcAGGGAAcAuA	996	559
AD-26085	GuucccuGAGAcAuuAGAu	338	AUCuAAUGUCUcAGGGAAC	997	562
AD-26086	uAGAuGAGGGcAuGcAGAu	339	AUCUGcAUGCCCUcAUCuA	998	576
AD-26087	GAGGGcAuGcAGAucccAu	340	AUGGGAUCUGcAUGCCCUC	999	581
AD-26088	GGcAuGcAGAucccAucuA	341	uAGAUGGGAUCUGcAUGCC	1000	584
AD-26089	AGAucccAucuAcAcAGuu	342	AACUGUGuAGAUGGGAUCU	1001	591
AD-26090	cccAucuAcAcAGuuuGAu	343	AUcAAACUGUGuAGAUGGG	1002	595
AD-26091	AcAGuuuGAuGcuGcucAu	344	AUGAGcAGcAUcAAACUGU	1003	604
AD-26092	GAuGcuGcucAucccAcuA	345	uAGUGGGAUGAGcAGcAUC	1004	611
AD-26093	AuGcuGcucAucccAcuAA	346	UuAGUGGGAUGAGcAGcAU	1005	612
AD-26094	uGcuGcucAucccAcuAAu	347	AUuAGUGGGAUGAGcAGcA	1006	613
AD-26095	cccAcuAAuGuccAGcGuu	348	AACGCUGGAcAUuAGUGGG	1007	623
AD-26096	cAGcGuuuGGcuGAAccAu	349	AUGGUUcAGCcAAACGCUG	1008	635
AD-26097	uGGcuGAAccAucAcAGAu	350	AUCUGUGAUGGUUcAGCcA	1009	642
AD-26098	AAccAucAcAGAuGcuGAA	351	UUcAGcAUCUGUGAUGGUU	1010	648
AD-26099	AccAucAcAGAuGcuGAAA	352	UUUcAGcAUCUGUGAUGGU	1011	649
AD-26100	AucAcAGAuGcuGAAAcAu	353	AUGUUUcAGcAUCUGUGAU	1012	652
AD-26101	GAuGcuGAAAcAuGcAGuu	354	AACUGcAUGUUUcAGcAUC	1013	658
AD-26102	cuGAAAcAuGcAGuuGuAA	355	UuAcAACUGcAUGUUUcAG	1014	662
AD-26103	AAcAuGcAGuuGuAAAcuu	356	AAGUUuAcAACUGcAUGUU	1015	666
AD-26104	AuGcAGuuGuAAAcuuGAu	357	AUcAAGUUuAcAACUGcAU	1016	669
AD-26105	uGcAGuuGuAAAcuuGAuu	358	AAUcAAGUUuAcAACUGcA	1017	670
AD-26106	cAGuuGuAAAcuuGAuuAA	359	UuAAUcAAGUUuAcAACUG	1018	672
AD-26107	cuuGAuuAAcuAucAAGAu	360	AUCUUGAuAGUuAAUcAAG	1019	682
AD-26108	GAuuAAcuAucAAGAuGAu	361	AUcAUCUUGAuAGUuAAUC	1020	685
AD-26109	cuAucAAGAuGAuGcAGAA	362	UUCUGcAUcAUCUUGAuAG	1021	691
AD-26110	GAAcuuGccAcAcGuGcAA	363	UUGcACGUGUGGcAAGUUC	1022	707
AD-26111	AAcuuGccAcAcGuGcAAu	364	AUUGcACGUGUGGcAAGUU	1023	708
AD-26112	cAcAcGuGcAAucccuGAA	365	UUcAGGGAUUGcACGUGUG	1024	715
AD-26123	GcAAucccuGAAcuGAcAA	366	UUGUcAGUUcAGGGAUUGC	1025	722
AD-26124	cAAucccuGAAcuGAcAAA	367	UUUGUcAGUUcAGGGAUUG	1026	723
AD-26125	AAucccuGAAcuGAcAAAA	368	UUUUGUcAGUUcAGGGAUU	1027	724
AD-26126	uGAAcuGAcAAAAcuGcuA	369	uAGcAGUUUUGUcAGUUcA	1028	730
AD-26127	GAAcuGAcAAAAcuGcuAA	370	UuAGcAGUUUUGUcAGUUC	1029	731
AD-26128	AAcuGAcAAAAcuGcuAAA	371	UUuAGcAGUUUUGUcAGUU	1030	732
AD-26129	AcuGAcAAAAcuGcuAAAu	372	AUUuAGcAGUUUUGUcAGU	1031	733
AD-26130	GAGGAccAGGuGGuGGuuA	373	uAACcACcACCUGGUCCUC	1032	755
AD-26131	AGGAccAGGuGGuGGuuAA	374	UuAACcACcACCUGGUCCU	1033	756
AD-26132	GGAccAGGuGGuGGuuAAu	375	AUuAACcACcACCUGGUCC	1034	757
AD-26133	GAccAGGuGGuGGuuAAuA	376	uAUuAACcACcACCUGGUC	1035	758

AD-26134	ucAcuuGcAAuAAuuAuAA	377	UuAuAAUuAUUGcAAGUGA	1036	1548
AD-26135	cuuGcAAuAAuuAuAAGAA	378	UUCUuAuAAUuAUUGcAAG	1037	1551
AD-26136	AccAGGuGGuGGuuAAuAA	379	UuAUuAACcACcACCUGGU	1038	759
AD-26137	GGcuGcAGuuAuGGuccAu	380	AUGGACcAuAACUGcAGCC	1039	778
AD-26138	GuuAuGGuccAucAGcuuu	381	AAAGCUGAUGGACcAuAAC	1040	785
AD-26139	AuGGuccAucAGcuuucuA	382	uAGAAAGCUGAUGGACcAU	1041	788
AD-26140	uGGuccAucAGcuuucuAA	383	UuAGAAAGCUGAUGGACcA	1042	789
AD-26141	ucGGGcuGGuGAcAGGGAA	384	UUCCCUGUcACcAGCCCGA	1043	1624
AD-26142	GGuccAucAGcuuucuAAA	385	UUuAGAAAGCUGAUGGACC	1044	790
AD-26143	GuccAucAGcuuucuAAAA	386	UUUuAGAAAGCUGAUGGAC	1045	791
AD-26144	GAAGcuuccAGAcAcGcuA	387	uAGCGUGUCUGGAAGCUUC	1046	812
AD-26145	AAGcuuccAGAcAcGcuAu	388	AuAGCGUGUCUGGAAGCUU	1047	813
AD-26146	cuuccAGAcAcGcuAucAu	389	AUGAuAGCGUGUCUGGAAG	1048	816
AD-26147	AGAcAcGcuAucAuGcGuu	390	AACGcAUGAuAGCGUGUCU	1049	821
AD-26148	ucAuGcGuucuccucAGAu	391	AUCUGAGGAGAACGcAUGA	1050	831
AD-26149	ccucAGAuGGuGucuGcuA	392	uAGcAGAcACcAUCUGAGG	1051	842
AD-26150	cucAGAuGGuGucuGcuAu	393	AuAGcAGAcACcAUCUGAG	1052	843
AD-26151	GuGucuGcuAuuGuAcGuA	394	uACGuAcAAuAGcAGAcAC	1053	851
AD-26152	cuGcuAuuGuAcGuAccAu	395	AUGGuACGuAcAAuAGcAG	1054	855
AD-26153	uuGuAcGuAccAuGcAGAA	396	UUCUGcAUGGuACGuAcAA	1055	861
AD-26154	uGuAcGuAccAuGcAGAAu	397	AUUCUGcAUGGuACGuAcA	1056	862
AD-26155	cGuAccAuGcAGAAuAcAA	398	UUGuAUUCUGcAUGGuACG	1057	866
AD-26156	cAuGcAGAAuAcAAAuGAu	399	AUcAUUUGuAUUCUGcAUG	1058	871
AD-26157	GcAGAAuAcAAAuGAuGuA	400	uAcAUcAUUUGuAUUCUGC	1059	874
AD-26158	GAAuAcAAAuGAuGuAGAA	401	UUCuAcAUcAUUUGuAUUC	1060	877
AD-26159	GAuGuAGAAAcAGcucGuu	402	AACGAGCUGUUUCuAcAUC	1061	887
AD-26160	GuuGuAccGcuGGGAccuu	403	AAGGUCCcAGCGGuAcAAC	1062	903
AD-26161	uAccGcuGGGAccuuGcAu	404	AUGcAAGGUCCcAGCGGuA	1063	907
AD-26162	ccGcuGGGAccuuGcAuAA	405	UuAUGcAAGGUCCcAGCGG	1064	909
AD-26163	uGGGAccuuGcAuAAccuu	406	AAGGUuAUGcAAGGUCCcA	1065	913
AD-26164	GGGAccuuGcAuAAccuuu	407	AAAGGUuAUGcAAGGUCCC	1066	914
AD-26165	cuuGcAuAAccuuucccAu	408	AUGGGAAAGGUuAUGcAAG	1067	919
AD-26166	ucuuuAAGucuGGAGGcAu	409	AUGCCUCcAGACUuAAAGA	1068	960
AD-26167	GcAuuccuGcccuGGuGAA	410	UUcACcAGGGcAGGAAUGC	1069	975
AD-26168	cAuuccuGcccuGGuGAAA	411	UUUcACcAGGGcAGGAAUG	1070	976
AD-26169	AuuccuGcccuGGuGAAAA	412	UUUUcACcAGGGcAGGAAU	1071	977
AD-26170	uuccuGcccuGGuGAAAAu	413	AUUUUcACcAGGGcAGGAA	1072	978
AD-26171	uGcccuGGuGAAAAuGcuu	414	AAGcAUUUUcACcAGGGcA	1073	982
AD-26172	cuGGuGAAAAuGcuuGGuu	415	AACcAAGcAUUUUcACcAG	1074	986
AD-26173	GcuuGGuucAccAGuGGAu	416	AUCcACUGGUGAACcAAGC	1075	997
AD-26174	cuuGGuucAccAGuGGAuu	417	AAUCcACUGGUGAACcAAG	1076	998
AD-26175	uGcGuGAGcAGGGuGccAu	418	AUGGcACCCUGCUcACGcA	1077	1848
AD-26176	GcGuGAGcAGGGuGccAuu	419	AAUGGcACCCUGCUcACGC	1078	1849

AD-26177	cAccAGuGGAuucuGuGuu	420	AAcAcAGAAUCcACUGGUG	1079	1005
AD-26178	cAGuGGAuucuGuGuuGuu	421	AAcAAcAcAGAAUCcACUG	1080	1008
AD-26179	AGuGGAuucuGuGuuGuuu	422	AAAcAAcAcAGAAUCcACU	1081	1009
AD-26180	GuGGAuucuGuGuuGuuuu	423	AAAAcAAcAcAGAAUCcAC	1082	1010
AD-26181	uGGAuucuGuGuuGuuuuA	424	uAAAAcAAcAcAGAAUCcA	1083	1011
AD-26182	GGAuucuGuGuuGuuuuAu	425	AuAAAAcAAcAcAGAAUCC	1084	1012
AD-26183	uGuGuuGuuuuAuGccAuu	426	AAUGGcAuAAAAcAAcAcA	1085	1018
AD-26184	GGGuGGGAcAcAGcAGcAA	427	UUGCUGCUGUGUCCcACCC	1086	1927
AD-26185	GuGuuGuuuuAuGccAuuA	428	uAAUGGcAuAAAAcAAcAC	1087	1019
AD-26186	uuGuuuuAuGccAuuAcAA	429	UUGuAAUGGcAuAAAAcAA	1088	1022
AD-26187	ccAuuAcAAcucuccAcAA	430	UUGUGGAGAGUUGuAAUGG	1089	1032
AD-26188	uAcAAcucuccAcAAccuu	431	AAGGUUGUGGAGAGUUGuA	1090	1036
AD-26189	AcAAcucuccAcAAccuuu	432	AAAGGUUGUGGAGAGUUGU	1091	1037
AD-26190	cAAcucuccAcAAccuuuu	433	AAAAGGUUGUGGAGAGUUG	1092	1038
AD-26191	AAcucuccAcAAccuuuuA	434	uAAAAGGUUGUGGAGAGUU	1093	1039
AD-26192	AcucuccAcAAccuuuuAu	435	AuAAAAGGUUGUGGAGAGU	1094	1040
AD-26193	cucuccAcAAccuuuuAuu	436	AAuAAAAGGUUGUGGAGAG	1095	1041
AD-26194	ucuccAcAAccuuuuAuuA	437	uAAuAAAAGGUUGUGGAGA	1096	1042
AD-26195	cAAccuuuuAuuAcAucAA	438	UUGAUGuAAuAAAAGGUUG	1097	1048
AD-26196	ccuuuuAuuAcAucAAGAA	439	UUCUUGAUGuAAuAAAAGG	1098	1051
AD-26197	uuAcAucAAGAAGGAGcuA	440	uAGCUCCUUCUUGAUGuAA	1099	1058
AD-26198	uAcAucAAGAAGGAGcuAA	441	UuAGCUCCUUCUUGAUGuA	1100	1059
AD-26199	cAucAAGAAGGAGcuAAAA	442	UUUuAGCUCCUUCUUGAUG	1101	1061
AD-26200	AucAAGAAGGAGcuAAAAu	443	AUUUuAGCUCCUUCUUGAU	1102	1062
AD-26201	GcuAAAAuGGcAGuGcGuu	444	AACGcACUGCcAUUUuAGC	1103	1073
AD-26202	uAAAAuGGcAGuGcGuuuA	445	uAAACGcACUGCcAUUUuA	1104	1075
AD-26203	AAAuGGuuGccuuGcucAA	446	UUGAGcAAGGcAACcAUUU	1105	1110
AD-26204	GccuGuuccccuGAGGGuA	447	uACCCUcAGGGGAAcAGGC	1106	206
AD-26205	uGGuuGccuuGcucAAcAA	448	UUGUUGAGcAAGGcAACcA	1107	1113
AD-26206	GGuuGccuuGcucAAcAAA	449	UUUGUUGAGcAAGGcAACC	1108	1114
AD-26207	GuuGccuuGcucAAcAAAA	450	UUUUGUUGAGcAAGGcAAC	1109	1115
AD-26208	GccuuGcucAAcAAAAcAA	451	UUGUUUUGUUGAGcAAGGC	1110	1118
AD-26209	ccuuGcucAAcAAAAcAAA	452	UUUGUUUUGUUGAGcAAGG	1111	1119
AD-26210	GuuAAAuucuuGGcuAuuA	453	uAAuAGCcAAGAAUUuAAC	1112	1139
AD-26211	uAuuAcGAcAGAcuGccuu	454	AAGGcAGUCUGUCGuAAuA	1113	1153
AD-26212	AuGGcAAccAAGAAAGcAA	455	UUGCUUUCUUGGUUGCcAU	1114	1185
AD-26213	AGuGGuGGAccccAAGcuu	456	AAGCUUGGGGUCcACcACU	1115	1220
AD-26214	GuGGuGGAccccAAGcuuu	457	AAAGCUUGGGGUCcACcAC	1116	1221
AD-26215	uGGuGGAccccAAGcuuuA	458	uAAAGCUUGGGGUCcACcA	1117	1222
AD-26216	uGGAccccAAGcuuuAGuA	459	uACuAAAGCUUGGGGUCcA	1118	1225
AD-26217	GGAccccAAGcuuuAGuAA	460	UuACuAAAGCUUGGGGUCC	1119	1226
AD-26218	GAccccAAGcuuuAGuAAA	461	UUuACuAAAGCUUGGGGUC	1120	1227
AD-26651	AccccAAGcuuuAGuAAAu	462	AUUuACuAAAGCUUGGGGU	1121	1228

AD-26652	ccccAAGcuuuAGuAAAuA	463	uAUUuACuAAAGCUUGGGG	1122	1229
AD-26653	cccAAGcuuuAGuAAAuAu	464	AuAUUuACuAAAGCUUGGG	1123	1230
AD-26654	ccAAGcuuuAGuAAAuAuA	465	uAuAUUuACuAAAGCUUGG	1124	1231
AD-26655	uAAAuAuAAuGAGGAccuA	466	uAGGUCCUcAUuAuAUUuA	1125	1242
AD-26656	AAAuAuAAuGAGGAccuAu	467	AuAGGUCCUcAUuAuAUUU	1126	1243
AD-26657	AAuAuAAuGAGGAccuAuA	468	uAuAGGUCCUcAUuAuAUU	1127	1244
AD-26658	AuAAuGAGGAccuAuAcuu	469	AAGuAuAGGUCCUcAUuAU	1128	1247
AD-26659	AAAcuAcuGuGGAccAcAA	470	UUGUGGUCcAcAGuAGUUU	1129	1271
AD-26660	ccAcAAGcAGAGuGcuGAA	471	UUcAGcACUCUGCUUGUGG	1130	1284
AD-26661	cAGAGuGcuGAAGGuGcuA	472	uAGcACCUUcAGcACUCUG	1131	1291
AD-26662	AGAGuGcuGAAGGuGcuAu	473	AuAGcACCUUcAGcACUCU	1132	1292
AD-26663	AuuGuAGAAGcuGGuGGAA	474	UUCcACcAGCUUCuAcAAU	1133	1337
AD-26664	uuGuAGAAGcuGGuGGAAu	475	AUUCcACcAGCUUCuAcAA	1134	1338
AD-26665	GcuGGuGGAAuGcAAGcuu	476	AAGCUUGcAUUCcACcAGC	1135	1346
AD-26666	cuGGuGGAAuGcAAGcuuu	477	AAAGCUUGcAUUCcACcAG	1136	1347
AD-26667	AGGAcuucAccuGAcAGAu	478	AUCUGUcAGGUGAAGUCCU	1137	1366
AD-26668	cuucAccuGAcAGAuccAA	479	UUGGAUCUGUcAGGUGAAG	1138	1370
AD-26669	ccuGAcAGAuccAAGucAA	480	UUGACUUGGAUCUGUcAGG	1139	1375
AD-26670	AGAuccAAGucAAcGucuu	481	AAGACGUUGACUUGGAUCU	1140	1381
AD-26671	uccAAGucAAcGucuuGuu	482	AAcAAGACGUUGACUUGGA	1141	1384
AD-26672	ucuuGuucAGAAcuGucuu	483	AAGAcAGUUCUGAAcAAGA	1142	1396
AD-26673	cuuGuucAGAAcuGucuuu	484	AAAGAcAGUUCUGAAcAAG	1143	1397
AD-26674	GucuuuGGAcucucAGGAA	485	UUCCUGAGAGUCcAAAGAC	1144	1410
AD-26675	ucuuuGGAcucucAGGAAu	486	AUUCCUGAGAGUCcAAAGA	1145	1411
AD-26676	uuGGAcucucAGGAAucuu	487	AAGAUUCCUGAGAGUCcAA	1146	1414
AD-26677	uGcccAGGGAGAAccccuu	488	AAGGGGUUCUCCCUGGGcA	1147	2371
AD-26678	uGGAcucucAGGAAucuuu	489	AAAGAUUCCUGAGAGUCcA	1148	1415
AD-26679	ucucAGGAAucuuucAGAu	490	AUCUGAAAGAUUCCUGAGA	1149	1420
AD-26680	AAucuuucAGAuGcuGcAA	491	UUGcAGcAUCUGAAAGAUU	1150	1427
AD-26681	cuuucAGAuGcuGcAAcuA	492	uAGUUGcAGcAUCUGAAAG	1151	1430
AD-26682	uucAGAuGcuGcAAcuAAA	493	UUuAGUUGcAGcAUCUGAA	1152	1432
AD-26683	uGcuGcAAcuAAAcAGGAA	494	UUCCUGUUuAGUUGcAGcA	1153	1438
AD-26684	uAAAcAGGAAGGGAuGGAA	495	UUCcAUCCCUUCCUGUUuA	1154	1447
AD-26685	AGGGAuGGAAGGucuccuu	496	AAGGAGACCUUCcAUCCCU	1155	1456
AD-26686	AGGucuccuuGGGAcucuu	497	AAGAGUCCcAAGGAGACCU	1156	1465
AD-26687	ucuccuuGGGAcucuuGuu	498	AAcAAGAGUCCcAAGGAGA	1157	1468
AD-26688	uGGGAcucuuGuucAGcuu	499	AAGCUGAAcAAGAGUCCcA	1158	1474
AD-26689	cuuGuucAGcuucuGGGuu	500	AACCcAGAAGCUGAAcAAG	1159	1481
AD-26690	ucAGcuucuGGGuucAGAu	501	AUCUGAACCcAGAAGCUGA	1160	1486
AD-26691	GcuucuGGGuucAGAuGAu	502	AUcAUCUGAACCcAGAAGC	1161	1489
AD-26692	cuucuGGGuucAGAuGAuA	503	uAUcAUCUGAACCcAGAAG	1162	1490
AD-26693	GGccAGGAuGccuuGGGuA	504	uACCcAAGGcAUCCUGGCC	1163	2441
AD-26694	uucuGGGuucAGAuGAuAu	505	AuAUcAUCUGAACCcAGAA	1164	1491

AD-26695	cuGGGuucAGAuGAuAuAA	506	UuAuAUcAUCUGAACCcAG	1165	1493
AD-26696	uGGGuucAGAuGAuAuAAA	507	UUuAuAUcAUCUGAACCcA	1166	1494
AD-26697	GucAccuGuGcAGcuGGAA	508	UUCcAGCUGcAcAGGUGAC	1167	1517
AD-26698	ucAccuGuGcAGcuGGAAu	509	AUUCcAGCUGcAcAGGUGA	1168	1518
AD-26699	cAccuGuGcAGcuGGAAuu	510	AAUUCcAGCUGcAcAGGUG	1169	1519
AD-26700	cuGuGcAGcuGGAAuucuu	511	AAGAAUUCcAGCUGcAcAG	1170	1522
AD-26701	uGuGcAGcuGGAAuucuuu	512	AAAGAAUUCcAGCUGcAcA	1171	1523
AD-26702	GcAGcuGGAAuucuuucuA	513	uAGAAAGAAUUCcAGCUGC	1172	1526
AD-26703	cAGcuGGAAuucuuucuAA	514	UuAGAAAGAAUUCcAGCUG	1173	1527
AD-26704	uuucuAAccucAcuuGcAA	515	UUGcAAGUGAGGUuAGAAA	1174	1539
AD-26705	uucuAAccucAcuuGcAAu	516	AUUGcAAGUGAGGUuAGAA	1175	1540
AD-26706	AccucAcuuGcAAuAAuuA	517	uAAUuAUUGcAAGUGAGGU	1176	1545
AD-26707	ccucAcuuGcAAuAAuuAu	518	AuAAUuAUUGcAAGUGAGG	1177	1546
AD-26708	cucAcuuGcAAuAAuuAuA	519	uAuAAUuAUUGcAAGUGAG	1178	1547
AD-26709	GucuGccAAGuGGGuGGuA	520	uACcACCcACUUGGcAGAC	1179	1580
AD-26710	ucuGccAAGuGGGuGGuAu	521	AuACcACCcACUUGGcAGA	1180	1581
AD-26711	GGGuGGuAuAGAGGcucuu	522	AAGAGCCUCuAuACcACCC	1181	1591
AD-26712	AuAGAGGcucuuGuGcGuA	523	uACGcAcAAGAGCCUCuAU	1182	1598
AD-26713	ucuuGuGcGuAcuGuccuu	524	AAGGAcAGuACGcAcAAGA	1183	1606
AD-26714	cuGGuGAcAGGGAAGAcAu	525	AUGUCUUCCCUGUcACcAG	1184	1629
AD-26715	AcAucAcuGAGccuGccAu	526	AUGGcAGGCUcAGUGAUGU	1185	1644
AD-26716	GccuGccAucuGuGcucuu	527	AAGAGcAcAGAUGGcAGGC	1186	1654
AD-26717	ucuGAccAGccGAcAccAA	528	UUGGUGUCGGCUGGUcAGA	1187	1678
AD-26718	GAccAGccGAcAccAAGAA	529	UUCUUGGUGUCGGCUGGUC	1188	1681
AD-26719	GAcAccAAGAAGcAGAGAu	530	AUCUCUGCUUCUUGGUGUC	1189	1689
AD-26720	AGcAGAGAuGGcccAGAAu	531	AUUCUGGGCcAUCUCUGCU	1190	1699
AD-26721	GAuGGcccAGAAuGcAGuu	532	AACUGcAUUCUGGGCcAUC	1191	1705
AD-26722	ccAGAAuGcAGuucGccuu	533	AAGGCGAACUGcAUUCUGG	1192	1711
AD-26723	AuGcAGuucGccuucAcuA	534	uAGUGAAGGCGAACUGcAU	1193	1716
AD-26724	uGcAGuucGccuucAcuAu	535	AuAGUGAAGGCGAACUGcA	1194	1717
AD-26725	ucGccuucAcuAuGGAcuA	536	uAGUCcAuAGUGAAGGCGA	1195	1723
AD-26726	ucAcuAuGGAcuAccAGuu	537	AACUGGuAGUCcAuAGUGA	1196	1729
AD-26727	uGGAcuAccAGuuGuGGuu	538	AACcAcAACUGGuAGUCcA	1197	1735
AD-26728	GGAcuAccAGuuGuGGuuA	539	uAACcAcAACUGGuAGUCC	1198	1736
AD-26729	GAcuAccAGuuGuGGuuAA	540	UuAACcAcAACUGGuAGUC	1199	1737
AD-26730	cAGuuGuGGuuAAGcucuu	541	AAGAGCUuAACcAcAACUG	1200	1743
AD-26731	AGuuGuGGuuAAGcucuuA	542	uAAGAGCUuAACcAcAACU	1201	1744
AD-26732	AAGcucuuAcAcccAccAu	543	AUGGUGGGUGuAAGAGCUU	1202	1754
AD-26733	cAucccAcuGGccucuGAu	544	AUcAGAGGCcAGUGGGAUG	1203	1770
AD-26734	AucccAcuGGccucuGAuA	545	uAUcAGAGGCcAGUGGGAU	1204	1771
AD-26735	ucccAcuGGccucuGAuAA	546	UuAUcAGAGGCcAGUGGGA	1205	1772
AD-26736	uGGccucuGAuAAAGGcuA	547	uAGCCUUuAUcAGAGGCcA	1206	1778
AD-26737	ucuGAuAAAGGcuAcuGuu	548	AAcAGuAGCCUUuAUcAGA	1207	1783

AD-26738	AuAAAGGcuAcuGuuGGAu	549	AUCcAAcAGuAGCCUUuAU	1208	1787
AD-26739	GGcuAcuGuuGGAuuGAuu	550	AAUcAAUCcAAcAGuAGCC	1209	1792
AD-26740	uGuuGGAuuGAuucGAAAu	551	AUUUCGAAUcAAUCcAAcA	1210	1798
AD-26741	uGccAuuccAcGAcuAGuu	552	AACuAGUCGUGGAAUGGcA	1211	1861
AD-26742	uuccAcGAcuAGuucAGuu	553	AACUGAACuAGUCGUGGAA	1212	1866
AD-26743	AcGAcuAGuucAGuuGcuu	554	AAGcAACUGAACuAGUCGU	1213	1870
AD-26744	AcuAGuucAGuuGcuuGuu	555	AAcAAGcAACUGAACuAGU	1214	1873
AD-26745	GuuGcuuGuucGuGcAcAu	556	AUGUGcACGAAcAAGcAAC	1215	1882
AD-26746	uGuucGuGcAcAucAGGAu	557	AUCCUGAUGUGcACGAAcA	1216	1888
AD-26747	GuucGuGcAcAucAGGAuA	558	uAUCCUGAUGUGcACGAAC	1217	1889
AD-26748	GGuGGGAcAcAGcAGcAAu	559	AUUGCUGCUGUGUCCcACC	1218	1928
AD-26749	GuGGGAcAcAGcAGcAAuu	560	AAUUGCUGCUGUGUCCcAC	1219	1929
AD-26750	uGGGAcAcAGcAGcAAuuu	561	AAAUUGCUGCUGUGUCCcA	1220	1930
AD-26751	GGGGuccGcAuGGAAGAAA	562	UUUCUUCcAUGCGGACCCC	1221	1955
AD-26752	GGGuccGcAuGGAAGAAAu	563	AUUUCUUCcAUGCGGACCC	1222	1956
AD-26753	ucAcAuccuAGcucGGGAu	564	AUCCCGAGCuAGGAUGUGA	1223	1999
AD-26754	cAuccuAGcucGGGAuGuu	565	AAcAUCCCGAGCuAGGAUG	1224	2002
AD-26755	uAGcucGGGAuGuucAcAA	566	UUGUGAAcAUCCCGAGCuA	1225	2007
AD-26756	GGGAuGuucAcAAccGAAu	567	AUUCGGUUGUGAAcAUCCC	1226	2013
AD-26757	GGAuGuucAcAAccGAAuu	568	AAUUCGGUUGUGAAcAUCC	1227	2014
AD-26758	cAGAGGAcuAAAuAccAuu	569	AAUGGuAUUuAGUCCUCUG	1228	2038
AD-26759	GGAcuAAAuAccAuuccAu	570	AUGGAAUGGuAUUuAGUCC	1229	2042
AD-26760	uAAAuAccAuuccAuuGuu	571	AAcAAUGGAAUGGuAUUuA	1230	2046
AD-26761	AAAuAccAuuccAuuGuuu	572	AAAcAAUGGAAUGGuAUUU	1231	2047
AD-26762	AuuGuuuGuGcAGcuGcuu	573	AAGcAGCUGcAcAAAcAAU	1232	2059
AD-26763	uuGuuuGuGcAGcuGcuuu	574	AAAGcAGCUGcAcAAAcAA	1233	2060
AD-26764	uGuuuGuGcAGcuGcuuuA	575	uAAAGcAGCUGcAcAAAcA	1234	2061
AD-26765	GuuuGuGcAGcuGcuuuAu	576	AuAAAGcAGCUGcAcAAAC	1235	2062
AD-26766	uuuGuGcAGcuGcuuuAuu	577	AAuAAAGcAGCUGcAcAAA	1236	2063
AD-26767	AGcuGcuuuAuucucccAu	578	AUGGGAGAAuAAAGcAGCU	1237	2070
AD-26768	GcuGcuuuAuucucccAuu	579	AAUGGGAGAAuAAAGcAGC	1238	2071
AD-26769	uuuAuucucccAuuGAAAA	580	UUUUcAAUGGGAGAAuAAA	1239	2076
AD-26770	AuucucccAuuGAAAAcAu	581	AUGUUUUcAAUGGGAGAAU	1240	2079
AD-26771	ucccAuuGAAAAcAuccAA	582	UUGGAUGUUUUcAAUGGGA	1241	2083
AD-26772	uGcAGGGGuccucuGuGAA	583	UUcAcAGAGGACCCCUGcA	1242	2110
AD-26773	AcuuGcucAGGAcAAGGAA	584	UUCCUUGUCCUGAGcAAGU	1243	2128
AD-26774	cAGcuccucuGAcAGAGuu	585	AACUCUGUcAGAGGAGCUG	1244	2178
AD-26775	AGcuccucuGAcAGAGuuA	586	uAACUCUGUcAGAGGAGCU	1245	2179
AD-26776	uccucuGAcAGAGuuAcuu	587	AAGuAACUCUGUcAGAGGA	1246	2182
AD-26777	AcAGAGuuAcuucAcucuA	588	uAGAGUGAAGuAACUCUGU	1247	2189
AD-26778	AGuuAcuucAcucuAGGAA	589	UUCCuAGAGUGAAGuAACU	1248	2193
AD-26779	GuuAcuucAcucuAGGAAu	590	AUUCCuAGAGUGAAGuAAC	1249	2194
AD-26780	AcuucAcucuAGGAAuGAA	591	UUcAUUCCuAGAGUGAAGU	1250	2197

AD-26781	GcuGcuGuuuuGuuccGAA	592	UUCGGAAcAAAAcAGcAGC	1251	2234
AD-26782	cuGcuGuuuuGuuccGAAu	593	AUUCGGAAcAAAAcAGcAG	1252	2235
AD-26783	GucuGAGGAcAAGccAcAA	594	UUGUGGCUUGUCCUcAGAC	1253	2254
AD-26784	uGAGGAcAAGccAcAAGAu	595	AUCUUGUGGCUUGUCCUcA	1254	2257
AD-26785	AcAAGccAcAAGAuuAcAA	596	UUGuAAUCUUGUGGCUUGU	1255	2262
AD-26786	AGccAcAAGAuuAcAAGAA	597	UUCUUGuAAUCUUGUGGCU	1256	2265
AD-26787	AGAuuAcAAGAAAcGGcuu	598	AAGCCGUUUCUUGuAAUCU	1257	2272
AD-26788	cAAGAAAcGGcuuucAGuu	599	AACUGAAAGCCGUUUCUUG	1258	2278
AD-26789	AGcuGAccAGcucucucuu	600	AAGAGAGAGCUGGUcAGCU	1259	2298
AD-26790	AccAGcucucucuucAGAA	601	UUCUGAAGAGAGAGCUGGU	1260	2303
AD-26791	uAuuGGuGcccAGGGAGAA	602	UUCUCCCUGGGcACcAAuA	1261	2365
AD-26792	cAGGGAGAAccccuuGGAu	603	AUCcAAGGGGUUCUCCCUG	1262	2375
AD-26793	AGGGAGAAccccuuGGAuA	604	uAUCcAAGGGGUUCUCCCU	1263	2376
AD-26794	ccuuGGAuAucGccAGGAu	605	AUCCUGGCGAuAUCcAAGG	1264	2386
AD-26795	uAucGccAGGAuGAuccuA	606	uAGGAUcAUCCUGGCGAuA	1265	2393
AD-26796	GccAGGAuGAuccuAGcuA	607	uAGCuAGGAUcAUCCUGGC	1266	2397
AD-26797	ccAGGAuGAuccuAGcuAu	608	AuAGCuAGGAUcAUCCUGG	1267	2398
AD-26798	GAuGAuccuAGcuAucGuu	609	AACGAuAGCuAGGAUcAUC	1268	2402
AD-26799	AuccuAGcuAucGuucuuu	610	AAAGAACGAuAGCuAGGAU	1269	2406
AD-26800	uccuAGcuAucGuucuuuu	611	AAAAGAACGAuAGCuAGGA	1270	2407
AD-26801	ucuuuucAcucuGGuGGAu	612	AUCcACcAGAGUGAAAAGA	1271	2420
AD-26802	cuuuucAcucuGGuGGAuA	613	uAUCcACcAGAGUGAAAAG	1272	2421
AD-26803	uuuucAcucuGGuGGAuAu	614	AuAUCcACcAGAGUGAAAA	1273	2422
AD-26804	uGGuGGAuAuGGccAGGAu	615	AUCCUGGCcAuAUCcACcA	1274	2431
AD-26805	GAuAuGGccAGGAuGccuu	616	AAGGcAUCCUGGCcAuAUC	1275	2436
AD-26806	ccuuGGGuAuGGAccccAu	617	AUGGGGUCcAuACCcAAGG	1276	2451
AD-26807	uGGGuAuGGAccccAuGAu	618	AUcAUGGGGUCcAuACCcA	1277	2454
AD-26808	uuGuAAAcuuGAuuAAcuA	619	uAGUuAAUcAAGUUuAcAA	1278	675
AD-26809	uGuAAAcuuGAuuAAcuAu	620	AuAGUuAAUcAAGUUuAcA	1279	676
AD-26810	AAAcuuGAuuAAcuAucAA	621	UUGAuAGUuAAUcAAGUUU	1280	679
AD-26811	uAuGGAccccAuGAuGGAA	622	UUCcAUcAUGGGGUCcAuA	1281	2458
AD-26812	GGAccccAuGAuGGAAcAu	623	AUGUUCcAUcAUGGGGUCC	1282	2461
AD-26813	ccAuGAuGGAAcAuGAGAu	624	AUCUcAUGUUCcAUcAUGG	1283	2466
AD-26814	AccAcccuGGuGcuGAcuA	625	uAGUcAGcACcAGGGUGGU	1284	2493
AD-26815	ccAcccuGGuGcuGAcuAu	626	AuAGUcAGcACcAGGGUGG	1285	2494
AD-26816	uGcuGAcuAuccAGuuGAu	627	AUcAACUGGAuAGUcAGcA	1286	2503
AD-26817	AGuuGAuGGGcuGccAGAu	628	AUCUGGcAGCCcAUcAACU	1287	2515
AD-26818	uGcccAGGAccucAuGGAu	629	AUCcAUGAGGUCCUGGGcA	1288	2542
AD-26819	GcAAucAGcuGGccuGGuu	630	AACcAGGCcAGCUGAUUGC	1289	2580
AD-26820	cAAucAGcuGGccuGGuuu	631	AAACcAGGCcAGCUGAUUG	1290	2581
AD-26821	GGuuuGAuAcuGAccuGuA	632	uAcAGGUcAGuAUcAAACC	1291	2595
AD-26822	AuAcuGAccuGuAAAucAu	633	AUGAUUuAcAGGUcAGuAU	1292	2601
AD-26823	uGAccuGuAAAucAuccuu	634	AAGGAUGAUUuAcAGGUcA	1293	2605

AD-26824	GAccuGuAAAucAuccuuu	635	AAAGGAUGAUUuAcAGGUC	1294	2606
AD-26825	AccuGuAAAucAuccuuuA	636	uAAAGGAUGAUUuAcAGGU	1295	2607
AD-26826	AAuAcAAAuGAuGuAGAAA	637	UUUCuAcAUcAUUUGuAUU	1296	878
AD-26900	uuuuAAGAAuAucuGuAAu	638	AUuAcAGAuAUUCUuAAAA	1297	2745
AD-26901	uAcAGcAAuuucuAAuuuu	639	AAAAUuAGAAAUUGCUGuA	1298	2872
AD-26902	cAcuAAuucAuAAucAcuc	640	GAGUGAUuAUGAAUuAGUG	1299	2915
AD-26903	AcuAAuucAuAAucAcucu	641	AGAGUGAUuAUGAAUuAGU	1300	2916
AD-26904	uAAuucAuAAucAcucuAA	642	UuAGAGUGAUuAUGAAUuA	1301	2918
AD-26905	AAuucAuAAucAcucuAAu	643	AUuAGAGUGAUuAUGAAUU	1302	2919
AD-26906	AAuuGuAAucuGAAuAAAG	644	CUUuAUUcAGAUuAcAAUU	1303	2939
AD-26907	uuuGuAuAAAAuAGAcAAA	645	UUUGUCuAUUUuAuAcAAA	1304	2978
AD-26908	uuGuAuAAAAuAGAcAAAu	646	AUUUGUCuAUUUuAuAcAA	1305	2979
AD-26909	uGuAuAAAAuAGAcAAAuA	647	uAUUUGUCuAUUUuAuAcA	1306	2980
AD-26910	GuAuAAAAuAGAcAAAuAG	648	CuAUUUGUCuAUUUuAuAC	1307	2981
AD-26911	AuAAAAuAGAcAAAuAGAA	649	UUCuAUUUGUCuAUUUuAU	1308	2983
AD-26912	uAAAAuAGAcAAAuAGAAA	650	UUUCuAUUUGUCuAUUUuA	1309	2984
AD-26913	AAAuAGAcAAAuAGAAAAu	651	AUUUUCuAUUUGUCuAUUU	1310	2986
AD-26914	uGGGAuAuGuAuGGGuAGG	652	CCuACCcAuAcAuAUCCcA	1311	3081
AD-26915	GGGAuAuGuAuGGGuAGGG	653	CCCuACCcAuAcAuAUCCC	1312	3082
AD-26916	cuAAuucAuAAucAcucuA	654	uAGAGUGAUuAUGAAUuAG	1313	2917
AD-26917	AAAuAGAAAAuGGuccAAu	655	AUUGGACcAUUUUCuAUUU	1314	2994
AD-26918	AAuAGAAAAuGGuccAAuu	656	AAUUGGACcAUUUUCuAUU	1315	2995
AD-26919	uuuGGAcAGuuuAccAGuu	657	AACUGGuAAACUGUCcAAA	1316	3134
AD-26920	AuucuuucuAAccucAcuu	658	AAGUGAGGUuAGAAAGAAU	1317	1535
AD-26921	uGGAuuGAuucGAAAucuu	659	AAGAUUUCGAAUcAAUCcA	1318	1801
Set1 254 A22 S26	ccAtAcAActGttttGAAA	6141	TTTcAAAAcAGTTGtATGG	6309	236
Set1 703 A22 S26	GAttAActAtcAAGAtGAt	6142	ATcATCTTGAtAGTtAATC	6310	685
Set1 709 A22 S26	ctAtcAAGAtGAtGcAGAA	6143	TTCTGcATcATCTTGAtAG	6311	691
Set1 895 A22 S26	GAAtAcAAAtGAtGtAGAA	6144	TTCtAcATcATTTGtATTC	6312	877
Set1 1816 A22 S26	tGttGGAttGAttcGAAAt	6145	ATTTCGAATcAATCcAAcA	6313	1798
Set1 1974 A22 S26	GGGtccGcAtGGAAGAAAt	6146	ATTTCTTCcATGCGGACCC	6314	1956
Set1 2425 A22 S26	tcctAGctAtcGttctttt	6147	AAAAGAACGAtAGCtAGGA	6315	2407
Set1 3146 A22 S26	AAGtGAAGAAtGcAcAAGA	6148	TCTTGTGcATTCTTcACTT	6316	3128
Set1 889 A22 S26	cAtGcAGAAtAcAAAtGAt	6149	ATcATTTGtATTCTGcATG	6317	871
Set1 1814 A22 S26	ActGttGGAttGAttcGAA	6150	TTCGAATcAATCcAAcAGT	6318	1796

Set1 1245 A22 S26	GAccccAAGctttAGtAAA	6151	TTtACtAAAGCTTGGGGTC	6319	1227
Set1 3196 A22 S26	AGccttGcttGttAAAttt	6152	AAATTtAAcAAGcAAGGCT	6320	3178
Set1 1450 A22 S26	ttcAGAtGctGcAActAAA	6153	TTtAGTTGcAGcATCTGAA	6321	1432
Set1 3169 A22 S26	AtcAcAAGAtGGAAtttAt	6154	AtAAATTCcATCTTGTGAT	6322	3151
Set1 3477 A22 S26	AAtAGAAAAtGGtccAAtt	6155	AATTGGACcATTTTCtATT	6323	3459
Set1 865 A22 S26	GAtGGtGtctGctAttGtA	6156	tAcAAtAGcAGAcACcATC	6324	847
Set1 1249 A22 S26	ccAAGctttAGtAAAtAtA	6157	tAtATTtACtAAAGCTTGG	6325	1231
Set1 1250 A22 S26	cAAGctttAGtAAAtAtAA	6158	TtAtATTtACtAAAGCTTG	6326	1232
Set1 2202 A22 S26	ctctGAcAGAGttActtcA	6159	TGAAGtAAcTcTGTcAGAG	6327	2184
Set1 1545 A22 S26	cAGctGGAAttctttctAA	6160	TtAGAAAGAATTCcAGCTG	6328	1527
Set1 1755 A22 S26	GActAccAGttGtGGttAA	6161	TtAACcAcAACTGGtAGTC	6329	1737
Set1 254 A25 S27	CCATACAACTGTTTTGAAA	6162	TTTCAAAACAGTTGTATGG	6330	236
Set1 703 A25 S27	GATTAACTATCAAGATGAT	6163	ATCATCTTGATAGTTAATC	6331	685
Set1 709 A25 S27	CTATCAAGATGATGCAGAA	6164	TTCTGCATCATCTTGATAG	6332	691
Set1 895 A25 S27	GAATACAAATGATGTAGAA	6165	TTCTACATCATTTGTATTC	6333	877
Set1 1816 A25 S27	TGTTGGATTGATTCGAAAT	6166	ATTTCGAATCAATCCAACA	6334	1798
Set1 1974 A25 S27	GGGTCCGCATGGAAGAAAT	6167	ATTTCTTCCATGCGGACCC	6335	1956
Set1 2425 A25 S27	TCCTAGCTATCGTTCTTTT	6168	AAAAGAACGATAGCTAGGA	6336	2407
Set1 3146 A25 S27	AAGTGAAGAATGCACAAGA	6169	TCTTGTGCATTCTTCACTT	6337	3128
Set1 889 A25 S27	CATGCAGAATACAAATGAT	6170	ATCATTTGTATTCTGCATG	6338	871
Set1 1814 A25 S27	ACTGTTGGATTGATTCGAA	6171	TTCGAATCAATCCAACAGT	6339	1796
Set1 1245 A25	GACCCCAAGCTTTAGTAAA	6172	TTTACTAAAGCTTGGGGTC	6340	1227

S27					
Set1 3196 A25 S27	AGCCTTGCTTGTTAAATTT	6173	AAATTTAACAAGCAAGGCT	6341	3178
Set1 1450 A25 S27	TTCAGATGCTGCAACTAAA	6174	TTTAGTTGCAGCATCTGAA	6342	1432
Set1 3169 A25 S27	ATCACAAGATGGAATTTAT	6175	ATAAATTCCATCTTGTGAT	6343	3151
Set1 3477 A25 S27	AATAGAAAATGGTCCAATT	6176	AATTGGACCATTTTCTATT	6344	3459
Set1 865 A25 S27	GATGGTGTCTGCTATTGTA	6177	TACAATAGCAGACACCATC	6345	847
Set1 1249 A25 S27	CCAAGCTTTAGTAAATATA	6178	TATATTTACTAAAGCTTGG	6346	1231
Set1 1250 A25 S27	CAAGCTTTAGTAAATATAA	6179	TTATATTTACTAAAGCTTG	6347	1232
Set1 2202 A25 S27	CTCTGACAGAGTTACTTCA	6180	TGAAGTAACTCTGTCAGAG	6348	2184
Set1 1545 A25 S27	CAGCTGGAATTCTTTCTAA	6181	TTAGAAAGAATTCCAGCTG	6349	1527
Set1 1755 A25 S27	GACTACCAGTTGTGGTTAA	6182	TTAACCACAACTGGTAGTC	6350	1737
Set1 254 A LO V1 S26	ccAtAcAActGttttGAAA	6183	TTtcAAAAcAGttGtAtGG	6351	236
Set1 703 A LO V1 S26	GAttAActAtcAAGAtGAt	6184	ATcAtcttGAtAGTtAAtc	6352	685
Set1 709 A LO V1 S26	ctAtcAAGAtGAtGcAGAA	6185	TTctGcAtcAtctTGAtAG	6353	691
Set1 895 A LO V1 S26	GAAtAcAAAtGAtGtAGAA	6186	TTctAcAtcAtttGtAttc	6354	877
Set1 1816 A LO V1 S26	tGttGGAttGAttcGAAAt	6187	ATttcGAAtcAAtCcAAcA	6355	1798
Set1 1974 A LO V1 S26	GGGtccGcAtGGAAGAAAt	6188	ATttcttccAtGcGGAccc	6356	1956
Set1 2425 A LO V1 S26	tcctAGctAtcGttctttt	6189	AAAAGAAcGAtAGCtAGGA	6357	2407
Set1 3146 A LO V1 S26	AAGtGAAGAAtGcAcAAGA	6190	TCttGtGcAttctTcActt	6358	3128

Set1 889 A LO V1 S26	cAtGcAGAAtAcAAAtGAt	6191	ATcAtttGtAttcTGcAtG	6359	871
Set1 1814 A LO V1 S26	ActGttGGAttGAttcGAA	6192	TTcGAAtcAAtccAAcAGt	6360	1796
Set1 1245 A LO V1 S26	GAccccAAGctttAGtAAA	6193	TTtActAAAGcttGGGGtc	6361	1227
Set1 3196 A LO V1 S26	AGccttGcttGttAAAttt	6194	AAAtttAAcAAGcAAGGct	6362	3178
Set1 1450 A LO V1 S26	ttcAGAtGctGcAActAAA	6195	TTtAGttGcAGcATctGAA	6363	1432
Set1 3169 A LO V1 S26	AtcAcAAGAtGGAAtttAt	6196	ATAAAttccAtctTGtGAt	6364	3151
Set1 3477 A LO V1 S26	AAtAGAAAAtGGtccAAtt	6197	AAttGGAccAtttTctAtt	6365	3459
Set1 865 A LO V1 S26	GAtGGtGtctGctAttGtA	6198	TAcAAtAGcAGAcAccAtc	6366	847
Set1 1249 A LO V1 S26	ccAAGctttAGtAAAtAtA	6199	TAtAtttActAAAGcttGG	6367	1231
Set1 1250 A LO V1 S26	cAAGctttAGtAAAtAtAA	6200	TTAtAtttActAAAGcttG	6368	1232
Set1 2202 A LO V1 S26	ctctGAcAGAGttActtcA	6201	TGAAGtAActctGTcAGAG	6369	2184
Set1 1545 A LO V1 S26	cAGctGGAAttctttctAA	6202	TTAGAAAGAAttcCAGctG	6370	1527
Set1 1755 A LO V1 S26	GActAccAGttGtGGttAA	6203	TTAAccAcAActGGtAGtc	6371	1737
Set1 254 A LO V2 S LO V1	ccAtACAaCTGtTTtGAaa	6204	TTtCAAaACaGTtGTATgg	6372	236
Set1 703 A LO V2 S LO V1	gaTtAACtATCaAGaTGat	6205	ATcATCtTGaTAgTTAAtc	6373	685
Set1 709 A LO V2 S LO V1	ctAtCAAgATGaTGcAGaa	6206	TTcTGCaTCaTCtTGATag	6374	691

Set1 895 A LO V2 S LO V1	gaAtACAaATGaTGtAGaa	6207	TTcTACaTCaTTtGTATtc	6375	877
Set1 1816 A LO V2 S LO V1	tgTtGGAtTGAtTCgAAat	6208	ATtTCGaATcAAtCCAAca	6376	1798
Set1 1974 A LO V2 S LO V1	ggGtCCGcATGgAAgAAat	6209	ATtTCTtCCaTGcGGACcc	6377	1956
Set1 2425 A LO V2 S LO V1	tcCtAGCtATCgTTcTTtt	6210	AAaAGAaCGaTAgCTAGga	6378	2407
Set1 3146 A LO V2 S LO V1	aaGtGAAgAATgCAcAAga	6211	TCtTGTgCAtTCtTCACtt	6379	3128
Set1 889 A LO V2 S LO V1	caTgCAGaATAcAAaTGat	6212	ATcATTtGTaTTcTGCAtg	6380	871
Set1 1814 A LO V2 S LO V1	acTgTTGgATTgATtCGaa	6213	TTcGAAtCAaTCcAACAgt	6381	1796
Set1 1245 A LO V2 S LO V1	gaCcCCAaGCTtTAgTAaa	6214	TTtACTaAAgCTtGGGGtc	6382	1227
Set1 3196 A LO V2 S LO V1	agCcTTGcTTGtTAaATtt	6215	AAaTTTaACaAGcAAGGct	6383	3178
Set1 1450 A LO V2 S LO V1	ttCaGATgCTGcAAcTAaa	6216	TTtAGTtGCaGCaTCTGaa	6384	1432
Set1 3169 A LO V2 S LO V1	atCaCAAgATGgAAtTTat	6217	ATaAATtCCaTCtTGTGat	6385	3151
Set1 3477 A LO V2 S LO V1	aaTaGAAaATGgTCcAAtt	6218	AAtTGGaCCaTTtTCTAtt	6386	3459
Set1 865 A LO V2 S LO V1	gaTgGTGtCTGcTAtTGta	6219	TAcAATaGCaGAcACCAtc	6387	847
Set1 1249 A LO V2 S LO V1	ccAaGCTtTAGtAAaTAta	6220	TAtATTtACtAAaGCTTgg	6388	1231
Set1 1250 A LO V2 S LO V1	caAgCTTtAGTaAAtATaa	6221	TTaTATtTAcTAaAGCTtg	6389	1232
Set1 2202 A	ctCtGACaGAGtTAcTTca	6222	TGaAGTaACtCTgTCAGag	6390	2184

LO V2 S LO V1					
Set1 1545 A LO V2 S LO V1	caGcTGGaATTcTTtCTaa	6223	TTaGAAaGAaTTcCAGCtg	6391	1527
Set1 1755 A LO V2 S LO V1	gaCtACCaGTTgTGgTTaa	6224	TTaACCaCAaCTgGTAGtc	6392	1737
Set2 254 A LO V3 S LO V2	ccAtACAaCTGtTTtGAaa	6225	TTtCAAaACaGTtGTATgg	6393	236
Set2 703 A LO V3 S LO V2	gaTtAACtATCaAGaTGat	6226	ATcATCtTGaTAgTTAAtc	6394	685
Set2 709 A LO V3 S LO V2	ctAtCAAgATGaTGcAGaa	6227	TTcTGCaTCaTCtTGATag	6395	691
Set2 895 A LO V3 S LO V2	gaAtACAaATGaTGtAGaa	6228	TTcTACaTCaTTtGTATtc	6396	877
Set2 1816 A LO V3 S LO V2	tgTtGGAtTGAtTCgAAat	6229	ATtTCGaATcAAtCCAAca	6397	1798
Set2 1974 A LO V3 S LO V2	ggGtCCGcATGgAAgAAat	6230	ATtTCTtCCaTGcGGACcc	6398	1956
Set2 2425 A LO V3 S LO V2	tcCtAGCtATCgTTcTTtt	6231	AAaAGAaCGaTAgCTAGga	6399	2407
Set2 3146 A LO V3 S LO V2	aaGtGAAgAATgCAcAAga	6232	TCtTGTgCAtTCtTCACtt	6400	3128
Set2 889 A LO V3 S LO V2	caTgCAGaATAcAAaTGat	6233	ATcATTtGTaTTcTGCAtg	6401	871
Set2 1814 A LO V3 S LO V2	acTgTTGgATTgATtCGaa	6234	TTcGAAtCAaTCcAACAgt	6402	1796
Set2 1245 A LO V3 S LO V2	gaCcCCAaGCTtTAgTAaa	6235	TTtACTaAAgCTtGGGGtc	6403	1227
Set2 3196 A LO V3 S LO V2	agCcTTGcTTGtTAaATtt	6236	AAaTTTaACaAGcAAGGct	6404	3178
Set2 1450 A LO V3 S LO V2	ttCaGATgCTGcAAcTAaa	6237	TTtAGTtGCaGCaTCTGaa	6405	1432
Set2 3169 A	atCaCAAgATGgAAtTTat	6238	ATaAATtCCaTCtTGTGat	6406	3151

LO V3 S LO V2					
Set2 3477 A LO V3 S LO V2	aaTaGAAaATGgTCcAAtt	6239	AAtTGGaCCaTTtTCTAtt	6407	3459
Set2 865 A LO V3 S LO V2	gaTgGTGtCTGcTAtTGta	6240	TAcAATaGCaGAcACCAtc	6408	847
Set2 1249 A LO V3 S LO V2	ccAaGCTtTAGtAAaTAta	6241	TAtATTtACtAAaGCTTgg	6409	1231
Set2 1250 A LO V3 S LO V2	caAgCTTtAGTaAAtATaa	6242	TTaTATtTAcTAaAGCTtg	6410	1232
Set2 2202 A LO V3 S LO V2	ctCtGACAGAGTTAcTTca	6243	TGaAGTaACtCTgTCAGag	6411	2184
Set2 1545 A LO V3 S LO V2	caGcTGGaATTcTTtCTaa	6244	TTaGAAaGAaTTcCAGCtg	6412	1527
Set2 1755 A LO V3 S LO V2	gaCtACCaGTTgTGgTTaa	6245	TTaACCaCAaCTgGTAGtc	6413	1737
Set2 254 A LO V4 S LO V1	ccAtACAaCTGtTTtGAaa	6246	tTtCAAaACaGTtGTATgg	6414	236
Set2 703 A LO V4 S LO V1	gaTtAACtATCaAGaTGat	6247	aTcATCtTGaTAgTTAAtc	6415	685
Set2 709 A LO V4 S LO V1	ctAtCAAgATGaTGcAGaa	6248	tTcTGCaTCaTCtTGATag	6416	691
Set2 895 A LO V4 S LO V1	gaAtACAaATGaTGtAGaa	6249	tTcTACaTCaTTtGTATtc	6417	877
Set2 1816 A LO V4 S LO V1	tgTtGGAtTGAtTCgAAat	6250	aTtTCGaATcAAtCCAAca	6418	1798
Set2 1974 A LO V4 S LO V1	ggGtCCGcATGgAAgAAat	6251	aTtTCTtCCaTGcGGACcc	6419	1956
Set2 2425 A LO V4 S LO V1	tcCtAGCtATCgTTcTTtt	6252	aAaAGAaCGaTAgCTAGga	6420	2407
Set2 3146 A LO V4 S LO V1	aaGtGAAgAATgCAcAAga	6253	tCtTGTgCAtTCtTCACtt	6421	3128
Set2 889 A LO V4	caTgCAGaATAcAAaTGat	6254	aTcATTtGTaTTcTGCAtg	6422	871

S LO V1					
Set2 1814 A LO V4 S LO V1	acTgTTGgATTgATtCGaa	6255	tTcGAAtCAaTCcAACAgt	6423	1796
Set2 1245 A LO V4 S LO V1	gaCcCCAaGCTtTAgTAaa	6256	tTtACTaAAgCTtGGGGtc	6424	1227
Set2 3196 A LO V4 S LO V1	agCcTTGcTTGtTAaATtt	6257	aAaTTTaACaAGcAAGGct	6425	3178
Set2 1450 A LO V4 S LO V1	ttCaGATgCTGcAAcTAaa	6258	tTtAGTtGCaGCaTCTGaa	6426	1432
Set2 3169 A LO V4 S LO V1	atCaCAAgATGgAAtTTat	6259	aTaAATtCCaTCtTGTGat	6427	3151
Set2 3477 A LO V4 S LO V1	aaTaGAAaATGgTCcAAtt	6260	aAtTGGaCCaTTtTCTAtt	6428	3459
Set2 865 A LO V4 S LO V1	gaTgGTGtCTGcTAtTGta	6261	tAcAATaGCaGAcACCAtc	6429	847
Set2 1249 A LO V4 S LO V1	ccAaGCTtTAGtAAaTAta	6262	tAtATTtACtAAaGCTTgg	6430	1231
Set2 1250 A LO V4 S LO V1	caAgCTTtAGTaAAtATaa	6263	tTaTATtTAcTAaAGCTtg	6431	1232
Set2 2202 A LO V4 S LO V1	ctCtGACaGAGtTAcTTca	6264	tGaAGTaACtCTgTCAGag	6432	2184
Set2 1545 A LO V4 S LO V1	caGcTGGaATTcTTtCTaa	6265	tTaGAAaGAaTTcCAGCtg	6433	1527
Set2 1755 A LO V4 S LO V1	gaCtACCaGTTgTGgTTaa	6266	tTaACCaCAaCTgGTAGtc	6434	1737
Set2 254 A LO V5 S LO V1	ccAtACAaCTGtTTtGAaa	6267	tTtCAAaACaGTtGTATgg	6435	236
Set2 703 A LO V5 S LO V1	gaTtAACtATCaAGaTGat	6268	aTcATCtTGaTAgTTAAtc	6436	685
Set2 709 A LO V5 S LO V1	ctAtCAAgATGaTGcAGaa	6269	tTcTGCaTCaTCtTGATag	6437	691
Set2 895 A LO V5	gaAtACAaATGaTGtAGaa	6270	tTcTACaTCaTTtGTATtc	6438	877

S LO V1					
Set2 1816 A LO V5 S LO V1	tgTtGGAtTGAtTCgAAat	6271	aTtTCGaATcAAtCCAAca	6439	1798
Set2 1974 A LO V5 S LO V1	ggGtCCGcATGgAAgAAat	6272	aTtTCTtCCaTGcGGACcc	6440	1956
Set2 2425 A LO V5 S LO V1	tcCtAGCtATCgTTcTTtt	6273	aAaAGAaCGaTAgCTAGga	6441	2407
Set2 3146 A LO V5 S LO V1	aaGtGAAgAATgCAcAAga	6274	tCtTGTgCAtTCtTCACtt	6442	3128
Set2 889 A LO V5 S LO V1	caTgCAGaATAcAAaTGat	6275	aTcATTtGTaTTcTGCAtg	6443	871
Set2 1814 A LO V5 S LO V1	acTgTTGgATTgATtCGaa	6276	tTcGAAtCAaTCcAACAgt	6444	1796
Set2 1245 A LO V5 S LO V1	gaCcCCAaGCTtTAgTAaa	6277	tTtACTaAAgCTtGGGGtc	6445	1227
Set2 3196 A LO V5 S LO V1	agCcTTGcTTGtTAaATtt	6278	aAaTTTaACaAGcAAGGct	6446	3178
Set2 1450 A LO V5 S LO V1	ttCaGATgCTGcAAcTAaa	6279	tTtAGTtGCaGCaTCTGaa	6447	1432
Set2 3169 A LO V5 S LO V1	atCaCAAgATGgAAtTTat	6280	aTaAATtCCaTCtTGTGat	6448	3151
Set2 3477 A LO V5 S LO V1	aaTaGAAaATGgTCcAAtt	6281	aAtTGGaCCaTTtTCTAtt	6449	3459
Set2 865 A LO V5 S LO V1	gaTgGTGtCTGcTAtTGta	6282	tAcAATaGCaGAcACCAtc	6450	847
Set2 1249 A LO V5 S LO V1	ccAaGCTtTAGtAAaTAta	6283	tAtATTtACtAAaGCTTgg	6451	1231
Set2 1250 A LO V5 S LO V1	caAgCTTtAGTaAAtATaa	6284	tTaTATtTAcTAaAGCTtg	6452	1232
Set2 2202 A LO V5 S LO V1	ctCtGACaGAGtTAcTTca	6285	tGaAGTaACtCTgTCAGag	6453	2184

Set2 1545 A LO V5 S LO V1	caGcTGGaATTcTTtCTaa	6286	tTaGAAaGAaTTcCAGCtg	6454	1527
Set2 1755 A LO V5 S LO V1	gaCtACCaGTTgTGgTTaa	6287	tTaACCaCAaCTgGTAGtc	6455	1737
Set2 254 A48 S26	ccAtAcAActGttttGAAA	6288	tTTcAAAAcAGTTGtATGG	6456	236
Set2 703 A48 S26	GAttAActAtcAAGAtGAt	6289	aTcATCTTGAtAGTtAATC	6457	685
Set2 709 A48 S26	ctAtcAAGAtGAtGcAGAA	6290	tTCTGcATcATCTTGAtAG	6458	691
Set2 895 A48 S26	GAAtAcAAAtGAtGtAGAA	6291	tTCtAcATcATTTGtATTC	6459	877
Set2 1816 A48 S26	tGttGGAttGAttcGAAAt	6292	aTTTCGAATcAATCcAAcA	6460	1798
Set2 1974 A48 S26	GGGtccGcAtGGAAGAAAt	6293	aTTTCTTCcATGCGGACCC	6461	1956
Set2 2425 A48 S26	tcctAGctAtcGttctttt	6294	aAAAGAACGAtAGCtAGGA	6462	2407
Set2 3146 A48 S26	AAGtGAAGAAtGcAcAAGA	6295	tCTTGTGcATTCTTcACTT	6463	3128
Set2 889 A48 S26	cAtGcAGAAtAcAAAtGAt	6296	aTcATTTGtATTCTGcATG	6464	871
Set2 1814 A48 S26	ActGttGGAttGAttcGAA	6297	tTCGAATcAATCcAAcAGT	6465	1796
Set2 1245 A48 S26	GAccccAAGctttAGtAAA	6298	tTtACtAAAGCTTGGGGTC	6466	1227
Set2 3196 A48 S26	AGccttGcttGttAAAttt	6299	aAATTtAAcAAGcAAGGCT	6467	3178
Set2 1450 A48 S26	ttcAGAtGctGcAActAAA	6300	tTtAGTTGcAGcATCTGAA	6468	1432
Set2 3169 A48 S26	AtcAcAAGAtGGAatttAt	6301	atAAATTCcATCTTGTGAT	6469	3151
Set2 3477 A48 S26	AAtAGAAAAtGGtccAAtt	6302	aATTGGACcATTTTCtATT	6470	3459
Set2 865 A48 S26	GAtGGtGtctGctAttGtA	6303	tAcAAtAGcAGAcACcATC	6471	847
Set2 1249 A48 S26	ccAAGctttAGtAAAtAtA	6304	tAtATTtACtAAAGCTTGG	6472	1231
Set2 1250 A48 S26	cAAGctttAGtAAAtAtAA	6305	ttAtATTtACtAAAGCTTG	6473	1232
Set2 2202 A48 S26	ctctGAcAGAGttActtcA	6306	tGAAGtAAcTcTGTcAGAG	6474	2184

Set2 1545 A48 S26	cAGctGGAAttctttctAA	6307	ttAGAAAGAATTCcAGCTG	6475	1527
Set2 1755 A48 S26	GActAccAGttGtGGttAA	6308	ttAACcAcAACTGGtAGTC	6476	1737

Nickname	First Strand Sequence	SEQ ID NO:	Second Strand Sequence	SEQ ID NO:
hs_ CTNNB1_ 1816_ AD26740_ A22S26	uGuuGGAuuGAuucGAAAuuu	6477	AUUUCGAAUcAAUCcAAcAuu	6486
hs_ CTNNB1_ 3477_ AD-26918-A22S26	AAuAGAAAAuGGuccAAuuuu	6478	AAUUGGACcAUUUUCuAUUuu	6487
hs_ CTNNB1_ 1814_ AD18983_ A22S26	AcuGuuGGAuuGAuucGAAuu	6479	UUCGAAUcAAUCcAAcAGUuu	6488
hs_ CTNNB1_ 709_ AD26109_ A22S26	cuAucAAGAuGAuGcAGAAuu	6480	UUCUGcAUcAUCUUGAuAGuu	6489
hs_ CTNNB1_ 254_ AD-26034-A22S26	ccAuAcAAcuGuuuuGAAAuu	6481	UUUcAAAAcAGUUGuAUGGuu	6490
hs_ CTNNB1_ 3169_ AD-25944-A22S26	AucAcAAGAuGGAAuuuAuuu	6482	AuAAAUUCcAUCUUGUGAUuu	6491
hs_ CTNNB1_ 703_ AD-26108-A22S26	AUcAUCUUGAuAGUuAAUCuu	6483	uccuAGcuAucGuucuuuuuu	6492
hs_ CTNNB1_ 2425_ AD-26800-A22S26	uccuAGcuAucGuucuuuuuu	6484	AAAAGAACGAuAGCuAGGAuu	6493
hs_ CTNNB1_ 1974_ AD-26752-A22S26	GGGuccGcAuGGAAGAAAuuu	6485	AUUUCUUCcAUGCGGACCCuu	6494

[00783] "Position" indicates the position of the RNAi agent in the human Beta-Catenin sequence NM_001098210.1.

[00784] The sequences in Table 3 are represented by the abbreviations in Table 3A:

TABLE 3A. ABBREVIATIONS

Abbreviation[a]	Nucleotide(s)
A	adenosine-5'-phosphate
C	cytidine-5'-phosphate
G	guanosine-5'-phosphate
dT	2'-deoxy-thymidine-5'-phosphate
U	uridine-5'-phosphate
c	2'-O-methylcytidine-5'-phosphate
u	2'-O-methyluridine-5'-phosphate
sdT	2'-deoxy Thymidine 5'-phosphorothioate

[00785] Modified and unmodified variants of the RNAi agents of Tables 1, 2 and 3 are easily conceived by one of skill in the art. Unmodified variants include those which do not comprise a modification of the base (such as provided in Table 3). In several cases, a pyrimidine in the sense strand is modified; and/or a pyrimidine preceding a "A" base in the anti-sense strand is modified. Modifications involving other positions (or the absence of a modification at a particular base) are easily conceived.

[00786] In general, the sense strand is heavily modified, and the anti-sense strand lightly modified. Some modifications are placed at sites predicted to be sensitive to endonucleases. Some modifications are designed to eliminate an immune response to the RNAi agent while preserving activity. Some modifications serve more than one purpose.

[00787] RNAi agents are also on occasion referenced by a "ND" prefix rather than "AD"; thus RNAi agents designated AD-18892 and ND-18892, for example, are identical and comprise the same sequence.

[00788] Of the RNAi agents listed herein, many were synthesized, as described in Example 2, and tested in vitro, as described in Example 3.

[00789] EXAMPLE 1A

[00790] Overlapping siRNAs

[00791] Some of the siRNAs listed above overlap each other in sequence. The following table presents a compilation of groups of RNAi agents, wherein each member of a group overlaps with each other member of the same group by at least 12 nt. A 12-nt portion of the overlap of the sense strands and a 12-nt portion of the overlap of the anti-sense strand are presented. Thus, for example, AD-26022 and AD-26204 share the common technical feature of the sequence of CCUGUUCCCCUG (SEQ ID NO: 1319) in the sense strand, and the sequence of CAGGGGAACAGG (SEQ ID NO: 2714) in the anti-sense strand. Note of course that only a 12-nt portion of the overlap is shown; many groups of RNAi agents will overlap by more than 12 nt. The position within the gene is also indicated.

[00792] The disclosure also encompasses subgroups of the disclosed groups of overlapping RNAi agents. For example, the disclosure contemplates the group of AD-26027, AD-26024, AD-26028, AD-26026, AD-26025, which all share the sequences of SEQ ID NOs: 1334 and 2729. However, the disclosure also contemplates all subgroups or partial groups within this group, e.g., AD-26027 and AD-26024; AD-26027, AD-26024, AD-26028, and AD-26026; AD-26028, AD-26026, and AD-26025; AD-26027 and AD-26028; AD-26028 and AD-26025; etc. The disclosure thus encompasses any subgroup within a disclosed group of overlapping RNAi agents. The sequences of members of these subgroups can be combined with any other element disclosed herein

(e.g., modification, sets of modification, 5' and/or 3' end cap(s), blunt end(s), overhang(s), ligand(s), additional treatment(s) or method(s), pharmaceutical carrier(s), additional RNAi agent(s), etc.), provided that such combinations are not mututally exclusive (e.g., a RNAi agent comprising two strands cannot by definition have both two blunt ends and two overhangs).

TABLE 4. Groups of overlapping RNAi agents to Beta-Catenin

Position	Sense overlap	SEQ ID NO:	Anti-sense overlap	SEQ ID NO:	Overlapping groups of RNAi agents
206	CCUGUUCCCCUG	1319	CAGGGGAACAGG	2714	AD-26022, AD-26204
207	CUGUUCCCCUGA	1320	UCAGGGGAACAG	2715	AD-26022, AD-26204
208	UGUUCCCCUGAG	1321	CUCAGGGGAACA	2716	AD-26022, AD-26023
209	GUUCCCCUGAGG	1322	CCUCAGGGGAAC	2717	AD-26022, AD-26023, AD-26204
210	UUCCCCUGAGGG	1323	CCCUCAGGGGAA	2718	AD-26022, AD-26023, AD-26204
211	UCCCCUGAGGGU	1324	ACCCUCAGGGGA	2719	AD-26022, AD-26023, AD-26204
212	CCCCUGAGGGUA	1325	UACCCUCAGGGG	2720	AD-26022, AD-26023, AD-26204
213	CCCUGAGGGUAU	1326	AUACCCUCAGGG	2721	AD-26022, AD-26023
214	CCUGAGGGUAUU	1327	AAUACCCUCAGG	2722	AD-26024, AD-26023
215	CUGAGGGUAUUU	1328	AAAUACCCUCAG	2723	AD-26024, AD-26025
216	UGAGGGUAUUUG	1329	CAAAUACCCUCA	2724	AD-26024, AD-26026
217	GAGGGUAUUUGA	1330	UCAAAUACCCUC	2725	AD-26024, AD-26025
218	AGGGUAUUUGAA	1331	UUCAAAUACCCU	2726	AD-26024, AD-26026, AD-26025
219	GGGUAUUUGAAG	1332	CUUCAAAUACCC	2727	AD-26024, AD-26026, AD-26025
220	GGUAUUUGAAGU	1333	ACUUCAAAUACC	2728	AD-26027, AD-26024, AD-26026, AD-26025
221	GUAUUUGAAGUA	1334	UACUUCAAAUAC	2729	AD-26027, AD-26024, AD-26028, AD-26026, AD-26025
222	UAUUUGAAGUAU	1335	AUACUUCAAAUA	2730	AD-26027, AD-26028, AD-26026, AD-26025
223	AUUUGAAGUAUA	1336	UAUACUUCAAAU	2731	AD-26027, AD-26028
224	UUUGAAGUAUAC	1337	GUAUACUUCAAA	2732	AD-26027, AD-26029
225	UUGAAGUAUACC	1338	GGUAUACUUCAA	2733	AD-26029, AD-26028
226	UGAAGUAUACCA	1339	UGGUAUACUUCA	2734	AD-26027, AD-26029, AD-26028
227	GAAGUAUACCAU	1340	AUGGUAUACUUC	2735	AD-26027, AD-26029, AD-26028
228	AAGUAUACCAUA	1341	UAUGGUAUACUU	2736	AD-26029, AD-26028
229	AGUAUACCAUAC	1342	GUAUGGUAUACU	2737	AD-26029, AD-26030
230	GUAUACCAUACA	1343	UGUAUGGUAUAC	2738	AD-26031, AD-26029, AD-26030
231	UAUACCAUACAA	1344	UUGUAUGGUAUA	2739	AD-26032, AD-26031, AD-26029, AD-26030

232	AUACCAUACAAC	1345	GUUGUAUGGUAU	2740	AD-26032, AD-26031
233	UACCAUACAACU	1346	AGUUGUAUGGUA	2741	AD-26032, AD-26031, AD-26030
234	ACCAUACAACUG	1347	CAGUUGUAUGGU	2742	AD-26032, AD-26031, AD-26033, AD-26030
235	CCAUACAACUGU	1348	ACAGUUGUAUGG	2743	AD-26032, AD-26034, AD-26031, AD-26033, AD-26030
236	CAUACAACUGUU	1349	AACAGUUGUAUG	2744	AD-26032, AD-26034, AD-26031, AD-26033, AD-26030
237	AUACAACUGUUU	1350	AAACAGUUGUAU	2745	AD-26032, AD-26034, AD-26031, AD-26033
238	UACAACUGUUUU	1351	AAAACAGUUGUA	2746	AD-26032, AD-26034, AD-26033
239	ACAACUGUUUUG	1352	CAAAACAGUUGU	2747	AD-26034, AD-26033
240	CAACUGUUUUGA	1353	UCAAAACAGUUG	2748	AD-26034, AD-26033
241	AACUGUUUUGAA	1354	UUCAAAACAGUU	2749	AD-26034, AD-26033
250	GAAAAUCCAGCG	1355	CGCUGGAUUUUC	2750	AD-19763, AD-26035
251	AAAAUCCAGCGU	1356	ACGCUGGAUUUU	2751	AD-26036, AD-19763, AD-26035
252	AAAUCCAGCGUG	1357	CACGCUGGAUUU	2752	AD-26036, AD-19763, AD-26035
253	AAUCCAGCGUGG	1358	CCACGCUGGAUU	2753	AD-26036, AD-26035
254	AUCCAGCGUGGA	1359	UCCACGCUGGAU	2754	AD-26036, AD-26035
255	UCCAGCGUGGAC	1360	GUCCACGCUGGA	2755	AD-26036, AD-26035
256	CCAGCGUGGACA	1361	UGUCCACGCUGG	2756	AD-26036, AD-26035, AD-26037
257	CAGCGUGGACAA	1362	UUGUCCACGCUG	2757	AD-26036, AD-26035, AD-26037
258	AGCGUGGACAAU	1363	AUUGUCCACGCU	2758	AD-26036, AD-26037
261	GUGGACAAUGGC	1364	GCCAUUGUCCAC	2759	AD-26038, AD-26037
262	UGGACAAUGGCU	1365	AGCCAUUGUCCA	2760	AD-26038, AD-26037
263	GGACAAUGGCUA	1366	UAGCCAUUGUCC	2761	AD-26038, AD-26037
264	GACAAUGGCUAC	1367	GUAGCCAUUGUC	2762	AD-18896, AD-26038
265	ACAAUGGCUACU	1368	AGUAGCCAUUGU	2763	AD-18896, AD-26038, AD-18953
266	CAAUGGCUACUC	1369	GAGUAGCCAUUG	2764	AD-18896, AD-26038, AD-18953
267	AAUGGCUACUCA	1370	UGAGUAGCCAUU	2765	AD-18896, AD-26038, AD-18953
268	AUGGCUACUCAA	1371	UUGAGUAGCCAU	2766	AD-18896, AD-26038, AD-18953, AD-26040
269	UGGCUACUCAAG	1372	CUUGAGUAGCCA	2767	AD-18896, AD-26041, AD-18953, AD-26040
270	GGCUACUCAAGC	1373	GCUUGAGUAGCC	2768	AD-18896, AD-26041, AD-26039, AD-18953, AD-26040
271	GCUACUCAAGCU	1374	AGCUUGAGUAGC	2769	AD-18896, AD-26041, AD-18953, AD-26040
272	CUACUCAAGCUG	1375	CAGCUUGAGUAG	2770	AD-26041, AD-26042, AD-18953, AD-26040

273	UACUCAAGCUGA	1376	UCAGCUUGAGUA	2771	AD-26041, AD-26042, AD-26040
274	ACUCAAGCUGAU	1377	AUCAGCUUGAGU	2772	AD-26041, AD-26042, AD-26039, AD-26040
275	CUCAAGCUGAUU	1378	AAUCAGCUUGAG	2773	AD-26041, AD-26042, AD-26040
276	UCAAGCUGAUUU	1379	AAAUCAGCUUGA	2774	AD-26041, AD-26042
290	UGGAGUUGGACA	1380	UGUCCAACUCCA	2775	AD-26043, AD-26044
291	GGAGUUGGACAU	1381	AUGUCCAACUCC	2776	AD-26043, AD-26044
294	GUUGGACAUGGC	1382	GCCAUGUCCAAC	2777	AD-26045, AD-26044
295	UUGGACAUGGCC	1383	GGCCAUGUCCAA	2778	AD-26045, AD-26044
296	UGGACAUGGCCA	1384	UGGCCAUGUCCA	2779	AD-26045, AD-26044
297	GGACAUGGCCAU	1385	AUGGCCAUGUCC	2780	AD-26045, AD-26044
306	CAUGGAACCAGA	1386	UCUGGUUCCAUG	2781	AD-26047, AD-26046
307	AUGGAACCAGAC	1387	GUCUGGUUCCAU	2782	AD-26047, AD-26046
308	UGGAACCAGACA	1388	UGUCUGGUUCCA	2783	AD-26047, AD-26046
309	GGAACCAGACAG	1389	CUGUCUGGUUCC	2784	AD-26047, AD-26046
310	GAACCAGACAGA	1390	UCUGUCUGGUUC	2785	AD-26047, AD-26046
311	AACCAGACAGAA	1391	UUCUGUCUGGUU	2786	AD-26047, AD-26046
316	GACAGAAAAGCG	1392	CGCUUUUCUGUC	2787	AD-26050, AD-26049
317	ACAGAAAAGCGG	1393	CCGCUUUUCUGU	2788	AD-26050, AD-26049
318	CAGAAAAGCGGC	1394	GCCGCUUUUCUG	2789	AD-26050, AD-26049
319	AGAAAAGCGGCU	1395	AGCCGCUUUUCU	2790	AD-26050, AD-26049
320	GAAAAGCGGCUG	1396	CAGCCGCUUUUC	2791	AD-26050, AD-26049
321	AAAAGCGGCUGU	1397	ACAGCCGCUUUU	2792	AD-26050, AD-26049
322	AAAGCGGCUGUU	1398	AACAGCCGCUUU	2793	AD-26050, AD-26049
323	AAGCGGCUGUUA	1399	UAACAGCCGCUU	2794	AD-26050, AD-19743
330	UGUUAGUCACUG	1400	CAGUGACUAACA	2795	AD-26051, AD-19743
337	CACUGGCAGCAA	1401	UUGCUGCCAGUG	2796	AD-26051, AD-26052
338	ACUGGCAGCAAC	1402	GUUGCUGCCAGU	2797	AD-26053, AD-26052
339	CUGGCAGCAACA	1403	UGUUGCUGCCAG	2798	AD-26053, AD-26052
340	UGGCAGCAACAG	1404	CUGUUGCUGCCA	2799	AD-26053, AD-26052
341	GGCAGCAACAGU	1405	ACUGUUGCUGCC	2800	AD-26053, AD-26052
342	GCAGCAACAGUC	1406	GACUGUUGCUGC	2801	AD-26053, AD-26052
343	CAGCAACAGUCU	1407	AGACUGUUGCUG	2802	AD-26053, AD-26052
344	AGCAACAGUCUU	1408	AAGACUGUUGCU	2803	AD-26053, AD-26052
353	CUUACCUGGACU	1409	AGUCCAGGUAAG	2804	AD-26054, AD-26055
354	UUACCUGGACUC	1410	GAGUCCAGGUAA	2805	AD-26054, AD-26055
355	UACCUGGACUCU	1411	AGAGUCCAGGUA	2806	AD-26054, AD-26055
356	ACCUGGACUCUG	1412	CAGAGUCCAGGU	2807	AD-26054, AD-26055
357	CCUGGACUCUGG	1413	CCAGAGUCCAGG	2808	AD-26056, AD-26055
358	CUGGACUCUGGA	1414	UCCAGAGUCCAG	2809	AD-26054, AD-26056, AD-26055
359	UGGACUCUGGAA	1415	UUCCAGAGUCCA	2810	AD-26054, AD-26056, AD-26055
360	GGACUCUGGAAU	1416	AUUCCAGAGUCC	2811	AD-26056, AD-26055
366	UGGAAUCCAUUC	1417	GAAUGGAUUCCA	2812	AD-19072, AD-18925
367	GGAAUCCAUUCU	1418	AGAAUGGAUUCC	2813	AD-19072, AD-18925
368	GAAUCCAUUCUG	1419	CAGAAUGGAUUC	2814	AD-19072, AD-18925
369	AAUCCAUUCUGG	1420	CCAGAAUGGAUU	2815	AD-19072, AD-18925
370	AUCCAUUCUGGU	1421	ACCAGAAUGGAU	2816	AD-19072, AD-18925

371	UCCAUUCUGGUG	1422	CACCAGAAUGGA	2817	AD-19072, AD-18925
372	CCAUUCUGGUGC	1423	GCACCAGAAUGG	2818	AD-19072, AD-18925
401	CUCUGAGUGGUA	1424	UACCACUCAGAG	2819	AD-26060, AD-26059
402	UCUGAGUGGUAA	1425	UUACCACUCAGA	2820	AD-26060, AD-26059
403	CUGAGUGGUAAA	1426	UUUACCACUCAG	2821	AD-26060, AD-26059
417	CAAUCCUGAGGA	1427	UCCUCAGGAUUG	2822	AD-26062, AD-26061
418	AAUCCUGAGGAA	1428	UUCCUCAGGAUU	2823	AD-26062, AD-26061
423	UGAGGAAGAGGA	1429	UCCUCUUCCUCA	2824	AD-26062, AD-26063
424	GAGGAAGAGGAU	1430	AUCCUCUUCCUC	2825	AD-26062, AD-26063
441	UACCUCCCAAGU	1431	ACUUGGGAGGUA	2826	AD-26065, AD-26064
442	ACCUCCCAAGUC	1432	GACUUGGGAGGU	2827	AD-26065, AD-26064
443	CCUCCCAAGUCC	1433	GGACUUGGGAGG	2828	AD-26065, AD-26064
444	CUCCCAAGUCCU	1434	AGGACUUGGGAG	2829	AD-26065, AD-26064
445	UCCCAAGUCCUG	1435	CAGGACUUGGGA	2830	AD-26065, AD-26064
446	CCCAAGUCCUGU	1436	ACAGGACUUGGG	2831	AD-26065, AD-26064
447	CCAAGUCCUGUA	1437	UACAGGACUUGG	2832	AD-26065, AD-26064
457	UAUGAGUGGGAA	1438	UUCCCACUCAUA	2833	AD-26066, AD-26067
459	UGAGUGGGAACA	1439	UGUUCCCACUCA	2834	AD-26070, AD-26067
460	GAGUGGGAACAG	1440	CUGUUCCCACUC	2835	AD-26071, AD-26070, AD-26067
461	AGUGGGAACAGG	1441	CCUGUUCCCACU	2836	AD-26071, AD-26070, AD-26067
462	GUGGGAACAGGG	1442	CCCUGUUCCCAC	2837	AD-26071, AD-26070, AD-26067
463	UGGGAACAGGGA	1443	UCCCUGUUCCCA	2838	AD-26071, AD-26070, AD-26067
464	GGGAACAGGGAU	1444	AUCCCUGUUCCC	2839	AD-26071, AD-26070, AD-26067
465	GGAACAGGGAUU	1445	AAUCCCUGUUCC	2840	AD-26071, AD-26070
466	GAACAGGGAUUU	1446	AAAUCCCUGUUC	2841	AD-26071, AD-26070
477	UUCUCAGUCCUU	1447	AAGGACUGAGAA	2842	AD-26073, AD-26072
480	UCAGUCCUUCAC	1448	GUGAAGGACUGA	2843	AD-26074, AD-26073
481	CAGUCCUUCACU	1449	AGUGAAGGACUG	2844	AD-26074, AD-26073
482	AGUCCUUCACUC	1450	GAGUGAAGGACU	2845	AD-26074, AD-26073
483	GUCCUUCACUCA	1451	UGAGUGAAGGAC	2846	AD-26074, AD-26073
484	UCCUUCACUCAA	1452	UUGAGUGAAGGA	2847	AD-26074, AD-26073
486	CUUCACUCAAGA	1453	UCUUGAGUGAAG	2848	AD-26074, AD-26075
487	UUCACUCAAGAA	1454	UUCUUGAGUGAA	2849	AD-26074, AD-26075
492	UCAAGAACAAGU	1455	ACUUGUUCUUGA	2850	AD-26076, AD-26075
493	CAAGAACAAGUA	1456	UACUUGUUCUUG	2851	AD-26076, AD-26075
511	AUUGAUGGACAG	1457	CUGUCCAUCAAU	2852	AD-26077, AD-26078
512	UUGAUGGACAGU	1458	ACUGUCCAUCAA	2853	AD-26077, AD-26078
513	UGAUGGACAGUA	1459	UACUGUCCAUCA	2854	AD-26077, AD-26078
523	UAUGCAAUGACU	1460	AGUCAUUGCAUA	2855	AD-19757, AD-19756
524	AUGCAAUGACUC	1461	GAGUCAUUGCAU	2856	AD-19757, AD-19756
525	UGCAAUGACUCG	1462	CGAGUCAUUGCA	2857	AD-19757, AD-19756
526	GCAAUGACUCGA	1463	UCGAGUCAUUGC	2858	AD-19757, AD-19756
534	UCGAGCUCAGAG	1464	CUCUGAGCUCGA	2859	AD-19744, AD-26079
535	CGAGCUCAGAGG	1465	CCUCUGAGCUCG	2860	AD-19744, AD-26079
536	GAGCUCAGAGGG	1466	CCCUCUGAGCUC	2861	AD-19744, AD-26079
537	AGCUCAGAGGGU	1467	ACCCUCUGAGCU	2862	AD-19744, AD-26079

538	GCUCAGAGGGUA	1468	UACCCUCUGAGC	2863	AD-19744, AD-26079
541	CAGAGGGUACGA	1469	UCGUACCCUCUG	2864	AD-26080, AD-19744
542	AGAGGGUACGAG	1470	CUCGUACCCUCU	2865	AD-26080, AD-26081
543	GAGGGUACGAGC	1471	GCUCGUACCCUC	2866	AD-26080, AD-26081
544	AGGGUACGAGCU	1472	AGCUCGUACCCU	2867	AD-26080, AD-26081
545	GGGUACGAGCUG	1473	CAGCUCGUACCC	2868	AD-26080, AD-26081
546	GGUACGAGCUGC	1474	GCAGCUCGUACC	2869	AD-26080, AD-26082
547	GUACGAGCUGCU	1475	AGCAGCUCGUAC	2870	AD-26080, AD-26081, AD-26082
548	UACGAGCUGCUA	1476	UAGCAGCUCGUA	2871	AD-26080, AD-26081, AD-26082
549	ACGAGCUGCUAU	1477	AUAGCAGCUCGU	2872	AD-26081, AD-26082
558	UAUGUUCCCUGA	1478	UCAGGGAACAUA	2873	AD-26084, AD-26083
559	AUGUUCCCUGAG	1479	CUCAGGGAACAU	2874	AD-26084, AD-26083
560	UGUUCCCUGAGA	1480	UCUCAGGGAACA	2875	AD-26084, AD-26083
561	GUUCCCUGAGAC	1481	GUCUCAGGGAAC	2876	AD-26084, AD-26085, AD-26083
562	UUCCCUGAGACA	1482	UGUCUCAGGGAA	2877	AD-26084, AD-26085, AD-26083
563	UCCCUGAGACAU	1483	AUGUCUCAGGGA	2878	AD-26084, AD-26085, AD-26083
564	CCCUGAGACAUU	1484	AAUGUCUCAGGG	2879	AD-26084, AD-26085, AD-26083
565	CCUGAGACAUUA	1485	UAAUGUCUCAGG	2880	AD-26084, AD-26085
576	AGAUGAGGGCAU	1486	AUGCCCUCAUCU	2881	AD-26086, AD-18911
577	GAUGAGGGCAUG	1487	CAUGCCCUCAUC	2882	AD-26086, AD-18911
578	AUGAGGGCAUGC	1488	GCAUGCCCUCAU	2883	AD-19011, AD-18911
579	UGAGGGCAUGCA	1489	UGCAUGCCCUCA	2884	AD-26086, AD-19011, AD-18911
580	GAGGGCAUGCAG	1490	CUGCAUGCCCUC	2885	AD-18911, AD-26087
581	AGGGCAUGCAGA	1491	UCUGCAUGCCCU	2886	AD-18959, AD-26086, AD-18911, AD-26087
582	GGGCAUGCAGAU	1492	AUCUGCAUGCCC	2887	AD-18911, AD-26087
583	GGCAUGCAGAUC	1493	GAUCUGCAUGCC	2888	AD-26088, AD-18911, AD-26087
584	GCAUGCAGAUCC	1494	GGAUCUGCAUGC	2889	AD-26088, AD-26087
585	CAUGCAGAUCCC	1495	GGGAUCUGCAUG	2890	AD-26088, AD-18959, AD-19011, AD-26087
586	AUGCAGAUCCCA	1496	UGGGAUCUGCAU	2891	AD-26088, AD-26087
587	UGCAGAUCCCAU	1497	AUGGGAUCUGCA	2892	AD-26088, AD-18959
588	GCAGAUCCCAUC	1498	GAUGGGAUCUGC	2893	AD-26088, AD-18959
590	AGAUCCCAUCUA	1499	UAGAUGGGAUCU	2894	AD-26088, AD-26089
594	CCCAUCUACACA	1500	UGUGUAGAUGGG	2895	AD-26089, AD-26090
595	CCAUCUACACAG	1501	CUGUGUAGAUGG	2896	AD-26089, AD-26090
596	CAUCUACACAGU	1502	ACUGUGUAGAUG	2897	AD-26089, AD-26090
597	AUCUACACAGUU	1503	AACUGUGUAGAU	2898	AD-26089, AD-26090
610	GAUGCUGCUCAU	1504	AUGAGCAGCAUC	2899	AD-26091, AD-26092
611	AUGCUGCUCAUC	1505	GAUGAGCAGCAU	2900	AD-26092, AD-26093
612	UGCUGCUCAUCC	1506	GGAUGAGCAGCA	2901	AD-26092, AD-26094
613	GCUGCUCAUCCC	1507	GGGAUGAGCAGC	2902	AD-26092, AD-26093
614	CUGCUCAUCCCA	1508	UGGGAUGAGCAG	2903	AD-26092, AD-26093, AD-26094

615	UGCUCAUCCCAC	1509	GUGGGAUGAGCA	2904	AD-26092, AD-26093, AD-26094
616	GCUCAUCCCACU	1510	AGUGGGAUGAGC	2905	AD-26092, AD-26093, AD-26094
617	CUCAUCCCACUA	1511	UAGUGGGAUGAG	2906	AD-26092, AD-26094
618	UCAUCCCACUAA	1512	UUAGUGGGAUGA	2907	AD-19070, AD-18949, AD-26093, AD-26094
619	CAUCCCACUAAU	1513	AUUAGUGGGAUG	2908	AD-18949, AD-19048, AD-18954, AD-26094
620	AUCCCACUAAUG	1514	CAUUAGUGGGAU	2909	AD-19070, AD-18918, AD-19048, AD-18954
621	UCCCACUAAUGU	1515	ACAUUAGUGGGA	2910	AD-19070, AD-18949, AD-18918, AD-19048, AD-18954
622	CCCACUAAUGUC	1516	GACAUUAGUGGG	2911	AD-26095, AD-19070, AD-18918, AD-19048, AD-18954
623	CCACUAAUGUCC	1517	GGACAUUAGUGG	2912	AD-26095, AD-18949, AD-18918, AD-19048, AD-18954
624	CACUAAUGUCCA	1518	UGGACAUUAGUG	2913	AD-26095, AD-18949, AD-18918, AD-19048, AD-18954
625	ACUAAUGUCCAG	1519	CUGGACAUUAGU	2914	AD-26095, AD-18918, AD-19048
626	CUAAUGUCCAGC	1520	GCUGGACAUUAG	2915	AD-26095, AD-18918, AD-19048
627	UAAUGUCCAGCG	1521	CGCUGGACAUUA	2916	AD-26095, AD-18918
636	GCGUUUGGCUGA	1522	UCAGCCAAACGC	2917	AD-26096, AD-19765
637	CGUUUGGCUGAA	1523	UUCAGCCAAACG	2918	AD-26096, AD-19765
638	GUUUGGCUGAAC	1524	GUUCAGCCAAAC	2919	AD-26096, AD-19765
639	UUUGGCUGAACC	1525	GGUUCAGCCAAA	2920	AD-26096, AD-19765
640	UUGGCUGAACCA	1526	UGGUUCAGCCAA	2921	AD-26096, AD-18974, AD-19765
641	UGGCUGAACCAU	1527	AUGGUUCAGCCA	2922	AD-26096, AD-19765, AD-26097
642	GGCUGAACCAUC	1528	GAUGGUUCAGCC	2923	AD-18974, AD-19000, AD-19765, AD-26097
643	GCUGAACCAUCA	1529	UGAUGGUUCAGC	2924	AD-18974, AD-19765, AD-26097
644	CUGAACCAUCAC	1530	GUGAUGGUUCAG	2925	AD-18974, AD-19000
645	UGAACCAUCACA	1531	UGUGAUGGUUCA	2926	AD-18974, AD-26097
646	GAACCAUCACAG	1532	CUGUGAUGGUUC	2927	AD-18974, AD-19000, AD-26097
647	AACCAUCACAGA	1533	UCUGUGAUGGUU	2928	AD-18974, AD-19000, AD-26098, AD-26097
648	ACCAUCACAGAU	1534	AUCUGUGAUGGU	2929	AD-19000, AD-26098, AD-26099, AD-26097
649	CCAUCACAGAUG	1535	CAUCUGUGAUGG	2930	AD-19000, AD-26098, AD-26099
650	CAUCACAGAUGC	1536	GCAUCUGUGAUG	2931	AD-26098, AD-26099
651	AUCACAGAUGCU	1537	AGCAUCUGUGAU	2932	AD-26100, AD-26098

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653	CACAGAUGCUGA	1539	UCAGCAUCUGUG	2934	AD-26100, AD-26098, AD-26099
654	ACAGAUGCUGAA	1540	UUCAGCAUCUGU	2935	AD-26100, AD-26099
655	CAGAUGCUGAAA	1541	UUUCAGCAUCUG	2936	AD-26100, AD-26099
657	GAUGCUGAAACA	1542	UGUUUCAGCAUC	2937	AD-26100, AD-26101
658	AUGCUGAAACAU	1543	AUGUUUCAGCAU	2938	AD-26100, AD-26101
661	CUGAAACAUGCA	1544	UGCAUGUUUCAG	2939	AD-26101, AD-26102
662	UGAAACAUGCAG	1545	CUGCAUGUUUCA	2940	AD-26101, AD-26102
663	GAAACAUGCAGU	1546	ACUGCAUGUUUC	2941	AD-26101, AD-26102
664	AAACAUGCAGUU	1547	AACUGCAUGUUU	2942	AD-26101, AD-26102
665	AACAUGCAGUUG	1548	CAACUGCAUGUU	2943	AD-26103, AD-26102
666	ACAUGCAGUUGU	1549	ACAACUGCAUGU	2944	AD-26103, AD-26102
667	CAUGCAGUUGUA	1550	UACAACUGCAUG	2945	AD-26103, AD-26102
668	AUGCAGUUGUAA	1551	UUACAACUGCAU	2946	AD-26104, AD-26103, AD-26102
669	UGCAGUUGUAAA	1552	UUUACAACUGCA	2947	AD-26105, AD-26103
670	GCAGUUGUAAAC	1553	GUUUACAACUGC	2948	AD-26105, AD-26104, AD-26103
671	CAGUUGUAAACU	1554	AGUUUACAACUG	2949	AD-26105, AD-26104, AD-26103, AD-26106
672	AGUUGUAAACUU	1555	AAGUUUACAACU	2950	AD-26105, AD-26103, AD-26106
673	GUUGUAAACUUG	1556	CAAGUUUACAAC	2951	AD-26105, AD-26104, AD-26106
674	UUGUAAACUUGA	1557	UCAAGUUUACAA	2952	AD-26105, AD-26808, AD-26104, AD-26106
675	UGUAAACUUGAU	1558	AUCAAGUUUACA	2953	AD-26105, AD-26808, AD-26104, AD-26106, AD-26809
676	GUAAACUUGAUU	1559	AAUCAAGUUUAC	2954	AD-26105, AD-26808, AD-26106, AD-26809
677	UAAACUUGAUUA	1560	UAAUCAAGUUUA	2955	AD-26808, AD-26106, AD-26809
678	AAACUUGAUUAA	1561	UUAAUCAAGUUU	2956	AD-26808, AD-26810, AD-26106, AD-26809
679	AACUUGAUUAAC	1562	GUUAAUCAAGUU	2957	AD-26808, AD-26810, AD-26809
680	ACUUGAUUAACU	1563	AGUUAAUCAAGU	2958	AD-26808, AD-26809
681	CUUGAUUAACUA	1564	UAGUUAAUCAAG	2959	AD-26107, AD-26808, AD-26810, AD-26809
682	UUGAUUAACUAU	1565	AUAGUUAAUCAA	2960	AD-26107, AD-26810, AD-26809
683	UGAUUAACUAUC	1566	GAUAGUUAAUCA	2961	AD-26107, AD-26810
684	GAUUAACUAUCA	1567	UGAUAGUUAAUC	2962	AD-26107, AD-26810, AD-26108
685	AUUAACUAUCAA	1568	UUGAUAGUUAAU	2963	AD-26107, AD-26108
686	UUAACUAUCAAG	1569	CUUGAUAGUUAA	2964	AD-26107, AD-26108
687	UAACUAUCAAGA	1570	UCUUGAUAGUUA	2965	AD-26107, AD-26108
688	AACUAUCAAGAU	1571	AUCUUGAUAGUU	2966	AD-26107, AD-26108
690	CUAUCAAGAUGA	1572	UCAUCUUGAUAG	2967	AD-26109, AD-26108
691	UAUCAAGAUGAU	1573	AUCAUCUUGAUA	2968	AD-26109, AD-26108

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709	CUUGCCACACGU	1576	ACGUGUGGCAAG	2971	AD-26110, AD-26111
710	UUGCCACACGUG	1577	CACGUGUGGCAA	2972	AD-26110, AD-26111
711	UGCCACACGUGC	1578	GCACGUGUGGCA	2973	AD-26110, AD-26111
712	GCCACACGUGCA	1579	UGCACGUGUGGC	2974	AD-26110, AD-26111
713	CCACACGUGCAA	1580	UUGCACGUGUGG	2975	AD-26110, AD-26111
714	CACACGUGCAAU	1581	AUUGCACGUGUG	2976	AD-26112, AD-26111
721	GCAAUCCCUGAA	1582	UUCAGGGAUUGC	2977	AD-26112, AD-26123
722	CAAUCCCUGAAC	1583	GUUCAGGGAUUG	2978	AD-26124, AD-26123
723	AAUCCCUGAACU	1584	AGUUCAGGGAUU	2979	AD-26124, AD-26125
724	AUCCCUGAACUG	1585	CAGUUCAGGGAU	2980	AD-26124, AD-26123
725	UCCCUGAACUGA	1586	UCAGUUCAGGGA	2981	AD-26124, AD-26125
726	CCCUGAACUGAC	1587	GUCAGUUCAGGG	2982	AD-26124, AD-26123
727	CCUGAACUGACA	1588	UGUCAGUUCAGG	2983	AD-26124, AD-26123, AD-26125
728	CUGAACUGACAA	1589	UUGUCAGUUCAG	2984	AD-26124, AD-26123, AD-26125
729	UGAACUGACAAA	1590	UUUGUCAGUUCA	2985	AD-26124, AD-26125, AD-26126
730	GAACUGACAAAA	1591	UUUUGUCAGUUC	2986	AD-26125, AD-26126
731	AACUGACAAAAC	1592	GUUUUGUCAGUU	2987	AD-26128, AD-26126, AD-26127
732	ACUGACAAAACU	1593	AGUUUUGUCAGU	2988	AD-26128, AD-26126, AD-26129
733	CUGACAAAACUG	1594	CAGUUUUGUCAG	2989	AD-26128, AD-26126, AD-26129
734	UGACAAAACUGC	1595	GCAGUUUUGUCA	2990	AD-26128, AD-26127, AD-26129
735	GACAAAACUGCU	1596	AGCAGUUUUGUC	2991	AD-26128, AD-26126, AD-26129
736	ACAAAACUGCUA	1597	UAGCAGUUUUGU	2992	AD-26128, AD-26126, AD-26127, AD-26129
737	CAAAACUGCUAA	1598	UUAGCAGUUUUG	2993	AD-26128, AD-26127, AD-26129
738	AAAACUGCUAAA	1599	UUUAGCAGUUUU	2994	AD-26128, AD-26129
755	AGGACCAGGUGG	1600	CCACCUGGUCCU	2995	AD-26131, AD-26130
756	GGACCAGGUGGU	1601	ACCACCUGGUCC	2996	AD-26132, AD-26131, AD-26130
757	GACCAGGUGGUG	1602	CACCACCUGGUC	2997	AD-26132, AD-26133, AD-26131, AD-26130
758	ACCAGGUGGUGG	1603	CCACCACCUGGU	2998	AD-26132, AD-26133, AD-26131, AD-26130, AD-26136
759	CCAGGUGGUGGU	1604	ACCACCACCUGG	2999	AD-26132, AD-26131, AD-26136
760	CAGGUGGUGGUU	1605	AACCACCACCUG	3000	AD-26132, AD-26133, AD-26131, AD-26136
761	AGGUGGUGGUUA	1606	UAACCACCACCU	3001	AD-26132, AD-26131, AD-26130, AD-26136
762	GGUGGUGGUUAA	1607	UUAACCACCACC	3002	AD-26132, AD-26131
763	GUGGUGGUUAAU	1608	AUUAACCACCAC	3003	AD-26132, AD-26133,

					AD-26136
764	UGGUGGUUAAUA	1609	UAUUAACCACCA	3004	AD-26133, AD-26136
784	GUUAUGGUCCAU	1610	AUGGACCAUAAC	3005	AD-26138, AD-26137
787	AUGGUCCAUCAG	1611	CUGAUGGACCAU	3006	AD-26138, AD-26139
788	UGGUCCAUCAGC	1612	GCUGAUGGACCA	3007	AD-26138, AD-26139, AD-26140
789	GGUCCAUCAGCU	1613	AGCUGAUGGACC	3008	AD-26142, AD-26140
790	GUCCAUCAGCUU	1614	AAGCUGAUGGAC	3009	AD-26143, AD-26142, AD-26140
791	UCCAUCAGCUUU	1615	AAAGCUGAUGGA	3010	AD-26139, AD-26143, AD-26142, AD-26140
792	CCAUCAGCUUUC	1616	GAAAGCUGAUGG	3011	AD-26143, AD-26142, AD-26140
793	CAUCAGCUUUCU	1617	AGAAAGCUGAUG	3012	AD-26139, AD-26143, AD-26142, AD-26140
794	AUCAGCUUUCUA	1618	UAGAAAGCUGAU	3013	AD-26143, AD-26142, AD-26140
795	UCAGCUUUCUAA	1619	UUAGAAAGCUGA	3014	AD-26143, AD-26142
796	CAGCUUUCUAAA	1620	UUUAGAAAGCUG	3015	AD-26143, AD-26142
811	GAAGCUUCCAGA	1621	UCUGGAAGCUUC	3016	AD-26144, AD-18950
812	AAGCUUCCAGAC	1622	GUCUGGAAGCUU	3017	AD-26144, AD-18950
813	AGCUUCCAGACA	1623	UGUCUGGAAGCU	3018	AD-26145, AD-26144, AD-18950
814	GCUUCCAGACAC	1624	GUGUCUGGAAGC	3019	AD-26145, AD-26144
815	CUUCCAGACACG	1625	CGUGUCUGGAAG	3020	AD-26145, AD-26144
816	UUCCAGACACGC	1626	GCGUGUCUGGAA	3021	AD-26146, AD-26144
817	UCCAGACACGCU	1627	AGCGUGUCUGGA	3022	AD-26145, AD-26146, AD-26144
818	CCAGACACGCUA	1628	UAGCGUGUCUGG	3023	AD-26145, AD-26146
819	CAGACACGCUAU	1629	AUAGCGUGUCUG	3024	AD-26145, AD-26146
820	AGACACGCUAUC	1630	GAUAGCGUGUCU	3025	AD-26146, AD-26147
821	GACACGCUAUCA	1631	UGAUAGCGUGUC	3026	AD-19745, AD-26146
822	ACACGCUAUCAU	1632	AUGAUAGCGUGU	3027	AD-19745, AD-26146, AD-26147
823	CACGCUAUCAUG	1633	CAUGAUAGCGUG	3028	AD-19745, AD-26147
824	ACGCUAUCAUGC	1634	GCAUGAUAGCGU	3029	AD-19745, AD-19739, AD-26147
825	CGCUAUCAUGCG	1635	CGCAUGAUAGCG	3030	AD-19745, AD-19746, AD-19739
826	GCUAUCAUGCGU	1636	ACGCAUGAUAGC	3031	AD-19766, AD-19739, AD-26147
827	CUAUCAUGCGUU	1637	AACGCAUGAUAG	3032	AD-19766, AD-19745, AD-19739, AD-26147
828	UAUCAUGCGUUC	1638	GAACGCAUGAUA	3033	AD-19766, AD-19745, AD-19739
829	AUCAUGCGUUCU	1639	AGAACGCAUGAU	3034	AD-19766, AD-19746, AD-19739
830	UCAUGCGUUCUC	1640	GAGAACGCAUGA	3035	AD-19739, AD-26148
831	CAUGCGUUCUCC	1641	GGAGAACGCAUG	3036	AD-19739, AD-26148
832	AUGCGUUCUCCU	1642	AGGAGAACGCAU	3037	AD-19746, AD-26148
842	CUCAGAUGGUGU	1643	ACACCAUCUGAG	3038	AD-26150, AD-26149
843	UCAGAUGGUGUC	1644	GACACCAUCUGA	3039	AD-26150, AD-26149

844	CAGAUGGUGUCU	1645	AGACACCAUCUG	3040	AD-26150, AD-26149
845	AGAUGGUGUCUG	1646	CAGACACCAUCU	3041	AD-26150, AD-26149
846	GAUGGUGUCUGC	1647	GCAGACACCAUC	3042	AD-26150, AD-26149
847	AUGGUGUCUGCU	1648	AGCAGACACCAU	3043	AD-26150, AD-26149
848	UGGUGUCUGCUA	1649	UAGCAGACACCA	3044	AD-26150, AD-26149
854	CUGCUAUUGUAC	1650	GUACAAUAGCAG	3045	AD-26151, AD-26152
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919	UUGCAUAACCUU	1690	AAGGUUAUGCAA	3085	AD-19759, AD-26163, AD-26164, AD-26165
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979	CCUGCCCUGGUG	1700	CACCAGGGCAGG	3095	AD-26170, AD-26168
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982	GCCCUGGUGAAA	1703	UUUCACCAGGGC	3098	AD-26170, AD-26171, AD-26168, AD-26169
983	CCCUGGUGAAAA	1704	UUUUCACCAGGG	3099	AD-26170, AD-26171, AD-26169
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1013	AUUCUGUGUUGU	1724	ACAACACAGAAU	3119	AD-26181, AD-26178, AD-26179, AD-26182
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1018	GUGUUGUUUUAU	1729	AUAAAACAACAC	3124	AD-26183, AD-26182, AD-26185
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1116	UGCCUUGCUCAA	1786	UUGAGCAAGGCA	3181	AD-26206, AD-26203, AD-26207
1117	GCCUUGCUCAAC	1787	GUUGAGCAAGGC	3182	AD-26205, AD-26208, AD-26207
1118	CCUUGCUCAACA	1788	UGUUGAGCAAGG	3183	AD-26206, AD-26205, AD-26208, AD-26207, AD-26209
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1222	GGUGGACCCCAA	1798	UUGGGGUCCACC	3193	AD-26215, AD-26057, AD-26213
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1228	CCCCAAGCUUUA	1804	UAAAGCUUGGGG	3199	AD-26215, AD-26652, AD-26217, AD-26216, AD-26218
1229	CCCAAGCUUUAG	1805	CUAAAGCUUGGG	3200	AD-26651, AD-26652, AD-26217, AD-26216, AD-26653, AD-26218
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1231	CAAGCUUUAGUA	1807	UACUAAAGCUUG	3202	AD-26654, AD-26651, AD-26652, AD-26217,

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1233	AGCUUUAGUAAA	1809	UUUACUAAAGCU	3204	AD-26654, AD-26651, AD-26652, AD-26068, AD-26653, AD-26069, AD-26218
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1245	UAUAAUGAGGAC	1818	GUCCUCAUUAUA	3213	AD-26655, AD-26656, AD-26657
1246	AUAAUGAGGACC	1819	GGUCCUCAUUAU	3214	AD-26655, AD-26656, AD-26657
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1289	GCAGAGUGCUGA	1828	UCAGCACUCUGC	3223	AD-18945, AD-26660, AD-19046
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1293	AGUGCUGAAGGU	1832	ACCUUCAGCACU	3227	AD-19046, AD-26661, AD-26662
1294	GUGCUGAAGGUG	1833	CACCUUCAGCAC	3228	AD-19046, AD-26662
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1314	CUGCUCUAGUAA	1838	UUACUAGAGCAG	3233	AD-19768, AD-19748
1315	UGCUCUAGUAAU	1839	AUUACUAGAGCA	3234	AD-19768, AD-19748
1316	GCUCUAGUAAUA	1840	UAUUACUAGAGC	3235	AD-19768, AD-19748
1317	CUCUAGUAAUAA	1841	UUAUUACUAGAG	3236	AD-19768, AD-19748
1318	UCUAGUAAUAAG	1842	CUUAUUACUAGA	3237	AD-19768, AD-19748
1319	CUAGUAAUAAGC	1843	GCUUAUUACUAG	3238	AD-19768, AD-19748
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1340	UAGAAGCUGGUG	1847	CACCAGCUUCUA	3242	AD-26664, AD-26663
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1343	AAGCUGGUGGAA	1850	UUCCACCAGCUU	3245	AD-26664, AD-26663
1346	CUGGUGGAAUGC	1851	GCAUUCCACCAG	3246	AD-26665, AD-26666
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1348	GGUGGAAUGCAA	1853	UUGCAUUCCACC	3248	AD-26665, AD-26666
1349	GUGGAAUGCAAG	1854	CUUGCAUUCCAC	3249	AD-26665, AD-26666
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1352	GAAUGCAAGCUU	1857	AAGCUUGCAUUC	3252	AD-26665, AD-26666
1369	CUUCACCUGACA	1858	UGUCAGGUGAAG	3253	AD-26667, AD-26668
1370	UUCACCUGACAG	1859	CUGUCAGGUGAA	3254	AD-26667, AD-26668
1371	UCACCUGACAGA	1860	UCUGUCAGGUGA	3255	AD-26667, AD-26668
1372	CACCUGACAGAU	1861	AUCUGUCAGGUG	3256	AD-26667, AD-26668
1374	CCUGACAGAUCC	1862	GGAUCUGUCAGG	3257	AD-26669, AD-26668
1375	CUGACAGAUCCA	1863	UGGAUCUGUCAG	3258	AD-26669, AD-26668
1376	UGACAGAUCCAA	1864	UUGGAUCUGUCA	3259	AD-26669, AD-26668
1380	AGAUCCAAGUCA	1865	UGACUUGGAUCU	3260	AD-26669, AD-26670
1381	GAUCCAAGUCAA	1866	UUGACUUGGAUC	3261	AD-26669, AD-26670
1383	UCCAAGUCAACG	1867	CGUUGACUUGGA	3262	AD-26671, AD-26670
1384	CCAAGUCAACGU	1868	ACGUUGACUUGG	3263	AD-26671, AD-26670
1385	CAAGUCAACGUC	1869	GACGUUGACUUG	3264	AD-26671, AD-26670
1386	AAGUCAACGUCU	1870	AGACGUUGACUU	3265	AD-26671, AD-26670
1387	AGUCAACGUCUU	1871	AAGACGUUGACU	3266	AD-26671, AD-26670
1396	CUUGUUCAGAAC	1872	GUUCUGAACAAG	3267	AD-26672, AD-26673
1397	UUGUUCAGAACU	1873	AGUUCUGAACAA	3268	AD-26672, AD-26673
1398	UGUUCAGAACUG	1874	CAGUUCUGAACA	3269	AD-26672, AD-26673
1399	GUUCAGAACUGU	1875	ACAGUUCUGAAC	3270	AD-26672, AD-26673
1400	UUCAGAACUGUC	1876	GACAGUUCUGAA	3271	AD-26672, AD-26673
1401	UCAGAACUGUCU	1877	AGACAGUUCUGA	3272	AD-26672, AD-26673
1402	CAGAACUGUCUU	1878	AAGACAGUUCUG	3273	AD-26672, AD-26673
1406	ACUGUCUUUGGA	1879	UCCAAAGACAGU	3274	AD-19056, AD-19079
1407	CUGUCUUUGGAC	1880	GUCCAAAGACAG	3275	AD-19056, AD-19079
1408	UGUCUUUGGACU	1881	AGUCCAAAGACA	3276	AD-19056, AD-19079
1409	GUCUUUGGACUC	1882	GAGUCCAAAGAC	3277	AD-26674, AD-19056, AD-19079
1410	UCUUUGGACUCU	1883	AGAGUCCAAAGA	3278	AD-26674, AD-26675, AD-19056, AD-19079

1411	CUUUGGACUCUC	1884	GAGAGUCCAAAG	3279	AD-26674, AD-19056, AD-19079
1412	UUUGGACUCUCA	1885	UGAGAGUCCAAA	3280	AD-26674, AD-26675, AD-19079
1413	UUGGACUCUCAG	1886	CUGAGAGUCCAA	3281	AD-26675, AD-26676, AD-19079
1414	UGGACUCUCAGG	1887	CCUGAGAGUCCA	3282	AD-26674, AD-26675, AD-26676, AD-26678
1415	GGACUCUCAGGA	1888	UCCUGAGAGUCC	3283	AD-26674, AD-26676, AD-26678
1416	GACUCUCAGGAA	1889	UUCCUGAGAGUC	3284	AD-26674, AD-26675, AD-26676, AD-26678
1417	ACUCUCAGGAAU	1890	AUUCCUGAGAGU	3285	AD-26675, AD-26676, AD-26678
1418	CUCUCAGGAAUC	1891	GAUUCCUGAGAG	3286	AD-26676, AD-26678
1419	UCUCAGGAAUCU	1892	AGAUUCCUGAGA	3287	AD-26679, AD-26676, AD-26678
1420	CUCAGGAAUCUU	1893	AAGAUUCCUGAG	3288	AD-26679, AD-26678
1421	UCAGGAAUCUUU	1894	AAAGAUUCCUGA	3289	AD-26679, AD-26678
1426	AAUCUUUCAGAU	1895	AUCUGAAAGAUU	3290	AD-26679, AD-26680
1429	CUUUCAGAUGCU	1896	AGCAUCUGAAAG	3291	AD-26681, AD-26680
1430	UUUCAGAUGCUG	1897	CAGCAUCUGAAA	3292	AD-26681, AD-26680
1431	UUCAGAUGCUGC	1898	GCAGCAUCUGAA	3293	AD-26682, AD-26680
1432	UCAGAUGCUGCA	1899	UGCAGCAUCUGA	3294	AD-26682, AD-26681
1433	CAGAUGCUGCAA	1900	UUGCAGCAUCUG	3295	AD-26682, AD-26681, AD-26680
1434	AGAUGCUGCAAC	1901	GUUGCAGCAUCU	3296	AD-26682, AD-26681
1435	GAUGCUGCAACU	1902	AGUUGCAGCAUC	3297	AD-26682, AD-26681
1436	AUGCUGCAACUA	1903	UAGUUGCAGCAU	3298	AD-26682, AD-26681
1437	UGCUGCAACUAA	1904	UUAGUUGCAGCA	3299	AD-26682, AD-26683
1438	GCUGCAACUAAA	1905	UUUAGUUGCAGC	3300	AD-26682, AD-26683
1467	UCUCCUUGGGAC	1906	GUCCCAAGGAGA	3301	AD-26687, AD-26686
1468	CUCCUUGGGACU	1907	AGUCCCAAGGAG	3302	AD-26687, AD-26686
1469	UCCUUGGGACUC	1908	GAGUCCCAAGGA	3303	AD-26687, AD-26686
1470	CCUUGGGACUCU	1909	AGAGUCCCAAGG	3304	AD-26687, AD-26686
1471	CUUGGGACUCUU	1910	AAGAGUCCCAAG	3305	AD-26687, AD-26686
1473	UGGGACUCUUGU	1911	ACAAGAGUCCCA	3306	AD-26688, AD-26687
1474	GGGACUCUUGUU	1912	AACAAGAGUCCC	3307	AD-26688, AD-26687
1480	CUUGUUCAGCUU	1913	AAGCUGAACAAG	3308	AD-26689, AD-26688
1485	UCAGCUUCUGGG	1914	CCCAGAAGCUGA	3309	AD-26689, AD-26690
1486	CAGCUUCUGGGU	1915	ACCCAGAAGCUG	3310	AD-26689, AD-26690
1487	AGCUUCUGGGUU	1916	AACCCAGAAGCU	3311	AD-26689, AD-26690
1488	GCUUCUGGGUUC	1917	GAACCCAGAAGC	3312	AD-26691, AD-26690
1489	CUUCUGGGUUCA	1918	UGAACCCAGAAG	3313	AD-26692, AD-26691, AD-26690
1490	UUCUGGGUUCAG	1919	CUGAACCCAGAA	3314	AD-26692, AD-26691, AD-26694, AD-26690
1491	UCUGGGUUCAGA	1920	UCUGAACCCAGA	3315	AD-26692, AD-26694, AD-26690
1492	CUGGGUUCAGAU	1921	AUCUGAACCCAG	3316	AD-26692, AD-26691, AD-26694, AD-26695, AD-26690

1493	UGGGUUCAGAUG	1922	CAUCUGAACCCA	3317	AD-26692, AD-26691, AD-26696, AD-26694, AD-26695
1494	GGGUUCAGAUGA	1923	UCAUCUGAACCC	3318	AD-26692, AD-26691, AD-26696, AD-26694
1495	GGUUCAGAUGAU	1924	AUCAUCUGAACC	3319	AD-26692, AD-26691, AD-26694, AD-26695
1496	GUUCAGAUGAUA	1925	UAUCAUCUGAAC	3320	AD-26696, AD-26694, AD-26695
1497	UUCAGAUGAUAU	1926	AUAUCAUCUGAA	3321	AD-26696, AD-26694, AD-26695
1498	UCAGAUGAUAUA	1927	UAUAUCAUCUGA	3322	AD-26696, AD-26695
1499	CAGAUGAUAUAA	1928	UUAUAUCAUCUG	3323	AD-26696, AD-26695
1503	UGAUAUAAAUGU	1929	ACAUUUAUAUCA	3324	AD-18994, AD-18927
1504	GAUAUAAAUGUG	1930	CACAUUUAUAUC	3325	AD-19045, AD-18994
1505	AUAUAAAUGUGG	1931	CCACAUUUAUAU	3326	AD-19045, AD-18927
1506	UAUAAAUGUGGU	1932	ACCACAUUUAUA	3327	AD-18994, AD-18927
1507	AUAAAUGUGGUC	1933	GACCACAUUUAU	3328	AD-19045, AD-18994, AD-18927
1508	UAAAUGUGGUCA	1934	UGACCACAUUUA	3329	AD-19045, AD-18994, AD-18927
1509	AAAUGUGGUCAC	1935	GUGACCACAUUU	3330	AD-19045, AD-18994
1510	AAUGUGGUCACC	1936	GGUGACCACAUU	3331	AD-19045, AD-18994
1517	UCACCUGUGCAG	1937	CUGCACAGGUGA	3332	AD-26697, AD-26698
1518	CACCUGUGCAGC	1938	GCUGCACAGGUG	3333	AD-26697, AD-26698
1519	ACCUGUGCAGCU	1939	AGCUGCACAGGU	3334	AD-26697, AD-26699
1520	CCUGUGCAGCUG	1940	CAGCUGCACAGG	3335	AD-26697, AD-26699, AD-26698
1521	CUGUGCAGCUGG	1941	CCAGCUGCACAG	3336	AD-26700, AD-26697, AD-26699, AD-26698
1522	UGUGCAGCUGGA	1942	UCCAGCUGCACA	3337	AD-26700, AD-26697, AD-26699, AD-26701, AD-26698
1523	GUGCAGCUGGAA	1943	UUCCAGCUGCAC	3338	AD-26700, AD-26699, AD-26701, AD-26698
1524	UGCAGCUGGAAU	1944	AUUCCAGCUGCA	3339	AD-26700, AD-26699, AD-26701, AD-26698
1525	GCAGCUGGAAUU	1945	AAUUCCAGCUGC	3340	AD-26700, AD-26699, AD-26701, AD-26702
1526	CAGCUGGAAUUC	1946	GAAUUCCAGCUG	3341	AD-26700, AD-26701, AD-26702
1527	AGCUGGAAUUCU	1947	AGAAUUCCAGCU	3342	AD-26700, AD-26703, AD-26702
1528	GCUGGAAUUCUU	1948	AAGAAUUCCAGC	3343	AD-26700, AD-26703, AD-26701, AD-26702
1529	CUGGAAUUCUUU	1949	AAAGAAUUCCAG	3344	AD-26703, AD-26701, AD-26702
1530	UGGAAUUCUUUC	1950	GAAAGAAUUCCA	3345	AD-26703, AD-26702
1531	GGAAUUCUUUCU	1951	AGAAAGAAUUCC	3346	AD-26703, AD-26702
1532	GAAUUCUUUCUA	1952	UAGAAAGAAUUC	3347	AD-26703, AD-26702
1538	UUUCUAACCUCA	1953	UGAGGUUAGAAA	3348	AD-26704, AD-26920
1539	UUCUAACCUCAC	1954	GUGAGGUUAGAA	3349	AD-26704, AD-26920,

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1540	UCUAACCUCACU	1955	AGUGAGGUUAGA	3350	AD-26704, AD-26920, AD-26705, AD-18899
1541	CUAACCUCACUU	1956	AAGUGAGGUUAG	3351	AD-26704, AD-26920, AD-26705, AD-18899, AD-18917
1542	UAACCUCACUUG	1957	CAAGUGAGGUUA	3352	AD-26704, AD-26705, AD-18899, AD-18917
1543	AACCUCACUUGC	1958	GCAAGUGAGGUU	3353	AD-26704, AD-19074, AD-26705, AD-18899, AD-18917
1544	ACCUCACUUGCA	1959	UGCAAGUGAGGU	3354	AD-26704, AD-26706, AD-19074, AD-26705, AD-18899, AD-18917
1545	CCUCACUUGCAA	1960	UUGCAAGUGAGG	3355	AD-26704, AD-26706, AD-26707, AD-19074, AD-26705, AD-18899, AD-18917
1546	CUCACUUGCAAU	1961	AUUGCAAGUGAG	3356	AD-26706, AD-26707, AD-19074, AD-26708, AD-26705, AD-18899, AD-18917
1547	UCACUUGCAAUA	1962	UAUUGCAAGUGA	3357	AD-26706, AD-26134, AD-26707, AD-19074, AD-26708, AD-18899, AD-18917
1548	CACUUGCAAUAA	1963	UUAUUGCAAGUG	3358	AD-26706, AD-26134, AD-26707, AD-19074, AD-26708, AD-18917
1549	ACUUGCAAUAAU	1964	AUUAUUGCAAGU	3359	AD-26706, AD-26134, AD-26707, AD-19074, AD-26708
1550	CUUGCAAUAAUU	1965	AAUUAUUGCAAG	3360	AD-26706, AD-26134, AD-26707, AD-19074, AD-26708, AD-26135
1551	UUGCAAUAAUUA	1966	UAAUUAUUGCAA	3361	AD-26706, AD-26134, AD-26707, AD-26708, AD-26135
1552	UGCAAUAAUUAU	1967	AUAAUUAUUGCA	3362	AD-26134, AD-26707, AD-26708, AD-26135
1553	GCAAUAAUUAUA	1968	UAUAAUUAUUGC	3363	AD-26134, AD-26708, AD-26135
1554	CAAUAAUUAUAA	1969	UUAUAAUUAUUG	3364	AD-26134, AD-26135
1580	UCUGCCAAGUGG	1970	CCACUUGGCAGA	3365	AD-26710, AD-26709
1581	CUGCCAAGUGGG	1971	CCCACUUGGCAG	3366	AD-26710, AD-26709
1582	UGCCAAGUGGGU	1972	ACCCACUUGGCA	3367	AD-26710, AD-26709
1583	GCCAAGUGGGUG	1973	CACCCACUUGGC	3368	AD-26710, AD-26709
1584	CCAAGUGGGUGG	1974	CCACCCACUUGG	3369	AD-26710, AD-26709
1585	CAAGUGGGUGGU	1975	ACCACCCACUUG	3370	AD-26710, AD-26709
1586	AAGUGGGUGGUA	1976	UACCACCCACUU	3371	AD-26710, AD-26709
1597	AUAGAGGCUCUU	1977	AAGAGCCUCUAU	3372	AD-26712, AD-26711
1628	CUGGUGACAGGG	1978	CCCUGUCACCAG	3373	AD-26714, AD-26141

1629	UGGUGACAGGGA	1979	UCCCUGUCACCA	3374	AD-26714, AD-26141
1630	GGUGACAGGGAA	1980	UUCCCUGUCACC	3375	AD-26714, AD-26141
1637	GGGAAGACAUCA	1981	UGAUGUCUUCCC	3376	AD-18938, AD-19064
1638	GGAAGACAUCAC	1982	GUGAUGUCUUCC	3377	AD-18938, AD-18937
1639	GAAGACAUCACU	1983	AGUGAUGUCUUC	3378	AD-18938, AD-19064
1640	AAGACAUCACUG	1984	CAGUGAUGUCUU	3379	AD-19064, AD-18937
1641	AGACAUCACUGA	1985	UCAGUGAUGUCU	3380	AD-18938, AD-19064, AD-18937
1642	GACAUCACUGAG	1986	CUCAGUGAUGUC	3381	AD-18938, AD-19064, AD-18937
1643	ACAUCACUGAGC	1987	GCUCAGUGAUGU	3382	AD-18938, AD-19064, AD-18937, AD-26715
1644	CAUCACUGAGCC	1988	GGCUCAGUGAUG	3383	AD-18938, AD-18937, AD-26715
1645	AUCACUGAGCCU	1989	AGGCUCAGUGAU	3384	AD-18937, AD-26715
1654	CCUGCCAUCUGU	1990	ACAGAUGGCAGG	3385	AD-26716, AD-18990
1655	CUGCCAUCUGUG	1991	CACAGAUGGCAG	3386	AD-26716, AD-18990
1656	UGCCAUCUGUGC	1992	GCACAGAUGGCA	3387	AD-26716, AD-18990
1657	GCCAUCUGUGCU	1993	AGCACAGAUGGC	3388	AD-26716, AD-18990, AD-19061
1658	CCAUCUGUGCUC	1994	GAGCACAGAUGG	3389	AD-26716, AD-18990, AD-18893, AD-19061
1659	CAUCUGUGCUCU	1995	AGAGCACAGAUG	3390	AD-26716, AD-18946, AD-18990, AD-18893, AD-19061
1660	AUCUGUGCUCUU	1996	AAGAGCACAGAU	3391	AD-26716, AD-18946, AD-18990, AD-19082, AD-18893, AD-19061
1661	UCUGUGCUCUUC	1997	GAAGAGCACAGA	3392	AD-18946, AD-18990, AD-19082, AD-18893, AD-19061
1662	CUGUGCUCUUCG	1998	CGAAGAGCACAG	3393	AD-18946, AD-19082, AD-19061
1663	UGUGCUCUUCGU	1999	ACGAAGAGCACA	3394	AD-18946, AD-19082, AD-18893, AD-19061
1664	GUGCUCUUCGUC	2000	GACGAAGAGCAC	3395	AD-18946, AD-18904, AD-19082, AD-18893, AD-19061
1665	UGCUCUUCGUCA	2001	UGACGAAGAGCA	3396	AD-18946, AD-18904, AD-19082, AD-18893
1666	GCUCUUCGUCAU	2002	AUGACGAAGAGC	3397	AD-18946, AD-18932, AD-18904, AD-19082
1667	CUCUUCGUCAUC	2003	GAUGACGAAGAG	3398	AD-18932, AD-19082, AD-18943
1668	UCUUCGUCAUCU	2004	AGAUGACGAAGA	3399	AD-18932, AD-18904, AD-18943
1669	CUUCGUCAUCUG	2005	CAGAUGACGAAG	3400	AD-18904, AD-19002, AD-18943
1670	UUCGUCAUCUGA	2006	UCAGAUGACGAA	3401	AD-18932, AD-18904, AD-19002, AD-18943
1671	UCGUCAUCUGAC	2007	GUCAGAUGACGA	3402	AD-18904, AD-18943
1672	CGUCAUCUGACC	2008	GGUCAGAUGACG	3403	AD-18932, AD-19002,

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1673	GUCAUCUGACCA	2009	UGGUCAGAUGAC	3404	AD-18932, AD-18943
1674	UCAUCUGACCAG	2010	CUGGUCAGAUGA	3405	AD-19002, AD-18943
1677	UCUGACCAGCCG	2011	CGGCUGGUCAGA	3406	AD-26717, AD-19761
1678	CUGACCAGCCGA	2012	UCGGCUGGUCAG	3407	AD-26717, AD-19761
1679	UGACCAGCCGAC	2013	GUCGGCUGGUCA	3408	AD-26717, AD-19761
1680	GACCAGCCGACA	2014	UGUCGGCUGGUC	3409	AD-26717, AD-19761
1681	ACCAGCCGACAC	2015	GUGUCGGCUGGU	3410	AD-26717, AD-26718
1682	CCAGCCGACACC	2016	GGUGUCGGCUGG	3411	AD-26717, AD-26718, AD-19761
1683	CAGCCGACACCA	2017	UGGUGUCGGCUG	3412	AD-26717, AD-26718, AD-19761
1684	AGCCGACACCAA	2018	UUGGUGUCGGCU	3413	AD-26717, AD-26718
1704	GAUGGCCCAGAA	2019	UUCUGGGCCAUC	3414	AD-26721, AD-26720
1705	AUGGCCCAGAAU	2020	AUUCUGGGCCAU	3415	AD-26721, AD-26720
1710	CCAGAAUGCAGU	2021	ACUGCAUUCUGG	3416	AD-26721, AD-26722
1711	CAGAAUGCAGUU	2022	AACUGCAUUCUG	3417	AD-26721, AD-26722
1713	GAAUGCAGUUCG	2023	CGAACUGCAUUC	3418	AD-26722, AD-19741
1714	AAUGCAGUUCGC	2024	GCGAACUGCAUU	3419	AD-26722, AD-19741
1715	AUGCAGUUCGCC	2025	GGCGAACUGCAU	3420	AD-26722, AD-19741, AD-26723
1716	UGCAGUUCGCCU	2026	AGGCGAACUGCA	3421	AD-26724, AD-26722, AD-19741, AD-26723
1717	GCAGUUCGCCUU	2027	AAGGCGAACUGC	3422	AD-26724, AD-19741, AD-26723
1718	CAGUUCGCCUUC	2028	GAAGGCGAACUG	3423	AD-26724, AD-26723
1719	AGUUCGCCUUCA	2029	UGAAGGCGAACU	3424	AD-26724, AD-19741
1720	GUUCGCCUUCAC	2030	GUGAAGGCGAAC	3425	AD-19741, AD-26723
1721	UUCGCCUUCACU	2031	AGUGAAGGCGAA	3426	AD-26724, AD-26723
1722	UCGCCUUCACUA	2032	UAGUGAAGGCGA	3427	AD-26724, AD-26725, AD-26723
1723	CGCCUUCACUAU	2033	AUAGUGAAGGCG	3428	AD-26724, AD-26725
1728	UCACUAUGGACU	2034	AGUCCAUAGUGA	3429	AD-26725, AD-26726
1729	CACUAUGGACUA	2035	UAGUCCAUAGUG	3430	AD-26725, AD-26726
1734	UGGACUACCAGU	2036	ACUGGUAGUCCA	3431	AD-26727, AD-26726
1735	GGACUACCAGUU	2037	AACUGGUAGUCC	3432	AD-26727, AD-26728
1736	GACUACCAGUUG	2038	CAACUGGUAGUC	3433	AD-26728, AD-26729
1737	ACUACCAGUUGU	2039	ACAACUGGUAGU	3434	AD-26727, AD-26729
1738	CUACCAGUUGUG	2040	CACAACUGGUAG	3435	AD-26727, AD-26728, AD-26729
1739	UACCAGUUGUGG	2041	CCACAACUGGUA	3436	AD-26727, AD-26728, AD-26729
1740	ACCAGUUGUGGU	2042	ACCACAACUGGU	3437	AD-26727, AD-26728, AD-26729
1741	CCAGUUGUGGUU	2043	AACCACAACUGG	3438	AD-26727, AD-26728, AD-26729
1742	CAGUUGUGGUUA	2044	UAACCACAACUG	3439	AD-26728, AD-26730, AD-26729
1743	AGUUGUGGUUAA	2045	UUAACCACAACU	3440	AD-26731, AD-26730, AD-26729
1744	GUUGUGGUUAAG	2046	CUUAACCACAAC	3441	AD-26731, AD-26730
1745	UUGUGGUUAAGC	2047	GCUUAACCACAA	3442	AD-26731, AD-26730

1746	UGUGGUUAAGCU	2048	AGCUUAACCACA	3443	AD-26731, AD-26730
1747	GUGGUUAAGCUC	2049	GAGCUUAACCAC	3444	AD-26731, AD-26730
1748	UGGUUAAGCUCU	2050	AGAGCUUAACCA	3445	AD-26731, AD-26730
1749	GGUUAAGCUCUU	2051	AAGAGCUUAACC	3446	AD-26731, AD-26730
1770	AUCCCACUGGCC	2052	GGCCAGUGGGAU	3447	AD-26734, AD-26733
1771	UCCCACUGGCCU	2053	AGGCCAGUGGGA	3448	AD-26734, AD-26733, AD-26735
1772	CCCACUGGCCUC	2054	GAGGCCAGUGGG	3449	AD-26734, AD-18963, AD-26733, AD-26735
1773	CCACUGGCCUCU	2055	AGAGGCCAGUGG	3450	AD-26734, AD-18930, AD-18963, AD-26733, AD-26735
1774	CACUGGCCUCUG	2056	CAGAGGCCAGUG	3451	AD-26734, AD-18930, AD-18963, AD-26733, AD-26735, AD-19078
1775	ACUGGCCUCUGA	2057	UCAGAGGCCAGU	3452	AD-26734, AD-18930, AD-18963, AD-26733, AD-18948, AD-19078
1776	CUGGCCUCUGAU	2058	AUCAGAGGCCAG	3453	AD-26734, AD-18963, AD-26733, AD-26735, AD-18948, AD-19078
1777	UGGCCUCUGAUA	2059	UAUCAGAGGCCA	3454	AD-26734, AD-18930, AD-26736, AD-18963, AD-26735, AD-18948, AD-19078
1778	GGCCUCUGAUAA	2060	UUAUCAGAGGCC	3455	AD-18930, AD-26736, AD-18963, AD-26735, AD-18948, AD-19078
1779	GCCUCUGAUAAA	2061	UUUAUCAGAGGC	3456	AD-18930, AD-26736, AD-18963, AD-18948, AD-19078
1780	CCUCUGAUAAAG	2062	CUUUAUCAGAGG	3457	AD-18930, AD-26736, AD-18948, AD-19078
1781	CUCUGAUAAAGG	2063	CCUUUAUCAGAG	3458	AD-26736, AD-18948, AD-19078
1782	UCUGAUAAAGGC	2064	GCCUUUAUCAGA	3459	AD-26736, AD-18948, AD-26737
1783	CUGAUAAAGGCU	2065	AGCCUUUAUCAG	3460	AD-26736, AD-26737
1784	UGAUAAAGGCUA	2066	UAGCCUUUAUCA	3461	AD-26736, AD-26737
1786	AUAAAGGCUACU	2067	AGUAGCCUUUAU	3462	AD-26738, AD-26737
1787	UAAAGGCUACUG	2068	CAGUAGCCUUUA	3463	AD-26738, AD-26737
1788	AAAGGCUACUGU	2069	ACAGUAGCCUUU	3464	AD-26738, AD-26737
1789	AAGGCUACUGUU	2070	AACAGUAGCCUU	3465	AD-26738, AD-26737
1791	GGCUACUGUUGG	2071	CCAACAGUAGCC	3466	AD-26738, AD-26739
1792	GCUACUGUUGGA	2072	UCCAACAGUAGC	3467	AD-26738, AD-26739
1793	CUACUGUUGGAU	2073	AUCCAACAGUAG	3468	AD-26738, AD-26739
1795	ACUGUUGGAUUG	2074	CAAUCCAACAGU	3469	AD-18983, AD-26739
1796	CUGUUGGAUUGA	2075	UCAAUCCAACAG	3470	AD-18983, AD-26739, AD-18897
1797	UGUUGGAUUGAU	2076	AUCAAUCCAACA	3471	AD-26740, AD-18983, AD-26739, AD-18897
1798	GUUGGAUUGAUU	2077	AAUCAAUCCAAC	3472	AD-26740, AD-26739,

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1799	UUGGAUUGAUUC	2078	GAAUCAAUCCAA	3473	AD-26740, AD-18983, AD-18897
1800	UGGAUUGAUUCG	2079	CGAAUCAAUCCA	3474	AD-26740, AD-18897, AD-26921
1801	GGAUUGAUUCGA	2080	UCGAAUCAAUCC	3475	AD-26740, AD-18983, AD-18897, AD-26921
1802	GAUUGAUUCGAA	2081	UUCGAAUCAAUC	3476	AD-18983, AD-18897, AD-26921
1803	AUUGAUUCGAAA	2082	UUUCGAAUCAAU	3477	AD-26740, AD-18897, AD-26921
1804	UUGAUUCGAAAU	2083	AUUUCGAAUCAA	3478	AD-26740, AD-26921
1848	GCGUGAGCAGGG	2084	CCCUGCUCACGC	3479	AD-26175, AD-26176
1849	CGUGAGCAGGGU	2085	ACCCUGCUCACG	3480	AD-26175, AD-26176
1850	GUGAGCAGGGUG	2086	CACCCUGCUCAC	3481	AD-26175, AD-26176
1851	UGAGCAGGGUGC	2087	GCACCCUGCUCA	3482	AD-26175, AD-26176
1852	GAGCAGGGUGCC	2088	GGCACCCUGCUC	3483	AD-26175, AD-26176
1853	AGCAGGGUGCCA	2089	UGGCACCCUGCU	3484	AD-26175, AD-26176
1854	GCAGGGUGCCAU	2090	AUGGCACCCUGC	3485	AD-26175, AD-26176
1859	GUGCCAUUCCAC	2091	GUGGAAUGGCAC	3486	AD-19742, AD-19749
1860	UGCCAUUCCACG	2092	CGUGGAAUGGCA	3487	AD-26741, AD-19749
1861	GCCAUUCCACGA	2093	UCGUGGAAUGGC	3488	AD-26741, AD-19742
1862	CCAUUCCACGAC	2094	GUCGUGGAAUGG	3489	AD-26741, AD-19742, AD-19749
1863	CAUUCCACGACU	2095	AGUCGUGGAAUG	3490	AD-26741, AD-19742, AD-19749, AD-19762
1864	AUUCCACGACUA	2096	UAGUCGUGGAAU	3491	AD-26741, AD-19742, AD-19749
1865	UUCCACGACUAG	2097	CUAGUCGUGGAA	3492	AD-26742, AD-26741, AD-19742, AD-19749, AD-19762
1866	UCCACGACUAGU	2098	ACUAGUCGUGGA	3493	AD-26742, AD-26741, AD-19749, AD-19762
1867	CCACGACUAGUU	2099	AACUAGUCGUGG	3494	AD-26742, AD-26741, AD-19751, AD-19762
1868	CACGACUAGUUC	2100	GAACUAGUCGUG	3495	AD-26742, AD-19751, AD-19762, AD-19752
1869	ACGACUAGUUCA	2101	UGAACUAGUCGU	3496	AD-26742, AD-26743, AD-19751, AD-19762
1870	CGACUAGUUCAG	2102	CUGAACUAGUCG	3497	AD-26742, AD-26743, AD-19751, AD-19762, AD-19752
1871	GACUAGUUCAGU	2103	ACUGAACUAGUC	3498	AD-26742, AD-26743, AD-19751, AD-19752
1872	ACUAGUUCAGUU	2104	AACUGAACUAGU	3499	AD-26742, AD-26743, AD-19751, AD-19752, AD-26744
1873	CUAGUUCAGUUG	2105	CAACUGAACUAG	3500	AD-26743, AD-19752, AD-26744
1874	UAGUUCAGUUGC	2106	GCAACUGAACUA	3501	AD-26743, AD-19751, AD-19752, AD-26744
1875	AGUUCAGUUGCU	2107	AGCAACUGAACU	3502	AD-26743, AD-19753,

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1878	UCAGUUGCUUGU	2110	ACAAGCAACUGA	3505	AD-19753, AD-26744
1879	CAGUUGCUUGUU	2111	AACAAGCAACUG	3506	AD-19753, AD-26744
1881	GUUGCUUGUUCG	2112	CGAACAAGCAAC	3507	AD-19753, AD-26745
1882	UUGCUUGUUCGU	2113	ACGAACAAGCAA	3508	AD-19753, AD-26745
1887	UGUUCGUGCACA	2114	UGUGCACGAACA	3509	AD-26746, AD-26745
1888	GUUCGUGCACAU	2115	AUGUGCACGAAC	3510	AD-26746, AD-26747, AD-26745
1889	UUCGUGCACAUC	2116	GAUGUGCACGAA	3511	AD-26746, AD-26747
1890	UCGUGCACAUCA	2117	UGAUGUGCACGA	3512	AD-26746, AD-26747
1891	CGUGCACAUCAG	2118	CUGAUGUGCACG	3513	AD-26746, AD-26747
1892	GUGCACAUCAGG	2119	CCUGAUGUGCAC	3514	AD-26746, AD-26747
1893	UGCACAUCAGGA	2120	UCCUGAUGUGCA	3515	AD-26746, AD-26747
1894	GCACAUCAGGAU	2121	AUCCUGAUGUGC	3516	AD-26746, AD-26747
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1908	CCAGCGCCGUAC	2123	GUACGGCGCUGG	3518	AD-19738, AD-19754
1909	CAGCGCCGUACG	2124	CGUACGGCGCUG	3519	AD-19738, AD-19754
1910	AGCGCCGUACGU	2125	ACGUACGGCGCU	3520	AD-19738, AD-19754
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1912	CGCCGUACGUCC	2127	GGACGUACGGCG	3522	AD-19738, AD-19754
1927	GGUGGGACACAG	2128	CUGUGUCCCACC	3523	AD-26184, AD-26748
1928	GUGGGACACAGC	2129	GCUGUGUCCCAC	3524	AD-26749, AD-26184, AD-26748
1929	UGGGACACAGCA	2130	UGCUGUGUCCCA	3525	AD-26749, AD-26750, AD-26184, AD-26748
1930	GGGACACAGCAG	2131	CUGCUGUGUCCC	3526	AD-26749, AD-26750, AD-26184
1931	GGACACAGCAGC	2132	GCUGCUGUGUCC	3527	AD-26749, AD-26184, AD-26748
1932	GACACAGCAGCA	2133	UGCUGCUGUGUC	3528	AD-26749, AD-26750, AD-26184, AD-26748
1933	ACACAGCAGCAA	2134	UUGCUGCUGUGU	3529	AD-26750, AD-26184, AD-26748
1934	CACAGCAGCAAU	2135	AUUGCUGCUGUG	3530	AD-26749, AD-26750, AD-26748
1935	ACAGCAGCAAUU	2136	AAUUGCUGCUGU	3531	AD-26749, AD-26750
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1956	GGUCCGCAUGGA	2138	UCCAUGCGGACC	3533	AD-26751, AD-26752
1957	GUCCGCAUGGAA	2139	UUCCAUGCGGAC	3534	AD-26751, AD-26752
1958	UCCGCAUGGAAG	2140	CUUCCAUGCGGA	3535	AD-26751, AD-26752
1959	CCGCAUGGAAGA	2141	UCUUCCAUGCGG	3536	AD-26751, AD-26752
1960	CGCAUGGAAGAA	2142	UUCUUCCAUGCG	3537	AD-26751, AD-26752
1961	GCAUGGAAGAAA	2143	UUUCUUCCAUGC	3538	AD-26751, AD-26752
2001	CAUCCUAGCUCG	2144	CGAGCUAGGAUG	3539	AD-26753, AD-26754
2002	AUCCUAGCUCGG	2145	CCGAGCUAGGAU	3540	AD-26753, AD-26754
2003	UCCUAGCUCGGG	2146	CCCGAGCUAGGA	3541	AD-26753, AD-26754
2004	CCUAGCUCGGGA	2147	UCCCGAGCUAGG	3542	AD-26753, AD-26754
2005	CUAGCUCGGGAU	2148	AUCCCGAGCUAG	3543	AD-26753, AD-26754
2006	UAGCUCGGGAUG	2149	CAUCCCGAGCUA	3544	AD-26755, AD-26754

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2008	GCUCGGGAUGUU	2151	AACAUCCCGAGC	3546	AD-26755, AD-26754
2011	CGGGAUGUUCAC	2152	GUGAACAUCCCG	3547	AD-26755, AD-20124
2012	GGGAUGUUCACA	2153	UGUGAACAUCCC	3548	AD-26756, AD-26755, AD-20124
2013	GGAUGUUCACAA	2154	UUGUGAACAUCC	3549	AD-26756, AD-26755, AD-26757, AD-20124
2014	GAUGUUCACAAC	2155	GUUGUGAACAUC	3550	AD-26756, AD-26757, AD-20124
2015	AUGUUCACAACC	2156	GGUUGUGAACAU	3551	AD-26756, AD-26757, AD-20124
2016	UGUUCACAACCG	2157	CGGUUGUGAACA	3552	AD-26756, AD-19750, AD-20124
2017	GUUCACAACCGA	2158	UCGGUUGUGAAC	3553	AD-19750, AD-26757, AD-20124
2018	UUCACAACCGAA	2159	UUCGGUUGUGAA	3554	AD-26756, AD-19750, AD-26757, AD-20124
2019	UCACAACCGAAU	2160	AUUCGGUUGUGA	3555	AD-26756, AD-19750, AD-26757
2020	CACAACCGAAUU	2161	AAUUCGGUUGUG	3556	AD-19750, AD-26757
2041	GGACUAAAUACC	2162	GGUAUUUAGUCC	3557	AD-26758, AD-26759
2042	GACUAAAUACCA	2163	UGGUAUUUAGUC	3558	AD-26758, AD-26759
2043	ACUAAAUACCAU	2164	AUGGUAUUUAGU	3559	AD-26758, AD-26759
2044	CUAAAUACCAUU	2165	AAUGGUAUUUAG	3560	AD-26758, AD-26759
2045	UAAAUACCAUUC	2166	GAAUGGUAUUUA	3561	AD-26760, AD-26759
2046	AAAUACCAUUCC	2167	GGAAUGGUAUUU	3562	AD-26760, AD-26761, AD-26759
2047	AAUACCAUUCCA	2168	UGGAAUGGUAUU	3563	AD-26760, AD-26759
2048	AUACCAUUCCAU	2169	AUGGAAUGGUAU	3564	AD-26760, AD-26761, AD-26759, AD-18982
2049	UACCAUUCCAUU	2170	AAUGGAAUGGUA	3565	AD-26760, AD-19062, AD-18982
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2051	CCAUUCCAUUGU	2172	ACAAUGGAAUGG	3567	AD-26761, AD-19062, AD-18982
2052	CAUUCCAUUGUU	2173	AACAAUGGAAUG	3568	AD-26760, AD-26761, AD-19062
2053	AUUCCAUUGUUU	2174	AAACAAUGGAAU	3569	AD-26761, AD-19062, AD-18982
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2055	UCCAUUGUUUGU	2176	ACAAACAAUGGA	3571	AD-19062, AD-18982
2059	UUGUUUGUGCAG	2177	CUGCACAAACAA	3572	AD-26763, AD-26762
2060	UGUUUGUGCAGC	2178	GCUGCACAAACA	3573	AD-26764, AD-26763, AD-26762
2061	GUUUGUGCAGCU	2179	AGCUGCACAAAC	3574	AD-26764, AD-26765, AD-26763, AD-26762
2062	UUUGUGCAGCUG	2180	CAGCUGCACAAA	3575	AD-26764, AD-26765, AD-26766, AD-26763, AD-26762
2063	UUGUGCAGCUGC	2181	GCAGCUGCACAA	3576	AD-26764, AD-26765, AD-26766, AD-26763

2064	UGUGCAGCUGCU	2182	AGCAGCUGCACA	3577	AD-26764, AD-26766, AD-26763, AD-26762
2065	GUGCAGCUGCUU	2183	AAGCAGCUGCAC	3578	AD-26765, AD-26766, AD-26763, AD-26762
2066	UGCAGCUGCUUU	2184	AAAGCAGCUGCA	3579	AD-26764, AD-26765, AD-26766, AD-26763
2067	GCAGCUGCUUUA	2185	UAAAGCAGCUGC	3580	AD-26764, AD-26765, AD-26766
2068	CAGCUGCUUUAU	2186	AUAAAGCAGCUG	3581	AD-26765, AD-26766
2069	AGCUGCUUUAUU	2187	AAUAAAGCAGCU	3582	AD-26766, AD-26767
2070	GCUGCUUUAUUC	2188	GAAUAAAGCAGC	3583	AD-26768, AD-26767
2071	CUGCUUUAUUCU	2189	AGAAUAAAGCAG	3584	AD-26768, AD-26767
2072	UGCUUUAUUCUC	2190	GAGAAUAAAGCA	3585	AD-26768, AD-26767
2073	GCUUUAUUCUCC	2191	GGAGAAUAAAGC	3586	AD-26768, AD-18928
2074	CUUUAUUCUCCC	2192	GGGAGAAUAAAG	3587	AD-26768, AD-18928, AD-26767
2075	UUUAUUCUCCCA	2193	UGGGAGAAUAAA	3588	AD-26769, AD-18928, AD-26767
2076	UUAUUCUCCCAU	2194	AUGGGAGAAUAA	3589	AD-26769, AD-26768, AD-18928, AD-26767
2077	UAUUCUCCCAUU	2195	AAUGGGAGAAUA	3590	AD-26769, AD-26768, AD-18928
2078	AUUCUCCCAUUG	2196	CAAUGGGAGAAU	3591	AD-26770, AD-18928
2079	UUCUCCCAUUGA	2197	UCAAUGGGAGAA	3592	AD-26769, AD-26770
2080	UCUCCCAUUGAA	2198	UUCAAUGGGAGA	3593	AD-26769, AD-26770
2081	CUCCCAUUGAAA	2199	UUUCAAUGGGAG	3594	AD-26769, AD-26770
2082	UCCCAUUGAAAA	2200	UUUUCAAUGGGA	3595	AD-26771, AD-26769, AD-26770
2083	CCCAUUGAAAAC	2201	GUUUUCAAUGGG	3596	AD-26771, AD-26770
2084	CCAUUGAAAACA	2202	UGUUUUCAAUGG	3597	AD-26771, AD-26770
2085	CAUUGAAAACAU	2203	AUGUUUUCAAUG	3598	AD-26771, AD-26770
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2101	AGAGUAGCUGCA	2205	UGCAGCUACUCU	3600	AD-18962, AD-18895
2102	GAGUAGCUGCAG	2206	CUGCAGCUACUC	3601	AD-18962, AD-18895
2104	GUAGCUGCAGGG	2207	CCCUGCAGCUAC	3602	AD-18962, AD-18976
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2106	AGCUGCAGGGGU	2209	ACCCCUGCAGCU	3604	AD-19003, AD-18962, AD-18976
2107	GCUGCAGGGGUC	2210	GACCCCUGCAGC	3605	AD-18962, AD-18976
2108	CUGCAGGGGUCC	2211	GGACCCCUGCAG	3606	AD-19003, AD-18976
2109	UGCAGGGGUCCU	2212	AGGACCCCUGCA	3607	AD-19003, AD-26772, AD-18976
2110	GCAGGGGUCCUC	2213	GAGGACCCCUGC	3608	AD-19003, AD-26772, AD-18976
2111	CAGGGGUCCUCU	2214	AGAGGACCCCUG	3609	AD-18923, AD-19003, AD-26772, AD-18976
2112	AGGGGUCCUCUG	2215	CAGAGGACCCCU	3610	AD-18923, AD-19003, AD-18955, AD-26772
2113	GGGGUCCUCUGU	2216	ACAGAGGACCCC	3611	AD-18923, AD-18955, AD-26772
2114	GGGUCCUCUGUG	2217	CACAGAGGACCC	3612	AD-18923, AD-18934, AD-18955, AD-26772

2115	GGUCCUCUGUGA	2218	UCACAGAGGACC	3613	AD-18923, AD-18934, AD-19052, AD-18912, AD-18955
2116	GUCCUCUGUGAA	2219	UUCACAGAGGAC	3614	AD-18923, AD-19052, AD-18912, AD-18955, AD-26772
2117	UCCUCUGUGAAC	2220	GUUCACAGAGGA	3615	AD-18923, AD-18934, AD-19052, AD-18912, AD-18955
2118	CCUCUGUGAACU	2221	AGUUCACAGAGG	3616	AD-18923, AD-18934, AD-18973, AD-19052, AD-18912, AD-18955
2119	CUCUGUGAACUU	2222	AAGUUCACAGAG	3617	AD-18934, AD-18973, AD-19052, AD-18912, AD-18955
2120	UCUGUGAACUUG	2223	CAAGUUCACAGA	3618	AD-18934, AD-18973, AD-19052, AD-18912
2121	CUGUGAACUUGC	2224	GCAAGUUCACAG	3619	AD-18973, AD-19052, AD-18912
2122	UGUGAACUUGCU	2225	AGCAAGUUCACA	3620	AD-18973, AD-19047
2123	GUGAACUUGCUC	2226	GAGCAAGUUCAC	3621	AD-18973, AD-19047, AD-18971
2124	UGAACUUGCUCA	2227	UGAGCAAGUUCA	3622	AD-18973, AD-19047, AD-18971, AD-18961
2125	GAACUUGCUCAG	2228	CUGAGCAAGUUC	3623	AD-18973, AD-19047, AD-18971, AD-18961
2126	AACUUGCUCAGG	2229	CCUGAGCAAGUU	3624	AD-19047, AD-18984, AD-18971, AD-18961
2127	ACUUGCUCAGGA	2230	UCCUGAGCAAGU	3625	AD-19047, AD-18984, AD-26773, AD-18971, AD-18961
2128	CUUGCUCAGGAC	2231	GUCCUGAGCAAG	3626	AD-19047, AD-18984, AD-26773, AD-18971
2129	UUGCUCAGGACA	2232	UGUCCUGAGCAA	3627	AD-19047, AD-18984, AD-26773, AD-18971, AD-18961
2130	UGCUCAGGACAA	2233	UUGUCCUGAGCA	3628	AD-18984, AD-26773, AD-18971, AD-18961
2131	GCUCAGGACAAG	2234	CUUGUCCUGAGC	3629	AD-18984, AD-26773, AD-18961
2132	CUCAGGACAAGG	2235	CCUUGUCCUGAG	3630	AD-18984, AD-26773
2133	UCAGGACAAGGA	2236	UCCUUGUCCUGA	3631	AD-18984, AD-26773
2178	AGCUCCUCUGAC	2237	GUCAGAGGAGCU	3632	AD-26775, AD-26774
2179	GCUCCUCUGACA	2238	UGUCAGAGGAGC	3633	AD-26775, AD-26774
2180	CUCCUCUGACAG	2239	CUGUCAGAGGAG	3634	AD-26775, AD-26774
2181	UCCUCUGACAGA	2240	UCUGUCAGAGGA	3635	AD-26775, AD-26774
2182	CCUCUGACAGAG	2241	CUCUGUCAGAGG	3636	AD-26775, AD-26776
2183	CUCUGACAGAGU	2242	ACUCUGUCAGAG	3637	AD-26776, AD-26774
2184	UCUGACAGAGUU	2243	AACUCUGUCAGA	3638	AD-26775, AD-26776, AD-26774
2185	CUGACAGAGUUA	2244	UAACUCUGUCAG	3639	AD-26775, AD-26776
2188	ACAGAGUUACUU	2245	AAGUAACUCUGU	3640	AD-26777, AD-26776

2191	GAGUUACUUCAC	2246	GUGAAGUAACUC	3641	AD-26777, AD-19755
2192	AGUUACUUCACU	2247	AGUGAAGUAACU	3642	AD-26777, AD-26778, AD-19755
2193	GUUACUUCACUC	2248	GAGUGAAGUAAC	3643	AD-26777, AD-26779, AD-26778, AD-19755
2194	UUACUUCACUCU	2249	AGAGUGAAGUAA	3644	AD-26777, AD-26779, AD-19755
2195	UACUUCACUCUA	2250	UAGAGUGAAGUA	3645	AD-26777, AD-26778, AD-19755
2196	ACUUCACUCUAG	2251	CUAGAGUGAAGU	3646	AD-26780, AD-26778, AD-19755
2197	CUUCACUCUAGG	2252	CCUAGAGUGAAG	3647	AD-26779, AD-26780, AD-26778, AD-19755
2198	UUCACUCUAGGA	2253	UCCUAGAGUGAA	3648	AD-26779, AD-26780, AD-26778, AD-19755
2199	UCACUCUAGGAA	2254	UUCCUAGAGUGA	3649	AD-26779, AD-26780, AD-26778
2200	CACUCUAGGAAU	2255	AUUCCUAGAGUG	3650	AD-26779, AD-26780
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2235	UGCUGUUUUGUU	2257	AACAAAACAGCA	3652	AD-26782, AD-26781
2236	GCUGUUUUGUUC	2258	GAACAAAACAGC	3653	AD-26782, AD-26781
2237	CUGUUUUGUUCC	2259	GGAACAAAACAG	3654	AD-26782, AD-26781
2238	UGUUUUGUUCCG	2260	CGGAACAAAACA	3655	AD-26782, AD-26781
2239	GUUUUGUUCCGA	2261	UCGGAACAAAAC	3656	AD-26782, AD-26781
2240	UUUUGUUCCGAA	2262	UUCGGAACAAAA	3657	AD-26782, AD-26781
2256	UGAGGACAAGCC	2263	GGCUUGUCCUCA	3658	AD-26783, AD-26784
2257	GAGGACAAGCCA	2264	UGGCUUGUCCUC	3659	AD-26783, AD-26784
2258	AGGACAAGCCAC	2265	GUGGCUUGUCCU	3660	AD-26783, AD-26784
2259	GGACAAGCCACA	2266	UGUGGCUUGUCC	3661	AD-26783, AD-26784
2260	GACAAGCCACAA	2267	UUGUGGCUUGUC	3662	AD-26783, AD-26784
2261	ACAAGCCACAAG	2268	CUUGUGGCUUGU	3663	AD-26784, AD-26785
2262	CAAGCCACAAGA	2269	UCUUGUGGCUUG	3664	AD-26784, AD-26785
2263	AAGCCACAAGAU	2270	AUCUUGUGGCUU	3665	AD-26784, AD-26785
2264	AGCCACAAGAUU	2271	AAUCUUGUGGCU	3666	AD-26786, AD-26785
2265	GCCACAAGAUUA	2272	UAAUCUUGUGGC	3667	AD-26786, AD-26785
2266	CCACAAGAUUAC	2273	GUAAUCUUGUGG	3668	AD-26786, AD-26785
2267	CACAAGAUUACA	2274	UGUAAUCUUGUG	3669	AD-26786, AD-26785
2268	ACAAGAUUACAA	2275	UUGUAAUCUUGU	3670	AD-26786, AD-26785
2271	AGAUUACAAGAA	2276	UUCUUGUAAUCU	3671	AD-26786, AD-26787
2277	CAAGAAACGGCU	2277	AGCCGUUUCUUG	3672	AD-26788, AD-26787
2278	AAGAAACGGCUU	2278	AAGCCGUUUCUU	3673	AD-26788, AD-26787
2302	ACCAGCUCUCUC	2279	GAGAGAGCUGGU	3674	AD-26790, AD-26789
2303	CCAGCUCUCUCU	2280	AGAGAGAGCUGG	3675	AD-26790, AD-26789
2304	CAGCUCUCUCUU	2281	AAGAGAGAGCUG	3676	AD-26790, AD-26789
2325	GCCAAUGGCUUG	2282	CAAGCCAUUGGC	3677	AD-18909, AD-18910
2326	CCAAUGGCUUGG	2283	CCAAGCCAUUGG	3678	AD-18909, AD-18910, AD-19080
2327	CAAUGGCUUGGA	2284	UCCAAGCCAUUG	3679	AD-18909, AD-18947, AD-18910, AD-19080
2328	AAUGGCUUGGAA	2285	UUCCAAGCCAUU	3680	AD-18909, AD-19051, AD-18947, AD-18910, AD-19080

2329	AUGGCUUGGAAU	2286	AUUCCAAGCCAU	3681	AD-18909, AD-19051, AD-18947, AD-18978, AD-18910
2330	UGGCUUGGAAUG	2287	CAUUCCAAGCCA	3682	AD-18909, AD-19051, AD-18947, AD-18978, AD-19080
2331	GGCUUGGAAUGA	2288	UCAUUCCAAGCC	3683	AD-18909, AD-19051, AD-18947, AD-18978, AD-18910, AD-19080
2332	GCUUGGAAUGAG	2289	CUCAUUCCAAGC	3684	AD-19051, AD-18947, AD-18978, AD-18910, AD-19080
2333	CUUGGAAUGAGA	2290	UCUCAUUCCAAG	3685	AD-19051, AD-18947, AD-18978, AD-19080
2334	UUGGAAUGAGAC	2291	GUCUCAUUCCAA	3686	AD-19051, AD-18947, AD-18978
2335	UGGAAUGAGACU	2292	AGUCUCAUUCCA	3687	AD-19051, AD-18978
2370	UGCCCAGGGAGA	2293	UCUCCCUGGGCA	3688	AD-26677, AD-26791
2371	GCCCAGGGAGAA	2294	UUCUCCCUGGGC	3689	AD-26677, AD-26791
2374	CAGGGAGAACCC	2295	GGGUUCUCCCUG	3690	AD-26792, AD-26677
2375	AGGGAGAACCCC	2296	GGGGUUCUCCCU	3691	AD-26793, AD-26677
2376	GGGAGAACCCCU	2297	AGGGGUUCUCCC	3692	AD-26793, AD-26792
2377	GGAGAACCCCUU	2298	AAGGGGUUCUCC	3693	AD-26793, AD-26792, AD-26677
2378	GAGAACCCCUUG	2299	CAAGGGGUUCUC	3694	AD-26793, AD-26792
2379	AGAACCCCUUGG	2300	CCAAGGGGUUCU	3695	AD-26793, AD-26792
2380	GAACCCCUUGGA	2301	UCCAAGGGGUUC	3696	AD-26793, AD-26792
2381	AACCCCUUGGAU	2302	AUCCAAGGGGUU	3697	AD-26793, AD-26792
2385	CCUUGGAUAUCG	2303	CGAUAUCCAAGG	3698	AD-26794, AD-19063
2386	CUUGGAUAUCGC	2304	GCGAUAUCCAAG	3699	AD-26794, AD-19063
2387	UUGGAUAUCGCC	2305	GGCGAUAUCCAA	3700	AD-18979, AD-26794, AD-19063
2388	UGGAUAUCGCCA	2306	UGGCGAUAUCCA	3701	AD-18979, AD-19001, AD-26794, AD-19063
2389	GGAUAUCGCCAG	2307	CUGGCGAUAUCC	3702	AD-18979, AD-18941, AD-19001, AD-26794, AD-19063
2390	GAUAUCGCCAGG	2308	CCUGGCGAUAUC	3703	AD-18979, AD-18941, AD-19001, AD-18900, AD-26794, AD-19063
2391	AUAUCGCCAGGA	2309	UCCUGGCGAUAU	3704	AD-18979, AD-18941, AD-19001, AD-18900, AD-26794
2392	UAUCGCCAGGAU	2310	AUCCUGGCGAUA	3705	AD-18979, AD-18941, AD-19001, AD-18900, AD-26794, AD-26795
2393	AUCGCCAGGAUG	2311	CAUCCUGGCGAU	3706	AD-18979, AD-18941, AD-19001, AD-26795
2394	UCGCCAGGAUGA	2312	UCAUCCUGGCGA	3707	AD-18979, AD-18941, AD-19001, AD-18900, AD-26795
2395	CGCCAGGAUGAU	2313	AUCAUCCUGGCG	3708	AD-18941, AD-19001,

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2396	GCCAGGAUGAUC	2314	GAUCAUCCUGGC	3709	AD-18941, AD-26796, AD-26795
2397	CCAGGAUGAUCC	2315	GGAUCAUCCUGG	3710	AD-26796, AD-18900, AD-26795, AD-26797
2398	CAGGAUGAUCCU	2316	AGGAUCAUCCUG	3711	AD-26796, AD-26795, AD-26797
2399	AGGAUGAUCCUA	2317	UAGGAUCAUCCU	3712	AD-26796, AD-26795
2400	GGAUGAUCCUAG	2318	CUAGGAUCAUCC	3713	AD-26796, AD-26797
2401	GAUGAUCCUAGC	2319	GCUAGGAUCAUC	3714	AD-26796, AD-26798, AD-26797
2402	AUGAUCCUAGCU	2320	AGCUAGGAUCAU	3715	AD-26796, AD-26797
2403	UGAUCCUAGCUA	2321	UAGCUAGGAUCA	3716	AD-26796, AD-26798, AD-26797
2404	GAUCCUAGCUAU	2322	AUAGCUAGGAUC	3717	AD-26798, AD-26797
2405	AUCCUAGCUAUC	2323	GAUAGCUAGGAU	3718	AD-26799, AD-26798
2406	UCCUAGCUAUCG	2324	CGAUAGCUAGGA	3719	AD-26799, AD-26800
2407	CCUAGCUAUCGU	2325	ACGAUAGCUAGG	3720	AD-26799, AD-26798
2408	CUAGCUAUCGUU	2326	AACGAUAGCUAG	3721	AD-26799, AD-26798, AD-26800
2409	UAGCUAUCGUUC	2327	GAACGAUAGCUA	3722	AD-26799, AD-26800
2410	AGCUAUCGUUCU	2328	AGAACGAUAGCU	3723	AD-26799, AD-26800
2411	GCUAUCGUUCUU	2329	AAGAACGAUAGC	3724	AD-26799, AD-26800
2412	CUAUCGUUCUUU	2330	AAAGAACGAUAG	3725	AD-26799, AD-26800
2419	UCUUUUCACUCU	2331	AGAGUGAAAAGA	3726	AD-18951, AD-26801
2420	CUUUUCACUCUG	2332	CAGAGUGAAAAG	3727	AD-18951, AD-26802, AD-26801
2421	UUUUCACUCUGG	2333	CCAGAGUGAAAA	3728	AD-18951, AD-26803, AD-26802, AD-26801
2422	UUUCACUCUGGU	2334	ACCAGAGUGAAA	3729	AD-18951, AD-26802, AD-26801
2423	UUCACUCUGGUG	2335	CACCAGAGUGAA	3730	AD-18951, AD-26803, AD-26801
2424	UCACUCUGGUGG	2336	CCACCAGAGUGA	3731	AD-26803, AD-26802
2425	CACUCUGGUGGA	2337	UCCACCAGAGUG	3732	AD-26803, AD-26801
2426	ACUCUGGUGGAU	2338	AUCCACCAGAGU	3733	AD-26803, AD-26802, AD-26801
2427	CUCUGGUGGAUA	2339	UAUCCACCAGAG	3734	AD-26803, AD-26802
2435	GAUAUGGCCAGG	2340	CCUGGCCAUAUC	3735	AD-26805, AD-26804
2436	AUAUGGCCAGGA	2341	UCCUGGCCAUAU	3736	AD-26805, AD-26804
2437	UAUGGCCAGGAU	2342	AUCCUGGCCAUA	3737	AD-26805, AD-26804
2440	GGCCAGGAUGCC	2343	GGCAUCCUGGCC	3738	AD-26693, AD-26805
2441	GCCAGGAUGCCU	2344	AGGCAUCCUGGC	3739	AD-26693, AD-26805
2442	CCAGGAUGCCUU	2345	AAGGCAUCCUGG	3740	AD-26693, AD-26805
2453	UGGGUAUGGACC	2346	GGUCCAUACCCA	3741	AD-26806, AD-26807
2454	GGGUAUGGACCC	2347	GGGUCCAUACCC	3742	AD-26806, AD-26807
2455	GGUAUGGACCCC	2348	GGGGUCCAUACC	3743	AD-26806, AD-26807
2456	GUAUGGACCCCA	2349	UGGGGUCCAUAC	3744	AD-26806, AD-26807
2457	UAUGGACCCCAU	2350	AUGGGGUCCAUA	3745	AD-26806, AD-26811, AD-26807
2458	AUGGACCCCAUG	2351	CAUGGGGUCCAU	3746	AD-26811, AD-26807
2459	UGGACCCCAUGA	2352	UCAUGGGGUCCA	3747	AD-26811, AD-26807

2460	GGACCCCAUGAU	2353	AUCAUGGGGUCC	3748	AD-26811, AD-26807, AD-26812
2461	GACCCCAUGAUG	2354	CAUCAUGGGGUC	3749	AD-26811, AD-26812
2462	ACCCCAUGAUGG	2355	CCAUCAUGGGGU	3750	AD-26811, AD-26812
2463	CCCCAUGAUGGA	2356	UCCAUCAUGGGG	3751	AD-26811, AD-26812
2464	CCCAUGAUGGAA	2357	UUCCAUCAUGGG	3752	AD-26811, AD-26812
2465	CCAUGAUGGAAC	2358	GUUCCAUCAUGG	3753	AD-26813, AD-26812
2466	CAUGAUGGAACA	2359	UGUUCCAUCAUG	3754	AD-26813, AD-26812
2467	AUGAUGGAACAU	2360	AUGUUCCAUCAU	3755	AD-26813, AD-26812
2493	CCACCCUGGUGC	2361	GCACCAGGGUGG	3756	AD-26814, AD-26815
2494	CACCCUGGUGCU	2362	AGCACCAGGGUG	3757	AD-26814, AD-26815
2495	ACCCUGGUGCUG	2363	CAGCACCAGGGU	3758	AD-26814, AD-26815
2496	CCCUGGUGCUGA	2364	UCAGCACCAGGG	3759	AD-26814, AD-26815, AD-19057
2497	CCUGGUGCUGAC	2365	GUCAGCACCAGG	3760	AD-19071, AD-26814, AD-26815, AD-19057
2498	CUGGUGCUGACU	2366	AGUCAGCACCAG	3761	AD-19071, AD-26814, AD-26815, AD-18970, AD-19057
2499	UGGUGCUGACUA	2367	UAGUCAGCACCA	3762	AD-19071, AD-26814, AD-26815, AD-18970, AD-19057, AD-18892
2500	GGUGCUGACUAU	2368	AUAGUCAGCACC	3763	AD-19071, AD-26815, AD-18970, AD-19057, AD-18892
2501	GUGCUGACUAUC	2369	GAUAGUCAGCAC	3764	AD-19071, AD-18970, AD-19057, AD-18892
2502	UGCUGACUAUCC	2370	GGAUAGUCAGCA	3765	AD-19071, AD-26816, AD-18970, AD-19057, AD-18892
2503	GCUGACUAUCCA	2371	UGGAUAGUCAGC	3766	AD-19071, AD-19042, AD-26816, AD-18970, AD-19057
2504	CUGACUAUCCAG	2372	CUGGAUAGUCAG	3767	AD-19071, AD-19042, AD-26816, AD-18970, AD-18919, AD-18892
2505	UGACUAUCCAGU	2373	ACUGGAUAGUCA	3768	AD-19042, AD-18944, AD-18970, AD-18919, AD-18892
2506	GACUAUCCAGUU	2374	AACUGGAUAGUC	3769	AD-19042, AD-26816, AD-18944, AD-18908, AD-18919, AD-18892
2507	ACUAUCCAGUUG	2375	CAACUGGAUAGU	3770	AD-19042, AD-26816, AD-18967, AD-18944, AD-18908, AD-18919
2508	CUAUCCAGUUGA	2376	UCAACUGGAUAG	3771	AD-19042, AD-26816, AD-18967, AD-18944, AD-18908, AD-19077, AD-18919
2509	UAUCCAGUUGAU	2377	AUCAACUGGAUA	3772	AD-19042, AD-26816, AD-18967, AD-18944, AD-18908, AD-19077,

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2510	AUCCAGUUGAUG	2378	CAUCAACUGGAU	3773	AD-19042, AD-18967, AD-18944, AD-18908, AD-19077, AD-18919
2511	UCCAGUUGAUGG	2379	CCAUCAACUGGA	3774	AD-18967, AD-18944, AD-18908, AD-19077, AD-18919
2512	CCAGUUGAUGGG	2380	CCCAUCAACUGG	3775	AD-18967, AD-18944, AD-18908, AD-19077
2513	CAGUUGAUGGGC	2381	GCCCAUCAACUG	3776	AD-18967, AD-18908, AD-19077
2514	AGUUGAUGGGCU	2382	AGCCCAUCAACU	3777	AD-26817, AD-18967, AD-19077
2515	GUUGAUGGGCUG	2383	CAGCCCAUCAAC	3778	AD-26817, AD-19077
2544	CCAGGACCUCAU	2384	AUGAGGUCCUGG	3779	AD-19073, AD-26818
2545	CAGGACCUCAUG	2385	CAUGAGGUCCUG	3780	AD-19073, AD-26818
2546	AGGACCUCAUGG	2386	CCAUGAGGUCCU	3781	AD-19073, AD-26818
2547	GGACCUCAUGGA	2387	UCCAUGAGGUCC	3782	AD-19073, AD-26818
2548	GACCUCAUGGAU	2388	AUCCAUGAGGUC	3783	AD-19073, AD-26818
2580	CAAUCAGCUGGC	2389	GCCAGCUGAUUG	3784	AD-26819, AD-26820
2581	AAUCAGCUGGCC	2390	GGCCAGCUGAUU	3785	AD-26819, AD-26820
2582	AUCAGCUGGCCU	2391	AGGCCAGCUGAU	3786	AD-26819, AD-18989, AD-26820
2583	UCAGCUGGCCUG	2392	CAGGCCAGCUGA	3787	AD-18975, AD-26819, AD-18989, AD-26820
2584	CAGCUGGCCUGG	2393	CCAGGCCAGCUG	3788	AD-18975, AD-26819, AD-18989, AD-26820
2585	AGCUGGCCUGGU	2394	ACCAGGCCAGCU	3789	AD-18975, AD-19060, AD-26819, AD-18989, AD-26820
2586	GCUGGCCUGGUU	2395	AACCAGGCCAGC	3790	AD-18975, AD-18898, AD-26819, AD-18989, AD-26820
2587	CUGGCCUGGUUU	2396	AAACCAGGCCAG	3791	AD-18975, AD-19060, AD-18898, AD-18989, AD-26820
2588	UGGCCUGGUUUG	2397	CAAACCAGGCCA	3792	AD-18975, AD-19059, AD-19060, AD-18964, AD-18898, AD-18989
2589	GGCCUGGUUUGA	2398	UCAAACCAGGCC	3793	AD-18920, AD-19059, AD-19060, AD-18964, AD-18898, AD-18989
2590	GCCUGGUUUGAU	2399	AUCAAACCAGGC	3794	AD-18975, AD-18920, AD-19059, AD-19060, AD-18964, AD-18898
2591	CCUGGUUUGAUA	2400	UAUCAAACCAGG	3795	AD-18922, AD-19059, AD-19060, AD-18907, AD-18964, AD-18898
2592	CUGGUUUGAUAC	2401	GUAUCAAACCAG	3796	AD-18922, AD-18920, AD-19060, AD-18907, AD-18964, AD-18898
2593	UGGUUUGAUACU	2402	AGUAUCAAACCA	3797	AD-18905, AD-18922,

					AD-18920, AD-18907, AD-18964
2594	GGUUUGAUACUG	2403	CAGUAUCAAACC	3798	AD-18905, AD-18920, AD-26821, AD-18907, AD-18964
2595	GUUUGAUACUGA	2404	UCAGUAUCAAAC	3799	AD-18922, AD-18920, AD-19059, AD-26821, AD-18986
2596	UUUGAUACUGAC	2405	GUCAGUAUCAAA	3800	AD-18905, AD-18922, AD-18920, AD-26821, AD-18907, AD-19066, AD-18986
2597	UUGAUACUGACC	2406	GGUCAGUAUCAA	3801	AD-18905, AD-26821, AD-18907, AD-18986
2598	UGAUACUGACCU	2407	AGGUCAGUAUCA	3802	AD-18905, AD-18999, AD-18907, AD-18965, AD-19066
2599	GAUACUGACCUG	2408	CAGGUCAGUAUC	3803	AD-18905, AD-26821, AD-18999, AD-18965, AD-19066, AD-18986
2600	AUACUGACCUGU	2409	ACAGGUCAGUAU	3804	AD-26822, AD-18905, AD-18965, AD-19066, AD-18986
2601	UACUGACCUGUA	2410	UACAGGUCAGUA	3805	AD-26822, AD-26821, AD-18999, AD-18965, AD-19066, AD-18986
2602	ACUGACCUGUAA	2411	UUACAGGUCAGU	3806	AD-26822, AD-18999, AD-18965, AD-19066, AD-18986
2603	CUGACCUGUAAA	2412	UUUACAGGUCAG	3807	AD-26822, AD-18999, AD-18965, AD-19066
2604	UGACCUGUAAAU	2413	AUUUACAGGUCA	3808	AD-26822, AD-18999, AD-18965, AD-26823
2605	GACCUGUAAAUC	2414	GAUUUACAGGUC	3809	AD-26822, AD-26824, AD-18999, AD-26823
2606	ACCUGUAAAUCA	2415	UGAUUUACAGGU	3810	AD-26822, AD-26824, AD-26825, AD-26823
2607	CCUGUAAAUCAU	2416	AUGAUUUACAGG	3811	AD-26822, AD-26824, AD-26825, AD-26823
2608	CUGUAAAUCAUC	2417	GAUGAUUUACAG	3812	AD-26824, AD-26825, AD-26823
2609	UGUAAAUCAUCC	2418	GGAUGAUUUACA	3813	AD-26824, AD-26823
2610	GUAAAUCAUCCU	2419	AGGAUGAUUUAC	3814	AD-26825, AD-26823
2611	UAAAUCAUCCUU	2420	AAGGAUGAUUUA	3815	AD-26824, AD-26825, AD-26823
2612	AAAUCAUCCUUU	2421	AAAGGAUGAUUU	3816	AD-26824, AD-26825
2628	GUAACAAUACAA	2422	UUGUAUUGUUAC	3817	AD-18933, AD-19053
2629	UAACAAUACAAA	2423	UUUGUAUUGUUA	3818	AD-18933, AD-19053
2630	AACAAUACAAAU	2424	AUUUGUAUUGUU	3819	AD-18933, AD-19053
2631	ACAAUACAAAUG	2425	CAUUUGUAUUGU	3820	AD-18933, AD-19053
2632	CAAUACAAAUGG	2426	CCAUUUGUAUUG	3821	AD-18933, AD-19053, AD-25889

2633	AAUACAAAUGGA	2427	UCCAUUUGUAUU	3822	AD-18933, AD-25889
2634	AUACAAAUGGAU	2428	AUCCAUUUGUAU	3823	AD-18933, AD-25889
2635	UACAAAUGGAUU	2429	AAUCCAUUUGUA	3824	AD-18933, AD-25889
2636	ACAAAUGGAUUU	2430	AAAUCCAUUUGU	3825	AD-25890, AD-25889
2637	CAAAUGGAUUUU	2431	AAAAUCCAUUUG	3826	AD-25890, AD-25889
2638	AAAUGGAUUUUG	2432	CAAAAUCCAUUU	3827	AD-25890, AD-25889
2648	UGGGAGUGACUC	2433	GAGUCACUCCCA	3828	AD-25892, AD-25891
2649	GGGAGUGACUCA	2434	UGAGUCACUCCC	3829	AD-25892, AD-25891
2650	GGAGUGACUCAA	2435	UUGAGUCACUCC	3830	AD-25892, AD-25891
2651	GAGUGACUCAAG	2436	CUUGAGUCACUC	3831	AD-25892, AD-25891
2652	AGUGACUCAAGA	2437	UCUUGAGUCACU	3832	AD-25892, AD-25891
2653	GUGACUCAAGAA	2438	UUCUUGAGUCAC	3833	AD-25892, AD-25891
2654	UGACUCAAGAAG	2439	CUUCUUGAGUCA	3834	AD-25892, AD-25891
2663	AAGUGAAGAAUG	2440	CAUUCUUCACUU	3835	AD-25894, AD-25893
2664	AGUGAAGAAUGC	2441	GCAUUCUUCACU	3836	AD-25894, AD-25938
2665	GUGAAGAAUGCA	2442	UGCAUUCUUCAC	3837	AD-25893, AD-25938
2666	UGAAGAAUGCAC	2443	GUGCAUUCUUCA	3838	AD-25894, AD-25893
2667	GAAGAAUGCACA	2444	UGUGCAUUCUUC	3839	AD-25894, AD-25893, AD-25938
2668	AAGAAUGCACAA	2445	UUGUGCAUUCUU	3840	AD-25894, AD-25893, AD-25938
2669	AGAAUGCACAAG	2446	CUUGUGCAUUCU	3841	AD-25894, AD-25893, AD-25938
2670	GAAUGCACAAGA	2447	UCUUGUGCAUUC	3842	AD-25894, AD-25938
2682	AUGGAUCACAAG	2448	CUUGUGAUCCAU	3843	AD-25940, AD-25939
2683	UGGAUCACAAGA	2449	UCUUGUGAUCCA	3844	AD-25941, AD-25940, AD-25939
2684	GGAUCACAAGAU	2450	AUCUUGUGAUCC	3845	AD-25941, AD-25940, AD-25942, AD-25939
2685	GAUCACAAGAUG	2451	CAUCUUGUGAUC	3846	AD-25941, AD-25940, AD-25942, AD-25939, AD-25943
2686	AUCACAAGAUGG	2452	CCAUCUUGUGAU	3847	AD-25941, AD-25940, AD-25944, AD-25942, AD-25939, AD-25943
2687	UCACAAGAUGGA	2453	UCCAUCUUGUGA	3848	AD-25941, AD-25940, AD-25944, AD-25942, AD-25943
2688	CACAAGAUGGAA	2454	UUCCAUCUUGUG	3849	AD-25941, AD-25944, AD-25942, AD-25939, AD-25943
2689	ACAAGAUGGAAU	2455	AUUCCAUCUUGU	3850	AD-25941, AD-25940, AD-25944, AD-25942, AD-25943
2690	CAAGAUGGAAUU	2456	AAUUCCAUCUUG	3851	AD-25941, AD-25944, AD-25942, AD-25943
2691	AAGAUGGAAUUU	2457	AAAUUCCAUCUU	3852	AD-25944, AD-25942, AD-25943
2692	AGAUGGAAUUUA	2458	UAAAUUCCAUCU	3853	AD-25944, AD-25943
2693	GAUGGAAUUUAU	2459	AUAAAUUCCAUC	3854	AD-25944, AD-25895
2694	AUGGAAUUUAUC	2460	GAUAAAUUCCAU	3855	AD-25895, AD-25896
2695	UGGAAUUUAUCA	2461	UGAUAAAUUCCA	3856	AD-25895, AD-25896,

					AD-25945
2696	GGAAUUUAUCAA	2462	UUGAUAAAUUCC	3857	AD-25895, AD-25896, AD-25897, AD-25945
2697	GAAUUUAUCAAA	2463	UUUGAUAAAUUC	3858	AD-25895, AD-25896, AD-25898, AD-25897, AD-25945
2698	AAUUUAUCAAAC	2464	GUUUGAUAAAUU	3859	AD-25895, AD-25899, AD-25896, AD-25898, AD-25945
2699	AUUUAUCAAACC	2465	GGUUUGAUAAAU	3860	AD-25895, AD-25896, AD-25898, AD-25897, AD-25945
2700	UUUAUCAAACCC	2466	GGGUUUGAUAAA	3861	AD-25895, AD-25899, AD-25896, AD-25898, AD-25897, AD-25945
2701	UUAUCAAACCCU	2467	AGGGUUUGAUAA	3862	AD-25899, AD-25896, AD-25897, AD-18929, AD-25945
2702	UAUCAAACCCUA	2468	UAGGGUUUGAUA	3863	AD-25899, AD-25898, AD-25897, AD-18929, AD-25945
2703	AUCAAACCCUAG	2469	CUAGGGUUUGAU	3864	AD-18996, AD-25899, AD-18915, AD-25898, AD-25897, AD-18929
2704	UCAAACCCUAGC	2470	GCUAGGGUUUGA	3865	AD-18996, AD-25899, AD-18915, AD-25898, AD-18929
2705	CAAACCCUAGCC	2471	GGCUAGGGUUUG	3866	AD-18935, AD-18996, AD-25899, AD-18915
2706	AAACCCUAGCCU	2472	AGGCUAGGGUUU	3867	AD-18915, AD-18942, AD-18929
2707	AACCCUAGCCUU	2473	AAGGCUAGGGUU	3868	AD-18913, AD-18935, AD-18996, AD-18915
2708	ACCCUAGCCUUG	2474	CAAGGCUAGGGU	3869	AD-18913, AD-18996, AD-18915, AD-18942, AD-18929, AD-25946
2709	CCCUAGCCUUGC	2475	GCAAGGCUAGGG	3870	AD-18913, AD-18935, AD-18996, AD-25947, AD-18915, AD-25946
2710	CCUAGCCUUGCU	2476	AGCAAGGCUAGG	3871	AD-18913, AD-25948, AD-18935, AD-25947, AD-18915, AD-18942, AD-25946
2711	CUAGCCUUGCUU	2477	AAGCAAGGCUAG	3872	AD-18913, AD-25948, AD-18935, AD-25949, AD-25947, AD-18942, AD-25946
2712	UAGCCUUGCUUG	2478	CAAGCAAGGCUA	3873	AD-18913, AD-25948, AD-18935, AD-25950, AD-25947, AD-18942, AD-25946
2713	AGCCUUGCUUGU	2479	ACAAGCAAGGCU	3874	AD-18913, AD-25948, AD-25951, AD-25949,

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2714	GCCUUGCUUGUU	2480	AACAAGCAAGGC	3875	AD-18913, AD-25948, AD-25951, AD-25950, AD-25949, AD-25947, AD-25946
2715	CCUUGCUUGUUA	2481	UAACAAGCAAGG	3876	AD-25948, AD-25951, AD-25950, AD-25949, AD-25947, AD-25946
2716	CUUGCUUGUUAA	2482	UUAACAAGCAAG	3877	AD-25948, AD-25951, AD-25950, AD-25949, AD-25947
2717	UUGCUUGUUAAA	2483	UUUAACAAGCAA	3878	AD-25948, AD-25951, AD-25950, AD-25949
2718	UGCUUGUUAAAU	2484	AUUUAACAAGCA	3879	AD-25951, AD-25950, AD-25949
2719	GCUUGUUAAAUU	2485	AAUUUAACAAGC	3880	AD-25951, AD-25950
2750	GAAUAUCUGUAA	2486	UUACAGAUAUUC	3881	AD-25900, AD-26900
2751	AAUAUCUGUAAU	2487	AUUACAGAUAUU	3882	AD-25900, AD-26900, AD-25901
2752	AUAUCUGUAAUG	2488	CAUUACAGAUAU	3883	AD-25900, AD-25902, AD-25901
2753	UAUCUGUAAUGG	2489	CCAUUACAGAUA	3884	AD-25900, AD-25902, AD-25901
2754	AUCUGUAAUGGU	2490	ACCAUUACAGAU	3885	AD-25900, AD-25901
2755	UCUGUAAUGGUA	2491	UACCAUUACAGA	3886	AD-25902, AD-25901
2756	CUGUAAUGGUAC	2492	GUACCAUUACAG	3887	AD-25900, AD-25902, AD-25901
2757	UGUAAUGGUACU	2493	AGUACCAUUACA	3888	AD-25900, AD-25902
2758	GUAAUGGUACUG	2494	CAGUACCAUUAC	3889	AD-25902, AD-25901
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2833	UUAAGUCUCUCG	2496	CGAGAGACUUAA	3891	AD-25903, AD-25952, AD-25904
2834	UAAGUCUCUCGU	2497	ACGAGAGACUUA	3892	AD-25903, AD-25952, AD-25904, AD-25953
2835	AAGUCUCUCGUA	2498	UACGAGAGACUU	3893	AD-25954, AD-25903, AD-25952, AD-25904, AD-25953
2836	AGUCUCUCGUAG	2499	CUACGAGAGACU	3894	AD-25954, AD-25903, AD-25952, AD-25904, AD-25953, AD-25905
2837	GUCUCUCGUAGU	2500	ACUACGAGAGAC	3895	AD-25954, AD-25903, AD-25952, AD-25904, AD-25953
2838	UCUCUCGUAGUG	2501	CACUACGAGAGA	3896	AD-25954, AD-25952, AD-25904, AD-25953, AD-25905
2839	CUCUCGUAGUGU	2502	ACACUACGAGAG	3897	AD-25954, AD-25952, AD-25904, AD-25953, AD-25905
2840	UCUCGUAGUGUU	2503	AACACUACGAGA	3898	AD-25954, AD-25952, AD-25953, AD-25905

2841	CUCGUAGUGUUA	2504	UAACACUACGAG	3899	AD-25954, AD-25955, AD-25953, AD-25905
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2844	GUAGUGUUAAGU	2507	ACUUAACACUAC	3902	AD-25907, AD-25906, AD-25955
2845	UAGUGUUAAGUU	2508	AACUUAACACUA	3903	AD-25907, AD-25908, AD-25906, AD-25955, AD-25909
2846	AGUGUUAAGUUA	2509	UAACUUAACACU	3904	AD-25907, AD-25908, AD-25956, AD-25906, AD-25955, AD-25909
2847	GUGUUAAGUUAU	2510	AUAACUUAACAC	3905	AD-25907, AD-25908, AD-25956, AD-25957, AD-25906, AD-25955, AD-25909
2848	UGUUAAGUUAUA	2511	UAUAACUUAACA	3906	AD-25907, AD-25908, AD-25956, AD-25957, AD-25906, AD-25909
2849	GUUAAGUUAUAG	2512	CUAUAACUUAAC	3907	AD-25907, AD-25908, AD-25956, AD-25957, AD-25906, AD-25909
2850	UUAAGUUAUAGU	2513	ACUAUAACUUAA	3908	AD-25907, AD-25956, AD-25957, AD-25909
2851	UAAGUUAUAGUG	2514	CACUAUAACUUA	3909	AD-25908, AD-25956, AD-25957, AD-25909
2852	AAGUUAUAGUGA	2515	UCACUAUAACUU	3910	AD-25956, AD-25957, AD-25909
2853	AGUUAUAGUGAA	2516	UUCACUAUAACU	3911	AD-25956, AD-25957
2871	UACAGCAAUUUC	2517	GAAAUUGCUGUA	3912	AD-26901, AD-25958
2872	ACAGCAAUUUCU	2518	AGAAAUUGCUGU	3913	AD-26901, AD-25958
2873	CAGCAAUUUCUA	2519	UAGAAAUUGCUG	3914	AD-26901, AD-25958
2874	AGCAAUUUCUAA	2520	UUAGAAAUUGCU	3915	AD-26901, AD-25958
2875	GCAAUUUCUAAU	2521	AUUAGAAAUUGC	3916	AD-26901, AD-25958
2876	CAAUUUCUAAUU	2522	AAUUAGAAAUUG	3917	AD-26901, AD-25958
2877	AAUUUCUAAUUU	2523	AAAUUAGAAAUU	3918	AD-26901, AD-25958
2901	UAAUGGUGUAGA	2524	UCUACACCAUUA	3919	AD-18936, AD-19054
2902	AAUGGUGUAGAA	2525	UUCUACACCAUU	3920	AD-18936, AD-19054
2903	AUGGUGUAGAAC	2526	GUUCUACACCAU	3921	AD-18936, AD-19010, AD-19054
2904	UGGUGUAGAACA	2527	UGUUCUACACCA	3922	AD-18936, AD-19009, AD-19010, AD-19054
2905	GGUGUAGAACAC	2528	GUGUUCUACACC	3923	AD-18936, AD-19009, AD-18939, AD-19054
2906	GUGUAGAACACU	2529	AGUGUUCUACAC	3924	AD-18966, AD-19009, AD-19010, AD-18939, AD-19054
2907	UGUAGAACACUA	2530	UAGUGUUCUACA	3925	AD-18966, AD-19009, AD-18902, AD-19010, AD-18939, AD-19054

2908	GUAGAACACUAA	2531	UUAGUGUUCUAC	3926	AD-18966, AD-19009, AD-18902, AD-19010, AD-18939, AD-19054, AD-19076
2909	UAGAACACUAAU	2532	AUUAGUGUUCUA	3927	AD-18966, AD-19009, AD-18902, AD-19010, AD-18939, AD-19076
2910	AGAACACUAAUU	2533	AAUUAGUGUUCU	3928	AD-18966, AD-19009, AD-19010, AD-18939, AD-19076
2911	GAACACUAAUUC	2534	GAAUUAGUGUUC	3929	AD-18966, AD-18902, AD-18914, AD-18939, AD-19076
2912	AACACUAAUUCA	2535	UGAAUUAGUGUU	3930	AD-18966, AD-18902, AD-18914, AD-25911, AD-19076
2913	ACACUAAUUCAU	2536	AUGAAUUAGUGU	3931	AD-18966, AD-18902, AD-18914, AD-25912, AD-19076
2914	CACUAAUUCAUA	2537	UAUGAAUUAGUG	3932	AD-18902, AD-18914, AD-25912, AD-25911, AD-26902
2915	ACUAAUUCAUAA	2538	UUAUGAAUUAGU	3933	AD-18914, AD-25912, AD-25911, AD-26903, AD-26902, AD-19076
2916	CUAAUUCAUAAU	2539	AUUAUGAAUUAG	3934	AD-18914, AD-25912, AD-25911, AD-26903, AD-26902
2917	UAAUUCAUAAUC	2540	GAUUAUGAAUUA	3935	AD-26916, AD-25911, AD-26903, AD-26902, AD-26904
2918	AAUUCAUAAUCA	2541	UGAUUAUGAAUU	3936	AD-26905, AD-26916, AD-18914, AD-25912, AD-25911, AD-26903, AD-26902, AD-26904
2919	AUUCAUAAUCAC	2542	GUGAUUAUGAAU	3937	AD-26905, AD-26916, AD-25912, AD-25911, AD-26903, AD-26902, AD-26904
2920	UUCAUAAUCACU	2543	AGUGAUUAUGAA	3938	AD-26905, AD-26916, AD-25912, AD-26903, AD-26902, AD-26904
2921	UCAUAAUCACUC	2544	GAGUGAUUAUGA	3939	AD-26905, AD-26916, AD-26903, AD-26902, AD-26904
2922	CAUAAUCACUCU	2545	AGAGUGAUUAUG	3940	AD-26905, AD-26916, AD-26903, AD-26904
2923	AUAAUCACUCUA	2546	UAGAGUGAUUAU	3941	AD-26905, AD-26916, AD-26904
2924	UAAUCACUCUAA	2547	UUAGAGUGAUUA	3942	AD-26905, AD-26904
2938	AAUUGUAAUCUG	2548	CAGAUUACAAUU	3943	AD-25913, AD-26906
2939	AUUGUAAUCUGA	2549	UCAGAUUACAAU	3944	AD-25913, AD-26906, AD-25914

2940	UUGUAAUCUGAA	2550	UUCAGAUUACAA	3945	AD-25913, AD-26906, AD-25915, AD-25914
2941	UGUAAUCUGAAU	2551	AUUCAGAUUACA	3946	AD-25916, AD-25913, AD-26906, AD-25915, AD-25914
2942	GUAAUCUGAAUA	2552	UAUUCAGAUUAC	3947	AD-25916, AD-25913, AD-26906, AD-25914
2943	UAAUCUGAAUAA	2553	UUAUUCAGAUUA	3948	AD-26906, AD-25915, AD-25914
2944	AAUCUGAAUAAA	2554	UUUAUUCAGAUU	3949	AD-25916, AD-25913, AD-26906, AD-25915, AD-25914
2945	AUCUGAAUAAAG	2555	CUUUAUUCAGAU	3950	AD-25916, AD-26906, AD-25915, AD-25914
2946	UCUGAAUAAAGU	2556	ACUUUAUUCAGA	3951	AD-25916, AD-25915, AD-25914
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2979	UGUAUAAAAUAG	2559	CUAUUUUAUACA	3954	AD-26908, AD-26907, AD-26909
2980	GUAUAAAAUAGA	2560	UCUAUUUUAUAC	3955	AD-26908, AD-26909
2981	UAUAAAAUAGAC	2561	GUCUAUUUUAUA	3956	AD-26908, AD-26910, AD-26907, AD-26909
2982	AUAAAAUAGACA	2562	UGUCUAUUUUAU	3957	AD-26910, AD-26911, AD-26907, AD-26909
2983	UAAAAUAGACAA	2563	UUGUCUAUUUUA	3958	AD-26908, AD-26910, AD-26911, AD-26907, AD-26909
2984	AAAAUAGACAAA	2564	UUUGUCUAUUUU	3959	AD-26908, AD-26910, AD-26912, AD-26911, AD-26907, AD-26909
2985	AAAUAGACAAAU	2565	AUUUGUCUAUUU	3960	AD-26908, AD-26912, AD-26911, AD-26913, AD-26909
2986	AAUAGACAAAUA	2566	UAUUUGUCUAUU	3961	AD-26910, AD-26912, AD-26911, AD-26913, AD-26909
2987	AUAGACAAAUAG	2567	CUAUUUGUCUAU	3962	AD-26910, AD-26912, AD-26911, AD-26913
2988	UAGACAAAUAGA	2568	UCUAUUUGUCUA	3963	AD-26912, AD-26911
2989	AGACAAAUAGAA	2569	UUCUAUUUGUCU	3964	AD-26912, AD-26911, AD-26913
2990	GACAAAUAGAAA	2570	UUUCUAUUUGUC	3965	AD-25917, AD-26913
2991	ACAAAUAGAAAA	2571	UUUUCUAUUUGU	3966	AD-26913, AD-25918
2992	CAAAUAGAAAAU	2572	AUUUUCUAUUUG	3967	AD-25917, AD-25959, AD-25918
2993	AAAUAGAAAAUG	2573	CAUUUUCUAUUU	3968	AD-25917, AD-25959, AD-26917, AD-25918
2994	AAUAGAAAAUGG	2574	CCAUUUUCUAUU	3969	AD-25917, AD-26918, AD-25959, AD-26917
2995	AUAGAAAAUGGU	2575	ACCAUUUUCUAU	3970	AD-25917, AD-26918, AD-25959, AD-26917,

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2996	UAGAAAAUGGUC	2576	GACCAUUUUCUA	3971	AD-25917, AD-26918, AD-25959, AD-26917, AD-25919, AD-25918, AD-25960
2997	AGAAAAUGGUCC	2577	GGACCAUUUUCU	3972	AD-25917, AD-26918, AD-25920, AD-25959, AD-26917, AD-25919, AD-25918, AD-25960
2998	GAAAAUGGUCCA	2578	UGGACCAUUUUC	3973	AD-26918, AD-25920, AD-25959, AD-26917, AD-25919, AD-25918, AD-25960
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3001	AAUGGUCCAAUU	2581	AAUUGGACCAUU	3976	AD-26918, AD-25920, AD-25919, AD-25960
3002	AUGGUCCAAUUA	2582	UAAUUGGACCAU	3977	AD-25920, AD-25919, AD-25960
3003	UGGUCCAAUUAG	2583	CUAAUUGGACCA	3978	AD-25920, AD-25919
3028	AUGCUUAAAAUA	2584	UAUUUUAAGCAU	3979	AD-18985, AD-18992
3029	UGCUUAAAAUAA	2585	UUAUUUUAAGCA	3980	AD-18985, AD-18992
3030	GCUUAAAAUAAG	2586	CUUAUUUUAAGC	3981	AD-18985, AD-18992
3031	CUUAAAAUAAGC	2587	GCUUAUUUUAAG	3982	AD-18985, AD-18992, AD-19081
3032	UUAAAAUAAGCA	2588	UGCUUAUUUUAA	3983	AD-18985, AD-19081
3033	UAAAAUAAGCAG	2589	CUGCUUAUUUUA	3984	AD-18985, AD-18992, AD-19081, AD-19044
3034	AAAAUAAGCAGG	2590	CCUGCUUAUUUU	3985	AD-18985, AD-18992, AD-19081
3035	AAAUAAGCAGGU	2591	ACCUGCUUAUUU	3986	AD-18985, AD-19044
3036	AAUAAGCAGGUG	2592	CACCUGCUUAUU	3987	AD-18993, AD-19081, AD-19044
3037	AUAAGCAGGUGG	2593	CCACCUGCUUAU	3988	AD-18993, AD-18894, AD-19081, AD-19044
3038	UAAGCAGGUGGA	2594	UCCACCUGCUUA	3989	AD-19043, AD-18993, AD-18894, AD-19044
3039	AAGCAGGUGGAU	2595	AUCCACCUGCUU	3990	AD-19043, AD-18956, AD-18993, AD-18894
3040	AGCAGGUGGAUC	2596	GAUCCACCUGCU	3991	AD-19043, AD-18956, AD-18993, AD-18894, AD-19044, AD-18958
3041	GCAGGUGGAUCU	2597	AGAUCCACCUGC	3992	AD-19043, AD-18956, AD-18993, AD-18894, AD-18958
3042	CAGGUGGAUCUA	2598	UAGAUCCACCUG	3993	AD-19043, AD-18956, AD-18894, AD-18969, AD-18958, AD-19058

3043	AGGUGGAUCUAU	2599	AUAGAUCCACCU	3994	AD-19069, AD-19043, AD-18956, AD-18993, AD-18894, AD-18969, AD-18958, AD-19058
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3045	GUGGAUCUAUUU	2601	AAAUAGAUCCAC	3996	AD-19069, AD-19043, AD-18956, AD-18969, AD-18958, AD-19058
3046	UGGAUCUAUUUC	2602	GAAAUAGAUCCA	3997	AD-19069, AD-18956, AD-18969, AD-18958, AD-19058
3047	GGAUCUAUUUCA	2603	UGAAAUAGAUCC	3998	AD-19069, AD-18969, AD-18958, AD-19058
3048	GAUCUAUUUCAU	2604	AUGAAAUAGAUC	3999	AD-19069, AD-18969, AD-19058
3049	AUCUAUUUCAUG	2605	CAUGAAAUAGAU	4000	AD-19069, AD-19058
3077	AUUUGGGAUAUG	2606	CAUAUCCCAAAU	4001	AD-25921, AD-25922
3078	UUUGGGAUAUGU	2607	ACAUAUCCCAAA	4002	AD-25961, AD-25921, AD-25922
3079	UUGGGAUAUGUA	2608	UACAUAUCCCAA	4003	AD-25961, AD-25923, AD-25921, AD-25922
3080	UGGGAUAUGUAU	2609	AUACAUAUCCCA	4004	AD-25961, AD-25923, AD-26914, AD-25921, AD-25922
3081	GGGAUAUGUAUG	2610	CAUACAUAUCCC	4005	AD-25961, AD-25923, AD-26915, AD-26914, AD-25921, AD-25922
3082	GGAUAUGUAUGG	2611	CCAUACAUAUCC	4006	AD-25961, AD-25923, AD-25924, AD-26915, AD-26914, AD-25921, AD-25922
3083	GAUAUGUAUGGG	2612	CCCAUACAUAUC	4007	AD-25961, AD-25923, AD-25924, AD-26915, AD-25962, AD-26914, AD-25921, AD-25922
3084	AUAUGUAUGGGU	2613	ACCCAUACAUAU	4008	AD-25961, AD-25923, AD-25924, AD-26915, AD-25962, AD-26914, AD-25922
3085	UAUGUAUGGGUA	2614	UACCCAUACAUA	4009	AD-25961, AD-25923, AD-25924, AD-26915, AD-25962, AD-26914
3086	AUGUAUGGGUAG	2615	CUACCCAUACAU	4010	AD-25923, AD-25924, AD-26915, AD-25962, AD-26914
3087	UGUAUGGGUAGG	2616	CCUACCCAUACA	4011	AD-25924, AD-26915, AD-25962, AD-26914
3088	GUAUGGGUAGGG	2617	CCCUACCCAUAC	4012	AD-25924, AD-26915, AD-25962
3089	UAUGGGUAGGGU	2618	ACCCUACCCAUA	4013	AD-25924, AD-25962

3093	GGUAGGGUAAAU	2619	AUUUACCCUACC	4014	AD-18998, AD-25963
3094	GUAGGGUAAAUC	2620	GAUUUACCCUAC	4015	AD-18998, AD-25963, AD-18995
3095	UAGGGUAAAUCA	2621	UGAUUUACCCUA	4016	AD-18998, AD-25963, AD-18995
3096	AGGGUAAAUCAG	2622	CUGAUUUACCCU	4017	AD-18998, AD-25963, AD-18995
3097	GGGUAAAUCAGU	2623	ACUGAUUUACCC	4018	AD-18998, AD-25963, AD-18981, AD-18995
3098	GGUAAAUCAGUA	2624	UACUGAUUUACC	4019	AD-18921, AD-18998, AD-25963, AD-18981, AD-18995
3099	GUAAAUCAGUAA	2625	UUACUGAUUUAC	4020	AD-18921, AD-18998, AD-18981, AD-18995
3100	UAAAUCAGUAAG	2626	CUUACUGAUUUA	4021	AD-18921, AD-18998, AD-18981, AD-19050, AD-18995
3101	AAAUCAGUAAGA	2627	UCUUACUGAUUU	4022	AD-18921, AD-18968, AD-18981, AD-19050
3102	AAUCAGUAAGAG	2628	CUCUUACUGAUU	4023	AD-18921, AD-18968, AD-18981, AD-19050, AD-19005
3103	AUCAGUAAGAGG	2629	CCUCUUACUGAU	4024	AD-18921, AD-18968, AD-18981, AD-19050, AD-18903, AD-19005
3104	UCAGUAAGAGGU	2630	ACCUCUUACUGA	4025	AD-18921, AD-18968, AD-18972, AD-18981, AD-19050, AD-18903, AD-19005
3105	CAGUAAGAGGUG	2631	CACCUCUUACUG	4026	AD-18921, AD-18968, AD-18972, AD-19050, AD-18903, AD-19005
3106	AGUAAGAGGUGU	2632	ACACCUCUUACU	4027	AD-18968, AD-19050, AD-18903, AD-19005
3107	GUAAGAGGUGUU	2633	AACACCUCUUAC	4028	AD-18972, AD-19050, AD-18903, AD-19005
3108	UAAGAGGUGUUA	2634	UAACACCUCUUA	4029	AD-18968, AD-18972, AD-18903, AD-25964, AD-19005
3109	AAGAGGUGUUAU	2635	AUAACACCUCUU	4030	AD-18972, AD-18903, AD-25964, AD-19005
3110	AGAGGUGUUAUU	2636	AAUAACACCUCU	4031	AD-18972, AD-18903, AD-25925, AD-25926, AD-25964
3111	GAGGUGUUAUUU	2637	AAAUAACACCUC	4032	AD-25925, AD-25926, AD-25964
3112	AGGUGUUAUUUG	2638	CAAAUAACACCU	4033	AD-25927, AD-25925, AD-25926, AD-25964
3113	GGUGUUAUUUGG	2639	CCAAAUAACACC	4034	AD-25927, AD-25926, AD-25964
3114	GUGUUAUUUGGA	2640	UCCAAAUAACAC	4035	AD-25927, AD-25925, AD-25926, AD-25964

3115	UGUUAUUUGGAA	2641	UUCCAAAUAACA	4036	AD-25925, AD-25926, AD-25964
3116	GUUAUUUGGAAC	2642	GUUCCAAAUAAC	4037	AD-25927, AD-25925, AD-25926
3117	UUAUUUGGAACC	2643	GGUUCCAAAUAA	4038	AD-25927, AD-25926
3123	GGAACCUUGUUU	2644	AAACAAGGUUCC	4039	AD-25929, AD-25928
3124	GAACCUUGUUUU	2645	AAAACAAGGUUC	4040	AD-25930, AD-25928
3125	AACCUUGUUUUG	2646	CAAAACAAGGUU	4041	AD-25930, AD-25929, AD-25928
3126	ACCUUGUUUUGG	2647	CCAAAACAAGGU	4042	AD-25930, AD-25929
3127	CCUUGUUUUGGA	2648	UCCAAAACAAGG	4043	AD-25930, AD-25929, AD-25928
3128	CUUGUUUUGGAC	2649	GUCCAAAACAAG	4044	AD-25930, AD-25929, AD-25928
3129	UUGUUUUGGACA	2650	UGUCCAAAACAA	4045	AD-25929, AD-25928
3130	UGUUUUGGACAG	2651	CUGUCCAAAACA	4046	AD-25930, AD-25929
3131	GUUUUGGACAGU	2652	ACUGUCCAAAAC	4047	AD-25930, AD-25931
3132	UUUUGGACAGUU	2653	AACUGUCCAAAA	4048	AD-25932, AD-25931
3133	UUUGGACAGUUU	2654	AAACUGUCCAAA	4049	AD-25932, AD-26919, AD-25931
3134	UUGGACAGUUUA	2655	UAAACUGUCCAA	4050	AD-25933, AD-26919, AD-25931
3135	UGGACAGUUUAC	2656	GUAAACUGUCCA	4051	AD-25933, AD-25932, AD-26919, AD-25931
3136	GGACAGUUUACC	2657	GGUAAACUGUCC	4052	AD-25933, AD-25932, AD-25931
3137	GACAGUUUACCA	2658	UGGUAAACUGUC	4053	AD-25932, AD-26919, AD-25931
3138	ACAGUUUACCAG	2659	CUGGUAAACUGU	4054	AD-25933, AD-25932, AD-26919, AD-25931
3139	CAGUUUACCAGU	2660	ACUGGUAAACUG	4055	AD-25933, AD-25932, AD-26919
3140	AGUUUACCAGUU	2661	AACUGGUAAACU	4056	AD-25933, AD-26919
3145	ACCAGUUGCCUU	2662	AAGGCAACUGGU	4057	AD-18940, AD-18916
3146	CCAGUUGCCUUU	2663	AAAGGCAACUGG	4058	AD-18940, AD-18906, AD-18916
3147	CAGUUGCCUUUU	2664	AAAAGGCAACUG	4059	AD-18940, AD-18906, AD-18916
3148	AGUUGCCUUUUA	2665	UAAAAGGCAACU	4060	AD-18940, AD-19075, AD-18916
3149	GUUGCCUUUUAU	2666	AUAAAAGGCAAC	4061	AD-19075, AD-18906, AD-18916
3150	UUGCCUUUUAUC	2667	GAUAAAAGGCAA	4062	AD-18940, AD-19075, AD-18906, AD-18916
3151	UGCCUUUUAUCC	2668	GGAUAAAAGGCA	4063	AD-18940, AD-19075, AD-18906, AD-18916
3152	GCCUUUUAUCCC	2669	GGGAUAAAAGGC	4064	AD-18906, AD-18916
3153	CCUUUUAUCCCA	2670	UGGGAUAAAAGG	4065	AD-26017, AD-19075, AD-18906, AD-18997
3154	CUUUUAUCCCAA	2671	UUGGGAUAAAAG	4066	AD-26017, AD-19075, AD-18997
3155	UUUUAUCCCAAA	2672	UUUGGGAUAAAA	4067	AD-26017, AD-18997

3156	UUUAUCCCAAAG	2673	CUUUGGGAUAAA	4068	AD-26017, AD-18997
3157	UUAUCCCAAAGU	2674	ACUUUGGGAUAA	4069	AD-26017, AD-18997
3158	UAUCCCAAAGUU	2675	AACUUUGGGAUA	4070	AD-26017, AD-18997, AD-18988
3159	AUCCCAAAGUUG	2676	CAACUUUGGGAU	4071	AD-18997, AD-18988
3160	UCCCAAAGUUGU	2677	ACAACUUUGGGA	4072	AD-19067, AD-18997, AD-18988
3161	CCCAAAGUUGUU	2678	AACAACUUUGGG	4073	AD-19067, AD-19083
3162	CCAAAGUUGUUG	2679	CAACAACUUUGG	4074	AD-19083, AD-18988
3163	CAAAGUUGUUGU	2680	ACAACAACUUUG	4075	AD-19067, AD-19083, AD-19049, AD-18988
3164	AAAGUUGUUGUA	2681	UACAACAACUUU	4076	AD-19067, AD-19083, AD-18952, AD-19049, AD-18988
3165	AAGUUGUUGUAA	2682	UUACAACAACUU	4077	AD-19067, AD-19083, AD-18957, AD-18952, AD-19049, AD-18988
3166	AGUUGUUGUAAC	2683	GUUACAACAACU	4078	AD-19067, AD-19083, AD-18957, AD-18952, AD-19049
3167	GUUGUUGUAACC	2684	GGUUACAACAAC	4079	AD-19067, AD-19083, AD-18957, AD-25934, AD-18952, AD-19049
3168	UUGUUGUAACCU	2685	AGGUUACAACAA	4080	AD-19083, AD-18957, AD-25934, AD-18952, AD-25935, AD-19049
3169	UGUUGUAACCUG	2686	CAGGUUACAACA	4081	AD-18957, AD-25934, AD-18952, AD-26018, AD-25935, AD-19049
3170	GUUGUAACCUGC	2687	GCAGGUUACAAC	4082	AD-26019, AD-18957, AD-25934, AD-18952, AD-26018, AD-25935, AD-19049
3171	UUGUAACCUGCU	2688	AGCAGGUUACAA	4083	AD-26019, AD-18957, AD-25936, AD-25934, AD-18952, AD-26018, AD-25935
3172	UGUAACCUGCUG	2689	CAGCAGGUUACA	4084	AD-26019, AD-18957, AD-25936, AD-25934, AD-26018, AD-25935
3173	GUAACCUGCUGU	2690	ACAGCAGGUUAC	4085	AD-26019, AD-25936, AD-25934, AD-26018
3174	UAACCUGCUGUG	2691	CACAGCAGGUUA	4086	AD-26019, AD-25936, AD-25934, AD-26018, AD-25935
3175	AACCUGCUGUGA	2692	UCACAGCAGGUU	4087	AD-26019, AD-25936, AD-26018, AD-25935
3176	ACCUGCUGUGAU	2693	AUCACAGCAGGU	4088	AD-26019, AD-25936, AD-26018
3177	CCUGCUGUGAUA	2694	UAUCACAGCAGG	4089	AD-26019, AD-25936
3197	CAAGAGAAAAUG	2695	CAUUUUCUCUUG	4090	AD-26020, AD-25937
3198	AAGAGAAAAUGC	2696	GCAUUUUCUCUU	4091	AD-26020, AD-26021,

					AD-25937
3199	AGAGAAAAUGCG	2697	CGCAUUUUCUCU	4092	AD-26020, AD-26021
3200	GAGAAAAUGCGG	2698	CCGCAUUUUCUC	4093	AD-26020, AD-26021
3201	AGAAAAUGCGGU	2699	ACCGCAUUUUCU	4094	AD-26020, AD-26021
3202	GAAAAUGCGGUU	2700	AACCGCAUUUUC	4095	AD-26020, AD-26021
3203	AAAAUGCGGUUA	2701	UAACCGCAUUUU	4096	AD-26020, AD-26021
3204	AAAUGCGGUUAU	2702	AUAACCGCAUUU	4097	AD-26020, AD-26021
3220	AAUGGUUCAGAA	2703	UUCUGAACCAUU	4098	AD-18960, AD-18987
3221	AUGGUUCAGAAU	2704	AUUCUGAACCAU	4099	AD-18960, AD-18987, AD-19008
3222	UGGUUCAGAAUU	2705	AAUUCUGAACCA	4100	AD-18960, AD-18987, AD-19008
3223	GGUUCAGAAUUA	2706	UAAUUCUGAACC	4101	AD-18980, AD-18987, AD-19008
3224	GUUCAGAAUUAA	2707	UUAAUUCUGAAC	4102	AD-18960, AD-18987, AD-19008
3225	UUCAGAAUUAAA	2708	UUUAAUUCUGAA	4103	AD-18960, AD-18980, AD-19008
3226	UCAGAAUUAAAC	2709	GUUUAAUUCUGA	4104	AD-18960, AD-18980, AD-18987, AD-19008
3227	CAGAAUUAAACU	2710	AGUUUAAUUCUG	4105	AD-18980, AD-18987, AD-19008
3228	AGAAUUAAACUU	2711	AAGUUUAAUUCU	4106	AD-18980, AD-19008
3229	GAAUUAAACUUU	2712	AAAGUUUAAUUC	4107	AD-18980, AD-19007
3230	AAUUAAACUUUU	2713	AAAAGUUUAAUU	4108	AD-18980, AD-19007

[00793] **EXAMPLE 2**

[00794] **Synthesis of Beta-Catenin RNAi Agent Sequences**

[00795] **Beta-Catenin RNAi agent sequence selection**

[00796] 479 sense and 479 anti-sense CTNNB1-derived RNAi agent oligos listed herein are synthesized and formed into duplexes.

[00797] **Synthesis of Beta-Catenin sequences**

[00798] **Synthesis:**

[00799] Beta-Catenin sequences are synthesized on MerMade 192 synthesizer at 1 μmol scale.

[00800] 958 single strand sequences (corresponding to 479 RNAi agent duplexes) are synthesized for the human Beta-Catenin gene. For all the sequences, 'endolight' chemistry is applied as detailed below.

- All pyrimidines (cytosine and uridine) in the sense strand are replaced with corresponding 2'-O-Methyl bases (2' O-Methyl C and 2'-O-Methyl U)
- In the anti-sense strand, pyrimidines (C and U) adjacent to (towards 5' position) ribo A nucleoside are replaced with their corresponding 2-O-Methyl nucleosides
- A two base dTdT extension at 3' end of both sense and anti-sense sequences is

introduced. This two base overhang has a phosphodiester linkage

- The sequence file is converted to a text file to make it compatible for loading in the MerMade 192 synthesis software

[00801] The synthesis of Beta-Catenin sequences uses solid supported oligonucleotide synthesis using phosphoramidite chemistry

[00802] The synthesis of the above sequences is performed at 1 μm scale in 96-well plates and 192 sequences are made per run. The amidite solutions are prepared at 0.1M concentration and ethyl thio tetrazole (0.6M in acetonitrile) is used as activator.

[00803] Cleavage and De-protection:

[00804] The synthesized sequences are cleaved and de-protected in 96-well plates, using methylamine in the first step and triethylamine ^{3}HF in the second step. The crude sequences thus obtained are precipitated using acetone: ethanol mix and the pellet is re-suspended in 0.02M sodium acetate buffer. Samples from each sequence are analyzed by LC-MS and the resulting mass data confirms the identity of the sequences. A selected set of samples are also analyzed by IEX chromatography.

[00805] Purification:

[00806] Next step in the process is purification. All sequences are purified on AKTA explorer purification system using Source 15Q column. Purification is performed using a column and in-line buffer heater set at 60°C. A single peak corresponding to the full length sequence is collected in the eluent and is subsequently analyzed for purity by ion exchange chromatography.

[00807] The purified sequences are desalted on a Sephadex G25 column using AKTA purifier. The desalted Beta-Catenin sequences are analyzed for concentration and purity. The single strands are then annealed to form RNAi agent duplexes. Each duplex is made at a concentration of 10 μM in 1x PBS.

[00808] A detailed list of Beta-Catenin single strands and duplexes are shown herein, in Example 1, above. The duplexes are used in in vitro screening to test their ability to knock down Beta-Catenin gene level, Example 3, below.

[00809] EXAMPLE 3

[00810] In vitro screening of Beta-Catenin RNAi Agents

[00811] In vitro screening:

[00812] RNAi agents listed herein (Example 1) and synthesized as described in Example 2, are tested for activity in vitro.

[00813] Cell culture and transfections:

[00814] HeLa cells (ATCC, Manassas, VA) are grown to near confluence at 37°C in an atmosphere of 5% CO_2 in Eagle's Minimum Essential Medium (EMEM, ATCC) supplemented with 10% FBS, streptomycin, and glutamine (ATCC) before being released from the plate by trypsinization. Reverse transfection is carried out by adding 5 μl of Opti-MEM to 5 μl of RNAi agent duplexes per well into a 96-well plate along with 10 μl of Opti-MEM plus 0.2 μl of Lipofectamine RNAiMax per well (Invitrogen, Carlsbad, CA. cat # 13778-150) and incubated at room temperature for 15 minutes. For assays performed at 24 hours, 80 μl of complete growth media without antibiotic containing ~2 $x10^4$ HeLa cells are then added to the RNAi agent mixture. For assays performed at 120 hours, 80 μl of complete growth media without antibiotic containing ~2 $x10^4$ HeLa cells are then added to the RNAi agent mixture. Cells are incubated for either 24 or 48 hours prior to RNA purification. Single dose experiments are performed at 10nM and in some cases 0.1nM final duplex concentration and dose response experiments are done at 10, 1, 0.5, 0.1, 0.05, 0.01, 0.005, 0.001, 0.0005, 0.0001, 0.00005, 0.00001 nM final duplex concentration.

[00815] Total RNA isolation using MagMAX-96 Total RNA Isolation Kit (Applied Biosystem, Foster City CA, part #: AM1830):

[00816] Cells are harvested and lysed in 140 μl of Lysis/Binding Solution then mixed for 1 minute at 850 rpm using and Eppendorf Thermomixer (the mixing speed is the same throughout the process). Twenty micro liters of magnetic beads and Lysis/Binding Enhancer mixture are added into cell-lysate and mixed for 5 minutes. Magnetic beads are captured using magnetic stand and the supernatant is removed without disturbing the beads. After removing supernatant, magnetic beads are washed with Wash Solution 1 (isopropanol added) and mixed for 1 minute. Beads are captured again and supernatant removed. Beads are then washed with 150 μl Wash Solution 2 (Ethanol added), captured and supernatant is removed. 50 μl of DNase mixture (MagMax turbo DNase Buffer and Turbo DNase) is then added to the beads and they are mixed for 10 to 15 minutes. After mixing, 100 μl of RNA Rebinding Solution is added and mixed for 3 minutes. Supernatant is removed and magnetic beads are washed again with 150 μl Wash Solution 2 and mixed for 1 minute and supernatant is removed completely. The magnetic beads are mixed for 2 minutes to dry before RNA is eluted with 50 μl of water.

[00817] cDNA synthesis using ABI High capacity cDNA reverse transcription kit (Applied Biosystems, Foster City, CA, Cat #4368813):

[00818] A master mix of 2 μl 10X Buffer, 0.8 μl 25X dNTPs, 2 μl Random primers, 1 μl

Reverse Transcriptase, 1 µl RNase inhibitor and 3.2 µl of H_2O per reaction are added into 10 µl total RNA. cDNA is generated using a Bio-Rad C-1000 or S-1000 thermal cycler (Hercules, CA) through the following steps: 25°C 10 min, 37°C 120 min, 85°C 5 sec, 4°C hold.

[00819] Real time PCR:

[00820] 2 µl of cDNA are added to a master mix containing 1 µl 18S TaqMan Probe (Applied Biosystems Cat # 4319413E), 1ul β-catenin TaqMan probe (Applied Biosystems cat # HS00170025_m1) and 10 µl TaqMan Universal PCR Master Mix (Applied Biosystems Cat #4324018) per well in a MicroAmp Optical 96 well plate (Applied Biosystems cat # 4326659). Real time PCR is done in an ABI 7900HT Real Time PCR system (Applied Biosystems) using the ΔΔCt(RQ) assay. Each duplex is tested in two independent transfections and each transfections is assayed in duplicate, unless otherwise noted in the summary tables.

[00821] Real time data are analyzed using the ΔΔCt method and normalized to assays performed with cells transfected with 10 nM AD-1955 (a control RNAi agent that does not bind to Beta-Catenin) to calculate relative fold-change.

[00822] The results are shown below. Table 5 shows the results of experiments performed at 0.1 or 10 nM final duplex concentration for single dose screens with each of the Beta-Catenin duplexes. The "Residual Gene Activity" (Fold-Change) indicates the residual gene level, at 10 nm or 0.1 nM. Thus, for AD-18892, a "Residual Gene Activity" at 10 nM at 24 hr of 0.054 indicates 5.4% remaining gene activity, or 94.6% gene knock-down. The Avg. EC50 (nM) indicates the estimated EC50 (concentration estimated to give 50% gene knock-down in HeLa cells), as calculated from available data collected at 10nM, 1nM, 0.1nM, 0.01nM, and 0.001nM. "NA" indicates data is not available.

TABLE 5. Analysis of RNAi agents to Beta-Catenin

Duplex	Sense SEQ ID NO:	Anti-sense SEQ ID NO:	Residual Gene Activity 10 nM 24hr	Residual Gene Activity 0.1nM 120hr	Avg. EC50 (nM)
AD-18892	1	660	0.054	0.47	NA
AD-18893	2	661	0.026	NA	0.008
AD-18894	3	662	0.068	NA	0.005
AD-18895	4	663	0.466	NA	NA
AD-18896	5	664	0.244	NA	NA
AD-18897	6	665	0.054	NA	0.028
AD-18898	7	666	0.903	NA	NA
AD-18899	8	667	0.301	NA	NA
AD-18900	9	668	1.157	NA	NA

AD-18901	10	669	0.359	NA	NA
AD-18902	11	670	0.058	NA	0.005
AD-18903	12	671	0.052	NA	0.002
AD-18904	13	672	0.690	NA	NA
AD-18905	14	673	0.198	NA	1.260
AD-18906	15	674	0.248	NA	NA
AD-18907	16	675	0.379	NA	NA
AD-18908	17	676	0.157	NA	NA
AD-18909	18	677	0.441	NA	NA
AD-18910	19	678	0.385	NA	NA
AD-18911	20	679	0.186	NA	1.664
AD-18912	21	680	0.221	NA	NA
AD-18913	22	681	0.124	NA	0.018
AD-18914	23	682	0.058	NA	0.002
AD-18915	24	683	0.242	NA	NA
AD-18916	25	684	0.530	NA	NA
AD-18917	26	685	0.527	0.66	NA
AD-18918	27	686	1.161	NA	NA
AD-18919	28	687	0.387	NA	NA
AD-18920	29	688	1.124	NA	NA
AD-18921	30	689	0.752	NA	NA
AD-18922	31	690	0.587	NA	NA
AD-18923	32	691	0.773	NA	NA
AD-18925	33	692	0.738	NA	NA
AD-18926	34	693	0.193	NA	0.033
AD-18927	35	694	0.091	NA	0.764
AD-18928	36	695	0.228	NA	NA
AD-18929	37	696	0.069	NA	NA
AD-18930	38	697	0.428	NA	NA
AD-18931	39	698	1.195	NA	NA
AD-18932	40	699	0.876	NA	NA
AD-18933	41	700	0.047	NA	0.001
AD-18934	42	701	0.651	NA	NA
AD-18935	43	702	0.419	NA	NA
AD-18936	44	703	0.125	NA	0.158
AD-18937	45	704	0.839	NA	NA
AD-18938	46	705	0.436	NA	NA
AD-18939	47	706	0.068	NA	0.011
AD-18940	48	707	0.515	NA	NA
AD-18941	49	708	0.421	NA	NA
AD-18942	50	709	1.397	NA	NA
AD-18943	51	710	0.990	NA	NA
AD-18944	52	711	0.550	NA	NA

AD-18945	53	712	0.193	NA	0.780
AD-18946	54	713	0.086	0.47	NA
AD-18947	55	714	0.397	NA	NA
AD-18948	56	715	0.885	NA	NA
AD-18949	57	716	0.863	NA	NA
AD-18950	58	717	0.103	NA	0.145
AD-18951	59	718	0.184	NA	0.519
AD-18952	60	719	0.382	NA	NA
AD-18953	61	720	1.349	NA	NA
AD-18954	62	721	0.766	NA	NA
AD-18955	63	722	0.649	0.64	NA
AD-18956	64	723	0.240	NA	NA
AD-18957	65	724	1.198	NA	NA
AD-18958	66	725	0.083	NA	0.012
AD-18959	67	726	0.713	NA	NA
AD-18960	68	727	0.188	NA	0.310
AD-18961	69	728	0.105	NA	0.209
AD-18962	70	729	0.942	NA	NA
AD-18963	71	730	0.037	0.37	0.049
AD-18964	72	731	0.907	NA	NA
AD-18965	73	732	0.440	0.48	NA
AD-18966	74	733	0.042	NA	0.000
AD-18967	75	734	0.695	NA	NA
AD-18968	76	735	0.158	NA	0.134
AD-18969	77	736	0.073	NA	0.004
AD-18970	78	737	0.810	NA	NA
AD-18971	79	738	0.336	NA	NA
AD-18972	80	739	0.332	NA	NA
AD-18973	81	740	0.707	NA	NA
AD-18974	82	741	0.038	NA	0.007
AD-18975	83	742	0.184	0.73	NA
AD-18976	84	743	0.094	NA	0.118
AD-18977	85	744	0.965	NA	NA
AD-18978	86	745	0.848	NA	NA
AD-18979	87	746	0.375	NA	NA
AD-18980	88	747	0.052	NA	NA
AD-18981	89	748	0.090	NA	0.004
AD-18982	90	749	0.156	NA	0.156
AD-18983	91	750	0.026	0.23	0.070
AD-18984	92	751	0.913	NA	NA
AD-18985	93	752	0.578	NA	NA
AD-18986	94	753	0.073	NA	0.003
AD-18987	95	754	0.626	NA	NA

AD-18988	96	755	0.379	NA	NA
AD-18989	97	756	0.879	NA	NA
AD-18990	98	757	0.299	NA	NA
AD-18991	99	758	0.112	NA	0.454
AD-18992	100	759	1.171	NA	NA
AD-18993	101	760	0.802	NA	NA
AD-18994	102	761	0.071	NA	0.313
AD-18995	103	762	0.096	NA	0.006
AD-18996	104	763	0.450	NA	NA
AD-18997	105	764	0.226	NA	NA
AD-18998	106	765	0.279	NA	NA
AD-18999	107	766	0.337	NA	NA
AD-19000	108	767	0.134	NA	0.347
AD-19001	109	768	0.470	0.71	NA
AD-19002	110	769	0.619	NA	NA
AD-19003	111	770	0.610	NA	NA
AD-19004	112	771	0.066	NA	0.007
AD-19005	113	772	0.274	NA	NA
AD-19006	114	773	0.139	NA	0.994
AD-19007	115	774	0.655	NA	NA
AD-19008	116	775	0.088	NA	0.001
AD-19009	117	776	0.066	NA	0.000
AD-19010	118	777	0.227	NA	NA
AD-19011	119	778	0.721	NA	NA
AD-19012	120	779	0.175	NA	0.181
AD-19042	121	780	0.283	NA	NA
AD-19043	122	781	0.131	NA	0.006
AD-19044	123	782	0.333	NA	NA
AD-19045	124	783	0.553	NA	NA
AD-19046	125	784	0.947	NA	NA
AD-19047	126	785	0.774	NA	NA
AD-19048	127	786	0.838	NA	NA
AD-19049	128	787	0.938	NA	NA
AD-19050	129	788	0.070	NA	0.001
AD-19051	130	789	0.551	NA	NA
AD-19052	131	790	0.818	NA	NA
AD-19053	132	791	0.364	NA	NA
AD-19054	133	792	0.075	NA	0.002
AD-19055	134	793	0.210	NA	NA
AD-19056	135	794	0.085	NA	0.019
AD-19057	136	795	0.599	NA	NA
AD-19058	137	796	0.577	NA	NA
AD-19059	138	797	0.728	NA	NA

AD-19060	139	798	1.072	NA	NA
AD-19061	140	799	0.885	NA	NA
AD-19062	141	800	0.810	NA	NA
AD-19063	142	801	0.741	NA	NA
AD-19064	143	802	0.591	NA	NA
AD-19065	144	803	0.323	NA	NA
AD-19066	145	804	0.086	0.48	NA
AD-19067	146	805	0.138	NA	NA
AD-19068	147	806	0.321	NA	NA
AD-19069	148	807	0.135	NA	1.403
AD-19070	149	808	0.892	NA	NA
AD-19071	150	809	0.658	NA	NA
AD-19072	151	810	0.704	NA	NA
AD-19073	152	811	0.838	NA	NA
AD-19074	153	812	0.042	NA	0.008
AD-19075	154	813	0.841	NA	NA
AD-19076	155	814	0.037	NA	0.002
AD-19077	156	815	0.226	NA	NA
AD-19078	157	816	0.719	NA	NA
AD-19079	158	817	0.545	NA	NA
AD-19080	159	818	0.092	NA	0.172
AD-19081	160	819	0.203	NA	8.936
AD-19082	161	820	0.055	NA	0.090
AD-19083	162	821	0.404	NA	NA
AD-19738	163	822	1.361	NA	NA
AD-19739	164	823	0.970	NA	NA
AD-19740	165	824	0.679	NA	NA
AD-19741	166	825	0.168	NA	NA
AD-19742	167	826	0.958	NA	NA
AD-19743	168	827	0.839	NA	NA
AD-19744	169	828	0.978	NA	NA
AD-19745	170	829	0.852	NA	NA
AD-19746	171	830	0.086	NA	NA
AD-19747	172	831	0.187	NA	NA
AD-19748	173	832	0.794	NA	NA
AD-19749	174	833	0.115	NA	NA
AD-19750	175	834	0.317	NA	NA
AD-19751	176	835	0.591	NA	NA
AD-19752	177	836	0.089	NA	NA
AD-19753	178	837	0.091	NA	NA
AD-19754	179	838	0.756	NA	NA
AD-19755	180	839	0.443	NA	NA
AD-19756	181	840	0.529	NA	NA

AD-19757	182	841	0.265	NA	NA
AD-19758	183	842	0.139	NA	NA
AD-19759	184	843	0.465	NA	NA
AD-19760	185	844	0.213	NA	NA
AD-19761	186	845	1.234	NA	NA
AD-19762	187	846	0.085	NA	NA
AD-19763	188	847	0.593	NA	NA
AD-19765	189	848	0.031	NA	NA
AD-19766	190	849	0.469	NA	NA
AD-19767	191	850	0.587	NA	NA
AD-19768	192	851	0.780	NA	NA
AD-20124	193	852	0.123	0.44	NA
AD-25889	194	853	0.605	0.73	NA
AD-25890	195	854	0.034	0.49	NA
AD-25891	196	855	0.041	0.16	0.050
AD-25892	197	856	0.099	0.34	NA
AD-25893	198	857	0.062	0.23	0.040
AD-25894	199	858	0.033	0.13	0.004
AD-25895	200	859	0.113	0.60	NA
AD-25896	201	860	0.276	0.74	NA
AD-25897	202	861	0.213	0.82	NA
AD-25898	203	862	0.127	0.79	NA
AD-25899	204	863	0.729	0.61	NA
AD-25900	205	864	0.094	0.64	NA
AD-25901	206	865	0.842	0.91	NA
AD-25902	207	866	0.054	0.24	NA
AD-25903	208	867	0.646	0.96	NA
AD-25904	209	868	0.681	0.83	NA
AD-25905	210	869	0.680	1.61	NA
AD-25906	211	870	0.413	0.96	NA
AD-25907	212	871	0.091	0.90	NA
AD-25908	213	872	0.355	0.72	NA
AD-25909	214	873	0.189	0.76	NA
AD-25910	215	874	0.048	0.48	0.070
AD-25911	216	875	0.134	0.81	NA
AD-25912	217	876	0.095	0.66	NA
AD-25913	218	877	0.291	0.94	NA
AD-25914	219	878	0.057	0.47	0.054
AD-25915	220	879	0.453	0.79	NA
AD-25916	221	880	0.219	0.79	NA
AD-25917	222	881	0.143	0.73	NA
AD-25918	223	882	0.075	0.29	0.013
AD-25919	224	883	0.123	0.68	NA

AD-25920	225	884	0.255	0.69	NA
AD-25921	226	885	0.637	0.81	NA
AD-25922	227	886	0.283	0.83	NA
AD-25923	228	887	0.575	0.64	NA
AD-25924	229	888	0.118	0.52	NA
AD-25925	230	889	0.242	0.96	NA
AD-25926	231	890	0.150	0.67	NA
AD-25927	232	891	0.394	0.72	NA
AD-25928	233	892	0.138	0.62	NA
AD-25929	234	893	0.073	0.50	NA
AD-25930	235	894	0.095	0.71	NA
AD-25931	236	895	0.076	0.77	NA
AD-25932	237	896	0.073	0.61	NA
AD-25933	238	897	0.113	0.79	NA
AD-25934	239	898	0.223	0.46	NA
AD-25935	240	899	0.288	0.78	NA
AD-25936	241	900	0.413	0.78	NA
AD-25937	242	901	0.838	0.77	NA
AD-25938	243	902	0.038	0.08	0.006
AD-25939	244	903	0.078	0.21	NA
AD-25940	245	904	0.063	0.31	NA
AD-25941	246	905	0.025	0.19	0.008
AD-25942	247	906	0.029	0.20	0.016
AD-25943	248	907	0.037	0.44	0.080
AD-25944	249	908	0.038	0.23	0.007
AD-25945	250	909	0.045	0.26	NA
AD-25946	251	910	0.107	0.46	NA
AD-25947	252	911	0.100	0.72	NA
AD-25948	253	912	0.159	0.33	NA
AD-25949	254	913	0.104	0.39	NA
AD-25950	255	914	0.026	0.26	0.010
AD-25951	256	915	0.026	0.28	0.007
AD-25952	257	916	0.349	0.80	NA
AD-25953	258	917	0.120	0.65	NA
AD-25954	259	918	0.550	0.92	NA
AD-25955	260	919	0.067	0.53	NA
AD-25956	261	920	0.039	0.40	0.042
AD-25957	262	921	0.105	0.64	NA
AD-25958	263	922	0.044	0.38	0.024
AD-25959	264	923	0.169	0.59	NA
AD-25960	265	924	0.060	0.37	0.044
AD-25961	266	925	0.162	0.67	NA
AD-25962	267	926	0.684	0.76	NA

AD-25963	268	927	0.106	0.48	0.275
AD-25964	269	928	0.033	0.47	0.050
AD-26017	270	929	0.113	0.87	NA
AD-26018	271	930	0.060	0.37	NA
AD-26019	272	931	0.106	0.42	NA
AD-26020	273	932	0.043	0.50	NA
AD-26021	274	933	0.046	0.69	NA
AD-26022	275	934	0.109	0.83	NA
AD-26023	276	935	0.637	0.80	NA
AD-26024	277	936	0.226	0.73	NA
AD-26025	278	937	0.252	0.96	NA
AD-26026	279	938	0.088	0.58	NA
AD-26027	280	939	0.228	0.96	NA
AD-26028	281	940	0.025	0.28	0.050
AD-26029	282	941	0.067	0.76	NA
AD-26030	283	942	0.275	0.52	NA
AD-26031	284	943	0.030	0.25	0.012
AD-26032	285	944	0.078	0.50	NA
AD-26033	286	945	0.353	0.69	NA
AD-26034	287	946	0.022	0.16	0.009
AD-26035	288	947	0.106	0.36	NA
AD-26036	289	948	0.336	0.63	NA
AD-26037	290	949	0.136	0.45	NA
AD-26038	291	950	0.215	0.46	NA
AD-26039	292	951	0.591	0.69	NA
AD-26040	293	952	0.046	0.15	0.099
AD-26041	294	953	0.324	0.67	NA
AD-26042	295	954	0.026	0.38	0.010
AD-26043	296	955	0.026	0.09	0.075
AD-26044	297	956	0.034	0.37	NA
AD-26045	298	957	0.531	0.77	NA
AD-26046	299	958	0.531	0.58	NA
AD-26047	300	959	0.023	0.47	0.058
AD-26048	301	960	0.397	0.95	NA
AD-26049	302	961	0.212	0.65	NA
AD-26050	303	962	0.204	0.95	NA
AD-26051	304	963	0.619	0.57	NA
AD-26052	305	964	0.037	0.55	NA
AD-26053	306	965	0.369	0.71	NA
AD-26054	307	966	0.616	0.78	NA
AD-26055	308	967	0.424	0.64	NA
AD-26056	309	968	0.168	0.81	NA
AD-26057	310	969	0.086	0.28	NA

AD-26058	311	970	0.456	0.67	NA
AD-26059	312	971	0.169	0.47	NA
AD-26060	313	972	0.057	0.19	0.139
AD-26061	314	973	0.050	0.42	NA
AD-26062	315	974	0.110	0.64	NA
AD-26063	316	975	0.021	0.74	NA
AD-26064	317	976	0.785	0.62	NA
AD-26065	318	977	0.678	0.84	NA
AD-26066	319	978	0.035	0.44	NA
AD-26067	320	979	0.305	0.51	NA
AD-26068	321	980	0.028	0.50	0.102
AD-26069	322	981	0.046	0.50	NA
AD-26070	323	982	0.446	0.64	NA
AD-26071	324	983	0.074	0.48	NA
AD-26072	325	984	0.742	0.84	NA
AD-26073	326	985	0.086	0.33	NA
AD-26074	327	986	0.227	0.55	NA
AD-26075	328	987	0.092	0.74	NA
AD-26076	329	988	0.029	0.24	0.159
AD-26077	330	989	0.191	0.70	NA
AD-26078	331	990	0.032	0.32	0.106
AD-26079	332	991	0.131	0.55	NA
AD-26080	333	992	0.589	0.86	NA
AD-26081	334	993	0.538	0.66	NA
AD-26082	335	994	0.021	0.42	0.039
AD-26083	336	995	0.049	0.25	NA
AD-26084	337	996	0.334	0.75	NA
AD-26085	338	997	0.192	0.69	NA
AD-26086	339	998	0.524	0.62	NA
AD-26087	340	999	0.276	0.71	NA
AD-26088	341	1000	0.101	0.83	NA
AD-26089	342	1001	0.821	0.93	NA
AD-26090	343	1002	0.367	0.77	NA
AD-26091	344	1003	0.022	0.32	0.057
AD-26092	345	1004	0.246	0.75	NA
AD-26093	346	1005	0.570	0.70	NA
AD-26094	347	1006	0.145	0.57	NA
AD-26095	348	1007	0.073	0.58	NA
AD-26096	349	1008	0.109	0.51	NA
AD-26097	350	1009	0.145	0.57	NA
AD-26098	351	1010	0.101	0.43	NA
AD-26099	352	1011	0.171	0.68	NA
AD-26100	353	1012	0.058	0.21	NA

AD-26101	354	1013	0.041	0.30	0.030
AD-26102	355	1014	0.169	0.93	NA
AD-26103	356	1015	0.209	0.61	NA
AD-26104	357	1016	0.016	0.22	0.058
AD-26105	358	1017	0.044	0.49	NA
AD-26106	359	1018	0.169	0.75	NA
AD-26107	360	1019	0.290	0.90	NA
AD-26108	361	1020	0.040	0.50	0.030
AD-26109	362	1021	0.024	0.22	0.025
AD-26110	363	1022	0.326	0.79	NA
AD-26111	364	1023	0.798	0.77	NA
AD-26112	365	1024	0.301	0.51	NA
AD-26123	366	1025	0.652	0.84	NA
AD-26124	367	1026	0.277	0.48	NA
AD-26125	368	1027	0.342	0.64	NA
AD-26126	369	1028	0.094	0.46	NA
AD-26127	370	1029	0.455	0.80	NA
AD-26128	371	1030	0.058	0.24	0.066
AD-26129	372	1031	0.409	0.57	NA
AD-26130	373	1032	0.892	0.80	NA
AD-26131	374	1033	0.067	0.41	0.104
AD-26132	375	1034	0.109	0.19	0.060
AD-26133	376	1035	0.790	0.85	NA
AD-26134	377	1036	0.046	0.27	0.103
AD-26135	378	1037	0.069	0.38	NA
AD-26136	379	1038	0.451	0.78	NA
AD-26137	380	1039	0.685	0.64	NA
AD-26138	381	1040	0.579	0.63	NA
AD-26139	382	1041	0.857	0.59	NA
AD-26140	383	1042	0.384	0.71	NA
AD-26141	384	1043	0.104	0.49	NA
AD-26142	385	1044	0.199	0.59	NA
AD-26143	386	1045	0.205	0.61	NA
AD-26144	387	1046	0.821	1.04	NA
AD-26145	388	1047	0.860	0.86	NA
AD-26146	389	1048	0.076	0.34	NA
AD-26147	390	1049	0.559	0.65	NA
AD-26148	391	1050	0.066	0.48	NA
AD-26149	392	1051	0.326	0.50	NA
AD-26150	393	1052	0.396	0.66	NA
AD-26151	394	1053	0.249	0.54	NA
AD-26152	395	1054	0.837	0.74	NA
AD-26153	396	1055	0.119	0.39	NA

AD-26154	397	1056	0.600	0.64	NA
AD-26155	398	1057	0.693	0.69	NA
AD-26156	399	1058	0.033	0.35	0.020
AD-26157	400	1059	0.220	0.74	NA
AD-26158	401	1060	0.031	0.40	0.033
AD-26159	402	1061	0.387	0.49	NA
AD-26160	403	1062	0.836	0.73	NA
AD-26161	404	1063	0.831	0.76	NA
AD-26162	405	1064	0.358	0.50	NA
AD-26163	406	1065	0.817	0.66	NA
AD-26164	407	1066	0.112	0.59	NA
AD-26165	408	1067	0.272	0.67	NA
AD-26166	409	1068	0.300	0.63	NA
AD-26167	410	1069	0.664	0.77	NA
AD-26168	411	1070	0.771	0.78	NA
AD-26169	412	1071	0.480	0.67	NA
AD-26170	413	1072	0.174	0.47	NA
AD-26171	414	1073	0.410	0.75	NA
AD-26172	415	1074	0.294	0.74	NA
AD-26173	416	1075	0.384	0.71	NA
AD-26174	417	1076	0.388	0.79	NA
AD-26175	418	1077	0.611	0.72	NA
AD-26176	419	1078	0.055	0.44	NA
AD-26177	420	1079	0.310	0.67	NA
AD-26178	421	1080	0.038	0.20	0.094
AD-26179	422	1081	0.042	0.33	0.108
AD-26180	423	1082	0.031	0.21	0.036
AD-26181	424	1083	0.041	0.08	0.034
AD-26182	425	1084	0.237	0.79	NA
AD-26183	426	1085	0.028	0.37	0.070
AD-26184	427	1086	0.189	0.54	NA
AD-26185	428	1087	0.357	0.76	NA
AD-26186	429	1088	0.066	0.60	NA
AD-26187	430	1089	0.298	0.60	NA
AD-26188	431	1090	0.159	0.51	NA
AD-26189	432	1091	0.143	0.51	NA
AD-26190	433	1092	0.063	0.34	NA
AD-26191	434	1093	0.674	0.82	NA
AD-26192	435	1094	0.446	0.75	NA
AD-26193	436	1095	0.058	0.36	0.055
AD-26194	437	1096	0.289	0.84	NA
AD-26195	438	1097	0.353	0.81	NA
AD-26196	439	1098	0.055	0.35	NA

AD-26197	440	1099	0.440	0.68	NA
AD-26198	441	1100	0.175	0.53	NA
AD-26199	442	1101	0.055	0.58	NA
AD-26200	443	1102	0.076	0.46	NA
AD-26201	444	1103	0.283	0.48	NA
AD-26202	445	1104	0.052	0.70	NA
AD-26203	446	1105	0.045	0.22	0.162
AD-26204	447	1106	0.660	0.73	NA
AD-26205	448	1107	0.324	0.76	NA
AD-26206	449	1108	0.520	1.12	NA
AD-26207	450	1109	0.367	0.75	NA
AD-26208	451	1110	0.795	0.73	NA
AD-26209	452	1111	0.112	0.54	NA
AD-26210	453	1112	0.030	0.39	NA
AD-26211	454	1113	0.124	0.25	NA
AD-26212	455	1114	0.151	0.45	NA
AD-26213	456	1115	0.223	0.63	NA
AD-26214	457	1116	0.513	0.66	NA
AD-26215	458	1117	0.102	0.29	NA
AD-26216	459	1118	0.496	0.58	NA
AD-26217	460	1119	0.410	0.77	NA
AD-26218	461	1120	0.041	0.15	0.026
AD-26651	462	1121	0.023	0.21	0.041
AD-26652	463	1122	0.025	0.21	0.026
AD-26653	464	1123	0.115	0.76	NA
AD-26654	465	1124	0.068	0.88	NA
AD-26655	466	1125	0.682	0.86	NA
AD-26656	467	1126	0.684	0.91	NA
AD-26657	468	1127	0.468	0.89	NA
AD-26658	469	1128	0.305	0.50	NA
AD-26659	470	1129	0.481	0.50	NA
AD-26660	471	1130	0.041	0.20	0.010
AD-26661	472	1131	0.194	0.77	NA
AD-26662	473	1132	0.717	1.00	NA
AD-26663	474	1133	0.546	1.02	NA
AD-26664	475	1134	0.030	0.36	NA
AD-26665	476	1135	0.037	0.25	0.008
AD-26666	477	1136	0.072	0.57	NA
AD-26667	478	1137	0.587	0.65	NA
AD-26668	479	1138	0.760	0.70	NA
AD-26669	480	1139	0.038	0.64	NA
AD-26670	481	1140	0.033	0.32	0.005
AD-26671	482	1141	0.091	0.71	NA

AD-26672	483	1142	0.084	0.56	NA
AD-26673	484	1143	0.027	0.18	0.012
AD-26674	485	1144	0.044	0.32	0.021
AD-26675	486	1145	0.063	0.67	NA
AD-26676	487	1146	0.617	0.81	NA
AD-26677	488	1147	0.138	0.50	NA
AD-26678	489	1148	0.055	0.34	NA
AD-26679	490	1149	0.052	0.44	NA
AD-26680	491	1150	0.191	0.42	NA
AD-26681	492	1151	0.092	0.57	NA
AD-26682	493	1152	0.035	0.11	0.007
AD-26683	494	1153	0.055	0.87	NA
AD-26684	495	1154	0.035	0.16	0.009
AD-26685	496	1155	0.034	0.37	NA
AD-26686	497	1156	0.821	0.77	NA
AD-26687	498	1157	0.151	0.29	NA
AD-26688	499	1158	0.094	0.69	NA
AD-26689	500	1159	0.086	0.61	NA
AD-26690	501	1160	0.047	0.36	NA
AD-26691	502	1161	0.030	0.24	0.020
AD-26692	503	1162	0.222	0.62	NA
AD-26693	504	1163	0.739	0.76	NA
AD-26694	505	1164	0.331	0.63	NA
AD-26695	506	1165	0.371	0.66	NA
AD-26696	507	1166	0.023	0.37	0.027
AD-26697	508	1167	1.024	0.80	NA
AD-26698	509	1168	0.047	0.22	NA
AD-26699	510	1169	0.145	0.71	NA
AD-26700	511	1170	0.028	0.08	0.005
AD-26701	512	1171	0.028	0.21	0.006
AD-26702	513	1172	0.046	0.43	NA
AD-26703	514	1173	0.193	0.65	NA
AD-26704	515	1174	0.027	0.36	0.010
AD-26705	516	1175	0.054	0.40	NA
AD-26706	517	1176	0.223	0.52	NA
AD-26707	518	1177	0.144	0.70	NA
AD-26708	519	1178	0.160	0.59	NA
AD-26709	520	1179	0.818	0.80	NA
AD-26710	521	1180	0.307	0.84	NA
AD-26711	522	1181	0.209	0.46	NA
AD-26712	523	1182	0.276	0.76	NA
AD-26713	524	1183	0.043	0.23	0.014
AD-26714	525	1184	0.108	0.65	NA

AD-26715	526	1185	0.777	0.67	NA
AD-26716	527	1186	0.551	0.69	NA
AD-26717	528	1187	0.643	0.80	NA
AD-26718	529	1188	0.821	0.70	NA
AD-26719	530	1189	0.053	0.35	NA
AD-26720	531	1190	0.148	0.62	NA
AD-26721	532	1191	0.906	0.92	NA
AD-26722	533	1192	0.042	0.38	0.033
AD-26723	534	1193	0.136	0.69	NA
AD-26724	535	1194	0.472	1.00	NA
AD-26725	536	1195	0.082	0.39	NA
AD-26726	537	1196	0.258	0.70	NA
AD-26727	538	1197	0.043	0.33	NA
AD-26728	539	1198	0.612	0.80	NA
AD-26729	540	1199	0.056	0.15	0.007
AD-26730	541	1200	0.038	0.13	0.007
AD-26731	542	1201	0.034	0.10	0.035
AD-26732	543	1202	0.853	0.74	NA
AD-26733	544	1203	0.805	0.77	NA
AD-26734	545	1204	0.580	0.77	NA
AD-26735	546	1205	0.457	1.02	NA
AD-26736	547	1206	0.701	0.75	NA
AD-26737	548	1207	0.066	0.33	NA
AD-26738	549	1208	0.327	0.79	NA
AD-26739	550	1209	0.102	0.44	NA
AD-26740	551	1210	0.030	0.08	0.006
AD-26741	552	1211	0.128	0.50	NA
AD-26742	553	1212	0.025	0.34	0.057
AD-26743	554	1213	0.033	0.38	0.061
AD-26744	555	1214	0.170	0.74	NA
AD-26745	556	1215	0.304	0.55	NA
AD-26746	557	1216	0.037	0.33	NA
AD-26747	558	1217	0.048	0.43	NA
AD-26748	559	1218	0.081	0.51	NA
AD-26749	560	1219	0.184	0.70	NA
AD-26750	561	1220	0.209	0.64	NA
AD-26751	562	1221	0.570	0.71	NA
AD-26752	563	1222	0.040	0.45	0.042
AD-26753	564	1223	0.153	0.61	NA
AD-26754	565	1224	0.518	0.79	NA
AD-26755	566	1225	0.064	0.27	NA
AD-26756	567	1226	0.146	0.48	NA
AD-26757	568	1227	0.035	0.22	0.047

AD-26758	569	1228	0.053	0.46	NA
AD-26759	570	1229	0.116	0.59	NA
AD-26760	571	1230	0.435	0.60	NA
AD-26761	572	1231	0.088	0.44	NA
AD-26762	573	1232	0.385	0.57	NA
AD-26763	574	1233	0.057	0.22	0.015
AD-26764	575	1234	0.120	0.47	NA
AD-26765	576	1235	0.058	0.43	NA
AD-26766	577	1236	0.183	0.72	NA
AD-26767	578	1237	0.582	0.57	NA
AD-26768	579	1238	0.042	0.39	NA
AD-26769	580	1239	0.071	0.52	NA
AD-26770	581	1240	0.398	0.58	NA
AD-26771	582	1241	0.576	0.71	NA
AD-26772	583	1242	0.784	0.64	NA
AD-26773	584	1243	0.353	0.58	NA
AD-26774	585	1244	0.069	0.55	NA
AD-26775	586	1245	0.506	0.86	NA
AD-26776	587	1246	0.079	0.26	NA
AD-26777	588	1247	0.363	0.73	NA
AD-26778	589	1248	0.101	0.40	NA
AD-26779	590	1249	0.040	0.34	0.109
AD-26780	591	1250	0.069	0.25	NA
AD-26781	592	1251	0.044	0.24	NA
AD-26782	593	1252	0.054	0.53	NA
AD-26783	594	1253	0.053	0.51	NA
AD-26784	595	1254	0.072	0.53	NA
AD-26785	596	1255	0.201	0.51	NA
AD-26786	597	1256	0.134	0.81	NA
AD-26787	598	1257	0.143	0.60	NA
AD-26788	599	1258	0.036	0.57	0.053
AD-26789	600	1259	0.418	0.74	NA
AD-26790	601	1260	0.122	0.62	NA
AD-26791	602	1261	0.305	0.73	NA
AD-26792	603	1262	0.346	0.76	NA
AD-26793	604	1263	0.391	0.63	NA
AD-26794	605	1264	0.077	0.40	NA
AD-26795	606	1265	0.586	0.65	NA
AD-26796	607	1266	0.392	0.70	NA
AD-26797	608	1267	0.063	0.73	NA
AD-26798	609	1268	0.249	0.62	NA
AD-26799	610	1269	0.345	0.66	NA
AD-26800	611	1270	0.034	0.20	0.025

AD-26801	612	1271	0.044	0.46	NA
AD-26802	613	1272	0.096	0.57	NA
AD-26803	614	1273	0.162	0.57	NA
AD-26804	615	1274	0.056	0.35	NA
AD-26805	616	1275	0.742	0.66	NA
AD-26806	617	1276	0.080	0.69	NA
AD-26807	618	1277	0.517	0.62	NA
AD-26808	619	1278	0.043	0.51	NA
AD-26809	620	1279	0.227	0.61	NA
AD-26810	621	1280	0.048	0.22	0.039
AD-26811	622	1281	0.333	0.85	NA
AD-26812	623	1282	0.522	0.84	NA
AD-26813	624	1283	0.044	0.33	0.076
AD-26814	625	1284	0.545	0.72	NA
AD-26815	626	1285	0.594	0.63	NA
AD-26816	627	1286	0.044	0.37	NA
AD-26817	628	1287	0.523	0.68	NA
AD-26818	629	1288	0.575	1.80	NA
AD-26819	630	1289	0.069	0.41	NA
AD-26820	631	1290	0.484	0.76	NA
AD-26821	632	1291	0.245	0.70	NA
AD-26822	633	1292	0.039	0.23	0.037
AD-26823	634	1293	0.062	0.09	0.033
AD-26824	635	1294	0.304	0.60	NA
AD-26825	636	1295	0.038	0.36	NA
AD-26826	637	1296	0.105	0.57	NA
AD-26900	638	1297	0.056	0.73	0.033
AD-26901	639	1298	0.065	0.68	NA
AD-26902	640	1299	0.053	0.42	NA
AD-26903	641	1300	0.075	0.59	NA
AD-26904	642	1301	0.051	0.38	NA
AD-26905	643	1302	0.084	0.45	NA
AD-26906	644	1303	0.186	0.76	NA
AD-26907	645	1304	0.610	0.82	NA
AD-26908	646	1305	0.073	0.78	NA
AD-26909	647	1306	0.235	0.99	NA
AD-26910	648	1307	0.077	0.78	NA
AD-26911	649	1308	0.193	0.96	NA
AD-26912	650	1309	0.074	0.73	NA
AD-26913	651	1310	0.141	0.88	NA
AD-26914	652	1311	0.519	0.64	NA
AD-26915	653	1312	0.587	0.71	NA
AD-26916	654	1313	0.063	0.62	NA

AD-26917	655	1314	0.076	0.55	NA
AD-26918	656	1315	0.069	0.28	0.029
AD-26919	657	1316	0.085	0.55	NA
AD-26920	658	1317	0.042	0.31	NA
AD-26921	659	1318	0.025	0.09	0.014

[00823] NA: data not available or not determined.

[00824] "Fold-Change" represents the residual level (in HeLa cells) at a particular time and concentration, relative to control. Thus, a "Fold-Change 10 nM 24hr" for AD-18892 of "0.054" indicates that, at a concentration of 10 nM, there was 5.4% residual Beta-Catenin level, or 94.6% gene knock-down, in HeLa cells at 24 hr after treating the cells with the RNAi agent.

[00825] "Fold-Change 0.1 nM 120hr" indicates the residual Beta-Catenin level at a concentration of 0.1 nM, measured at 120 hr.

[00826] "Avg. EC50 (nM)" indicates a concentration estimated, based on available data, to allow 50% gene knock-down in HeLa cells. Thus, for AD-18893, a concentration of 0.008 nM is estimated to knock down Beta-Catenin by 50%. To calculate estimated average EC50 figures, HeLa cells were treated with RNAi agents at concentrations of 10nM, 1nM, 0.1nM, 0.01nM, and 0.001nM of RNAi agent, and the data fit to a curve. The indicated EC50 is an estimated EC50 calculated from available data that is expected to give 50% gene knock-down of Beta-Catenin in HeLa cells.

[00827] Tables 1 to 8 thus disclose various RNAi agents capable of mediating gene knock-down of Beta-Catenin.

[00828] TABLE 6. Analysis of RNAi agents to Beta-Catenin

[00829] Additional duplexes targeting Beta-Catenin (listed in Table 3) were tested *in vitro* against HeLa cells. 48 hour results were measured; duplex concentration was 6 nM, 3 nM and 1.5 nM. Data in this table represents residual gene activity; thus Set1 254 A22 S26 showed 4.9% residual gene activity (e.g., 95.1% gene knockdown) at 48 hours at 6 nM in HeLa cells.

Nickname	AV HeLa set1-2 d3-6nM	AV HeLa set1-2 3nM	AV HeLa set1-2 1.5nM	SD HeLa set1-2 d3-6nM	SD HeLa set1-2 3nM	SD HeLa set1-2 1.5nM
Set1 254 A22 S26	4.9	11.1	22.5	1.6	2.1	1.6
Set1 703 A22 S26	4.8	12.4	29.0	1.5	2.4	7.3
Set1 709 A22 S26	6.5	13.9	30.7	1.1	2.0	7.1
Set1 895 A22 S26	5.9	13.1	48.0	0.8	3.9	25.6
Set1 1816 A22 S26	4.9	12.3	28.6	0.5	2.8	4.3
Set1 1974 A22 S26	6.6	12.5	36.9	1.0	0.9	0.6
Set1 2425 A22 S26	5.6	13.6	27.3	0.4	1.7	9.7
Set1 3146 A22 S26	4.5	9.3	21.0	1.1	1.2	2.9

Set1 889 A22 S26	8.6	14.2	37.9	3.4	3.7	17.1
Set1 1814 A22 S26	6.0	11.8	21.3	2.2	3.8	4.6
Set1 1245 A22 S26	6.7	12.0	28.2	2.6	2.5	8.7
Set1 3196 A22 S26	4.5	9.1	17.1	0.5	0.0	5.3
Set1 1450 A22 S26	4.4	12.5	25.4	0.3	3.6	2.7
Set1 3169 A22 S26	6.3	13.1	29.7	0.9	2.2	9.8
Set1 3477 A22 S26	9.6	19.8	40.9	2.0	2.6	10.9
Set1 865 A22 S26	12.0	24.5	57.3	3.3	7.5	14.2
Set1 1249 A22 S26	34.4	71.2	73.3	7.9	24.7	12.3
Set1 1250 A22 S26	12.0	30.6	61.6	2.0	8.4	4.2
Set1 2202 A22 S26	8.3	14.0	45.8	3.1	1.8	12.2
Set1 1545 A22 S26	34.4	62.0	81.5	11.6	4.1	12.5
Set1 1755 A22 S26	8.7	21.9	64.9	1.0	6.4	8.0
Set1 254 A25 S27	6.3	12.3	17.6	1.2	3.4	1.7
Set1 703 A25 S27	7.0	13.7	32.8	1.2	2.9	8.0
Set1 709 A25 S27	5.6	11.4	23.4	1.8	0.5	7.7
Set1 895 A25 S27	6.6	13.5	35.7	1.9	2.5	6.8
Set1 1816 A25 S27	7.8	15.6	26.4	1.3	1.2	4.8
Set1 1974 A25 S27	8.1	16.2	34.7	2.6	1.3	3.8
Set1 2425 A25 S27	7.8	16.5	35.3	1.0	2.2	2.5
Set1 3146 A25 S27	4.9	11.9	31.0	0.3	1.3	4.2
Set1 889 A25 S27	9.3	15.0	37.2	1.3	1.9	4.1
Set1 1814 A25 S27	6.2	13.7	43.2	1.1	0.9	6.1
Set1 1245 A25 S27	7.2	15.2	36.2	0.3	2.4	11.7
Set1 3196 A25 S27	5.5	10.3	24.2	1.4	0.8	2.1
Set1 1450 A25 S27	4.3	10.4	29.9	1.1	1.1	6.4
Set1 3169 A25 S27	4.3	11.5	22.0	0.4	2.3	2.7
Set1 3477 A25 S27	7.5	12.8	22.8	1.1	1.3	2.1
Set1 865 A25 S27	5.1	10.9	18.1	0.7	1.2	2.9
Set1 1249 A25 S27	8.0	22.9	37.2	1.8	5.1	6.7
Set1 1250 A25 S27	16.6	28.2	49.1	3.1	2.7	8.9
Set1 2202 A25 S27	6.1	10.0	29.2	2.3	3.6	4.8
Set1 1545 A25 S27	9.0	16.6	41.9	1.3	2.2	2.2
Set1 1755 A25 S27	5.8	15.1	33.8	1.2	2.2	6.1
Set1 254 A LO V1 S26	6.0	16.4	32.9	0.3	3.8	5.1
Set1 703 A LO V1 S26	8.1	22.7	50.3	2.8	3.4	16.2
Set1 709 A LO V1 S26	6.2	14.8	37.1	1.2	1.7	5.1
Set1 895 A LO V1 S26	42.7	63.9	82.3	7.8	15.5	10.2
Set1 1816 A LO V1 S26	6.9	16.9	43.4	0.9	1.4	15.1
Set1 1974 A LO V1 S26	9.0	18.5	36.8	1.4	3.6	6.8
Set1 2425 A LO V1 S26	5.5	13.9	30.0	0.4	1.6	7.5
Set1 3146 A LO V1 S26	12.1	27.7	61.2	1.5	2.7	3.8
Set1 889 A LO V1 S26	24.5	37.8	60.3	3.2	3.2	9.1

Set1 1814 A LO V1 S26	8.6	20.7	46.5	1.5	2.6	11.1
Set1 1245 A LO V1 S26	42.0	61.4	85.9	5.8	8.4	10.4
Set1 3196 A LO V1 S26	6.1	14.0	31.0	0.6	1.2	5.4
Set1 1450 A LO V1 S26	9.4	21.1	47.6	1.4	1.3	8.0
Set1 3169 A LO V1 S26	5.3	15.5	30.5	1.3	3.7	1.9
Set1 3477 A LO V1 S26	8.6	16.9	39.8	1.0	1.0	2.3
Set1 865 A LO V1 S26	5.5	18.1	34.5	0.9	3.1	11.0
Set1 1249 A LO V1 S26	61.0	90.3	82.0	5.6	29.0	6.6
Set1 1250 A LO V1 S26	11.3	23.1	58.2	0.9	3.0	5.1
Set1 2202 A LO V1 S26	5.7	14.5	45.2	1.0	1.4	1.5
Set1 1545 A LO V1 S26	5.6	13.1	38.6	0.4	0.9	3.2
Set1 1755 A LO V1 S26	39.5	53.6	77.5	3.8	3.3	5.0
Set1 254 A LO V2 S LO V1	8.7	18.6	44.9	2.5	1.4	6.6
Set1 703 A LO V2 S LO V1	39.9	51.7	75.8	3.9	3.2	9.9
Set1 709 A LO V2 S LO V1	9.2	20.3	45.0	1.2	0.7	8.7
Set1 895 A LO V2 S LO V1	33.3	64.9	84.8	1.8	6.5	5.8
Set1 1816 A LO V2 S LO V1	14.4	33.1	61.2	2.2	2.9	9.3
Set1 1974 A LO V2 S LO V1	56.7	65.4	91.8	15.4	5.6	6.7
Set1 2425 A LO V2 S LO V1	13.3	21.4	54.2	1.5	3.6	6.0
Set1 3146 A LO V2 S LO V1	9.7	16.7	32.7	2.0	1.7	5.0
Set1 889 A LO V2 S LO V1	18.0	34.6	58.8	1.4	4.2	7.0
Set1 1814 A LO V2 S LO V1	8.9	18.5	44.1	3.3	5.0	1.0
Set1 1245 A LO V2 S LO V1	52.2	43.1	93.4	13.1	4.1	6.2
Set1 3196 A LO V2 S LO V1	7.8	15.1	28.0	2.7	3.1	2.5
Set1 1450 A LO V2 S LO V1	6.6	14.4	35.0	0.4	2.0	4.0
Set1 3169 A LO V2 S LO V1	5.3	14.5	26.4	0.5	2.8	2.2
Set1 3477 A LO V2 S LO V1	9.4	22.0	35.2	1.5	0.8	1.6
Set1 865 A LO V2 S LO V1	11.2	18.5	45.9	5.4	4.2	18.2
Set1 1249 A LO V2 S LO V1	65.5	97.0	82.0	19.2	22.0	10.3
Set1 1250 A LO V2 S LO V1	49.4	62.9	92.4	6.3	19.6	22.4
Set1 2202 A LO V2 S LO V1	6.7	17.3	34.9	0.8	3.6	1.6
Set1 1545 A LO V2 S LO V1	17.9	32.6	58.3	1.2	5.0	8.2
Set1 1755 A LO V2 S LO V1	10.5	23.3	43.1	1.0	3.3	7.3
Set2 254 A LO V3 S LO V2	15.0	88.6	75.0	3.4	21.7	4.4
Set2 703 A LO V3 S LO V2	112.0	235.3	135.2	25.2	30.1	22.4
Set2 709 A LO V3 S LO V2	36.7	93.6	98.4	2.6	7.6	4.8
Set2 895 A LO V3 S LO V2	80.2	163.3	117.7	9.1	62.4	10.6
Set2 1816 A LO V3 S LO V2	66.3	113.1	116.6	10.0	22.2	12.6
Set2 1974 A LO V3 S LO V2	110.7	142.7	134.5	13.1	19.0	12.8
Set2 2425 A LO V3 S LO V2	50.9	119.3	151.5	13.1	20.2	7.0
Set2 3146 A LO V3 S LO V2	30.8	73.2	99.6	5.0	13.5	14.3
Set2 889 A LO V3 S LO V2	72.5	135.6	112.8	12.0	37.8	9.4
Set2 1814 A LO V3 S LO V2	80.7	129.6	133.9	23.6	13.9	15.2

Set2 1245 A LO V3 S LO V2	94.9	128.9	129.1	13.2	18.1	13.8
Set2 3196 A LO V3 S LO V2	20.5	69.2	89.8	1.4	8.7	15.8
Set2 1450 A LO V3 S LO V2	35.3	95.3	109.0	1.6	15.1	16.1
Set2 3169 A LO V3 S LO V2	26.2	90.9	85.7	8.9	26.1	7.7
Set2 3477 A LO V3 S LO V2	16.3	71.8	68.0	3.7	20.3	2.2
Set2 865 A LO V3 S LO V2	99.3	122.9	115.4	9.0	29.0	14.5
Set2 1249 A LO V3 S LO V2	62.7	114.9	113.5	7.5	19.6	3.4
Set2 1250 A LO V3 S LO V2	101.9	112.5	116.1	8.7	12.1	11.1
Set2 2202 A LO V3 S LO V2	72.2	118.5	129.7	7.1	22.3	7.5
Set2 1545 A LO V3 S LO V2	65.6	109.5	120.7	12.9	6.5	9.3
Set2 1755 A LO V3 S LO V2	84.7	140.6	146.9	11.1	52.2	13.5
Set2 254 A LO V4 S LO V1	11.2	50.5	59.8	1.4	4.6	4.5
Set2 703 A LO V4 S LO V1	29.1	94.0	100.5	3.4	10.3	6.1
Set2 709 A LO V4 S LO V1	6.3	25.9	32.9	0.2	2.6	2.2
Set2 895 A LO V4 S LO V1	26.4	86.4	108.5	1.2	6.5	30.8
Set2 1816 A LO V4 S LO V1	15.0	94.1	88.1	1.5	13.2	25.2
Set2 1974 A LO V4 S LO V1	47.3	100.2	126.0	9.1	4.5	21.6
Set2 2425 A LO V4 S LO V1	13.0	44.3	61.8	3.7	1.7	6.9
Set2 3146 A LO V4 S LO V1	11.8	36.2	34.8	2.5	2.4	3.6
Set2 889 A LO V4 S LO V1	28.9	79.6	79.8	9.2	13.4	10.7
Set2 1814 A LO V4 S LO V1	10.4	50.1	62.9	0.9	17.3	9.2
Set2 1245 A LO V4 S LO V1	31.7	88.0	105.1	5.3	18.8	14.2
Set2 3196 A LO V4 S LO V1	9.8	27.2	39.2	1.1	1.4	4.9
Set2 1450 A LO V4 S LO V1	8.9	27.8	44.0	2.1	7.6	10.9
Set2 3169 A LO V4 S LO V1	8.1	26.3	29.7	1.4	7.1	6.6
Set2 3477 A LO V4 S LO V1	7.9	19.2	29.1	0.6	2.5	9.5
Set2 865 A LO V4 S LO V1	6.2	23.8	33.4	0.6	0.7	5.6
Set2 1249 A LO V4 S LO V1	69.5	103.4	103.4	19.1	17.3	11.8
Set2 1250 A LO V4 S LO V1	61.4	90.3	94.6	15.3	12.4	11.7
Set2 2202 A LO V4 S LO V1	9.3	35.7	42.8	2.9	6.9	5.5
Set2 1545 A LO V4 S LO V1	32.8	68.0	92.2	6.1	17.1	23.2
Set2 1755 A LO V4 S LO V1	13.9	50.4	62.0	3.6	4.6	12.5
Set2 254 A LO V5 S LO V1	11.4	28.3	52.5	1.8	8.2	4.8
Set2 703 A LO V5 S LO V1	31.1	88.4	97.0	1.4	14.7	6.3
Set2 709 A LO V5 S LO V1	13.0	34.2	37.9	3.4	8.8	5.7
Set2 895 A LO V5 S LO V1	25.9	81.1	109.1	3.0	8.2	20.0
Set2 1816 A LO V5 S LO V1	12.9	42.3	53.7	2.5	7.0	12.1
Set2 1974 A LO V5 S LO V1	39.5	80.3	93.6	11.6	5.5	10.4
Set2 2425 A LO V5 S LO V1	11.5	38.8	59.9	1.4	5.4	3.3
Set2 3146 A LO V5 S LO V1	9.3	32.1	41.6	0.7	5.6	4.3
Set2 889 A LO V5 S LO V1	26.9	64.9	89.5	5.2	23.5	17.5
Set2 1814 A LO V5 S LO V1	11.0	47.9	79.5	1.5	9.1	11.6
Set2 1245 A LO V5 S LO V1	29.5	78.6	127.3	2.2	5.1	16.7

Set2 3196 A LO V5 S LO V1	8.1	28.6	55.6	0.7	9.8	9.7
Set2 1450 A LO V5 S LO V1	6.6	27.8	46.3	1.6	12.7	12.4
Set2 3169 A LO V5 S LO V1	7.8	24.2	32.6	1.5	0.8	5.5
Set2 3477 A LO V5 S LO V1	11.5	46.6	57.9	2.3	25.4	7.1
Set2 865 A LO V5 S LO V1	11.4	35.2	40.9	1.6	8.6	6.7
Set2 1249 A LO V5 S LO V1	52.0	82.3	89.6	3.2	3.0	12.9
Set2 1250 A LO V5 S LO V1	45.0	75.2	97.3	6.1	4.2	13.0
Set2 2202 A LO V5 S LO V1	5.8	26.1	35.7	0.8	5.2	4.2
Set2 1545 A LO V5 S LO V1	23.8	59.7	73.5	3.5	18.3	11.0
Set2 1755 A LO V5 S LO V1	10.8	40.5	73.9	0.8	10.6	4.8
Set2 254 A48 S26	7.3	20.0	36.8	0.8	1.5	1.7
Set2 703 A48 S26	7.4	27.7	48.1	0.7	2.6	5.7
Set2 709 A48 S26	10.3	35.4	42.0	0.3	12.1	1.3
Set2 895 A48 S26	8.7	30.7	64.5	0.7	6.6	8.0
Set2 1816 A48 S26	10.0	29.4	36.0	1.8	6.7	7.5
Set2 1974 A48 S26	9.3	27.7	45.1	1.3	7.5	2.3
Set2 2425 A48 S26	8.2	38.6	40.5	1.8	2.5	6.6
Set2 3146 A48 S26	5.8	22.4	28.5	0.5	2.2	5.6
Set2 889 A48 S26	7.2	21.9	30.6	0.9	5.9	2.8
Set2 1814 A48 S26	7.3	19.3	25.2	2.6	7.8	7.6
Set2 1245 A48 S26	8.3	47.7	58.2	2.0	19.3	10.5
Set2 3196 A48 S26	8.0	20.2	27.0	0.4	6.9	7.2
Set2 1450 A48 S26	7.5	27.4	40.4	1.8	9.7	6.6
Set2 3169 A48 S26	8.4	18.2	30.5	0.8	3.1	7.4
Set2 3477 A48 S26	12.5	44.1	59.8	2.2	10.3	5.5
Set2 865 A48 S26	13.0	38.2	42.5	2.4	5.3	8.4
Set2 1249 A48 S26	47.7	74.5	88.6	9.0	13.3	12.3
Set2 1250 A48 S26	11.5	56.4	66.0	2.4	7.2	7.4
Set2 2202 A48 S26	6.7	28.1	33.2	0.8	5.4	4.9
Set2 1545 A48 S26	37.0	72.7	61.7	10.9	13.6	24.3
Set2 1755 A48 S26	8.4	25.9	39.7	2.4	4.7	6.4

[00830] EXAMPLE 4

[00831] SCREENING IN INSENSITIVE CELLS

[00832] In various embodiments, preferred RNAi agents to Beta-Catenin are those which are specific to Beta-Catenin and, in effect, do not exhibit off-target effects. Thus, in order to continue lead selection, various RNAi agents to Beta-Catenin are tested against cell lines which produce little or no Beta-Catenin. The Beta-Catenin RNAi agents which do not greatly reduce viability of these so-called "insensitive cell lines" are thought to have little or not off-target effects. The "insensitive" cell lines used are NCI-H28 and RKO. NCI-H28 is a mesothelioma cell line in whch the Beta-Catenin gene has been deleted; RKO is a colorectal cell line which has low or no Beta-Catenin

expression.

[00833] 105 RNAi agents to Beta-Catenin found had been found to be effective in the dose-response analysis. These are tested against "insensitive" cell lines used are NCI-H28 and RKO at doses of 50 nM, 10 nM, 1 nM, 0.1 nM, and 0.0001 nM, and cell viability is determined at the time points of 3, 5 and 7 days.

[00834] The following RNAi agents demonstrate at least 80% viability (no more than 20% growth inhibition) of RKO cells and at least 80% viability of NCI-H28 cells on day 5, at 50 or 10 nM.

[00835] **TABLE 7.**

RNAi agent	IC50
AD-18963-b2	0.049
AD-25894-b1	0.004
AD-25914-b1	0.054
AD-25956-b1	0.042
AD-26028-b1	0.050
AD-26034-b1	0.009
AD-26108-b1	0.030
AD-26131-b1	0.104
AD-26134-b1	0.103
AD-26158-b1	0.033
AD-26193-b1	0.055
AD-26218-b1	0.026
AD-26652-b1	0.026
AD-26704-b1	0.010
AD-26900-b1	0.033
AD-26918-b1	0.029

[00836] The following RNAi agents demonstrate at least 80% viability (no more than 20% growth inhibition) of RKO cells and about 60 to 80% viability of NCI-H28 cells on day 5, at 50 or 10 nM.

[00837] **TABLE 8.**

RNAi Agent	IC50
AD-18983-b2	0.070
AD-25893-b1	0.040
AD-25918-b1	0.013
AD-25943-b1	0.080
AD-25944-b1	0.007
AD-25951-b1	0.007
AD-25958-b1	0.024
AD-26068-b1	0.102
AD-26109-b1	0.025
AD-26156-b1	0.020
AD-26673-b1	0.012
AD-26682-b1	0.007
AD-26696-b1	0.027
AD-26740-b1	0.006

AD-26752-b1	0.042
AD-26757-b1	0.047
AD-26779-b1	0.109
AD-26788-b1	0.053
AD-26800-b1	0.025

[00838] Thus, 35 RNAi agents to Beta-Catenin did not greatly reduce viability of cell lines which do not depend on Beta-Catenin; these 35 RNAi agents to Beta-Catenin are: AD-18963-b2, AD-18983-b2, AD-25893-b1, AD-25894-b1, AD-25914-b1, AD-25918-b1, AD-25943-b1, AD-25944-b1, AD-25951-b1, AD-25956-b1, AD-25958-b1, AD-26028-b1, AD-26034-b1, AD-26068-b1, AD-26108-b1, AD-26109-b1, AD-26131-b1, AD-26134-b1, AD-26156-b1, AD-26158-b1, AD-26193-b1, AD-26218-b1, AD-26652-b1, AD-26673-b1, AD-26682-b1, AD-26696-b1, AD-26704-b1, AD-26740-b1, AD-26752-b1, AD-26757-b1, AD-26779-b1, AD-26788-b1, AD-26800-b1, AD-26900-b1, and AD-26918-b1 (wherein "b1" indicates "batch 1").

[00839] **EXAMPLE 5**

[00840] **SCREENING IN SENSITIVE CELL LINES**

[00841] Further screening is performed on the 35 RNAi agents to Beta-Catenin which were able to reduce Beta-Catenin expression in vitro, and did which did not greatly reduce viability of cell lines which do not depend on Beta-Catenin, as shown in the previous Examples.

[00842] These 35 RNAi agents were tested on four colorectal cell lines with an APC mutation (LoVo, DLD-1, LS411N and SW403). In the wild-type Wnt pathway, Beta-Catenin protein is phosphorylated by GSK-3, and then degraded by APC; thus, Beta-Catenin protein levels do not accumulate. However, in the case of the APC mutation, the Beta-Catenin is not degraded and thus the protein accumulates. These four cell lines are, in fact, dependent on Beta-Catenin and stop growing if Beta-Catenin expression is down-regulated.

[00843] The cell lines are each treated with each of the 35 RNAi agents to Beta-Catenin at doses of 50 nM, 10 nM, 1 nM, 0.1 nM, and 0.0001 nM, and tested at 3, 5 and 7 days. The data used are from DLD-1 treated at 1 nM, LoVo at 1 nM, and LS411N at 0.1 nM, and data collected at 7 days. SW403 data is not used, as these data did not distinguish among the various siRNAs even at 0.1 nM.

[00844] The screening data for RNAi agents to Beta-Catenin in sensitive cell lines is presented below.

[00845] **TABLE 9. SCREENING DATA**

siRNA	Pos	Species	24 hr Average IC50 (nM)	DLD1 1 nM Day 7	LoVo 1 nM Day 7	LS411N 0.1 nM Day 7	PBMC
AD-18983	CDS	Hu, Cy, Mo	0.07	0.258	0.150	0.054	Neg
AD-26156	CDS	Hu, Cy, Mo	0.02	0.458	0.194	0.187	Neg
AD-25951	3' UTR	Hu, Cy	0.007	0.659	0.188	0.465	Neg
AD-26109	CDS	Hu, Cy	0.025	0.156	0.172	0.410	Neg
AD-26218	CDS	Hu, Cy	0.026	0.376	0.243	0.566	Neg
AD-25894	3' UTR	Hu, Cy	0.004	0.378	0.293	0.307	Neg
AD-26740	CDS	Hu, Cy	0.006	0.511	0.227	0.330	Neg
AD-26158	CDS	Hu, Cy	0.033	0.347	0.227	0.398	Neg
AD-26682	CDS	Hu, Cy	0.007	0.484	0.297	0.923	Neg
AD-26034	CDS	Hu, Cy	0.009	0.673	0.267	0.656	Neg
AD-25944	3' UTR	Hu, Cy	0.007	0.633	0.264	0.589	Neg
AD-26800	CDS	Hu, Cy	0.025	0.449	0.240	0.815	Neg
AD-26108	CDS	Hu, Cy	0.03	0.437	0.305	0.880	Neg
AD-26752	CDS	Hu, Cy	0.042	0.518	0.396	0.500	Neg
AD-26918	3' UTR	Hu, Cy	0.029	0.371	0.345	0.965	Neg

[00846] In this table, the position is shown, wherein CDS indicates the coding segment (or open reading frame), and 3'UTR indicates the 3' untranslated region. The species forms of Beta-Catenin to which the RNAi agents match is also shown. Thus, AD-18983 matches each of the hman (Hu), cynomolgus (Cy), and Mouse (Mo) forms of Beta-Catenin. The estimated 24-hr average IC50 is shown (in nM). The cell viability in DLD1, LoVo, and LS411N cells is shown. For AD-18983, "0.258" indicates that at 1 nM at day 7, there was 25.8% cell viability of DLD1 cells, or 74.2% viability reduction. Similarly, there was 15.0% cell viability of LoVo cells (85.5% viability reduction) at 1 nM, and 5.4% cell viability (94.6% viability reduction) of LS411N cells (at 0.1 nM). PBMC indicates the peripheral blood mononuclear cell assay used as a test to measure potential immunogenicity of RNAi agents; "Neg" indicates that the RNAi agents did not illicit an immune response, as indicated by an increase in INF-α and TNF-α.

[00847] Thus, the following RNAi agents to Beta-Catenin demonstrated a significant reduction of cell viability in at least one colorectal cell line that depends on Beta-Catenin for growth: AD-18963-b2, AD-25894-b1, AD-25944-b1, AD-25951-b1, AD-26034-b1, AD-26108-b1, AD-26109-b1, AD-26156-b1, AD-26158-b1, AD-26218-b1, AD-26682-b1, AD-26740-b1, AD-26752-b1, AD-26800-b1, and AD-26918-b1.

[00848] **EQUIVALENTS**

[00849] A composition of embodiment 1 is a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

[00850] The composition of embodiment 1, wherein the composition further comprises a second RNAi agent to Beta-Catenin.

[00851] The composition of embodiment 1, wherein the antisense strand is 30 or fewer nucleotides in length.

[00852] The composition of embodiment 1, wherein the sense strand and the antisense strand form a duplex region 15 to 30 nucleotide pairs in length.

[00853] The composition of embodiment 1, wherein the antisense strand and the sense strand are independently 19 to 23 nucleotides in length.

[00854] The composition of embodiment 1, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00855] The composition of embodiment 1, wherein the RNAi agent comprises at least one modified backbone and/or at least one 2'-modified nucleotide.

[00856] The composition of embodiment 1, wherein the RNAi agent comprises:

a) at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or

b) at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or

c) at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or

d) at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[00857] The composition of embodiment 1, wherein the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00858] The composition of embodiment 1, wherein the RNAi agent comprises a blunt end.

[00859] The composition of embodiment 1, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[00860] The composition of embodiment 1, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[00861] The composition of embodiment 1, wherein the RNAi agent is ligated to one or more agent selected from: one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan,

chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00862] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 60% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00863] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 70% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00864] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 80% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00865] The composition of embodiment 1, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 90% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00866] The composition of embodiment 1, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[00867] The composition of embodiment 1, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[00868] The composition of embodiment 1, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[00869] A composition of embodiment 2 is a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent specific to Beta-Catenin provided in Table 1.

[00870] The composition of embodiment 2, wherein the composition comprises a second RNAi agent to Beta-Catenin.

[00871] The composition of embodiment 2, wherein the second strand is 30 or fewer nucleotides in length.

[00872] The composition of embodiment 2, wherein the first strand and the second strand form a duplex region 15 to 30 nucleotide pairs in length.

[00873] The composition of embodiment 2, wherein the first strand and the second strand are independently 19 to 23 nucleotides in length.

[00874] The composition of embodiment 2, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00875] The composition of embodiment 2, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

[00876] The composition of embodiment 2, wherein the RNAi agent comprises:

at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide;

and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

The composition of embodiment 2, wherein the RNAi agent comprises one or more 2'-modifications selected from the group consisting of:

2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00877] The composition of embodiment 2, wherein the RNAi agent comprises a blunt end.

[00878] The composition of embodiment 2, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[00879] The composition of embodiment 2, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand.

[00880] The composition of embodiment 2, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: one or more diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00881] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 60% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00882] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 70% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00883] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting

expression of the Beta-Catenin gene by at least about 80% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00884] The composition of embodiment 2, wherein the RNAi agent is capable of inhibiting expression of the Beta-Catenin gene by at least about 90% at a concentration of 10 nM in HeLa, GTL-16, or SK-BR-3 cells in vitro.

[00885] The composition of embodiment 2, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[00886] The composition of embodiment 2, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[00887] The composition of embodiment 2, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[00888] A method of embodiment 3 is a method comprising a method of treating a Beta-Catenin-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

[00889] The method of embodiment 3, wherein the Beta-Catenin-related disease is cancer, autoimmune, or a viral disease.

[00890] The method of embodiment 3, wherein the Beta-Catenin-related disease is cancer.

[00891] The method of embodiment 3, wherein the method further comprises the step of administering an additional treatment for cancer, autoimmune, or a viral disease.

[00892] The method of embodiment 3, wherein the composition comprises a second RNAi agent to Beta-Catenin.

[00893] The method of embodiment 3, wherein the method further comprises the step of administering an additional RNAi agent to Beta-Catenin.

[00894] The method of embodiment 3, further comprising the administration of an additional treatment.

[00895] The method of embodiment 3, wherein the additional treatment is a composition.

[00896] The method of embodiment 3, wherein the additional treatment is a method.

[00897] The method of embodiment 3, wherein the additional treatment and the RNAi agent can be administered in any order.

[00898] A method of embodiment 4 is a method comprising a method of inhibiting the expression of the Beta-Catenin gene in an individual, comprising the step of administering to the

individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

[00899] The method of embodiment 4, wherein the individual is afflicted with or susceptible to a Beta-Catenin-related disease.

[00900] The method of embodiment 4, wherein the Beta-Catenin-related disease is cancer, autoimmune, or a viral disease.

[00901] The method of embodiment 4, wherein the Beta-Catenin-related disease is cancer.

[00902] The method of embodiment 4, further comprising the administration of an additional treatment.

[00903] The method of embodiment 4, wherein the additional treatment is a composition.

[00904] The method of embodiment 4, wherein the additional treatment is a method.

[00905] The method of embodiment 4, wherein the additional treatment and the RNAi agent can be administered in any order.

[00906] A composition of embodiment 5 is a composition comprising a medicament for use in an RNAi formulation comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

[00907] Any composition above in a pharmaceutically effective formulation.

[00908] The composition according to embodiment 5, for use in a method of treating a Beta-Catenin-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to embodiment 1.

[00909] The use of a composition according to embodiment 5, in the manufacture of a medicament for the treatment of a Beta-Catenin-related disease.

[00910] The use of embodiment 5, wherein the Beta-Catenin-related disease is cancer, autoimmune, or a viral disease.

[00911] The composition of embodiment 5, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

[00912] The composition of embodiment 5, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

ADDITIONAL EQUIVALENTS

[00913] A composition of embodiment 6 is a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous

nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00914] The composition of embodiment 6, wherein the composition further comprises a second RNAi agent to Beta-ENaC.

[00915] The composition of embodiment 6, wherein the antisense strand is 30 or fewer nucleotides in length.

[00916] The composition of embodiment 6, wherein the sense strand and the antisense strand form a duplex region 15 to 30 nucleotide pairs in length.

[00917] The composition of embodiment 6, wherein the antisense strand and the sense strand are independently 19 to 23 nucleotides in length.

[00918] The composition of embodiment 6, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00919] The composition of embodiment 6, wherein the RNAi agent comprises at least one modified backbone and/or at least one 2'-modified nucleotide.

[00920] The composition of embodiment 6, wherein the RNAi agent comprises:

a) at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or

b) at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide; and/or

c) at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide; and/or

d) at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[00921] The composition of embodiment 6, wherein the RNAi agent comprises a 2'-modification selected from the group consisting of: 2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00922] The composition of cla embodiment 6, wherein the RNAi agent comprises a blunt end.

[00923] The composition of embodiment 6, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[00924] The composition of embodiment 6, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand of the RNAi agent.

[00925] The composition of embodiment 6, wherein the RNAi agent is ligated to one or more agent selected from: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin,

steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00926] The composition of embodiment 6, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 60% at a concentration of 10 nM in H441 cells *in vitro*.

[00927] The composition of embodiment 6, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 70% at a concentration of 10 nM in H441 cells *in vitro*.

[00928] The composition of embodiment 6, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 80% at a concentration of 10 nM in H441 cells *in vitro*.

[00929] The composition of embodiment 6, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 90% at a concentration of 10 nM in H441 cells *in vitro*.

[00930] The composition of embodiment 6, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[00931] The composition of embodiment 6, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[00932] The composition of embodiment 6, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[00933] A composition of embodiment 7 is a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00934] The composition of embodiment 7, wherein the composition comprises a second RNAi agent to Beta-ENaC.

[00935] The composition of embodiment 7, wherein the second strand is 30 or fewer nucleotides in length.

[00936] The composition of embodiment 7, wherein the first strand and the second strand form a duplex region 15 to 30 nucleotide pairs in length.

[00937] The composition of embodiment 7, wherein the first strand and the second strand are independently 19 to 23 nucleotides in length.

[00938] The composition of embodiment 7, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00939] The composition of embodiment 7, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

[00940] The composition of embodiment 7, wherein the RNAi agent comprises:

at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide;

and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[00941] The composition of embodiment 7, wherein the RNAi agent comprises one or more 2'-modifications selected from the group consisting of:

2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00942] The composition of embodiment 7, wherein the RNAi agent comprises a blunt end.

[00943] The composition of embodiment 7, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[00944] The composition of embodiment 7, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand.

[00945] The composition of embodiment 7, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00946] The composition of embodiment 7, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 60% at a concentration of 10 nM in H441 cells *in vitro*.

[00947] The composition of embodiment 7, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 70% at a concentration of 10 nM in H441 cells *in vitro*.

[00948] The composition of embodiment 7, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 80% at a concentration of 10 nM in H441 cells *in vitro*.

[00949] The composition of embodiment 7, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 90% at a concentration of 10 nM in H441 cells *in vitro*.

[00950] The composition of embodiment 7, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[00951] The composition of embodiment 7, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[00952] The composition of embodiment 7, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[00953] A method of embodiment 8 is a method of treating a Beta-ENaC-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00954] The method of embodiment 8, wherein the Beta-ENaC-related disease is cystic fibrosis, pseudohypoaldosteronism type 1 (PHA1), Liddle's syndrome, hypertension, alkalosis, hypokalemia, and/or obesity-associated hypertension.

[00955] The method of embodiment 8, wherein the Beta-ENaC-related disease is cystic fibrosis.

[00956] The method of embodiment 8, wherein the method further comprises the step of administering an additional treatment for cystic fibrosis, pseudohypoaldosteronism type 1 (PHA1), Liddle's syndrome, hypertension, alkalosis, hypokalemia, and/or obesity-associated hypertension.

[00957] The method of embodiment 8, wherein the composition comprises a second RNAi agent to Beta-ENaC.

[00958] The method of embodiment 8, wherein the method further comprises the step of administering an additional RNAi agent to Beta-ENaC.

[00959] The method of embodiment 8, further comprising the administration of an additional treatment.

[00960] The method of embodiment 8, wherein the additional treatment is a composition.

[00961] The method of embodiment 8, wherein the additional treatment is a method.

[00962] The method of embodiment 8, wherein the additional treatment and the RNAi agent can be administered in any order.

[00963] A method of embodiment 9 is a method of inhibiting the expression of the Beta-ENaC gene in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00964] The method of embodiment 9, wherein the individual is afflicted with or susceptible to a Beta-ENaC-related disease.

[00965] The method of embodiment 9, wherein the Beta-ENaC-related disease is cystic fibrosis, pseudohypoaldosteronism type 1 (PHA1), Liddle's syndrome, hypertension, alkalosis, hypokalemia, and/or obesity-associated hypertension.

[00966] The method of embodiment 9, wherein the Beta-ENaC-related disease is cystic fibrosis.

[00967] The method of embodiment 9, further comprising the administration of an additional treatment.

[00968] The method of embodiment 9, wherein the additional treatment is a composition.

[00969] The method of embodiment 9, wherein the additional treatment is a method.

[00970] The method of embodiment 9, wherein the additional treatment and the RNAi agent can be administered in any order.

[00971] A medicament for use in an RNAi formulation comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00972] A composition of embodiment 10 is a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand comprises the sequence of the first strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00973] The composition of embodiment 10, wherein the composition comprises a second RNAi agent to Beta-ENaC.

[00974] The composition of embodiment 10, wherein the second strand is 30 or fewer nucleotides in length.

[00975] The composition of embodiment 10, wherein the first strand and the second strand form a duplex region 15 to 30 nucleotide pairs in length.

[00976] The composition of embodiment 10, wherein the first strand and the second strand are independently 19 to 23 nucleotides in length.

[00977] The composition of embodiment 10, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00978] The composition of embodiment 10, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

[00979] The composition of embodiment 10, wherein the RNAi agent comprises:

at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide;

and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[00980] The composition of embodiment 10, wherein the RNAi agent comprises one or more 2'-modifications selected from the group consisting of:

2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[00981] The composition of embodiment 10, wherein the RNAi agent comprises a blunt end.

[00982] The composition of embodiment 10, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[00983] The composition of embodiment 10, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand.

[00984] The composition of embodiment 10, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[00985] The composition of embodiment 10, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 60% at a concentration of 10 nM in H441 cells in vitro.

[00986] The composition of embodiment 10, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 70% at a concentration of 10 nM in H441 cells in vitro.

[00987] The composition of embodiment 10, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 80% at a concentration of 10 nM in H441 cells in vitro.

[00988] The composition of embodiment 10, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 90% at a concentration of 10 nM in H441 cells in vitro.

[00989] The composition of embodiment 10, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[00990] The composition of embodiment 10, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[00991] The composition of embodiment 10, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[00992] A composition of embodiment 11 is a composition comprising a RNAi agent comprising a first strand and a second strand, wherein the sequence of the first strand is the sequence of the first strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[00993] The composition of embodiment 11, wherein the composition comprises a second RNAi agent to Beta-ENaC.

[00994] The composition of embodiment 11, wherein the second strand is 30 or fewer nucleotides in length.

[00995] The composition of embodiment 11, wherein the first strand and the second strand form a duplex region 15 to 30 nucleotide pairs in length.

[00996] The composition of embodiment 11, wherein the first strand and the second strand are independently 19 to 23 nucleotides in length.

[00997] The composition of embodiment 11, wherein the RNAi agent comprises a modification that causes the RNAi agent to have increased stability in a biological sample or environment.

[00998] The composition of embodiment 11, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.

[00999] The composition of embodiment 11, wherein the RNAi agent comprises:

at least one 5'-uridine-adenine-3' (5'-ua-3') dinucleotide, wherein the uridine is a 2'-modified nucleotide; and/or at least one 5'-uridine-guanine-3' (5'-ug-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide;

and/or at least one 5'-cytidine-adenine-3' (5'-ca-3') dinucleotide, wherein the 5'-

cytidine is a 2'-modified nucleotide;

and/or at least one 5'-uridine-uridine-3' (5'-uu-3') dinucleotide, wherein the 5'-uridine is a 2'-modified nucleotide.

[001000] The composition of embodiment 11, wherein the RNAi agent comprises one or more 2'-modifications selected from the group consisting of:

2'-deoxy, 2'-deoxy-2'-fluoro, 2'-O-methyl, 2'-O-methoxyethyl (2'-O-MOE), 2'-O-aminopropyl (2'-O-AP), 2'-O-dimethylaminoethyl (2'-O-DMAOE), 2'-O-dimethylaminopropyl (2'-O-DMAP), 2'-O-dimethylaminoethyloxyethyl (2'-O-DMAEOE), and 2'-O-N-methylacetamido (2'-O-NMA).

[001001] The composition of embodiment 11, wherein the RNAi agent comprises a blunt end.

[001002] The composition of embodiment 11, wherein the RNAi agent comprises an overhang having 1 to 4 unpaired nucleotides.

[001003] The composition of embodiment 11, wherein the RNAi agent comprises an overhang at the 3'-end of the antisense strand.

[001004] The composition of embodiment 11, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

[001005] The composition of embodiment 11, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 60% at a concentration of 10 nM in H441 cells in vitro.

[001006] The composition of embodiment 11, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 70% at a concentration of 10 nM in H441 cells in vitro.

[001007] The composition of embodiment 11, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 80% at a concentration of 10 nM in H441 cells in vitro.

[001008] The composition of embodiment 11, wherein the RNAi agent is capable of inhibiting expression of the Beta-ENaC gene by at least about 90% at a concentration of 10 nM in H441 cells in vitro.

[001009] The composition of embodiment 11, wherein the RNAi has an EC50 of no more than about 0.1 nM.

[001010] The composition of embodiment 11, wherein the RNAi has an EC50 of no more than about 0.01 nM.

[001011] The composition of embodiment 11, wherein the RNAi has an EC50 of no more than about 0.001 nM.

[001012] A composition of embodiment 12 is any composition above in a pharmaceutically effective formulation.

[001013] The composition according to embodiment 12, for use in a method of treating a Beta-ENaC-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-ENaC provided in Table 1.

[001014] The use of a composition according to embodiment 12, in the manufacture of a medicament for the treatment of a Beta-ENaC-related disease.

[001015] The use of a composition according to embodiment 12, wherein the Beta-ENaC-related disease is cystic fibrosis, pseudohypoaldosteronism type 1 (PHA1), Liddle's syndrome, hypertension, alkalosis, hypokalemia, and/or obesity-associated hypertension.

[001016] The composition of embodiment 12, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

[001017] The composition of embodiment 12, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

[001018] Unless defined otherwise, the technical and scientific terms used herein have the same meaning as that usually understood by a specialist familiar with the field to which the disclosure belongs.

[001019] Unless indicated otherwise, all methods, steps, techniques and manipulations that are not specifically described in detail can be performed and have been performed in a manner known per se, as will be clear to the skilled person. Reference is for example again made to the standard handbooks and the general background art mentioned herein and to the further references cited therein. Unless indicated otherwise, each of the references cited herein is incorporated in its entirety by reference.

[001020] Claims to the invention are non-limiting and are provided below.

[001021] Although particular embodiments and claims have been disclosed herein in detail, this has been done by way of example for purposes of illustration only, and is not intended to be limiting with respect to the scope of the appended claims, or the scope of subject matter of claims of any

corresponding future application. In particular, it is contemplated by the inventors that various substitutions, alterations, and modifications may be made to the disclosure without departing from the spirit and scope of the disclosure as defined by the claims. The choice of nucleic acid starting material, clone of interest, or library type is believed to be a matter of routine for a person of ordinary skill in the art with knowledge of the embodiments described herein. Other aspects, advantages, and modifications considered to be within the scope of the following claims. Those skilled in the art will recognize or be able to ascertain, using no more than routine experimentation, many equivalents of the specific embodiments of the invention described herein. Such equivalents are intended to be encompassed by the following claims. Redrafting of claim scope in later filed corresponding applications may be due to limitations by the patent laws of various countries and should not be interpreted as giving up subject matter of the claims.

We claim:

1. A composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.
2. The composition of claim 1, wherein the composition further comprises a second RNAi agent to Beta-Catenin.
3. The composition of claim 1, wherein the RNAi agent comprises at least one modified backbone and/or at least one 2'-modified nucleotide.
4. The composition of claim 1, wherein the RNAi agent is ligated to one or more agent selected from: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.
5. A composition comprising a RNAi agent comprising a first strand and a second strand, wherein the first strand and second strand comprise at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the first and second strand, respectively, of a RNAi agent specific to Beta-Catenin provided in Table 1.
6. The composition of claim 1, wherein the composition comprises a second RNAi agent to Beta-Catenin.
7. The composition of claim 1, wherein the RNAi agent comprises a phosphorothioate and/or a 2'-modified nucleotide.
8. The composition of claim 1, wherein the RNAi agent is ligated to one or more agents, the agent selected from a: diagnostic compound, reporter group, cross-linking agent, nuclease-resistance conferring moiety, natural or unusual nucleobase, lipophilic molecule, cholesterol, lipid, lectin, steroid, uvaol, hecigenin, diosgenin, terpene, triterpene, sarsasapogenin, Friedelin, epifriedelanol-derivatized lithocholic acid, vitamin, carbohydrate, dextran, pullulan, chitin, chitosan, synthetic carbohydrate, oligo lactate 15-mer, natural polymer, low- or medium-molecular weight polymer, inulin, cyclodextrin, hyaluronic acid, protein, protein-binding agent, integrin-targeting molecule, polycationic, peptide, polyamine, peptide mimic, and/or transferrin.

9. A method of treating a Beta-Catenin-related disease in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

10. The method of claim 9, wherein the Beta-Catenin-related disease is selected from: adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, and chronic wounds and impaired wound healing.

11. The method of claim 9, wherein the method further comprises the step of administering an additional treatment for adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, and/or chronic wounds and impaired wound healing.

12. The method of claim 11, wherein the method further comprises the step of administering an additional RNAi agent to Beta-Catenin.

13. A method of inhibiting the expression of the Beta-Catenin gene in an individual, comprising the step of administering to the individual a therapeutically effective amount of a composition comprising a RNAi agent comprising a sense strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

14. The method of claim 13, wherein the Beta-Catenin-related disease is adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, and chronic wounds and/or impaired wound healing.

15. A medicament for use in an RNAi formulation comprising a RNAi agent comprising a sense

strand and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1.

16. Any composition above in a pharmaceutically effective formulation.

17. The composition according to claim 1, for use in a method of treating a Beta-Catenin-related disease in an individual, the method comprising the step of administering to the individual a therapeutically effective amount of a composition according to claim 1.

18. The use of a composition according to claim 1, in the manufacture of a medicament for the treatment of a Beta-Catenin-related disease.

19. The composition of claim 1, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

20. The composition of claim 5, wherein all the pyrimidines are 2' O-methyl-modified nucleotides.

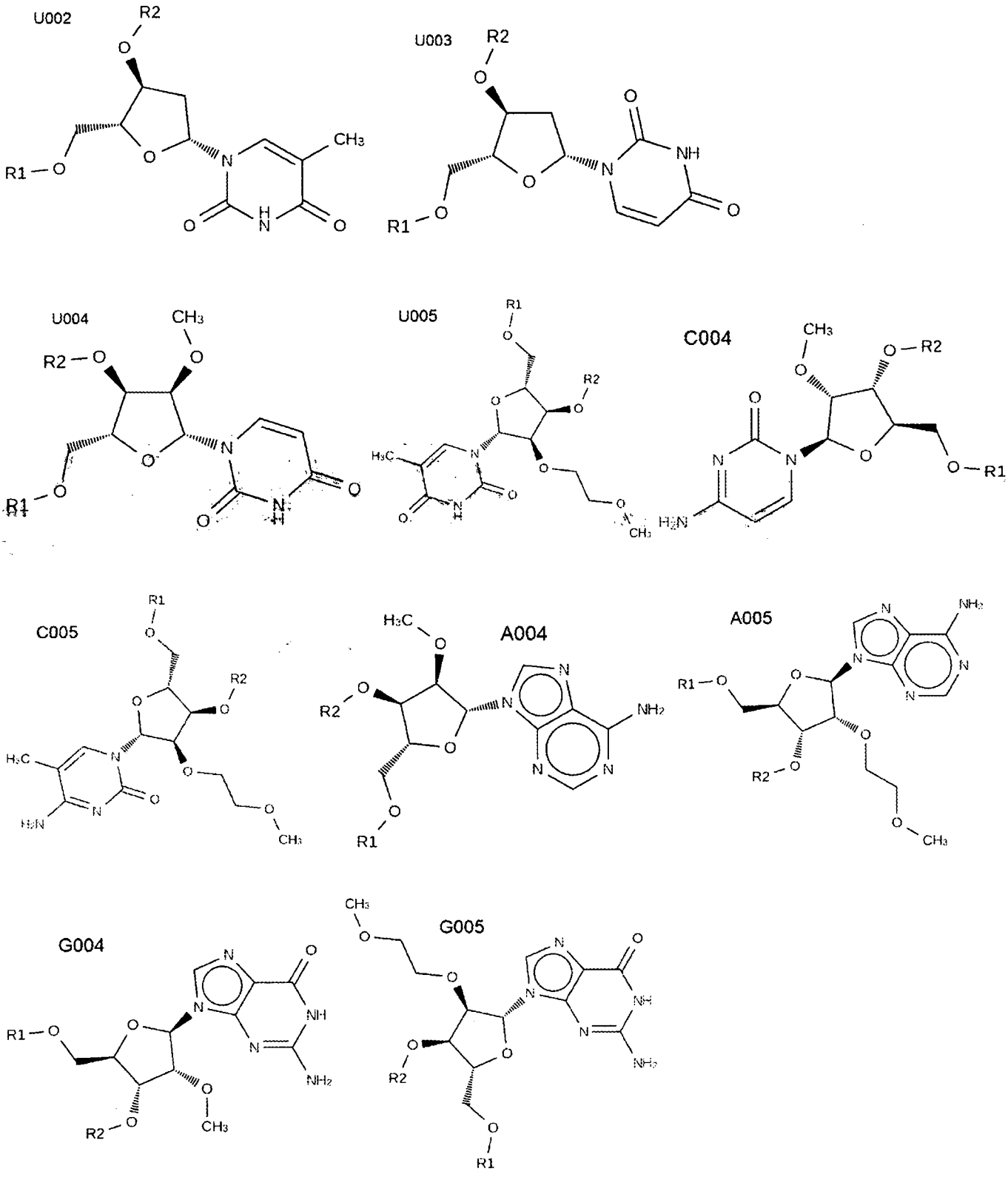


FIG. 1

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[Continued on next page]

(54) Title: RNAI AGENTS TO TREAT BETA-CATENIN RELATED DISEASES

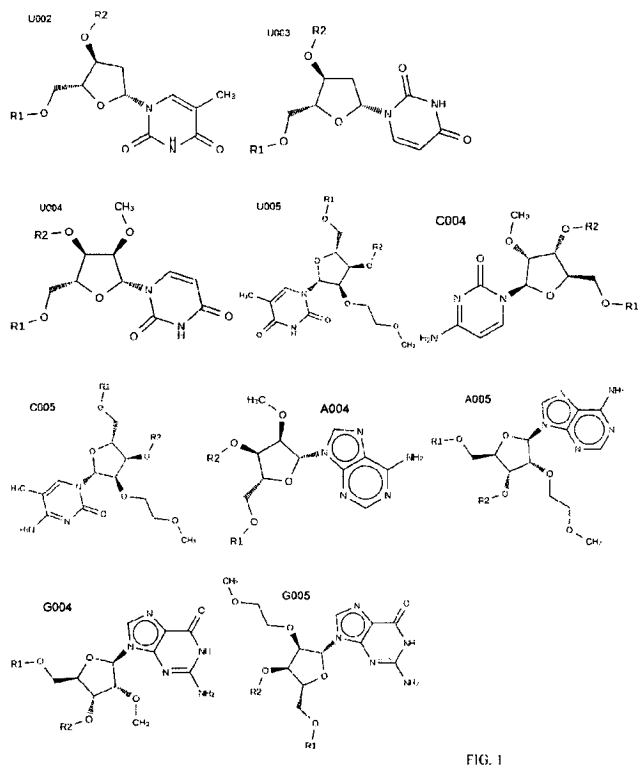


FIG. 1

(57) Abstract: The present disclosure relates to RNAi agents useful in methods of treating Beta-Catenin-related diseases such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to Beta-Catenin.

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(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2008/156702 A2 (CEQUENT PHARMACEUTICALS, INC. [US]; FRUEHAUF; VAZE; LAROUX; SAUER) 24 December 2008 (2008-12-24)	1,2,5,6, 9,13, 15-18
Y	page 43 - page 44; sequences 61, 62, 64, 67, 68, 69 the whole document	3,4,7,8, 10-12, 14,19,20

Y	WO 2006/031977 A2 (UNIVERSITY OF CALIFORNIA [US]; HEBROK; PASCA DI MAGLIANO) 23 March 2006 (2006-03-23) page 44 the whole document	3,4,7,8, 10-12, 14,19,20

Y	WO 2010/146055 A1 (INSTITUT CURIE [FR]; C.N.R.S. [FR]; UNIVERSITÉ PARIS-SUD 11 [FR]) 23 December 2010 (2010-12-23) page 34 the whole document	3,4,7,8, 10-12, 14,19,20

☐ Further documents are listed in the continuation of Box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
8 May 2013	02/08/2013

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2013/050159

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2008156702 A2	24-12-2008	EP 2173875 A2	14-04-2010
		EP 2176412 A2	21-04-2010
		US 2008311081 A1	18-12-2008
		US 2010092438 A1	15-04-2010
		US 2010239546 A1	23-09-2010
		WO 2008156661 A2	24-12-2008
		WO 2008156702 A2	24-12-2008
WO 2006031977 A2	23-03-2006	US 2009012018 A1	08-01-2009
		WO 2006031977 A2	23-03-2006
WO 2010146055 A1	23-12-2010	EP 2266550 A1	29-12-2010
		WO 2010146055 A1	23-12-2010

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20(partially)

A composition comprising a RNAi agent comprising a sense and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1, targeting position 2500 (AD-18892) and RNAi agents overlapping thereto (AD-18908, AD-18919, AD-18944, AD-18967, AD-19042, AD-19077, AD-26814, AD-26815, AD-26816, AD-26817).

2-816. claims: 1-20(partially)

A composition comprising a RNAi agent comprising a sense and an antisense strand, wherein the antisense strand comprises at least 15 contiguous nucleotides differing by 0, 1, 2, or 3 nucleotides from the antisense strand of a RNAi agent specific to Beta-Catenin provided in Table 1, taken individually, wherein invention 2 relates to duplex AD-18893, ... invention 816 relates to duplex SETI-895. The ISA will take into consideration overlapping molecules and will regroup the RNAi agents listed above accordingly, in case the Applicant paid additional search fees.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. (means)

   [ ] on paper

   [X] in electronic form

   b. (time)

   [ ] in the international application as filed

   [ ] together with the international application in electronic form

   [X] subsequently to this Authority for the purpose of search

2. [X] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-20(partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

(19)中华人民共和国国家知识产权局

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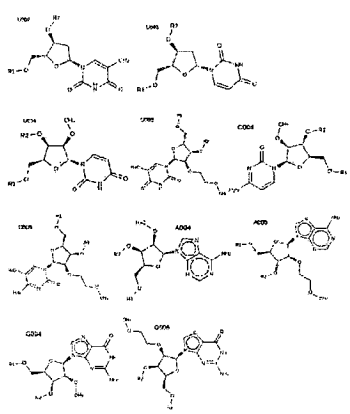
权利要求书2页 说明书298页 附图1页

(54)发明名称

治疗β-联蛋白相关疾病的有机组合物

(57)摘要

本公开涉及RNAi剂，所述RNAi剂可用于使用治疗有效量的针对β-联蛋白的RNAi剂治疗β-联蛋白相关疾病如结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮和慢性伤口以及受损的伤口愈合以及相似病和相关疾病的方法中。



CN 104302768 A

1. 一种组合物，其包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

2. 根据权利要求 1 所述的组合物，其中组合物还包含针对 β-联蛋白的第二 RNAi 剂。

3. 根据权利要求 1 所述的组合物，其中 RNAi 剂包含至少一条修饰的主链和/或至少一个 2' 修饰的核苷酸。

4. 根据权利要求 1 所述的组合物，其中 RNAi 剂连接至选自以下的一种或多种物质：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和/或转铁蛋白。

5. 一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链和第二链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的第一链和第二链分别差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

6. 根据权利要求 1 所述的组合物，其中组合物包含针对 β-联蛋白的第二 RNAi 剂。

7. 根据权利要求 1 所述的组合物，其中 RNAi 剂包含硫代磷酸酯和/或 2'-修饰的核苷酸。

8. 根据权利要求 1 所述的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和/或转铁蛋白。

9. 一种治疗个体中 β-联蛋白相关疾病的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

10. 根据权利要求 9 所述的方法，其中 β-联蛋白相关疾病选自：结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮和慢性伤口以及受损的伤口愈合。

11. 根据权利要求 9 所述的方法，其中所述方法还包括步骤：对结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮和/或慢性伤口以及

受损的伤口愈合施用额外的治疗。

12. 根据权利要求 11 所述的方法，其中方法还包括步骤：施用针对 β－联蛋白的额外 RNAi 剂。

13. 一种抑制个体中 β－联蛋白基因表达的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β－联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

14. 根据权利要求 13 所述的方法，其中 β－联蛋白相关疾病是结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、和慢性伤口和／或受损的伤口愈合。

15. 一种用于 RNAi 制剂中的药物，所述 RNAi 制剂包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β－联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

16. 以上的任何组合物，处于药学有效的制剂中。

17. 根据权利要求 1 所述的组合物，用于治疗个体中 β－联蛋白相关疾病的方法中，所述方法包括步骤：向所述个体施用治疗有效量的根据权利要求 1 所述的组合物。

18. 根据权利要求 1 所述的组合物的用途，用于制造治疗 β－联蛋白相关疾病的药物。

19. 根据权利要求 1 所述的组合物，其中全部嘧啶均是 2’O－甲基修饰的核苷酸。

20. 根据权利要求 5 所述的组合物，其中全部嘧啶均是 2’O－甲基修饰的核苷酸。

治疗 β-联蛋白相关疾病的有机组合物

[0001] 借助分泌型糖脂蛋白 Wnt 家族的信号传导是胚胎发育和组织稳态期间指导细胞增殖、细胞极性和细胞命运决定的基础机制之一。因此，Wnt 途径中的突变经常与人出生缺陷、癌症和其他疾病相关。一个关键 Wnt 途径是规范 Wnt 信号传导途径。

[0002] 转录辅助激活物 β-联蛋白是这条途径中的分子节点。在 Wnt 不存在的情况下，胞质 β-联蛋白蛋白质总是因轴蛋白复合体的作用而降解，所述轴蛋白复合体由支架蛋白-轴蛋白、肿瘤抑制物-腺瘤结肠息肉基因产物 (APC)、酪蛋白激酶 1(CK1) 和糖原合酶激酶 3(GSK3) 组成。CK1 和 GSK3 依次地磷酸化 β-联蛋白的氨基端区域，导致 β-联蛋白由 β-Trcp(E3 泛素连接酶亚基）识别并随后 β-联蛋白泛素化和蛋白酶体降解。

[0003] β-联蛋白的这种持续消除防止 β-联蛋白抵达细胞核，并且 Wnt 靶基因因而被结合 DNA 的 T 细胞因子 / 淋巴样增进因子 (TCF/LEF) 蛋白家族阻遏。当 Wnt 配体与 7 次跨膜卷曲蛋白 (Fz 或 Fzd) 受体和其辅助受体（低密度脂蛋白受体-相关蛋白 6(LRP6)）或其近亲 LRP5 结合时，Wnt/β-联蛋白途径激活。类似的 Wnt-Fz-LRP6 复合物的形成，连同支架蛋白蓬乱蛋白 (Dishevelled)(Dvl) 的再招募一起，导致 LRP6 磷酸化以及轴蛋白复合体激活和再招募至受体。这些事件导致抑制轴蛋白介导的 β-联蛋白磷酸化并且因而稳定 β-联蛋白，所述 β-联蛋白积累、穿行至细胞核以与 TCF/LEF 形成复合体并激活 Wnt 靶基因表达。

[0004] 鉴于 Wnt/β-联蛋白信号传导在发育和稳态中至关重要的作用，Wnt 途径组分的突变与许多病症和疾病相关毫不令人惊讶。McDonald 等人，2009Dev. Cell 17:9-26。已经充分记录失调的 Wnt/β-联蛋白信号传导与癌症相关、尤其与结直肠癌相关。Polakis 2007. Curr. Opin. Genet. Dev. 17:45-51。因 APC 缺乏或阻止 β-联蛋白降解的 β-联蛋白突变所致的组成型激活的 β-联蛋白信号传导导致造成细胞预先倾向于形成肿瘤的过多干细胞更新 / 增殖。实际上，干细胞中 APC 缺失或 β-联蛋白激活对于肠道瘤形成是必需的。Fuchs 2009Cell 137:811-819。

[0005] β-联蛋白中的突变、β-联蛋白的水平和细胞区室化改变和 Wnt/β-联蛋白途径的其他畸变因此直接或间接地参与许多疾病。在 β-联蛋白相关的一些癌症中，肿瘤生长需要 β-联蛋白，但是 β-联蛋白不扩增、过量表达或错误定位。

[0006] 需要与 β-联蛋白相关疾病相关的治疗。

发明简述

[0007] 本公开提供用于抑制靶基因 β-联蛋白的针对 β-联蛋白的 RNAi(RNA 干扰）剂，所述 RNAi 剂可用于治疗 β-联蛋白相关疾病，例如：结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突 (taste papillae)、皮肤癌、毛基质瘤、间变性甲状腺癌 (anaplastic thyroid carcinoma)、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合，以及相似和相关的疾病。本公开还涵盖一种治疗患有至少部分由 β-联蛋白表达介导的病态的人类受试者的方法，所述方法包括步骤：向受试者施用治疗有效量的针对 β-联蛋白的 RNAi 剂。

[0008] 本公开提供可用于减少受试者（例如哺乳动物，如人）中 β-联蛋白水平的特异性 RNAi 剂和方法。本公开特别地提供包含 β-联蛋白的至少 15 个或更多个连续核苷酸的双链 RNAi 剂。具体而言，本公开提供包含有义链和反义链的物质，其中所述有义链和/或反义链包含与例如表 1 中或本文中他处提供的 RNAi 剂及其修饰变体和未修饰变体的那些序列差异 0、1、2 或 3 个核苷酸的 15 个或更多个连续核苷酸的序列。未修饰的序列有时称作“通用序列 (generic)”。本公开还提供包含有义链和反义链的物质，其中所述有义链和/或反义链包含与例如表 1 中或本文中他处提供的 RNAi 剂及其修饰变体和未修饰变体的那些序列差异 0、1、2 或 3 个核苷酸的 19 个或更多个连续核苷酸的序列。有义链和反义链可以是连续的，或共价结合，例如，借助环或接头共价结合。在一个实施方案中，RNAi 剂特别可以包含每条链小于约 30 个核苷酸，例如，如 17 至 23 个核苷酸，18 至 22 个核苷酸，17 至 23 个核苷酸，和/或 19 至 21 个核苷酸，和/或 19 至 30 个核苷酸和/或如例如在表 1、2、3、4、5、6、7、8 和/或 9 中或本文中他处提供的那些核苷酸。

[0009] 双链 RNAi 剂质可以具有 0、1 或 2 个平末端，和/或从一个末端或 3’末端和/或 5’末端具有含 1、2、3 个或 4 个核苷酸（即，1 至 4 个核苷酸）的突出端。双链 RNAi 剂也可以任选地包含一个或两个 3’帽结构和/或一个或多个修饰的核苷酸。如本文中提供的序列的修饰变体包括这些变体，所述变体否则相同，但是含有天然存在的核苷酸对相应修饰核苷酸置换。

[0010] 另外，RNAi 剂可以仅含有天然存在的核糖核苷酸亚单位，或针对一个或多个替换核苷酸亚单位的糖、磷酸酯或碱基的一个或多个修饰，无论它们是否包含核糖核苷酸亚单位或脱氧核糖核苷酸亚单位。在一个实施方案中，公开 RNAi 剂的修饰变体具有替换尿苷的胸苷（作为 RNA，或优选地，DNA）。在一个实施方案中，公开 RNAi 剂的修饰变体包括这些 RNAi 剂，所述 RNAi 剂具有相同的序列（例如，相同碱基序列），但是具有针对一个或多个核苷酸亚基的糖、磷酸酯或碱基中一者或多者的一个或多个修饰。在一个实施方案中，所述修饰改善 RNAi 剂的功效、稳定性（例如，针对血清和/或肠液中的核酸酶）和/或降低免疫原性。本公开的一个方面涉及包含至少一个非天然核碱基 (nucleobase) 的双链寡核苷酸。在某些实施方案中，非天然核碱基是二氟甲苯基、硝基吲哚基、硝基吡咯基或硝基咪唑基。在一个特定实施方案中，非天然核碱基是二氟甲苯基。在某些实施方案中，两条寡核苷酸链中仅一条链含有非天然核碱基。在某些实施方案中，两条寡核苷酸链均含有非天然核碱基。

[0011] RNAi 剂可以任选地连接至配体，例如胆固醇或其衍生物，其中选择所述配体以改善 RNAi 剂的一种或多种特征，例如，稳定性、分布和/或细胞摄入。RNAi 剂可以是分离的或是用于本文所述方法的药物组合物的部分。药物组合物可以任选地包含两个或更多个 RNAi 剂，每一种涉及 β-联蛋白 mRNA 的相同或不同区段。任选地，药物组合物还可以包含用于任何 β-联蛋白相关疾病的任何已知治疗或与其联合使用。

[0012] 本公开还提供了用于减少细胞中 β-联蛋白 mRNA 水平的方法，特别在以 β-联蛋白过量表达或过多活性为特征的疾病情况下。这类方法包括向细胞施用一种或多种本公开的 RNAi 剂的步骤，如下文进一步描述。本发明的方法利用参与 RNA 干扰的细胞机制以选择性降解细胞中的靶 RNA，并且由使细胞与本公开的一种 RNAi 剂接触的步骤组成。本公开还涵盖一种治疗患有至少部分由 β-联蛋白表达、过量表达、过多活性或不恰当细胞区室化介导的病态的人类受试者的方法，所述方法包括步骤：向受试者施用治疗有效量的针对

β-联蛋白的 RNAi 剂。额外的方法涉及其中病情进展（例如，肿瘤生长）需要 β-联蛋白的病态，虽然 β-联蛋白未扩增、过量表达或错误定位。这类方法可以对细胞直接进行或可以通过向细胞或受试者施用本公开的一种或多种 RNAi 剂/药物组合物，而对哺乳动物受试者进行。减少细胞中的靶 β-联蛋白 RNA 导致所产生的编码的 β-联蛋白的量减少。在生物中，这种可以导致恢复 Wnt/β-联蛋白途径中的平衡，和/或阻止 β-联蛋白积累，和/或恢复 β-联蛋白的恰当细胞区室化，和/或 β-联蛋白活性和/或表达减少，和/或阻止 β-联蛋白介导的 Wnt 相关基因（如原癌基因 c-myc）激活，和/或改善、治疗和/或预防 β-联蛋白相关疾病。在 β-联蛋白相关的一些癌症中，肿瘤生长需要 β-联蛋白，但是 β-联蛋白不扩增、过量表达或错误定位。β-联蛋白表达水平或活性的减少因此应当限制肿瘤生长。

[0013] 本公开的方法和组合物，例如，该方法和 β-联蛋白 RNAi 剂组合物，可以以本文所述的任何剂量和/或制剂以及以本文所述的任何施用途径一起使用。

[0014] 在附图和下文描述中阐述本公开的一个或多个实施方案的详细内容。多种实施方案（例如，可以使用的 RNAi 剂的序列、修饰、末端帽结构、组合、配体、额外治疗或方法等）的不相互排斥的要素可以彼此组合。相互排斥的组合例如包括以下事实：包含两条链的 RNAi 剂按定义不能具有两个平末端和两个突出端。另外，任何 RNAi 剂序列可以与本文中公开的任何修饰或末端帽结构的集合组合，条件是该组合的要素不相互排他的。修饰、5' 末端帽结构和/或 3' 末端帽结构的任何组合可以随本文中公开的任何 RNAi 剂序列一起使用。任何 RNAi 剂可以与任何其他 RNAi 剂或其他治疗组合物或方法组合。本公开的其他特征、目的和优点将从本说明书、附图并从权利要求书中显而易见。

附图简述

[0015] 图 1 显示各种修饰的核苷酸：本文中公开了可以在 RNAi 剂中使用的 U002、U003、U004、U005、C004、C005、A004、A005、G005 和 G004。U002 表示作为 DNA 的 2'-脱氧胸苷。U003 表示 2'-脱氧尿苷。U004 表示具有带 2'-O-甲基修饰的 U 碱基的核苷酸。U005 表示带 2'-O-甲氧乙基（MOE）修饰的 U 碱基。C004 表示带 2'-O-甲基修饰的 C 碱基。C005 表示带 2'-O-甲氧乙基修饰的 C 碱基。A004 表示带 2'-O-甲基修饰的 A 碱基。A005 表示带 2'-O-甲氧乙基修饰的 A 碱基。G005 表示带 2'O-甲基修饰的 G 碱基。G004 表示带 2'O-甲基修饰的 G 碱基。以符号 U002，U003，U004 等书写的多核苷酸序列有时前缀有“X”（表示序列的起点），并且有时在碱基之间具有“p”，表示核苷之间的磷酸二酯键。

发明详述

[0016] 本公开涵盖用于抑制靶基因 β-联蛋白的针对 β-联蛋白的 RNAi 剂，所述 RNAi 剂可用于治疗 β-联蛋白相关疾病（例如，与 β-联蛋白中的突变和/或 β-联蛋白表达、区室化、水平和/或活性改变相关的疾病，和/通过调节 β-联蛋白的表达、水平和/或活性可治疗的疾病），如结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合，以及相似和相关的疾病。在 β-联蛋白相关的一些癌症中，肿瘤生长需要 β-联蛋白，但是 β-联蛋白不扩增、过量表达或错误定位。β-联蛋白表达水平或活性的减少因此应当限制肿瘤生长。本公开还涵盖一种治疗

患有至少部分由 β-联蛋白表达介导的病态的人类受试者的方法，所述方法包括步骤：向受试者施用治疗有效量的针对 β-联蛋白的 RNAi 剂。

[0017] 本公开的多种实施方案包括：

[0018] 包含本文所述的 RNAi 剂的反义链的 RNAi 剂。

[0019] 在一个实施方案中，本公开涉及一种组合物，其包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与例如表 1、2、3、4、5、6、7、8 和 / 或 9 中提供的针对 β-联蛋白特异的 RNAi 剂（或对 β-联蛋白特异的重叠性 RNAi 剂的任何集合）的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含了含有有义链和反义链的 RNAi 剂，其中有义链包含与来自本文提供的任何序列中的 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链包含与本文提供的任何 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，并且第二链包含与本文提供的任何 RNAi 剂的第二链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。在另一个实施方案中，本公开涉及一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链的序列包含本文提供的任何 RNAi 剂的第一链的序列。在另一个实施方案中，本公开涉及一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链的序列是本文提供的任何 RNAi 剂的第一链的序列。在另一个实施方案中，本公开涉及一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列包含本文提供的任何 RNAi 剂的第一链和 / 或第二链的序列。在另一个实施方案中，本公开涉及一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列是本文提供的任何 RNAi 剂的第一链和 / 或第二链的序列。在这些多样的实施方案中，RNAi 剂用于抑制靶基因 β-联蛋白。

[0020] 特定的双链体包括表 1 中列出的未修饰的序列和示例性修饰序列。除所描述的示例修饰之外，可以使用提供的核苷酸序列产生其他修饰的变体。

[0021] 表 1. 针对 β-联蛋白的 RNAi 剂的 SEQ ID NOs

[0022] 在表 1 中提供是各种 β-联蛋白 RNAi 双链体的名称 (nickname)；未修饰的有义序列和反义序列和 SEQ ID NOs；示例性修饰的有义序列和反义序列和 SEQ ID NOs；和 RNAi 剂在 β-联蛋白基因内部的位置。

	未修饰的序列		修饰序列的例子		
双链体	有义 SEQ ID NO:	反义 SEQ ID NO:	有义 SEQ ID NO:	反义 SEQ NO:	位置
AD-18892	4112	4771	1	660	2500
AD-18893	4113	4772	2	661	1659
AD-18894	4114	4773	3	662	3038
AD-18895	4115	4774	4	663	2096
AD-18896	4116	4775	5	664	265
AD-18897	4117	4776	6	665	1797
AD-18898	4118	4777	7	666	2587
AD-18899	4119	4778	8	667	1541
AD-18900	4120	4779	9	668	2391
AD-18901	4121	4780	10	669	954
AD-18902	4122	4781	11	670	2908
AD-18903	4123	4782	12	671	3104
AD-18904	4124	4783	13	672	1665
AD-18905	4125	4784	14	673	2594
AD-18906	4126	4785	15	674	3147
AD-18907	4127	4786	16	675	2592
AD-18908	4128	4787	17	676	2507
AD-18909	4129	4788	18	677	2325
AD-18910	4130	4789	19	678	2326

AD-18911	4131	4790	20	679	577
AD-18912	4132	4791	21	680	2116
AD-18913	4133	4792	22	681	2708
AD-18914	4134	4793	23	682	2912
AD-18915	4135	4794	24	683	2704
AD-18916	4136	4795	25	684	3146
AD-18917	4137	4796	26	685	1542
AD-18918	4138	4797	27	686	621
AD-18919	4139	4798	28	687	2505
AD-18920	4140	4799	29	688	2590
AD-18921	4141	4800	30	689	3099
AD-18922	4142	4801	31	690	2591
AD-18923	4143	4802	32	691	2112
AD-18925	4144	4803	33	692	366
AD-18926	4145	4804	34	693	2479
AD-18927	4146	4805	35	694	1502
AD-18928	4147	4806	36	695	2073
AD-18929	4148	4807	37	696	2702
AD-18930	4149	4808	38	697	1774
AD-18931	4150	4809	39	698	708
AD-18932	4151	4810	40	699	1667
AD-18933	4152	4811	41	700	2629
AD-18934	4153	4812	42	701	2114
AD-18935	4154	4813	43	702	2706
AD-18936	4155	4814	44	703	2899
AD-18937	4156	4815	45	704	1639
AD-18938	4157	4816	46	705	1638
AD-18939	4158	4817	47	706	2906
AD-18940	4159	4818	48	707	3145
AD-18941	4160	4819	49	708	2390
AD-18942	4161	4820	50	709	2707
AD-18943	4162	4821	51	710	1668
AD-18944	4163	4822	52	711	2506
AD-18945	4164	4823	53	712	1286
AD-18946	4165	4824	54	713	1660
AD-18947	4166	4825	55	714	2328
AD-18948	4167	4826	56	715	1776
AD-18949	4168	4827	57	716	619
AD-18950	4169	4828	58	717	807
AD-18951	4170	4829	59	718	2417
AD-18952	4171	4830	60	719	3165
AD-18953	4172	4831	61	720	266
AD-18954	4173	4832	62	721	618
AD-18955	4174	4833	63	722	2113
AD-18956	4175	4834	64	723	3040

AD-18957	4176	4835	65	724	3166
AD-18958	4177	4836	66	725	3041
AD-18959	4178	4837	67	726	582
AD-18960	4179	4838	68	727	3220
AD-18961	4180	4839	69	728	2125
AD-18962	4181	4840	70	729	2101
AD-18963	4182	4841	71	730	1773
AD-18964	4183	4842	72	731	2588
AD-18965	4184	4843	73	732	2598
AD-18966	4185	4844	74	733	2907
AD-18967	4186	4845	75	734	2508
AD-18968	4187	4846	76	735	3102
AD-18969	4188	4847	77	736	3042
AD-18970	4189	4848	78	737	2499
AD-18971	4190	4849	79	738	2124
AD-18972	4191	4850	80	739	3105
AD-18973	4192	4851	81	740	2119
AD-18974	4193	4852	82	741	641
AD-18975	4194	4853	83	742	2584
AD-18976	4195	4854	84	743	2105
AD-18977	4196	4855	85	744	1069
AD-18978	4197	4856	86	745	2330
AD-18979	4198	4857	87	746	2388
AD-18980	4199	4858	88	747	3224
AD-18981	4200	4859	89	748	3098
AD-18982	4201	4860	90	749	2049
AD-18983	4202	4861	91	750	1796
AD-18984	4203	4862	92	751	2127
AD-18985	4204	4863	93	752	3029
AD-18986	4205	4864	94	753	2596
AD-18987	4206	4865	95	754	3221
AD-18988	4207	4866	96	755	3159
AD-18989	4208	4867	97	756	2583
AD-18990	4209	4868	98	757	1655
AD-18991	4210	4869	99	758	874
AD-18992	4211	4870	100	759	3028
AD-18993	4212	4871	101	760	3037
AD-18994	4213	4872	102	761	1504
AD-18995	4214	4873	103	762	3095
AD-18996	4215	4874	104	763	2703
AD-18997	4216	4875	105	764	3154
AD-18998	4217	4876	106	765	3094
AD-18999	4218	4877	107	766	2599
AD-19000	4219	4878	108	767	643
AD-19001	4220	4879	109	768	2389

AD-19002	4221	4880	110	769	1669
AD-19003	4222	4881	111	770	2106
AD-19004	4223	4882	112	771	3170
AD-19005	4224	4883	113	772	3103
AD-19006	4225	4884	114	773	642
AD-19007	4226	4885	115	774	3230
AD-19008	4227	4886	116	775	3222
AD-19009	4228	4887	117	776	2905
AD-19010	4229	4888	118	777	2904
AD-19011	4230	4889	119	778	579
AD-19012	4231	4890	120	779	3171
AD-19042	4232	4891	121	780	2504
AD-19043	4233	4892	122	781	3039
AD-19044	4234	4893	123	782	3034
AD-19045	4235	4894	124	783	1505
AD-19046	4236	4895	125	784	1288
AD-19047	4237	4896	126	785	2123
AD-19048	4238	4897	127	786	620
AD-19049	4239	4898	128	787	3164
AD-19050	4240	4899	129	788	3101
AD-19051	4241	4900	130	789	2329
AD-19052	4242	4901	131	790	2115
AD-19053	4243	4902	132	791	2627
AD-19054	4244	4903	133	792	2902
AD-19055	4245	4904	134	793	262
AD-19056	4246	4905	135	794	1406
AD-19057	4247	4906	136	795	2497
AD-19058	4248	4907	137	796	3043
AD-19059	4249	4908	138	797	2589
AD-19060	4250	4909	139	798	2586
AD-19061	4251	4910	140	799	1658
AD-19062	4252	4911	141	800	2050
AD-19063	4253	4912	142	801	2385
AD-19064	4254	4913	143	802	1637
AD-19065	4255	4914	144	803	707
AD-19066	4256	4915	145	804	2597
AD-19067	4257	4916	146	805	3161
AD-19068	4258	4917	147	806	875
AD-19069	4259	4918	148	807	3044
AD-19070	4260	4919	149	808	617
AD-19071	4261	4920	150	809	2498
AD-19072	4262	4921	151	810	367
AD-19073	4263	4922	152	811	2545
AD-19074	4264	4923	153	812	1544
AD-19075	4265	4924	154	813	3148

AD-19076	4266	4925	155	814	2909
AD-19077	4267	4926	156	815	2509
AD-19078	4268	4927	157	816	1775
AD-19079	4269	4928	158	817	1407
AD-19080	4270	4929	159	818	2327
AD-19081	4271	4930	160	819	3031
AD-19082	4272	4931	161	820	1661
AD-19083	4273	4932	162	821	3162
AD-19738	4274	4933	163	822	1906
AD-19739	4275	4934	164	823	825
AD-19740	4276	4935	165	824	1838
AD-19741	4277	4936	166	825	1714
AD-19742	4278	4937	167	826	1859
AD-19743	4279	4938	168	827	324
AD-19744	4280	4939	169	828	535
AD-19745	4281	4940	170	829	822
AD-19746	4282	4941	171	830	826
AD-19747	4283	4942	172	831	851
AD-19748	4284	4943	173	832	1313
AD-19749	4285	4944	174	833	1860
AD-19750	4286	4945	175	834	2016
AD-19751	4287	4946	176	835	1868
AD-19752	4288	4947	177	836	1869
AD-19753	4289	4948	178	837	1876
AD-19754	4290	4949	179	838	1908
AD-19755	4291	4950	180	839	2192
AD-19756	4292	4951	181	840	520
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AD-19758	4294	4953	183	842	623
AD-19759	4295	4954	184	843	916
AD-19760	4296	4955	185	844	1153
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AD-19762	4298	4957	187	846	1864
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AD-19767	4302	4961	191	850	1028
AD-19768	4303	4962	192	851	1314
AD-20124	4304	4963	193	852	2012
AD-25889	4305	4964	194	853	2632
AD-25890	4306	4965	195	854	2637
AD-25891	4307	4966	196	855	2648
AD-25892	4308	4967	197	856	2649
AD-25893	4309	4968	198	857	2663
AD-25894	4310	4969	199	858	2664

AD-25895	4311	4970	200	859	2694
AD-25896	4312	4971	201	860	2695
AD-25897	4313	4972	202	861	2697
AD-25898	4314	4973	203	862	2698
AD-25899	4315	4974	204	863	2699
AD-25900	4316	4975	205	864	2751
AD-25901	4317	4976	206	865	2752
AD-25902	4318	4977	207	866	2753
AD-25903	4319	4978	208	867	2832
AD-25904	4320	4979	209	868	2833
AD-25905	4321	4980	210	869	2837
AD-25906	4322	4981	211	870	2843
AD-25907	4323	4982	212	871	2844
AD-25908	4324	4983	213	872	2845
AD-25909	4325	4984	214	873	2846
AD-25910	4326	4985	215	874	2859
AD-25911	4327	4986	216	875	2913
AD-25912	4328	4987	217	876	2914
AD-25913	4329	4988	218	877	2938
AD-25914	4330	4989	219	878	2940
AD-25915	4331	4990	220	879	2941
AD-25916	4332	4991	221	880	2942
AD-25917	4333	4992	222	881	2991
AD-25918	4334	4993	223	882	2992
AD-25919	4335	4994	224	883	2997
AD-25920	4336	4995	225	884	2998
AD-25921	4337	4996	226	885	3077
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AD-25924	4340	4999	229	888	3083
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AD-25926	4342	5001	231	890	3111
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AD-25928	4344	5003	233	892	3123
AD-25929	4345	5004	234	893	3124
AD-25930	4346	5005	235	894	3125
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AD-25935	4351	5010	240	899	3169
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AD-25937	4353	5012	242	901	3192
AD-25938	4354	5013	243	902	2665
AD-25939	4355	5014	244	903	2682

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AD-25941	4357	5016	246	905	2684
AD-25942	4358	5017	247	906	2685
AD-25943	4359	5018	248	907	2686
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AD-25946	4362	5021	251	910	2709
AD-25947	4363	5022	252	911	2710
AD-25948	4364	5023	253	912	2711
AD-25949	4365	5024	254	913	2712
AD-25950	4366	5025	255	914	2713
AD-25951	4367	5026	256	915	2714
AD-25952	4368	5027	257	916	2834
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AD-25954	4370	5029	259	918	2836
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AD-25956	4372	5031	261	920	2847
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AD-25958	4374	5033	263	922	2871
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AD-25960	4376	5035	265	924	2996
AD-25961	4377	5036	266	925	3079
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AD-26019	4383	5042	272	931	3171
AD-26020	4384	5043	273	932	3198
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AD-26022	4386	5045	275	934	207
AD-26023	4387	5046	276	935	208
AD-26024	4388	5047	277	936	215
AD-26025	4389	5048	278	937	216
AD-26026	4390	5049	279	938	217
AD-26027	4391	5050	280	939	221
AD-26028	4392	5051	281	940	222
AD-26029	4393	5052	282	941	225
AD-26030	4394	5053	283	942	230
AD-26031	4395	5054	284	943	231
AD-26032	4396	5055	285	944	232
AD-26033	4397	5056	286	945	235
AD-26034	4398	5057	287	946	236
AD-26035	4399	5058	288	947	251
AD-26036	4400	5059	289	948	252

AD-26037	4401	5060	290	949	257
AD-26038	4402	5061	291	950	262
AD-26039	4403	5062	292	951	268
AD-26040	4404	5063	293	952	269
AD-26041	4405	5064	294	953	270
AD-26042	4406	5065	295	954	273
AD-26043	4407	5066	296	955	285
AD-26044	4408	5067	297	956	291
AD-26045	4409	5068	298	957	295
AD-26046	4410	5069	299	958	305
AD-26047	4411	5070	300	959	307
AD-26048	4412	5071	301	960	111
AD-26049	4413	5072	302	961	316
AD-26050	4414	5073	303	962	317
AD-26051	4415	5074	304	963	331
AD-26052	4416	5075	305	964	338
AD-26053	4417	5076	306	965	339
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AD-26056	4420	5079	309	968	358
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AD-26058	4422	5081	311	970	383
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AD-26062	4426	5085	315	974	418
AD-26063	4427	5086	316	975	424
AD-26064	4428	5087	317	976	441
AD-26065	4429	5088	318	977	442
AD-26066	4430	5089	319	978	451
AD-26067	4431	5090	320	979	458
AD-26068	4432	5091	321	980	1232
AD-26069	4433	5092	322	981	1233
AD-26070	4434	5093	323	982	460
AD-26071	4435	5094	324	983	461
AD-26072	4436	5095	325	984	471
AD-26073	4437	5096	326	985	478
AD-26074	4438	5097	327	986	481
AD-26075	4439	5098	328	987	487
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AD-26077	4441	5100	330	989	507
AD-26078	4442	5101	331	990	512
AD-26079	4443	5102	332	991	532
AD-26080	4444	5103	333	992	542
AD-26081	4445	5104	334	993	543

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AD-26083	4447	5106	336	995	558
AD-26084	4448	5107	337	996	559
AD-26085	4449	5108	338	997	562
AD-26086	4450	5109	339	998	576
AD-26087	4451	5110	340	999	581
AD-26088	4452	5111	341	1000	584
AD-26089	4453	5112	342	1001	591
AD-26090	4454	5113	343	1002	595
AD-26091	4455	5114	344	1003	604
AD-26092	4456	5115	345	1004	611
AD-26093	4457	5116	346	1005	612
AD-26094	4458	5117	347	1006	613
AD-26095	4459	5118	348	1007	623
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AD-26097	4461	5120	350	1009	642
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AD-26099	4463	5122	352	1011	649
AD-26100	4464	5123	353	1012	652
AD-26101	4465	5124	354	1013	658
AD-26102	4466	5125	355	1014	662
AD-26103	4467	5126	356	1015	666
AD-26104	4468	5127	357	1016	669
AD-26105	4469	5128	358	1017	670
AD-26106	4470	5129	359	1018	672
AD-26107	4471	5130	360	1019	682
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AD-26109	4473	5132	362	1021	691
AD-26110	4474	5133	363	1022	707
AD-26111	4475	5134	364	1023	708
AD-26112	4476	5135	365	1024	715
AD-26123	4477	5136	366	1025	722
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AD-26127	4481	5140	370	1029	731
AD-26128	4482	5141	371	1030	732
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AD-26130	4484	5143	373	1032	755
AD-26131	4485	5144	374	1033	756
AD-26132	4486	5145	375	1034	757
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AD-26135	4489	5148	378	1037	1551
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AD-26138	4492	5151	381	1040	785
AD-26139	4493	5152	382	1041	788
AD-26140	4494	5153	383	1042	789
AD-26141	4495	5154	384	1043	1624
AD-26142	4496	5155	385	1044	790
AD-26143	4497	5156	386	1045	791
AD-26144	4498	5157	387	1046	812
AD-26145	4499	5158	388	1047	813
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AD-26147	4501	5160	390	1049	821
AD-26148	4502	5161	391	1050	831
AD-26149	4503	5162	392	1051	842
AD-26150	4504	5163	393	1052	843
AD-26151	4505	5164	394	1053	851
AD-26152	4506	5165	395	1054	855
AD-26153	4507	5166	396	1055	861
AD-26154	4508	5167	397	1056	862
AD-26155	4509	5168	398	1057	866
AD-26156	4510	5169	399	1058	871
AD-26157	4511	5170	400	1059	874
AD-26158	4512	5171	401	1060	877
AD-26159	4513	5172	402	1061	887
AD-26160	4514	5173	403	1062	903
AD-26161	4515	5174	404	1063	907
AD-26162	4516	5175	405	1064	909
AD-26163	4517	5176	406	1065	913
AD-26164	4518	5177	407	1066	914
AD-26165	4519	5178	408	1067	919
AD-26166	4520	5179	409	1068	960
AD-26167	4521	5180	410	1069	975
AD-26168	4522	5181	411	1070	976
AD-26169	4523	5182	412	1071	977
AD-26170	4524	5183	413	1072	978
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AD-26172	4526	5185	415	1074	986
AD-26173	4527	5186	416	1075	997
AD-26174	4528	5187	417	1076	998
AD-26175	4529	5188	418	1077	1848
AD-26176	4530	5189	419	1078	1849
AD-26177	4531	5190	420	1079	1005
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AD-26198	4552	5211	441	1100	1059
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AD-26211	4565	5224	454	1113	1153
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AD-26217	4571	5230	460	1119	1226
AD-26218	4572	5231	461	1120	1227
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AD-26661	4583	5242	472	1131	1291
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AD-26663	4585	5244	474	1133	1337
AD-26664	4586	5245	475	1134	1338
AD-26665	4587	5246	476	1135	1346
AD-26666	4588	5247	477	1136	1347
AD-26667	4589	5248	478	1137	1366
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AD-26670	4592	5251	481	1140	1381
AD-26671	4593	5252	482	1141	1384
AD-26672	4594	5253	483	1142	1396
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AD-26674	4596	5255	485	1144	1410
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AD-26702	4624	5283	513	1172	1526
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AD-26735	4657	5316	546	1205	1772
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AD-26746	4668	5327	557	1216	1888
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AD-26750	4672	5331	561	1220	1930
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AD-26758	4680	5339	569	1228	2038
AD-26759	4681	5340	570	1229	2042
AD-26760	4682	5341	571	1230	2046
AD-26761	4683	5342	572	1231	2047
AD-26762	4684	5343	573	1232	2059
AD-26763	4685	5344	574	1233	2060
AD-26764	4686	5345	575	1234	2061
AD-26765	4687	5346	576	1235	2062
AD-26766	4688	5347	577	1236	2063
AD-26767	4689	5348	578	1237	2070
AD-26768	4690	5349	579	1238	2071
AD-26769	4691	5350	580	1239	2076
AD-26770	4692	5351	581	1240	2079
AD-26771	4693	5352	582	1241	2083
AD-26772	4694	5353	583	1242	2110
AD-26773	4695	5354	584	1243	2128
AD-26774	4696	5355	585	1244	2178
AD-26775	4697	5356	586	1245	2179
AD-26776	4698	5357	587	1246	2182
AD-26777	4699	5358	588	1247	2189
AD-26778	4700	5359	589	1248	2193
AD-26779	4701	5360	590	1249	2194
AD-26780	4702	5361	591	1250	2197
AD-26781	4703	5362	592	1251	2234
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AD-26783	4705	5364	594	1253	2254
AD-26784	4706	5365	595	1254	2257
AD-26785	4707	5366	596	1255	2262
AD-26786	4708	5367	597	1256	2265
AD-26787	4709	5368	598	1257	2272
AD-26788	4710	5369	599	1258	2278
AD-26789	4711	5370	600	1259	2298
AD-26790	4712	5371	601	1260	2303
AD-26791	4713	5372	602	1261	2365
AD-26792	4714	5373	603	1262	2375
AD-26793	4715	5374	604	1263	2376

AD-26794	4716	5375	605	1264	2386
AD-26795	4717	5376	606	1265	2393
AD-26796	4718	5377	607	1266	2397
AD-26797	4719	5378	608	1267	2398
AD-26798	4720	5379	609	1268	2402
AD-26799	4721	5380	610	1269	2406
AD-26800	4722	5381	611	1270	2407
AD-26801	4723	5382	612	1271	2420
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AD-26803	4725	5384	614	1273	2422
AD-26804	4726	5385	615	1274	2431
AD-26805	4727	5386	616	1275	2436
AD-26806	4728	5387	617	1276	2451
AD-26807	4729	5388	618	1277	2454
AD-26808	4730	5389	619	1278	675
AD-26809	4731	5390	620	1279	676
AD-26810	4732	5391	621	1280	679
AD-26811	4733	5392	622	1281	2458
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AD-26815	4737	5396	626	1285	2494
AD-26816	4738	5397	627	1286	2503
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AD-26823	4745	5404	634	1293	2605
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AD-26825	4747	5406	636	1295	2607
AD-26826	4748	5407	637	1296	878
AD-26900	4749	5408	638	1297	2745
AD-26901	4750	5409	639	1298	2872
AD-26902	4751	5410	640	1299	2915
AD-26903	4752	5411	641	1300	2916
AD-26904	4753	5412	642	1301	2918
AD-26905	4754	5413	643	1302	2919
AD-26906	4755	5414	644	1303	2939
AD-26907	4756	5415	645	1304	2978
AD-26908	4757	5416	646	1305	2979
AD-26909	4758	5417	647	1306	2980
AD-26910	4759	5418	648	1307	2981
AD-26911	4760	5419	649	1308	2983

AD-26912	4761	5420	650	1309	2984
AD-26913	4762	5421	651	1310	2986
AD-26914	4763	5422	652	1311	3081
AD-26915	4764	5423	653	1312	3082
AD-26916	4765	5424	654	1313	2917
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AD-26918	4767	5426	656	1315	2995
AD-26919	4768	5427	657	1316	3134
AD-26920	4769	5428	658	1317	1535
AD-26921	4770	5429	659	1318	1801
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SET1 3477	6105	6126	6239	6407	3459
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SET1 703	6106	6127	6226	6394	685
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SET1 889	6109	6130	6296	6464	871
SET1 895	6110	6131	6228	6396	877
SET1 895	6110	6131	6249	6417	877
SET1 895	6110	6131	6270	6438	877
SET1 895	6110	6131	6291	6459	877

[0023] 本公开的多种实施方案

[0024] 针对 β－联蛋白的各种 RNAi 剂在表 1、2、3、4、5、6、7、8 和／或 9 中公开。

[0025] 表 1、表 2 和表 3 提供多种针对 β-联蛋白的 RNAi 剂的序列、SEQ ID NOs 和位置，包括未修饰的序列和示例性修饰的序列。表 2 中的序列未修饰。

[0026] 表 3 提供多种针对 β-联蛋白的 RNAi 剂的有义链和反义链的示例性修饰序列的序列和 SEQ ID NOs。本公开还涵盖这些序列的未修饰形式，和包含其他修饰或修饰样式的不同形式（但是碱基序列相同）。

[0027] 在表 3 的序列中，小写字母（例如，c、u）表示修饰的核苷酸，而大写字母（例如，C、U、A、G）表示未修饰的核苷酸。在表 3 中，显示每个序列的修饰形式的例子。然而，本公开涵盖这些序列的未修饰形式和包含额外或替代性修饰的其他形式。因而，例如，AD-18892 可以任选地在有义链中具有未修饰的（或“通用性”）序列 UGGUGCUGACUAUCCAGUU(SEQ ID NO:429) 并且在反义链中具有序列 AACUGGAUAGUCAGCACCA(SEQ ID NO:430)。本公开还涵盖双链体的替代性经修饰形式，其在有义链中包含 UGGUGCUGACUAUCCAGUU(SEQ ID NO:429) 并且在反义链中包含 AACUGGAUAGUCAGCACCA(SEQ ID NO:430)。

[0028] 在表 1、2、3、4、5、6、7 和 8 的序列中，修饰的和未修饰的序列可以任选地在 3’ 末端包含序列“dTdT”、“dTsdT”或“UU”。因此，例如，AD-18892 可以任选地在有义链中具有修饰的序列 uGGuGcuGAcuAuccAGuudTdT(SEQ ID NO:6136) 或 uGGuGcuGAcuAuccAGuudTsdT(SEQ ID NO:6137)；并且在反义链中具有修饰的序列 AACUGGAuAGUcAGcACcAdTdT(SEQ ID NO:6138) 或 AACUGGAuAGUcAGcACcAdTsdT(SEQ ID NO:6139)。如下表 3 中所示，dT 是 2’-脱氧胸苷 -5’- 磷酸并且 sdT 是 2’- 脱氧胸苷 5’- 硫代磷酸酯。在公开的序列中，末端二核苷酸“UU”是 2’-OMe-U 2’-OMe-U，并且末端 TT 和末端 UU 均不处于倒转 / 反方向。在多种实施方案中，也可以使用作为标准 RNA 的 UU。

[0029] 末端二胸苷（或 TT 或 dTdT 或 sdTsdT 或 UU 等）不是 β-联蛋白靶序列的部分，而是常作为突出端安置以保护 siRNA 末端免受核酸酶作用的二胸苷二核苷酸的修饰变体（见，例如，Elbashir 等人，2001Nature 411:494-498；Elbashir 等人，2001EMBO J. 20:6877-6888；和 Kraynack 等人，2006RNA 12:163-176)。从这些参考文献中已知末端二核苷酸增强核酸酶抗性但不有助于靶识别。在任何修饰或未修饰的序列上，如本领域已知，可以使用 3’ 末端帽结构代替末端二核苷酸以使末端免遭核酸酶降解，条件是 3’ 末端帽结构能够稳定 RNAi 剂（例如，抵抗核酸酶）并不过度干扰 siRNA 活性。

[0030] 表 4 提供针对 β-联蛋白的重叠性 RNAi 剂的集合。

[0031] 表 5 至表 9 中提供各种 β-联蛋白 RNAi 剂的活性水平。

[0032] 包含本文所述的 RNAi 剂的反义链的 RNAi 剂

[0033] 在一个特定的具体实施方案中，本公开涉及一种组合物，其包含用于抑制靶基因 β-联蛋白的 RNAi 剂，所述 RNAi 剂包含反义链，其中反义链包含与针对 β-联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述反义链选自那些在本文提供和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体中的反义链。

[0034] 在一个实施方案中，该组合物包含用于抑制靶基因 β-联蛋白的 RNAi 剂，所述 RNAi 剂包含有义链和反义链，其中有义链的序列和反义链的序列分别是本文提供的任何 RNAi 剂的有义链和反义链的序列。在一个实施方案中，该组合物包含用于抑制靶基因 β-联蛋白的 RNAi 剂，所述 RNAi 剂包含有义链和反义链，其中反义链的序列是本文提供的任何 RNAi 剂的反义链的序列。在一个实施方案中，该组合物包含用于抑制靶基因 β-联蛋

白的RNAi剂，所述RNAi剂包含有义链和反义链，其中有义链的序列和反义链的序列分别是本文提供的任何RNAi剂的有义链和反义链的序列，还在一条链或两条链上包含额外的约6至20个核苷酸（例如，约6、7、8、9、10、11、12、13、14、15、16、17、18、19或20个核苷酸）。在一个实施方案中，该组合物包含用于抑制靶基因β-联蛋白的RNAi剂，所述RNAi剂包含有义链和反义链，其中反义链的序列是本文提供的任何RNAi剂的反义链的序列，还在一条链或两条链上包含额外的约6至20个核苷酸（例如，约6、7、8、9、10、11、12、13、14、15、16、17、18、19或20个核苷酸）。在这些多样的实施方案中，RNAi剂用于抑制靶基因β-联蛋白。

[0035] 下文描述这些实施方案的各种具体实施方案。

[0036] 在一个实施方案中，组合物还包含针对β-联蛋白的第二RNAi剂。在多种实施方案中，第二RNAi剂物理地与第一RNAi剂隔离，或这两者物理地连接（例如，共价连接或否则缀合），或组合在相同的药物组合物中。

[0037] 在一个实施方案中，反义链具有约30个或更少个核苷酸长度。

[0038] 在一个实施方案中，有义链和反义链形成长度约15至约30个核苷酸对的双链体区。

[0039] 在一个实施方案中，反义链具有约15至约36个核苷酸长度、约17至约30个核苷酸长度、约17至23个核苷酸长度，约19至约49个核苷酸长度或约19至约23个核苷酸长度。在一个实施方案中，反义链具有至少选自约15个核苷酸、约16个核苷酸、约17个核苷酸、约18个核苷酸、约19个核苷酸、约20个核苷酸、约21个核苷酸、约22个核苷酸、约23个核苷酸、约24个核苷酸、约25个核苷酸、约26个核苷酸、约27个核苷酸、约28个核苷酸、约29个核苷酸和约30个核苷酸的长度。

[0040] 在一个实施方案中，RNAi剂包含引起RNAi剂在生物样品或环境（例如，血清或肠道灌洗液）中具有增加的稳定性的修饰。

[0041] 在一个实施方案中，RNAi剂包含至少一个糖主链修饰（例如，硫代磷酸酯键）和/或至少一个2'修饰的核苷酸。在一个实施方案中，全部嘧啶均是2'O-甲基修饰的核苷酸。

[0042] 在一个实施方案中，RNAi剂包含：至少一个5'-尿苷-腺嘌呤-3'(5'-ua-3')二核苷酸，其中尿苷是2'-修饰的核苷酸；和/或至少一个5'-尿苷-鸟嘌呤-3'(5'-ug-3')二核苷酸，其中5'-尿苷是2'-修饰的核苷酸；和/或至少一个5'-胞苷-腺嘌呤-3'(5'-ca-3')二核苷酸，其中5'-胞苷是2'-修饰的核苷酸；和/或至少一个5'-尿苷-尿苷-3'(5'-uu-3')二核苷酸，其中5'-尿苷是2'-修饰的核苷酸。

[0043] 在一个实施方案中，RNAi剂包含选自以下的2'-修饰：2'-脱氧、2'-脱氧-2'-氟、2'-O-甲基、2'-O-甲氧乙基(2'-O-MOE)、2'-O-氨基丙基(2'-O-AP)、2'-O-二甲基氨基乙基(2'-O-DMAOE)、2'-O-二甲氨基丙基(2'-O-DMAP)、2'-O-二甲基氨基乙基氧乙基(2'-O-DMAEOE)和2'-O-N-甲基乙酰氨基(2'-O-NMA)。在一个实施方案中，全部嘧啶均是2'O-甲基修饰的核苷酸。

[0044] 在一个实施方案中，RNAi剂包含平末端。

[0045] 在一个实施方案中，RNAi剂包含具有1至4个非配对核苷酸突出端。

[0046] 在一个实施方案中，RNAi剂包含在RNAi剂的反义链的3'末端处包含突出端。

[0047] 在一个实施方案中，RNAi剂连接至一种或多种诊断化合物、报道基团、交联剂、赋

予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基(hecigenin)、薯蓣皂苷配基、萜、三萜、菝葜皂苷元(sarsasapogenin)、无羁萜、表木栓烷醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯15聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和/或转铁蛋白。

[0048] 在一个实施方案中,RNAi剂能够以10nM浓度在HeLa细胞中体外抑制β-联蛋白基因的表达至少约60%。

[0049] 在一个实施方案中,RNAi剂能够以10nM浓度在HeLa细胞中体外抑制β-联蛋白基因的表达至少约70%。

[0050] 在一个实施方案中,RNAi剂能够以10nM浓度在HeLa细胞中体外抑制β-联蛋白基因的表达至少约80%。

[0051] 在一个实施方案中,RNAi剂能够以10nM浓度在HeLa细胞中体外抑制β-联蛋白基因的表达至少约90%。

[0052] 在一个实施方案中,RNAi具有不多于约0.1nM的EC_{50}。

[0053] 在一个实施方案中,RNAi具有不多于约0.01nM的EC_{50}。

[0054] 在一个实施方案中,RNAi具有不多于约0.001nM的EC_{50}。

[0055] 包含第一链和第二链的RNAi剂

[0056] 在一个特定的具体实施方案中,本公开涉及一种组合物,其包含用于抑制靶基因β-联蛋白的RNAi剂,所述RNAi剂包含第一链和第二链,其中第一链和第二链包含分别与针对β-联蛋白的RNAi剂的第一链和第二链各自差异0、1、2或3个核苷酸的至少15个连续核苷酸,所述针对β-联蛋白的RNAi剂选自本文中提供的和例如在表1、2、3、4、5、6、7、8和/或9中列出的特定双链体。在这些多样的实施方案中,RNAi剂用于抑制靶基因β-联蛋白。

[0057] 下文描述这个实施方案的多种具体实施方案。

[0058] 在一个实施方案中,组合物还包含针对β-联蛋白的第二RNAi剂。在多种实施方案中,第二RNAi剂物理地与第一RNAi剂隔离,或这两者物理地连接(例如,共价连接或否则缀合),或组合在相同的药物组合物中。

[0059] 在一个实施方案中,反义链具有约30个或更少个核苷酸长度。

[0060] 在一个实施方案中,有义链和反义链形成长度约15至约30个核苷酸对的双链体区。

[0061] 在一个实施方案中,反义链具有约15至约36个核苷酸长度,包括约17至约23个核苷酸长度,并且包括约19至约23个核苷酸长度。在一个实施方案中,反义链具有至少选自约15个核苷酸、约16个核苷酸、约17个核苷酸、约18个核苷酸、约19个核苷酸、约20个核苷酸、约21个核苷酸、约22个核苷酸、约23个核苷酸、约24个核苷酸、约25个核苷酸、约26个核苷酸、约27个核苷酸、约28个核苷酸、约29个核苷酸和约30个核苷酸的长度。

[0062] 在一个实施方案中,RNAi剂包含引起RNAi剂在生物样品或环境(例如,血清或肠道灌洗液)中具有增加的稳定性的修饰。

[0063] 在一个实施方案中,RNAi剂包含至少一个糖主链修饰(例如,硫代磷酸酯键)和

/ 或至少一个 2' 修饰的核苷酸。在一个实施方案中，全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[0064] 在一个实施方案中，RNAi 剂包含：至少一个 5'- 尿苷 - 腺嘌呤 -3'(5'-ua-3') 二核苷酸，其中尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 鸟嘌呤 -3'(5'-ug-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 胞苷 - 腺嘌呤 -3'(5'-ca-3') 二核苷酸，其中 5'- 胞苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 尿苷 -3'(5'-uu-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸。

[0065] 在一个实施方案中，RNAi 剂包含选自以下的 2'- 修饰：2'- 脱氧、2'- 脱氧 -2'- 氟、2'-O- 甲基、2'-O- 甲氧乙基 (2'-O-MOE)、2'-O- 氨基丙基 (2'-O-AP)、2'-O- 二甲基氨基乙基 (2'-O-DMAOE)、2'-O- 二甲氨基丙基 (2'-O-DMAP)、2'-O- 二甲基氨基乙基氧乙基 (2'-O-DMAEOE) 和 2'-O-N- 甲基乙酰氨基 (2'-O-NMA)。

[0066] 在一个实施方案中，RNAi 剂包含平末端。

[0067] 在一个实施方案中，RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[0068] 在一个实施方案中，RNAi 剂包含在 RNAi 剂的反义链的 3' 末端处包含突出端。

[0069] 在一个实施方案中，RNAi 剂连接至一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[0070] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 HeLa 细胞中体外抑制 β- 联蛋白基因的表达至少约 60%。

[0071] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 HeLa 细胞中体外抑制 β- 联蛋白基因的表达至少约 70%。

[0072] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 HeLa 细胞中体外抑制 β- 联蛋白基因的表达至少约 80%。

[0073] 在一个实施方案中，RNAi 剂能够以 10nM 浓度在 HeLa 细胞中体外抑制 β- 联蛋白基因的表达至少约 90%。

[0074] 在一个实施方案中，RNAi 具有不多于约 0.1nM 的 EC_{50}。

[0075] 在一个实施方案中，RNAi 具有不多于约 0.01nM 的 EC_{50}。

[0076] 在一个实施方案中，RNAi 具有不多于约 0.001nM 的 EC_{50}。

[0077] 使用本文所述的 RNAi 剂治疗的方法

[0078] 在一个特定的具体实施方案中，本公开涉及一种治疗个体中 β- 联蛋白相关疾病的方法，包括步骤：向个体施用治疗有效量的包含本文中公开的任一种或多种 RNAi 剂的组合物。在这种方法的一个实施方案中，RNAi 剂至少包含反义链，其中反义链包含与针对 β- 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β- 联蛋白的 RNAi 剂选自本文提供的和如在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。在一个实施方案中，RNAi 剂包含有义链和反义链，其中有义链包含与针对 β- 联蛋白的 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β- 联

蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链包含与针对 β - 联蛋白的 RNAi 剂的第一链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列是针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。在这些多样的实施方案中，RNAi 剂用于抑制靶基因 β - 联蛋白。

[0079] 下文描述这些实施方案的各种特定具体实施方案。

[0080] 在一个实施方案中，β - 联蛋白相关疾病是结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口和 / 或受损的伤口愈合，和 / 或相似和相关的疾病。

[0081] 在一个实施方案中，β - 联蛋白相关疾病是癌症。

[0082] 在一个实施方案中，该方法还包括施用额外的治疗。在一个实施方案中，额外的治疗是治疗有效量的组合物。

[0083] 在一个实施方案中，额外的治疗是方法（或操作 (procedure)）。

[0084] 在一个实施方案中，额外的治疗和 RNAi 剂可以按任意顺序施用，或可以同时施用。

[0085] 在一个实施方案中，该方法还包括步骤：施用额外的治疗用于结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口和 / 或受损的伤口愈合，和 / 或相似和相关的疾病。

[0086] 在一个实施方案中，组合物包含针对 β - 联蛋白的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂隔离，或这两者物理地连接（例如，共价连接或否则缀合），或组合在相同的药物组合物中。

[0087] 在一个实施方案中，该方法还包括步骤：施用额外的 RNAi 剂，所述额外的 RNAi 剂包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的特定双链体。

[0088] 使用 RNAi 剂抑制 β - 联蛋白表达

[0089] 在一个特定的具体实施方案中，本公开涉及一种抑制个体中 β - 联蛋白基因表达的方法，包括步骤：向个体施用治疗有效量的包含本公开的任一种或多种 RNAi 剂的组合物。在一个实施方案中，RNAi 剂包含至少一种反义链，和 / 或包含有义链和反义链，其中反义链包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续

核苷酸，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和/或 9 中列出的那些特定双链体。在一个实施方案中，RNAi 剂包含有义链和反义链，其中反义链包含与针对 β-联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和/或 9 中列出的那些特定双链体。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含针对 β-联蛋白的 RNAi 剂的第一链的序列，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和/或 9 中列出的那些特定双链体。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列是针对 β-联蛋白的 RNAi 剂的第一链的序列，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和/或 9 中列出的那些特定双链体。

[0090] 下文描述这些实施方案的这个方面的多种实施方案。

[0091] 在一个实施方案中，个体罹患或易患 β-联蛋白相关疾病。

[0092] 在一个实施方案中，β-联蛋白相关疾病是结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口和/或受损的伤口愈合，和/或相似和相关的疾病。

[0093] 在一个实施方案中，β-联蛋白相关疾病是癌症。

[0094] 在一个实施方案中，该方法还包括施用额外的治疗。在一个实施方案中，额外的治疗是治疗有效量的组合物。

[0095] 在一个实施方案中，额外的治疗是方法（或操作）。

[0096] 在一个实施方案中，额外的治疗和 RNAi 剂可以按任意顺序施用或可以同时施用。

[0097] 在一个实施方案中，该方法还包括步骤：施用额外的治疗用于结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口和/或受损的伤口愈合，和/或相似和相关的疾病。

[0098] 在一个实施方案中，组合物包含针对 β-联蛋白的第二 RNAi 剂。在多种实施方案中，第二 RNAi 剂物理地与第一 RNAi 剂隔离，或这两者物理地连接（例如，共价连接或否则缀合），或组合在相同的药物组合物中。

[0099] 在一个实施方案中，该方法还包括步骤：施用额外的 RNAi 剂，所述额外的 RNAi 剂包含与针对 β-联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和/或 9 中列出的特定双链体。

[0100] 针对 β-联蛋白的 RNAi 剂的药物制剂

[0101] 在一个特定的具体实施方案中，本公开涉及一种包含本公开的任一种或多种 RNAi 剂的组合物。在一个实施方案中，RNAi 剂包含至少一种反义链，和/或包含有义链和反义链，其中反义链包含与针对 β-联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β-联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、

6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含与针对 β - 联蛋白的 RNAi 剂的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列是针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。

[0102] 在一个实施方案中，本公开涉及 RNAi 剂在制造用于治疗 β - 联蛋白相关疾病的药物中的用途，其中 RNAi 剂是本文中公开的任何 RNAi。在一个实施方案中，RNAi 剂包含有义链和反义链，其中反义链包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体。在一个实施方案中，RNAi 剂包含至少一种反义链，和 / 或包含有义链和反义链，其中反义链包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含与针对 β - 联蛋白的 RNAi 剂的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列包含针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。在一个实施方案中，RNAi 剂包含第一链和第二链，其中第一链的序列是针对 β - 联蛋白的 RNAi 剂的第一链的序列，所述针对 β - 联蛋白的 RNAi 剂选自本文提供的和在例如表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的那些特定双链体，其中组合物处于药学有效制剂中。

[0103] 包含不同于所公开序列的错配的针对 β - 联蛋白的 RNAi 剂的具体实施方案

[0104] 本文中公开了针对 β - 联蛋白的 RNAi 剂的多种具体实施方案。本公开涵盖表 1、2、3、4、5、6、7、8 和 / 或 9 中提供的示例性修饰序列，和相应的未修饰序列和其他修饰的序列（例如，修饰的变体和未修饰的变体）。本公开的具体实施方案包括了包含下述序列的 RNAi 剂及其修饰变体和未修饰变体，所述序列与表 1 中所列的任一 RNAi 剂差异 0、1、2 或 3 个核苷酸或 bp[碱基对)](例如，0、1、2 或 3 错配)。如下文以额外细节描述，错配在本文中定义为将两个序列最大限度地对齐并比较时碱基序列 (例如，A 替代 G) 或长度之间的差异。此外，如下文更详细地描述，“未修饰的变体”是其中碱基序列相同，但是没有一个碱基被修饰的变体；这种变体例如包括野生型 β - 联蛋白 mRNA 或基因的相应部分。“修饰的变体”含有对核苷酸、糖、磷酸酯或主链的一个或多个修饰 (或一个或多个减少或不同的修饰)，和 /

或一个或多个部分的添加；但是对碱基序列无改变、置换、添加或缺失。特定序列及其修饰变体或未修饰变体具有彼此之间 0 个错配。

[0105] 在一个具体实施方案，本公开包含 RNAi 剂，所述 RNAi 剂包含反义链，所述反义链包含与表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的任一 RNAi 剂的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0106] 在另一个具体实施方案中，RNAi 剂包含有义链，所述有义链包含与表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的任一 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0107] 定义

[0108] 出于便利，下文提供在本说明书、实施例和所附权利要求中使用的某些术语和短语的含义。如果本说明书的其他部分中某术语的用途和这个部分中所提供的其定义之间存在明显的不一致性，则这个部分中的定义应当占优。

[0109] 其他实施方案

[0110] 下文描述本公开的多种特定的具体实施方案。

[0111] 在一个实施方案中，本公开涉及根据任一个已公开实施方案的组合物，其用于治疗个体中 β - 联蛋白相关疾病的方法中，所述方法包括步骤：向该个体施用治疗有效量本公开的组合物。

[0112] 下文描述这个实施方案的多种特定的具体实施方案。

[0113] 在一个实施方案中，本公开涉及根据任一个以上实施方案的组合物，其用于抑制个体中 β - 联蛋白表达的方法中，所述方法包括步骤：向该个体施用治疗有效量的根据任一个公开的实施方案的组合物。

[0114] 本公开的一个实施方案是根据任一个以上实施方案的组合物在制造用于治疗 β - 联蛋白相关疾病的药物中的用途。

[0115] 在一个实施方案中，β - 联蛋白相关疾病选自癌症、病毒病或自身免疫性疾病。

[0116] 在一个实施方案中，本公开涉及任一个以上实施方案的用于治疗 β - 联蛋白相关疾病的组合物。

[0117] 在一个实施方案中，β - 联蛋白相关疾病选自癌症、病毒病或自身免疫性疾病。

[0118] 在一个实施方案中，本公开涉及一种抑制细胞中 β - 联蛋白表达的方法，所述方法包括步骤：向所述细胞引入包含 RNAi 剂的组合物，所述 RNAi 剂包含反义链，其中反义链包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文中公开的 β - 联蛋白 siRNA。

[0119] 在一个实施方案中，本公开涉及一种抑制细胞中 β - 联蛋白表达的方法，所述方法包括步骤：向所述细胞引入包含 RNAi 剂的组合物，所述 RNAi 剂包含有义链和反义链，其中反义链包含与针对 β - 联蛋白的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸并且有义链包含与针对 β - 联蛋白的 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述针对 β - 联蛋白的 RNAi 剂选自本文中公开的 β - 联蛋白 siRNA。

[0120] β - 联蛋白

[0121] “β - 联蛋白”意指基因、mRNA 和 / 或蛋白质，或编码该蛋白质的任何核酸，所述

蛋白质还命名为钙黏着蛋白相关蛋白 β1 ;CTNNB1 ;CTNNB ;CTNNB ;CTB1 ;FLJ25606 ;OMIM : 116806 ;MGI :88276HomoloGene :1434 ;OTTHUMP00000209288 ;DKFZp686D02253 ;HGNC : 2514 ;EntrezGene :1499 ;Ensembl :ENSG00000168036 ;UniProtKB :P35222 ;GC03P040551 ; GC03P041054 ;或 GC03P041201。见 :Kraus 等人,1994. Genomics23 :272-4。

[0122] β-联蛋白参与调节细胞黏附并参与通过 Wnt 途径的信号转导。它是构成黏着连接 (AJ) 的蛋白质复合体的部分。AJ 是上皮细胞层产生和维持必需的并且调节细胞生长和细胞之间的黏附。β-联蛋白还卯定肌动蛋白细胞骨架并且可能负责传输一旦上皮层完成则造成细胞停止分裂的接触抑制信号。

[0123] 对 β-联蛋白测序时,发现它是犰狳蛋白家族的成员。这些蛋白质具有特化用于蛋白质-蛋白质结合的所谓犰狳重复结构域的多重副本。当 β-联蛋白不与钙黏着蛋白和 α-联蛋白接合时,它可以与其他蛋白质如 ICAT 和 APC 相互作用。

[0124] β-联蛋白还参与 Wnt 途径。当 Wnt 不存在时,GSK-3(一种激酶)以组成型方式磷酸化 β-联蛋白。β-联蛋白与轴蛋白(支架蛋白)接合,所述轴蛋白与 GSK-3 和 APC(肿瘤抑制物-腺瘤结肠息肉基因产物 (adenomatosis polyposis coli)) 复合。通过促进 GSK-3 的活性,这种复合体的产生增加 β-联蛋白的磷酸化。当 β-联蛋白磷酸化时,它降解并且因此在细胞中不显著地积累。当 Wnt 与其受体卷曲蛋白 (frizzled, Fz) 结合时,将蓬乱蛋白 (dishevelled,Dsh) 招募至胞膜。GSK-3 因 Fz 激活 Dsh 而抑制。因为这种情况,导致 β-联蛋白在细胞质中积累并且可以转位至细胞核,在那里它执行几种功能。它可以与 TCF/LEF 转录因子联合发挥作用以激活参与不同过程(包括增殖、存活和基质重建)的靶基因。

[0125] β-联蛋白与许多其他蛋白相互作用,所述其他蛋白包括钙黏着蛋白、转录因子、轴蛋白、半乳糖凝集素 -3、β-半乳糖苷-结合蛋白、GSK-3、蛋白激酶 A、雄激素受体、APC、AXIN1、CBY1、CDH1、CDH2、CDH3、CDK5R1、CHUK、CTNNA1、CTNND1、EGFR、FHL2、HER2/neu、HNF4A、IKK2、LEF1、MAGI1、MUC1、NF5A1、PCAF、PHF17、斑珠蛋白、PTPN14、PTPRF、PRPRK、PSEN1、RuvB 样 1、SMAD7、SLC913R1、SMARCA4、USP9X 和 VE-钙黏着蛋白。

[0126] β-联蛋白与几种疾病相关。β-联蛋白本身可以充当癌基因。在结肠的腺瘤息肉中,其产物结合 β-联蛋白的 APC 基因突变。如下文更详细地描述,β-联蛋白中的突变、其过量表达和/或异常细胞区室化(例如,在细胞质和/或细胞核中异常积累)与多种疾病相关,包括 :结肠的腺瘤息肉、结直肠癌、基底细胞癌、毛基质瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、间变性甲状腺癌和子宫癌肉瘤。见 :Thompson 等人,2007Hepatology 45:1298-305 ; Wang 等 人,2008Cancer Epidemiol. Biomarkers Prev. 17:2101-8 ;Saldanha 等 人, Br. J. Dermatol. 151:157-64。

[0127] 细胞核和胞质积累(例如,不恰当的细胞区室化)富集于基底样乳腺癌中并且与不良结局相关。更经常在基底样原位癌中比其他亚型中观察到 β-联蛋白积累,表明这条途径的激活可能是在基底样肿瘤形成中的早期事件。Khramtsov 等人,2010Am. J. Pathol. 176:2911-2920。

[0128] β-联蛋白的序列和结构

[0129] 已经发现这个基因的编码相同蛋白质的三种人转录物变体 :NP_001091679.1 ;

NP_001091680.1；和 NP_001895.1。人 β-联蛋白的氨基酸序列和核苷酸序列在基因座 NM_001098209(登 录 号 NM_001098209XM_001133660XM_001133664XM_001133673XM_001133675；VERSION NM_001098209.1GI:148233337)；基因座 NM_001098210(登录号 NM_001098210；VERSION NM_001098210.1GI:148227671)；和基因座 NM_001904(登录号 NM_001904XM_942045XM_945648XM_945650XM_945651XM_945652XM_945653XM_945654XM_945655XM_945657；VERSION NM_001904.3GI:148228165) 中提供。

[0130] β-联蛋白的小鼠(小家鼠(Mus musculus))序列可作为 Q02248(CTNB1_MOUSE)；MGI:88276；NP_031640.1GI:6671684；NM007614.3 获得。大鼠(褐家鼠(Rattus norvegicus))序列可作为 Q9WU82(CTNB1_RAT) 获得；Li 等人，2002Gene 283:255-62。

[0131] 可以如此涉及对 β-联蛋白特异的 RNAi 剂，从而其序列完全匹配与人 β-联蛋白基因和来自试验动物的同源基因相对应的 mRNA 的序列。因而，完全相同的 RNAi 剂可以用于试验动物(例如，大鼠、小鼠、食蟹猴等)和人中。已经在包括人、小鼠和大鼠的许多物种中测定各种 β-联蛋白基因的序列(如上文所述)。

[0132] 食蟹猴 (Macaca fascicularis) 或“cyno”) 中的 β-联蛋白序列已经测定。

[0133] 下文显示 Cyno 和人 (NM_001098210.1) β-联蛋白 mRNA 序列的比对结果。

```
Human   AGGATACAGCGGCTTCTGCGCGACTTATAAGAGCTCCTTGTGCGGCGCCATTTTAAGCCT 60
Cyno    ----------------------------------------------CGCCATTTTAAGCCT 15
                                                      ***************

Human   CTCGGTCTGTGGCAGCAGCGTTGGCCCGGCCCCGGGAGCGGAGAGCGAGGGGAGGCGGAG 120
Cyno    CTTGGTCTGTGGCAGCCGTGTTGGCCCGGCCCCGAGAGCGGAGAGCGAGGGGAGGCGGAG 75
        ** ************* * *************** ************************

Human   ACGGAGGAAGGTCTGAGGAGCAGCTTCAGTCCCCGCCGAGCCGCCACCGCAGGTCGAGGA 180
Cyno    ACGGAGGAAGGTCCGAGGAGCAGCTTCAGTCCTCGCCGAGCCGCCACCGCAGGTCGAGGA 135
        ************* ****************. ****************************

Human   CGGTCGGACTCCCGCGGCGGGAGGAGCCTGTTCCCCTGAGGGTATTTGAAGTATACCATA 240
Cyno    CGGTCGGACTCCCGCGACGGGAGGAGCCTGTTCCCCTGAGGGTATTTGAAGTATACCATA 195
        ***************** ********************************************

Human   CAACTGTTTTGAAAATCCAGCGTGGACAATGGCTACTCAAGCTGATTTGATGGAGTTGGA 300
Cyno    CAACTGTTTTGAAAATCCAGCGTGGACAATGGCTACTCAAGCTGATTTGATGGAGTTGGA 255
        ************************************************************

Human   CATGGCCATGGAACCAGACAGAAAAGCGGCTGTTAGTCACTGGCAGCAACAGTCTTACCT 360
Cyno    CATGGCCATGGAACCAGACAGAAAAGCGGCTGTTAGTCACTGGCAGCAACAGTCTTACCT 315
        ************************************************************

Human   GGACTCTGGAATCCATTCTGGTGCCACTACCACAGCTCCTTCTCTGAGTGGTAAAGGCAA 420
Cyno    GGACTCTGGAATCCATTCTGGTGCCACTACCACAGCTCCTTCTCTGAGTGGTAAAGGCAA 375
        ************************************************************

Human   TCCTGAGGAAGAGGATGTGGATACCTCCCAAGTCCTGTATGAGTGGGAACAGGGATTTTC 480
Cyno    TCCTGAGGAAGAGGATGTGGATACCTCCCAAGTCCTGTATGAGTGGGAACAGGGATTTTC 435
        ************************************************************

Human   TCAGTCCTTCACTCAAGAACAAGTAGCTGATATTGATGGACAGTATGCAATGACTCGAGC 540
Cyno    TCAGTCCTTCACTCAAGAACAAGTAGCTGATATTGATGGACAGTATGCAATGACTCGAGC 495
        ************************************************************

Human   TCAGAGGGTACGAGCTGCTATGTTCCCTGAGACATTAGATGAGGGCATGCAGATCCCATC 600
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Cyno    TCAGAGGGTACGAGCTGCTATGTTCCCTGAGACATTAGATGAGGGCATGCAGATCCCATC 555
        ************************************************************

Human   TACACAGTTTGATGCTGCTCATCCCACTAATGTCCAGCGTTTGGCTGAACCATCACAGAT 660
Cyno    TACACAGTTTGATGCTGCTCATCCCACTAATGTCCAGCGTTTGGCTGAACCATCACAGAT 615
        ************************************************************

Human   GCTGAAACATGCAGTTGTAAACTTGATTAACTATCAAGATGATGCAGAACTTGCCACACG 720
Cyno    GCTGAAACATGCAGTTGTAAACTTGATTAACTATCAAGATGATGCAGAACTTGCCACACG 675
        ************************************************************

Human   TGCAATCCCTGAACTGACAAAACTGCTAAATGACGAGGACCAGGTGGTGGTTAATAAGGC 780
Cyno    TGCAATCCCTGAACTGACAAAACTGCTAAATGATGAGGACCAGGTGGTGGTTAATAAGGC 735
        ********************************** ***************************

Human   TGCAGTTATGGTCCATCAGCTTTCTAAAAAGGAAGCTTCCAGACACGCTATCATGCGTTC 840
Cyno    TGCAGTTATGGTCCATCAGCTTTCTAAAAAGGAAGCTTCCAGACACGCTATCATGCGTTC 795
        ************************************************************

Human   TCCTCAGATGGTGTCTGCTATTGTACGTACCATGCAGAATACAAATGATGTAGAAACAGC 900
Cyno    TCCTCAGATGGTGTCTGCTATTGTACGTACCATGCAGAATACAAATGATGTAGAAACAGC 855
        ************************************************************

Human   TCGTTGTACCGCTGGGACCTTGCATAACCTTTCCCATCATCGTGAGGGCTTACTGGCCAT 960
Cyno    TCGTTGTACCGCTGGGACCTTGCATAACCTTTCCCATCATCGGGAGGGCTTGTTGGCCAT 915
        ****************************************** ******** ********

Human   CTTTAAGTCTGGAGGCATTCCTGCCCTGGTGAAAATGCTTGGTTCACCAGTGGATTCTGT 1020
Cyno    CTTTAAGTCTGGAGGCATTCCTGCCCTGGTGAAAATGCTTGGTTCACCAGTGGATTCTGT 975
        ************************************************************

Human   GTTGTTTTATGCCATTACAACTCTCCACAACCTTTTATTACATCAAGAAGGAGCTAAAAT 1080
Cyno    GTTGTTTTATGCCATTACAACTCTCCACAACCTTTTATTACATCAAGAAGGAGCTAAAAT 1035
        ************************************************************

Human   GGCAGTGCGTTTAGCTGGTGGGCTGCAGAAAATGGTTGCCTTGCTCAACAAAACAAATGT 1140
Cyno    GGCAGTGCGTTTAGCTGGCGGGCTACAGAAAATGGTTGCCTTGCTCAACAAAACAAACGT 1095
        ****************** ***** ********************************** **

Human   TAAATTCTTGGCTATTACGACAGACTGCCTTCAAATTTTAGCTTATGGCAACCAAGAAAG 1200
Cyno    TAAATTCTTGGCTATTACGACAGACTGCCTTCAGATTTTAGCATATGGCAACCAAGAAAG 1155
        ********************************** ******** ****************

Human   CAAGCTCATCATACTGGCTAGTGGTGGACCCCAAGCTTTAGTAAATATAATGAGGACCTA 1260
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Cyno    CAAGCTGATCATACTGGCTAGTGGTGGACCCCAAGCTTTAGTAAATATAATGAGGACCTA 1215
        ****** **************************************************

Human   TACTTACGAAAAACTACTGTGGACCACAAGCAGAGTGCTGAAGGTGCTATCTGTCTGCTC 1320
Cyno    TACTTATGAGAAACTACTGTGGACCACAAGCAGAGTGCTGAAGGTGCTATCCGTCTGCTC 1275
        ****** ** ****************************************** ********

Human   TAGTAATAAGCCGGCTATTGTAGAAGCTGGTGGAATGCAAGCTTTAGGACTTCACCTGAC 1380
Cyno    TAGTAATAAGCCAGCTATTGTAGAAGCTGGTGGAATGCAAGCTTTAGGACTTCACCTGAC 1335
        ************ **********************************************

Human   AGATCCAAGTCAACGTCTTGTTCAGAACTGTCTTTGGACTCTCAGGAATCTTTCAGATGC 1440
Cyno    AGATCCAAGTCAACGTCTTGTTCAGAACTGTCTTTGGACTCTCAGGAATCTTTCAGATGC 1395
        ************************************************************

Human   TGCAACTAAACAGGAAGGGATGGAAGGTCTCCTTGGGACTCTTGTTCAGCTTCTGGGTTC 1500
Cyno    TGCAACTAAACAGGAAGGGATGGAAGGTCTCCTTGGGACTCTTGTTCAGCTTCTGGGTTC 1455
        ************************************************************

Human   AGATGATATAAATGTGGTCACCTGTGCAGCTGGAATTCTTTCTAACCTCACTTGCAATAA 1560
Cyno    AGATGATATAAATGTGGTCACCTGTGCAGCTGGAATTCTTTCTAACCTCACTTGCAATAA 1515
        ************************************************************

Human   TTATAAGAACAAGATGATGGTCTGCCAAGTGGGTGGTATAGAGGCTCTTGTGCGTACTGT 1620
Cyno    TTATAAGAATAAGATGATGGTCTGCCAAGTGGGTGGTATAGAGGCTCTTGTGCGTACTGT 1575
        ********* **********************************************

Human   CCTTCGGGCTGGTGACAGGGAAGACATCACTGAGCCTGCCATCTGTGCTCTTCGTCATCT 1680
Cyno    CCTTCGGGCTGGTGACAGGGAAGACATCACTGAGCCTGCCATCTGTGCTCTTCGTCATCT 1635
        ************************************************************

Human   GACCAGCCGACACCAAGAAGCAGAGATGGCCCAGAATGCAGTTCGCCTTCACTATGGACT 1740
Cyno    GACCAGCCGACACCAAGAAGCAGAGATGGCCCAGAATGCAGTTCGCCTTCACTATGGACT 1695
        ************************************************************

Human   ACCAGTTGTGGTTAAGCTCTTACACCCACCATCCCACTGGCCTCTGATAAAGGCTACTGT 1800
Cyno    ACCAGTTGTGGTTAAGCTCTTACACCCACCATCCCACTGGCCTCTGATAAAGGCTACTGT 1755
        ************************************************************

Human   TGGATTGATTCGAAATCTTGCCCTTTGTCCCGCAAATCATGCACCTTTGCGTGAGCAGGG 1860
Cyno    TGGATTGATTCGAAATCTTGCCCTTTGTCCAGCAAATCATGCACCTTTGCGTGAGCAGGG 1815
        ******************************** ****************************

Human   TGCCATTCCACGACTAGTTCAGTTGCTTGTTCGTGCACATCAGGATACCCAGCGCCGTAC 1920
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Cyno    TGCCATTCCACGACTAGTTCAGTTGCTTGTTCGTGCACATCAGGATACCCAGCGCCGTAC 1875
        ************************************************************

Human   GTCCATGGGTGGGACACAGCAGCAATTTGTGGAGGGGGTCCGCATGGAAGAAATAGTTGA 1980
Cyno    GTCCATGGGTGGGACACAGCAGCAATTTGTGGAGGGGGTCCGCATGGAAGAAATAGTTGA 1935
        ************************************************************

Human   AGGTTGTACCGGAGCCCTTCACATCCTAGCTCGGGATGTTCACAACCGAATTGTTATCAG 2040
Cyno    AGGTTGTACTGGAGCCCTTCACATCCTAGCTCGGGATGTTCACAACCGAATTGTAATCAG 1995
        ********* ****************************************** *****

Human   AGGACTAAATACCATTCCATTGTTTGTGCAGCTGCTTTATTCTCCCATTGAAAACATCCA 2100
Cyno    AGGACTAAATACCATTCCATTGTTTGTGCAGCTGCTTTATTCTCCCATTGAAAACATCCA 2055
        ************************************************************

Human   AAGAGTAGCTGCAGGGGTCCTCTGTGAACTTGCTCAGGACAAGGAAGCTGCAGAAGCTAT 2160
Cyno    AAGAGTAGCTGCAGGGGTCCTCTGTGAACTTGCTCAGGACAAGGAAGCTGCAGAAGCGAT 2115
        ********************************************************** **

Human   TGAAGCTGAGGGAGCCACAGCTCCTCTGACAGAGTTACTTCACTCTAGGAATGAAGGTGT 2220
Cyno    TGAAGCTGAGGGAGCCACAGCTCCTCTGACAGAGTTACTTCACTCTAGGAATGAAGGTGT 2175
        ************************************************************

Human   GGCGACATATGCAGCTGCTGTTTTGTTCCGAATGTCTGAGGACAAGCCACAAGATTACAA 2280
Cyno    GGCGACGTATGCAGCTGCTGTTTTGTTCCGAATGTCTGAGGACAAGCCACAAGATTACAA 2235
        ****** ******************************************************

Human   GAAACGGCTTTCAGTTGAGCTGACCAGCTCTCTCTTCAGAACAGAGCCAATGGCTTGGAA 2340
Cyno    GAAACGGCTTTCAGTTGAGCTGACCAGCTCTCTCTTCAGAACGGAGCCAATGGCTTGGAA 2295
        ******************************************* ******************

Human   TGAGACTGCTGATCTTGGACTTGATATTGGTGCCCAGGGAGAACCCCTTGGATATCGCCA 2400
Cyno    TGAGACTGCGGATCTTGGACTTGATATTGGTGCCCAGGGAGAACCCCTTGGATATCGCCA 2355
        ********* ****************************************************

Human   GGATGATCCTAGCTATCGTTCTTTTCACTCTGGTGGATATGGCCAGGATGCCTTGGGTAT 2460
Cyno    GGATGATCCTAGCTATCGTTCTTTTCACTCTGGTGGATATGGCCAGGATGCCTTGGGTAT 2415
        ************************************************************

Human   GGACCCCATGATGGAACATGAGATGGGTGGCCACCACCCTGGTGCTGACTATCCAGTTGA 2520
Cyno    GGACCCCATGATGGAACATGAGATGGGTGGCCACCACCCTGGTGCTGACTATCCAGTTGA 2475
        ************************************************************

Human   TGGGCTGCCAGATCTGGGGCATGCCCAGGACCTCATGGATGGGCTGCCTCCAGGTGACAG 2580
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Cyno    TGGGCTGCCAGATCTGGGACATGCCCAGGACCTCATGGATGGGCTGCCTCCAGGTGATAG 2535
        ****************** ************************************** **

Human   CAATCAGCTGGCCTGGTTTGATACTGACCTGTAAATCATCCTTTAG-------------- 2626
Cyno    CAATCAGCTGGCCTGGTTTGATACTGACCTGTAAATCATCCTTTAGCTGTATTGTCTGAA 2595
        *********************************************

Human   ------------------------------------------------------------
Cyno    CTTGCATTGTGATTGGCCTGTAGAGTTGCTGAGAGGGCTCGAGGGGTGGGCTGGTATCTC 2655

Human   ------------------------------------------------------------
Cyno    AGAAAGTGCCTGACACACTAACCAAGCTGAGTTTCCTATGGGAACAATTGAAGTAAACTT 2715

Human   -------------------------GAGTAACAATACAAATGGATTTTGGGAGTGACTCA 2661
Cyno    TTTGTTCTGGTCCTTTTTGGTCGAGGAGTAACAATACAAATGGATTTTGGGAGTGACTCA 2775
                                  ***********************************

Human   AGAAGTGAAGAATGCACAAGAATGGATCACAAGATGGAATTTATCAAACCCTAGCCTTGC 2721
Cyno    AGAAGTGAAGAATGCACAAGAATGGATCACAAGATGGAATTTATCAAACCCTAGCCTTGC 2835
        ************************************************************

Human   TTGTTAAATTTTTTTTTTTTTTTTTTAAGAATATCTGTAATGGTACTGACTTTGCTTGC 2781
Cyno    TTGTTAAATTTTTTTTTTTTTTTTTTAAGAATATCTGTAATGGTACTGACTTTGCTTGC 2895
        ************************************************************

Human   TTTGAAGTAGCTCTTTTTTTTTTTTTTTTTTTTTTTTGCAGTAACTGTTTTTTAAGTCT 2841
Cyno    TTTGAAGTAGCTCTTTTTTTTTTTTTTTTTTTTTTTTGCAGTAACTGTTTTTTAAGTCT 2955
        ************************************************************

Human   CTCGTAGTGTTAAGTTATAGTGAATACTGCTACAGCAATTTCTAATTTTTAAGAATTGAG 2901
Cyno    CTCGTAGTGTTAAGTTATAGTGAATACTGCTACAGCAATTTCTAATTTTTAAGAATTGAG 3015
        ************************************************************

Human   TAATGGTGTAGAACACTAATTCATAATCACTCTAATTAATTGTAATCTGAATAAAGTGTA 2961
Cyno    TAATGGTGTAGAACACTAATTCATAATCACTCTAAT-AATTGTAATCTGAATAAAGTGTA 3074
        ************************************ ************************

Human   ACAATTGTGTAGCCTTTTTGTATAAAATAGACAAATAGAAAATGGTCCAATTAGTTTCCT 3021
Cyno    ACA-TTGTGTAGCCTTTTTGTATAAAATAGACAAATAGAAAATGGTCCAATTAGTTTCCT 3133
        *** ********************************************************

Human   TTTTAATATGCTTAAAATAAGCAGGTGGATCTATTTCATGTTTTTGATCAAAAACT--AT 3079
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Cyno        TTTTAATATGCTTAAAATAAGCAGGTGGATCTATTTCATGTTTTTGATCAAAAACTTTAT 3193
            ************************************************************  **

Human       TTGGGATATGTATGGGTAGGGTAAATCAGTAAGAGGTGTTATTTGGAACCTTGTTTTGGA 3139
Cyno        TTGGGATATGTATGGGTAGGGTAAATCAGTAAGAGGTGTTATTTGGAACCTTGTTTTGGA 3253
            ************************************************************

Human       CAGTTTACCAGTTGCCTTTTATCCCAAAGTTGTTGTAACCTGCTGTGATACGATGCTTCA 3199
Cyno        CAGTTTACCAGTTGCCTTTTATCCCAAAGTTGTTGTAACCTGCTGTGATACAATGCTTCA 3313
            ************************************************** ********

Human       AGAGAAAATGCGGTTATAAAAAATGGTTCAGAATTAAACTTTTAATTCATTCGATTG 3256
Cyno        AGAGAAAATGCGGTTATAAAAAATGGTTCAGAA---------------------- 3346
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Human         (SEQ ID NO: 4112)
Cyno          (SEQ ID NO: 4113)
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[0134] 食蟹猴序列和人序列的起始密码子 (ATG) 和终止子 (TGA) 为粗体加下划线。人序列和食蟹猴序列之间匹配的核苷酸用星号 (*) 标记。可以通过比较以上序列 (SEQ ID NOs:4112 和 4113),轻易地确定给定的序列 (例如,siRNA 或双链体的第一链或第二链) 是否匹配 β - 联蛋白序列的有义链或反义链。

[0135] 针对 β - 联蛋白的 RNAi 剂的额外实施方案

[0136] 本公开涵盖针对 β - 联蛋白的 RNAi 剂的多种实施方案。

[0137] 在一个实施方案中,本公开的 β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA、大鼠 β - 联蛋白 mRNA 和食蟹猴 β - 联蛋白 mRNA 中相同的序列。这种序列同一性促进在人类试验之前的动物试验。在另一个实施方案中,β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA、小鼠 β - 联蛋白 mRNA 和食蟹猴 β - 联蛋白 mRNA 中相同的序列。在另一个实施方案中,β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA 和小鼠 β - 联蛋白 mRNA 中相同的序列。在另一个实施方案中,β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA、大鼠 β - 联蛋白 mRNA 和食蟹猴 β - 联蛋白 mRNA 中相同的序列。在另一个实施方案中,β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA、小鼠 β - 联蛋白 mRNA 和大鼠 β - 联蛋白 mRNA 中相同的序列。在另一个实施方案中,β - 联蛋白 RNAi 剂包含在人 β - 联蛋白 mRNA、大鼠 β - 联蛋白 mRNA 和食蟹猴 β - 联蛋白 mRNA 中相同的序列。

[0138] 在一个实施方案中,β - 联蛋白 RNAi 剂包含不匹配任何其他 mRNA 序列的序列。在一个实施方案中,β - 联蛋白 RNAi 剂包含与全部其他已知的非 β - 联蛋白 mRNA 差异至少 0、1、2 或 3 个核苷酸的序列。在多种实施方案中,β - 联蛋白 RNAi 剂敲减任何其他基因超过 5%、10%、15%、20%、25%、30% 或 40%。可以在体外,或通过使用各种基因的阵列测试 β - 联蛋白 RNAi 剂敲减其他基因的能力。

[0139] β - 联蛋白中的多种突变是已知的 ;这些突变中许多参与 β - 联蛋白相关疾病。这些突变包括在 33、37、41 和 45 处残基的突变,但是也已经在第 8、11、13、21、24、25、28、29、

32、34、39、47、48 和 55 位置处找到疾病相关性突变。在本公开的多种实施方案中，可以构思 RNAi 剂偏好地靶向突变（而非野生型）形式的 β-联蛋白。

[0140] 在其他实施方案中，本公开的 RNAi 剂与 5' 或 3' UTR[非翻译区)] 结合。

[0141] 可以直接测量 RNAi 剂降低 β-联蛋白水平的功效，例如，测量 β-联蛋白 mRNA 丰度的水平或蛋白质本身的水平或细胞分布。例如，β-联蛋白在细胞质和/或细胞核中的积累量与各种病态相关。在施用 RNAi 剂后，可以对细胞和组织检测 β-联蛋白在细胞质和细胞核中的积累。备选地，可以通过测量 β-联蛋白的任一种或多种已知活性的水平间接地测量 RNAi 的功效。例如，β-联蛋白定位至细胞核可以导致各种基因（包括 c-myc）的转录。在施用针对 β-联蛋白的 RNAi 剂后，可以测量由 β-联蛋白激活 c-myc 或其他基因的表达。

[0142] 在一个实施方案中，将本公开的 β-联蛋白 RNAi 剂施用至有需要的患者（例如，患有、疑似患有或易患以下疾病的患者：结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合，以及相似和相关的疾病）。

[0143] 也可以对患者施用多于一种对 β-联蛋白特异的 RNAi 剂。在一个实施方案中，本公开的 β-联蛋白 RNAi 剂可以任选地与适用于该疾病的一种或多种额外药剂一起施用。在一个实施方案中，本公开的 β-联蛋白 RNAi 剂可以任选地与任何其他适宜的额外治疗一起施用，其中所述的额外治疗可以是组合物或方法。

[0144] 多种病与 β-联蛋白中的突变（如上文所列的那些）相关，所述突变导致 β-联蛋白的过量表达、过多活性和/或不恰当细胞区室化。除 β-联蛋白之外的组分中的突变也可以激活 Wnt 信号传导途径。例如，APC（肿瘤抑制物-腺瘤结肠息肉基因产物）正常情况下控制 β-联蛋白活性。APC 正常情况下与糖原合酶激酶 3-β (GSK-3β) 和轴蛋白构成复合体。这种复合体结合细胞质中的 β-联蛋白。借助于酪蛋白激酶 (CK1)（其实施 β-联蛋白的初始磷酸化），GSK-3β 能够接着磷酸化 β-联蛋白。这将 β-联蛋白引向泛素化和细胞蛋白酶体降解，并且防止 β-联蛋白转运至细胞核。APC 突变因此可以导致 Wnt 信号传导途径的组成型激活。因此可以将针对 β-联蛋白的 RNAi 剂施用至存在病态的患者，所述病态不仅与 β-联蛋白中的突变相关，还与 Wnt 信号传导途径的其他组分（如 APC）中的突变相关。

[0145] 在结肠腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合以及相似和相关疾病的情况下，RNAi 剂和额外的疾病疗法可以按任意顺序、同时或依次地或随时间推移以一个或多个剂量施用。

[0146] 在这些 β-联蛋白相关疾病的治疗中，RNAi 剂和额外的疾病治疗可以按任意顺序、同时或依次地或随时间推移按多个剂量施用。RNAi 剂和额外治疗的施用可以例如是同时的，并行的、分别的或依次的。

[0147] 同时施用可以例如以与两种或更多种有效成分的一个固定组合的形式进行，或通

过同时施用独立配制的两种或更多种有效成分进行。依次使用（施用）优选地意指优选地在一个时间点施用某组合的一种或多种组分，在不同的时间点施用其他组分，即，以时间交错方式(chronically staggered manner)施用，从而该组合比独立施用的单一混合物显示出更高的效率（特别显示协同作用）。分别使用（施用）优选地意指在不同时间点彼此独立施用该组合的各个组分，优选地意指组分 (a) 和 (b) 如此施用，从而这两种化合物的明显可度量血液水平的重叠不以重叠方式存在（在相同的时间）。

[0148] 另外，两种或更多种依次、分别和同时施用的组合优选地是可能的，从而组合的组分 - 药物显示联合治疗效果，所述联合治疗效果超过以下情况时存在的效果：组合的组分 - 药物在如此大的时间区间分别使用，从而不能找到对其治疗效率的相互效应，协同效应是特别优选的。

[0149] 如本文所用的术语“延迟进展”意指施用该组合至正处于待治疗疾病的首次表现或复发的预备阶段或早期阶段中的患者，在所述患者中，例如诊断出相应疾病的前期形式，或所述患者处于例如医学治疗期间的某种状况，或因意外而产生的某种状况，在所述状况下相应疾病将有可能形成。

[0150] “联合治疗活性”或“联合治疗效果”意指化合物可以按这类时间区间（以时间交错方式，特别地以序列特异性方式）分别给予，从而它们优选地在待治疗的温血动物（特别是人）中仍显示（优选地显示协同）相互作用（联合治疗效果）。尤其可以通过追踪血液水平确定究竟是否为这种情形，所述血液水平显示两种化合物至少在某些时间区间期间存在于待治疗的人的血液中。

[0151] 额外的定义

[0152] 出于便利，下文提供在本说明书、实施例和所附权利要求中使用的某些术语和短语的含义。如果本说明书的其他部分中某术语的用途和这个章节 (document) 中所提供的其定义之间存在明显的不一致性，则这个章节中的定义应当占优。

[0153] 如本公开中通篇所用，冠词如“a”和“an”指该冠词的语法对象的一个或多于一个（至少一个）。

[0154] 针对 β - 联蛋白的 RNAi 剂

[0155] 在一个实施方案中，本公开涉及 β - 联蛋白 RNAi 剂或其他与编码 β - 联蛋白基因（或其部分）的 mRNA 互补的反义核酸，或编码该 siRNA(RNAi 剂）的至少一条链的重组表达载体或包含可以作为如下文定义的 RNAi 剂发挥作用的反义核酸的组合物。

[0156] 如本文所用，“反义”核酸包含与编码 β - 联蛋白的“有义”核酸互补（例如与双链 DNA 分子的编码链互补、与 mRNA 互补或与 β - 联蛋白基因的编码链互补）的核苷酸序列。

[0157] 如本文所用，术语“针对 β - 联蛋白的 RNAi 剂”、“对 β - 联蛋白特异的 RNAi 剂”、“针对 β - 联蛋白的 iRNA 剂”、“针对 β - 联蛋白的 siRNA”、“β - 联蛋白 siRNA”等指 siRNA（短抑制性 RNA）、shRNA（短或小发夹 RNA），iRNA（干扰 RNA）剂、RNAi(RNA 干扰）剂、dsRNA（双链 RNA）、微 RNA 等，并且指特异性靶向与 β - 联蛋白基因相对应的 mRNA、对其特异和 / 或与之结合的组合物。如本文所用，术语“反义核酸”或“包含反义核酸的组合物”等广泛地意在涵盖包含至少一条对其靶反义的核酸链的任何组合物；这包括但不限于任何 siRNA、shRNA、iRHA、dsRNA、微 RNA、反义寡核苷酸和包含反义核酸的任何其他组合物。

[0158] 如本文所用，术语“iRNA”和“RNAi”指一种物质，其含有 RNA（或其衍生物）并且

通过 RNA 诱导的沉默复合物 (RISC) 途径介导另一种 RNA 转录物的定向切割。在一个实施方案中，RNAi 剂是激活 RISC 复合物 / 途径的寡核苷酸组合物。在另一个实施方案中，RNAi 剂包含反义链序列（反义寡核苷酸）。RNAi 剂例如包括 siRNA、dsRNA 和 shRNA。RNAi 剂可以完全是 RNA，或可以包含主链或不是 RNA 的独立核苷酸，如 LNA、GNA、TNA、硼烷磷酸酯 RNA、FANA 等。独立核苷酸可以由 DNA（例如，末端 UU、TT 等）或独立核苷酸在 5' 末端或内部替换。然而，在任何情况下，本公开均不构思包含完全是 DNA 的两条链（例如，双链 DNA）的 RNAi 剂。

[0159] 在一个实施方案中，RNAi 包含单链。这种单链 RNAi 剂寡核苷酸或多核苷酸可以包含有义链或反义链，如 Sioud 2005J. Mol. Biol. 348:1079-1090 及其中参考文献所描述。因此，本公开涵盖具有单链的 RNAi 剂，所述单链包含本文所述的 RNAi 剂的有义链或反义链。

[0160] 本公开的 RNAi 剂靶向（例如，结合于、复性至等）β - 联蛋白 mRNA。对 β - 联蛋白特异的 RNAi 剂的使用导致 β - 联蛋白活性、水平和 / 或表达的减少，例如，靶基因或靶序列的“敲减”或“敲除”。特别地，在一个实施方案中，在病态以 β - 联蛋白的过量表达或过多活性为特征的情况下，针对 β - 联蛋白的 RNAi 剂的施用敲减 β - 联蛋白靶，足以恢复 β - 联蛋白活性的正常水平。

[0161] 在一个实施方案中，RNAi 包含单链（如 shRNA，如本文所述）。在其他实施方案中，RNAi 剂包含单链，因为有义链和反义链是连续的、由环连接或否则是连接的。

[0162] 在多种实施方案中，一条链或两条链带切口。

[0163] 在一个实施方案中，单链 RNAi 剂寡核苷酸或多核苷酸可以包含有义链和 / 或反义链。见，例如，Sioud 2005J. Mol. Biol. 348:1079-1090 及其中引用的参考文献。因此，本公开涵盖具有单链的 RNAi 剂，所述单链包含本文所述的 RNAi 剂的有义链或反义链。

[0164] 在本公开中特别有用的 RNAi 剂包括可以与 β - 联蛋白 mRNA 的某个区域特异性结合并且具有以下一个或多个性质的那些：在 β - 联蛋白的编码区段结合；在 5' 非翻译区和编码区段的起始密码子的交界处或其附近结合；在 mRNA 的翻译起始位点处或其附近结合；在 β - 联蛋白基因的第三外显子中结合；在外显子和内含子的交界处或其附近结合；与其他基因的 mRNA 少量结合或不结合（少量脱靶效应或无“脱靶效应”）；在不是双链区或茎区（例如，在环部分或单链部分中）的一个区域或多个区域内或其附近与 β - 联蛋白 mRNA 结合；激发少量免疫原性或不激发免疫原性；在 β - 联蛋白 mRNA 序列中各个动物物种（包括人、小鼠、大鼠、食蟹猴等）之间保守的区段内结合，原因是保守序列的存在促进使用各种实验室动物检验；与 mRNA 的双链区域结合；与 AT 丰富区域结合（例如，至少约 50%、51%、52%、53%、54%、55%、56%、57%、58%、59 或 60% AT 丰度）；和 / 或缺少已知或疑似减低 siRNA 活性的特定序列，例如，GG 序列在 5' 末端的存在，这可以减少 RNAi 剂的双链部分的分离。在多种实施方案中，对 β - 联蛋白特异的 RNAi 剂可以是具有这些性质中一种性质或多种性质的双链 RNA。

[0165] 如本文所用，术语“双链 RNA”或“dsRNA”指包含第一链和第二链的 RNAi 剂；例如，包含具有杂交双链体区（即，其中来自第一链和第二链的核苷酸碱基配对的区域）的 RNA 分子或分子复合物的组合物，其中所述杂交双链体区包含两条反平行的和基本上互补的核酸链，其将称作具有相对于靶 RNA 的“有义”方向”和“反义”方向。相对于 mRNA 靶，反义链也称作“引导”链，并且有义链也称作“载客”链。载客链可以包含以下至少一种或更多种情

况：与另一条链相比一个或多个额外的核苷酸（例如，凸出或 1 核苷酸环）、与另一条链相比的切刻、缺口等。在多种实施方案中，RNAi 剂包含第一链和第二链。在多种实施方案中，第一链是有义链并且第二链是反义链。在其他实施方案中，第一链是反义链并且第二链是有义链。

[0166] 双链体区可以具有允许经 RISC 途径特异性降解所期望的靶的任何长度，但是一般范围是从 9 至 36 碱基对（“bp”）的长度，例如，15-30 个碱基对长度。考虑一个在 9 和 36 个碱基对之间的双链体，该双链体可以具有这个范围内的任何长度，例如，9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35 或 36 碱基对（bp）及其之间的任何子范围，包括但不限于 15-30 个碱基对、15-26 个碱基对、15-23 个碱基对、15-22 个碱基对、15-21 个碱基对、15-20 个碱基对、15-19 个碱基对、15-18 个碱基对、15-17 个碱基对、18-30 个碱基对、18-26 个碱基对、18-23 个碱基对、18-22 个碱基对、18-21 个碱基对、18-20 个碱基对、19-30 个碱基对、19-26 个碱基对、19-23 个碱基对、19-22 个碱基对、19-21 个碱基对、19-20 个碱基对、19 个碱基对、20-30 个碱基对、20-26 个碱基对、20-25 个碱基对、20-24 个碱基对、20-23 个碱基对、20-22 个碱基对、20-21 个碱基对、20 个碱基对、21-30 个碱基对、21-26 个碱基对、21-25 个碱基对、21-24 个碱基对、21-23 个碱基对、21-22 个碱基对、21 个碱基对、22 个碱基对或 23 个碱基对。细胞中通过 Dicer 和相似酶加工产生的 dsRNA 通常具有范围 19-22 的碱基对长度。dsRNA 的双链体区的一条链包含与靶 RNA 的区域基本上互补的序列。形成双链体结构的两条链可以来自具有至少一个自身互补双链体区域的单个 RNA 分子，或可以由杂交以形成该双链体的两个或更多个独立 RNA 分子组成。在双链体区从单个分子的两条链形成的情况下，该分子可以具有由形成双链体结构的一条链的 3’-端和相应另一条链的 5’-端之间的单链核苷酸链（本文中称作“发夹环”，例如，如存在于 shRNA 构建体中）分隔的双链体区。发夹环可以包含至少一个非配对核苷酸；在一些实施方案中，发夹环可以包含至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 20 个、至少 23 个或更多个非配对核苷酸。在 dsRNA 的两条基本上互补链由单独 RNA 分子构成的情况下，这些分子不需要共价连接，但是可以共价连接。在两条链由发夹环共价连接的情况下，构建体通常在本文中和本领域中称作“shRNA”。在两条链借助发夹环之外的方式共价连接的情况下，连接结构称作“接头”。

[0167] 术语“RNAi 剂”和“siRNA”还在本文中用来指如上文所述的可用于 RNA 干扰的 dsRNA。

[0168] 在本公开的多种实施方案中，组合物涉及针对 β-联蛋白的 RNAi 剂及其修饰变体和未修饰变体，其中所述 RNAi 剂包含有义链和/或反义链，所述有义链包含与本文中公开的、特别在表 1、2、3、4、5、6、7、8 和/或 9 中公开的任何 RNAi 剂的有义链具有 0、1、2 或 3 个错配的至少 15 个连续核苷酸，所述反义链包含与本文中公开的、特别在表 1、2、3、4、5、6、7、8 和/或 9 中公开的任何 RNAi 剂的反义链具有 0、1、2 或 3 个错配的至少 15 个连续核苷酸。

[0169] 包含不同于所公开序列的错配的针对 β-联蛋白的 RNAi 剂

[0170] 本文中公开了针对 β-联蛋白的 RNAi 剂的各种具体实施方案；在表 1、2 和 3 中提供示例序列。本公开的具体实施方案包括了包含下述序列的 RNAi 剂及其修饰变体和未修饰变体，所述序列与表 1、2、3、4、5、6、7、8 和/或 9 中所列的任一 RNAi 剂差异 0、1、2 或 3 个核苷酸或 bp[碱基对)](例如，0、1、2 或 3 错配)。

[0171] 错配在本文中定义为将两个序列最大限度地对齐并比较时碱基序列或长度之间的差异。将错配定义为一个位置，其中一个序列的碱基不匹配另一个序列的碱基。因此例如，如果一个序列中的某个位置具有特定碱基（例如，A）并且另一个序列上的相应位置具有不同的碱基（例如，G），则计为错配。例如用 T、C、G 或 U 置换 A 将构成错配。用 T、A、C 或 U 置换 G 也将构成错配。用 T、G、A 或 U 置换 C 也将构成错配。用 A、C 或 G 置换 U 将构成错配。然而注意，在给定的链上，U 可以由 T 替换（作为 RNA 或，优选地，DNA，例如，2'－脱氧－胸苷）；用 T 替换 U 不是错配，因为 U 或 A 可以与对侧链上的 A 配对。RNAi 剂因此可以包含一些 DNA 碱基，例如，T 或末端 TT 或 UU。

[0172] 例如，如果一个序列中的某个位置具有碱基（例如，A），并且另一个序列中的相应位置没有碱基（例如，该位置是包含磷酸酯－糖主链但是不包含碱基的非碱基核苷酸），则计为错配。任何一个序列中（或有义链或反义链中）的单链切刻不计为错配。因此，作为一个非限制性例子，如果一个序列包含序列 AG，但是另一个序列包含在 A 和 G 之间具有单链切刻的序列 AG，则将不计为错配。如果一个序列包含 C 并且另一个序列在相同位置包含修饰的 C（例如，2'－修饰），则将不计为错配。

[0173] 此外，如果在不修饰碱基的情况下对 RNAi 剂的糖、磷酸酯或主链进行修饰，则不计为错配。因而，作为 RNA 的序列 UGGUGCUGACUAUCCAGUU(SEQ ID NO:429) 和作为 PNA（肽核酸）的相同序列彼此具有 0 个错配。

[0174] 还应指出，表 1、2、3、4、5、6、7、8 和／或 9 中的 RNAi 剂的序列包括包含修饰的序列，如表 3 中详述。例如，RNAi 剂 AD-18892 的一个修饰变体包含序列 uGGuGcuGAcuAuccAGuudTdT(SEQ ID NO:6132) 和 AACUGGAuAGUcAGcACcAdTdT(SEQ ID NO:660) 的链。应当指出，将 dTdT(2'－脱氧胸苷 -5'－磷酸和 2'－脱氧胸苷 -5'－磷酸）或在一些情况下将 TT 或 UU 作为帽结构或延长物添加至两个 3' 末端，但是在计算错配总数时不包括这种帽结构或延长物。此外，序列 uGGuGcuGAcuAuccAGuu(SEQ ID NO:1) 包含来自 β－联蛋白基因的相应部分或 UGGUGCUGACUAUCCAGUU(SEQ ID NO:4771) 的修饰。在这种情况下，小写体“c”表示 2'-O- 甲基胞苷 -5'－磷酸，并且小写体“u”表示 2'-O- 甲基尿苷 -5'－磷酸。大写体“A”、“C”、“G”和“U”分别表示未修饰的腺苷 -5'－磷酸、胞苷 -5'－磷酸、鸟苷 -5'－磷酸和尿苷 -5'－磷酸。对序列之间的 0、1、2 或 3 个错配计数时，修饰的 c 置换未修饰的 C 不计为错配。对于表 1、2、3、4、5、6、7、8 和／或 9 中的全部序列均是如此。因而，将 (a) 在测试序列和修饰的序列（例如，AD-18892 的序列或表 1、2、3、4、5、6、7、8 和／或 9 中的任何其他序列）之间，和 (b) 在相同测试序列和来自 β－联蛋白基因的相应未修饰序列（例如，β－联蛋白基因的与 AD-18892 或表 1 中任何其他序列相对应的部分）之间和 (c) 在修饰的序列和具有相同碱基序列的差异性修饰的序列之间计算相等数目的错配。

[0175] 在一个具体实施方案中，本公开包含 RNAi 剂及其修饰变体和未修饰变体，所述 RNAi 剂包含反义链，所述反义链包含与表 1、2、3、4、5、6、7、8 和／或 9 中列出的任一 RNAi 剂的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个或 19 个连续核苷酸。

[0176] 应当指出本公开涉及所公开序列的“修饰变体和未修饰变体”。

[0177] 特定序列的“未修饰变体”（也称作“通用序列”）是 β－联蛋白的不带任何修饰的相应部分。例如，AD-18892 的修饰变体（或“通用序列”）包含序列 uGGuGcuGAcuAuccAGuudTdT(SEQ ID NO:6132) 的链；相应的“未修饰变体”是野生型 β－联

蛋白序列的不带修饰或末端 dTdT 的相应部分，即，UGGUGCUGACUAUCCAGUU(SEQ ID NO：6140)，如上文所述。表 1、2、3、4、5、6、7、8 和 / 或 9 的序列的“未修饰变体”具有不带碱基修饰或末端 dTdT 的相同序列。一个给出的序列及其“未修饰变体”差异 0 个核苷酸（并且没有错配）。

[0178] 特定序列的“修饰变体”包含主链、糖、磷酸酯或碱基的一个或多个（或一个或多个更少）修饰，但是没有任何碱基置换（例如，G 置换 C，或 A 置换 G）；因此一个给出的序列及其修饰变体差异 0 个核苷酸（并且没有错配）。作为一个非限制性例子，序列 uGGuGcuGAcuAuccAGuu(SEQ ID NO：1) 的修饰变体是 UGGuGcuGAcUAuccAGuu(SEQ ID NO：6089)。作为另一个例子，作为 RNA 的给出序列 [例如，uGGuGcuGAcuAuccAGuu(SEQ ID NO：1)] 和作为 PNA 的相同序列彼此是修饰变体并且差异 0 个核苷酸（并且没有错配）。类似地，作为锁核酸 (LNA)、吗啉代、苏糖核酸 (TNA) 或二醇核酸 (GNA) 或 FANA 的相同序列（没有碱基置换）将是具有 0 个错配的修饰变体。

[0179] 如下文详述，将给定位置处的单核苷酸用修饰形式的相同核苷酸置换将产生修饰变体（具有 0 个错配）。

[0180] 在另一个具体实施方案中，RNAi 剂包含有义链，所述有义链包含与表 1、2、3、4、5、6、7、8 和 / 或 9 中列出的任一 RNAi 剂的有义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，及其修饰变体和未修饰变体。

[0181] 本公开的针对 β - 联蛋白的 RNAi 剂可以用于 RNA 干扰。

[0182] RNAi 剂序列的修饰

[0183] 本公开涵盖未修饰的序列和示例性修饰序列，如在表 1、2 和 3 中公开的那些。

[0184] 本公开还涵盖所公开的序列的任何其他修饰（例如，修饰变体）。

[0185] 例如，本公开涵盖了给定位置处的单核苷酸用修饰形式的相同核苷酸置换的 RNAi 剂。因而，核苷酸 (A、G、C 或 U) 可以由相应的 5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶、次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶、5- 羧甲基氨基甲基 -2- 硫代尿苷、5- 羧甲基氨基甲基尿嘧啶、二氢尿嘧啶、β -D- 半乳糖基 Q 核苷 (beta-D-galactosylqueosine)、肌苷、N6- 异戊烯基腺嘌呤、1- 甲基鸟嘌呤、1- 甲基肌苷、2,2- 二甲基鸟嘌呤、2- 甲基腺嘌呤、2- 甲基鸟嘌呤、3- 甲基胞嘧啶、5- 甲基胞嘧啶、N6- 腺嘌呤、7- 甲基鸟嘌呤、5- 甲氨基甲基尿嘧啶、5- 甲氧氨基甲基 -2- 硫尿嘧啶、β -D- 甘露糖基 Q 核苷 (beta-D-mannosylqueosine)、5’- 甲氧基羧基甲基尿嘧啶、5- 甲氧基尿嘧啶、2- 甲基硫代 -N6- 异戊烯基腺嘌呤、尿嘧啶 -5- 羟基乙酸 (v)、wybutoxosine、假尿嘧啶、Q 核苷 (queosine)、2- 硫胞嘧啶、5- 甲基 -2- 硫尿嘧啶、2- 硫尿嘧啶、4- 硫尿嘧啶、5- 甲基尿嘧啶、尿嘧啶 -5- 羟基乙酸甲酯 (oxyacetic acid methylester)、尿嘧啶 -5- 羟基乙酸 (v)、5- 甲基 -2- 硫尿嘧啶、3-(3- 氨基 -3-N-2- 羧丙基）尿嘧啶、(acp3)w 或 2,6- 二氨基嘌呤替换。

[0186] 额外的修饰变体包括向 RNAi 剂添加任何其他部分（例如，a 放射标记物或其他标签或缀合物）；条件是碱基序列相同，其他部分的添加产生“修饰变体”（无错配）。

[0187] 可以使用各种修饰集合。这些包括以下式样，所述样式用于本文中公开的各种筛选中。

A22S26

A22a 全部 UA 作为 2’-OMe-U A 并且全部 CA 作为 2’-OMe-C A

S26a 全部 U 作为 2’-OMe-U 并且全部 C 作为 2’-OMe-C

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A25S27

A25a wt RNA

S27a wt RNA

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A48S26

A48a 全部 UA 作为 2’-OMe-U A 并且全部 CA 作为 2’-OMe-C A，首个 5’-N 是 DNA

S26a 全部 U 作为 2’-OMe-U 并且全部 C 作为 2’-OMe-C

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A51S26

A51a 全部 U 作为 2’-OMe-U 并且全部 C 作为 2’-OMe-C，例外位置是 1、2 和 14

S26a 全部 U 作为 2’-OMe-U 并且全部 C 作为 2’-OMe-C

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A52S36

A52a 在位置 3、7、10 和 13 处的 2’-OMe-N，在位置 18 和 19 处的 2’-MOE-N

S36a 在位置 4、8、12 和 15 处的 2’-OMe-N，在位置 1、2、18 和 19 处的 2’-MOE-N

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A53S37

A53a 在位置 3、7、10、13、18 和 19 处的 2’-MOE-N

S37a 在位置 1、2、4、8、12、15、18 和 19 处的 2’-MOE-N

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A54S36

A54a 在位置 3、7、10 和 13 处的 2’-OMe-N，在位置 18 和 19 处的 2’-MOE-N，在位置 1 处的 DNA

S36a 在位置 4、8、12 和 15 处的 2’-OMe-N，在位置 1、2、18 和 19 处的 2’-MOE-N

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

A55S36

A55a 在位置 3、7、10 和 13 处的 2’-OMe-N，在位置 18 和 19 处的 2’-MOE-N，

在位置 1 处的 2’-F-N

S36a 在位置 4、8、12 和 15 处的 2’-OMe-N，在位置 1、2、18 和 19 处的 2’-MOE-N

全部 3’突出端作为 2’-OMe-U 2’-OMe-U

[0188] 除这些修饰和修饰样式（例如，式样）之外，可以使用核酸修饰的常识产生所提供序列的其他修饰或修饰集合。

[0189] RNA 干扰

[0190] RNA 干扰 (RNAi) 是一项转录后定向基因沉默技术，该技术使用双链 RNA(dsRNA) 以降解含有与 dsRNA 相同的序列的信使 RNA(mRNA)。当核糖核酸酶 III(Dicer) 将较长 dsRNA 切割成称作 siRNA 的较短片段时，RNAi 的过程出现。由 Dicer 产生的 siRNA（小干扰性 RNA)

一般长约 21 至 23 个核苷酸并且包含约 19 个碱基对双链体（不过人工 siRNA 或 RNAi 剂可以更短，和 / 或平末端化，和 / 或包含一个或多个末端帽结构）。较小的 RNA 区段随后介导靶 mRNA 的降解。Dicer 也已经涉及从结构保守的前体 RNA 中切出 21- 和 22- 个核苷酸时序小 RNA(stRNA)，这些时序小 RNA 涉及翻译性控制。Hutvagner 等人，2001Science 293:834。RNAi 反应的特征还在于常称作 RNA 诱导性沉默复合物 (RISC) 的核酸内切酶复合物，所述核酸内切酶复合物介导切割与 RNAi 剂的反义链互补的单链 mRNA。靶 RNA 的切割在与 siRNA 双链体的反义链互补的区域的中部发生。

[0191] 在一个方面，RNA 干扰剂包括与靶 RNA 序列相互作用以指导切割靶 RNA 的单链 RNA。不希望受理论约束，引入植物和无脊椎动物细胞中的长双链 RNA 被称作 Dicer 的 III 型核酸内切酶分解成 siRNA。Sharp 等人，2001Genes Dev. 15:485。核糖核酸酶 III 型样酶 Dicer 将 dsRNA 加工成至具有特征性双碱基 3' 突出端的 19-23 碱基对短干扰性 RNA。Bernstein 等人，2001Nature 409:363。siRNA 随后被掺入 RNA 诱导性沉默复合物 (RISC) 中，在那里，一种或多种解旋酶解开 siRNA 双链体，从而使得现在未配对的 siRNA 链之一充当引导靶识别的“引导链”成为可能。Nykanen 等人，2001Cell 107:309。一旦与反义引导链适宜的靶 mRNA 结合，RISC 内部的一种或多种核酸内切酶切割靶以引起沉默。Elbashir 等人，2001Genes Dev. 15:188。因此，在一个方面，本公开涉及了促进实现靶基因沉默的 RISC 复合物形成的单链 RNA。

[0192] 还已经在多种系统中研究 RNA 干扰。在果蝇胚胎裂解物中的工作 (Elbashir 等人，2001EMBO J. 20:6877 和 Tuschl 等人，国际 PCT 公开号 WO 01/75164) 已经揭示对多种系统（特别包括哺乳动物）中介导高效 RNAi 活性为必需的 siRNA 长度、结构、化学组成和序列的某些要求。这些研究已经显示，当含有 3' 端二核苷酸突出端时 21- 核苷酸 siRNA 双链体最有活性。耐受用 2'- 脱氧核苷酸 (2'-H) 置换 3' 端 siRNA 突出端核苷酸。此外，siRNA 活性通常需要在 siRNA 双链体的靶互补链上的 5'- 磷酸酯。对治疗用途最重要的是，短于 50bp 或左右的 siRNA 双链体在哺乳动物细胞中不激活干扰素反应。见，例如 Tuschl 等人，WO01/752164。

[0193] 其他已经报道了各种 RNAi 和基因沉默系统。例如，Churikov 等人，国际 PCT 公开号 WO 01/42443 描述了使用某些 dsRNA 修改生物的遗传特征的某些方法。Reed 等人，国际 PCT 公开号 WO 01/68836 描述了用于植物中基因沉默的某些方法。Honer 等人，国际 PCT 公开号 WO 01/70944 描述了使用转基因线虫作为帕金森病模型，利用某些 dsRNA 筛选药物的某些方法。Arndt 等人，国际 PCT 公开号 WO01/92513 描述了通过使用增强 RNAi 的因子介导基因阻抑作用的某些方法。Tuschl 等人，国际 PCT 公开号 WO 02/44321 描述了某些合成性 siRNA 构建体。Pachuk 等人，国际 PCT 公开号 WO 00/63364，和 Satishchandran 等人，国际 PCT 公开号 WO 01/04313 描述了使用载体表达的某些长（超过 250bp）dsRNA 抑制某些多核苷酸序列的功能的某些方法和组合物。Kreutzer 等人，国际 PCT 公开号 WO 02/055692，WO02/055693 和 EP 1144623B1 描述了用于使用 dsRNA 抑制基因表达的某些方法。Graham 等人，国际 PCT 公开号 WO 99/49029 和 WO 01/70949 和 AU 4037501 描述了载体表达的某些 siRNA 分子。Fire 等人，美国专利号 6,506,559 描述了使用介导 RNAi 的某些长 dsRNA(299bp-1033bp) 构建体体外抑制基因表达的某些方法。Martinez 等人，2002Cell，110，563-574 描述了某些单链 siRNA 构建体，包括在 HeLa 细胞中介导 RNA 干扰的某些 5'- 磷酸化单链 siRNA。Harborth

等人，2003，Anti-sense & Nucleic Acid Drug Development 13:83-105 描述了某些化学修饰和结构修饰的 siRNA 分子。Chiu 和 Rana 2003RNA 9:1034-1048 描述了某些化学修饰和结构修饰的 siRNA 分子。Woolf 等人，国际 PCT 公开号 WO 03/064626 和 WO 03/064625 描述了某些化学修饰的 dsRNA 构建体。

[0194] 用于 RNAi 合成的试剂盒是可商业获得的，例如，从 New England Biolabs 和 Ambion 可商业获得。

[0195] 本公开的 RNAi 剂靶向（例如，结合于、复性至等）β-联蛋白 mRNA。针对 β-联蛋白的 RNAi 剂的使用导致 β-联蛋白活性、水平和/或表达的减少，例如，靶基因或靶序列的“敲减”或“敲除”。特别地，在一个实施方案中，在病态以 β-联蛋白的过量表达或过多活性或不恰当细胞区室化为特征的情况下，针对 β-联蛋白的 RNAi 剂的施用敲减 β-联蛋白靶，足以恢复 β-联蛋白活性的正常水平。

[0196] 合适的 RNAi 剂可以通过本领域已知的任何方法选择或是本领域普通技术人员可构思的。例如，选择标准可以包括以下一个或多个步骤：初始分析 β-联蛋白基因序列和设计 RNAi 剂；这种设计可以考虑跨物种的序列相似性（人、食蟹猴、小鼠等）和与其他（非 β-联蛋白）基因的不相似性；体外筛选 RNAi 剂（例如，在 HeLa 细胞中以 10nM）；在 HeLa 细胞中确定 EC_{50}；确定用 RNAi 剂处理的细胞的生存力，所述细胞包括不需要 β-联蛋白用于存活的不敏感细胞（例如，NCI-H28 或 RKO）或需要 β-联蛋白用于存活的敏感细胞（例如，LoVo、DLD-1、LS411N 或 SW403））；例如用人 PBMC（外周血单核细胞细胞）检验以测试 TNF-α 水平以估计免疫原性，其中较不想要免疫刺激性序列；在人全血测定法中检验，其中新鲜人血液用 RNAi 剂处理并且确定细胞因子/趋化因子水平［例如，TNF-α（肿瘤坏死因子-α）和/或 MCP1（单核细胞趋化蛋白 1）］，其中较不想要免疫刺激性序列；在试验动物中使用 Hep3B 皮下肿瘤在体内确定基因敲减；β-联蛋白靶基因调节作用分析，例如，使用药效动力学（PD）标志物，例如，Wnt/β-联蛋白途径的其他组分，其中 β-联蛋白敲减导致剂量依赖性减少这些组分的丰度；并且优化 RNAi 剂的特定修饰。

[0197] 本文所述的 dsRNA 分子（RNAi 剂）因此可用于 β-联蛋白基因的 RNA 干扰。

[0198] RNAi 剂的特征：有义链、反义链和（任选的）突出端

[0199] 在多种实施方案中，RNAi 剂包含第一链和第二链，例如，有义链和反义链。任选地，双链体的一个或两个末端含有非配对核苷酸，在本文中称作“突出端”。

[0200] 术语“反义链”指 RNAi 剂的包含与靶序列基本上互补的区域的链。如本文所用，术语“互补区域”指反义链上与序列（例如，如本文定义的靶序列）基本上互补的区域。在互补区域不与靶序列完全互补的情况下，错配可以存在于分子的内部或末端区域内。通常，最耐受的错配存在于末端区域内，例如，在 5’ 和/或 3’ 末端的 5、4、3 或 2 个核苷酸内部。

[0201] 如本文所用，术语“有义链”指 RNAi 的链，所述链包含与如本文中定义该术语时的反义链的的区域基本上互补的区域。

[0202] 基因的序列可以在个体之间变动，特别地在编码区段内部的摇摆位置处或在非翻译区中；个体也可以在编码序列方面彼此不同，导致 mRNA 中额外的差异。如果需要并且在需要的情况下，RNAi 剂的有义链和反义链的序列因此可以设计成对应于个体患者的序列。也可以在序列方面修饰 RNAi 剂以降低免疫原性、与非预期 mRNA 的结合（例如，“脱靶效应”）或以增加血液中的稳定性。这些序列变体与 RNAi 剂的碱基或 5’ 或 3’ 或其他末端帽

结构的化学修饰无关。在 β-联蛋白的情况下，已经公开三种人转录物：NP_001091679.1；NP_001091680.1；和 NP_001895.1。这些转录物之间的变体可以用来设计针对 β-联蛋白的 RNAi 剂。

[0203] RNAi 剂可以包含突出端、平末端和/或末端帽结构。RNAi 剂可以具有 0、1 或 2 个突出端；在 0 个核苷酸突出端情况下，它们平末端化。RNAi 剂可以具有 0、1 或 2 个平末端。在“平末端化 RNAi 剂”中，两条链以碱基配对方式终止；因此平末端化分子缺少 3’或 5’单链核苷酸突出端。

[0204] 如本文所用，术语“突出端”或“核苷酸突出端”指至少一个非配对核苷酸，其从 RNAi 剂的双链体结构的两条链的至少一条链的末端突出。例如，当 dsRNA 的一条链的 3’-端延伸超过另一条链的 5’-端时或反之亦然，存在一个突出端。dsRNA 可以包含至少一个核苷酸的突出端；备选地，该突出端可以包含至少 2 个核苷酸、至少 3 个核苷酸、至少 4 个核苷酸、至少 5 个或更多个核苷酸。突出端可以包含核苷酸/核苷类似物（包括脱氧核苷酸/核苷）或由其组成。突出端可以在有义链、反义链或其任意组合上。另外，突出端的核苷酸可以存在于 dsRNA 的反义或有义链的 5’末端、3’末端或两个末端上。

[0205] RNAi 剂也可以任选地包含帽结构。术语“帽结构”等包括与双链核苷酸双链体的末端连接的化学部分，但是在本文中用来排除作为核苷酸或核苷的化学部分。“3’帽结构”连接在核苷酸或寡核苷酸的 3’末端处并保护分子例如免遭核酸酶（如血清或肠液中的那些核酸酶）作用。有用 3’帽结构将增加稳定性（例如，减少降解，例如，被核酸酶降解）并且依旧允许 RNAi 活性。多种 3’末端帽结构如例如在 WO 2005/021749 和 WO2007/128477；和美国专利号 8,084,600 和 8,097,716 中公开的那样。“5’帽结构”连接在核苷酸或寡核苷酸的 5’末端处。帽结构不应当干扰（或过度干扰）RNAi 活性。

[0206] 本公开因此构思了包含反义链的对 β-联蛋白特异的 RNAi 剂。在一个更具体的实施方案中，本公开构思对 β-联蛋白特异的 RNAi 剂，所述 RNAi 剂包含第一链和第二链，例如，有义链和反义链（其可以任选地是连续的或经接头或环连接）或反义链和有义链（其可以任选地是连续的或经接头或环连接），所述第一链和第二链一起包含双链区或互补区，并且可以还任选地包含一个或两个突出端，和/或一个或帽结构，和/或糖、磷酸酯或碱基的修饰，和/或额外部分。所述 RNAi 剂用来引起 β-联蛋白基因的 RNA 干扰。

[0207] 靶和互补序列

[0208] 本公开的 RNAi 剂靶向（例如，特异性结合于、复性至等）编码 β-联蛋白基因的 mRNA。对 β-联蛋白特异的 RNAi 剂的使用导致 β-联蛋白活性，水平和/或表达和/或细胞分布/区室化的减少，例如，靶基因或靶序列的“敲减”或“敲除”。特别地在一个实施方案中，在病态以 β-联蛋白的过量表达或过多活性为特征的情况下，针对 β-联蛋白的 RNAi 剂的施用敲减 β-联蛋白基因，足以恢复 β-联蛋白活性的正常水平、丰度或细胞分布。

[0209] 如本文所用，“靶序列”或“靶基因”指基因转录期间形成的 mRNA 分子（例如，β-联蛋白基因）的核苷酸序列的连续部分，包括作为初级转录物产物的 RNA 加工的产物的 mRNA。该序列的靶部分将至少长到足以充当 iRNA 指导在这个部分或其附近切割的底物。例如，靶序列总体上将是从 9-36 个核苷酸 (nt) 长度，例如，15-30 个核苷酸长度，包括其之间的全部子范围。作为一个非限制性实例，靶序列可以具有 15-30 个核苷酸、15-26 个核苷酸、15-23 个核苷酸、15-22 个核苷酸、15-21 个核苷酸、15-20 个核苷酸、15-19 个核苷酸、15-18 个核

苷酸、15-17 个核苷酸、18-30 个核苷酸、18-26 个核苷酸、18-23 个核苷酸、18-22 个核苷酸、18-21 个核苷酸、18-20 个核苷酸、19-30 个核苷酸、19-26 个核苷酸、19-23 个核苷酸、19-22 个核苷酸、19-21 个核苷酸、19-20 个核苷酸、19 个核苷酸、20-30 个核苷酸、20-26 个核苷酸、20-25 个核苷酸、20-24 个核苷酸、20-23 个核苷酸、20-22 个核苷酸、20-21 个核苷酸、20 个核苷酸、21-30 个核苷酸、21-26 个核苷酸、21-25 个核苷酸、21-24 个核苷酸、21-23 个核苷酸、或者 21-22 个核苷酸、21 个核苷酸、22 个核苷酸或 23 个核苷酸。RNAi 的有义链和反义链包含与靶核酸（β-联蛋白）的序列互补的序列。

[0210] 如本文所用，术语“包含某个序列的链”指寡核苷酸，其包含由使用标准核苷酸命名所指的序列描述的核苷酸链。

[0211] 如本文所用并且除非另外说明，否则术语“互补的”指包含第一核苷酸序列的寡核苷酸或多核苷酸在某些条件下与包含第二核苷酸序列的寡核苷酸或多核苷酸杂交和形成双链体结构的能力。这类条件可以例如是严格的，例如，400mM NaCl，40mM PIPES pH 6.4，1mM EDTA，50℃或 70℃持续 12-16 小时，随后洗涤。可以使用其他条件，如在如生物内部可能遭遇的生理相关条件。技术人员将能够根据杂交核苷酸的最终应用，确定最适宜检验两个序列的互补性的条件集合。

[0212] 在 RNAi 剂内部（例如，如本文所述的 dsRNA 内部）的互补序列包括针对一个或两个核苷酸序列的整个长度范围内与包含第二核苷酸序列的寡核苷酸或多核苷酸碱基配对的包含了第一核苷酸序列的寡核苷酸或多核苷酸。这类序列可以在本文中称作彼此“完全互补”。然而，在第一序列相对于本文中第二序列称作“基本上互补”的情况下，这两个序列可以是完全互补的，或一旦杂交为至多 30 个碱基对的双链体时，则它们可以形成 1 个或多个、但通常不多于 5、4、3 或 2 个错配碱基对，同时仍保留在最相关于其最终应用的条件下杂交的能力，例如，通过 RISC 途径抑制基因表达。然而，在两个寡核苷酸设计成一旦杂交就形成双链体的一个或多个单链突出端的情况下，就互补性的确定而言，这类突出端不应当视作错配。例如，出于本文所述的目的，仍可以将包含长 21 个核苷酸的一个寡核苷酸和长 23 个核苷酸的另一个寡核苷酸的 dsRNA 称作“完全互补的”，其中较长的寡核苷酸包含与较短寡核苷酸完全互补的 21 个核苷酸的序列。如上文所述，术语“突出端”描述在双链核苷酸双链体的 3’ 或 5’ 末端处的非配对核苷酸。在一个实施方案中，突出端长 1 至 4 个核苷酸并且在 3’ 末端上。

[0213] 如本文所用，“互补”序列也可以包含非 Watson-Crick 碱基对和 / 或从非天然和修饰的核苷酸形成的碱基对或完全由其形成，只要以上关于它们杂交能力的要求得到满足。这类非 Watson-Crick 碱基对包括但不限于 G:U 摇摆或 Hoogstein 碱基配对。

[0214] 术语“互补的”、“完全互补的”和“基本上互补的”在此可以进一步相对于 dsRNA 的有义链和反义链之间或 RNAi 剂的反义链和靶序列之间的碱基匹配使用，如将从它们使用的上下文来理解。本公开的 RNAi 剂可以包含与本文中公开的靶序列（DNA）的序列互补的序列。例如，如果公开的靶序列是 DNA，则 RNAi 剂可以包含这样一种链，所述链与该 DNA 互补（反平行并且具有与靶的序列成氢键的碱基序列）并且例如是 RNA 或具有少数 DNA 置换的 RNA，或备选性主链如 FANA、PNA、GNA、TNA、硼烷磷酸酯或 LNA，或具有少数置换的 RNA，所述少数置换是 FANA、PNA、GNA、TNA、硼烷磷酸酯或 LNA 等。

[0215] 如本文所用，“与信使 RNA(mRNA) 的至少部分基本上互补”的多核苷酸指与目的

mRNA(例如,编码 β-联蛋白的 mRNA)的连续部分基本上互补的多核苷酸。例如,如果一种多核苷酸与编码 β-联蛋白的 mRNA 的非间断部分基本上互补,则该序列与 β-联蛋白 mRNA 的至少一部分互补。

[0216] 因而,本公开的 RNAi 剂互补于或基本上互补于与靶基因 β-联蛋白相对应的 mRNA 中的靶序列并且是双链的,包含有义链和反义链(其可以是连续的、借助环连接或否则接合的),其中双链区域应当长 9 至 36bp 长(特别地例如长 19 至 22bp 或 19 至 23bp),并且可以进一步任选地包含 3' 突出端或 5' 突出端,并且该 RNAi 剂可以进一步包含 3' 帽结构。RNAi 剂介导 RNA 干扰,下调或抑制 β-联蛋白的水平、表达和/或活性,和/或建立或重建大约正常水平的 β-联蛋白和/或 β-联蛋白活性,或与 β-联蛋白相关的其他生物学功能。

[0217] 双链 RNA

[0218] 如本文所用,术语"双链 RNA"或"dsRNA"指包含第一链和第二链的 RNAi 剂;例如包含具有杂交双链体区的 RNA 分子或分子复合物的组合物,所述杂交双链体区包含两条反平行的和基本上互补的核酸链,其将称作具有相对于靶 RNA 的"有义"方向和"反义"方向。相对于 mRNA 靶,反义链也称作"引导"链,并且有义链也称作"载客 (passenger)"链。载客链可以包含以下至少一个种或更多种情况:与另一条链相比一个或多个额外的核苷酸(例如,凸出或 1 核苷酸环)、与另一条链相比的切刻、缺口等。在多种实施方案中,第一链是有义链并且第二链是反义链。在其他实施方案中,第一链是反义链,并且第二链是有义链。

[0219] 双链体区可以具有允许经 RISC 途径特异性降解所需靶 RNA 的任何长度,但是一般范围将是从 9 至 36 碱基对("bp")的长度,例如,15-30 个碱基对长度。考虑一个在 9 和 36 碱基对之间的双链体,该双链体可以具有这个范围内的任何长度,例如,9、10、11、12、13、14、15、16、17、18、19、20、21、22、23、24、25、26、27、28、29、30、31、32、33、34、35 或 36bp 及其之间的任何子范围,包括但不限于 15-30 个碱基对、15-26bp、15-23bp、15-22bp、15-21bp、15-20bp、15-19bp、15-18bp、15-17bp、18-30bp、18-26bp、18-23bp、18-22bp、18-21bp、18-20bp、19-30bp、19-26bp、19-23bp、19-22bp、19-21bp、19-20bp、19bp、20-30bp、20-26bp、20-25bp、20-24bp、20-23bp、20-22bp、20-21bp、20bp、21-30bp、21-26bp、21-25bp、21-24bp、21-23bp、21-22bp、21bp、22bp 或 23bp。细胞中通过 Dicer 和相似酶加工产生的 dsRNA 通常具有范围约 19 至约 22 个碱基对长度。dsRNA 的双链体区的一条链包含与靶 RNA 的区域基本上互补的序列。形成双链体结构的两条链可以来自具有至少一个自身互补双链体区域的单个 RNA 分子,或可以由杂交以形成该双链体的两个或更多个独立 RNA 分子组成。在双链体区从单个分子的两个自身互补区形成的情况下,该分子可以具有由形成双链体结构的一条链的 3'-端和相应另一条链的 5'-端之间的单链核苷酸链(本文中称作"发夹环",例如,如存在于 shRNA 构建体中)分隔的双链体区。发夹环可以包含至少一个非配对核苷酸;在一些实施方案中,发夹环可以包含至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 20 个、至少 23 个或更多个非配对核苷酸。在 dsRNA 的两条基本上互补链由单独 RNA 分子构成的情况下,这些分子不需要共价连接,但是可以共价连接。在两条链由发夹环共价连接的情况下,构建体通常在本文中和本领域中称作"shRNA"。在两条链借助发夹环之外的方式共价连接的情况下,连接结构称作"接头"。术语"siRNA"也在本文中用来指如上文所述的 dsRNA。

[0220] 降低或正常化 β-联蛋白水平、表达、细胞分布和/或活性的 RNAi 剂

[0221] 用于靶向 β-联蛋白的示例性 RNAi 剂包括结合于相应于本文提供的 β-联蛋白基因的 mRNA。表 1、2、3、4、5、6、7、8 和/或 9 中提供针对 β-联蛋白的示例性 RNAi 剂。

[0222] 本领域已知的任何方法可以用来测量 β-联蛋白 RNAi 剂引起的 β-联蛋白活性、浓度、细胞分布(例如,定位至膜但是不定位至细胞质或细胞核)和/或表达的变化。测量可以在施用 RNAi 剂之前、期间和之后的多个时间点进行,以确定 RNAi 剂的作用。

[0223] 本公开的 RNAi 剂沉默 β-联蛋白基因、抑制其表达、下调其表达和/或阻抑其表达,从而在多种细胞区室中实现大致正常水平的 β-联蛋白活性、表达和/或浓度和/或分布。

[0224] 此外,在多种实施方案中,取决于疾病状况和生物学背景,可接受的是,使用本公开的 RNAi 剂建立低于正常水平或高于正常水平的 β-联蛋白表达、活性和/或浓度水平。

[0225] RNAi 剂及其修饰的类型

[0226] 包含反义核酸的 RNAi 剂或组合物下调细胞中特定蛋白质表达的用途是本领域熟知的。RNAi 剂包含与另一个核酸(例如,mRNA)的编码链互补并且能够与之形成氢键的序列。因此,在多种实施方案中,本公开的 RNAi 剂涵盖了靶向(例如,互补于、能够与之形成特定氢氢键等)本文中例如表 1、2、3、4、5、6、7、8 和/或 9 中所提出的任何序列的任何 RNAi 剂。

[0227] 与 mRNA 互补的反义序列可以与 mRNA 的编码区、5' 或 3' 非翻译区和/或桥接编码区和非翻译区的区域和/或其部分互补。另外,RNAi 剂可以与编码 mRNA 的基因的调节区,例如转录或翻译起始序列或调节元件互补。特别地,RNAi 剂或任何其部分可以与 mRNA 的编码链上起始密码子之前或跨越该起始密码子的区域或 3' 非翻译区互补。

[0228] 可以根据 Watson 和 Crick 碱基配对规则设计 RNAi 剂分子。RNAi 剂可以与 β-联蛋白 mRNA 的完整编码区互补,但更特别地是仅对 β-联蛋白 mRNA 的编码区或非编码区的一部分是反义的寡核苷酸。例如,反义寡核苷酸可以与 β-联蛋白 mRNA 的翻译起点周围的区域互补。反义寡核苷酸可以例如具有约 5、10、15、19、20、21、22、23、24、25、30、35、40、45 或 50 个核苷酸长度。

[0229] RNAi 剂可以在内部和/或在一个或两个末端处具有修饰。在末端处的修饰可以帮助稳定 RNAi 剂,保护它免遭血液中的核酸酶降解。

[0230] RNAi 剂也可以任选地设计成与 mRNA 的已知或预测的暴露区和/或单链区(例如,环)复性。

[0231] 可以使用化学合成和酶连接反应,利用本领域已知的方法构建 RNAi 剂。例如,可以使用天然存在的核苷酸或多种修饰的核苷酸化学地合成 RNAi 剂,其中设计所述修饰的核苷酸以降低脱靶效应,和/或增加分子的生物稳定性或增加反义核酸与有义核酸之间所形成的双链体的物理稳定性,例如,可以使用硫代磷酸酯衍生物和吖啶取代的核苷酸。

[0232] "G"、"C"、"A"、"T"和"U"各自通常表示分别含有鸟嘌呤、胞嘧啶、腺嘌呤、胸苷和尿嘧啶作为碱基的核苷酸。然而,术语"核糖核苷酸"或"核苷酸"也可以指修饰的核苷酸或代用替换部分。技术人员充分了解,鸟嘌呤、胞嘧啶、腺嘌呤和尿嘧啶可以由其他部分替换,而基本上不改变包含携带这类替换部分的核苷酸的寡核苷酸的碱基配对特性。例如,而不限于,包含肌苷作为其碱基的核苷酸可以与含有腺嘌呤、胞嘧啶或尿嘧啶的核苷酸发生

碱基配对。因此，含有尿嘧啶、鸟嘌呤或腺嘌呤的核苷酸可以在本公开中表征的 dsRNA 的核苷酸序列中由含有例如肌苷的核苷酸替换。在另一个实例中，寡核苷酸中任何地方的腺嘌呤和胞嘧啶可以分别地替换为鸟嘌呤和尿嘧啶，以形成与靶 mRNA 的 G-U 摇摆碱基配对。含有这类替换部分的序列适用于本公开中表征的组合物和方法。

[0233] 技术人员将认识到术语“RNA 分子”或“核糖核酸分子”不仅包括如自然界中表达或存在（即天然存在）的 RNA 分子，还包括如本文所述或如本领域已知的包含一个或多个核糖核苷酸 / 核糖核苷类似物或衍生物的非天然存在的 RNA 类似物和衍生物。严格地说，“核糖核苷”包含核苷碱基和核糖，并且“核糖核苷酸”是具有 1 个、2 个或 3 个磷酸酯部分的核糖核苷。然而，如本文所用，术语“核糖核苷”和“核糖核苷酸”可以视为等同的。例如，如下文所述，可以在核碱基结构或在核糖 - 磷酸酯主链结构方面修饰 RNA。然而，包含核糖核苷类似物或衍生物的分子必须保留形成双链体的能力。作为非限制性例子，RNA 分子也可以包含至少一个修饰的核糖核苷，所述修饰的核苷酸包括但不限于 2’-O- 甲基修饰的核苷酸、包含 5’ 硫代磷酸酯基的核苷、与胆甾烯基衍生物或十二烷酸双癸酰胺基连接的末端核苷、锁核苷 (locked nucleoside)、非碱基核苷、2’- 脱氧 -2’- 氟修饰的核苷、2’- 氨基修饰的核苷、2’- 烷基修饰的核苷、吗啉代核苷、非锁核糖核苷酸（例如，无环核苷酸单体，如 WO 2008/147824 中所述）、磷酰胺酯或包含非天然碱基的核苷，或其任意组合。备选地，RNA 分子可以包含至少两个修饰的核糖核苷、至少 3 个、至少 4 个、至少 5 个、至少 6 个、至少 7 个、至少 8 个、至少 9 个、至少 10 个、至少 15 个、至少 20 个或更多个修饰的核糖核苷，直到 dsRNA 分子的整个长度。对于 RNA 分子中这些多个修饰的核糖核苷中的每一个，修饰不需要是相同的。在一个实施方案中，被构思用本文所述方法和组合物中的修饰 RNA 是具有形成所需双链体结构的能力并且经 RISC 途径允许或介导靶 RNA 特异性降解的肽核酸 (PNA)。在一些情况下，RNA 分子可以包含为 DNA 的末端二核苷酸（例如，TT）和 / 或少数内部（例如，碱基配对性）DNA 碱基（例如，少于 RNA 碱基的数目），例如，置换 U 的 T。

[0234] 可以用来产生 RNAi 剂的修饰核苷酸的例子包括 5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶、次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶、5- 羧甲基氨基甲基 -2- 硫代尿苷、5- 羧甲基氨基甲基尿嘧啶、二氢尿嘧啶、β -D- 半乳糖基 Q 核苷、肌苷、N6- 异戊烯基腺嘌呤、1- 甲基鸟嘌呤、1- 甲基肌苷、2,2- 二甲基鸟嘌呤、2- 甲基腺嘌呤、2- 甲基鸟嘌呤、3- 甲基胞嘧啶、5- 甲基胞嘧啶、N6- 腺嘌呤、7- 甲基鸟嘌呤、5- 甲氨基甲基尿嘧啶、5- 甲氧氨基甲基 -2- 硫尿嘧啶、β -D- 甘露糖基 Q 核苷、5’- 甲氧基羧基甲基尿嘧啶、5- 甲氧基尿嘧啶、2- 甲基硫代 -N6- 异戊烯基腺嘌呤、尿嘧啶 -5- 羟基乙酸 (v)、wybutoxosine、假尿嘧啶、Q 核苷、2- 硫胞嘧啶、5- 甲基 -2- 硫尿嘧啶、2- 硫尿嘧啶、4- 硫尿嘧啶、5- 甲基尿嘧啶、尿嘧啶 -5- 羟基乙酸甲酯、尿嘧啶 -5- 羟基乙酸 (v)、5- 甲基 -2- 硫尿嘧啶、3-(3- 氨基 -3-N-2- 羧丙基）尿嘧啶、(acp3)w 和 2,6- 二氨基嘌呤。

[0235] 本文中公开的序列的“修饰变体”包括包含相同序列，但是在碱基、糖、磷酸酯或主链中具有修饰（但不是碱基置换，例如，A 置换为 G，或 C 置换为 U）的任何变体。因而，修饰的变体可以包含上文描述的任何修饰的核苷酸（例如，5- 氟尿嘧啶、5- 溴尿嘧啶、5- 氯尿嘧啶、5- 碘尿嘧啶，次黄嘌呤、黄嘌呤、4- 乙酰胞嘧啶、5-（羧基羟甲基）尿嘧啶等）。当碱基由相应的修饰碱基替换（例如，A 替换为修饰的 A）时，这些修饰的核苷酸不构成错配或碱基差异。因此，在特定位置处具有 U 的给定序列和在相同序列的相应位置处包含 5- 氟尿嘧

啶、5-溴尿嘧啶、5-氯尿嘧啶或5-碘尿嘧啶的修饰变体将差异0个核苷酸（或没有错配）；然而，在特定位置处具有C的给定序列和具有5-氟尿嘧啶的不同序列（其中除此之外，两个序列相同）将差异1个核苷酸（1个错配）。

[0236] 在一个实施方案中，本公开涵盖本文中公开的任何RNAi剂的任何修饰变体。修饰变体含有相同的序列，但可以经修饰以在磷酸酯、糖、碱基、核苷酸等中含有修饰。例如，修饰的变体可以含有本文中列出的一个或多个修饰的核苷酸，例如C由2'-修饰的C替换（这类序列将差异0个错配）。

[0237] 在一个方面，修饰的核糖核苷包括脱氧核糖核苷。在这种情况下，RNAi剂可以包含一个或多个脱氧核苷，包括例如脱氧核苷突出端或在dsRNA的双链部分内部的一个或多个脱氧核苷。然而，不证自明的是在任何情况下术语"RNAi剂"不涵盖双链DNA分子。

[0238] 用脱氧核糖核苷酸替换具有双核苷酸3'突出端的21聚RNAi剂双链体的3'端核苷酸突出区段未对RNAi活性产生不良作用。用脱氧核糖核苷酸替换RNAi剂的每个末端上的至多4个核苷酸已经被良好耐受，而用脱氧核糖核苷酸完全置换导致无RNAi活性。国际PCT公开号WO00/44914和Beach等人的国际PCT公开号WO 01/68836初步表明，siRNA可以包括针对磷酸酯-糖主链或核苷的修饰以包含至少一个氮杂原子或硫杂原子。Kreutzer等人的加拿大专利申请号2,359,180还描述为了对抗双链RNA依赖性蛋白激酶PKR激活而用于dsRNA构建体中的某些化学修饰，具体而言，2'-氨基核苷酸或2'-O-甲基核苷酸和含有2'-O亚甲基桥或4'-C亚甲基桥的核苷酸。额外的3'端核苷酸突出端包括dT（脱氧胸苷）、2'-O,4'-C-亚乙基胸苷（eT）和2-羟乙基磷酸酯（hp）。

[0239] 用长（>25核苷酸）siRNA转录物，Parrish等人，2000Molecular Cell 6:1077-1087测试了靶向秀丽隐杆线虫（C.elegans）中unc-22基因的某些化学修饰。作者描述通过用T7和T3RNA聚合酶掺入硫代磷酸酯核苷酸类似物将硫代磷酸酯残基引入这些siRNA转录物中并且观察到具有两个硫代磷酸酯修饰的碱基的RNA在作为RNAi的有效性方面也具有大幅度降低。另外，Parrish等人报道硫代磷酸酯修饰多于两个残基在体外大幅度去稳定化RNA，从而不能分析干扰活性。Id.at 1081。作者还测试在长siRNA转录物中核苷酸糖的2'-位置处的某些修饰并且发现用脱氧核苷酸置换核糖核苷酸导致干扰活性大幅度降低，特别在尿苷至胸苷和/或胞苷至脱氧胞苷置换的情况下。Id.此外，作者测试了某些碱基修饰，包括在siRNA的有义链和反义链中用4-硫尿嘧啶、5-溴尿嘧啶、5-碘尿嘧啶和3-（氨基烯丙基）尿嘧啶置换尿嘧啶和用肌苷置换鸟苷。在4-硫尿嘧啶和5-溴尿嘧啶置换似乎被耐受的情况下，Parrish报道，在任一条链掺入时，肌苷导致干扰活性大幅度降低。Parrish还报道在反义链中掺入5-碘尿嘧啶和3-（氨基烯丙基）尿嘧啶也导致RNAi活性大幅度降低。

[0240] 本领域技术人员将理解，可以使用本领域已知的任何常规方法合成并根据需要修饰siRNA（见Henschel等人，2004DEQOR:a web-based tool for the design and quality control of siRNAs.Nucleic Acids Research 32（网络服务器发行）:W113-W120）。另外，本领域技术人员将显而易见，存在可用于反义寡核苷酸、siRNA或shRNA表达构建体/载体的多种调节序列（例如，组成型或诱导型启动子、组织特异性启动子或其功能性片段等）。

[0241] 本领域中存在几种例子，它们描述可以引入核酸分子中的糖修饰、碱基修饰、磷酸酯修饰和主链修饰，伴随核酸分子的核酸酶稳定性和功效显著增强。例如，通过用

抗核酸酶基团修饰而修饰寡核苷酸以增强稳定性和/或增强生物活性，例如，2'-氨基、2'-C-烯丙基、2'-氟、2'-O-甲基、2'-O-烯丙基、2'-H、核苷酸碱基修饰（综述见 Usman 和 Cedergren1992TIBS. 17:34 ;Usman 等人，1994Nucleic Acids Symp. Ser. 31:163 ;Burgin 等人，1996Biochemistry 35:14090）。本领域中广泛描述了核酸分子的糖修饰。

[0242] 已经描述 RNAi 剂的额外修饰和缀合。Soutschek 等人 2004Nature 432:173-178 提出胆固醇借助吡咯烷接头与 RNAi 剂的有义链的 3' 末端缀合，因而产生共价的和不可逆的缀合物。也可以对 siRNA 进行化学修饰（包括与其他分子缀合）以改善体内药动力停留时间和效率。

[0243] 在本公开的多种实施方案中，针对 β-联蛋白的 RNAi 剂包含至少一个 5'-尿苷-腺嘌呤-3'（5'-ua-3'）二核苷酸，其中尿苷是 2'-修饰的核苷酸；至少一个 5'-尿苷-鸟嘌呤-3'（5'-ug-3'）二核苷酸，其中 5'-尿苷是 2'-修饰的核苷酸；至少一个 5'-胞苷-腺嘌呤-3'（5'-ca-3'）二核苷酸，其中 5'-胞苷是 2'-修饰的核苷酸；和/或至少一个 5'-尿苷-尿苷-3'（5'-uu-3'）二核苷酸，其中 5'-尿苷是 2'-修饰的核苷酸。

[0244] 在本公开的多种实施方案中，RNAi 剂包含选自以下的 2'-修饰：2'-脱氧、2'-脱氧-2'-氟、2'-O-甲基、2'-O-甲氧乙基（2'-O-MOE）、2'-O-氨基丙基（2'-O-AP）、2'-O-二甲基氨基乙基（2'-O-DMAOE）、2'-O-二甲氨基丙基（2'-O-DMAP）、2'-O-二甲基氨基乙基氧乙基（2'-O-DMAEOE）和 2'-O-N-甲基乙酰氨基（2'-O-NMA）。

[0245] 在另一个实施方案中，RNAi 包含空位或丢失性碱基。例如，磷酸酯-糖主链可以存在，但是碱基丢失。

[0246] 在另一个实施方案中，RNAi 剂具有单链切刻（例如，主链中的断口或丢失键）。在多种实施方案中，单链切刻可以在有义链或反义链或这两种链中。

[0247] 这种切刻可以例如在有义链中，产生内部分段的小干扰性 RNA 或 sisiRNA，其可以比没有切刻的相应 RNAi 剂具有更少的脱靶效应。

[0248] 反义核酸或 RNAi 剂也可以具有备选性主链如锁核酸（LNA）、吗啉代、肽核酸（PNA）、苏糖核酸（TNA）或二醇核酸（GNA）、FANA、硼烷磷酸酯 RNA 或具有少量核苷酸的原发 RNA，这些核苷酸由 DNA、LNA、PNA、TNA、GNA、FANA、硼烷磷酸酯等置换和/或它可以是标记的（例如，放射标记或否则加标签）。

[0249] 一条链或两条链可以包含备选性主链。

[0250] 在又一个实施方案中，由本公开的方法使用的 RNAi 剂可以包括 α-端基异构的核酸分子。α-端基异构的核酸分子与互补性 RNA 形成特定双链杂交分子，其中与常见 β-单元相反，所述链相互平行分布。Gaultier 等人，1987Nucleic Acids. Res. 15:6625-6641。RNAi 剂也可以包含 2'-O-甲基核糖核苷酸（Inoue 等人，1987Nucleic Acids Res. 15:6131-6148）或嵌合 RNA-DNA 类似物（Inoue 等人，1987FEBS Lett. 215:327-330）。

[0251] 备选地，可以通过靶定与 β-联蛋白的调节区（例如启动子和/或增强子）互补的核苷酸序列以形成阻止 β-联蛋白基因转录的三螺旋结构，抑制基因表达。一般见 Helene, C. 1991Anticancer Drug Des. 6(6):569-84 ;Helene 等人，1992Ann. N. Y. Acad. Sci. 660:27-36 和 Maher, 1992, Bioassays 14(12):807-15。

[0252] RNAi 剂的产生

[0253] RNAi 剂可以在细胞内部使用已经向其中以反义方向亚克隆核酸（即，从插入的核酸转录的 RNA 将相对于目的靶核酸是反义方向）的表达载体以生物方式产生。RNAi 剂可以使用已经向其中亚克隆核酸作为 shRNA 构建体的表达载体以生物方式产生（即，从插入的核酸转录的 RNA 将具有相对于目的靶核酸处于反义方向的第一区域、包含环或铰合部的第二区域和相对于目的靶核酸处于有义方向的第三区域，其中转录物的第一区域和第三区域优选地彼此杂交，因而形成茎 - 环结构）。

[0254] 产生 RNAi 剂的方法是本领域熟知的并且是本领域普通技术人员可获得的。

[0255] 用于合成 RNAi 的试剂盒是从例如 New England Biolabs 和 Ambion 可商业获得的。

[0256] RNAi 剂的递送

[0257] 本公开的 RNAi 剂可以通过本领域已知的任何手段递送或引入（例如，至体外细胞、至试验动物或至人）。

[0258] 本公开的 RNAi 剂一般施用至受试者或原位产生，从而它们与编码 β - 联蛋白的细胞 mRNA 和 / 或基因组 DNA 杂交并且通过抑制转录和 / 或翻译来抑制表达。RNAi 剂的施用途径的例子包括在组织部位直接注射。备选地，RNAi 剂可以经修饰以靶向所选择的细胞并且随后全身施用。例如，对于全身性施用，可以修饰反义分子，从而它们与所选细胞表面上表达的受体或抗原特异性地结合，例如通过将所述反义核酸分子连接至与细胞表面受体或抗原结合的肽或抗体连接而做到这一点。也可以使用本领域熟知的和例如在 US20070111230 中描述的载体递送反义核酸分子至细胞。为实现反义分子的足够胞内浓度，优选其中反义核酸分子处于 pol II 或 pol III 强启动子控制下的载体构建体。

[0259] 当提到 RNAi 剂时，“引入细胞中”意指促进或实现摄入或吸收入细胞中，如本领域技术人员所理解。吸收或摄取 RNAi 剂可以通过无协助扩散作用或主动细胞过程或通过助剂或装置进行。这个术语的含义不限于体外细胞；也可以将 RNAi 剂“引入细胞中”，其中所述细胞是活生物的部分。在这种情况下，引入细胞中将包括递送至生物。例如，对于体内递送，可以将 RNAi 剂注射入组织部位或全身施用。体内递送也可以借助 β - 葡聚糖递送系统，如在美国专利号 5,032,401 和 5,607,677 和美国公开号 2005/0281781 中描述的那些。体外引入细胞中包括本领域已知的方法如电穿孔法和脂质体转染法。其他方案在下文描述或是本领域已知的。

[0260] 递送 RNAi 剂至组织是个问题，因为该物质必须抵达靶器官并且还必须进入靶细胞的细胞质。RNA 不能渗透细胞膜，因此全身性递送裸 RNA 剂不可能成功。RNA 因血清中的 RNA 酶活性迅速降解。出于这些原因，已经构思递送 RNAi 剂至靶细胞的其他机制。本领域已知的方法包括但不限于：病毒递送法（逆转录病毒、腺病毒、慢病毒、杆状病毒、AAV）；脂质体法（脂质转染胺 (lipofectamine)、阳离子 DOTAP、中性 DOPC) 或纳米粒子法（阳离子聚合物、PEI)、细菌递送法 (tkRNAi)、电穿孔法以及还包括改善稳定性的 siRNA 化学修饰法 (LNA)。Xia 等人，2002Nat. Biotechnol. 20 和 Devroe 等人，2002. BMC Biotechnol. 21:15 公开了将 siRNA 掺入病毒载体中。Porphysome 也可以用来递送 RNAi 剂。Lovell 等人，2001Nature Mater. 10:324-32；和 WO 2011/044671。构思了用于递送 RNAi 剂的其他系统并且可以通过仍待寻找和 / 或由 FDA 或其他管理机关批准的各种方法递送本公开的 RNAi 剂。本公开的 RNAi 剂可以在合适的药物组合物中递送。下文更详细地描述这些药物组合物中的几种。

[0261] RNAi 剂的药物组合物

[0262] 如本文中使用，“药物组合物”包含药学有效量的一种或多种 β-联蛋白 RNAi 剂、可药用载体和任选地与 RNAi 剂协同发挥作用的额外疾病治疗剂。额外的疾病治疗剂可以是针对 β-联蛋白的额外 RNAi 剂和/或针对另一个基因的额外 RNAi 剂。如本文所用，“药理有效量”、“治疗有效量”或简单地“有效量”指有效产生预期药理、治疗或预防结果的 RNAi 剂的量。例如，如果与疾病或病症相关的可度量参数存在至少 10%下降时认为给定的临床治疗有效，则用于治疗这种疾病或病症的药物的治疗有效量是实现该参数下降至少 10%所需要的量。在这个实施方案中，治疗有效量的靶向 β-联蛋白的 RNAi 剂可以减少 β-联蛋白蛋白质水平至少 10%。在额外的实施方案中，给定的临床治疗视为有效，其中存在与疾病或病症相关的可度量参数的至少 15%、20%、25%、30%、35%、40%、45%、50%、55%、60%、65%、70%、75%、80%、85%、90 或 95%减少，并且用于治疗该疾病或病症的药物的治疗有效量是分别实现该参数减少至少 15%、20%、25%、30%、35%、40%、45%、50%、55%、60%、65%、70%、75%、80%、85%、90 或 95%所必需的量。

[0263] 术语“可药用载体”指用于施用治疗药的载体。这类载体包括但不限于盐水、缓冲盐水、右旋糖、水、甘油、乙醇及及它们的组合。该术语特别地排除细胞培养基。对于口服施用的药物，可药用载体包括但不限于可药用的赋形剂如惰性稀释剂、崩解剂、粘合剂、润滑剂、甜味剂、矫味剂、着色剂和防腐剂。合适的惰性稀释剂包括碳酸钠和碳酸钙、磷酸钠和磷酸钙和乳糖，而玉米淀粉和海藻酸是合适的崩解剂。粘合剂可以包括淀粉和明胶，而如果存在，则润滑剂通常将是硬脂酸镁、硬脂酸或滑石。如果需要，片剂可以用多种材料如甘油单硬脂酸酯或甘油基二硬脂酸酯包衣以延缓胃肠道中的吸收。下文进一步描述药物制剂中所包含的药剂。

[0264] 包含 β-联蛋白 RNAi 剂的药物组合物可以处于固体形式，例如，散剂、颗粒剂、片剂、丸剂、胶囊锭剂(gelcap)、明胶胶囊剂、脂质体剂、栓剂、可咀嚼形式或贴剂。包含 β-联蛋白 RNAi 剂的药物组合物也可以按液态形式呈现，例如，溶液剂、乳剂、混悬剂、酏剂或糖浆剂。适宜的液态支持物可以例如是水、有机溶剂如多元醇，如丙三醇或二醇（包括丙二醇和聚乙二醇）或乙醇、Cremophor EL 或它们在水中处于不同比例的混合物。组合物可以包含用白蛋白或表面活性剂包覆的纳米尺度的非晶态或晶态颗粒。

[0265] 适宜的支持物可以例如包括抗细菌药和抗真菌药、缓冲剂、磷酸钙、纤维素、甲基纤维素、三氯叔丁醇、可可脂、着色剂、糊精、乳化剂、肠衣、矫味剂、明胶、等渗剂、卵磷脂、硬脂酸镁、香味剂、多元醇如甘露醇、注射用有机酯如油酸乙酯、尼泊金酯、苯酚山梨酸、聚乙二醇、聚乙烯吡咯烷酮、磷酸盐缓冲盐水(PBS)、防腐剂、丙二醇、羧甲基纤维素钠、氯化钠、山梨醇、各种糖（包括但不限于蔗糖、果糖、半乳糖、乳糖和海藻糖）、淀粉、栓剂蜡、滑石、植物油如橄榄油和玉米油、维生素、蜡和/或润湿剂。对于 β-联蛋白 RNAi 剂，优选的支持物包括葡聚糖和水，例如水中的 5%右旋糖(D5W)。

[0266] 药物组合物的生物惰性部分可以任选地是可蚀的，允许定时释放 RNAi 剂。

[0267] 药物组合物可以包含有助于递送、稳定性、功效或降低免疫原性的额外组分。

[0268] 包含针对 β-联蛋白的 RNAi 剂的药物组合物的额外组分

[0269] 可以添加包含针对 β-联蛋白的 RNAi 剂的药物组合物的额外组分以有助于递送、稳定性、功效或降低免疫原性。

[0270] 先前已经使用脂质体用于药物递送（例如，递送化疗药）。脂质体（例如，阳离子脂质体）在PCT公开WO 02/100435A1，WO 03/015757A1，和WO 04029213A2；美国专利号5,962,016；5,030,453；和6,680,068；和美国专利申请2004/0208921中描述。在WO 04/002453A1中还描述产生脂质体的方法。另外，已经将中性脂质掺入阳离子脂质体中（例如，Farhood等人，1995）。

[0271] 阳离子脂质体已经用来递送RNAi剂至各种细胞类型（Sioud和Sorensen，2003；美国专利申请2004/0204377；Duxbury等人，2004；Donze和Picard，2002）。

[0272] 中性脂质体的用途在Miller等人，1998和美国专利申请2003/0012812中公开。

[0273] 如本文所用，术语“SNALP”指稳定的核酸-脂质粒子。SNALP代表包被缩减（reduced）的含水内部的脂质囊泡，其中所述含水内部包含核酸如iRNA或从中转录出iRNA的质粒。SNALP例如在美国专利申请公开号20060240093、20070135372中并且在国际申请号WO2009082817中描述。

[0274] 使用基于脂质、基于胺和基于聚合物的技术的化学转染在来自Ambion Inc.，Austin，Tex.；和Novagen，EMD Biosciences，Inc，Merck KGaA分公司，Darmstadt，德国）的产品；Ovcharenko D(2003)“Efficient delivery of siRNAs to human primary cells.”Ambion TechNotes 10(5):15-16)中公开。另外，Song等人(Nat Med.在线发表(Fete 10，2003)doi：10.1038/nm828)和其他人[Caplen等人，2001Proc.Natl.Acad.Sci.(USA)，98:9742-9747；和McCaffrey等人，Nature 414:34-39]公开了以通过注射siRNA至哺乳动物的循环系统中高效地转染肝脏细胞。

[0275] 多种分子已经用于细胞特异性递送RNAi剂。例如，鱼精蛋白的核酸浓缩特性已经与特异性抗体组合以递送siRNA。Song等人，2005Nat Biotech.23:709-717。自装配聚乙二醇化聚阳离子聚乙烯亚胺(PEI)也已经用来浓缩并保护siRNA。Schiffelers等人，2004Nucl.Acids Res.32:e149，141-110。

[0276] 含有siRNA的纳米粒子则成功地被递送至过量表达整联蛋白的肿瘤新生血管。Hu-Lieskovan等人，2005Cancer Res.65:8984-8992。

[0277] 可以借助例如脂质纳米粒子(LNP)；中性脂质体(NL)；聚合物纳米粒子；双链RNA结合基序(dsRBMs)；或借助对RNAi剂的修饰（例如，与dsRNA共价接合）递送本公开的RNAi剂。

[0278] 脂质纳米粒子(LNP)是基于阳离子脂质的自装配系统。这些纳米粒子可以包含例如中性脂质（脂质体基体）；阳离子脂质（用于加载siRNA）；胆固醇（用于稳定脂质体）；和PEG-脂质（用于稳定制剂、电荷屏蔽和延长血流中的循环）。

[0279] 阳离子脂质可以包括例如头部基团、接头、尾部和胆固醇尾。LNP可以具有例如良好的肿瘤递送、血液中延长的循环、小粒子（例如，小于100nm）和在肿瘤微环境（其具有低pH并低氧）中的稳定性。

[0280] 中性脂质体(NL)是非阳离子脂质类的粒子。

[0281] 聚合物纳米粒子是自装配聚合物类的粒子。

[0282] 双链RNA结合基序(dsRBMs)是将需要修饰的自装配RNA结合蛋白。

[0283] 本公开的多种实施方案中，针对β-联蛋白的RNAi剂连接至一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、

脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和转铁蛋白。

[0284] 可以在药物组合物中制备本公开的 RNAi 剂，所述药物组合物包含适于施用 RNAi 剂的特定方法的多种组分。

[0285] 包含 RNAi 剂的药物组合物的施用

[0286] 包含 β-联蛋白的 RNAi 剂的药物组合物可以通过以下途径施用：经颊途径、吸入（包括吹入和深度吸入）途径、经鼻途径、经口途径、肠胃外途径、植入途径、借助硬膜外、动脉内、关节内、被膜内、心内、脑室内、颅内、皮内、肌内、眶内、经眼、腹膜内、椎管内、胸骨内、鞘内、静脉内、蛛网膜下、被膜下、皮下、表皮下、经内皮、经气管、经血管、直肠、舌下、局部和/或阴道途径注射或输注。可以通过注射、输注、皮肤贴片或本领域已知的任何其他方法做到这点。可以粉化、雾化、气雾化、微粒化或其他适当地用于递送的制剂。如果是液体，施用可以是缓慢的或借助快速浓注，不过在本领域已知的一些情况下，快速浓注可能导致物质经肾丢失。

[0287] 包含 β-联蛋白 RNAi 剂的药物组合物可以用本领域已知的医疗器械施用。例如，在一个特定实施方案中，可以用无针皮下注射装置（如美国专利号 5,399,163、5,383,851、5,312,335、5,064,413、4,941,880、4,790,824 或 4,596,556 中公开的装置）施用 RNAi 剂。用于本公开中的熟知植入物和模块的例子包括：美国专利号 4,487,603，其公开用于以受控速率分配药物的可植入式微量输注泵；美国专利号 4,486,194，其公开用于经皮肤施用药物的治疗装置；美国专利号 4,447,233，其公开用于以精确输注速率递送药物的药物输注泵；美国专利号 4,447,224，其公开用于连续递送药物的可变流量植入式输注装置；美国专利号 4,439,196，其公开具有多腔区室的渗透性药物递送系统；和美国专利号 4,475,196，其公开公开渗透性药物递送系统。许多其他的此类植入物、递送系统和模块是本领域技术人员已知的。

[0288] 在某些实施方案中，可以配制包含 RNAi 剂的药物组合物以确保正确体内分布。施用针对 β-联蛋白的 RNAi 剂可以是全身性的（整个身体）或，特别地，定向至表达 β-联蛋白（或过量表达 β-联蛋白或显示其过多活性）的组织或器官。用于靶向这些特定组织或器官的方法在本文中描述和/或是本领域已知的。例如，它们可以配制在脂质体中。对于制造脂质体的方法，见，例如，美国专利 4,522,811；5,374,548；和 5,399,331。脂质体可以包含一个或多个被选择性转运至特定细胞或器官中的部分，因而增强靶向的药物递送（见，例如 V. V. Ranade (1989) J. Clin. Pharmacol. 29:685）。

[0289] 示例性靶向部分包括叶酸或生物素（见，例如，授予 Low 等人的美国专利 5,416,016）；甘露糖苷 (Umezawa 等人，(1988) Biochem. Biophys. Res. Commun. 153:1038)；抗体 (P. G. Bloeman 等人，(1995) FEBS Lett. 357:140；M. Owais 等人，(1995) Antimicrob. Agents Chemother. 39:180)；表面活性蛋白质 A 受体 (Briscoe 等人，(1995) Am. J. Physiol. 1233:134)，其不同的种类可以构成本公开的制剂，以及已发明分子的组分；p120 (Schreier 等人，(1994) J. Biol. Chem. 269:9090)；还见 K. Keinanen；

M. L. Laukkanen(1994)FEBS Lett. 346:123 ;J. J. Killion ;I. J. Fidler(1994) Immunomethods 4:273。

[0290] 本公开因此涵盖用于治疗 β-联蛋白相关疾病的包含一种或多种针对 β-联蛋白的 RNAi 剂的药物组合物,所述 RNAi 剂可以任选地包含多种修饰和/或额外组分。

[0291] 测量 RNAi 剂对 β-联蛋白活性、水平、表达或区室化的影响

[0292] 本领域已知的任何方法可以用来测量由 β-联蛋白 RNAi 剂引起或改变的 β-联蛋白活性、水平、细胞分布和/或表达的变化。测量可以在施用 RNAi 剂之前、期间和之后的多个时间点进行,以确定 RNAi 剂的作用。

[0293] 术语"沉默"、"抑制……的表达"、"下调……的表达"、"抑制……的表达"等,只要它们涉及 β-联蛋白基因,在此均指至少部分地阻抑 β-联蛋白基因的表达,如通过 β-联蛋白 mRNA 的量减少所展示,其中可以从第一细胞或细胞群中分离或在其中检测到所述 mRNA,在所述第一细胞或细胞群中,β-联蛋白基因转录并且所述第一细胞或细胞群已经被处理,从而与基本上与第一细胞或细胞群相同的但尚未如此处理的第二细胞或细胞群(对照细胞)相比,β-联蛋白基因的表达被抑制。抑制程度通常以下式表述

$$\frac{(\text{对照细胞中的 mRNA})-(\text{处理细胞中的 mRNA})}{(\text{对照细胞中的 mRNA})} * 100\% \qquad \text{等式 1}$$

[0294] 备选地,抑制的程度可以就与 β-联蛋白基因表达功能性联系的参数减少(例如,β-联蛋白基因编码的蛋白质的量等)而言给出。原则上,可以在以组成型方式或通过基因组工程化而表达 β-联蛋白的任何细胞中并且通过任何适宜的测定法确定 β-联蛋白基因沉默。然而,当需要参考或对照以确定给定的 RNAi 剂是否抑制 β-联蛋白基因表达到某种程度并且因此属于本公开,下文实施例中提供的测定法应当充当这类参考。

[0295] 例如,在某些情况下,通过施用本公开中表征的 RNAi 剂阻抑 β-联蛋白基因的表达至少约 10%、15%、20%、25%、30%、35%、40%、45%或 50%。在一些实施方案中,通过施用本公开中表征的 RNAi 剂阻抑 β-联蛋白基因至少约 60%、70%或 80%。在一些实施方案中,通过施用如本文所述的 RNAi 剂阻抑 β-联蛋白基因至少约 85%、90%或 95%或更多。

[0296] 可以首先在体外(例如,使用测试细胞如 HeLa 细胞)测试 RNAi 剂抑制 β-联蛋白的能力。

[0297] 随后例如使用 PBMC(外周血单核细胞细胞)测定法,可以对可在体外抑制 β-联蛋白的 RNAi 剂测试免疫刺激作用。也可以在动物试验中测试 RNAi 剂。试验动物和对照动物包括过量表达或不足表达 β-联蛋白的那些,例如,如 Chenn 等人,2003Cer. Cortex 13:599-606 中所述。抑制或改变 β-联蛋白水平、活性和/或表达的 RNAi 剂可以用于治疗多种 β-联蛋白相关疾病的药物中。

[0298] 在 β-联蛋白或 β-联蛋白相关疾病的症状的语境中,"较低的"意指这类水平的统计显著减少。减少可以例如是至少 10%、至少 20%、至少 30%、至少 40%、至少 50%、至少 60%、至少 70%、至少 80%、至少 90%、至少 95%或更多。如果,对于一种具体疾病,或对于患有一种具体疾病的个体,β-联蛋白的水平或表达升高,用本公开的 β-联蛋白 RNAi 剂治疗可以特别地减少 β-联蛋白的水平或表达到文献中视为对未患这种疾病的个体而

言的正常范围内的水平。

[0299] 可以通过评价 mRNA（例如，借助 RNA 印迹或 PCR）或蛋白质（例如，蛋白质印迹法）测量 β－联蛋白的水平或表达。可以通过测量 β－联蛋白基因转录速率（例如，借助 RNA 印迹；或逆转录酶聚合酶链反应或实时聚合酶链反应）确定 RNAi 剂对 β－联蛋白表达的影响。可以对（细胞表面表达的）β－联蛋白的水平进行直接测量，例如通过其中表达 β－联蛋白的组织的蛋白质印迹法。也可以确定 β－联蛋白在各种细胞区室（胞膜、细胞质和细胞核）中的存在。

[0300] 如本文所用，“下调”指 β－联蛋白的生物活性和／或表达的任何统计显著减少，包括完全阻断活性（即，完全抑制）和／或表达。例如，“下调”可以指 β－联蛋白水平，活性和／或表达减少至少约 10％、20％、30％、40％、50％、60％、70％、80％、90％或 100％。

[0301] 如本文所用，术语“抑制”或“抑制”β－联蛋白指 β－联蛋白的生物学水平、活性和／或表达的任何统计显著减少，包括完全阻断活性和／或表达。例如，“抑制”可以指 β－联蛋白水平，活性和／或表达减少至少约 10％、20％、30％、40％、50％、60％、70％、80％、90％或 100％。如本文所用，当提到任何其他生物因子或组合物时，术语“抑制”类似地指水平、活性和／或表达的明显减少。

[0302] “水平”意指 β－联蛋白 RNAi 剂可以改变 β－联蛋白的水平，例如，β－联蛋白 mRNA 的水平或 β－联蛋白的水平或 β－联蛋白的活性水平。

[0303] 一些疾病，如结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合，以及相似和相关的疾病，以过多的和／或突变的 β－联蛋白活性和／或细胞内部异常 β－联蛋白分布为特征。因而，在多种实施方案中，施用针对 β－联蛋白的 RNAi 剂特别地建立或重新建立 β－联蛋白活性、表达、分布和／或浓度的正常水平或大致正常水平。

[0304] 就水平、表达和／或活性而言，“正常”或“大致正常”意指约 50％、约 60％、约 70％、约 80％、约 90％、和／或约 100％；和／或不多于约 100％、约 120％、约 130％、约 140％或约 150％的 β－联蛋白在健康细胞区室、细胞、组织或器官中的水平、表达或活性。在一个实施方案中，施用适宜量的适宜 β－联蛋白 RNAi 剂将 β－联蛋白水平、活性和／或表达水平恢复到健康细胞、组织或器官的 β－联蛋白水平、活性和／或表达水平的约 50％至约 150％、更具体地约 60％至约 140％、更具体地至约 70％至约 130％、更具体地至约 80％至约 120％、更具体地至约 90％至约 110％和最具体地至约 100％。向患有 β－联蛋白相关疾病的患者施用 β－联蛋白 RNAi 因此特别地将 β－联蛋白水平、活性和／或表达恢复到大约正常的水平，如通过直接测量 β－联蛋白 mRNA 或蛋白质水平或间接测定（如分析组织学样品或组织样品的水平）所测定的。本公开的 RNAi 剂也可以实现 β－联蛋白在细胞内部（例如，在细胞膜中但是不在细胞质或细胞核中）分布的正常水平或大致正常水平。

[0305] 在 β－联蛋白相关的一些癌症中，肿瘤生长需要 β－联蛋白，但是 β－联蛋白不扩增、过量表达或错误定位。β－联蛋白表达、水平或活性的减少因此应当限制肿瘤生长。本公开因此涵盖下述方法，其中降低 β－联蛋白表达、水平或活性到低于正常的表达、水平或活性。

[0306] 此外，在多种实施方案中，取决于疾病状况和生物学背景，可接受的是，使用本公开的 RNAi 剂建立低于正常水平或高于正常水平的 β-联蛋白表达、活性和/或浓度水平。

[0307] β-联蛋白相关疾病

[0308] 本公开涵盖针对 β-联蛋白的 RNAi 剂和向人和非人动物施用该 RNAi 剂以治疗各种 β-联蛋白相关疾病。

[0309] “β-联蛋白相关疾病”意指与 β-联蛋白的水平、表达、细胞位置和/或活性方面突变和/或功能障碍相关的任何疾病，和/或可以通过调节 β-联蛋白的水平、表达、细胞位置和/或活性进行治疗、预防和/或改善的任何疾病。在一些情况下，“β-联蛋白相关疾病”包括这样的癌症，其中肿瘤生长需要 β-联蛋白，但是 β-联蛋白不扩增、不过量表达或不错误定位。β-联蛋白表达、水平或活性的减少因此应当限制肿瘤生长。在本公开的多种实施方案中，β-联蛋白相关疾病可以用针对 β-联蛋白的 RNAi 剂治疗和/或改善。

[0310] β-联蛋白相关疾病经常是与规范 Wnt/β-联蛋白途径中的异常相关。Wnt 信号传导几乎参与胚胎发育的每个方面并且还控制许多成年组织中的稳态自我更新。Wnt 途径中的种系突变造成几种遗传性疾病，并且体细胞突变与肠和多种其他组织的癌症相关。在 Wnt 途径中，当 Wnt 受体复合体不被配体结合时，丝氨酸/苏氨酸激酶 CK1 和 GSK3α/β 使 β-联蛋白磷酸化。磷酸化的 β-联蛋白由 F 框 /WD 重复序列蛋白 β-TrCP（专用型 E3 泛素连接酶复合体的组分）识别。在泛素化后，引导 β-联蛋白遭蛋白酶体快速破坏。在细胞核中，Groucho 与 TCF(T 细胞因子）的结合抑制 Wnt 靶基因（包括原癌基因 c-myc）的转录。然而，细胞核中的 β-联蛋白积累可以导致这些 Wnt 靶基因的激活。例如，一旦被 Wnt 结合，则卷曲蛋白 (Fz)/LRP 辅助受体复合物激活规范信号传导途径。Fz 与 Dsh（一种在 β-联蛋白和激酶 GSK3β 上游发挥作用的胞质蛋白）相互作用。Wnt 信号传导控制 GSK3β 和酪蛋白激酶 I-γ (CK1γ) 对 LRP 的磷酸化，因此调节轴蛋白的对接作用。召集轴蛋白离开破坏复合物导致 β-联蛋白在细胞质中的稳定化。一旦在细胞核中，β-联蛋白将 Groucho 从 TCF/LEF 替代出来以促进 Wnt 靶基因（包括 c-myc）的转录。Moon 等人，2002science 296:1644-1646；Nelson 等人，2004Science 303:1483-1487；和 Clevers 2006Cell 127:469-480；和其中引用的参考文献。

[0311] B-联蛋白相关疾病因此经常与该蛋白质的突变形式和/或升高水平的突变或野生型 β-联蛋白和/或 β-联蛋白在细胞质和/或细胞核中的存在相关。在正常胃粘膜中，β-联蛋白定位至细胞膜。Clements 等人，2002Cancer Res. 62:3503-6。如上文所示，在不存在生长信号或分化信号的情况下，胞质 β-联蛋白在 APC（肿瘤抑制物-腺瘤结肠息肉基因产物）蛋白和 GSK-3β 的控制下快速代谢。在一些癌细胞、慢性伤口和其他患病细胞和组织中，β-联蛋白在细胞质中积累。核转位也可以发生。β-联蛋白积累可以导致与 T 细胞因子 4 或转录激活物的淋巴样增进因子家族相互作用，并且可以导致一些发育相关基因和/或原癌基因（包括 c-myc）的激活。Behrens 等人，1996Nature 382:638-642；和 He 等人，1998Science281:1509-1512。

[0312] 如上文所示，β-联蛋白在蛋白酶体中代谢，其中 β-联蛋白在高度保守的 Ser 和 Thr 残基 (Ser33、Ser37、Thr41 和 Ser45) 定向磷酸化和在 NH_2 端中泛素化后降解。在这些 Ser 残基和 Thr 残基中的突变导致 β-联蛋白积累并且与各种癌症相关。在突变热点 Ser37 至 Phe37 处突变与 SK23mel（黑色素瘤）细胞系中的 β-联蛋白积累和增加的半

寿期相关。Rubinfeld 等人，1997Science 275:1790-1792。624mel 细胞系中的 Ser45 至 Tyr45 突变还增加 β-联蛋白的半寿期。Rubinfeld 等人，1997。这些残基的导致 β-联蛋白积累的其他缺失和突变在 Funayama 等人，1995J. Cell Biol. 128:959；Munemitsu 等人，1996Mol. Cell. Biol. 16:4088；Yost 等人，1996Genes Dev. 10:1443 和 Ha 等人，2002Acta Derm. Venereol. 82:428-431 中描述。β-联蛋白的变更磷酸化还与乳腺癌相关。Sommers 等人，1994Cancer Res. 54:3544-3552。

[0313] 在 4 个 Ser 残基和 Thr 残基外部的 β-联蛋白也已经与病态相关。在前列腺癌细胞系中检测到天冬氨酸 32 至 Tyr 的邻近突变。Voeller 等人，1998Cancer Res. 58:2520-2523。HSC-39 胃癌细胞系中存在从 +82 至 +402 的一个 321bp 缺失。Kawanishi 等人，1995Mol. Cell. Biol. 15:1175-1181。在第 32、33、34、37 和 41 位置处的其他突变已经与毛基质瘤（来源和病原学未知的皮肤肿瘤）相关。Chan 等人，1999Nature Genet. 21:410-413。与胃癌相关的额外突变存在于第 8、11、13、21、24、25、28、29、32、37、39、47、48 和 55 位置处。Clements 等人，2002CancerRes. 62:3503-3506。在 Miyaki 等人，1999Cancer Res. 59:4506-4509 中描述了结直肠肿瘤中的多种突变。总之，β-联蛋白在第 8、11、13、21、24、25、28、29、32、33、34、37、39、41、45、47、48 和 55 位置处的突变已经与各种癌症和其他病态相关。

[0314] 此外，HSC-39 胃癌细胞系中出现从 +82 至 +402 的一个 321bp 缺失。Kawanishi 等人，1995Mol. Cell. Biol. 15:1175-1181。（在这 4 个 Ser 残基和 Thr 残基区域内部和外部的）额外 β-联蛋白突变已经与髓母细胞瘤、内膜样卵巢癌、子宫内膜癌、肝细胞癌和前列腺腺癌相关。Zurawel 等人，1998Cancer Res. 58:896-899；Palacios 等人，1998Cancer Res. 58:1344-1347；Fukuchi 等 人，1998Cancer Res. 58:3526-3528；Miyoshi 等 人，1998Cancer Res. 58:2524-2527；Voeller 等人，1998Cancer Res. 2520-2523；和 Iwao 等人，1998Cancer Res. 58:1021-1026；和 Garcia-Rostan 等人，1999Cancer Res. 59:1811-1815。

[0315] 遗传环境或生物化学环境的变更也可以改变 β-联蛋白水平或活性。过量胞内 β-联蛋白在具有缺陷型 APC 的结肠和其他癌细胞中表达。Munemitsu 等人，1995Proc. Natl. Acad. Sci. USA 92:3046。减少的细胞-细胞黏附由伴随 v-src 基因转染的 β-联蛋白的酪氨酸磷酸化引起。Behrens 等人，1993J. Cell Biol. 120:757-766；Hamaguchi 等人，1993EMBO J. 12:307-314；Matsuyoshi 等人，1992J. Cell Biol. 118:703-714。

[0316] 此外，术语“β-联蛋白相关疾病”包括这些疾病，其中 β-联蛋白（处于正常形式、突变体形式和/或处于升高水平的正常形式或突变体形式和/或细胞内部定位改变）直接或间接造成参与病态的因子的表达、水平或活性增加；例如，核 β-联蛋白激活参与几种疾病的 c-myc 的产生。此外，“β-联蛋白相关疾病”包括与 Wnt/β-联蛋白途径中异常相关的那些疾病。例如，Wnt/β-联蛋白途径的异常与各种癌症、骨质疏松症、衰老、少牙畸形和退行性疾病相关。Clevers 等人，2006Cell 127:469-480；Moon 等人，2004Nat. Rev. Genet. 5:691-701；He 等人，2004Develop. 131:1663-1677；Logan 等人，2004Ann. Rev. Cell. Dev. Biol. 20:781-810。此外，Wilm 肿瘤（儿科肾癌）有时与 WTX 基因（最近发现参与 Wnt/β-联蛋白途径的肿瘤抑制基因）中的突变相关。Huang 等人，2008. Curr. Opin. Cell Biol. 20:119-125。

[0317] 具体而言，术语“β-联蛋白相关疾病”包括结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素

瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合。见 :Delektorskaya 等人,2008. Bull. Exp. Biol. Med. 146:616-619 ;Li 等人,2005World J. Gastroent. 11:2117-23 ;Liu 等人,2010J. Dental Res. 89:318-330 ;Noda 等人,1009Br. J. Cancer 100:1647-1658 ;Saegusa 等人,2009Am. J. Pathol. 174:2107-2115 ;Saldanha 等人,Br. J. Dermatol. 151:157 - 64 ;Stojadinovic 等人,Am. J. Pathol. 167:59-69 ;Thompson 等人,2007Hepatology 45:1298 - 305 ;Wang 等人,2008Cancer Epidemiol. Biomarkers Prev. 17:2101 - 8。

[0318] 针对 β - 联蛋白的 RNAi 剂可以用来治疗 β - 联蛋白相关疾病,特别是与变更的 β - 联蛋白表达、活性、区室化和 / 或水平相关或其中病情进展需要 β - 联蛋白(例如,肿瘤生长)的那些疾病。

[0319] 用于治疗 β - 联蛋白相关疾病的针对 β - 联蛋白的 RNAi 剂

[0320] 可以将本文所述的针对 β - 联蛋白的 RNAi 剂配制成可以施用至人或非人动物的药物组合物。这些组合物可以包含一种或多种 RNAi 剂,和任选地,可用于治疗 β - 联蛋白相关疾病的额外治疗。它们可以作为早期 / 预防性疗法的部分施用,并且可以按治疗有效的剂量施用。药物组合物可以包含药用载体并且可以通过本领域已知的任何方法施用。下文以额外细节描述本公开的这些各个方面。

[0321] 针对 β - 联蛋白的 RNAi 剂可以施用至人和非人动物用于治 β - 联蛋白相关疾病。

[0322] 在本公开的一个实施方案中,包含 β - 联蛋白 RNAi 剂的组合物可以施用至非人动物。例如,组合物可以给予鸡、火鸡、家畜动物(如羊、猪、马、牛等)、伴侣动物(例如,猫和犬)并且可以在治疗结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合以及相似和相关疾病方面具有功效。在每种情况下,将选择针对 β - 联蛋白的 RNAi 剂以匹配该动物基因组的 β - 联蛋白序列,并特别地以含有来自该动物基因组的全部其他基因中的至少 1 个核苷酸错配。本公开的 RNAi 剂因此可以用于治疗人和非人动物中的 β - 联蛋白相关疾病。

[0323] 如本文中在 β - 联蛋白表达的情境下所用,术语“治疗”、“疗法”等指减弱或减轻 β - 联蛋白表达所介导的病理过程。在本公开的内容下谈及下文描述的任何其他病况情况时(除 β - 联蛋白表达所介导的病理过程之外的),术语“治疗”、“疗法”等意指减弱或减轻与这种病况相关的至少一种症状,或减缓或逆转这种病况的进展或预期进展。

[0324] “治疗”还意指预防、治疗、治愈患者病况或患者病况的任何其他变化,所述其他变化表示改善身体状况或不存在身体状况变劣。“治疗”意指对 β - 联蛋白相关疾病(结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合,以及相似和相关的疾病)的治疗或对患者具有的任何其他病痛的任何适宜治疗。如本文所用,术语“治疗”和“疗法”指预防性或阻止性治疗和治愈性或病情改善性治疗,包括治疗存在感染疾病或疑似患有疾病的风险的患者,以及已经生病或

诊断为患有疾病的患者。术语“治疗”和“疗法”还指在未患有疾病但是可能易于形成不健康状况的个体中维持和/或促进健康。在一个实施方案中,“治疗”不涵盖病态的预防。因而,本公开可用于罹患 β-联蛋白相关疾病的个体或易患 β-联蛋白相关疾病的个体中抑制 β-联蛋白基因的表达和/或治疗 β-联蛋白相关疾病。“罹患”β-联蛋白相关疾病的个体已经展示作为该疾病特征的可检测症状,或否则已经临床上证实暴露于或携带 β-联蛋白相关疾病病原体或标志物。作为非限制性例子,罹患 β-联蛋白相关疾病的个体可以显示外在症状;或可以不显示外在症状,但是可以用临床试验证实在血液中携带与 β-联蛋白相关疾病相关的蛋白质标志物或与病原体相关的蛋白质或遗传物质。

[0325] 如果早期施用而非晚期施用,则对一些 β-联蛋白相关疾病的治疗可以更有效。因而,在一个具体实施方案中,将针对 β-联蛋白的 RNAi 剂早期、在疾病表现之前和/或作为预防药施用,而不是在疾病建立后施用。

[0326] 相对于针对 β-联蛋白的 RNAi 剂额外使用或与其一起使用的额外治疗

[0327] β-联蛋白相关疾病的治疗因此可以包括各种治疗,包含 β-联蛋白 RNAi 剂,并且任选地还包括额外治疗,其可以是方法(或操作),和/或额外组合物(例如,药剂或额外的 RNAi 剂)。

[0328] β-联蛋白相关疾病包括结肠的腺瘤息肉、结直肠癌、基底细胞癌、乳腺癌、肾癌、Wilm 肿瘤、髓母细胞瘤、卵巢癌、肾上腺皮质肿瘤、胃癌、肝癌、黑色素瘤、胰腺癌、前列腺癌、肾癌、异位性齿和味乳突、皮肤癌、毛基质瘤、间变性甲状腺癌、和子宫癌肉瘤、少牙畸形、骨质疏松症、衰老、退行性疾病、褥疮、慢性伤口以及受损的伤口愈合,以及相似和相关的疾病。针对这些疾病中任一种疾病的已知治疗的用途处于本领域普通技术人员的能力范围内。任何这类额外的治疗可以与针对 β-联蛋白的 RNAi 剂联合使用。

[0329] 可以在施用针对 β-联蛋白的 RNAi 剂之前、同时或之后施用的这些额外治疗包括:5-氟-29-脱氧尿苷、7-羟星形孢菌素、戈舍瑞林植入物、抗生素、贝伐珠单抗、比卡鲁胺、博来霉素、喜树碱(camptothecin)、卡铂、西妥昔单抗、顺铂、秋水仙胺(colcemid)、放线菌酮(cycloheximide)、环磷酰胺、阿糖胞苷、阿糖胞苷(Ara-C)、达卡巴嗪、多西他赛、阿霉素、依地福新(edelfosine)、ehlorambucil、表鬼臼毒素、表柔比星、埃罗替尼、雌莫司汀、依托泊苷、芬维 A 胺、非那雄胺、夫拉平度(Flavopiridol)、氟达拉滨、氟尿嘧啶、吉非替尼、吉西他滨(gemeitabine)、戈舍瑞林、六甲蜜胺、羟基脲、异环磷酰胺、依立替康、L-天冬酰胺酶、亮丙瑞林、美法仑(meiphalan)、巯基嘌呤、甲氨蝶呤、mitixantrone、丝裂霉素、米托蒽醌、氮芥、奥曲肽、紫杉醇、pirubicin、嘌呤霉素、沙格司亭、星形孢菌素、类固醇、他莫昔芬、紫杉酚、喃氟啶、替尼泊苷、拓扑替康、曲妥珠单抗、UFT、1-羟基-2-咪唑-1-基-膦酰基乙基)膦酸一水合物(以商品名称**Zometa®**由 Novartis 出售)、2-氯-N-[4-氯-3-(2-吡啶基)苯基]-4-(甲磺酰基)-苯甲酰胺(也称作 GDC-0449、并且在 PCT 公开号 WO 06/028958 中描述)、GDC0941(PCT 公开号 WO 09/036082 和 WO 09/055730)、BEZ235 或 NVP-BEZ 235(PCT 公开号 WO 06/122806)、ABT-263(PCT 公开号 WO09/155386)、5-阿扎胞苷(以商品名称**Vidaza®**出售)、地西他滨(以商品名称**Dacogen®**出售)、6-硫鸟嘌呤(以商品名称**Purinethol®**出售)、培美曲塞(以商品名称**Alimta®**出售)、阿夫土珠单抗(afutuzumab)(从**Roche®**可获得)、PEG 化非格司亭(以商品名称**Neulasta®**

由 Amgen 出售）、来那度胺（也称作 CC-5013，以商品名称 **Revlimid®** 出售）、沙立度胺（以商品名称 **Thalomid®** 出售）、阿伦珠单抗 (alemtuzumab)（以商品名称 **Campath®** 出售）、阿利维甲酸（以商品名称 **Panretin®** 出售）、维甲酸 (tretinoin)（全反式维甲酸，也称作 ATRA，以商品名称 **Vesanoid®** 出售）、异维甲酸、贝沙罗汀（以商品名称 **Targretin®** 出售）、阿伏西地（美国专利号 5621002）、氨磷汀（以商品名称 **Ethyol®** 出售）、甲酰四氢叶酸，氨鲁米特（以商品名称 **Cytadren®** 出售）、阿那格雷（以商品名称 **Agrylin®** 出售）、抗恶心药物，三氧化二砷（以商品名称 **Trisenox®** 出售）、天冬酰胺酶（也称作 L-天冬酰胺酶，欧文氏菌属 (Erwinia) L-天冬酰胺酶以商品名称 **Elspar®** 和 **Kidrolase®** 出售）、阿昔替尼、卡介菌 (bacillus calmette-guerin)（以商品名称 **theraCys®** 和 **TICE®** BCG 出售）、地尼白介素 2（以商品名称 **Ontak®** 出售）、硼替佐米（以商品名称 **Velcade®** 出售）、丙氨酸布立尼布 ((S)-((R)-1-(4-(4-氟-2-甲基-1H-吲哚-5-基氧)-5-甲基吡咯并[2,1-f][1,2,4]三嗪-6-基氧）丙-2-基)2-氨基丙酸，也称作 BMS-582664）、卡巴他赛 (1-羟基-7β,10β-二甲氧基-9-氧代-5β,20-环氧紫杉 (epoxytax)-11-烯-2α,4,13α-三基-4-乙酸酯-2-苯甲酸酯-13-[(2R,3S)-3-{[(叔丁氧基）羰基]氨基}-2-羟基-3-苯基丙酸酯）、larotaxel ((2α,3ξ,4α,5β,7α,10β,13α)-4,10-双（乙酰氧基）-13-({(2R,3S)-3-[(叔丁氧羰基）氨基]-2-羟基-3-苯基丙酰基}氧)-1-羟基-9-氧代-5,20-环氧-7,19-环紫杉-11-烯-2-基苯甲酸酯）、卡培他滨（按商标 **Xeloda®** 由 Roche 出售）、卡索匹坦（以商品名称 **Rezonic®** 和 **Zunrisa®** 由 GlaxoSmithKline 出售）、由 GlaxoSmithKline 出售的 **Cervarix®**、由 Merck 出售的 **Gardasil®**、克拉屈滨（也称作 2-氯脱氧腺苷 (2-CdA)，以商品名称 Leustatin™ 出售）、Claribine (2-氯脱氧腺苷，以商品名称 **leustatin®** 出售）、达西珠单抗 (dacetuzumab)（也称作 SGN-40 或 huS2C6，从 Seattle Genetics, Inc 可获得）、达贝泊汀 α（以商品名称 **Aranesp®** 由 Amgen 出售）、柔红霉素、地西他滨（以商品名称 **Dacogen®** 出售）、地拉罗司 (Deferasinox)（以商品名称 **Exjade®** 由 Novartis 出售）、地诺单抗 (denosumab)（以商品名称 **Prolia®** 由 Amgen 出售）、度拉纳明（也称作 AMG-951，从 Amgen/Genentech 可获得）、依洛珠单抗 (elotuzumab) (HuLuc63，CAS 编号 915296-00-3)、艾曲泊帕（以商品名称 **Promacta®** 和 **Revolade®** 由 GlaxoSmithKline 出售）、依托泊苷（也称作 VP-16 和磷酸依托泊苷，以商品名称 **Toposar®**、**VePesid®** 和 **Etopophos®** 出售）、替尼泊苷（也称作 VM-26，以商品名称 **Vumon®** 出售）、依西美坦（按商标 **Aromasin®** 由 Pfizer 出售）、来曲唑（以商品名称 **femara®** 由 Novartis 出售）、阿那曲唑（以商品名称 **Arimidex®** 出售）、芬妥木单抗 (figitumumab)（也称作 CP-751,871，从 ACC Corp 可获得）、罗妥木单抗 (robatumumab) (CAS 编号 934235-44-6)、非

格司亭（以商品名称**Neupogen®**由Amgen出售）、氟尿苷（以商品名称**FUDR®**出售）、氟甲睾酮（以商品名称出售**Halotestin®**）、氟维司群（以商品名称出售**Faslodex®**）、吉非替尼（Gefitnib）（以商品名称**Iressa®**出售）、N-[4-[(3-氯-4-氟苯基）氨基]-7-[[(3″ S″)-四氢-3-呋喃基]氧]-6-喹唑啉基]-4(二甲基氨基)-2-丁烯酰胺（butenamide）以商品名称**Tovok®**由Boehringer Ingelheim出售）、吉妥珠单抗奥佐米星（以商品名称**Mylotarg®**由Pfizer/Wyeth出售）、氢化可的松（也称作可的松、氢化可的松琥珀酸钠、氢化可的松磷酸钠并且以商品名称**Ala-Cort®**、磷酸氢化可的松、**Solu-Cortef®**、Hydrocort **Acetate®**和**Lanacort®**出售）、地塞米松（dexamethazone）((8S,9R,10S,11S,13S,14S,16R,17R)-9-氟-11,17-二羟基-17-(2-羟乙酰基)-10,13,16-三甲基-6,7,8,9,10,11,12,13,14,15,16,17-氢化联苯二酐(Dodecahydro)-3H-环戊二烯并[a]phenanthren-3-酮）、泼尼松龙（prednisolone）（以商品名称**Delta-Cortel®**、**Orapred®**、**Pediapred®**和**Prelone®**出售）、泼尼松（以商品名称**Deltasone®**、Liquid **Red®**、**Meticorten®**和**Orasone®**出售）、甲泼尼龙（也称作6-甲泼尼龙、醋酸甲泼尼龙、甲泼尼龙琥珀酸钠以商品名称**Duralone®**、**Medralone®**、**Medrol®**、**M-Prednisol®**和**Solu-Medrol®**出售）、替伊莫单抗（Ibritumomab tiuxetan）（以商品名称**Zevalin®**出售）、伊达比星（以商品名称**Idamycin®**、Idamycin **PFS®**出售）、伊珠单抗（Inotuzumab）奥加米星（也称作CMC-544和WAY-207294，从Hangzhou Sage Chemical Co.,Ltd.可获得）、白介素-2（也称作阿地白介素和IL-2，以商品名称**Proleukin®**出售）、白介素-11（也称作奥普瑞白介素（oprevelkin），以商品名称**Neumega®**出售）、α干扰素α（也称作IFN-α，以商品名称**Intron®** A和**Roferon-A®**出售）、依立替康（按商标**Camptosar®**由Pfizer出售）、盐酸拓扑替康（以商品名称**Hycamtin®**由GlaxoSmithKline出售）、伊沙匹隆（以商品名称**Lxempra®**由Bristol-Myers Squibb出售）、拉帕替尼或二甲苯磺酸拉帕替尼（lapatinib ditosylate）（按商标**Tykerb®**由GlaxoSmithKline出售）、亮丙瑞林或醋酸亮丙瑞林（以商品名称**Viadure®**由BayerAG出售、以商品名称**Eligard®**由Sanofi-Aventis出售和以商品名称**Lupron®**由Abbott Lab出售）、Linifanib(N-[4-(3-氨基-1H-吲唑-4-基）苯基]-N'-(2-氟-5-甲基苯基）脲，也称作ABT869，从Genentech可获得）、苹果酸舒尼替尼（以商品名称索坦（Sutent）由Pfizer出售）、波舒替尼(4-[(2,4-二氯-5-甲氧苯基）氨基]-6-甲氧基-7-[3-(4-甲基哌嗪-1-基）丙氧基]喹啉-3-甲腈，也称作SKI-606，并且在美国专利号6,780,996中描述）、达沙替尼（以商品名称**Sprycel®**由Bristol-Myers Squibb出售）、armala（也称作帕唑帕尼，以商品名称**Votrient®**由GlaxoSmithKline出售）、伊马替尼和甲磺酸伊马替尼（以商品名称

Gilvec®和**Gleevec®**由 Novartis 出售）、甲地孕酮（也称作醋酸甲地孕酮，以商品名称**Megace®**出售）、莫特塞尼 (N-(2,3-二氢-3,3-二甲基-1H-吲哚-6-基)-2-[(4-吡啶基甲基）氨基]-3-吡啶甲酰胺并且在 PCT 公开号 WO 02/066470 中描述）、帕瑞肽（也称作 SOM230 并且在 PCT 公开号 WO 02/010192 中描述）、索拉非尼（以商品名称**Nexavar®**出售）、奈拉滨 (nelarabine)((2R,3S,4R,5R)-2-(2-氨基-6-甲氧基-嘌呤-9-基)-5-氧杂环戊烷-3,4-二醇，以商品名称**Arranon®**和**Atriance®**由 GlaxoSmithKline 出售）、来那替尼 (neratinib)（也称作 HKI-272,(2E)-N-[4-[[3-氯-4-[(吡啶-2-基）甲氧基]苯基]氨基]-3-氰基-7-乙氧基喹啉-6-基]-4-(二甲氨基）丁-2-烯酰胺 (enamide) 并且在 PCT 公开号 WO 05/028443 中描述）、盐酸尼洛替尼（以商品名称**Tasigna®**由 Novartis 出售）、尼鲁米特（以商品名称**Nilandron®**和**Anandron®**出售）、比卡鲁胺（以商品名称**Casodex®**出售）、氟他胺（以商品名称 Fulexin™ 出售）、N-甲基-2-[[3-[(E)-2-吡啶-2-基乙烯基]-1H-吲唑-6-基]磺酰基 (sulfanyl)] 苯甲酰胺，也称作 AG013736，并且在 PCT 公开号 WO 01/002369 中描述、奥曲肽（也称作醋酸奥曲肽，以商品名称**Sandostatin®**和 Sandostatin **LAR®**出售）、奥当卡替（还称作 MK-0822,N-(1-氰基环丙基)-4-氟-N^2-{(1S)-2,2,2-三氟-1-[4'-(甲磺酰基）联苯-4-基]乙基}-L-亮酰胺，从 Lanzhou Chon Chemicals、ACC Corp. 和 ChemieTek 可获得，并且在 PCT 公开号 WO03/075836 中描述）、奥普瑞白介素（以商品名称**Neumega®**由 Pfizer/Wyeth 出售）、奥沙利铂（以商品名称**Eloxatin®**由 Sanofi-Aventis 出售并且在美国专利号 4,169,846 中描述）、帕利夫明（以商品名称 **Kepivance®**由 Amgen 出售）、帕米膦酸二钠（以商品名称 **Aredia®**出售）、唑来膦酸（以商品名称 **Zometa®**出售）、帕尼单抗（以商品名称 **Vectibix®**由 Amgen 出售）、喷司他丁（以商品名称 **Nipent®**出售）、培妥珠单抗（按商标 **Omnitarg®**由 Genentech 出售）、雷洛昔芬（以商品名称 **Evista®** 出售）、利妥昔单抗（按商标 **Riuxan®** 和 **MabThera®** 由 Genentech/Roche 出售）、罗米司亭 (Romiplostim)（以商品名称 **Nplate®** 由 Amgen 出售）、他莫昔芬（以商品名称 **Novaldex®**出售）、坦螺旋霉素 (17-烯丙氨基-17-去甲氧基格尔德霉素，也称作 KOS-953 和 17-AAG，从 SIGMA 可获得，并且在美国专利号 4,261,989 中描述）、替莫唑胺（以商品名称 **Temodar®**和 **Temodal®**由 Schering-Plough/Merck 出售）、更生霉素（也称作放线菌素 D 并且以商品名称 **Cosmegen®** 出售）、美法仑（也称作 L-PAM、L-沙可来新和苯丙氨酸氮芥，以商品名称 **Alkeran®** 出售）、六甲蜜胺（也称作六甲氰胺 (HMM)，以商品名称 **Hexalen®** 出售）、卡莫司汀（以商品名称 **BiCNU®**出售）、苯达莫司汀（以商品名称 **Treanda®**出售）、白消安（以商品名称 **Busulfex®**和 **Myleran®**出售）、卡铂（以商品名称 **Paraplatin®** 出售）、罗莫司汀（也称作 CCNU，以商品名称 **CeeNU®** 出售）、顺铂（也称作 CDDP，以商

品名称**Platinol®**和**Platinol®**-AQ出售）、苯丁酸氮芥（以商品名称**Leukeran®**出售）、环磷酰胺（以商品名称**Cytoxan®**和**Neosar®**出售）、达卡巴嗪（也称作DTIC、DIC和咪唑甲酰胺，以商品名称**DTIC-Dome®**出售）、六甲蜜胺（也称作六甲氰胺(HMM)，以商品名称**Hexalen®**出售）、异环磷酰胺（以商品名称**Ifex®**出售）、甲基苄肼（以商品名称**Matulane®**出售）、氮芥（也称作氮芥、氮氯嗪和盐酸氮芥，以商品名称出售**Mustargen®**）、链佐星（以商品名称**Zanosar®**出售）、噻替哌（也称作硫代磷酰胺(thiophosphoamide)、TESPA和TSPA，以商品名称**Thioplex®**出售），坦罗莫司（以商品名称**Torisel®**由Pfizer出售）、地磷莫司（正式地称作deferolimus，(1R,2R,4S)-4-[(2R)-2[(1R,9S,12S,15R,16E,18R,19R,21R,23S,24E,26E,28Z,30S,32S,35R)-1,18-二羟基-19,30-二甲氧基-15,17,21,23,29,35-六甲基-2,3,10,14,20-五氧代-11,36-二氧代-4-氮杂三环[30.3.1.04,9]三十六烷(hexatriaconta)-16,24,26,28-四烯-12-基]丙基]-2-甲氧环己基二甲基次膦酸盐，也称作AP23573和MK8669，并且在PCT公开号WO 03/064383中描述）、依维莫司（以商品名称**Afinitor®**由Novartis出售）、托瑞米芬（以商品名称**Fareston®**出售）、托西莫单抗(tositumomab)（按商标**Bexxar®**由GlaxoSmithKline出售）、奥法木单抗(ofatumumab)（按商标**Arzerra®**由GlaxoSmithKline出售）、曲美木单抗(tremelimumab)（从Pfizer可获得的IgG2单克隆抗体，以前称作ticilimumab、CP-675,206）、伊匹木单抗(CTLA-4抗体，也称作MDX-010、CAS编号77202-00-9）、长春碱（也称作硫酸长春碱、长春花碱和VLB，以商品名称**Alkaban-AQ®**和**Velban®**出售）、长春新碱（也称作硫酸长春新碱、LCR和VCR，以商品名称**Oncovin®**和Vincasar **Pfs®**出售）、长春瑞滨（以商品名称**Navelbine®**出售）、伏立诺他(Voninostat)（以商品名称**Zolinza®**由Merck出售）、扎利罗登（也称作SR57746，1-[2-(2-萘基）乙基]-4-[3-（三氟甲基）苯基]-1,2,3,6-四氢吡啶，并且在美国专利号5,266,573中描述）、XL-518（也称作GDC-0973，Cas编号1029872-29-4，从ACC Corp.可获得）；司美替尼(5-[(4-溴-2-氯苯基）氨基]-4-氟-N-(2-羟基乙氧基)-1-甲基-1H-苯并咪唑-6-甲酰胺，也称作AZD6244或ARRY142886，在PCT公开号WO2003077914中描述）；2-[(2-氯-4-碘苯基）氨基]-N-（环丙基甲氧基)-3,4-二氟-苯甲酰胺（也称作CI-1040或PD184352并且在PCT公开号WO2000035436中描述）；N-[(2R)-2,3-二羟基丙氧基]-3,4-二氟-2-[(2-氟-4-碘苯基）氨基]-苯甲酰胺（也称作PD0325901并且在PCT公开号WO2002006213中描述）；2,3-双[氨基[(2-氨基苯基）硫代]亚甲基]-丁二腈（也称作U0126并且在美国专利号2,779,780中描述）；N-[3,4-二氟-2-[(2-氟-4-碘苯基）氨基]-6-甲氧苯基]-1-[(2R)-2,3-二羟基丙基]-环丙烷磺酰胺（也称作RDEA119或BAY869766并且在PCT公开号WO2007014011中描述）；(3S,4R,5Z,8S,9S,11E)-14-（乙基氨基)-8,9,16-三羟基-3,4-二甲基-3,4,9,19-四氢-1H-2-苯并噁环十四烷(benzoxacyclotetradecine)-1,7(8H)-二酮]（也称作E6201并且在PCT公开号WO2003076424中描述）；2'-氨基-3'-甲氧基黄酮（也称作PD98059，从德国Biaffin GmbH & Co.,KG可获

得）；AS-703026（CAS 编号 1204531-26-9）；AZD-8330（也称作 ARRY-424704 或 ARRY-704，CAS 编号 1204531-17-8）；ARRY-438162（CAS 编号 1073666-70-2）；GSK-1120212（CAS 编号 1204531-25-8）；RO-4987665（CAS 编号 1204531-24-7）；和 TAK-733；抗再吸收剂、双膦酸盐、骨同化剂、降钙素、钙、钙盐、雌激素类似物、雷洛昔芬、RANKL 抑制剂、氟化钠、雷奈酸锶、特立帕肽和维生素 D。

[0330] 额外治疗和 RNAi 剂的剂量可以由本领域普通技术人员并且如本文所述那样容易地确定。

[0331] RNAi 剂的剂量和有效量

[0332] 本公开的 RNAi 剂以治疗有效量的剂量施用至有需要的患者。

[0333] “有效量”或“治疗有效量”是治疗个体的疾病或医学状况，或更一般地向个体提供营养个体、生理益处或医学益处的量。如本文所用，短语“治疗有效量”和“预防有效量”指在治疗、预防或管理由 β－联蛋白表达介导的病理过程或由 β－联蛋白表达介导的病理过程的明显症状时提供治疗益处的量。治疗有效的具体量可以由普通医疗执业者轻易地确定，并且可以根据本领域已知的因素变动，例如，由 β－联蛋白表达介导的病理过程的类型、患者病史和年龄、由 β－联蛋白表达介导的病理过程的阶段和施用抑制由 β－联蛋白表达介导的病理过程其他药物。

[0334] 在本公开的多种实施方案中，患者的年龄至少约 1、3、6 或 9 个月、或 1、5、10、20、30、40、50、55、60、65、70 或 75 岁。在本公开的多种实施方案中，患者的年龄不超过约 1、3、6 或 9 个月、或 1、5、10、20、30、40、50、55、60、65、70、75、80、90 或 100 岁。在多种实施方案中，患者具有至少约 5、10、15、20、30、40、50、60、70、80、90、100、120、140、160、180、200、220、240、260、280、300、320、340、360、380 或 400lbs 的体重。在本公开的多种实施方案中，患者具有不多于约 5、10、15、20、30、40、50、60、70、80、90、100、120、140、160、180、200、220、240、260、280、300、320、340、360、380 或 400lbs 的体重。

[0335] 在本公开的多种实施方案中，剂量［仅计量有效成分）］可以是至少约 1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000ng、1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000 微克、1、5、10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000mg。在本公开的多种实施方案中，剂量可以是不多于约 10、25、50、100、200、250、300、350、400、450、500、550、600、650、700、750、800、850、900、950 或 1000mg。在本公开的多种实施方案中，可以将该剂量施用每日至少多于 1 次、每日 1 次、每周多于 1 次、每周 1 次、每两周 1 次、每月 1 次和／或每 2、3、4、5、6、7、8、9、10、11 或 12 个月施用 1 次或其组合。

[0336] 在本公开的多种实施方案中，剂量与个体的体重或身体表面积相关。可以变动实际剂量水平以获得有效药物的量，其中在对患者无毒的情况下，所述量有效用于特定的患者、组合物和施用模式。选择的剂量水平将取决于多种药物代谢动力学因素，包括所用的特定 RNAi 剂的活性、施用途径、RNAi 剂的排泄速率、治疗的持续时间、与 RNAi 剂组合使用的其他药物、化合物和／或材料、患者的年龄、性别、重量、状况、总体健康和既往医史等医学领域熟知的因素。具有本领域普通技术的医师或兽医师可以轻易地确定所需要的 RNAi 的有效量。合适的剂量将是这种量，它是有效产生治疗效果的最低剂量或低到足在不造成副

作用的情况下产生治疗效果的剂量。

[0337] 除一种或多种针对 β-联蛋白的 RNAi 剂的治疗有效剂量之外，本公开的药物组合物可以包含与 RNAi 剂协同发挥作用或与之联合使用的额外疾病治疗药。例如，药物组合物可以包含针对 β-联蛋白的额外拮抗剂。

[0338] 针对 β-联蛋白的 RNAi 剂的额外实施方案

[0339] 在一个特定实施方案中，本公开涵盖一种包含一种或多种 β-联蛋白 RNAi 剂的组合物。在一个实施方案中，本公开包含了含有有义链和反义链的 RNAi 剂。在一个实施方案中，反义链由表 1、2、3、4、5、6、7、8 和/或 9 中列出的 RNAi 剂的反义链的序列组成、基本上由其组成或包含所述序列。在一个实施方案中，反义链由至少 15 个连续核苷酸的序列组成、基本上由其组成或包含所述序列，所述序列与表 1、2、3、4、5、6、7、8 和/或 9 中列出的任何 RNAi 剂的反义链的序列具有 0、1、2 或 3 个错配。在一个实施方案中，反义链由表 1、2、3、4、5、6、7、8 和/或 9 中列出的 RNAi 剂的反义链的序列组成，并且还包含 0、1、2、3、4、5、6、7、8、9 或 10 个核苷酸。在一个实施方案中，反义链由这样的序列组成，所述序列与表 1、2、3、4、5、6、7、8 和/或 9 中列出的 RNAi 剂的反义链的序列具有 0、1、2 或 3 个错配，并且还包含 0、1、2、3、4、5、6、7、8、9 或 10 个核苷酸。

[0340] 在本公开的多种实施方案中，要求保护的本公开的组合物具下述条件：它不包含表 1、2 或 3 中列出的任何特定单独 RNAi 剂。在本公开的多种实施方案中，针对 β-联蛋白的 RNAi 剂具有下述条件：它不具有在专利或科学文献例如 WO 2006/086772、US 20070207974、US 20070042381、US 20050255487、US 2007/0275914、US 20070039072、US 20060193870 或 US 20080113351 中公开的任何 β-联蛋白 RNAi 剂的序列。

RNAi 剂的额外实施方案

[0341] 在另一个具体实施方案中，RNAi 剂包含表 1 中列出的任一种 RNAi 剂及其修饰的变体和未修饰的变体。

[0342] 在另一个具体实施方案中，RNAi 剂包含表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂及其修饰变体和未修饰变体的有义链。

[0343] 在另一个具体实施方案中，RNAi 剂包含表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链。

[0344] 在另一个具体实施方案中，RNAi 剂包含具有下述序列的有义链，所述序列由表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂及其修饰变体和未修饰变体的有义链的序列组成。

[0345] 在另一个具体实施方案中，RNAi 剂包含具有下述序列的反义链，所述序列由表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链的序列组成。

[0346] 在另一个具体实施方案中，RNAi 剂包含具有下述序列的有义链，所述序列由表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂的有义链的序列组成，和/或具有下述序列的反义链，所述序列由表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂的反义链的序列组成。

[0347] 在另一个具体实施方案中，RNAi 剂具有由表 1、2、3、4、5、6、7、8 和/或 9 中列出的任一种 RNAi 剂及其修饰变体和未修饰变体的序列组成的序列。

[0348] 包含一种或多种针对 β-联蛋白的有效 RNAi 剂的实施方案

[0349] 在本公开的多种实施方案中，本公开包含在HeLa细胞中以体外浓度10nM或0.1nM展示至少约40%、50%、60%、70%、80%、90%或95%的 β-联蛋白基因敲减作用（分别不多于约60%、50%、40%、30%、20%、10%或5%残余基因活性）的 RNAi 剂。

[0350] 在本公开的多种实施方案中，该组合物包含一种或多种 RNAi 剂能够在 24 小时在10nM 实现≤0.05、≤0.10、≤0.20、≤0.30、≤0.40 的倍数变化（分别表示在HeLa 细胞中在 24 小时在 10nM浓度时至少 95%、90%、80%、70%或60%的 β-联蛋白基因敲减作用）。本文表格中公开了能够实现这些活性水平的 RNAi 剂。

[0351] 包含一种或多种针对 β-联蛋白的有效 RNAi 剂的实施方案

[0352] 在本公开的多种实施方案中，该组合物包含一种或多种 RNAi 剂能够在 120 小时在0.1nM 实现≤0.30、≤0.20 或≤0.10 倍数变化（分别表示在 HeLa 细胞中在 120 小时在0.1nM 浓度时至少 70%、80%或 90%的 β-联蛋白基因敲减作用）。本文表格中公开了能够实现这些活性水平的 RNAi 剂。

[0353] 包含一种或多种针对 β-联蛋白的具有低 EC_{50} 的 RNAi 剂的多种实施方案

[0354] 在本公开的多种实施方案中，组合物包含能够在HeLa 细胞中以低浓度介导 β-联蛋白的50%基因敲减作用（EC_{50}）的一种或多种RNAi 剂。对于本文中列出的许多RNAi 剂，计算估计的 EC_{50}。细胞用 10nM、1nM、0.1nM、0.01nM 和 0.001nM RNAi 剂处理，并将数据拟合成曲线。所示的 EC_{50} 是从可用数据计算的估计的 EC_{50}，其中预期所述估计的 EC_{50} 在 HeLa 细胞中产生 β-联蛋白的 50%基因敲减。在本公开的多种实施方案中，组合物包能够在 HeLa 细胞中以 100、75、50、25、10、5、2.5、1、0.75、0.5、0.25、0.2、0.12、0.1、0.09、0.08、0.07、0.06、0.05、0.04、0.03 或 0.02nM 或更小浓度介导 50%基因敲减作用（EC_{50}）的一种或多种 RNAi 剂。本文表格中公开了能够实现这些活性水平的 RNAi 剂。

[0355] 针对 β-联蛋白的 RNAi 剂的具体实施方案

[0356] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含有义链和反义链，其中反义链包含与来自表 1、2、3、4、5、6、7、8 和/或 9 的任一种 RNAi 剂及其修饰变体或未修饰变体的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0357] 在一个实施方案中，该组合物包含任一种或多种包含有义链和反义链的 RNAi 剂，其中反义链包含与来自表 1、2、3、4、5、6、7、8 和/或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链差异 0 个核苷酸的至少 15 个连续核苷酸。

[0358] 在一个实施方案中，本公开涉及一种组合物，其包含来自表 1、2、3、4、5、6、7、8 和/或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的任一者或多者。

[0359] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含反义链，所述反义链包含来自表 1、2、3、4、5、6、7、8 和/或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链的序列。

[0360] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含反义链，所述反义链由来自表 1、2、3、4、5、6、7、8 和/或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的反义链的序列组成。

[0361] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述

RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1、2、3、4、5、6、7、8 和 / 或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的第一链的序列。

[0362] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链和第二链的序列是来自表 1、2、3、4、5、6、7、8 和 / 或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的第一链和第二链的序列。

[0363] 在一个实施方案中，本公开涉及一种包含任一种或多种 RNAi 剂的组合物，所述 RNAi 剂包含第一链和第二链，其中第一链的序列是来自表 1、2、3、4、5、6、7、8 和 / 或 9 的任一种 RNAi 剂及其修饰变体和未修饰变体的第一链的序列，其中第一链和 / 或第二链进一步还包含至多约 20 个额外的核苷酸。

[0364] 针对 β - 联蛋白的特异性 RNAi 剂的额外实施方案

[0365] 在一个实施方案中，本公开包含一种 RNAi 剂，所述 RNAi 剂包含第一链和第二链，其中第一链包含与来自表 1、2、3、4、5、6、7、8 和 / 或 9 的任一种 RNAi 剂或其修饰变体或未修饰变体的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0366] 因而，在多种实施方案中，本公开涉及一种包含以下任一者或多者的组合物：

[0367] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26104 或其修饰变体或未修饰变体。

[0368] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26063 或其修饰变体或未修饰变体。

[0369] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26082 或其修饰变体或未修饰变体。

[0370] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26034 或其修饰变体或未修饰变体。

[0371] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26091 或其修饰变体或未修饰变体。

[0372] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26047 或其修饰变体或未修饰变体。

[0373] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26651 或其修饰变体或未修饰变体。

[0374] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26696 或其修饰变体或未修饰变体。

[0375] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26109 或其修饰变体或未修饰变体。

[0376] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25941 或其修饰变体或未修饰变体。

[0377] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26028 或其修饰变体或未修饰变体。

[0378] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26652 或其修饰变体或未修饰变体。

[0379] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26742 或其修饰变体或未修饰变体。

[0380] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26921 或其修饰变体或未修饰变体。

[0381] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18893 或其修饰变体或未修饰变体。

[0382] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18983 或其修饰变体或未修饰变体。

[0383] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25950 或其修饰变体或未修饰变体。

[0384] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25951 或其修饰变体或未修饰变体。

[0385] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26042 或其修饰变体或未修饰变体。

[0386] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26043 或其修饰变体或未修饰变体。

[0387] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26673 或其修饰变体或未修饰变体。

[0388] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26704 或其修饰变体或未修饰变体。

[0389] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26068 或其修饰变体或未修饰变体。

[0390] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26183 或其修饰变体或未修饰变体。

[0391] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26700 或其修饰变体或未修饰变体。

[0392] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26701 或其修饰变体或未修饰变体。

[0393] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25942 或其修饰变体或未修饰变体。

[0394] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26076 或其修饰变体或未修饰变体。

[0395] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26031 或其修饰变体或未修饰变体。

[0396] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26210 或其修饰变体或未修饰变体。

[0397] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26664 或其修饰变体或未修饰变体。

[0398] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26691 或其修饰变体或未修饰变体。

[0399] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26740 或其修饰变体或未修饰变体。

[0400] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19765 或其修饰变体或未修饰变体。

[0401] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26158 或其修饰变体或未修饰变体。

[0402] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26180 或其修饰变体或未修饰变体。

[0403] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26078 或其修饰变体或未修饰变体。

[0404] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25894 或其修饰变体或未修饰变体。

[0405] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25964 或其修饰变体或未修饰变体。

[0406] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26156 或其修饰变体或未修饰变体。

[0407] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26670 或其修饰变体或未修饰变体。

[0408] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26743 或其修饰变体或未修饰变体。

[0409] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25890 或其修饰变体或未修饰变体。

[0410] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26044 或其修饰变体或未修饰变体。

[0411] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26685 或其修饰变体或未修饰变体。

[0412] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26731 或其修饰变体或未修饰变体。

[0413] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26800 或其修饰变体或未修饰变体。

[0414] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26066 或其修饰变体或未修饰变体。

[0415] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26682 或其修饰变体或未修饰变体。

[0416] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26684 或其修饰变体或未修饰变体。

[0417] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26757 或其修饰变体或未修饰变体。

[0418] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26788 或其修饰变体或未修饰变体。

[0419] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18963 或其修饰变体或未修饰变体。

[0420] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19076 或其修饰变体或未修饰变体。

[0421] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25943 或其修饰变体或未修饰变体。

[0422] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26052 或其修饰变体或未修饰变体。

[0423] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26665 或其修饰变体或未修饰变体。

[0424] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26746 或其修饰变体或未修饰变体。

[0425] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18974 或其修饰变体或未修饰变体。

[0426] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25938 或其修饰变体或未修饰变体。

[0427] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25944 或其修饰变体或未修饰变体。

[0428] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26178 或其修饰变体或未修饰变体。

[0429] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26669 或其修饰变体或未修饰变体。

[0430] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26730 或其修饰变体或未修饰变体。

[0431] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26825 或其修饰变体或未修饰变体。

[0432] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25956 或其修饰变体或未修饰变体。

[0433] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26822 或其修饰变体或未修饰变体。

[0434] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26108 或其修饰变体或未修饰变体。

[0435] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26752 或其修饰变体或未修饰变体。

[0436] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26779 或其修饰变体或未修饰变体。

[0437] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25891 或其修饰变体或未修饰变体。

[0438] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26101 或其修饰变体或未修饰变体。

[0439] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26181 或其修饰变体或未修饰变体。

[0440] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26218 或其修饰变体或未修饰变体。

[0441] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26660 或其修饰变体或未修饰变体。

[0442] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18966 或其修饰变体或未修饰变体。

[0443] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19074 或其修饰变体或未修饰变体。

[0444] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26179 或其修饰变体或未修饰变体。

[0445] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26722 或其修饰变体或未修饰变体。

[0446] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26768 或其修饰变体或未修饰变体。

[0447] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26920 或其修饰变体或未修饰变体。

[0448] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26020 或其修饰变体或未修饰变体。

[0449] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26713 或其修饰变体或未修饰变体。

[0450] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26727 或其修饰变体或未修饰变体。

[0451] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26808 或其修饰变体或未修饰变体。

[0452] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25958 或其修饰变体或未修饰变体。

[0453] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26105 或其修饰变体或未修饰变体。

[0454] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26674 或其修饰变体或未修饰变体。

[0455] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26781 或其修饰变体或未修饰变体。

[0456] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26801 或其修饰变体或未修饰变体。

[0457] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26813 或其修饰变体或未修饰变体。

[0458] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26816 或其修饰变体或未修饰变体。

[0459] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25945 或其修饰变体或未修饰变体。

[0460] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26203 或其修饰变体或未修饰变体。

[0461] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26021 或其修饰变体或未修饰变体。

[0462] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26040 或其修饰变体或未修饰变体。

[0463] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26069 或其修饰变体或未修饰变体。

[0464] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26134 或其修饰变体或未修饰变体。

[0465] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26702 或其修饰变体或未修饰变体。

[0466] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18933 或其修饰变体或未修饰变体。

[0467] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26690 或其修饰变体或未修饰变体。

[0468] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26698 或其修饰变体或未修饰变体。

[0469] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25910 或其修饰变体或未修饰变体。

[0470] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26747 或其修饰变体或未修饰变体。

[0471] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26810 或其修饰变体或未修饰变体。

[0472] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26083 或其修饰变体或未修饰变体。

[0473] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26061 或其修饰变体或未修饰变体。

[0474] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26904 或其修饰变体或未修饰变体。

[0475] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18903 或其修饰变体或未修饰变体。

[0476] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18980 或其修饰变体或未修饰变体。

[0477] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26202 或其修饰变体或未修饰变体。

[0478] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26679 或其修饰变体或未修饰变体。

[0479] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26719 或其修饰变体或未修饰变体。

[0480] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26758 或其修饰变体或未修饰变体。

[0481] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26783 或其修饰变体或未修饰变体。

[0482] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26902 或其修饰变体或未修饰变体。

[0483] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18892 或其修饰变体或未修饰变体。

[0484] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18897 或其修饰变体或未修饰变体。

[0485] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25902 或其修饰变体或未修饰变体。

[0486] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26705 或其修饰变体或未修饰变体。

[0487] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26782 或其修饰变体或未修饰变体。

[0488] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19082 或其修饰变体或未修饰变体。

[0489] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26176 或其修饰变体或未修饰变体。

[0490] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26196 或其修饰变体或未修饰变体。

[0491] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26199 或其修饰变体或未修饰变体。

[0492] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26678 或其修饰变体或未修饰变体。

[0493] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26683 或其修饰变体或未修饰变体。

[0494] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26729 或其修饰变体或未修饰变体。

[0495] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26804 或其修饰变体或未修饰变体。

[0496] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26900 或其修饰变体或未修饰变体。

[0497] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25914 或其修饰变体或未修饰变体。

[0498] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26060 或其修饰变体或未修饰变体。

[0499] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26763 或其修饰变体或未修饰变体。

[0500] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18902 或其修饰变体或未修饰变体。

[0501] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18914 或其修饰变体或未修饰变体。

[0502] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26100 或其修饰变体或未修饰变体。

[0503] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26128 或其修饰变体或未修饰变体。

[0504] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26193 或其修饰变体或未修饰变体。

[0505] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26765 或其修饰变体或未修饰变体。

[0506] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25960 或其修饰变体或未修饰变体。

[0507] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26018 或其修饰变体或未修饰变体。

[0508] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25893 或其修饰变体或未修饰变体。

[0509] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26823 或其修饰变体或未修饰变体。

[0510] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25940 或其修饰变体或未修饰变体。

[0511] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26190 或其修饰变体或未修饰变体。

[0512] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26675 或其修饰变体或未修饰变体。

[0513] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26797 或其修饰变体或未修饰变体。

[0514] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26916 或其修饰变体或未修饰变体。

[0515] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26755 或其修饰变体或未修饰变体。

[0516] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26901 或其修饰变体或未修饰变体。

[0517] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19004 或其修饰变体或未修饰变体。

[0518] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19009 或其修饰变体或未修饰变体。

[0519] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26148 或其修饰变体或未修饰变体。

[0520] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26186 或其修饰变体或未修饰变体。

[0521] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26737 或其修饰变体或未修饰变体。

[0522] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25955 或其修饰变体或未修饰变体。

[0523] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26029 或其修饰变体或未修饰变体。

[0524] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26131 或其修饰变体或未修饰变体。

[0525] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18894 或其修饰变体或未修饰变体。

[0526] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18939 或其修饰变体或未修饰变体。

[0527] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26654 或其修饰变体或未修饰变体。

[0528] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18929 或其修饰变体或未修饰变体。

[0529] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26135 或其修饰变体或未修饰变体。

[0530] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26774 或其修饰变体或未修饰变体。

[0531] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26780 或其修饰变体或未修饰变体。

[0532] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26819 或其修饰变体或未修饰变体。

[0533] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26918 或其修饰变体或未修饰变体。

[0534] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19050 或其修饰变体或未修饰变体。

[0535] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18994 或其修饰变体或未修饰变体。

[0536] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26769 或其修饰变体或未修饰变体。

[0537] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26666 或其修饰变体或未修饰变体。

[0538] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26784 或其修饰变体或未修饰变体。

[0539] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18969 或其修饰变体或未修饰变体。

[0540] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18986 或其修饰变体或未修饰变体。

[0541] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25929 或其修饰变体或未修饰变体。

[0542] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25932 或其修饰变体或未修饰变体。

[0543] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26095 或其修饰变体或未修饰变体。

[0544] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26908 或其修饰变体或未修饰变体。

[0545] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26071 或其修饰变体或未修饰变体。

[0546] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26912 或其修饰变体或未修饰变体。

[0547] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19054 或其修饰变体或未修饰变体。

[0548] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25918 或其修饰变体或未修饰变体。

[0549] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26903 或其修饰变体或未修饰变体。

[0550] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25931 或其修饰变体或未修饰变体。

[0551] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26146 或其修饰变体或未修饰变体。

[0552] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26200 或其修饰变体或未修饰变体。

[0553] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26917 或其修饰变体或未修饰变体。

[0554] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26794 或其修饰变体或未修饰变体。

[0555] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26910 或其修饰变体或未修饰变体。

[0556] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-25939 或其修饰变体或未修饰变体。

[0557] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26032 或其修饰变体或未修饰变体。

[0558] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26776 或其修饰变体或未修饰变体。

[0559] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26806 或其修饰变体或未修饰变体。

[0560] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26748 或其修饰变体或未修饰变体。

[0561] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26725 或其修饰变体或未修饰变体。

[0562] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-18958 或其修饰变体或未修饰变体。

[0563] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26672 或其修饰变体或未修饰变体。

[0564] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26905 或其修饰变体或未修饰变体。

[0565] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-19056 或其修饰变体或未修饰变体。

[0566] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-19762 或其修饰变体或未修饰变体。

[0567] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26919 或其修饰变体或未修饰变体。

[0568] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-18946 或其修饰变体或未修饰变体。

[0569] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-19066 或其修饰变体或未修饰变体。

[0570] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-19746 或其修饰变体或未修饰变体。

[0571] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26057 或其修饰变体或未修饰变体。

[0572] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26073 或其修饰变体或未修饰变体。

[0573] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸：AD-26689 或其修饰变体或未修饰变体。

[0574] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19008 或其修饰变体或未修饰变体。

[0575] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26026 或其修饰变体或未修饰变体。

[0576] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26761 或其修饰变体或未修饰变体。

[0577] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19752 或其修饰变体或未修饰变体。

[0578] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18981 或其修饰变体或未修饰变体。

[0579] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18927 或其修饰变体或未修饰变体。

[0580] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19753 或其修饰变体或未修饰变体。

[0581] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25907 或其修饰变体或未修饰变体。

[0582] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26671 或其修饰变体或未修饰变体。

[0583] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19080 或其修饰变体或未修饰变体。

[0584] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26075 或其修饰变体或未修饰变体。

[0585] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26681 或其修饰变体或未修饰变体。

[0586] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18976 或其修饰变体或未修饰变体。

[0587] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25900 或其修饰变体或未修饰变体。

[0588] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26126 或其修饰变体或未修饰变体。

[0589] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26688 或其修饰变体或未修饰变体。

[0590] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25912 或其修饰变体或未修饰变体。

[0591] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25930 或其修饰变体或未修饰变体。

[0592] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18995 或其修饰变体或未修饰变体。

[0593] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26802 或其修饰变体或未修饰变体。

[0594] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25892 或其修饰变体或未修饰变体。

[0595] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25947 或其修饰变体或未修饰变体。

[0596] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26088 或其修饰变体或未修饰变体。

[0597] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26098 或其修饰变体或未修饰变体。

[0598] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26778 或其修饰变体或未修饰变体。

[0599] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26215 或其修饰变体或未修饰变体。

[0600] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26739 或其修饰变体或未修饰变体。

[0601] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18950 或其修饰变体或未修饰变体。

[0602] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25949 或其修饰变体或未修饰变体。

[0603] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26141 或其修饰变体或未修饰变体。

[0604] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18961 或其修饰变体或未修饰变体。

[0605] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25957 或其修饰变体或未修饰变体。

[0606] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26826 或其修饰变体或未修饰变体。

[0607] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25963 或其修饰变体或未修饰变体。

[0608] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26019 或其修饰变体或未修饰变体。

[0609] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26035 或其修饰变体或未修饰变体。

[0610] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25946 或其修饰变体或未修饰变体。

[0611] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26714 或其修饰变体或未修饰变体。

[0612] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26022 或其修饰变体或未修饰变体。

[0613] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26096 或其修饰变体或未修饰变体。

[0614] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26132 或其修饰变体或未修饰变体。

[0615] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26062 或其修饰变体或未修饰变体。

[0616] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18991 或其修饰变体或未修饰变体。

[0617] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26164 或其修饰变体或未修饰变体。

[0618] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26209 或其修饰变体或未修饰变体。

[0619] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25895 或其修饰变体或未修饰变体。

[0620] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25933 或其修饰变体或未修饰变体。

[0621] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26017 或其修饰变体或未修饰变体。

[0622] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19749 或其修饰变体或未修饰变体。

[0623] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26653 或其修饰变体或未修饰变体。

[0624] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26759 或其修饰变体或未修饰变体。

[0625] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25924 或其修饰变体或未修饰变体。

[0626] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26153 或其修饰变体或未修饰变体。

[0627] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25953 或其修饰变体或未修饰变体。

[0628] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26764 或其修饰变体或未修饰变体。

[0629] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26790 或其修饰变体或未修饰变体。

[0630] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-20124 或其修饰变体或未修饰变体。

[0631] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25919 或其修饰变体或未修饰变体。

[0632] 包含第一链和第二链的 RNAi 剂,其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18913 或其修饰变体或未修饰变体。

[0633] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26211 或其修饰变体或未修饰变体。

[0634] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18936 或其修饰变体或未修饰变体。

[0635] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25898 或其修饰变体或未修饰变体。

[0636] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26741 或其修饰变体或未修饰变体。

[0637] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19043 或其修饰变体或未修饰变体。

[0638] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26079 或其修饰变体或未修饰变体。

[0639] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19000 或其修饰变体或未修饰变体。

[0640] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25911 或其修饰变体或未修饰变体。

[0641] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26786 或其修饰变体或未修饰变体。

[0642] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19069 或其修饰变体或未修饰变体。

[0643] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26037 或其修饰变体或未修饰变体。

[0644] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26723 或其修饰变体或未修饰变体。

[0645] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19067 或其修饰变体或未修饰变体。

[0646] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25928 或其修饰变体或未修饰变体。

[0647] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26677 或其修饰变体或未修饰变体。

[0648] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19006 或其修饰变体或未修饰变体。

[0649] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19758 或其修饰变体或未修饰变体。

[0650] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26913 或其修饰变体或未修饰变体。

[0651] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25917 或其修饰变体或未修饰变体。

[0652] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26189 或其修饰变体或未修饰变体。

[0653] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26787 或其修饰变体或未修饰变体。

[0654] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26707 或其修饰变体或未修饰变体。

[0655] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26094 或其修饰变体或未修饰变体。

[0656] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26097 或其修饰变体或未修饰变体。

[0657] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26699 或其修饰变体或未修饰变体。

[0658] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26756 或其修饰变体或未修饰变体。

[0659] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26720 或其修饰变体或未修饰变体。

[0660] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25926 或其修饰变体或未修饰变体。

[0661] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26212 或其修饰变体或未修饰变体。

[0662] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26687 或其修饰变体或未修饰变体。

[0663] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26753 或其修饰变体或未修饰变体。

[0664] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18982 或其修饰变体或未修饰变体。

[0665] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18908 或其修饰变体或未修饰变体。

[0666] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18968 或其修饰变体或未修饰变体。

[0667] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25948 或其修饰变体或未修饰变体。

[0668] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26188 或其修饰变体或未修饰变体。

[0669] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26708 或其修饰变体或未修饰变体。

[0670] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25961 或其修饰变体或未修饰变体。

[0671] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26803 或其修饰变体或未修饰变体。

[0672] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19741 或其修饰变体或未修饰变体。

[0673] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26056 或其修饰变体或未修饰变体。

[0674] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25959 或其修饰变体或未修饰变体。

[0675] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26059 或其修饰变体或未修饰变体。

[0676] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26102 或其修饰变体或未修饰变体。

[0677] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26106 或其修饰变体或未修饰变体。

[0678] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26744 或其修饰变体或未修饰变体。

[0679] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26099 或其修饰变体或未修饰变体。

[0680] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26170 或其修饰变体或未修饰变体。

[0681] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19012 或其修饰变体或未修饰变体。

[0682] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26198 或其修饰变体或未修饰变体。

[0683] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26766 或其修饰变体或未修饰变体。

[0684] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18951 或其修饰变体或未修饰变体。

[0685] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18975 或其修饰变体或未修饰变体。

[0686] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26749 或其修饰变体或未修饰变体。

[0687] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18911 或其修饰变体或未修饰变体。

[0688] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26906 或其修饰变体或未修饰变体。

[0689] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-19747 或其修饰变体或未修饰变体。

[0690] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18960 或其修饰变体或未修饰变体。

[0691] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异

0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-25909 或其修饰变体或未修饰变体。

[0692] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26184 或其修饰变体或未修饰变体。

[0693] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26077 或其修饰变体或未修饰变体。

[0694] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26680 或其修饰变体或未修饰变体。

[0695] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26085 或其修饰变体或未修饰变体。

[0696] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18926 或其修饰变体或未修饰变体。

[0697] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18945 或其修饰变体或未修饰变体。

[0698] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26703 或其修饰变体或未修饰变体。

[0699] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26911 或其修饰变体或未修饰变体。

[0700] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26661 或其修饰变体或未修饰变体。

[0701] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-18905 或其修饰变体或未修饰变体。

[0702] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :AD-26142 或其修饰变体或未修饰变体。

[0703] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1245 或其修饰变体或未修饰变体。

[0704] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1249 或其修饰变体或未修饰变体。

[0705] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1250 或其修饰变体或未修饰变体。

[0706] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1450 或其修饰变体或未修饰变体。

[0707] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1545 或其修饰变体或未修饰变体。

[0708] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1755 或其修饰变体或未修饰变体。

[0709] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1814 或其修饰变体或未修饰变体。

[0710] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1816 或其修饰变体或未修饰变体。

[0711] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_1974 或其修饰变体或未修饰变体。

[0712] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_2202 或其修饰变体或未修饰变体。

[0713] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_2425 或其修饰变体或未修饰变体。

[0714] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_254 或其修饰变体或未修饰变体。

[0715] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_3146 或其修饰变体或未修饰变体。

[0716] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_3169 或其修饰变体或未修饰变体。

[0717] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_3196 或其修饰变体或未修饰变体。

[0718] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_3477 或其修饰变体或未修饰变体。

[0719] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_703 或其修饰变体或未修饰变体。

[0720] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_709 或其修饰变体或未修饰变体。

[0721] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_865 或其修饰变体或未修饰变体。

[0722] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_889 或其修饰变体或未修饰变体。

[0723] 包含第一链和第二链的 RNAi 剂，其中第一链包含与以下者的第一链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸 :Set1_895 或其修饰变体或未修饰变体。

[0724] 在多种实施方案中，第一链和第二链可以是有义链和反义链，或反义链和有义链。

[0725] 针对 β - 联蛋白的特异性 RNAi 剂的额外实施方案

[0726] 在一个实施方案中，本公开包含一种 RNAi 剂，所述 RNAi 剂包含反义链和 / 或有义链，所述反义链包含与表 1、2、3、4、5、6、7、8 和 / 或 9 中的任一种 RNAi 及其修饰变体和未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与表 1、2、3、4、5、6、7、8 和 / 或 9 中的任一种 RNAi 及其修饰变体和未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0727] 因而，在多种实施方案中，本公开涉及一种包含以下任一者或多者的组合物 :

[0728] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26104 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26104 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0729] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26063 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26063 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0730] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26082 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26082 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0731] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26034 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26034 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0732] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26091 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26091 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0733] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26047 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26047 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0734] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26651 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26651 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0735] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26696 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26696 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0736] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26109 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26109 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0737] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25941 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25941 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0738] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26028 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26028 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0739] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26652 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26652 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0740] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26742 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26742 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0741] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26921 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26921 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0742] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18893 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18893 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0743] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18983 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18983 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0744] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25950 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25950 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0745] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25951 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25951 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0746] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26042 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26042 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0747] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26043 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26043 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0748] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26673 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26673 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0749] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26704 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26704 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0750] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26068 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26068 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0751] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26183 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26183 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0752] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26700 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26700 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0753] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26701 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26701 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0754] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25942 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25942 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0755] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26076 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26076 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0756] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26031 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26031 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0757] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26210 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26210 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0758] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26664 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-26664 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0759] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26691 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26691 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0760] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26740 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26740 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0761] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19765 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19765 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0762] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26158 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26158 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0763] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26180 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26180 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0764] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26078 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26078 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0765] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25894 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25894 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0766] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25964 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25964 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0767] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26156 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26156 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0768] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26670 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26670 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0769] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26743 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26743 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0770] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25890 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25890 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0771] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26044 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26044 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0772] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26685 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26685 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0773] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26731 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26731 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0774] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26800 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26800 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0775] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26066 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26066 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0776] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26682 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26682 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0777] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26684 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26684 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0778] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26757 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26757 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0779] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26788 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26788 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0780] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18963 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18963 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0781] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19076 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19076 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0782] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25943 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25943 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0783] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26052 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26052 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0784] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26665 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26665 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0785] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26746 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26746 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0786] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18974 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18974 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0787] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25938 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25938 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0788] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25944 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25944 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0789] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26178 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26178 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0790] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26669 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26669 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0791] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26730 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26730 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0792] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26825 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26825 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0793] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25956 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25956 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0794] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26822 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26822 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0795] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26108 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26108 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0796] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26752 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26752 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0797] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26779 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-26779 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0798] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25891 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25891 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0799] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26101 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26101 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0800] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26181 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26181 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0801] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26218 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26218 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0802] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26660 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26660 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0803] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18966 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18966 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0804] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19074 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19074 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0805] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26179 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26179 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0806] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26722 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26722 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0807] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26768 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26768 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0808] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26920 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26920 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0809] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26020 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26020 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0810] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26713 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26713 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0811] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26727 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26727 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0812] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26808 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26808 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0813] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25958 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25958 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0814] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26105 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26105 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0815] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26674 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26674 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0816] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26781 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26781 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0817] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26801 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26801 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0818] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26813 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26813 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0819] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26816 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26816 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0820] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25945 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25945 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0821] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26203 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26203 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0822] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26021 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26021 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0823] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26040 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26040 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0824] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26069 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26069 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0825] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26134 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26134 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0826] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26702 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26702 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0827] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18933 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18933 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0828] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26690 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26690 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0829] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26698 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26698 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0830] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25910 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25910 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0831] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26747 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26747 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0832] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26810 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26810 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0833] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26083 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26083 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0834] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26061 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26061 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0835] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26904 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26904 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0836] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18903 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-18903 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0837] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18980 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18980 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0838] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26202 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26202 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0839] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26679 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26679 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0840] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26719 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26719 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0841] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26758 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26758 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0842] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26783 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26783 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0843] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26902 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26902 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0844] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18892 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18892 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0845] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18897 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18897 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0846] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25902 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25902 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0847] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26705 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26705 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0848] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26782 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26782 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0849] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19082 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19082 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0850] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26176 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26176 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0851] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26196 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26196 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0852] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26199 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26199 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0853] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26678 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26678 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0854] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26683 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26683 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0855] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26729 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26729 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0856] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26804 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26804 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0857] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26900 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26900 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0858] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25914 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25914 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0859] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26060 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26060 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0860] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26763 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26763 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0861] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18902 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18902 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0862] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18914 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18914 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0863] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26100 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26100 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0864] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26128 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26128 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0865] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26193 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26193 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0866] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26765 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26765 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0867] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25960 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25960 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0868] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26018 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26018 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0869] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25893 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25893 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0870] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26823 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26823 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0871] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25940 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25940 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0872] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26190 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26190 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0873] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26675 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26675 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0874] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26797 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26797 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0875] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26916 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-26916 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0876] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26755 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26755 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0877] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26901 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26901 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0878] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19004 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19004 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0879] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19009 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19009 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0880] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26148 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26148 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0881] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26186 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26186 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0882] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26737 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26737 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0883] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25955 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25955 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0884] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26029 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26029 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0885] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26131 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26131 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0886] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18894 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18894 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0887] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18939 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18939 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0888] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26654 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26654 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0889] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18929 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18929 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0890] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26135 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26135 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0891] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26774 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26774 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0892] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26780 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26780 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0893] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26819 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26819 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0894] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26918 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26918 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0895] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19050 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19050 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0896] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18994 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18994 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0897] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26769 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26769 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0898] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26666 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26666 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0899] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26784 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26784 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0900] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18969 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18969 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0901] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18986 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18986 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0902] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25929 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25929 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0903] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25932 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25932 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0904] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26095 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26095 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0905] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26908 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26908 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0906] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26071 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26071 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0907] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26912 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26912 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0908] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19054 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19054 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0909] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25918 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25918 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0910] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26903 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26903 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0911] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25931 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25931 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0912] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26146 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26146 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0913] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26200 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26200 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0914] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26917 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-26917 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0915] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26794 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26794 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0916] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26910 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26910 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0917] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25939 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25939 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0918] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26032 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26032 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0919] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26776 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26776 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0920] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26806 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26806 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0921] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26748 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26748 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0922] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26725 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26725 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0923] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18958 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18958 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0924] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26672 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26672 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0925] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26905 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26905 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0926] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19056 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19056 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0927] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19762 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19762 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0928] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26919 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26919 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0929] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18946 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18946 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0930] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19066 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19066 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0931] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19746 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19746 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0932] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26057 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26057 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0933] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26073 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26073 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0934] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26689 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26689 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0935] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19008 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19008 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0936] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26026 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26026 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0937] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26761 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26761 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0938] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19752 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19752 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0939] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18981 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18981 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0940] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18927 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18927 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0941] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19753 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19753 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0942] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25907 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25907 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0943] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26671 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26671 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0944] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19080 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19080 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0945] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26075 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26075 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0946] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26681 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26681 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0947] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18976 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18976 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0948] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25900 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25900 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0949] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26126 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26126 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0950] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26688 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26688 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0951] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25912 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25912 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0952] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25930 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25930 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0953] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18995 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-18995 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0954] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26802 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26802 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0955] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25892 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25892 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0956] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25947 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25947 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0957] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26088 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26088 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0958] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26098 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26098 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0959] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26778 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26778 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0960] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26215 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26215 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0961] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26739 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 26739 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0962] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18950 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18950 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0963] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25949 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25949 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0964] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26141 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26141 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0965] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18961 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18961 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0966] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25957 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25957 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0967] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26826 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26826 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0968] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25963 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25963 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0969] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26019 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26019 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0970] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26035 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26035 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0971] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25946 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25946 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0972] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26714 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26714 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0973] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26022 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26022 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0974] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26096 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26096 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0975] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26132 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26132 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0976] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26062 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26062 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0977] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18991 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18991 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0978] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26164 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26164 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0979] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26209 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26209 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0980] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25895 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25895 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0981] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25933 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25933 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0982] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26017 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26017 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[0983] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19749 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19749 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0984] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26653 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26653 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0985] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26759 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26759 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0986] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25924 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25924 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0987] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26153 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26153 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0988] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25953 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25953 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0989] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26764 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26764 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0990] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26790 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26790 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0991] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-20124 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-20124 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0992] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25919 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-25919 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0993] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18913 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18913 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0994] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26211 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26211 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0995] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18936 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18936 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0996] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25898 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25898 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0997] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26741 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26741 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0998] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19043 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19043 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[0999] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26079 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26079 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1000] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19000 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19000 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1001] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25911 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25911 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1002] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26786 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26786 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1003] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19069 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19069 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1004] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26037 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26037 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1005] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26723 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26723 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1006] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19067 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19067 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1007] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25928 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25928 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1008] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26677 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26677 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1009] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19006 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19006 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1010] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19758 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19758 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1011] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26913 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26913 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1012] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25917 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25917 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1013] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26189 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26189 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1014] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26787 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26787 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1015] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26707 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26707 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1016] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26094 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26094 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1017] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26097 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26097 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1018] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26699 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26699 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1019] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26756 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26756 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1020] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26720 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26720 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1021] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25926 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25926 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[1022] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26212 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26212 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1023] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26687 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26687 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1024] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26753 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26753 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1025] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18982 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18982 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1026] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18908 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18908 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1027] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18968 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18968 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1028] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25948 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25948 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1029] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26188 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26188 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1030] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26708 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26708 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1031] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25961 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 AD-25961 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1032] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26803 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26803 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1033] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19741 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19741 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1034] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26056 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26056 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1035] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25959 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25959 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1036] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26059 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26059 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1037] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26102 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26102 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1038] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26106 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26106 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1039] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26744 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26744 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1040] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26099 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26099 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1041] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26170 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26170 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1042] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19012 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19012 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1043] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26198 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26198 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1044] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26766 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26766 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1045] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18951 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18951 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1046] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18975 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18975 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1047] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26749 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26749 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1048] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18911 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18911 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1049] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26906 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26906 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1050] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-19747 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-19747 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1051] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18960 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18960 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1052] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-25909 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-25909 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1053] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26184 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26184 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1054] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26077 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26077 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1055] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26680 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26680 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1056] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26085 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26085 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1057] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18926 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18926 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1058] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18945 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18945 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1059] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26703 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26703 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1060] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26911 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26911 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸

的至少 15 个连续核苷酸。

[1061] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26661 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26661 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1062] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-18905 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-18905 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1063] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 AD-26142 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 AD-26142 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1064] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1245 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1245 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1065] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1249 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1249 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1066] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1250 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1250 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1067] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1450 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1450 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1068] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1545 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1545 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1069] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1755 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1755 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1070] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1814 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义

链包含与 Set1_1814 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1071] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1816 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1816 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1072] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_1974 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_1974 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1073] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_2202 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_2202 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1074] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_2425 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_2425 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1075] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_254 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_254 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1076] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_3146 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_3146 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1077] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_3169 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_3169 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1078] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_3196 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_3196 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1079] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_3477 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_3477 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1080] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_703 或其修饰变体

或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_703 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1081] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_709 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_709 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1082] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_865 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_865 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1083] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_889 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_889 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[1084] 包含反义链和 / 或有义链的 RNAi 剂，所述反义链包含与 Set1_895 或其修饰变体或未修饰变体的反义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，所述有义链包含与 Set1_895 或其修饰变体或未修饰变体的有义链的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

涵盖针对 β - 联蛋白的特异性 RNAi 剂的额外的实施方案

[1085] 在多种实施方案中，本公开涉及一种包含以下任一者或多者的组合物：

[001] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26104 的反义链的序列。

[002] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26063 的反义链的序列。

[003] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26082 的反义链的序列。

[004] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26034 的反义链的序列。

[005] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26091 的反义链的序列。

[006] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26047 的反义链的序列。

[007] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26651 的反义链的序列。

[008] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26696 的反义链的序列。

[009] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26109 的反义链的序列。

[0010] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25941 的反义链的序列。

[0011] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26028 的反义链的序列。

[0012] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26652 的反义链的序列。

[0013] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26742 的反义链的序列。

[0014] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26921 的反义链的序列。

[0015] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18893 的反义链的序列。

[0016] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18983 的反义链的序列。

[0017] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25950 的反义链的序列。

[0018] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25951 的反义链的序列。

[0019] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26042 的反义链的序列。

[0020] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26043 的反义链的序列。

[0021] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26673 的反义链的序列。

[0022] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26704 的反义链的序列。

[0023] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26068 的反义链的序列。

[0024] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26183 的反义链的序列。

[0025] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26700 的反义链的序列。

[0026] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26701 的反义链的序列。

[0027] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25942 的反义链的序列。

[0028] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26076 的反义链的序列。

[0029] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26031 的反义链的序

列。

[0030] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26210 的反义链的序列。

[0031] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26664 的反义链的序列。

[0032] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26691 的反义链的序列。

[0033] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26740 的反义链的序列。

[0034] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-19765 的反义链的序列。

[0035] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26158 的反义链的序列。

[0036] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26180 的反义链的序列。

[0037] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26078 的反义链的序列。

[0038] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25894 的反义链的序列。

[0039] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25964 的反义链的序列。

[0040] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26156 的反义链的序列。

[0041] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26670 的反义链的序列。

[0042] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26743 的反义链的序列。

[0043] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25890 的反义链的序列。

[0044] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26044 的反义链的序列。

[0045] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26685 的反义链的序列。

[0046] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26731 的反义链的序列。

[0047] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26800 的反义链的序列。

[0048] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26066 的反义链的序列。

[0049] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26682 的反义链的序列。

[0050] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26684 的反义链的序列。

[0051] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26757 的反义链的序列。

[0052] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26788 的反义链的序列。

[0053] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18963 的反义链的序列。

[0054] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-19076 的反义链的序列。

[0055] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25943 的反义链的序列。

[0056] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26052 的反义链的序列。

[0057] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26665 的反义链的序列。

[0058] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26746 的反义链的序列。

[0059] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18974 的反义链的序列。

[0060] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25938 的反义链的序列。

[0061] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25944 的反义链的序列。

[0062] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26178 的反义链的序列。

[0063] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26669 的反义链的序列。

[0064] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26730 的反义链的序列。

[0065] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26825 的反义链的序列。

[0066] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25956 的反义链的序列。

[0067] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26822 的反义链的序列。

[0068] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26108 的反义链的序

列。

[0069] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26752 的反义链的序列。

[0070] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26779 的反义链的序列。

[0071] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25891 的反义链的序列。

[0072] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26101 的反义链的序列。

[0073] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26181 的反义链的序列。

[0074] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26218 的反义链的序列。

[0075] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26660 的反义链的序列。

[0076] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18966 的反义链的序列。

[0077] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-19074 的反义链的序列。

[0078] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26179 的反义链的序列。

[0079] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26722 的反义链的序列。

[0080] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26768 的反义链的序列。

[0081] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26920 的反义链的序列。

[0082] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26020 的反义链的序列。

[0083] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26713 的反义链的序列。

[0084] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26727 的反义链的序列。

[0085] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26808 的反义链的序列。

[0086] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25958 的反义链的序列。

[0087] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26105 的反义链的序列。

[0088] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26674 的反义链的序列。

[0089] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26781 的反义链的序列。

[0090] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26801 的反义链的序列。

[0091] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26813 的反义链的序列。

[0092] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26816 的反义链的序列。

[0093] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25945 的反义链的序列。

[0094] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26203 的反义链的序列。

[0095] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26021 的反义链的序列。

[0096] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26040 的反义链的序列。

[0097] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26069 的反义链的序列。

[0098] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26134 的反义链的序列。

[0099] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26702 的反义链的序列。

[00100] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18933 的反义链的序列。

[00101] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26690 的反义链的序列。

[00102] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26698 的反义链的序列。

[00103] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25910 的反义链的序列。

[00104] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26747 的反义链的序列。

[00105] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26810 的反义链的序列。

[00106] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26083 的反义链的序列。

[00107] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26061 的反义链的序

列。

[00108] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26904的反义链的序列。

[00109] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18903的反义链的序列。

[00110] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18980的反义链的序列。

[00111] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26202的反义链的序列。

[00112] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26679的反义链的序列。

[00113] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26719的反义链的序列。

[00114] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26758的反义链的序列。

[00115] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26783的反义链的序列。

[00116] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26902的反义链的序列。

[00117] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18892的反义链的序列。

[00118] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18897的反义链的序列。

[00119] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25902的反义链的序列。

[00120] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26705的反义链的序列。

[00121] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26782的反义链的序列。

[00122] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19082的反义链的序列。

[00123] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26176的反义链的序列。

[00124] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26196的反义链的序列。

[00125] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26199的反义链的序列。

[00126] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26678的反义链的序列。

[00127] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26683的反义链的序列。

[00128] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26729的反义链的序列。

[00129] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26804的反义链的序列。

[00130] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26900的反义链的序列。

[00131] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25914的反义链的序列。

[00132] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26060的反义链的序列。

[00133] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26763的反义链的序列。

[00134] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18902的反义链的序列。

[00135] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18914的反义链的序列。

[00136] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26100的反义链的序列。

[00137] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26128的反义链的序列。

[00138] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26193的反义链的序列。

[00139] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26765的反义链的序列。

[00140] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25960的反义链的序列。

[00141] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26018的反义链的序列。

[00142] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25893的反义链的序列。

[00143] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26823的反义链的序列。

[00144] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25940的反义链的序列。

[00145] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26190的反义链的序列。

[00146] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26675的反义链的序

列。

[00147] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26797的反义链的序列。

[00148] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26916的反义链的序列。

[00149] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26755的反义链的序列。

[00150] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26901的反义链的序列。

[00151] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19004的反义链的序列。

[00152] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19009的反义链的序列。

[00153] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26148的反义链的序列。

[00154] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26186的反义链的序列。

[00155] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26737的反义链的序列。

[00156] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25955的反义链的序列。

[00157] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26029的反义链的序列。

[00158] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26131的反义链的序列。

[00159] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18894的反义链的序列。

[00160] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18939的反义链的序列。

[00161] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26654的反义链的序列。

[00162] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18929的反义链的序列。

[00163] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26135的反义链的序列。

[00164] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26774的反义链的序列。

[00165] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26780的反义链的序列。

[00166] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26819的反义链的序列。

[00167] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26918的反义链的序列。

[00168] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19050的反义链的序列。

[00169] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18994的反义链的序列。

[00170] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26769的反义链的序列。

[00171] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26666的反义链的序列。

[00172] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26784的反义链的序列。

[00173] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18969的反义链的序列。

[00174] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18986的反义链的序列。

[00175] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25929的反义链的序列。

[00176] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25932的反义链的序列。

[00177] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26095的反义链的序列。

[00178] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26908的反义链的序列。

[00179] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26071的反义链的序列。

[00180] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26912的反义链的序列。

[00181] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19054的反义链的序列。

[00182] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25918的反义链的序列。

[00183] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26903的反义链的序列。

[00184] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25931的反义链的序列。

[00185] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26146的反义链的序

列。

[00186] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26200的反义链的序列。

[00187] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26917的反义链的序列。

[00188] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26794的反义链的序列。

[00189] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26910的反义链的序列。

[00190] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25939的反义链的序列。

[00191] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26032的反义链的序列。

[00192] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26776的反义链的序列。

[00193] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26806的反义链的序列。

[00194] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26748的反义链的序列。

[00195] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26725的反义链的序列。

[00196] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18958的反义链的序列。

[00197] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26672的反义链的序列。

[00198] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26905的反义链的序列。

[00199] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19056的反义链的序列。

[00200] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19762的反义链的序列。

[00201] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26919的反义链的序列。

[00202] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18946的反义链的序列。

[00203] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19066的反义链的序列。

[00204] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19746的反义链的序列。

[00205] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26057的反义链的序列。

[00206] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26073的反义链的序列。

[00207] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26689的反义链的序列。

[00208] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19008的反义链的序列。

[00209] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26026的反义链的序列。

[00210] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26761的反义链的序列。

[00211] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19752的反义链的序列。

[00212] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18981的反义链的序列。

[00213] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18927的反义链的序列。

[00214] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19753的反义链的序列。

[00215] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25907的反义链的序列。

[00216] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26671的反义链的序列。

[00217] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19080的反义链的序列。

[00218] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26075的反义链的序列。

[00219] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26681的反义链的序列。

[00220] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18976的反义链的序列。

[00221] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25900的反义链的序列。

[00222] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26126的反义链的序列。

[00223] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26688的反义链的序列。

[00224] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25912的反义链的序

列。

[00225] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25930的反义链的序列。

[00226] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18995的反义链的序列。

[00227] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26802的反义链的序列。

[00228] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25892的反义链的序列。

[00229] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25947的反义链的序列。

[00230] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26088的反义链的序列。

[00231] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26098的反义链的序列。

[00232] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26778的反义链的序列。

[00233] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26215的反义链的序列。

[00234] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26739的反义链的序列。

[00235] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18950的反义链的序列。

[00236] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25949的反义链的序列。

[00237] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26141的反义链的序列。

[00238] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18961的反义链的序列。

[00239] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25957的反义链的序列。

[00240] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26826的反义链的序列。

[00241] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25963的反义链的序列。

[00242] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26019的反义链的序列。

[00243] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26035的反义链的序列。

[00244] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25946的反义链的序列。

[00245] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26714的反义链的序列。

[00246] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26022的反义链的序列。

[00247] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26096的反义链的序列。

[00248] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26132的反义链的序列。

[00249] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26062的反义链的序列。

[00250] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18991的反义链的序列。

[00251] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26164的反义链的序列。

[00252] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26209的反义链的序列。

[00253] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25895的反义链的序列。

[00254] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25933的反义链的序列。

[00255] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26017的反义链的序列。

[00256] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19749的反义链的序列。

[00257] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26653的反义链的序列。

[00258] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26759的反义链的序列。

[00259] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25924的反义链的序列。

[00260] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26153的反义链的序列。

[00261] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25953的反义链的序列。

[00262] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26764的反义链的序列。

[00263] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26790的反义链的序

列。

[00264] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-20124的反义链的序列。

[00265] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25919的反义链的序列。

[00266] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18913的反义链的序列。

[00267] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26211的反义链的序列。

[00268] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18936的反义链的序列。

[00269] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25898的反义链的序列。

[00270] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26741的反义链的序列。

[00271] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19043的反义链的序列。

[00272] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26079的反义链的序列。

[00273] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19000的反义链的序列。

[00274] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25911的反义链的序列。

[00275] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26786的反义链的序列。

[00276] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19069的反义链的序列。

[00277] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26037的反义链的序列。

[00278] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26723的反义链的序列。

[00279] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19067的反义链的序列。

[00280] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25928的反义链的序列。

[00281] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26677的反义链的序列。

[00282] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19006的反义链的序列。

[00283] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19758的反义链的序列。

[00284] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26913的反义链的序列。

[00285] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25917的反义链的序列。

[00286] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26189的反义链的序列。

[00287] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26787的反义链的序列。

[00288] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26707的反义链的序列。

[00289] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26094的反义链的序列。

[00290] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26097的反义链的序列。

[00291] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26699的反义链的序列。

[00292] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26756的反义链的序列。

[00293] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26720的反义链的序列。

[00294] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25926的反义链的序列。

[00295] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26212的反义链的序列。

[00296] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26687的反义链的序列。

[00297] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26753的反义链的序列。

[00298] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18982的反义链的序列。

[00299] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18908的反义链的序列。

[00300] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18968的反义链的序列。

[00301] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25948的反义链的序列。

[00302] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26188的反义链的序

列。

[00303] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26708的反义链的序列。

[00304] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25961的反义链的序列。

[00305] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26803的反义链的序列。

[00306] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19741的反义链的序列。

[00307] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26056的反义链的序列。

[00308] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-25959的反义链的序列。

[00309] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26059的反义链的序列。

[00310] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26102的反义链的序列。

[00311] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26106的反义链的序列。

[00312] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26744的反义链的序列。

[00313] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26099的反义链的序列。

[00314] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26170的反义链的序列。

[00315] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-19012的反义链的序列。

[00316] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26198的反义链的序列。

[00317] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26766的反义链的序列。

[00318] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18951的反义链的序列。

[00319] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18975的反义链的序列。

[00320] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-26749的反义链的序列。

[00321] 包含有义链和反义链的RNAi剂，其中反义链的序列是AD-18911的反义链的序列。

[00322] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26906 的反义链的序列。

[00323] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-19747 的反义链的序列。

[00324] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18960 的反义链的序列。

[00325] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-25909 的反义链的序列。

[00326] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26184 的反义链的序列。

[00327] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26077 的反义链的序列。

[00328] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26680 的反义链的序列。

[00329] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26085 的反义链的序列。

[00330] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18926 的反义链的序列。

[00331] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18945 的反义链的序列。

[00332] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26703 的反义链的序列。

[00333] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26911 的反义链的序列。

[00334] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26661 的反义链的序列。

[00335] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-18905 的反义链的序列。

[00336] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 AD-26142 的反义链的序列。

[00337] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1245 的反义链的序列。

[00338] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1249 的反义链的序列。

[00339] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1250 的反义链的序列。

[00340] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1450 的反义链的序列。

[00341] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1545 的反义链的

序列。

[00342] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1755 的反义链的序列。

[00343] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1814 的反义链的序列。

[00344] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1816 的反义链的序列。

[00345] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_1974 的反义链的序列。

[00346] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_2202 的反义链的序列。

[00347] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_2425 的反义链的序列。

[00348] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_254 的反义链的序列。

[00349] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_3146 的反义链的序列。

[00350] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_3169 的反义链的序列。

[00351] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_3196 的反义链的序列。

[00352] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_3477 的反义链的序列。

[00353] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_703 的反义链的序列。

[00354] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_709 的反义链的序列。

[00355] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_865 的反义链的序列。

[00356] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_889 的反义链的序列。

[00357] 包含有义链和反义链的 RNAi 剂，其中反义链的序列是 Set1_895 的反义链的序列。

涵盖针对 β-联蛋白的特异性 RNAi 剂的额外的实施方案

[001086] 在多种实施方案中，本公开涉及一种包含以下任一者或多者的组合物：

[00358] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26104 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00359] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26063 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00360] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26082 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00361] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26034 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00362] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26091 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00363] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26047 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00364] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26651 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00365] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26696 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00366] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26109 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00367] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25941 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00368] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26028 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00369] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26652 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00370] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26742 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00371] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26921 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00372] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18893 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00373] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18983 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00374] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25950 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00375] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25951 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00376] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26042 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00377] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26043 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00378] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26673 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00379] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26704 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00380] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26068 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00381] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26183 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00382] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26700 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00383] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26701 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00384] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25942 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00385] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26076 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00386] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26031 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00387] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26210 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00388] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26664 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00389] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26691 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00390] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26740 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00391] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19765 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00392] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26158 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00393] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26180 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00394] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26078 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00395] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25894 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00396] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25964 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00397] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26156 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00398] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26670 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00399] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26743 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00400] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25890 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00401] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26044 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00402] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26685 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00403] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26731 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00404] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26800 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00405] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26066 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00406] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26682 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00407] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26684 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00408] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26757 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00409] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26788 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00410] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18963 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00411] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19076 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00412] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25943 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00413] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26052 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00414] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26665 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00415] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26746 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00416] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18974 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00417] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25938 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00418] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25944 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00419] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26178 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00420] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26669 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00421] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26730 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00422] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26825 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00423] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25956 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00424] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26822 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00425] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26108 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00426] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26752 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00427] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26779 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00428] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25891 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00429] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26101 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00430] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26181 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00431] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26218 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00432] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26660 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00433] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18966 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00434] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19074 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00435] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26179 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00436] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26722 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00437] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26768 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00438] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26920 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00439] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26020 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00440] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26713 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00441] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26727 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00442] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26808 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00443] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25958 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00444] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26105 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00445] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26674 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00446] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26781 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00447] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26801 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00448] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26813 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00449] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26816 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00450] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25945 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00451] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26203 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00452] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26021 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00453] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26040 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00454] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26069 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00455] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26134 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00456] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26702 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00457] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18933 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00458] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26690 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00459] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26698 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00460] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25910 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00461] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26747 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00462] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26810 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00463] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26083 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00464] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26061 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00465] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26904 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00466] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18903 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00467] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18980 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00468] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26202 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00469] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26679 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00470] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26719 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00471] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26758 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00472] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26783 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00473] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26902 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00474] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18892 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00475] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18897 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00476] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25902 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00477] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26705 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00478] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26782 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00479] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19082 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00480] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26176 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00481] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26196 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00482] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26199 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00483] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26678 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00484] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26683 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00485] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26729 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00486] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26804 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00487] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26900 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00488] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25914 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00489] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26060 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00490] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26763 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00491] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18902 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00492] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18914 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00493] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26100 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00494] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26128 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00495] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26193 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00496] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26765 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00497] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25960 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00498] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26018 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00499] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25893 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00500] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26823 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00501] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25940 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00502] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26190 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00503] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26675 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00504] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26797 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00505] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26916 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00506] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26755 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00507] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26901 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00508] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19004 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00509] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19009 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00510] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26148 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00511] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26186 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00512] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26737 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00513] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25955 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00514] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26029 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00515] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26131 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00516] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18894 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00517] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18939 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00518] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26654 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00519] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18929 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00520] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26135 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00521] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26774 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00522] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26780 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00523] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26819 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00524] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26918 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00525] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19050 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00526] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18994 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00527] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26769 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00528] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26666 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00529] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26784 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00530] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18969 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00531] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18986 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00532] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25929 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00533] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25932 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00534] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26095 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00535] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26908 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00536] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26071 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00537] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26912 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00538] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19054 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00539] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25918 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00540] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26903 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00541] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25931 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00542] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26146 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00543] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26200 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00544] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26917 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00545] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26794 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00546] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26910 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00547] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25939 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00548] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26032 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00549] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26776 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00550] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26806 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00551] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26748 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00552] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26725 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00553] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18958 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00554] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26672 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00555] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26905 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00556] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19056 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00557] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19762 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00558] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26919 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00559] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18946 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00560] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19066 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00561] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19746 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00562] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26057 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00563] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26073 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00564] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26689 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00565] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19008 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00566] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26026 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00567] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26761 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00568] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19752 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00569] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18981 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00570] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18927 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00571] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19753 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00572] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25907 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00573] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26671 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00574] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19080 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00575] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26075 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00576] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26681 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00577] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18976 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00578] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25900 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00579] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26126 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00580] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26688 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00581] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25912 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00582] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25930 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00583] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18995 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00584] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26802 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00585] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25892 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00586] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25947 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00587] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26088 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00588] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26098 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00589] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26778 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00590] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26215 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00591] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26739 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00592] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18950 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00593] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25949 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00594] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26141的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00595] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-18961的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00596] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-25957的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00597] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26826的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00598] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-25963的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00599] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26019的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00600] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26035的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00601] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-25946的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00602] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26714的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00603] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26022的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00604] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26096的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00605] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26132的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00606] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26062的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00607] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-18991的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00608] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26164的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00609] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26209的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00610] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-25895的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00611] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-25933的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00612] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-26017的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00613] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是AD-19749的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00614] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26653 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00615] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26759 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00616] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25924 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00617] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26153 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00618] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25953 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00619] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26764 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00620] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26790 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00621] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-20124 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00622] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25919 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00623] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18913 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00624] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26211 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00625] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18936 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00626] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25898 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00627] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26741 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00628] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19043 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00629] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26079 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00630] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19000 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00631] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25911 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00632] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26786 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00633] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19069 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00634] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26037 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00635] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26723 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00636] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19067 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00637] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25928 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00638] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26677 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00639] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19006 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00640] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19758 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00641] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26913 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00642] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25917 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00643] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26189 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00644] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26787 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00645] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26707 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00646] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26094 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00647] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26097 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00648] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26699 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00649] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26756 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00650] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26720 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00651] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25926 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00652] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26212 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00653] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26687 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00654] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26753 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00655] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18982 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00656] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18908 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00657] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18968 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00658] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25948 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00659] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26188 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00660] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26708 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00661] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25961 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00662] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26803 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00663] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19741 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00664] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26056 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00665] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25959 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00666] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26059 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00667] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26102 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00668] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26106 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00669] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26744 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00670] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26099 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00671] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26170 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00672] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19012 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00673] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26198 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00674] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26766 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00675] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18951 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00676] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18975 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00677] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26749 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00678] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18911 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00679] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26906 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00680] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-19747 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00681] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18960 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00682] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-25909 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00683] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26184 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00684] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26077 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00685] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26680 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00686] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26085 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00687] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18926 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00688] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18945 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00689] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26703 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00690] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26911 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00691] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26661 的第

一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00692] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-18905 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00693] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 AD-26142 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00694] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1245 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00695] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1249 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00696] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1250 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00697] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1450 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00698] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1545 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00699] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1755 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00700] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1814 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00701] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1816 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00702] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_1974 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00703] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_2202 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00704] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_2425 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00705] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_254 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00706] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_3146 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00707] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_3169 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00708] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_3196 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00709] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_3477 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00710] 包含第一链和第二链的 RNAi 剂，其中第一链或第二链的序列是 Set1_703 的第一链或第二链的序列，并且其中第一链和 / 或第二链还包含至多约 20 个额外的核苷酸。

[00711] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是Set1_709的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00712] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是Set1_865的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00713] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是Set1_889的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00714] 包含第一链和第二链的RNAi剂，其中第一链或第二链的序列是Set1_895的第一链或第二链的序列，并且其中第一链和/或第二链还包含至多约20个额外的核苷酸。

[00715] 针对β-联蛋白的特异性RNAi剂的额外实施方案。

[00716] 在多种实施方案中，本公开涉及：

[00717] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6096和/或6117或其修饰变体或未修饰变体或由其组成。

[00718] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6097和/或6118或其修饰变体或未修饰变体或由其组成。

[00719] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6098和/或6119或其修饰变体或未修饰变体或由其组成。

[00720] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6100和/或6121或其修饰变体或未修饰变体或由其组成。

[00721] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6101和/或6122或其修饰变体或未修饰变体或由其组成。

[00722] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6103和/或6124或其修饰变体或未修饰变体或由其组成。

[00723] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6105和/或6126或其修饰变体或未修饰变体或由其组成。

[00724] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6106和/或6127或其修饰变体或未修饰变体或由其组成。

[00725] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别是SEQ ID NOs:6107和/或6128或其修饰变体或未修饰变体或由其组成。

[00726] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别包含SEQ ID NOs:6096和/或6117的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约30个核苷酸长度。

[00727] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别包含SEQ ID NOs:6097和/或6118的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约30个核苷酸长度。

[00728] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别包含SEQ ID NOs:6098和/或6119的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约30个核苷酸长度。

[00729] 包含第一链和第二链的RNAi剂，其中第一链和/或第二链的序列分别包含SEQ ID NOs:6100和/或6121的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于

约 30 个核苷酸长度。

[00730] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6101 和 / 或 6122 的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00731] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6103 和 / 或 6124 的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00732] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6105 和 / 或 6126 的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00733] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6106 和 / 或 6127 的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00734] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6107 和 / 或 6128 的序列，或其未修饰的变体，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00735] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6096 和 / 或 6117 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00736] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6097 和 / 或 6118 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00737] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6098 和 / 或 6119 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00738] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6100 和 / 或 6121 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00739] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6101 和 / 或 6122 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00740] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6103 和 / 或 6124 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00741] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6105 和 / 或 6126 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00742] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6106 和 / 或 6127 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和

第二链各自具有不多于约 30 个核苷酸长度。

[00743] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含 SEQ ID NOs:6107 和 / 或 6128 或其未修饰的变体的序列的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00744] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6096 和 / 或 6117 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00745] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6097 和 / 或 6118 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00746] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6098 和 / 或 6119 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00747] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6100 和 / 或 6121 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00748] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6101 和 / 或 6122 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00749] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6103 和 / 或 6124 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00750] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6105 和 / 或 6126 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00751] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6106 和 / 或 6127 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00752] 包含第一链和第二链的 RNAi 剂，其中第一链和 / 或第二链的序列分别包含与 SEQ ID NOs:6107 和 / 或 6128 或其未修饰的变体的序列差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸，其中第一链和第二链各自具有不多于约 30 个核苷酸长度。

[00753] 在多种实施方案中，第一链和第二链可以是有义链和反义链，或反义链和有义链。

[00754] 还包含额外核苷酸的针对 β - 联蛋白的特异性 RNAi 剂的额外实施方案。

[00755] 在本公开的多种实施方案中，RNAi 剂包含由至少 15 个连续核苷酸的下述序列组成的反义链，所述序列与来自表 1、2、3、4、5、6、7、8 和 / 或 9 的任一种 RNAi 剂或其修饰变体或未修饰变体的反义链的序列具有 0、1、2 或 3 个错配，其中反义链任选地还包含 0、1、2、3、4、5、6、7、8、9 或 10 个或更多个核苷酸（或其任何范围，例如，0-1、1-2、1-3、1-4、1-5、1-6、1-7、1-8、1-9、1-10、2-3、2-4 或 2-5 个核苷酸等）。[00756] 包含针对 β - 联蛋白的 RNAi 剂

的重叠群组的额外实施方案

[00757] 在本公开的多种实施方案中，本公开涉及具有重叠序列的 RNAi 剂群组。因而，本公开涵盖 RNAi 剂群组，其中该群组中的每种 RNAi 剂与相同群组中的每种其他 RNAi 重叠至少 5、6、7、8、9、10、11、12、13、14、15、16、17、18、19 或更多个核苷酸。在一个实施方案中，该重叠是至少 12 个核苷酸。表 4 中显示重叠的序列群组。

[00758] 表 4 显示，例如，AD-26022 和 AD-26204 在有义链中共有 CCUGUUCCCCUG(SEQ ID NO:1319) 的序列的共同技术特征并且在反义链中共有 CAGGGGAACAGG(SEQ ID NO:2714) 的序列的共同技术特征。当然应指出，仅显示重叠的 12 核苷酸部分；许多组的 RNAi 剂将重叠超过 12 个核苷酸。还显示在基因内部的位置。

[00759] 本公开因此涵盖多种实施方案，所述实施方案包含重叠性 RNAi 剂的群组，例如 (1) 包含 AD-26022 和 AD-26204 的序列的 RNAi 剂；(2) 由 AD-26022 和 AD-26204 的序列组成的 RNAi 剂；(3) 包含了含有 AD-26022 和 AD-26204 的序列的有义链和 / 或反义链的 RNAi 剂；(4) RNAi 剂，其包含了含有与 AD-26022 和 AD-26204 的序列具有 0 至 3 个错配的 15 个连续核苷酸的有义链和 / 或反义链；(5) RNAi 剂，其包含了含有与 AD-26022 和 AD-26204 的序列具有 0 至 3 个错配的 15 个连续核苷酸的有义链；(6) RNAi 剂，其包含了含有与 AD-26022 和 AD-26204 的序列具有 0 至 3 个错配的 15 个连续核苷酸的反义链等，以及反映 RNAi 剂的全部重叠群组的相似的实施方案。

[00760] 因而，在多种实施方案中，本公开的 RNAi 剂包含有义链和反义链（它们可以任选地共价连接、借助环或接头连接或是连续的），其中有义链和 / 或反义链由至少 15 个连续核苷酸的序列组成、基本上由所述序列组成或包含所述序列，所述序列与表 1、2、3、4、5、6、7、8 和 / 或 9 中公开的任一种或多种 RNAi 剂（或来自表 4 的重叠性 RNAi 剂群组的任何成员）的有义链和 / 或反义链分别具有 0、1、2 或 3 个核苷酸或 bp 错配，任选地还包含 0-10 个核苷酸或 bp。

[00761] 额外的定义

[00762] 如本文中和权利要求中所用的冠词“a”和“an”指该冠词的一个或多于一个（至少一个）语法对象。

[00763] 术语“RNAi 剂、”“RNAi 剂”、“RNAi 剂 (s)”等均指而不限于本公开的一种或多种 RNAi 剂。

[00764] 本文中公开的针对 β- 联蛋白的 RNAi 剂的具体例子双链体的名称偶尔具有跟随数字的后缀“b”。这个数字表示批次。因此，后缀“b1”指示“批次 1”。因而，命名为例如“AD-18892-b1”的 RNAi 双链体特别来自批次 1 并且具有与命名为“AD-18892”的任何 RNAi 剂相同的序列。

[00765] 除非另外定义，否则本文所用的技术术语和科学术语具有与熟悉本公开所属技术领域的专业人员通常所理解的相同意思。

[00766] 除非另外指明，否则如技术人员将显而易见，没有详细描述的全部方法、步骤、技术和操作可以按本身已知的方式进行并且已经按本身已知的方式进行。例如再次参考本文中提到的标准手册和一般背景技术并参考其中所引用的其他参考文献。

[00767] 对本公开的权利要求是非限制的并且在下文提供。

[00768] 虽然已经在本文中详细公开具体实施方案和权利要求，但是这仅出于说明目

的以举例方式进行，并且不意在限制所附权利要求书的范围或任何相应未来应用的权利要求的主题的范围。具体而言，发明人构思了可以对本公开作出各种替换、改变和修改而不脱离如权利要求书所定义的本公开的精神和范围。认为选择核酸起始材料、目的克隆或文库类型是知晓本文所述的实施方案的本领域技术人员的例行工作。其他方面、优点和修改视为处于以下权利要求的范围内。对稍后提交的相应申请中权利要求书范围的重新起草可以归因于各个国家的专利法的限制并且不应当解读为放弃权利要求的主题。

[00769] 所描述的针对 β-联蛋白的RNAi剂的各种额外制剂和明显变体可以由本领域普通技术人员构思。以下实施例中描述了针对 β-联蛋白的RNAi剂的非限制性例子，所述例子不限制如权利要求书中所述的本公开的范围。

[00770] 实施例 1

[00771] 生物信息学和 β-联蛋白 RNAi 剂 (siRNA) 序列

[00772] 生物信息学

[00773] 转录物

[00774] 实施RNAi剂设计以鉴定靶向人 β-联蛋白基因 (CTNNB1) 的RNAi剂。该设计使用来自NCBI（国家生物技术信息中心）参考序列集合的CTNNB1转录物NM_001098210.1。全部RNAi剂双链体均设计成与全部三种人CTNNB1转录物 (NM_001098210.1、NM_001098209.1 和 NM_001904.3) 具有 100%同一性。

[00775]siRNA 设计和特异性预测

[00776] 从每个序列预测了全部可能的 19 聚物的预测特异性。使用 FASTA 算法，将CTNNB1RNAi 剂用于针对人转录组（定义为人 NCBI 参考序列集合内部的 NM_ 记录和 XM_ 记录的集合）的综合检索中。perl 脚本' parseFasta.pl' 随后用来剖析比对结果并基于 siRNA 和任何潜在 ' 脱靶 ' 转录物之间错配的位置和数目产生评分。将脱靶评分加权以强调 siRNA 的“种子”区域内（距分子 5' 末端的位置 2-9 中）的差异。通过汇总独立错配评分，向来自 FASTA 检索的每个寡聚物 - 转录物对给予错配评分；将位置 2-9 中的错配计为 2.8，将切割位点位置 10-11 中的错配计为 1.2，并且将区域 12-19 中的错配计为 1.0。通过比较从每种寡聚物的种子衍生的 3 种不同六聚物所衍生的七聚物和八聚物的频率实施额外的脱靶预测。相对于 5' 起点距离位置 2-7 的六聚物用来产生 2 种七聚物和 1 种八聚物。通过添加一个 3' A 至六聚物产生所述 ' 七聚物 1'；通过添加一个 5' A 至六聚物产生所述 ' 七聚物 2'；通过添加在六聚物的 5' 末端和 3' 末端都添加 A 产生所述 ' 八聚物'。事先计算人 3' UTRome（定义为来自其中清晰限定编码区（ 'CDS'）末端的 NCBI 参考序列数据库的转录组的子序列）中八聚物和七聚物的频率。使用来自八聚物频率范围的中位值，将八聚物频率对七聚物频率归一化。随后通过计算 ((3X 归一化八聚物计数)+(2X 七聚物 2 计数)+(1X 七聚物 1 计数)) 的总和，计算出“mirSeedScore”。

[00777] 两条 RNAi 剂链均根据计算的评分分配至一个特异性分类：将高于 3 的评分看做高度特异性，将等于 3 的评分看做特异性并且将 2.2 和 2.8 之间的评分看做中等特异性。借助反义链的特异性分选 RNAi 剂。排除与已知人微 RNA 种子区域完美匹配的寡核苷酸。

表 2. 针对 β-联蛋白的 RNAi 剂：未修饰的序列

双链体	有义序列	有义 SEQ ID NO:	反义序列	反义 SEQ ID NO:	位置
AD-18892	UGGUGCUGACUAUCCAGUU	4771	AACUGGAUAGUCAGCACCA	5430	2500
AD-18893	CCAUCUGUGCUCUUCGUCA	4772	UGACGAAGAGCACAGAUGG	5431	1659
AD-18894	AUAAGCAGGUGGAUCUAUU	4773	AAUAGAUCCACCUGCUUAU	5432	3038
AD-18895	AUCCAAAGAGUAGCUGCAG	4774	CUGCAGCUACUCUUUGGAU	5433	2096
AD-18896	GACAAUGGCUACUCAAGCU	4775	AGCUUGAGUAGCCAUUGUC	5434	265
AD-18897	CUGUUGGAUUGAUUCGAAA	4776	UUUCGAAUCAAUCCAACAG	5435	1797
AD-18898	GCUGGCCUGGUUUGAUACU	4777	AGUAUCAAACCAGGCCAGC	5436	2587
AD-18899	UCUAACCUCACUUGCAAUA	4778	UAUUGCAAGUGAGGUUAGA	5437	1541
AD-18900	GAUAUCGCCAGGAUGAUCC	4779	GGAUCAUCCUGGCGAUAUC	5438	2391
AD-18901	UGGCCAUCUUUAAGUCUGG	4780	CCAGACUUAAAGAUGGCCA	5439	954
AD-18902	UGUAGAACACUAAUUCAUA	4781	UAUGAAUUAGUGUUCUACA	5440	2908
AD-18903	AUCAGUAAGAGGUGUUAUU	4782	AAUAACACCUCUUACUGAU	5441	3104
AD-18904	GUGCUCUUCGUCAUCUGAC	4783	GUCAGAUGACGAAGAGCAC	5442	1665
AD-18905	UGGUUUGAUACUGACCUGU	4784	ACAGGUCAGUAUCAAACCA	5443	2594
AD-18906	CCAGUUGCCUUUUAUCCCA	4785	UGGGAUAAAAGGCAACUGG	5444	3147
AD-18907	CCUGGUUUGAUACUGACCU	4786	AGGUCAGUAUCAAACCAGG	5445	2592
AD-18908	GACUAUCCAGUUGAUGGGC	4787	GCCCAUCAACUGGAUAGUC	5446	2507
AD-18909	AGCCAAUGGCUUGGAAUGA	4788	UCAUUCCAAGCCAUUGGCU	5447	2325
AD-18910	GCCAAUGGCUUGGAAUGAG	4789	CUCAUUCCAAGCCAUUGGC	5448	2326
AD-18911	AGAUGAGGGCAUGCAGAUC	4790	GAUCUGCAUGCCCUCAUCU	5449	577
AD-18912	GGUCCUCUGUGAACUUGCU	4791	AGCAAGUUCACAGAGGACC	5450	2116
AD-18913	AACCCUAGCCUUGCUUGUU	4792	AACAAGCAAGGCUAGGGUU	5451	2708
AD-18914	GAACACUAAUUCAUAAUCA	4793	UGAUUAUGAAUUAGUGUUC	5452	2912
AD-18915	AUCAAACCCUAGCCUUGCU	4794	AGCAAGGCUAGGGUUUGAU	5453	2704
AD-18916	ACCAGUUGCCUUUUAUCCC	4795	GGGAUAAAAGGCAACUGGU	5454	3146
AD-18917	CUAACCUCACUUGCAAUAA	4796	UUAUUGCAAGUGAGGUUAG	5455	1542
AD-18918	AUCCCACUAAUGUCCAGCG	4797	CGCUGGACAUUAGUGGGAU	5456	621

AD-18919	CUGACUAUCCAGUUGAUGG	4798	CCAUCAACUGGAUAGUCAG	5457	2505
AD-18920	GGCCUGGUUUGAUACUGAC	4799	GUCAGUAUCAAACCAGGCC	5458	2590
AD-18921	GGUAAAUCAGUAAGAGGUG	4800	CACCUCUUACUGAUUUACC	5459	3099
AD-18922	GCCUGGUUUGAUACUGACC	4801	GGUCAGUAUCAAACCAGGC	5460	2591
AD-18923	CAGGGGUCCUCUGUGAACU	4802	AGUUCACAGAGGACCCCUG	5461	2112
AD-18925	CUGGAAUCCAUUCUGGUGC	4803	GCACCAGAAUGGAUUCCAG	5462	366
AD-18926	UGAGAUGGGUGGCCACCAC	4804	GUGGUGGCCACCCAUCUCA	5463	2479
AD-18927	GAUGAUAUAAAUGUGGUCA	4805	UGACCACAUUUAUAUCAUC	5464	1502
AD-18928	UGCUUUAUUCUCCCAUUGA	4806	UCAAUGGGAGAAUAAAGCA	5465	2073
AD-18929	UUAUCAAACCCUAGCCUUG	4807	CAAGGCUAGGGUUUGAUAA	5466	2702
AD-18930	CCACUGGCCUCUGAUAAAG	4808	CUUUAUCAGAGGCCAGUGG	5467	1774
AD-18931	AACUUGCCACACGUGCAAU	4809	AUUGCACGUGUGGCAAGUU	5468	708
AD-18932	GCUCUUCGUCAUCUGACCA	4810	UGGUCAGAUGACGAAGAGC	5469	1667
AD-18933	GUAACAAUACAAAUGGAUU	4811	AAUCCAUUUGUAUUGUUAC	5470	2629
AD-18934	GGGGUCCUCUGUGAACUUG	4812	CAAGUUCACAGAGGACCCC	5471	2114
AD-18935	CAAACCCUAGCCUUGCUUG	4813	CAAGCAAGGCUAGGGUUUG	5472	2706
AD-18936	GAGUAAUGGUGUAGAACAC	4814	GUGUUCUACACCAUUACUC	5473	2899
AD-18937	GGAAGACAUCACUGAGCCU	4815	AGGCUCAGUGAUGUCUUCC	5474	1639
AD-18938	GGGAAGACAUCACUGAGCC	4816	GGCUCAGUGAUGUCUUCCC	5475	1638
AD-18939	GGUGUAGAACACUAAUUCA	4817	UGAAUUAGUGUUCUACACC	5476	2906
AD-18940	UACCAGUUGCCUUUUAUCC	4818	GGAUAAAAGGCAACUGGUA	5477	3145
AD-18941	GGAUAUCGCCAGGAUGAUC	4819	GAUCAUCCUGGCGAUAUCC	5478	2390
AD-18942	AAACCCUAGCCUUGCUUGU	4820	ACAAGCAAGGCUAGGGUUU	5479	2707
AD-18943	CUCUUCGUCAUCUGACCAG	4821	CUGGUCAGAUGACGAAGAG	5480	1668
AD-18944	UGACUAUCCAGUUGAUGGG	4822	CCCAUCAACUGGAUAGUCA	5481	2506
AD-18945	ACAAGCAGAGUGCUGAAGG	4823	CCUUCAGCACUCUGCUUGU	5482	1286
AD-18946	CAUCUGUGCUCUUCGUCAU	4824	AUGACGAAGAGCACAGAUG	5483	1660
AD-18947	CAAUGGCUUGGAAUGAGAC	4825	GUCUCAUUCCAAGCCAUUG	5484	2328
AD-18948	ACUGGCCUCUGAUAAAGGC	4826	GCCUUUAUCAGAGGCCAGU	5485	1776
AD-18949	UCAUCCCACUAAUGUCCAG	4827	CUGGACAUUAGUGGGAUGA	5486	619
AD-18950	AAAAGGAAGCUUCCAGACA	4828	UGUCUGGAAGCUUCCUUUU	5487	807
AD-18951	CGUUCUUUUCACUCUGGUG	4829	CACCAGAGUGAAAAGAACG	5488	2417
AD-18952	AAAGUUGUUGUAACCUGCU	4830	AGCAGGUUACAACAACUUU	5489	3165
AD-18953	ACAAUGGCUACUCAAGCUG	4831	CAGCUUGAGUAGCCAUUGU	5490	266
AD-18954	CUCAUCCCACUAAUGUCCA	4832	UGGACAUUAGUGGGAUGAG	5491	618
AD-18955	AGGGGUCCUCUGUGAACUU	4833	AAGUUCACAGAGGACCCCU	5492	2113
AD-18956	AAGCAGGUGGAUCUAUUUC	4834	GAAAUAGAUCCACCUGCUU	5493	3040
AD-18957	AAGUUGUUGUAACCUGCUG	4835	CAGCAGGUUACAACAACUU	5494	3166
AD-18958	AGCAGGUGGAUCUAUUUCA	4836	UGAAAUAGAUCCACCUGCU	5495	3041
AD-18959	AGGGCAUGCAGAUCCCAUC	4837	GAUGGGAUCUGCAUGCCCU	5496	582
AD-18960	AAAUGGUUCAGAAUUAAAC	4838	GUUUAAUUCUGAACCAUUU	5497	3220
AD-18961	UGAACUUGCUCAGGACAAG	4839	CUUGUCCUGAGCAAGUUCA	5498	2125
AD-18962	AAGAGUAGCUGCAGGGGUC	4840	GACCCCUGCAGCUACUCUU	5499	2101
AD-18963	CCCACUGGCCUCUGAUAAA	4841	UUUAUCAGAGGCCAGUGGG	5500	1773

AD-18964	CUGGCCUGGUUUGAUACUG	4842	CAGUAUCAAACCAGGCCAG	5501	2588
AD-18965	UUGAUACUGACCUGUAAAU	4843	AUUUACAGGUCAGUAUCAA	5502	2598
AD-18966	GUGUAGAACACUAAUUCAU	4844	AUGAAUUAGUGUUCUACAC	5503	2907
AD-18967	ACUAUCCAGUUGAUGGGCU	4845	AGCCCAUCAACUGGAUAGU	5504	2508
AD-18968	AAAUCAGUAAGAGGUGUUA	4846	UAACACCUCUUACUGAUUU	5505	3102
AD-18969	GCAGGUGGAUCUAUUUCAU	4847	AUGAAAUAGAUCCACCUGC	5506	3042
AD-18970	CUGGUGCUGACUAUCCAGU	4848	ACUGGAUAGUCAGCACCAG	5507	2499
AD-18971	GUGAACUUGCUCAGGACAA	4849	UUGUCCUGAGCAAGUUCAC	5508	2124
AD-18972	UCAGUAAGAGGUGUUAUUU	4850	AAAUAACACCUCUUACUGA	5509	3105
AD-18973	CCUCUGUGAACUUGCUCAG	4851	CUGAGCAAGUUCACAGAGG	5510	2119
AD-18974	UUGGCUGAACCAUCACAGA	4852	UCUGUGAUGGUUCAGCCAA	5511	641
AD-18975	UCAGCUGGCCUGGUUUGAU	4853	AUCAAACCAGGCCAGCUGA	5512	2584
AD-18976	GUAGCUGCAGGGGUCCUCU	4854	AGAGGACCCCUGCAGCUAC	5513	2105
AD-18977	AGGAGCUAAAAUGGCAGUG	4855	CACUGCCAUUUUAGCUCCU	5514	1069
AD-18978	AUGGCUUGGAAUGAGACUG	4856	CAGUCUCAUUCCAAGCCAU	5515	2330
AD-18979	UUGGAUAUCGCCAGGAUGA	4857	UCAUCCUGGCGAUAUCCAA	5516	2388
AD-18980	GGUUCAGAAUUAAACUUUU	4858	AAAAGUUUAAUUCUGAACC	5517	3224
AD-18981	GGGUAAAUCAGUAAGAGGU	4859	ACCUCUUACUGAUUUACCC	5518	3098
AD-18982	AUACCAUUCCAUUGUUUGU	4860	ACAAACAAUGGAAUGGUAU	5519	2049
AD-18983	ACUGUUGGAUUGAUUCGAA	4861	UUCGAAUCAAUCCAACAGU	5520	1796
AD-18984	AACUUGCUCAGGACAAGGA	4862	UCCUUGUCCUGAGCAAGUU	5521	2127
AD-18985	AUGCUUAAAAUAAGCAGGU	4863	ACCUGCUUAUUUUAAGCAU	5522	3029
AD-18986	GUUUGAUACUGACCUGUAA	4864	UUACAGGUCAGUAUCAAAC	5523	2596
AD-18987	AAUGGUUCAGAAUUAAACU	4865	AGUUUAAUUCUGAACCAUU	5524	3221
AD-18988	UAUCCCAAAGUUGUUGUAA	4866	UUACAACAACUUUGGGAUA	5525	3159
AD-18989	AUCAGCUGGCCUGGUUUGA	4867	UCAAACCAGGCCAGCUGAU	5526	2583
AD-18990	CCUGCCAUCUGUGCUCUUC	4868	GAAGAGCACAGAUGGCAGG	5527	1655
AD-18991	GCAGAAUACAAAUGAUGUA	4869	UACAUCAUUUGUAUUCUGC	5528	874
AD-18992	UAUGCUUAAAAUAAGCAGG	4870	CCUGCUUAUUUUAAGCAUA	5529	3028
AD-18993	AAUAAGCAGGUGGAUCUAU	4871	AUAGAUCCACCUGCUUAUU	5530	3037
AD-18994	UGAUAUAAAUGUGGUCACC	4872	GGUGACCACAUUUAUAUCA	5531	1504
AD-18995	GUAGGGUAAAUCAGUAAGA	4873	UCUUACUGAUUUACCCUAC	5532	3095
AD-18996	UAUCAAACCCUAGCCUUGC	4874	GCAAGGCUAGGGUUUGAUA	5533	2703
AD-18997	CCUUUUAUCCCAAAGUUGU	4875	ACAACUUUGGGAUAAAAGG	5534	3154
AD-18998	GGUAGGGUAAAUCAGUAAG	4876	CUUACUGAUUUACCCUACC	5535	3094
AD-18999	UGAUACUGACCUGUAAAUC	4877	GAUUUACAGGUCAGUAUCA	5536	2599
AD-19000	GGCUGAACCAUCACAGAUG	4878	CAUCUGUGAUGGUUCAGCC	5537	643
AD-19001	UGGAUAUCGCCAGGAUGAU	4879	AUCAUCCUGGCGAUAUCCA	5538	2389
AD-19002	UCUUCGUCAUCUGACCAGC	4880	GCUGGUCAGAUGACGAAGA	5539	1669
AD-19003	UAGCUGCAGGGGUCCUCUG	4881	CAGAGGACCCCUGCAGCUA	5540	2106
AD-19004	UGUUGUAACCUGCUGUGAU	4882	AUCACAGCAGGUUACAACA	5541	3170
AD-19005	AAUCAGUAAGAGGUGUUAU	4883	AUAACACCUCUUACUGAUU	5542	3103
AD-19006	UGGCUGAACCAUCACAGAU	4884	AUCUGUGAUGGUUCAGCCA	5543	642
AD-19007	GAAUUAAACUUUUAAUUCA	4885	UGAAUUAAAAGUUUAAUUC	5544	3230

AD-19008	AUGGUUCAGAAUUAAACUU	4886	AAGUUUAAUUCUGAACCAU	5545	3222
AD-19009	UGGUGUAGAACACUAAUUC	4887	GAAUUAGUGUUCUACACCA	5546	2905
AD-19010	AUGGUGUAGAACACUAAUU	4888	AAUUAGUGUUCUACACCAU	5547	2904
AD-19011	AUGAGGGCAUGCAGAUCCC	4889	GGGAUCUGCAUGCCCUCAU	5548	579
AD-19012	GUUGUAACCUGCUGUGAUA	4890	UAUCACAGCAGGUUACAAC	5549	3171
AD-19042	GCUGACUAUCCAGUUGAUG	4891	CAUCAACUGGAUAGUCAGC	5550	2504
AD-19043	UAAGCAGGUGGAUCUAUUU	4892	AAAUAGAUCCACCUGCUUA	5551	3039
AD-19044	UAAAAUAAGCAGGUGGAUC	4893	GAUCCACCUGCUUAUUUUA	5552	3034
AD-19045	GAUAUAAAUGUGGUCACCU	4894	AGGUGACCACAUUUAUAUC	5553	1505
AD-19046	AAGCAGAGUGCUGAAGGUG	4895	CACCUUCAGCACUCUGCUU	5554	1288
AD-19047	UGUGAACUUGCUCAGGACA	4896	UGUCCUGAGCAAGUUCACA	5555	2123
AD-19048	CAUCCCACUAAUGUCCAGC	4897	GCUGGACAUUAGUGGGAUG	5556	620
AD-19049	CAAAGUUGUUGUAACCUGC	4898	GCAGGUUACAACAACUUUG	5557	3164
AD-19050	UAAAUCAGUAAGAGGUGUU	4899	AACACCUCUUACUGAUUUA	5558	3101
AD-19051	AAUGGCUUGGAAUGAGACU	4900	AGUCUCAUUCCAAGCCAUU	5559	2329
AD-19052	GGGUCCUCUGUGAACUUGC	4901	GCAAGUUCACAGAGGACCC	5560	2115
AD-19053	GAGUAACAAUACAAAUGGA	4902	UCCAUUUGUAUUGUUACUC	5561	2627
AD-19054	UAAUGGUGUAGAACACUAA	4903	UUAGUGUUCUACACCAUUA	5562	2902
AD-19055	GUGGACAAUGGCUACUCAA	4904	UUGAGUAGCCAUUGUCCAC	5563	262
AD-19056	AACUGUCUUUGGACUCUCA	4905	UGAGAGUCCAAAGACAGUU	5564	1406
AD-19057	CCCUGGUGCUGACUAUCCA	4906	UGGAUAGUCAGCACCAGGG	5565	2497
AD-19058	CAGGUGGAUCUAUUUCAUG	4907	CAUGAAAUAGAUCCACCUG	5566	3043
AD-19059	UGGCCUGGUUUGAUACUGA	4908	UCAGUAUCAAACCAGGCCA	5567	2589
AD-19060	AGCUGGCCUGGUUUGAUAC	4909	GUAUCAAACCAGGCCAGCU	5568	2586
AD-19061	GCCAUCUGUGCUCUUCGUC	4910	GACGAAGAGCACAGAUGGC	5569	1658
AD-19062	UACCAUUCCAUUGUUUGUG	4911	CACAAACAAUGGAAUGGUA	5570	2050
AD-19063	CCCUUGGAUAUCGCCAGGA	4912	UCCUGGCGAUAUCCAAGGG	5571	2385
AD-19064	AGGGAAGACAUCACUGAGC	4913	GCUCAGUGAUGUCUUCCCU	5572	1637
AD-19065	GAACUUGCCACACGUGCAA	4914	UUGCACGUGUGGCAAGUUC	5573	707
AD-19066	UUUGAUACUGACCUGUAAA	4915	UUUACAGGUCAGUAUCAAA	5574	2597
AD-19067	UCCCAAAGUUGUUGUAACC	4916	GGUUACAACAACUUUGGGA	5575	3161
AD-19068	CAGAAUACAAAUGAUGUAG	4917	CUACAUCAUUUGUAUUCUG	5576	875
AD-19069	AGGUGGAUCUAUUUCAUGU	4918	ACAUGAAAUAGAUCCACCU	5577	3044
AD-19070	GCUCAUCCCACUAAUGUCC	4919	GGACAUUAGUGGGAUGAGC	5578	617
AD-19071	CCUGGUGCUGACUAUCCAG	4920	CUGGAUAGUCAGCACCAGG	5579	2498
AD-19072	UGGAAUCCAUUCUGGUGCC	4921	GGCACCAGAAUGGAUUCCA	5580	367
AD-19073	CCAGGACCUCAUGGAUGGG	4922	CCCAUCCAUGAGGUCCUGG	5581	2545
AD-19074	AACCUCACUUGCAAUAAUU	4923	AAUUAUUGCAAGUGAGGUU	5582	1544
AD-19075	CAGUUGCCUUUUAUCCCAA	4924	UUGGGAUAAAAGGCAACUG	5583	3148
AD-19076	GUAGAACACUAAUUCAUAA	4925	UUAUGAAUUAGUGUUCUAC	5584	2909
AD-19077	CUAUCCAGUUGAUGGGCUG	4926	CAGCCCAUCAACUGGAUAG	5585	2509
AD-19078	CACUGGCCUCUGAUAAAGG	4927	CCUUUAUCAGAGGCCAGUG	5586	1775
AD-19079	ACUGUCUUUGGACUCUCAG	4928	CUGAGAGUCCAAAGACAGU	5587	1407
AD-19080	CCAAUGGCUUGGAAUGAGA	4929	UCUCAUUCCAAGCCAUUGG	5588	2327

AD-19081	GCUUAAAAUAAGCAGGUGG	4930	CCACCUGCUUAUUUUAAGC	5589	3031
AD-19082	AUCUGUGCUCUUCGUCAUC	4931	GAUGACGAAGAGCACAGAU	5590	1661
AD-19083	CCCAAAGUUGUUGUAACCU	4932	AGGUUACAACAACUUUGGG	5591	3162
AD-19738	UACCCAGCGCCGUACGUCC	4933	GGACGUACGGCGCUGGGUA	5592	1906
AD-19739	ACGCUAUCAUGCGUUCUCC	4934	GGAGAACGCAUGAUAGCGU	5593	825
AD-19740	CAUGCACCUUUGCGUGAGC	4935	GCUCACGCAAAGGUGCAUG	5594	1838
AD-19741	GAAUGCAGUUCGCCUUCAC	4936	GUGAAGGCGAACUGCAUUC	5595	1714
AD-19742	GGUGCCAUUCCACGACUAG	4937	CUAGUCGUGGAAUGGCACC	5596	1859
AD-19743	AAGCGGCUGUUAGUCACUG	4938	CAGUGACUAACAGCCGCUU	5597	324
AD-19744	UCGAGCUCAGAGGGUACGA	4939	UCGUACCCUCUGAGCUCGA	5598	535
AD-19745	GACACGCUAUCAUGCGUUC	4940	GAACGCAUGAUAGCGUGUC	5599	822
AD-19746	CGCUAUCAUGCGUUCUCCU	4941	AGGAGAACGCAUGAUAGCG	5600	826
AD-19747	GUGUCUGCUAUUGUACGUA	4942	UACGUACAAUAGCAGACAC	5601	851
AD-19748	GUCUGCUCUAGUAAUAAGC	4943	GCUUAUUACUAGAGCAGAC	5602	1313
AD-19749	GUGCCAUUCCACGACUAGU	4944	ACUAGUCGUGGAAUGGCAC	5603	1860
AD-19750	AUGUUCACAACCGAAUUGU	4945	ACAAUUCGGUUGUGAACAU	5604	2016
AD-19751	CCACGACUAGUUCAGUUGC	4946	GCAACUGAACUAGUCGUGG	5605	1868
AD-19752	CACGACUAGUUCAGUUGCU	4947	AGCAACUGAACUAGUCGUG	5606	1869
AD-19753	AGUUCAGUUGCUUGUUCGU	4948	ACGAACAAGCAACUGAACU	5607	1876
AD-19754	CCCAGCGCCGUACGUCCAU	4949	AUGGACGUACGGCGCUGGG	5608	1908
AD-19755	GAGUUACUUCACUCUAGGA	4950	UCCUAGAGUGAAGUAACUC	5609	2192
AD-19756	ACAGUAUGCAAUGACUCGA	4951	UCGAGUCAUUGCAUACUGU	5610	520
AD-19757	UAUGCAAUGACUCGAGCUC	4952	GAGCUCGAGUCAUUGCAUA	5611	524
AD-19758	CCCACUAAUGUCCAGCGUU	4953	AACGCUGGACAUUAGUGGG	5612	623
AD-19759	GACCUUGCAUAACCUUUCC	4954	GGAAAGGUUAUGCAAGGUC	5613	916
AD-19760	UAUUACGACAGACUGCCUU	4955	AAGGCAGUCUGUCGUAAUA	5614	1153
AD-19761	AUCUGACCAGCCGACACCA	4956	UGGUGUCGGCUGGUCAGAU	5615	1677
AD-19762	CAUUCCACGACUAGUUCAG	4957	CUGAACUAGUCGUGGAAUG	5616	1864
AD-19763	GUUUUGAAAAUCCAGCGUG	4958	CACGCUGGAUUUUCAAAAC	5617	246
AD-19765	GCGUUUGGCUGAACCAUCA	4959	UGAUGGUUCAGCCAAACGC	5618	637
AD-19766	ACACGCUAUCAUGCGUUCU	4960	AGAACGCAUGAUAGCGUGU	5619	823
AD-19767	UAUGCCAUUACAACUCUCC	4961	GGAGAGUUGUAAUGGCAUA	5620	1028
AD-19768	UCUGCUCUAGUAAUAAGCC	4962	GGCUUAUUACUAGAGCAGA	5621	1314
AD-20124	CGGGAUGUUCACAACCGAA	4963	UUCGGUUGUGAACAUCCCG	5622	2012
AD-25889	ACAAUACAAAUGGAUUUUG	4964	CAAAAUCCAUUUGUAUUGU	5623	2632
AD-25890	ACAAAUGGAUUUUGGGAGU	4965	ACUCCCAAAAUCCAUUUGU	5624	2637
AD-25891	UUGGGAGUGACUCAAGAAG	4966	CUUCUUGAGUCACUCCCAA	5625	2648
AD-25892	UGGGAGUGACUCAAGAAGU	4967	ACUUCUUGAGUCACUCCCA	5626	2649
AD-25893	GAAGUGAAGAAUGCACAAG	4968	CUUGUGCAUUCUUCACUUC	5627	2663
AD-25894	AAGUGAAGAAUGCACAAGA	4969	UCUUGUGCAUUCUUCACUU	5628	2664
AD-25895	GAUGGAAUUUAUCAAACCC	4970	GGGUUUGAUAAAUUCCAUC	5629	2694
AD-25896	AUGGAAUUUAUCAAACCCU	4971	AGGGUUUGAUAAAUUCCAU	5630	2695
AD-25897	GGAAUUUAUCAAACCCUAG	4972	CUAGGGUUUGAUAAAUUCC	5631	2697
AD-25898	GAAUUUAUCAAACCCUAGC	4973	GCUAGGGUUUGAUAAAUUC	5632	2698

AD-25899	AAUUUAUCAAACCCUAGCC	4974	GGCUAGGGUUUGAUAAAUU	5633	2699
AD-25900	GAAUAUCUGUAAUGGUACU	4975	AGUACCAUUACAGAUAUUC	5634	2751
AD-25901	AAUAUCUGUAAUGGUACUG	4976	CAGUACCAUUACAGAUAUU	5635	2752
AD-25902	AUAUCUGUAAUGGUACUGA	4977	UCAGUACCAUUACAGAUAU	5636	2753
AD-25903	UUUUAAGUCUCUCGUAGUG	4978	CACUACGAGAGACUUAAAA	5637	2832
AD-25904	UUUAAGUCUCUCGUAGUGU	4979	ACACUACGAGAGACUUAAA	5638	2833
AD-25905	AGUCUCUCGUAGUGUUAAG	4980	CUUAACACUACGAGAGACU	5639	2837
AD-25906	UCGUAGUGUUAAGUUAUAG	4981	CUAUAACUUAACACUACGA	5640	2843
AD-25907	CGUAGUGUUAAGUUAUAGU	4982	ACUAUAACUUAACACUACG	5641	2844
AD-25908	GUAGUGUUAAGUUAUAGUG	4983	CACUAUAACUUAACACUAC	5642	2845
AD-25909	UAGUGUUAAGUUAUAGUGA	4984	UCACUAUAACUUAACACUA	5643	2846
AD-25910	UAGUGAAUACUGCUACAGC	4985	GCUGUAGCAGUAUUCACUA	5644	2859
AD-25911	AACACUAAUUCAUAAUCAC	4986	GUGAUUAUGAAUUAGUGUU	5645	2913
AD-25912	ACACUAAUUCAUAAUCACU	4987	AGUGAUUAUGAAUUAGUGU	5646	2914
AD-25913	UAAUUGUAAUCUGAAUAAA	4988	UUUAUUCAGAUUACAAUUA	5647	2938
AD-25914	AUUGUAAUCUGAAUAAAGU	4989	ACUUUAUUCAGAUUACAAU	5648	2940
AD-25915	UUGUAAUCUGAAUAAAGUG	4990	CACUUUAUUCAGAUUACAA	5649	2941
AD-25916	UGUAAUCUGAAUAAAGUGU	4991	ACACUUUAUUCAGAUUACA	5650	2942
AD-25917	GACAAAUAGAAAAUGGUCC	4992	GGACCAUUUUCUAUUUGUC	5651	2991
AD-25918	ACAAAUAGAAAAUGGUCCA	4993	UGGACCAUUUUCUAUUUGU	5652	2992
AD-25919	UAGAAAAUGGUCCAAUUAG	4994	CUAAUUGGACCAUUUUCUA	5653	2997
AD-25920	AGAAAAUGGUCCAAUUAGU	4995	ACUAAUUGGACCAUUUUCU	5654	2998
AD-25921	UAUUUGGGAUAUGUAUGGG	4996	CCCAUACAUAUCCCAAAUA	5655	3077
AD-25922	AUUUGGGAUAUGUAUGGGU	4997	ACCCAUACAUAUCCCAAAU	5656	3078
AD-25923	UUGGGAUAUGUAUGGGUAG	4998	CUACCCAUACAUAUCCCAA	5657	3080
AD-25924	GGAUAUGUAUGGGUAGGGU	4999	ACCCUACCCAUACAUAUCC	5658	3083
AD-25925	AAGAGGUGUUAUUUGGAAC	5000	GUUCCAAAUAACACCUCUU	5659	3110
AD-25926	AGAGGUGUUAUUUGGAACC	5001	GGUUCCAAAUAACACCUCU	5660	3111
AD-25927	GAGGUGUUAUUUGGAACCU	5002	AGGUUCCAAAUAACACCUC	5661	3112
AD-25928	UGGAACCUUGUUUUGGACA	5003	UGUCCAAAACAAGGUUCCA	5662	3123
AD-25929	GGAACCUUGUUUUGGACAG	5004	CUGUCCAAAACAAGGUUCC	5663	3124
AD-25930	GAACCUUGUUUUGGACAGU	5005	ACUGUCCAAAACAAGGUUC	5664	3125
AD-25931	GUUUUGGACAGUUUACCAG	5006	CUGGUAAACUGUCCAAAAC	5665	3132
AD-25932	UUUUGGACAGUUUACCAGU	5007	ACUGGUAAACUGUCCAAAA	5666	3133
AD-25933	UUGGACAGUUUACCAGUUG	5008	CAACUGGUAAACUGUCCAA	5667	3135
AD-25934	GUUGUUGUAACCUGCUGUG	5009	CACAGCAGGUUACAACAAC	5668	3168
AD-25935	UUGUUGUAACCUGCUGUGA	5010	UCACAGCAGGUUACAACAA	5669	3169
AD-25936	UUGUAACCUGCUGUGAUAC	5011	GUAUCACAGCAGGUUACAA	5670	3172
AD-25937	AUGCUUCAAGAGAAAAUGC	5012	GCAUUUUCUCUUGAAGCAU	5671	3192
AD-25938	AGUGAAGAAUGCACAAGAA	5013	UUCUUGUGCAUUCUUCACU	5672	2665
AD-25939	AAUGGAUCACAAGAUGGAA	5014	UUCCAUCUUGUGAUCCAUU	5673	2682
AD-25940	AUGGAUCACAAGAUGGAAU	5015	AUUCCAUCUUGUGAUCCAU	5674	2683
AD-25941	UGGAUCACAAGAUGGAAUU	5016	AAUUCCAUCUUGUGAUCCA	5675	2684
AD-25942	GGAUCACAAGAUGGAAUUU	5017	AAAUUCCAUCUUGUGAUCC	5676	2685

AD-25943	GAUCACAAGAUGGAAUUUA	5018	UAAAUUCCAUCUUGUGAUC	5677	2686
AD-25944	AUCACAAGAUGGAAUUUAU	5019	AUAAAUUCCAUCUUGUGAU	5678	2687
AD-25945	UGGAAUUUAUCAAACCCUA	5020	UAGGGUUUGAUAAAUUCCA	5679	2696
AD-25946	ACCCUAGCCUUGCUUGUUA	5021	UAACAAGCAAGGCUAGGGU	5680	2709
AD-25947	CCCUAGCCUUGCUUGUUAA	5022	UUAACAAGCAAGGCUAGGG	5681	2710
AD-25948	CCUAGCCUUGCUUGUUAAA	5023	UUUAACAAGCAAGGCUAGG	5682	2711
AD-25949	CUAGCCUUGCUUGUUAAAU	5024	AUUUAACAAGCAAGGCUAG	5683	2712
AD-25950	UAGCCUUGCUUGUUAAAUU	5025	AAUUUAACAAGCAAGGCUA	5684	2713
AD-25951	AGCCUUGCUUGUUAAAUUU	5026	AAAUUUAACAAGCAAGGCU	5685	2714
AD-25952	UUAAGUCUCUCGUAGUGUU	5027	AACACUACGAGAGACUUAA	5686	2834
AD-25953	UAAGUCUCUCGUAGUGUUA	5028	UAACACUACGAGAGACUUA	5687	2835
AD-25954	AAGUCUCUCGUAGUGUUAA	5029	UUAACACUACGAGAGACUU	5688	2836
AD-25955	CUCGUAGUGUUAAGUUAUA	5030	UAUAACUUAACACUACGAG	5689	2842
AD-25956	AGUGUUAAGUUAUAGUGAA	5031	UUCACUAUAACUUAACACU	5690	2847
AD-25957	GUGUUAAGUUAUAGUGAAU	5032	AUUCACUAUAACUUAACAC	5691	2848
AD-25958	CUACAGCAAUUUCUAAUUU	5033	AAAUUAGAAAUUGCUGUAG	5692	2871
AD-25959	CAAAUAGAAAAUGGUCCAA	5034	UUGGACCAUUUUCUAUUUG	5693	2993
AD-25960	AUAGAAAAUGGUCCAAUUA	5035	UAAUUGGACCAUUUUCUAU	5694	2996
AD-25961	UUUGGGAUAUGUAUGGGUA	5036	UACCCAUACAUAUCCCAAA	5695	3079
AD-25962	GAUAUGUAUGGGUAGGGUA	5037	UACCCUACCCAUACAUAUC	5696	3084
AD-25963	UGGGUAGGGUAAAUCAGUA	5038	UACUGAUUUACCCUACCCA	5697	3092
AD-25964	UAAGAGGUGUUAUUUGGAA	5039	UUCCAAAUAACACCUCUUA	5698	3109
AD-26017	UGCCUUUUAUCCCAAAGUU	5040	AACUUUGGGAUAAAAGGCA	5699	3152
AD-26018	UGUUGUAACCUGCUGUGAU	5041	AUCACAGCAGGUUACAACA	5700	3170
AD-26019	GUUGUAACCUGCUGUGAUA	5042	UAUCACAGCAGGUUACAAC	5701	3171
AD-26020	CAAGAGAAAAUGCGGUUAU	5043	AUAACCGCAUUUUCUCUUG	5702	3198
AD-26021	AAGAGAAAAUGCGGUUAUA	5044	UAUAACCGCAUUUUCUCUU	5703	3199
AD-26022	CCUGUUCCCCUGAGGGUAU	5045	AUACCCUCAGGGGAACAGG	5704	207
AD-26023	CUGUUCCCCUGAGGGUAUU	5046	AAUACCCUCAGGGGAACAG	5705	208
AD-26024	CCUGAGGCUAUUUGAAGUA	5047	UACUUCAAAUACCCUCAGG	5706	215
AD-26025	CUGAGGGUAUUUGAAGUAU	5048	AUACUUCAAAUACCCUCAG	5707	216
AD-26026	UGAGGGUAUUUGAAGUAUA	5049	UAUACUUCAAAUACCCUCA	5708	217
AD-26027	GGUAUUUGAAGUAUACCAU	5050	AUGGUAUACUUCAAAUACC	5709	221
AD-26028	GUAUUUGAAGUAUACCAUA	5051	UAUGGUAUACUUCAAAUAC	5710	222
AD-26029	UUUGAAGUAUACCAUACAA	5052	UUGUAUGGUAUACUUCAAA	5711	225
AD-26030	AGUAUACCAUACAACUGUU	5053	AACAGUUGUAUGGUAUACU	5712	230
AD-26031	GUAUACCAUACAACUGUUU	5054	AAACAGUUGUAUGGUAUAC	5713	231
AD-26032	UAUACCAUACAACUGUUUU	5055	AAAACAGUUGUAUGGUAUA	5714	232
AD-26033	ACCAUACAACUGUUUUGAA	5056	UUCAAAACAGUUGUAUGGU	5715	235
AD-26034	CCAUACAACUGUUUUGAAA	5057	UUUCAAAACAGUUGUAUGG	5716	236
AD-26035	GAAAAUCCAGCGUGGACAA	5058	UUGUCCACGCUGGAUUUUC	5717	251
AD-26036	AAAAUCCAGCGUGGACAAU	5059	AUUGUCCACGCUGGAUUUU	5718	252
AD-26037	CCAGCGUGGACAAUGGCUA	5060	UAGCCAUUGUCCACGCUGG	5719	257
AD-26038	GUGGACAAUGGCUACUCAA	5061	UUGAGUAGCCAUUGUCCAC	5720	262

AD-26039	AAUGGCUACUCAAGCUGAU	5062	AUCAGCUUGAGUAGCCAUU	5721	268
AD-26040	AUGGCUACUCAAGCUGAUU	5063	AAUCAGCUUGAGUAGCCAU	5722	269
AD-26041	UGGCUACUCAAGCUGAUUU	5064	AAAUCAGCUUGAGUAGCCA	5723	270
AD-26042	CUACUCAAGCUGAUUUGAU	5065	AUCAAAUCAGCUUGAGUAG	5724	273
AD-26043	AUUUGAUGGAGUUGGACAU	5066	AUGUCCAACUCCAUCAAAU	5725	285
AD-26044	UGGAGUUGGACAUGGCCAU	5067	AUGGCCAUGUCCAACUCCA	5726	291
AD-26045	GUUGGACAUGGCCAUGGAA	5068	UUCCAUGGCCAUGUCCAAC	5727	295
AD-26046	GCCAUGGAACCAGACAGAA	5069	UUCUGUCUGGUUCCAUGGC	5728	305
AD-26047	CAUGGAACCAGACAGAAAA	5070	UUUUCUGUCUGGUUCCAUG	5729	307
AD-26048	GGAGGCGGAGACGGAGGAA	5071	UUCCUCCGUCUCCGCCUCC	5730	111
AD-26049	AGACAGAAAAGCGGCUGUU	5072	AACAGCCGCUUUUCUGUCU	5731	316
AD-26050	GACAGAAAAGCGGCUGUUA	5073	UAACAGCCGCUUUUCUGUC	5732	317
AD-26051	UGUUAGUCACUGGCAGCAA	5074	UUGCUGCCAGUGACUAACA	5733	331
AD-26052	CACUGGCAGCAACAGUCUU	5075	AAGACUGUUGCUGCCAGUG	5734	338
AD-26053	ACUGGCAGCAACAGUCUUA	5076	UAAGACUGUUGCUGCCAGU	5735	339
AD-26054	UCUUACCUGGACUCUGGAA	5077	UUCCAGAGUCCAGGUAAGA	5736	353
AD-26055	CUUACCUGGACUCUGGAAU	5078	AUUCCAGAGUCCAGGUAAG	5737	354
AD-26056	CCUGGACUCUGGAAUCCAU	5079	AUGGAUUCCAGAGUCCAGG	5738	358
AD-26057	GGCUAGUGGUGGACCCCAA	5080	UUGGGGUCCACCACUAGCC	5739	1216
AD-26058	GCCACUACCACAGCUCCUU	5081	AAGGAGCUGUGGUAGUGGC	5740	383
AD-26059	UCCUUCUCUGAGUGGUAAA	5082	UUUACCACUCAGAGAAGGA	5741	397
AD-26060	CUCUGAGUGGUAAAGGCAA	5083	UUGCCUUUACCACUCAGAG	5742	402
AD-26061	UAAAGGCAAUCCUGAGGAA	5084	UUCCUCAGGAUUGCCUUUA	5743	412
AD-26062	CAAUCCUGAGGAAGAGGAU	5085	AUCCUCUUCCUCAGGAUUG	5744	418
AD-26063	UGAGGAAGAGGAUGUGGAU	5086	AUCCACAUCCUCUUCCUCA	5745	424
AD-26064	AUACCUCCCAAGUCCUGUA	5087	UACAGGACUUGGGAGGUAU	5746	441
AD-26065	UACCUCCCAAGUCCUGUAU	5088	AUACAGGACUUGGGAGGUA	5747	442
AD-26066	AGUCCUGUAUGAGUGGGAA	5089	UUCCCACUCAUACAGGACU	5748	451
AD-26067	UAUGAGUGGGAACAGGGAU	5090	AUCCCUGUUCCCACUCAUA	5749	458
AD-26068	CAAGCUUUAGUAAAUAUAA	5091	UUAUAUUUACUAAAGCUUG	5750	1232
AD-26069	AAGCUUUAGUAAAUAUAAU	5092	AUUAUAUUUACUAAAGCUU	5751	1233
AD-26070	UGAGUGGGAACAGGGAUUU	5093	AAAUCCCUGUUCCCACUCA	5752	460
AD-26071	GAGUGGGAACAGGGAUUUU	5094	AAAAUCCCUGUUCCCACUC	5753	461
AD-26072	AGGGAUUUUCUCAGUCCUU	5095	AAGGACUGAGAAAAUCCCU	5754	471
AD-26073	UUCUCAGUCCUUCACUCAA	5096	UUGAGUGAAGGACUGAGAA	5755	478
AD-26074	UCAGUCCUUCACUCAAGAA	5097	UUCUUGAGUGAAGGACUGA	5756	481
AD-26075	CUUCACUCAAGAACAAGUA	5098	UACUUGUUCUUGAGUGAAG	5757	487
AD-26076	UCAAGAACAAGUAGCUGAU	5099	AUCAGCUACUUGUUCUUGA	5758	493
AD-26077	CUGAUAUUGAUGGACAGUA	5100	UACUGUCCAUCAAUAUCAG	5759	507
AD-26078	AUUGAUGGACAGUAUGCAA	5101	UUGCAUACUGUCCAUCAAU	5760	512
AD-26079	GACUCGAGCUCAGAGGGUA	5102	UACCCUCUGAGCUCGAGUC	5761	532
AD-26080	CAGAGGGUACGAGCUGCUA	5103	UAGCAGCUCGUACCCUCUG	5762	542
AD-26081	AGAGGGUACGAGCUGCUAU	5104	AUAGCAGCUCGUACCCUCU	5763	543
AD-26082	GGGUACGAGCUGCUAUGUU	5105	AACAUAGCAGCUCGUACCC	5764	546

AD-26083	CUAUGUUCCCUGAGACAUU	5106	AAUGUCUCAGGGAACAUAG	5765	558
AD-26084	UAUGUUCCCUGAGACAUUA	5107	UAAUGUCUCAGGGAACAUA	5766	559
AD-26085	GUUCCCUGAGACAUUAGAU	5108	AUCUAAUGUCUCAGGGAAC	5767	562
AD-26086	UAGAUGAGGGCAUGCAGAU	5109	AUCUGCAUGCCCUCAUCUA	5768	576
AD-26087	GAGGGCAUGCAGAUCCCAU	5110	AUGGGAUCUGCAUGCCCUC	5769	581
AD-26088	GGCAUGCAGAUCCCAUCUA	5111	UAGAUGGGAUCUGCAUGCC	5770	584
AD-26089	AGAUCCCAUCUACACAGUU	5112	AACUGUGUAGAUGGGAUCU	5771	591
AD-26090	CCCAUCUACACAGUUUGAU	5113	AUCAAACUGUGUAGAUGGG	5772	595
AD-26091	ACAGUUUGAUGCUGCUCAU	5114	AUGAGCAGCAUCAAACUGU	5773	604
AD-26092	GAUGCUGCUCAUCCCACUA	5115	UAGUGGGAUGAGCAGCAUC	5774	611
AD-26093	AUGCUGCUCAUCCCACUAA	5116	UUAGUGGGAUGAGCAGCAU	5775	612
AD-26094	UGCUGCUCAUCCCACUAAU	5117	AUUAGUGGGAUGAGCAGCA	5776	613
AD-26095	CCCACUAAUGUCCAGCGUU	5118	AACGCUGGACAUUAGUGGG	5777	623
AD-26096	CAGCGUUUGGCUGAACCAU	5119	AUGGUUCAGCCAAACGCUG	5778	635
AD-26097	UGGCUGAACCAUCACAGAU	5120	AUCUGUGAUGGUUCAGCCA	5779	642
AD-26098	AACCAUCACAGAUGCUGAA	5121	UUCAGCAUCUGUGAUGGUU	5780	648
AD-26099	ACCAUCACAGAUGCUGAAA	5122	UUUCAGCAUCUGUGAUGGU	5781	649
AD-26100	AUCACAGAUGCUGAAACAU	5123	AUGUUUCAGCAUCUGUGAU	5782	652
AD-26101	GAUGCUGAAACAUGCAGUU	5124	AACUGCAUGUUUCAGCAUC	5783	658
AD-26102	CUGAAACAUGCAGUUGUAA	5125	UUACAACUGCAUGUUUCAG	5784	662
AD-26103	AACAUGCAGUUGUAAACUU	5126	AAGUUUACAACUGCAUGUU	5785	666
AD-26104	AUGCAGUUGUAAACUUGAU	5127	AUCAAGUUUACAACUGCAU	5786	669
AD-26105	UGCAGUUGUAAACUUGAUU	5128	AAUCAAGUUUACAACUGCA	5787	670
AD-26106	CAGUUGUAAACUUGAUUAA	5129	UUAAUCAAGUUUACAACUG	5788	672
AD-26107	CUUGAUUAACUAUCAAGAU	5130	AUCUUGAUAGUUAAUCAAG	5789	682
AD-26108	GAUUAACUAUCAAGAUGAU	5131	AUCAUCUUGAUAGUUAAUC	5790	685
AD-26109	CUAUCAAGAUGAUGCAGAA	5132	UUCUGCAUCAUCUUGAUAG	5791	691
AD-26110	GAACUUGCCACACGUGCAA	5133	UUGCACGUGUGGCAAGUUC	5792	707
AD-26111	AACUUGCCACACGUGCAAU	5134	AUUGCACGUGUGGCAAGUU	5793	708
AD-26112	CACACGUGCAAUCCCUGAA	5135	UUCAGGGAUUGCACGUGUG	5794	715
AD-26123	GCAAUCCCUGAACUGACAA	5136	UUGUCAGUUCAGGGAUUGC	5795	722
AD-26124	CAAUCCCUGAACUGACAAA	5137	UUUGUCAGUUCAGGGAUUG	5796	723
AD-26125	AAUCCCUGAACUGACAAAA	5138	UUUUGUCAGUUCAGGGAUU	5797	724
AD-26126	UGAACUGACAAAACUGCUA	5139	UAGCAGUUUUGUCAGUUCA	5798	730
AD-26127	GAACUGACAAAACUGCUAA	5140	UUAGCAGUUUUGUCAGUUC	5799	731
AD-26128	AACUGACAAAACUGCUAAA	5141	UUUAGCAGUUUUGUCAGUU	5800	732
AD-26129	ACUGACAAAACUGCUAAAU	5142	AUUUAGCAGUUUUGUCAGU	5801	733
AD-26130	GAGGACCAGGUGGUGGUUA	5143	UAACCACCACCUGGUCCUC	5802	755
AD-26131	AGGACCAGGUGGUGGUUAA	5144	UUAACCACCACCUGGUCCU	5803	756
AD-26132	GGACCAGGUGGUGGUUAAU	5145	AUUAACCACCACCUGGUCC	5804	757
AD-26133	GACCAGGUGGUGGUUAAUA	5146	UAUUAACCACCACCUGGUC	5805	758
AD-26134	UCACUUGCAAUAAUUAUAA	5147	UUAUAAUUAUUGCAAGUGA	5806	1548
AD-26135	CUUGCAAUAAUUAUAAGAA	5148	UUCUUAUAAUUAUUGCAAG	5807	1551
AD-26136	ACCAGGUGGUGGUUAAUAA	5149	UUAUUAACCACCACCUGGU	5808	759

AD-26137	GGCUGCAGUUAUGGUCCAU	5150	AUGGACCAUAACUGCAGCC	5809	778
AD-26138	GUUAUGGUCCAUCAGCUUU	5151	AAAGCUGAUGGACCAUAAC	5810	785
AD-26139	AUGGUCCAUCAGCUUUCUA	5152	UAGAAAGCUGAUGGACCAU	5811	788
AD-26140	UGGUCCAUCAGCUUUCUAA	5153	UUAGAAAGCUGAUGGACCA	5812	789
AD-26141	UCGGGCUGGUGACAGGGAA	5154	UUCCCUGUCACCAGCCCGA	5813	1624
AD-26142	GGUCCAUCAGCUUUCUAAA	5155	UUUAGAAAGCUGAUGGACC	5814	790
AD-26143	GUCCAUCAGCUUUCUAAAA	5156	UUUUAGAAAGCUGAUGGAC	5815	791
AD-26144	GAAGCUUCCAGACACGCUA	5157	UAGCGUGUCUGGAAGCUUC	5816	812
AD-26145	AAGCUUCCAGACACGCUAU	5158	AUAGCGUGUCUGGAAGCUU	5817	813
AD-26146	CUUCCAGACACGCUAUCAU	5159	AUGAUAGCGUGUCUGGAAG	5818	816
AD-26147	AGACACGCUAUCAUGCGUU	5160	AACGCAUGAUAGCGUGUCU	5819	821
AD-26148	UCAUGCGUUCUCCUCAGAU	5161	AUCUGAGGAGAACGCAUGA	5820	831
AD-26149	CCUCAGAUGGUGUCUGCUA	5162	UAGCAGACACCAUCUGAGG	5821	842
AD-26150	CUCAGAUGGUGUCUGCUAU	5163	AUAGCAGACACCAUCUGAG	5822	843
AD-26151	GUGUCUGCUAUUGUACGUA	5164	UACGUACAAUAGCAGACAC	5823	851
AD-26152	CUGCUAUUGUACGUACCAU	5165	AUGGUACGUACAAUAGCAG	5824	855
AD-26153	UUGUACGUACCAUGCAGAA	5166	UUCUGCAUGGUACGUACAA	5825	861
AD-26154	UGUACGUACCAUGCAGAAU	5167	AUUCUGCAUGGUACGUACA	5826	862
AD-26155	CGUACCAUGCAGAAUACAA	5168	UUGUAUUCUGCAUGGUACG	5827	866
AD-26156	CAUGCAGAAUACAAAUGAU	5169	AUCAUUUGUAUUCUGCAUG	5828	871
AD-26157	GCAGAAUACAAAUGAUGUA	5170	UACAUCAUUUGUAUUCUGC	5829	874
AD-26158	GAAUACAAAUGAUGUAGAA	5171	UUCUACAUCAUUUGUAUUC	5830	877
AD-26159	GAUGUAGAAACAGCUCGUU	5172	AACGAGCUGUUUCUACAUC	5831	887
AD-26160	GUUGUACCGCUGGGACCUU	5173	AAGGUCCCAGCGGUACAAC	5832	903
AD-26161	UACCGCUGGGACCUUGCAU	5174	AUGCAAGGUCCCAGCGGUA	5833	907
AD-26162	CCGCUGGGACCUUGCAUAA	5175	UUAUGCAAGGUCCCAGCGG	5834	909
AD-26163	UGGGACCUUGCAUAACCUU	5176	AAGGUUAUGCAAGGUCCCA	5835	913
AD-26164	GGGACCUUGCAUAACCUUU	5177	AAAGGUUAUGCAAGGUCCC	5836	914
AD-26165	CUUGCAUAACCUUUCCCAU	5178	AUGGGAAAGGUUAUGCAAG	5837	919
AD-26166	UCUUUAAGUCUGGAGGCAU	5179	AUGCCUCCAGACUUAAAGA	5838	960
AD-26167	GCAUUCCUGCCCUGGUGAA	5180	UUCACCAGGGCAGGAAUGC	5839	975
AD-26168	CAUUCCUGCCCUGGUGAAA	5181	UUUCACCAGGGCAGGAAUG	5840	976
AD-26169	AUUCCUGCCCUGGUGAAAA	5182	UUUUCACCAGGGCAGGAAU	5841	977
AD-26170	UUCCUGCCCUGGUGAAAAU	5183	AUUUUCACCAGGGCAGGAA	5842	978
AD-26171	UGCCCUGGUGAAAAUGCUU	5184	AAGCAUUUUCACCAGGGCA	5843	982
AD-26172	CUGGUGAAAAUGCUUGGUU	5185	AACCAAGCAUUUUCACCAG	5844	986
AD-26173	GCUUGGUUCACCAGUGGAU	5186	AUCCACUGGUGAACCAAGC	5845	997
AD-26174	CUUGGUUCACCAGUGGAUU	5187	AAUCCACUGGUGAACCAAG	5846	998
AD-26175	UGCGUGAGCAGGGUGCCAU	5188	AUGGCACCCUGCUCACGCA	5847	1848
AD-26176	GCGUGAGCAGGGUGCCAUU	5189	AAUGGCACCCUGCUCACGC	5848	1849
AD-26177	CACCAGUGGAUUCUGUGUU	5190	AACACAGAAUCCACUGGUG	5849	1005
AD-26178	CAGUGGAUUCUGUGUUGUU	5191	AACAACACAGAAUCCACUG	5850	1008
AD-26179	AGUGGAUUCUGUGUUGUUU	5192	AAACAACACAGAAUCCACU	5851	1009
AD-26180	GUGGAUUCUGUGUUGUUUU	5193	AAAACAACACAGAAUCCAC	5852	1010

AD-26181	UGGAUUCUGUGUUGUUUUA	5194	UAAAACAACACAGAAUCCA	5853	1011
AD-26182	GGAUUCUGUGUUGUUUUAU	5195	AUAAAACAACACAGAAUCC	5854	1012
AD-26183	UGUGUUGUUUUAUGCCAUU	5196	AAUGGCAUAAAACAACACA	5855	1018
AD-26184	GGGUGGGACACAGCAGCAA	5197	UUGCUGCUGUGUCCCACCC	5856	1927
AD-26185	GUGUUGUUUUAUGCCAUUA	5198	UAAUGGCAUAAAACAACAC	5857	1019
AD-26186	UUGUUUUAUGCCAUUACAA	5199	UUGUAAUGGCAUAAAACAA	5858	1022
AD-26187	CCAUUACAACUCUCCACAA	5200	UUGUGGAGAGUUGUAAUGG	5859	1032
AD-26188	UACAACUCUCCACAACCUU	5201	AAGGUUGUGGAGAGUUGUA	5860	1036
AD-26189	ACAACUCUCCACAACCUUU	5202	AAAGGUUGUGGAGAGUUGU	5861	1037
AD-26190	CAACUCUCCACAACCUUUU	5203	AAAAGGUUGUGGAGAGUUG	5862	1038
AD-26191	AACUCUCCACAACCUUUUA	5204	UAAAAGGUUGUGGAGAGUU	5863	1039
AD-26192	ACUCUCCACAACCUUUUAU	5205	AUAAAAGGUUGUGGAGAGU	5864	1040
AD-26193	CUCUCCACAACCUUUUAUU	5206	AAUAAAAGGUUGUGGAGAG	5865	1041
AD-26194	UCUCCACAACCUUUUAUUA	5207	UAAUAAAAGGUUGUGGAGA	5866	1042
AD-26195	CAACCUUUUAUUACAUCAA	5208	UUGAUGUAAUAAAAGGUUG	5867	1048
AD-26196	CCUUUUAUUACAUCAAGAA	5209	UUCUUGAUGUAAUAAAAGG	5868	1051
AD-26197	UUACAUCAAGAAGGAGCUA	5210	UAGCUCCUUCUUGAUGUAA	5869	1058
AD-26198	UACAUCAAGAAGGAGCUAA	5211	UUAGCUCCUUCUUGAUGUA	5870	1059
AD-26199	CAUCAAGAAGGAGCUAAAA	5212	UUUUAGCUCCUUCUUGAUG	5871	1061
AD-26200	AUCAAGAAGGAGCUAAAAU	5213	AUUUUAGCUCCUUCUUGAU	5872	1062
AD-26201	GCUAAAAUGGCAGUGCGUU	5214	AACGCACUGCCAUUUUAGC	5873	1073
AD-26202	UAAAAUGGCAGUGCGUUUA	5215	UAAACGCACUGCCAUUUUA	5874	1075
AD-26203	AAAUGGUUGCCUUGCUCAA	5216	UUGAGCAAGGCAACCAUUU	5875	1110
AD-26204	GCCUGUUCCCCUGAGGGUA	5217	UACCCUCAGGGGAACAGGC	5876	206
AD-26205	UGGUUGCCUUGCUCAACAA	5218	UUGUUGAGCAAGGCAACCA	5877	1113
AD-26206	GGUUGCCUUGCUCAACAAA	5219	UUUGUUGAGCAAGGCAACC	5878	1114
AD-26207	GUUGCCUUGCUCAACAAAA	5220	UUUUGUUGAGCAAGGCAAC	5879	1115
AD-26208	GCCUUGCUCAACAAAACAA	5221	UUGUUUUGUUGAGCAAGGC	5880	1118
AD-26209	CCUUGCUCAACAAAACAAA	5222	UUUGUUUUGUUGAGCAAGG	5881	1119
AD-26210	GUUAAAUUCUUGGCUAUUA	5223	UAAUAGCCAAGAAUUUAAC	5882	1139
AD-26211	UAUUACGACAGACUGCCUU	5224	AAGGCAGUCUGUCGUAAUA	5883	1153
AD-26212	AUGGCAACCAAGAAAGCAA	5225	UUGCUUUCUUGGUUGCCAU	5884	1185
AD-26213	AGUGGUGGACCCCAAGCUU	5226	AAGCUUGGGGUCCACCACU	5885	1220
AD-26214	GUGGUGGACCCCAAGCUUU	5227	AAAGCUUGGGGUCCACCAC	5886	1221
AD-26215	UGGUGGACCCCAAGCUUUA	5228	UAAAGCUUGGGGUCCACCA	5887	1222
AD-26216	UGGACCCCAAGCUUUAGUA	5229	UACUAAAGCUUGGGGUCCA	5888	1225
AD-26217	GGACCCCAAGCUUUAGUAA	5230	UUACUAAAGCUUGGGGUCC	5889	1226
AD-26218	GACCCCAAGCUUUAGUAAA	5231	UUUACUAAAGCUUGGGGUC	5890	1227
AD-26651	ACCCCAAGCUUUAGUAAAU	5232	AUUUACUAAAGCUUGGGGU	5891	1228
AD-26652	CCCCAAGCUUUAGUAAAUA	5233	UAUUUACUAAAGCUUGGGG	5892	1229
AD-26653	CCCAAGCUUUAGUAAAUAU	5234	AUAUUUACUAAAGCUUGGG	5893	1230
AD-26654	CCAAGCUUUAGUAAAUAUA	5235	UAUAUUUACUAAAGCUUGG	5894	1231
AD-26655	UAAAUAUAAUGAGGACCUA	5236	UAGGUCCUCAUUAUAUUUA	5895	1242
AD-26656	AAAUAUAAUGAGGACCUAU	5237	AUAGGUCCUCAUUAUAUUU	5896	1243

AD-26657	AAUAUAAUGAGGACCUAUA	5238	UAUAGGUCCUCAUUAUAUU	5897	1244
AD-26658	AUAAUGAGGACCUAUACUU	5239	AAGUAUAGGUCCUCAUUAU	5898	1247
AD-26659	AAACUACUGUGGACCACAA	5240	UUGUGGUCCACAGUAGUUU	5899	1271
AD-26660	CCACAAGCAGAGUGCUGAA	5241	UUCAGCACUCUGCUUGUGG	5900	1284
AD-26661	CAGAGUGCUGAAGGUGCUA	5242	UAGCACCUUCAGCACUCUG	5901	1291
AD-26662	AGAGUGCUGAAGGUGCUAU	5243	AUAGCACCUUCAGCACUCU	5902	1292
AD-26663	AUUGUAGAAGCUGGUGGAA	5244	UUCCACCAGCUUCUACAAU	5903	1337
AD-26664	UUGUAGAAGCUGGUGGAAU	5245	AUUCCACCAGCUUCUACAA	5904	1338
AD-26665	GCUGGUGGAAUGCAAGCUU	5246	AAGCUUGCAUUCCACCAGC	5905	1346
AD-26666	CUGGUGGAAUGCAAGCUUU	5247	AAAGCUUGCAUUCCACCAG	5906	1347
AD-26667	AGGACUUCACCUGACAGAU	5248	AUCUGUCAGGUGAAGUCCU	5907	1366
AD-26668	CUUCACCUGACAGAUCCAA	5249	UUGGAUCUGUCAGGUGAAG	5908	1370
AD-26669	CCUGACAGAUCCAAGUCAA	5250	UUGACUUGGAUCUGUCAGG	5909	1375
AD-26670	AGAUCCAAGUCAACGUCUU	5251	AAGACGUUGACUUGGAUCU	5910	1381
AD-26671	UCCAAGUCAACGUCUUGUU	5252	AACAAGACGUUGACUUGGA	5911	1384
AD-26672	UCUUGUUCAGAACUGUCUU	5253	AAGACAGUUCUGAACAAGA	5912	1396
AD-26673	CUUGUUCAGAACUGUCUUU	5254	AAAGACAGUUCUGAACAAG	5913	1397
AD-26674	GUCUUUGGACUCUCAGGAA	5255	UUCCUGAGAGUCCAAAGAC	5914	1410
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AD-26677	UGCCCAGGGAGAACCCCUU	5258	AAGGGGUUCUCCCUGGGCA	5917	2371
AD-26678	UGGACUCUCAGGAAUCUUU	5259	AAAGAUUCCUGAGAGUCCA	5918	1415
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AD-26680	AAUCUUUCAGAUGCUGCAA	5261	UUGCAGCAUCUGAAAGAUU	5920	1427
AD-26681	CUUUCAGAUGCUGCAACUA	5262	UAGUUGCAGCAUCUGAAAG	5921	1430
AD-26682	UUCAGAUGCUGCAACUAAA	5263	UUUAGUUGCAGCAUCUGAA	5922	1432
AD-26683	UGCUGCAACUAAACAGGAA	5264	UUCCUGUUUAGUUGCAGCA	5923	1438
AD-26684	UAAACAGGAAGGGAUGGAA	5265	UUCCAUCCCUUCCUGUUUA	5924	1447
AD-26685	AGGGAUGGAAGGUCUCCUU	5266	AAGGAGACCUUCCAUCCCU	5925	1456
AD-26686	AGGUCUCCUUGGGACUCUU	5267	AAGAGUCCCAAGGAGACCU	5926	1465
AD-26687	UCUCCUUGGGACUCUUGUU	5268	AACAAGAGUCCCAAGGAGA	5927	1468
AD-26688	UGGGACUCUUGUUCAGCUU	5269	AAGCUGAACAAGAGUCCCA	5928	1474
AD-26689	CUUGUUCAGCUUCUGGGUU	5270	AACCCAGAAGCUGAACAAG	5929	1481
AD-26690	UCAGCUUCUGGGUUCAGAU	5271	AUCUGAACCCAGAAGCUGA	5930	1486
AD-26691	GCUUCUGGGUUCAGAUGAU	5272	AUCAUCUGAACCCAGAAGC	5931	1489
AD-26692	CUUCUGGGUUCAGAUGAUA	5273	UAUCAUCUGAACCCAGAAG	5932	1490
AD-26693	GGCCAGGAUGCCUUGGGUA	5274	UACCCAAGGCAUCCUGGCC	5933	2441
AD-26694	UUCUGGGUUCAGAUGAUAU	5275	AUAUCAUCUGAACCCAGAA	5934	1491
AD-26695	CUGGGUUCAGAUGAUAUAA	5276	UUAUAUCAUCUGAACCCAG	5935	1493
AD-26696	UGGGUUCAGAUGAUAUAAA	5277	UUUAUAUCAUCUGAACCCA	5936	1494
AD-26697	GUCACCUGUGCAGCUGGAA	5278	UUCCAGCUGCACAGGUGAC	5937	1517
AD-26698	UCACCUGUGCAGCUGGAAU	5279	AUUCCAGCUGCACAGGUGA	5938	1518
AD-26699	CACCUGUGCAGCUGGAAUU	5280	AAUUCCAGCUGCACAGGUG	5939	1519
AD-26700	CUGUGCAGCUGGAAUUCUU	5281	AAGAAUUCCAGCUGCACAG	5940	1522

AD-26701	UGUGCAGCUGGAAUUCUUU	5282	AAAGAAUUCCAGCUGCACA	5941	1523
AD-26702	GCAGCUGGAAUUCUUUCUA	5283	UAGAAAGAAUUCCAGCUGC	5942	1526
AD-26703	CAGCUGGAAUUCUUUCUAA	5284	UUAGAAAGAAUUCCAGCUG	5943	1527
AD-26704	UUUCUAACCUCACUUGCAA	5285	UUGCAAGUGAGGUUAGAAA	5944	1539
AD-26705	UUCUAACCUCACUUGCAAU	5286	AUUGCAAGUGAGGUUAGAA	5945	1540
AD-26706	ACCUCACUUGCAAUAAUUA	5287	UAAUUAUUGCAAGUGAGGU	5946	1545
AD-26707	CCUCACUUGCAAUAAUUAU	5288	AUAAUUAUUGCAAGUGAGG	5947	1546
AD-26708	CUCACUUGCAAUAAUUAUA	5289	UAUAAUUAUUGCAAGUGAG	5948	1547
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AD-26711	GGGUGGUAUAGAGGCUCUU	5292	AAGAGCCUCUAUACCACCC	5951	1591
AD-26712	AUAGAGGCUCUUGUGCGUA	5293	UACGCACAAGAGCCUCUAU	5952	1598
AD-26713	UCUUGUGCGUACUGUCCUU	5294	AAGGACAGUACGCACAAGA	5953	1606
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AD-26715	ACAUCACUGAGCCUGCCAU	5296	AUGGCAGGCUCAGUGAUGU	5955	1644
AD-26716	GCCUGCCAUCUGUGCUCUU	5297	AAGAGCACAGAUGGCAGGC	5956	1654
AD-26717	UCUGACCAGCCGACACCAA	5298	UUGGUGUCGGCUGGUCAGA	5957	1678
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AD-26721	GAUGGCCCAGAAUGCAGUU	5302	AACUGCAUUCUGGGCCAUC	5961	1705
AD-26722	CCAGAAUGCAGUUCGCCUU	5303	AAGGCGAACUGCAUUCUGG	5962	1711
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AD-26724	UGCAGUUCGCCUUCACUAU	5305	AUAGUGAAGGCGAACUGCA	5964	1717
AD-26725	UCGCCUUCACUAUGGACUA	5306	UAGUCCAUAGUGAAGGCGA	5965	1723
AD-26726	UCACUAUGGACUACCAGUU	5307	AACUGGUAGUCCAUAGUGA	5966	1729
AD-26727	UGGACUACCAGUUGUGGUU	5308	AACCACAACUGGUAGUCCA	5967	1735
AD-26728	GGACUACCAGUUGUGGUUA	5309	UAACCACAACUGGUAGUCC	5968	1736
AD-26729	GACUACCAGUUGUGGUUAA	5310	UUAACCACAACUGGUAGUC	5969	1737
AD-26730	CAGUUGUGGUUAAGCUCUU	5311	AAGAGCUUAACCACAACUG	5970	1743
AD-26731	AGUUGUGGUUAAGCUCUUA	5312	UAAGAGCUUAACCACAACU	5971	1744
AD-26732	AAGCUCUUACACCCACCAU	5313	AUGGUGGGUGUAAGAGCUU	5972	1754
AD-26733	CAUCCCACUGGCCUCUGAU	5314	AUCAGAGGCCAGUGGGAUG	5973	1770
AD-26734	AUCCCACUGGCCUCUGAUA	5315	UAUCAGAGGCCAGUGGGAU	5974	1771
AD-26735	UCCCACUGGCCUCUGAUAA	5316	UUAUCAGAGGCCAGUGGGA	5975	1772
AD-26736	UGGCCUCUGAUAAAGGCUA	5317	UAGCCUUUAUCAGAGGCCA	5976	1778
AD-26737	UCUGAUAAAGGCUACUGUU	5318	AACAGUAGCCUUUAUCAGA	5977	1783
AD-26738	AUAAAGGCUACUGUUGGAU	5319	AUCCAACAGUAGCCUUUAU	5978	1787
AD-26739	GGCUACUGUUGGAUUGAUU	5320	AAUCAAUCCAACAGUAGCC	5979	1792
AD-26740	UGUUGGAUUGAUUCGAAAU	5321	AUUUCGAAUCAAUCCAACA	5980	1798
AD-26741	UGCCAUUCCACGACUAGUU	5322	AACUAGUCGUGGAAUGGCA	5981	1861
AD-26742	UUCCACGACUAGUUCAGUU	5323	AACUGAACUAGUCGUGGAA	5982	1866
AD-26743	ACGACUAGUUCAGUUGCUU	5324	AAGCAACUGAACUAGUCGU	5983	1870
AD-26744	ACUAGUUCAGUUGCUUGUU	5325	AACAAGCAACUGAACUAGU	5984	1873

AD-26745	GUUGCUUGUUCGUGCACAU	5326	AUGUGCACGAACAAGCAAC	5985	1882
AD-26746	UGUUCGUGCACAUCAGGAU	5327	AUCCUGAUGUGCACGAACA	5986	1888
AD-26747	GUUCGUGCACAUCAGGAUA	5328	UAUCCUGAUGUGCACGAAC	5987	1889
AD-26748	GGUGGGACACAGCAGCAAU	5329	AUUGCUGCUGUGUCCCACC	5988	1928
AD-26749	GUGGGACACAGCAGCAAUU	5330	AAUUGCUGCUGUGUCCCAC	5989	1929
AD-26750	UGGGACACAGCAGCAAUUU	5331	AAAUUGCUGCUGUGUCCCA	5990	1930
AD-26751	GGGGUCCGCAUGGAAGAAA	5332	UUUCUUCCAUGCGGACCCC	5991	1955
AD-26752	GGGUCCGCAUGGAAGAAAU	5333	AUUUCUUCCAUGCGGACCC	5992	1956
AD-26753	UCACAUCCUAGCUCGGGAU	5334	AUCCCGAGCUAGGAUGUGA	5993	1999
AD-26754	CAUCCUAGCUCGGGAUGUU	5335	AACAUCCCGAGCUAGGAUG	5994	2002
AD-26755	UAGCUCGGGAUGUUCACAA	5336	UUGUGAACAUCCCGAGCUA	5995	2007
AD-26756	GGGAUGUUCACAACCGAAU	5337	AUUCGGUUGUGAACAUCCC	5996	2013
AD-26757	GGAUGUUCACAACCGAAUU	5338	AAUUCGGUUGUGAACAUCC	5997	2014
AD-26758	CAGAGGACUAAAUACCAUU	5339	AAUGGUAUUUAGUCCUCUG	5998	2038
AD-26759	GGACUAAAUACCAUUCCAU	5340	AUGGAAUGGUAUUUAGUCC	5999	2042
AD-26760	UAAAUACCAUUCCAUUGUU	5341	AACAAUGGAAUGGUAUUUA	6000	2046
AD-26761	AAAUACCAUUCCAUUGUUU	5342	AAACAAUGGAAUGGUAUUU	6001	2047
AD-26762	AUUGUUUGUGCAGCUGCUU	5343	AAGCAGCUGCACAAACAAU	6002	2059
AD-26763	UUGUUUGUGCAGCUGCUUU	5344	AAAGCAGCUGCACAAACAA	6003	2060
AD-26764	UGUUUGUGCAGCUGCUUUA	5345	UAAAGCAGCUGCACAAACA	6004	2061
AD-26765	GUUUGUGCAGCUGCUUUAU	5346	AUAAAGCAGCUGCACAAAC	6005	2062
AD-26766	UUUGUGCAGCUGCUUUAUU	5347	AAUAAAGCAGCUGCACAAA	6006	2063
AD-26767	AGCUGCUUUAUUCUCCCAU	5348	AUGGGAGAAUAAAGCAGCU	6007	2070
AD-26768	GCUGCUUUAUUCUCCCAUU	5349	AAUGGGAGAAUAAAGCAGC	6008	2071
AD-26769	UUUAUUCUCCCAUUGAAAA	5350	UUUUCAAUGGGAGAAUAAA	6009	2076
AD-26770	AUUCUCCCAUUGAAAACAU	5351	AUGUUUUCAAUGGGAGAAU	6010	2079
AD-26771	UCCCAUUGAAAACAUCCAA	5352	UUGGAUGUUUUCAAUGGGA	6011	2083
AD-26772	UGCAGGGGUCCUCUGUGAA	5353	UUCACAGAGGACCCCUGCA	6012	2110
AD-26773	ACUUGCUCAGGACAAGGAA	5354	UUCCUUGUCCUGAGCAAGU	6013	2128
AD-26774	CAGCUCCUCUGACAGAGUU	5355	AACUCUGUCAGAGGAGCUG	6014	2178
AD-26775	AGCUCCUCUGACAGAGUUA	5356	UAACUCUGUCAGAGGAGCU	6015	2179
AD-26776	UCCUCUGACAGAGUUACUU	5357	AAGUAACUCUGUCAGAGGA	6016	2182
AD-26777	ACAGAGUUACUUCACUCUA	5358	UAGAGUGAAGUAACUCUGU	6017	2189
AD-26778	AGUUACUUCACUCUAGGAA	5359	UUCCUAGAGUGAAGUAACU	6018	2193
AD-26779	GUUACUUCACUCUAGGAAU	5360	AUUCCUAGAGUGAAGUAAC	6019	2194
AD-26780	ACUUCACUCUAGGAAUGAA	5361	UUCAUUCCUAGAGUGAAGU	6020	2197
AD-26781	GCUGCUGUUUUGUUCCGAA	5362	UUCGGAACAAAACAGCAGC	6021	2234
AD-26782	CUGCUGUUUUGUUCCGAAU	5363	AUUCGGAACAAAACAGCAG	6022	2235
AD-26783	GUCUGAGGACAAGCCACAA	5364	UUGUGGCUUGUCCUCAGAC	6023	2254
AD-26784	UGAGGACAAGCCACAAGAU	5365	AUCUUGUGGCUUGUCCUCA	6024	2257
AD-26785	ACAAGCCACAAGAUUACAA	5366	UUGUAAUCUUGUGGCUUGU	6025	2262
AD-26786	AGCCACAAGAUUACAAGAA	5367	UUCUUGUAAUCUUGUGGCU	6026	2265
AD-26787	AGAUUACAAGAAACGGCUU	5368	AAGCCGUUUCUUGUAAUCU	6027	2272
AD-26788	CAAGAAACGGCUUUCAGUU	5369	AACUGAAAGCCGUUUCUUG	6028	2278

AD-26789	AGCUGACCAGCUCUCUCUU	5370	AAGAGAGAGCUGGUCAGCU	6029	2298
AD-26790	ACCAGCUCUCUCUUCAGAA	5371	UUCUGAAGAGAGAGCUGGU	6030	2303
AD-26791	UAUUGGUGCCCAGGGAGAA	5372	UUCUCCCUGGGCACCAAUA	6031	2365
AD-26792	CAGGGAGAACCCCUUGGAU	5373	AUCCAAGGGGUUCUCCCUG	6032	2375
AD-26793	AGGGAGAACCCCUUGGAUA	5374	UAUCCAAGGGGUUCUCCCU	6033	2376
AD-26794	CCUUGGAUAUCGCCAGGAU	5375	AUCCUGGCGAUAUCCAAGG	6034	2386
AD-26795	UAUCGCCAGGAUGAUCCUA	5376	UAGGAUCAUCCUGGCGAUA	6035	2393
AD-26796	GCCAGGAUGAUCCUAGCUA	5377	UAGCUAGGAUCAUCCUGGC	6036	2397
AD-26797	CCAGGAUGAUCCUAGCUAU	5378	AUAGCUAGGAUCAUCCUGG	6037	2398
AD-26798	GAUGAUCCUAGCUAUCGUU	5379	AACGAUAGCUAGGAUCAUC	6038	2402
AD-26799	AUCCUAGCUAUCGUUCUUU	5380	AAAGAACGAUAGCUAGGAU	6039	2406
AD-26800	UCCUAGCUAUCGUUCUUUU	5381	AAAAGAACGAUAGCUAGGA	6040	2407
AD-26801	UCUUUUCACUCUGGUGGAU	5382	AUCCACCAGAGUGAAAAGA	6041	2420
AD-26802	CUUUUCACUCUGGUGGAUA	5383	UAUCCACCAGAGUGAAAAG	6042	2421
AD-26803	UUUUCACUCUGGUGGAUAU	5384	AUAUCCACCAGAGUGAAAA	6043	2422
AD-26804	UGGUGGAUAUGGCCAGGAU	5385	AUCCUGGCCAUAUCCACCA	6044	2431
AD-26805	GAUAUGGCCAGGAUGCCUU	5386	AAGGCAUCCUGGCCAUAUC	6045	2436
AD-26806	CCUUGGGUAUGGACCCCAU	5387	AUGGGGUCCAUACCCAAGG	6046	2451
AD-26807	UGGGUAUGGACCCCAUGAU	5388	AUCAUGGGGUCCAUACCCA	6047	2454
AD-26808	UUGUAAACUUGAUUAACUA	5389	UAGUUAAUCAAGUUUACAA	6048	675
AD-26809	UGUAAACUUGAUUAACUAU	5390	AUAGUUAAUCAAGUUUACA	6049	676
AD-26810	AAACUUGAUUAACUAUCAA	5391	UUGAUAGUUAAUCAAGUUU	6050	679
AD-26811	UAUGGACCCCAUGAUGGAA	5392	UUCCAUCAUGGGGUCCAUA	6051	2458
AD-26812	GGACCCCAUGAUGGAACAU	5393	AUGUUCCAUCAUGGGGUCC	6052	2461
AD-26813	CCAUGAUGGAACAUGAGAU	5394	AUCUCAUGUUCCAUCAUGG	6053	2466
AD-26814	ACCACCCUGGUGCUGACUA	5395	UAGUCAGCACCAGGGUGGU	6054	2493
AD-26815	CCACCCUGGUGCUGACUAU	5396	AUAGUCAGCACCAGGGUGG	6055	2494
AD-26816	UGCUGACUAUCCAGUUGAU	5397	AUCAACUGGAUAGUCAGCA	6056	2503
AD-26817	AGUUGAUGGGCUGCCAGAU	5398	AUCUGGCAGCCCAUCAACU	6057	2515
AD-26818	UGCCCAGGACCUCAUGGAU	5399	AUCCAUGAGGUCCUGGGCA	6058	2542
AD-26819	GCAAUCAGCUGGCCUGGUU	5400	AACCAGGCCAGCUGAUUGC	6059	2580
AD-26820	CAAUCAGCUGGCCUGGUUU	5401	AAACCAGGCCAGCUGAUUG	6060	2581
AD-26821	GGUUUGAUACUGACCUGUA	5402	UACAGGUCAGUAUCAAACC	6061	2595
AD-26822	AUACUGACCUGUAAAUCAU	5403	AUGAUUUACAGGUCAGUAU	6062	2601
AD-26823	UGACCUGUAAAUCAUCCUU	5404	AAGGAUGAUUUACAGGUCA	6063	2605
AD-26824	GACCUGUAAAUCAUCCUUU	5405	AAAGGAUGAUUUACAGGUC	6064	2606
AD-26825	ACCUGUAAAUCAUCCUUUA	5406	UAAAGGAUGAUUUACAGGU	6065	2607
AD-26826	AAUACAAAUGAUGUAGAAA	5407	UUUCUACAUCAUUUGUAUU	6066	878
AD-26900	UUUUAAGAAUAUCUGUAAU	5408	AUUACAGAUAUUCUUAAAA	6067	2745
AD-26901	UACAGCAAUUUCUAAUUUU	5409	AAAAUUAGAAAUUGCUGUA	6068	2872
AD-26902	CACUAAUUCAUAAUCACUC	5410	GAGUGAUUAUGAAUUAGUG	6069	2915
AD-26903	ACUAAUUCAUAAUCACUCU	5411	AGAGUGAUUAUGAAUUAGU	6070	2916
AD-26904	UAAUUCAUAAUCACUCUAA	5412	UUAGAGUGAUUAUGAAUUA	6071	2918
AD-26905	AAUUCAUAAUCACUCUAAU	5413	AUUAGAGUGAUUAUGAAUU	6072	2919

AD-26906	AAUUGUAAUCUGAAUAAAG	5414	CUUUAUUCAGAUUACAAUU	6073	2939
AD-26907	UUUGUAUAAAAUAGACAAA	5415	UUUGUCUAUUUUAUACAAA	6074	2978
AD-26908	UUGUAUAAAAUAGACAAAU	5416	AUUUGUCUAUUUUAUACAA	6075	2979
AD-26909	UGUAUAAAAUAGACAAAUA	5417	UAUUUGUCUAUUUUAUACA	6076	2980
AD-26910	GUAUAAAAUAGACAAAUAG	5418	CUAUUUGUCUAUUUUAUAC	6077	2981
AD-26911	AUAAAAUAGACAAAUAGAA	5419	UUCUAUUUGUCUAUUUUAU	6078	2983
AD-26912	UAAAAUAGACAAAUAGAAA	5420	UUUCUAUUUGUCUAUUUUA	6079	2984
AD-26913	AAAUAGACAAAUAGAAAAU	5421	AUUUUCUAUUUGUCUAUUU	6080	2986
AD-26914	UGGGAUAUGUAUGGGUAGG	5422	CCUACCCAUACAUAUCCCA	6081	3081
AD-26915	GGGAUAUGUAUGGGUAGGG	5423	CCCUACCCAUACAUAUCCC	6082	3082
AD-26916	CUAAUUCAUAAUCACUCUA	5424	UAGAGUGAUUAUGAAUUAG	6083	2917
AD-26917	AAAUAGAAAAUGGUCCAAU	5425	AUUGGACCAUUUUCUAUUU	6084	2994
AD-26918	AAUAGAAAAUGGUCCAAUU	5426	AAUUGGACCAUUUUCUAUU	6085	2995
AD-26919	UUUGGACAGUUUACCAGUU	5427	AACUGGUAAACUGUCCAAA	6086	3134
AD-26920	AUUCUUUCUAACCUCACUU	5428	AAGUGAGGUUAGAAAGAAU	6087	1535
AD-26921	UGGAUUGAUUCGAAAUCUU	5429	AAGAUUUCGAAUCAAUCCA	6088	1801
SET1_1245	GACCCCAAGCUUUAGUAAA	6090	UUUACUAAAGCUUGGGGUC	6111	1227
SET1_1249	CCAAGCUUUAGUAAAUAUA	6091	UAUAUUUACUAAAGCUUGG	6112	1231
SET1_1250	CAAGCUUUAGUAAAUAUAA	6092	UUAUAUUUACUAAAGCUUG	6113	1232
SET1_1450	UUCAGAUGCUGCAACUAAA	6093	UUUAGUUGCAGCAUCUGAA	6114	1432
SET1_1545	CAGCUGGAAUUCUUUCUAA	6094	UUAGAAAGAAUUCCAGCUG	6115	1527
SET1_1755	GACUACCAGUUGUGGUUAA	6095	UUAACCACAACUGGUAGUC	6116	1737
SET1_1814	ACUGUUGGAUUGAUUCGAA	6096	UUCGAAUCAAUCCAACAGU	6117	1796
SET1_1816	UGUUGGAUUGAUUCGAAAU	6097	AUUUCGAAUCAAUCCAACA	6118	1798
SET1_1974	GGGUCCGCAUGGAAGAAAU	6098	AUUUCUUCCAUGCGGACCC	6119	1956
SET1_2202	CUCUGACAGAGUUACUUCA	6099	UGAAGUAACUCUGUCAGAG	6120	2184
SET1_2425	UCCUAGCUAUCGUUCUUUU	6100	AAAAGAACGAUAGCUAGGA	6121	2407
SET1_254	CCAUACAACUGUUUUGAAA	6101	UUUCAAAACAGUUGUAUGG	6122	236
SET1_3146	AAGUGAAGAAUGCACAAGA	6102	UCUUGUGCAUUCUUCACUU	6123	3128
SET1_3169	AUCACAAGAUGGAAUUUAU	6103	AUAAAUUCCAUCUUGUGAU	6124	3151
SET1_3196	AGCCUUGCUUGUUAAAUUU	6104	AAAUUUAACAAGCAAGGCU	6125	3178
SET1_3477	AAUAGAAAAUGGUCCAAUU	6105	AAUUGGACCAUUUUCUAUU	6126	3459
SET1_703	GAUUAACUAUCAAGAUGAU	6106	AUCAUCUUGAUAGUUAAUC	6127	685
SET1_709	CUAUCAAGAUGAUGCAGAA	6107	UUCUGCAUCAUCUUGAUAG	6128	691
SET1_865	GAUGGUGUCUGCUAUUGUA	6108	UACAAUAGCAGACACCAUC	6129	847
SET1_889	CAUGCAGAAUACAAAUGAU	6109	AUCAUUUGUAUUCUGCAUG	6130	871
SET1_895	GAAUACAAAUGAUGUAGAA	6110	UUCUACAUCAUUUGUAUUC	6131	877

[00778] 表 3 中列出修饰的序列;本文中列出具体修饰。表 2 中的序列对应于没有修饰或 dTdT 延长的野生型 β-联蛋白基因的部分。还提供位置。在这些表中的序列内,小写字母(例如,c、u)表示修饰的核苷酸,而大写字母(例如,C、U、A、G)表示未修饰的核苷酸。在表 3 中,显示序列的修饰形式。然而,本公开涵盖这些序列的未修饰形式和包含额外或替代性修饰的其他形式。因而,例如,AD-18892 可以任选地在有义链中具有未修饰的序列 uGGuGcuGAcuAuccAGuu(SEQ ID NO:429) 并且在反义链中具有序列

AACUGGAuAGUcAGcACcA(SEQ ID NO:430)。本公开还涵盖双链体的替代性经修饰形式,所述双链体在有义链中包含 uGGuGcuGAcuAuccAGuu(SEQ ID NO:429) 并且在反义链中包含 AACUGGAuAGUcAGcACcA(SEQ ID NO:430)。

[00779] 在表 1、2 和 3 的序列中,修饰的和未修饰的序列可以任选地在 3' 末端包含序列"dTsdT"或"UU"。在本文公开的序列中,TT 和 UU 二核苷酸不处于反转 / 反方向并且"UU"是 2' -OMe-U 2' -OMe-U。

[00780] 因此,例如,AD-18892 可以任选地在有义链中具有修饰的序列 uGGuGcuGAcuAuccAGuudTdT(SEQ ID NO:6132) 或 uGGuGcuGAcuAuccAGuudTsdT(SEQ ID NO:6133);并且在反义链中具有修饰的序列 AACUGGAuAGUcAGcACcAdTdT(SEQ ID NO:6134) 或 AACUGGAuAGUcAGcACcAdTsdT(SEQ ID NO:6135)。如下表 3 中所示,dT 是 2'- 脱氧胸苷 -5'- 磷酸并且 sdT 是 2'- 脱氧胸苷 5'- 硫代磷酸酯。[00781] 在这个表的几个序列中,名称"Set1_#"可以前置前缀"hsCTNNB1_"。因而,"Set1_254"又命名为"hsCTNNB1_Set1_254"。数字从基因上位置的一种类型计算推出。因而,名称 Set1_1245、Set1_1249、Set1_1250、Set1_1450、Set1_1545、Set1_1755、Set1_1814、Set1_1816、Set1_1974、Set1_2202、Set1_2425、Set1_254、Set1_3146、Set1_3169、Set1_3196、Set1_3477、Set1_703、Set1_709、Set1_865、Set1_889、Set1_895 表示与位置 1245、1249、1250、1450、1545、1755、1814、1816、1974、2202、2425、254、3146、3169、3196、3477、703、709、865、889、895 的一个类型计算分别对应的双链体(或其修饰的变体)。然而,使用与这个表中其他序列不同的参数,计算这些位置导致 18nt 的移位。因而,"Set1_254"指与位置 236 对应的序列。还指出,下划线 (_) 有时由空格 () 替换;因此,例如,"Set1_3169"与"Set13169"相同;并且"hsCTNNB1_Set2_254_A48_S26"与"hsCTNNB1Set2254A48S26"相同。

[00782] 此外,额外的后缀可以附着于名称以表示具有相同序列(例如,相同的核苷酸序列)、但是具有不同修饰的不同变体。因而,"hsCTNNB1_Set1_1245"内部划分的双链体变体尤其包括:hsCTNNB1_Set1_254_A22_S26;hsCTNNB1_Set1_254_A25_S27;hsCTNNB1_Set1_254_A_LO_V1_S26;hsCTNNB1_Set1_254_A_LO_V2_S_LO_V1;hsCTNNB1_Set2_254_A_LO_V3_S_LO_V2;hsCTNNB1_Set2_254_A_LO_V4_S_LO_V1;hsCTNNB1_Set2_254_A_LO_V5_S_LO_V1;和 hsCTNNB1_Set2_254_A48_S26。

表 3. β- 联蛋白 RNAi 剂:实施例修饰的序列

双链体	有义序列	有义 SEQ ID NO:	反义序列	反义 SEQ ID NO:	位置
AD-18892	uGGuGcuGAcuAuccAGuu	1	AACUGGAuAGUcAGcACcA	660	2500
AD-18893	ccAucuGuGcucuucGucA	2	UGACGAAGAGcAcAGAUGG	661	1659
AD-18894	AuAAGcAGGuGGAucuAuu	3	AAuAGAUCcACCUGCUuAU	662	3038
AD-18895	AuccAAAGAGuAGcuGcAG	4	CUGcAGCuACUCUUUGGAU	663	2096
AD-18896	GAcAAuGGcuAcucAAGcu	5	AGCUUGAGuAGCcAUUGUC	664	265
AD-18897	cuGuuGGAuuGAuucGAAA	6	UUUCGAAUcAAUCcAAcAG	665	1797
AD-18898	GcuGGccuGGuuuGAuAcu	7	AGuAUcAAACcAGGCcAGC	666	2587
AD-18899	ucuAAccucAcuuGcAAuA	8	uAUUGcAAGUGAGGUuAGA	667	1541
AD-18900	GAuAucGccAGGAuGAucc	9	GGAUcAUCCUGGCGAuAUC	668	2391
AD-18901	uGGccAucuuuAAGucuGG	10	CcAGACUuAAAGAUGGCcA	669	954
AD-18902	uGuAGAAcAcuAAuucAuA	11	uAUGAAUuAGUGUUCuAcA	670	2908
AD-18903	AucAGuAAGAGGuGuuAuu	12	AAuAAcACCUCUuACUGAU	671	3104
AD-18904	GuGcucuucGucAucuGAc	13	GUcAGAUGACGAAGAGcAC	672	1665
AD-18905	uGGuuuGAuAcuGAccuGu	14	AcAGGUcAGuAUcAAACcA	673	2594
AD-18906	ccAGuuGccuuuuAucccA	15	UGGGAuAAAAGGcAACUGG	674	3147
AD-18907	ccuGGuuuGAuAcuGAccu	16	AGGUcAGuAUcAAACcAGG	675	2592
AD-18908	GAcuAuccAGuuGAuGGGc	17	GCCcAUcAACUGGAuAGUC	676	2507
AD-18909	AGccAAuGGcuuGGAAuGA	18	UcAUUCcAAGCcAUUGGCU	677	2325
AD-18910	GccAAuGGcuuGGAAuGAG	19	CUcAUUCcAAGCcAUUGGC	678	2326
AD-18911	AGAuGAGGGcAuGcAGAuc	20	GAUCUGcAUGCCCUcAUCU	679	577
AD-18912	GGuccucuGuGAAcuuGcu	21	AGcAAGUUcAcAGAGGACC	680	2116
AD-18913	AAcccuAGccuuGcuuGuu	22	AAcAAGcAAGGCuAGGGUU	681	2708
AD-18914	GAAcAcuAAuucAuAAucA	23	UGAUuAUGAAUuAGUGUUC	682	2912
AD-18915	AucAAAcccuAGccuuGcu	24	AGcAAGGCuAGGGUUUGAU	683	2704

AD-18916	AccAGuuGccuuuuAuccc	25	GGGAuAAAAGGcAACUGGU	684	3146
AD-18917	cuAAccucAcuuGcAAuAA	26	UuAUUGcAAGUGAGGUuAG	685	1542
AD-18918	AucccAcuAAuGuccAGcG	27	CGCUGGAcAUuAGUGGGAU	686	621
AD-18919	cuGAcuAuccAGuuGAuGG	28	CcAUcAACUGGAuAGUcAG	687	2505
AD-18920	GGccuGGuuuGAuAcuGAc	29	GUcAGuAUcAAACcAGGCC	688	2590
AD-18921	GGuAAAucAGuAAGAGGuG	30	cACCUCUuACUGAUUuACC	689	3099
AD-18922	GccuGGuuuGAuAcuGAcc	31	GGUcAGuAUcAAACcAGGC	690	2591
AD-18923	cAGGGGuccucuGuGAAcu	32	AGUUcAcAGAGGACCCCUG	691	2112
AD-18925	cuGGAAuccAuucuGGuGc	33	GcACcAGAAUGGAUUCcAG	692	366
AD-18926	uGAGAuGGGuGGccAccAc	34	GUGGUGGCcACCcAUCUcA	693	2479
AD-18927	GAuGAuAuAAAuGuGGucA	35	UGACcAcAUUuAuAUcAUC	694	1502
AD-18928	uGcuuuAuucucccAuuGA	36	UcAAUGGGAGAAuAAAGcA	695	2073
AD-18929	uuAucAAAcccuAGccuuG	37	cAAGGCuAGGGUUUGAuAA	696	2702
AD-18930	ccAcuGGccucuGAuAAAG	38	CUUuAUcAGAGGCcAGUGG	697	1774
AD-18931	AAcuuGccAcAcGuGcAAu	39	AUUGcACGUGUGGcAAGUU	698	708
AD-18932	GcucuucGucAucuGAccA	40	UGGUcAGAUGACGAAGAGC	699	1667
AD-18933	GuAAcAAuAcAAAuGGAuu	41	AAUCcAUUUGuAUUGUuAC	700	2629
AD-18934	GGGGuccucuGuGAAcuuG	42	cAAGUUcAcAGAGGACCCC	701	2114
AD-18935	cAAAcccuAGccuuGcuuG	43	cAAGcAAGGCuAGGGUUUG	702	2706
AD-18936	GAGuAAuGGuGuAGAAcAc	44	GUGUUCuAcACcAUuACUC	703	2899
AD-18937	GGAAGAcAucAcuGAGccu	45	AGGCUcAGUGAUGUCUUCC	704	1639
AD-18938	GGGAAGAcAucAcuGAGcc	46	GGCUcAGUGAUGUCUUCCC	705	1638
AD-18939	GGuGuAGAAcAcuAAuucA	47	UGAAUuAGUGUUCuAcACC	706	2906
AD-18940	uAccAGuuGccuuuuAucc	48	GGAuAAAAGGcAACUGGuA	707	3145
AD-18941	GGAuAucGccAGGAuGAuc	49	GAUcAUCCUGGCGAuAUCC	708	2390
AD-18942	AAAcccuAGccuuGcuuGu	50	AcAAGcAAGGCuAGGGUUU	709	2707
AD-18943	cucuucGucAucuGAccAG	51	CUGGUcAGAUGACGAAGAG	710	1668
AD-18944	uGAcuAuccAGuuGAuGGG	52	CCcAUcAACUGGAuAGUcA	711	2506
AD-18945	AcAAGcAGAGuGcuGAAGG	53	CCUUcAGcACUCUGCUUGU	712	1286
AD-18946	cAucuGuGcucuucGucAu	54	AUGACGAAGAGcAcAGAUG	713	1660
AD-18947	cAAuGGcuuGGAAuGAGAc	55	GUCUcAUUCcAAGCcAUUG	714	2328
AD-18948	AcuGGccucuGAuAAAGGc	56	GCCUUuAUcAGAGGCcAGU	715	1776
AD-18949	ucAucccAcuAAuGuccAG	57	CUGGAcAUuAGUGGGAUGA	716	619
AD-18950	AAAAGGAAGcuuccAGAcA	58	UGUCUGGAAGCUUCCUUUU	717	807
AD-18951	cGuucuuuucAcucuGGuG	59	cACcAGAGUGAAAAGAACG	718	2417
AD-18952	AAAGuuGuuGuAAccuGcu	60	AGcAGGUuAcAAcAACUUU	719	3165
AD-18953	AcAAuGGcuAcucAAGcuG	61	cAGCUUGAGuAGCcAUUGU	720	266
AD-18954	cucAucccAcuAAuGuccA	62	UGGAcAUuAGUGGGAUGAG	721	618
AD-18955	AGGGGuccucuGuGAAcuu	63	AAGUUcAcAGAGGACCCCU	722	2113
AD-18956	AAGcAGGuGGAucuAuuuc	64	GAAAuAGAUCcACCUGCUU	723	3040
AD-18957	AAGuuGuuGuAAccuGcuG	65	cAGcAGGUuAcAAcAACUU	724	3166
AD-18958	AGcAGGuGGAucuAuuucA	66	UGAAAuAGAUCcACCUGCU	725	3041
AD-18959	AGGGcAuGcAGAucccAuc	67	GAUGGGAUCUGcAUGCCCU	726	582
AD-18960	AAAuGGuucAGAAuuAAAc	68	GUUuAAUUCUGAACcAUUU	727	3220
AD-18961	uGAAcuuGcucAGGAcAAG	69	CUUGUCCUGAGcAAGUUcA	728	2125

AD-18962	AAGAGuAGcuGcAGGGGuc	70	GACCCCUGcAGCuACUCUU	729	2101
AD-18963	cccAcuGGccucuGAuAAA	71	UUuAUcAGAGGCcAGUGGG	730	1773
AD-18964	cuGGccuGGuuuGAuAcuG	72	cAGuAUcAAACcAGGCcAG	731	2588
AD-18965	uuGAuAcuGAccuGuAAAu	73	AUUuAcAGGUcAGuAUcAA	732	2598
AD-18966	GuGuAGAAcAcuAAuucAu	74	AUGAAUuAGUGUUCuAcAC	733	2907
AD-18967	AcuAuccAGuuGAuGGGcu	75	AGCCcAUcAACUGGAuAGU	734	2508
AD-18968	AAAucAGuAAGAGGuGuuA	76	uAAcACCUCUuACUGAUUU	735	3102
AD-18969	GcAGGuGGAucuAuuucAu	77	AUGAAAuAGAUCcACCUGC	736	3042
AD-18970	cuGGuGcuGAcuAuccAGu	78	ACUGGAuAGUcAGcACcAG	737	2499
AD-18971	GuGAAcuuGcucAGGAcAA	79	UUGUCCUGAGcAAGUUcAC	738	2124
AD-18972	ucAGuAAGAGGuGuuAuuu	80	AAAuAAcACCUCUuACUGA	739	3105
AD-18973	ccucuGuGAAcuuGcucAG	81	CUGAGcAAGUUcAcAGAGG	740	2119
AD-18974	uuGGcuGAAccAucAcAGA	82	UCUGUGAUGGUUcAGCcAA	741	641
AD-18975	ucAGcuGGccuGGuuuGAu	83	AUcAAACcAGGCcAGCUGA	742	2584
AD-18976	GuAGcuGcAGGGGuccucu	84	AGAGGACCCCUGcAGCuAC	743	2105
AD-18977	AGGAGcuAAAAuGGcAGuG	85	cACUGCcAUUUuAGCUCCU	744	1069
AD-18978	AuGGcuuGGAAuGAGAcuG	86	cAGUCUcAUUCcAAGCcAU	745	2330
AD-18979	uuGGAuAucGccAGGAuGA	87	UcAUCCUGGCGAuAUCcAA	746	2388
AD-18980	GGuucAGAAuuAAAcuuuu	88	AAAAGUUuAAUUCUGAACC	747	3224
AD-18981	GGGuAAAucAGuAAGAGGu	89	ACCUCUuACUGAUUuACCC	748	3098
AD-18982	AuAccAuuccAuuGuuuGu	90	AcAAAcAAUGGAAUGGuAU	749	2049
AD-18983	AcuGuuGGAuuGAuucGAA	91	UUCGAAUcAAUCcAAcAGU	750	1796
AD-18984	AAcuuGcucAGGAcAAGGA	92	UCCUUGUCCUGAGcAAGUU	751	2127
AD-18985	AuGcuuAAAAuAAGcAGGu	93	ACCUGCUuAUUUuAAGcAU	752	3029
AD-18986	GuuuGAuAcuGAccuGuAA	94	UuAcAGGUcAGuAUcAAAC	753	2596
AD-18987	AAuGGuucAGAAuuAAAcu	95	AGUUuAAUUCUGAACcAUU	754	3221
AD-18988	uAucccAAAGuuGuuGuAA	96	UuAcAAcAACUUUGGGAuA	755	3159
AD-18989	AucAGcuGGccuGGuuuGA	97	UcAAACcAGGCcAGCUGAU	756	2583
AD-18990	ccuGccAucuGuGcucuuc	98	GAAGAGcAcAGAUGGcAGG	757	1655
AD-18991	GcAGAAuAcAAAuGAuGuA	99	uAcAUcAUUUGuAUUCUGC	758	874
AD-18992	uAuGcuuAAAAuAAGcAGG	100	CCUGCUuAUUUuAAGcAuA	759	3028
AD-18993	AAuAAGcAGGuGGAucuAu	101	AuAGAUCcACCUGCUuAUU	760	3037
AD-18994	uGAuAuAAAuGuGGucAcc	102	GGUGACcAcAUUuAuAUcA	761	1504
AD-18995	GuAGGGuAAAucAGuAAGA	103	UCUuACUGAUUuACCCuAC	762	3095
AD-18996	uAucAAAcccuAGccuuGc	104	GcAAGGCuAGGGUUUGAuA	763	2703
AD-18997	ccuuuuAucccAAAGuuGu	105	AcAACUUUGGGAuAAAAGG	764	3154
AD-18998	GGuAGGGuAAAucAGuAAG	106	CUuACUGAUUuACCCuACC	765	3094
AD-18999	uGAuAcuGAccuGuAAAuc	107	GAUUuAcAGGUcAGuAUcA	766	2599
AD-19000	GGcuGAAccAucAcAGAuG	108	cAUCUGUGAUGGUUcAGCC	767	643
AD-19001	uGGAuAucGccAGGAuGAu	109	AUcAUCCUGGCGAuAUCcA	768	2389
AD-19002	ucuucGucAucuGAccAGc	110	GCUGGUcAGAUGACGAAGA	769	1669
AD-19003	uAGcuGcAGGGGuccucuG	111	cAGAGGACCCCUGcAGCuA	770	2106
AD-19004	uGuuGuAAccuGcuGuGAu	112	AUcAcAGcAGGUuAcAAcA	771	3170
AD-19005	AAucAGuAAGAGGuGuuAu	113	AuAAcACCUCUuACUGAUU	772	3103
AD-19006	uGGcuGAAccAucAcAGAu	114	AUCUGUGAUGGUUcAGCcA	773	642

AD-19007	GAAuuAAAcuuuuAAuucA	115	UGAAUuAAAAGUUuAAUUC	774	3230
AD-19008	AuGGuucAGAAuuAAAcuu	116	AAGUUuAAUUCUGAACcAU	775	3222
AD-19009	uGGuGuAGAAcAcuAAuuc	117	GAAUuAGUGUUCuAcACcA	776	2905
AD-19010	AuGGuGuAGAAcAcuAAuu	118	AAUuAGUGUUCuAcACcAU	777	2904
AD-19011	AuGAGGGcAuGcAGAuccc	119	GGGAUCUGcAUGCCCUcAU	778	579
AD-19012	GuuGuAAccuGcuGuGAuA	120	uAUcAcAGcAGGUuAcAAC	779	3171
AD-19042	GcuGAcuAuccAGuuGAuG	121	cAUcAACUGGAuAGUcAGC	780	2504
AD-19043	uAAGcAGGuGGAucuAuuu	122	AAAuAGAUCcACCUGCUuA	781	3039
AD-19044	uAAAAuAAGcAGGuGGAuc	123	GAUCcACCUGCUuAUUUuA	782	3034
AD-19045	GAuAuAAAuGuGGucAccu	124	AGGUGACcAcAUUuAuAUC	783	1505
AD-19046	AAGcAGAGuGcuGAAGGuG	125	cACCUUcAGcACUCUGCUU	784	1288
AD-19047	uGuGAAcuuGcucAGGAcA	126	UGUCCUGAGcAAGUUcAcA	785	2123
AD-19048	cAucccAcuAAuGuccAGc	127	GCUGGAcAUuAGUGGGAUG	786	620
AD-19049	cAAAGuuGuuGuAAccuGc	128	GcAGGUuAcAAcAACUUUG	787	3164
AD-19050	uAAAucAGuAAGAGGuGuu	129	AAcACCUCUuACUGAUUuA	788	3101
AD-19051	AAuGGcuuGGAAuGAGAcu	130	AGUCUcAUUCcAAGCcAUU	789	2329
AD-19052	GGGuccucuGuGAAcuuGc	131	GcAAGUUcAcAGAGGACCC	790	2115
AD-19053	GAGuAAcAAuAcAAAuGGA	132	UCcAUUUGuAUUGUuACUC	791	2627
AD-19054	uAAuGGuGuAGAAcAcuAA	133	UuAGUGUUCuAcACcAUuA	792	2902
AD-19055	GuGGAcAAuGGcuAcucAA	134	UUGAGuAGCcAUUGUCcAC	793	262
AD-19056	AAcuGucuuuGGAcucucA	135	UGAGAGUCcAAAGAcAGUU	794	1406
AD-19057	cccuGGuGcuGAcuAuccA	136	UGGAuAGUcAGcACcAGGG	795	2497
AD-19058	cAGGuGGAucuAuuucAuG	137	cAUGAAAuAGAUCcACCUG	796	3043
AD-19059	uGGccuGGuuuGAuAcuGA	138	UcAGuAUcAAACcAGGCcA	797	2589
AD-19060	AGcuGGccuGGuuuGAuAc	139	GuAUcAAACcAGGCcAGCU	798	2586
AD-19061	GccAucuGuGcucuucGuc	140	GACGAAGAGcAcAGAUGGC	799	1658
AD-19062	uAccAuuccAuuGuuuGuG	141	cAcAAAcAAUGGAAUGGuA	800	2050
AD-19063	cccuuGGAuAucGccAGGA	142	UCCUGGCGAuAUCcAAGGG	801	2385
AD-19064	AGGGAAGAcAucAcuGAGc	143	GCUcAGUGAUGUCUUCCCU	802	1637
AD-19065	GAAcuuGccAcAcGuGcAA	144	UUGcACGUGUGGcAAGUUC	803	707
AD-19066	uuuGAuAcuGAccuGuAAA	145	UUuAcAGGUcAGuAUcAAA	804	2597
AD-19067	ucccAAAGuuGuuGuAAcc	146	GGUuAcAAcAACUUUGGGA	805	3161
AD-19068	cAGAAuAcAAAuGAuGuAG	147	CuAcAUcAUUUGuAUUCUG	806	875
AD-19069	AGGuGGAucuAuuucAuGu	148	AcAUGAAAuAGAUCcACCU	807	3044
AD-19070	GcucAucccAcuAAuGucc	149	GGAcAUuAGUGGGAUGAGC	808	617
AD-19071	ccuGGuGcuGAcuAuccAG	150	CUGGAuAGUcAGcACcAGG	809	2498
AD-19072	uGGAAuccAuucuGGuGcc	151	GGcACcAGAAUGGAUUCcA	810	367
AD-19073	ccAGGAccucAuGGAuGGG	152	CCcAUCcAUGAGGUCCUGG	811	2545
AD-19074	AAccucAcuuGcAAuAAuu	153	AAUuAUUGcAAGUGAGGUU	812	1544
AD-19075	cAGuuGccuuuuAucccAA	154	UUGGGAuAAAAGGcAACUG	813	3148
AD-19076	GuAGAAcAcuAAuucAuAA	155	UuAUGAAUuAGUGUUCuAC	814	2909
AD-19077	cuAuccAGuuGAuGGGcuG	156	cAGCCcAUcAACUGGAuAG	815	2509
AD-19078	cAcuGGccucuGAuAAAGG	157	CCUUuAUcAGAGGCcAGUG	816	1775
AD-19079	AcuGucuuuGGAcucucAG	158	CUGAGAGUCcAAAGAcAGU	817	1407
AD-19080	ccAAuGGcuuGGAAuGAGA	159	UCUcAUUCcAAGCcAUUGG	818	2327

AD-19081	GcuuAAAAuAAGcAGGuGG	160	CcACCUGCUuAUUUuAAGC	819	3031
AD-19082	AucuGuGcucuucGucAuc	161	GAUGACGAAGAGcAcAGAU	820	1661
AD-19083	cccAAAGuuGuuGuAAccu	162	AGGUuAcAAcAACUUUGGG	821	3162
AD-19738	uAcccAGcGccGuAcGucc	163	GGACGuACGGCGCUGGGuA	822	1906
AD-19739	AcGcuAucAuGcGuucucc	164	GGAGAACGcAUGAuAGCGU	823	825
AD-19740	cAuGcAccuuuGcGuGAGc	165	GCUcACGcAAAGGUGcAUG	824	1838
AD-19741	GAAuGcAGuucGccuucAc	166	GUGAAGGCGAACUGcAUUC	825	1714
AD-19742	GGuGccAuuccAcGAcuAG	167	CuAGUCGUGGAAUGGcACC	826	1859
AD-19743	AAGcGGcuGuuAGucAcuG	168	cAGUGACuAAcAGCCGCUU	827	324
AD-19744	ucGAGcucAGAGGGuAcGA	169	UCGuACCCUCUGAGCUCGA	828	535
AD-19745	GAcAcGcuAucAuGcGuuc	170	GAACGcAUGAuAGCGUGUC	829	822
AD-19746	cGcuAucAuGcGuucuccu	171	AGGAGAACGcAUGAuAGCG	830	826
AD-19747	GuGucuGcuAuuGuAcGuA	172	uACGuAcAAuAGcAGAcAC	831	851
AD-19748	GucuGcucuAGuAAuAAGc	173	GCUuAUuACuAGAGcAGAC	832	1313
AD-19749	GuGccAuuccAcGAcuAGu	174	ACuAGUCGUGGAAUGGcAC	833	1860
AD-19750	AuGuucAcAAccGAAuuGu	175	AcAAUUCGGUUGUGAAcAU	834	2016
AD-19751	ccAcGAcuAGuucAGuuGc	176	GcAACUGAACuAGUCGUGG	835	1868
AD-19752	cAcGAcuAGuucAGuuGcu	177	AGcAACUGAACuAGUCGUG	836	1869
AD-19753	AGuucAGuuGcuuGuucGu	178	ACGAAcAAGcAACUGAACU	837	1876
AD-19754	cccAGcGccGuAcGuccAu	179	AUGGACGuACGGCGCUGGG	838	1908
AD-19755	GAGuuAcuucAcucuAGGA	180	UCCuAGAGUGAAGuAACUC	839	2192
AD-19756	AcAGuAuGcAAuGAcucGA	181	UCGAGUcAUUGcAuACUGU	840	520
AD-19757	uAuGcAAuGAcucGAGcuc	182	GAGCUCGAGUcAUUGcAuA	841	524
AD-19758	cccAcuAAuGuccAGcGuu	183	AACGCUGGAcAUuAGUGGG	842	623
AD-19759	GAccuuGcAuAAccuuucc	184	GGAAAGGUuAUGcAAGGUC	843	916
AD-19760	uAuuAcGAcAGAcuGccuu	185	AAGGcAGUCUGUCGuAAuA	844	1153
AD-19761	AucuGAccAGccGAcAccA	186	UGGUGUCGGCUGGUcAGAU	845	1677
AD-19762	cAuuccAcGAcuAGuucAG	187	CUGAACuAGUCGUGGAAUG	846	1864
AD-19763	GuuuuGAAAAuccAGcGuG	188	cACGCUGGAUUUUcAAAAC	847	246
AD-19765	GcGuuuGGcuGAAccAucA	189	UGAUGGUUcAGCcAAACGC	848	637
AD-19766	AcAcGcuAucAuGcGuucu	190	AGAACGcAUGAuAGCGUGU	849	823
AD-19767	uAuGccAuuAcAAcucucc	191	GGAGAGUUGuAAUGGcAuA	850	1028
AD-19768	ucuGcucuAGuAAuAAGcc	192	GGCUuAUuACuAGAGcAGA	851	1314
AD-20124	cGGGAuGuucAcAAccGAA	193	UUCGGUUGUGAAcAUCCCG	852	2012
AD-25889	AcAAuAcAAAuGGAuuuuG	194	cAAAAUCcAUUUGuAUUGU	853	2632
AD-25890	AcAAAuGGAuuuuGGGAGu	195	ACUCCcAAAAUCcAUUUGU	854	2637
AD-25891	uuGGGAGuGAcucAAGAAG	196	CUUCUUGAGUcACUCCcAA	855	2648
AD-25892	uGGGAGuGAcucAAGAAGu	197	ACUUCUUGAGUcACUCCcA	856	2649
AD-25893	GAAGuGAAGAAuGcAcAAG	198	CUUGUGcAUUCUUcACUUC	857	2663
AD-25894	AAGuGAAGAAuGcAcAAGA	199	UCUUGUGcAUUCUUcACUU	858	2664
AD-25895	GAuGGAAuuuAucAAAccc	200	GGGUUUGAuAAAUUCcAUC	859	2694
AD-25896	AuGGAAuuuAucAAAcccu	201	AGGGUUUGAuAAAUUCcAU	860	2695
AD-25897	GGAAuuuAucAAAcccuAG	202	CuAGGGUUUGAuAAAUUCC	861	2697
AD-25898	GAAuuuAucAAAcccuAGc	203	GCuAGGGUUUGAuAAAUUC	862	2698
AD-25899	AAuuuAucAAAcccuAGcc	204	GGCuAGGGUUUGAuAAAUU	863	2699

AD-25900	GAAuAucuGuAAuGGuAcu	205	AGuACcAUuAcAGAuAUUC	864	2751
AD-25901	AAuAucuGuAAuGGuAcuG	206	cAGuACcAUuAcAGAuAUU	865	2752
AD-25902	AuAucuGuAAuGGuAcuGA	207	UcAGuACcAUuAcAGAuAU	866	2753
AD-25903	uuuuAAGucucucGuAGuG	208	cACuACGAGAGACUuAAAA	867	2832
AD-25904	uuuAAGucucucGuAGuGu	209	AcACuACGAGAGACUuAAA	868	2833
AD-25905	AGucucucGuAGuGuuAAG	210	CUuAAcACuACGAGAGACU	869	2837
AD-25906	ucGuAGuGuuAAGuuAuAG	211	CuAuAACUuAAcACuACGA	870	2843
AD-25907	cGuAGuGuuAAGuuAuAGu	212	ACuAuAACUuAAcACuACG	871	2844
AD-25908	GuAGuGuuAAGuuAuAGuG	213	cACuAuAACUuAAcACuAC	872	2845
AD-25909	uAGuGuuAAGuuAuAGuGA	214	UcACuAuAACUuAAcACuA	873	2846
AD-25910	uAGuGAAuAcuGcuAcAGc	215	GCUGuAGcAGuAUUcACuA	874	2859
AD-25911	AAcAcuAAuucAuAAucAc	216	GUGAUuAUGAAUuAGUGUU	875	2913
AD-25912	AcAcuAAuucAuAAucAcu	217	AGUGAUuAUGAAUuAGUGU	876	2914
AD-25913	uAAuuGuAAucuGAAuAAA	218	UUuAUUcAGAUuAcAAUuA	877	2938
AD-25914	AuuGuAAucuGAAuAAAGu	219	ACUUuAUUcAGAUuAcAAU	878	2940
AD-25915	uuGuAAucuGAAuAAAGuG	220	cACUUuAUUcAGAUuAcAA	879	2941
AD-25916	uGuAAucuGAAuAAAGuGu	221	AcACUUuAUUcAGAUuAcA	880	2942
AD-25917	GAcAAAuAGAAAAuGGucc	222	GGACcAUUUUCuAUUUGUC	881	2991
AD-25918	AcAAAuAGAAAAuGGuccA	223	UGGACcAUUUUCuAUUUGU	882	2992
AD-25919	uAGAAAAuGGuccAAuuAG	224	CuAAUUGGACcAUUUUCuA	883	2997
AD-25920	AGAAAAuGGuccAAuuAGu	225	ACuAAUUGGACcAUUUUCU	884	2998
AD-25921	uAuuuGGGAuAuGuAuGGG	226	CCcAuAcAuAUCCcAAAuA	885	3077
AD-25922	AuuuGGGAuAuGuAuGGGu	227	ACCcAuAcAuAUCCcAAAU	886	3078
AD-25923	uuGGGAuAuGuAuGGGuAG	228	CuACCcAuAcAuAUCCcAA	887	3080
AD-25924	GGAuAuGuAuGGGuAGGGu	229	ACCCuACCcAuAcAuAUCC	888	3083
AD-25925	AAGAGGuGuuAuuuGGAAc	230	GUUCcAAAuAAcACCUCUU	889	3110
AD-25926	AGAGGuGuuAuuuGGAAcc	231	GGUUCcAAAuAAcACCUCU	890	3111
AD-25927	GAGGuGuuAuuuGGAAccu	232	AGGUUCcAAAuAAcACCUC	891	3112
AD-25928	uGGAAccuuGuuuuGGAcA	233	UGUCcAAAAcAAGGUUCcA	892	3123
AD-25929	GGAAccuuGuuuuGGAcAG	234	CUGUCcAAAAcAAGGUUCC	893	3124
AD-25930	GAAccuuGuuuuGGAcAGu	235	ACUGUCcAAAAcAAGGUUC	894	3125
AD-25931	GuuuuGGAcAGuuuAccAG	236	CUGGuAAACUGUCcAAAAC	895	3132
AD-25932	uuuuGGAcAGuuuAccAGu	237	ACUGGuAAACUGUCcAAAA	896	3133
AD-25933	uuGGAcAGuuuAccAGuuG	238	cAACUGGuAAACUGUCcAA	897	3135
AD-25934	GuuGuuGuAAccuGcuGuG	239	cAcAGcAGGUuAcAAcAAC	898	3168
AD-25935	uuGuuGuAAccuGcuGuGA	240	UcAcAGcAGGUuAcAAcAA	899	3169
AD-25936	uuGuAAccuGcuGuGAuAc	241	GuAUcAcAGcAGGUuAcAA	900	3172
AD-25937	AuGcuucAAGAGAAAAuGc	242	GcAUUUUCUCUUGAAGcAU	901	3192
AD-25938	AGuGAAGAAuGcAcAAGAA	243	UUCUUGUGcAUUCUUcACU	902	2665
AD-25939	AAuGGAucAcAAGAuGGAA	244	UUCcAUCUUGUGAUCcAUU	903	2682
AD-25940	AuGGAucAcAAGAuGGAAu	245	AUUCcAUCUUGUGAUCcAU	904	2683
AD-25941	uGGAucAcAAGAuGGAAuu	246	AAUUCcAUCUUGUGAUCcA	905	2684
AD-25942	GGAucAcAAGAuGGAAuuu	247	AAAUUCcAUCUUGUGAUCC	906	2685
AD-25943	GAucAcAAGAuGGAAuuuA	248	uAAAUUCcAUCUUGUGAUC	907	2686
AD-25944	AucAcAAGAuGGAAuuuAu	249	AuAAAUUCcAUCUUGUGAU	908	2687

AD-25945	uGGAAuuuAucAAAcccuA	250	uAGGGUUUGAuAAAUUCcA	909	2696
AD-25946	AcccuAGccuuGcuuGuuA	251	uAAcAAGcAAGGCuAGGGU	910	2709
AD-25947	cccuAGccuuGcuuGuuAA	252	UuAAcAAGcAAGGCuAGGG	911	2710
AD-25948	ccuAGccuuGcuuGuuAAA	253	UUuAAcAAGcAAGGCuAGG	912	2711
AD-25949	cuAGccuuGcuuGuuAAAu	254	AUUuAAcAAGcAAGGCuAG	913	2712
AD-25950	uAGccuuGcuuGuuAAAuu	255	AAUUuAAcAAGcAAGGCuA	914	2713
AD-25951	AGccuuGcuuGuuAAAuuu	256	AAAUUuAAcAAGcAAGGCU	915	2714
AD-25952	uuAAGucucucGuAGuGuu	257	AAcACuACGAGAGACUuAA	916	2834
AD-25953	uAAGucucucGuAGuGuuA	258	uAAcACuACGAGAGACUuA	917	2835
AD-25954	AAGucucucGuAGuGuuAA	259	UuAAcACuACGAGAGACUU	918	2836
AD-25955	cucGuAGuGuuAAGuuAuA	260	uAuAACUuAAcACuACGAG	919	2842
AD-25956	AGuGuuAAGuuAuAGuGAA	261	UUcACuAuAACUuAAcACU	920	2847
AD-25957	GuGuuAAGuuAuAGuGAAu	262	AUUcACuAuAACUuAAcAC	921	2848
AD-25958	cuAcAGcAAuuucuAAuuu	263	AAAUuAGAAAUUGCUGuAG	922	2871
AD-25959	cAAAuAGAAAAuGGuccAA	264	UUGGACcAUUUUCuAUUUG	923	2993
AD-25960	AuAGAAAAuGGuccAAuuA	265	uAAUUGGACcAUUUUCuAU	924	2996
AD-25961	uuuGGGAuAuGuAuGGGuA	266	uACCcAuAcAuAUCCcAAA	925	3079
AD-25962	GAuAuGuAuGGGuAGGGuA	267	uACCCuACCcAuAcAuAUC	926	3084
AD-25963	uGGGuAGGGuAAAucAGuA	268	uACUGAUUuACCCuACCcA	927	3092
AD-25964	uAAGAGGuGuuAuuuGGAA	269	UUCcAAAuAAcACCUCUuA	928	3109
AD-26017	uGccuuuuAucccAAAGuu	270	AACUUUGGGAuAAAAGGcA	929	3152
AD-26018	uGuuGuAAccuGcuGuGAu	271	AUcAcAGcAGGUuAcAAcA	930	3170
AD-26019	GuuGuAAccuGcuGuGAuA	272	uAUcAcAGcAGGUuAcAAC	931	3171
AD-26020	cAAGAGAAAAuGcGGuuAu	273	AuAACCGcAUUUUCUCUUG	932	3198
AD-26021	AAGAGAAAAuGcGGuuAuA	274	uAuAACCGcAUUUUCUCUU	933	3199
AD-26022	ccuGuuccccuGAGGGuAu	275	AuACCCUcAGGGGAAcAGG	934	207
AD-26023	cuGuuccccuGAGGGuAuu	276	AAuACCCUcAGGGGAAcAG	935	208
AD-26024	ccuGAGGGuAuuuGAAGuA	277	uACUUcAAAuACCCUcAGG	936	215
AD-26025	cuGAGGGuAuuuGAAGuAu	278	AuACUUcAAAuACCCUcAG	937	216
AD-26026	uGAGGGuAuuuGAAGuAuA	279	uAuACUUcAAAuACCCUcA	938	217
AD-26027	GGuAuuuGAAGuAuAccAu	280	AUGGuAuACUUcAAAuACC	939	221
AD-26028	GuAuuuGAAGuAuAccAuA	281	uAUGGuAuACUUcAAAuAC	940	222
AD-26029	uuuGAAGuAuAccAuAcAA	282	UUGuAUGGuAuACUUcAAA	941	225
AD-26030	AGuAuAccAuAcAAcuGuu	283	AAcAGUUGuAUGGuAuACU	942	230
AD-26031	GuAuAccAuAcAAcuGuuu	284	AAAcAGUUGuAUGGuAuAC	943	231
AD-26032	uAuAccAuAcAAcuGuuuu	285	AAAAcAGUUGuAUGGuAuA	944	232
AD-26033	AccAuAcAAcuGuuuuGAA	286	UUcAAAAcAGUUGuAUGGU	945	235
AD-26034	ccAuAcAAcuGuuuuGAAA	287	UUUcAAAAcAGUUGuAUGG	946	236
AD-26035	GAAAAuccAGcGuGGAcAA	288	UUGUCcACGCUGGAUUUUC	947	251
AD-26036	AAAAuccAGcGuGGAcAAu	289	AUUGUCcACGCUGGAUUUU	948	252
AD-26037	ccAGcGuGGAcAAuGGcuA	290	uAGCcAUUGUCcACGCUGG	949	257
AD-26038	GuGGAcAAuGGcuAcucAA	291	UUGAGuAGCcAUUGUCcAC	950	262
AD-26039	AAuGGcuAcucAAGcuGAu	292	AUcAGCUUGAGuAGCcAUU	951	268
AD-26040	AuGGcuAcucAAGcuGAuu	293	AAUcAGCUUGAGuAGCcAU	952	269
AD-26041	uGGcuAcucAAGcuGAuuu	294	AAAUcAGCUUGAGuAGCcA	953	270

AD-26042	cuAcucAAGcuGAuuuGAu	295	AUcAAAUcAGCUUGAGuAG	954	273
AD-26043	AuuuGAuGGAGuuGGAcAu	296	AUGUCcAACUCcAUcAAAU	955	285
AD-26044	uGGAGuuGGAcAuGGccAu	297	AUGGCcAUGUCcAACUCcA	956	291
AD-26045	GuuGGAcAuGGccAuGGAA	298	UUCcAUGGCcAUGUCcAAC	957	295
AD-26046	GccAuGGAAccAGAcAGAA	299	UUCUGUCUGGUUCcAUGGC	958	305
AD-26047	cAuGGAAccAGAcAGAAAA	300	UUUUCUGUCUGGUUCcAUG	959	307
AD-26048	GGAGGcGGAGAcGGAGGAA	301	UUCCUCCGUCUCCGCCUCC	960	111
AD-26049	AGAcAGAAAAGcGGcuGuu	302	AAcAGCCGCUUUUCUGUCU	961	316
AD-26050	GAcAGAAAAGcGGcuGuuA	303	uAAcAGCCGCUUUUCUGUC	962	317
AD-26051	uGuuAGucAcuGGcAGcAA	304	UUGCUGCcAGUGACuAAcA	963	331
AD-26052	cAcuGGcAGcAAcAGucuu	305	AAGACUGUUGCUGCcAGUG	964	338
AD-26053	AcuGGcAGcAAcAGucuuA	306	uAAGACUGUUGCUGCcAGU	965	339
AD-26054	ucuuAccuGGAcucuGGAA	307	UUCcAGAGUCcAGGuAAGA	966	353
AD-26055	cuuAccuGGAcucuGGAAu	308	AUUCcAGAGUCcAGGuAAG	967	354
AD-26056	ccuGGAcucuGGAAuccAu	309	AUGGAUUCcAGAGUCcAGG	968	358
AD-26057	GGcuAGuGGuGGAccccAA	310	UUGGGGUCcACcACuAGCC	969	1216
AD-26058	GccAcuAccAcAGcuccuu	311	AAGGAGCUGUGGuAGUGGC	970	383
AD-26059	uccuucucuGAGuGGuAAA	312	UUuACcACUcAGAGAAGGA	971	397
AD-26060	cucuGAGuGGuAAAGGcAA	313	UUGCCUUuACcACUcAGAG	972	402
AD-26061	uAAAGGcAAuccuGAGGAA	314	UUCCUcAGGAUUGCCUUuA	973	412
AD-26062	cAAuccuGAGGAAGAGGAu	315	AUCCUCUUCCUcAGGAUUG	974	418
AD-26063	uGAGGAAGAGGAuGuGGAu	316	AUCcAcAUCCUCUUCCUcA	975	424
AD-26064	AuAccucccAAGuccuGuA	317	uAcAGGACUUGGGAGGuAU	976	441
AD-26065	uAccucccAAGuccuGuAu	318	AuAcAGGACUUGGGAGGuA	977	442
AD-26066	AGuccuGuAuGAGuGGGAA	319	UUCCcACUcAuAcAGGACU	978	451
AD-26067	uAuGAGuGGGAAcAGGGAu	320	AUCCCUGUUCCcACUcAuA	979	458
AD-26068	cAAGcuuuAGuAAAuAuAA	321	UuAuAUUuACuAAAGCUUG	980	1232
AD-26069	AAGcuuuAGuAAAuAuAAu	322	AUuAuAUUuACuAAAGCUU	981	1233
AD-26070	uGAGuGGGAAcAGGGAuuu	323	AAAUCCCUGUUCCcACUcA	982	460
AD-26071	GAGuGGGAAcAGGGAuuuu	324	AAAAUCCCUGUUCCcACUC	983	461
AD-26072	AGGGAuuuucucAGuccuu	325	AAGGACUGAGAAAAUCCCU	984	471
AD-26073	uucucAGuccuucAcucAA	326	UUGAGUGAAGGACUGAGAA	985	478
AD-26074	ucAGuccuucAcucAAGAA	327	UUCUUGAGUGAAGGACUGA	986	481
AD-26075	cuucAcucAAGAAcAAGuA	328	uACUUGUUCUUGAGUGAAG	987	487
AD-26076	ucAAGAAcAAGuAGcuGAu	329	AUcAGCuACUUGUUCUUGA	988	493
AD-26077	cuGAuAuuGAuGGAcAGuA	330	uACUGUCcAUcAAuAUcAG	989	507
AD-26078	AuuGAuGGAcAGuAuGcAA	331	UUGcAuACUGUCcAUcAAU	990	512
AD-26079	GAcucGAGcucAGAGGGuA	332	uACCCUCUGAGCUCGAGUC	991	532
AD-26080	cAGAGGGuAcGAGcuGcuA	333	uAGcAGCUCGuACCCUCUG	992	542
AD-26081	AGAGGGuAcGAGcuGcuAu	334	AuAGcAGCUCGuACCCUCU	993	543
AD-26082	GGGuAcGAGcuGcuAuGuu	335	AAcAuAGcAGCUCGuACCC	994	546
AD-26083	cuAuGuucccuGAGAcAuu	336	AAUGUCUcAGGGAAcAuAG	995	558
AD-26084	uAuGuucccuGAGAcAuuA	337	uAAUGUCUcAGGGAAcAuA	996	559
AD-26085	GuucccuGAGAcAuuAGAu	338	AUCuAAUGUCUcAGGGAAC	997	562
AD-26086	uAGAuGAGGGcAuGcAGAu	339	AUCUGcAUGCCCUcAUCuA	998	576

AD-26087	GAGGGcAuGcAGAucccAu	340	AUGGGAUCUGcAUGCCCUC	999	581
AD-26088	GGcAuGcAGAucccAucuA	341	uAGAUGGGAUCUGcAUGCC	1000	584
AD-26089	AGAucccAucuAcAcAGuu	342	AACUGUGuAGAUGGGAUCU	1001	591
AD-26090	cccAucuAcAcAGuuuGAu	343	AUcAAACUGUGuAGAUGGG	1002	595
AD-26091	AcAGuuuGAuGcuGcucAu	344	AUGAGcAGcAUcAAACUGU	1003	604
AD-26092	GAuGcuGcucAucccAcuA	345	uAGUGGGAUGAGcAGcAUC	1004	611
AD-26093	AuGcuGcucAucccAcuAA	346	UuAGUGGGAUGAGcAGcAU	1005	612
AD-26094	uGcuGcucAucccAcuAAu	347	AUuAGUGGGAUGAGcAGcA	1006	613
AD-26095	cccAcuAAuGuccAGcGuu	348	AACGCUGGAcAUuAGUGGG	1007	623
AD-26096	cAGcGuuuGGcuGAAccAu	349	AUGGUUcAGCcAAACGCUG	1008	635
AD-26097	uGGcuGAAccAucAcAGAu	350	AUCUGUGAUGGUUcAGCcA	1009	642
AD-26098	AAccAucAcAGAuGcuGAA	351	UUcAGcAUCUGUGAUGGUU	1010	648
AD-26099	AccAucAcAGAuGcuGAAA	352	UUUcAGcAUCUGUGAUGGU	1011	649
AD-26100	AucAcAGAuGcuGAAAcAu	353	AUGUUUcAGcAUCUGUGAU	1012	652
AD-26101	GAuGcuGAAAcAuGcAGuu	354	AACUGcAUGUUUcAGcAUC	1013	658
AD-26102	cuGAAAcAuGcAGuuGuAA	355	UuAcAACUGcAUGUUUcAG	1014	662
AD-26103	AAcAuGcAGuuGuAAAcuu	356	AAGUUuAcAACUGcAUGUU	1015	666
AD-26104	AuGcAGuuGuAAAcuuGAu	357	AUcAAGUUuAcAACUGcAU	1016	669
AD-26105	uGcAGuuGuAAAcuuGAuu	358	AAUcAAGUUuAcAACUGcA	1017	670
AD-26106	cAGuuGuAAAcuuGAuuAA	359	UuAAUcAAGUUuAcAACUG	1018	672
AD-26107	cuuGAuuAAcuAucAAGAu	360	AUCUUGAuAGUuAAUcAAG	1019	682
AD-26108	GAuuAAcuAucAAGAuGAu	361	AUcAUCUUGAuAGUuAAUC	1020	685
AD-26109	cuAucAAGAuGAuGcAGAA	362	UUCUGcAUcAUCUUGAuAG	1021	691
AD-26110	GAAcuuGccAcAcGuGcAA	363	UUGcACGUGUGGcAAGUUC	1022	707
AD-26111	AAcuuGccAcAcGuGcAAu	364	AUUGcACGUGUGGcAAGUU	1023	708
AD-26112	cAcAcGuGcAAucccuGAA	365	UUcAGGGAUUGcACGUGUG	1024	715
AD-26123	GcAAucccuGAAcuGAcAA	366	UUGUcAGUUcAGGGAUUGC	1025	722
AD-26124	cAAucccuGAAcuGAcAAA	367	UUUGUcAGUUcAGGGAUUG	1026	723
AD-26125	AAucccuGAAcuGAcAAAA	368	UUUUGUcAGUUcAGGGAUU	1027	724
AD-26126	uGAAcuGAcAAAAcuGcuA	369	uAGcAGUUUUGUcAGUUcA	1028	730
AD-26127	GAAcuGAcAAAAcuGcuAA	370	UuAGcAGUUUUGUcAGUUC	1029	731
AD-26128	AAcuGAcAAAAcuGcuAAA	371	UUuAGcAGUUUUGUcAGUU	1030	732
AD-26129	AcuGAcAAAAcuGcuAAAu	372	AUUuAGcAGUUUUGUcAGU	1031	733
AD-26130	GAGGAccAGGuGGuGGuuA	373	uAACcACcACCUGGUCCUC	1032	755
AD-26131	AGGAccAGGuGGuGGuuAA	374	UuAACcACcACCUGGUCCU	1033	756
AD-26132	GGAccAGGuGGuGGuuAAu	375	AUuAACcACcACCUGGUCC	1034	757
AD-26133	GAccAGGuGGuGGuuAAuA	376	uAUuAACcACcACCUGGUC	1035	758
AD-26134	ucAcuuGcAAuAAuuAuAA	377	UuAuAAUuAUUGcAAGUGA	1036	1548
AD-26135	cuuGcAAuAAuuAuAAGAA	378	UUCUuAuAAUuAUUGcAAG	1037	1551
AD-26136	AccAGGuGGuGGuuAAuAA	379	UuAUuAACcACcACCUGGU	1038	759
AD-26137	GGcuGcAGuuAuGGuccAu	380	AUGGACcAuAACUGcAGCC	1039	778
AD-26138	GuuAuGGuccAucAGcuuu	381	AAAGCUGAUGGACcAuAAC	1040	785
AD-26139	AuGGuccAucAGcuuucuA	382	uAGAAAGCUGAUGGACcAU	1041	788
AD-26140	uGGuccAucAGcuuucuAA	383	UuAGAAAGCUGAUGGACcA	1042	789
AD-26141	ucGGGcuGGuGAcAGGGAA	384	UUCCCUGUcACcAGCCCGA	1043	1624

AD-26142	GGuccAucAGcuuucuAAA	385	UUuAGAAAGCUGAUGGACC	1044	790
AD-26143	GuccAucAGcuuucuAAAA	386	UUUuAGAAAGCUGAUGGAC	1045	791
AD-26144	GAAGcuuccAGAcAcGcuA	387	uAGCGUGUCUGGAAGCUUC	1046	812
AD-26145	AAGcuuccAGAcAcGcuAu	388	AuAGCGUGUCUGGAAGCUU	1047	813
AD-26146	cuuccAGAcAcGcuAucAu	389	AUGAuAGCGUGUCUGGAAG	1048	816
AD-26147	AGAcAcGcuAucAuGcGuu	390	AACGcAUGAuAGCGUGUCU	1049	821
AD-26148	ucAuGcGuucuccucAGAu	391	AUCUGAGGAGAACGcAUGA	1050	831
AD-26149	ccucAGAuGGuGucuGcuA	392	uAGcAGAcACcAUCUGAGG	1051	842
AD-26150	cucAGAuGGuGucuGcuAu	393	AuAGcAGAcACcAUCUGAG	1052	843
AD-26151	GuGucuGcuAuuGuAcGuA	394	uACGuAcAAuAGcAGAcAC	1053	851
AD-26152	cuGcuAuuGuAcGuAccAu	395	AUGGuACGuAcAAuAGcAG	1054	855
AD-26153	uuGuAcGuAccAuGcAGAA	396	UUCUGcAUGGuACGuAcAA	1055	861
AD-26154	uGuAcGuAccAuGcAGAAu	397	AUUCUGcAUGGuACGuAcA	1056	862
AD-26155	cGuAccAuGcAGAAuAcAA	398	UUGuAUUCUGcAUGGuACG	1057	866
AD-26156	cAuGcAGAAuAcAAAuGAu	399	AUcAUUUGuAUUCUGcAUG	1058	871
AD-26157	GcAGAAuAcAAAuGAuGuA	400	uAcAUcAUUUGuAUUCUGC	1059	874
AD-26158	GAAuAcAAAuGAuGuAGAA	401	UUCuAcAUcAUUUGuAUUC	1060	877
AD-26159	GAuGuAGAAAcAGcucGuu	402	AACGAGCUGUUUCuAcAUC	1061	887
AD-26160	GuuGuAccGcuGGGAccuu	403	AAGGUCCcAGCGGuAcAAC	1062	903
AD-26161	uAccGcuGGGAccuuGcAu	404	AUGcAAGGUCCcAGCGGuA	1063	907
AD-26162	ccGcuGGGAccuuGcAuAA	405	UuAUGcAAGGUCCcAGCGG	1064	909
AD-26163	uGGGAccuuGcAuAAccuu	406	AAGGUuAUGcAAGGUCCcA	1065	913
AD-26164	GGGAccuuGcAuAAccuuu	407	AAAGGUuAUGcAAGGUCCC	1066	914
AD-26165	cuuGcAuAAccuuucccAu	408	AUGGGAAAGGUuAUGcAAG	1067	919
AD-26166	ucuuuAAGucuGGAGGcAu	409	AUGCCUCcAGACUuAAAGA	1068	960
AD-26167	GcAuuccuGcccuGGuGAA	410	UUcACcAGGGcAGGAAUGC	1069	975
AD-26168	cAuuccuGcccuGGuGAAA	411	UUUcACcAGGGcAGGAAUG	1070	976
AD-26169	AuuccuGcccuGGuGAAAA	412	UUUUcACcAGGGcAGGAAU	1071	977
AD-26170	uuccuGcccuGGuGAAAAu	413	AUUUUcACcAGGGcAGGAA	1072	978
AD-26171	uGcccuGGuGAAAAuGcuu	414	AAGcAUUUUcACcAGGGcA	1073	982
AD-26172	cuGGuGAAAAuGcuuGGuu	415	AACcAAGcAUUUUcACcAG	1074	986
AD-26173	GcuuGGuucAccAGuGGAu	416	AUCcACUGGUGAACcAAGC	1075	997
AD-26174	cuuGGuucAccAGuGGAuu	417	AAUCcACUGGUGAACcAAG	1076	998
AD-26175	uGcGuGAGcAGGGuGccAu	418	AUGGcACCCUGCUcACGcA	1077	1848
AD-26176	GcGuGAGcAGGGuGccAuu	419	AAUGGcACCCUGCUcACGC	1078	1849
AD-26177	cAccAGuGGAuucuGuGuu	420	AAcAcAGAAUCcACUGGUG	1079	1005
AD-26178	cAGuGGAuucuGuGuuGuu	421	AAcAAcAcAGAAUCcACUG	1080	1008
AD-26179	AGuGGAuucuGuGuuGuuu	422	AAAcAAcAcAGAAUCcACU	1081	1009
AD-26180	GuGGAuucuGuGuuGuuuu	423	AAAAcAAcAcAGAAUCcAC	1082	1010
AD-26181	uGGAuucuGuGuuGuuuuA	424	uAAAAcAAcAcAGAAUCcA	1083	1011
AD-26182	GGAuucuGuGuuGuuuuAu	425	AuAAAAcAAcAcAGAAUCC	1084	1012
AD-26183	uGuGuuGuuuuAuGccAuu	426	AAUGGcAuAAAAcAAcAcA	1085	1018
AD-26184	GGGuGGGAcAcAGcAGcAA	427	UUGCUGCUGUGUCCcACCC	1086	1927
AD-26185	GuGuuGuuuuAuGccAuuA	428	uAAUGGcAuAAAAcAAcAC	1087	1019
AD-26186	uuGuuuuAuGccAuuAcAA	429	UUGuAAUGGcAuAAAAcAA	1088	1022

AD-26187	ccAuuAcAAcucuccAcAA	430	UUGUGGAGAGUUGuAAUGG	1089	1032
AD-26188	uAcAAcucuccAcAAccuu	431	AAGGUUGUGGAGAGUUGuA	1090	1036
AD-26189	AcAAcucuccAcAAccuuu	432	AAAGGUUGUGGAGAGUUGU	1091	1037
AD-26190	cAAcucuccAcAAccuuuu	433	AAAAGGUUGUGGAGAGUUG	1092	1038
AD-26191	AAcucuccAcAAccuuuuA	434	uAAAAGGUUGUGGAGAGUU	1093	1039
AD-26192	AcucuccAcAAccuuuuAu	435	AuAAAAGGUUGUGGAGAGU	1094	1040
AD-26193	cucuccAcAAccuuuuAuu	436	AAuAAAAGGUUGUGGAGAG	1095	1041
AD-26194	ucuccAcAAccuuuuAuuA	437	uAAuAAAAGGUUGUGGAGA	1096	1042
AD-26195	cAAccuuuuAuuAcAucAA	438	UUGAUGuAAuAAAAGGUUG	1097	1048
AD-26196	ccuuuuAuuAcAucAAGAA	439	UUCUUGAUGuAAuAAAAGG	1098	1051
AD-26197	uuAcAucAAGAAGGAGcuA	440	uAGCUCCUUCUUGAUGuAA	1099	1058
AD-26198	uAcAucAAGAAGGAGcuAA	441	UuAGCUCCUUCUUGAUGuA	1100	1059
AD-26199	cAucAAGAAGGAGcuAAAA	442	UUUuAGCUCCUUCUUGAUG	1101	1061
AD-26200	AucAAGAAGGAGcuAAAAu	443	AUUUuAGCUCCUUCUUGAU	1102	1062
AD-26201	GcuAAAAuGGcAGuGcGuu	444	AACGcACUGCcAUUUuAGC	1103	1073
AD-26202	uAAAAuGGcAGuGcGuuuA	445	uAAACGcACUGCcAUUUuA	1104	1075
AD-26203	AAAuGGuuGccuuGcucAA	446	UUGAGcAAGGcAACcAUUU	1105	1110
AD-26204	GccuGuuccccuGAGGGuA	447	uACCCUcAGGGGAAcAGGC	1106	206
AD-26205	uGGuuGccuuGcucAAcAA	448	UUGUUGAGcAAGGcAACcA	1107	1113
AD-26206	GGuuGccuuGcucAAcAAA	449	UUUGUUGAGcAAGGcAACC	1108	1114
AD-26207	GuuGccuuGcucAAcAAAA	450	UUUUGUUGAGcAAGGcAAC	1109	1115
AD-26208	GccuuGcucAAcAAAAcAA	451	UUGUUUUGUUGAGcAAGGC	1110	1118
AD-26209	ccuuGcucAAcAAAAcAAA	452	UUUGUUUUGUUGAGcAAGG	1111	1119
AD-26210	GuuAAAuucuuGGcuAuuA	453	uAAuAGCcAAGAAUUuAAC	1112	1139
AD-26211	uAuuAcGAcAGAcuGccuu	454	AAGGcAGUCUGUCGuAAuA	1113	1153
AD-26212	AuGGcAAccAAGAAAGcAA	455	UUGCUUUCUUGGUUGCcAU	1114	1185
AD-26213	AGuGGuGGAccccAAGcuu	456	AAGCUUGGGGUCcACcACU	1115	1220
AD-26214	GuGGuGGAccccAAGcuuu	457	AAAGCUUGGGGUCcACcAC	1116	1221
AD-26215	uGGuGGAccccAAGcuuuA	458	uAAAGCUUGGGGUCcACcA	1117	1222
AD-26216	uGGAccccAAGcuuuAGuA	459	uACuAAAGCUUGGGGUCcA	1118	1225
AD-26217	GGAccccAAGcuuuAGuAA	460	UuACuAAAGCUUGGGGUCC	1119	1226
AD-26218	GAccccAAGcuuuAGuAAA	461	UUuACuAAAGCUUGGGGUC	1120	1227
AD-26651	AccccAAGcuuuAGuAAAu	462	AUUuACuAAAGCUUGGGGU	1121	1228
AD-26652	ccccAAGcuuuAGuAAAuA	463	uAUUuACuAAAGCUUGGGG	1122	1229
AD-26653	cccAAGcuuuAGuAAAuAu	464	AuAUUuACuAAAGCUUGGG	1123	1230
AD-26654	ccAAGcuuuAGuAAAuAuA	465	uAuAUUuACuAAAGCUUGG	1124	1231
AD-26655	uAAAuAuAAuGAGGAccuA	466	uAGGUCCUcAUuAuAUUuA	1125	1242
AD-26656	AAAuAuAAuGAGGAccuAu	467	AuAGGUCCUcAUuAuAUUU	1126	1243
AD-26657	AAuAuAAuGAGGAccuAuA	468	uAuAGGUCCUcAUuAuAUU	1127	1244
AD-26658	AuAAuGAGGAccuAuAcuu	469	AAGuAuAGGUCCUcAUuAU	1128	1247
AD-26659	AAAcuAcuGuGGAccAcAA	470	UUGUGGUCcAcAGuAGUUU	1129	1271
AD-26660	ccAcAAGcAGAGuGcuGAA	471	UUcAGcACUCUGCUUGUGG	1130	1284
AD-26661	cAGAGuGcuGAAGGuGcuA	472	uAGcACCUUcAGcACUCUG	1131	1291
AD-26662	AGAGuGcuGAAGGuGcuAu	473	AuAGcACCUUcAGcACUCU	1132	1292
AD-26663	AuuGuAGAAGcuGGuGGAA	474	UUCcACcAGCUUCuAcAAU	1133	1337

AD-26664	uuGuAGAAGcuGGuGGAAu	475	AUUCcACcAGCUUCuAcAA	1134	1338
AD-26665	GcuGGuGGAAuGcAAGcuu	476	AAGCUUGcAUUCcACcAGC	1135	1346
AD-26666	cuGGuGGAAuGcAAGcuuu	477	AAAGCUUGcAUUCcACcAG	1136	1347
AD-26667	AGGAcuucAccuGAcAGAu	478	AUCUGUcAGGUGAAGUCCU	1137	1366
AD-26668	cuucAccuGAcAGAuccAA	479	UUGGAUCUGUcAGGUGAAG	1138	1370
AD-26669	ccuGAcAGAuccAAGucAA	480	UUGACUUGGAUCUGUcAGG	1139	1375
AD-26670	AGAuccAAGucAAcGucuu	481	AAGACGUUGACUUGGAUCU	1140	1381
AD-26671	uccAAGucAAcGucuuGuu	482	AAcAAGACGUUGACUUGGA	1141	1384
AD-26672	ucuuGuucAGAAcuGucuu	483	AAGAcAGUUCUGAAcAAGA	1142	1396
AD-26673	cuuGuucAGAAcuGucuuu	484	AAAGAcAGUUCUGAAcAAG	1143	1397
AD-26674	GucuuuGGAcucucAGGAA	485	UUCCUGAGAGUCcAAAGAC	1144	1410
AD-26675	ucuuuGGAcucucAGGAAu	486	AUUCCUGAGAGUCcAAAGA	1145	1411
AD-26676	uuGGAcucucAGGAAucuu	487	AAGAUUCCUGAGAGUCcAA	1146	1414
AD-26677	uGcccAGGGAGAAccccuu	488	AAGGGGUUCUCCCUGGGcA	1147	2371
AD-26678	uGGAcucucAGGAAucuuu	489	AAAGAUUCCUGAGAGUCcA	1148	1415
AD-26679	ucucAGGAAucuuucAGAu	490	AUCUGAAAGAUUCCUGAGA	1149	1420
AD-26680	AAucuuucAGAuGcuGcAA	491	UUGcAGcAUCUGAAAGAUU	1150	1427
AD-26681	cuuucAGAuGcuGcAAcuA	492	uAGUUGcAGcAUCUGAAAG	1151	1430
AD-26682	uucAGAuGcuGcAAcuAAA	493	UUuAGUUGcAGcAUCUGAA	1152	1432
AD-26683	uGcuGcAAcuAAAcAGGAA	494	UUCCUGUUuAGUUGcAGcA	1153	1438
AD-26684	uAAAcAGGAAGGGAuGGAA	495	UUCcAUCCCUUCCUGUUuA	1154	1447
AD-26685	AGGGAuGGAAGGucuccuu	496	AAGGAGACCUUCcAUCCCU	1155	1456
AD-26686	AGGucuccuuGGGAcucuu	497	AAGAGUCCcAAGGAGACCU	1156	1465
AD-26687	ucuccuuGGGAcucuuGuu	498	AAcAAGAGUCCcAAGGAGA	1157	1468
AD-26688	uGGGAcucuuGuucAGcuu	499	AAGCUGAAcAAGAGUCCcA	1158	1474
AD-26689	cuuGuucAGcuucuGGGuu	500	AACCcAGAAGCUGAAcAAG	1159	1481
AD-26690	ucAGcuucuGGGuucAGAu	501	AUCUGAACCcAGAAGCUGA	1160	1486
AD-26691	GcuucuGGGuucAGAuGAu	502	AUcAUCUGAACCcAGAAGC	1161	1489
AD-26692	cuucuGGGuucAGAuGAuA	503	uAUcAUCUGAACCcAGAAG	1162	1490
AD-26693	GGccAGGAuGccuuGGGuA	504	uACCcAAGGcAUCCUGGCC	1163	2441
AD-26694	uucuGGGuucAGAuGAuAu	505	AuAUcAUCUGAACCcAGAA	1164	1491
AD-26695	cuGGGuucAGAuGAuAuAA	506	UuAuAUcAUCUGAACCcAG	1165	1493
AD-26696	uGGGuucAGAuGAuAuAAA	507	UUuAuAUcAUCUGAACCcA	1166	1494
AD-26697	GucAccuGuGcAGcuGGAA	508	UUCcAGCUGcAcAGGUGAC	1167	1517
AD-26698	ucAccuGuGcAGcuGGAAu	509	AUUCcAGCUGcAcAGGUGA	1168	1518
AD-26699	cAccuGuGcAGcuGGAAuu	510	AAUUCcAGCUGcAcAGGUG	1169	1519
AD-26700	cuGuGcAGcuGGAAuucuu	511	AAGAAUUCcAGCUGcAcAG	1170	1522
AD-26701	uGuGcAGcuGGAAuucuuu	512	AAAGAAUUCcAGCUGcAcA	1171	1523
AD-26702	GcAGcuGGAAuucuuucuA	513	uAGAAAGAAUUCcAGCUGC	1172	1526
AD-26703	cAGcuGGAAuucuuucuAA	514	UuAGAAAGAAUUCcAGCUG	1173	1527
AD-26704	uuucuAAccucAcuuGcAA	515	UUGcAAGUGAGGUuAGAAA	1174	1539
AD-26705	uucuAAccucAcuuGcAAu	516	AUUGcAAGUGAGGUuAGAA	1175	1540
AD-26706	AccucAcuuGcAAuAAuuA	517	uAAUuAUUGcAAGUGAGGU	1176	1545
AD-26707	ccucAcuuGcAAuAAuuAu	518	AuAAUuAUUGcAAGUGAGG	1177	1546
AD-26708	cucAcuuGcAAuAAuuAuA	519	uAuAAUuAUUGcAAGUGAG	1178	1547

AD-26709	GucuGccAAGuGGGuGGuA	520	uACcACCcACUUGGcAGAC	1179	1580
AD-26710	ucuGccAAGuGGGuGGuAu	521	AuACcACCcACUUGGcAGA	1180	1581
AD-26711	GGGuGGuAuAGAGGcucuu	522	AAGAGCCUCuAuACcACCC	1181	1591
AD-26712	AuAGAGGcucuuGuGcGuA	523	uACGcAcAAGAGCCUCuAU	1182	1598
AD-26713	ucuuGuGcGuAcuGuccuu	524	AAGGAcAGuACGcAcAAGA	1183	1606
AD-26714	cuGGuGAcAGGGAAGAcAu	525	AUGUCUUCCCUGUcACcAG	1184	1629
AD-26715	AcAucAcuGAGccuGccAu	526	AUGGcAGGCUcAGUGAUGU	1185	1644
AD-26716	GccuGccAucuGuGcucuu	527	AAGAGcAcAGAUGGcAGGC	1186	1654
AD-26717	ucuGAccAGccGAcAccAA	528	UUGGUGUCGGCUGGUcAGA	1187	1678
AD-26718	GAccAGccGAcAccAAGAA	529	UUCUUGGUGUCGGCUGGUC	1188	1681
AD-26719	GAcAccAAGAAGcAGAGAu	530	AUCUCUGCUUCUUGGUGUC	1189	1689
AD-26720	AGcAGAGAuGGcccAGAAu	531	AUUCUGGGCcAUCUCUGCU	1190	1699
AD-26721	GAuGGcccAGAAuGcAGuu	532	AACUGcAUUCUGGGCcAUC	1191	1705
AD-26722	ccAGAAuGcAGuucGccuu	533	AAGGCGAACUGcAUUCUGG	1192	1711
AD-26723	AuGcAGuucGccuucAcuA	534	uAGUGAAGGCGAACUGcAU	1193	1716
AD-26724	uGcAGuucGccuucAcuAu	535	AuAGUGAAGGCGAACUGcA	1194	1717
AD-26725	ucGccuucAcuAuGGAcuA	536	uAGUCcAuAGUGAAGGCGA	1195	1723
AD-26726	ucAcuAuGGAcuAccAGuu	537	AACUGGuAGUCcAuAGUGA	1196	1729
AD-26727	uGGAcuAccAGuuGuGGuu	538	AACcAcAACUGGuAGUCcA	1197	1735
AD-26728	GGAcuAccAGuuGuGGuuA	539	uAACcAcAACUGGuAGUCC	1198	1736
AD-26729	GAcuAccAGuuGuGGuuAA	540	UuAACcAcAACUGGuAGUC	1199	1737
AD-26730	cAGuuGuGGuuAAGcucuu	541	AAGAGCUuAACcAcAACUG	1200	1743
AD-26731	AGuuGuGGuuAAGcucuuA	542	uAAGAGCUuAACcAcAACU	1201	1744
AD-26732	AAGcucuuAcAcccAccAu	543	AUGGUGGGUGuAAGAGCUU	1202	1754
AD-26733	cAucccAcuGGccucuGAu	544	AUcAGAGGCcAGUGGGAUG	1203	1770
AD-26734	AucccAcuGGccucuGAuA	545	uAUcAGAGGCcAGUGGGAU	1204	1771
AD-26735	ucccAcuGGccucuGAuAA	546	UuAUcAGAGGCcAGUGGGA	1205	1772
AD-26736	uGGccucuGAuAAAGGcuA	547	uAGCCUUuAUcAGAGGCcA	1206	1778
AD-26737	ucuGAuAAAGGcuAcuGuu	548	AAcAGuAGCCUUuAUcAGA	1207	1783
AD-26738	AuAAAGGcuAcuGuuGGAu	549	AUCcAAcAGuAGCCUUuAU	1208	1787
AD-26739	GGcuAcuGuuGGAuuGAuu	550	AAUcAAUCcAAcAGuAGCC	1209	1792
AD-26740	uGuuGGAuuGAuucGAAAu	551	AUUUCGAAUcAAUCcAAcA	1210	1798
AD-26741	uGccAuuccAcGAcuAGuu	552	AACuAGUCGUGGAAUGGcA	1211	1861
AD-26742	uuccAcGAcuAGuucAGuu	553	AACUGAACuAGUCGUGGAA	1212	1866
AD-26743	AcGAcuAGuucAGuuGcuu	554	AAGcAACUGAACuAGUCGU	1213	1870
AD-26744	AcuAGuucAGuuGcuuGuu	555	AAcAAGcAACUGAACuAGU	1214	1873
AD-26745	GuuGcuuGuucGuGcAcAu	556	AUGUGcACGAAcAAGcAAC	1215	1882
AD-26746	uGuucGuGcAcAucAGGAu	557	AUCCUGAUGUGcACGAAcA	1216	1888
AD-26747	GuucGuGcAcAucAGGAuA	558	uAUCCUGAUGUGcACGAAC	1217	1889
AD-26748	GGuGGGAcAcAGcAGcAAu	559	AUUGCUGCUGUGUCCcACC	1218	1928
AD-26749	GuGGGAcAcAGcAGcAAuu	560	AAUUGCUGCUGUGUCCcAC	1219	1929
AD-26750	uGGGAcAcAGcAGcAAuuu	561	AAAUUGCUGCUGUGUCCcA	1220	1930
AD-26751	GGGGuccGcAuGGAAGAAA	562	UUUCUUCcAUGCGGACCCC	1221	1955
AD-26752	GGGuccGcAuGGAAGAAAu	563	AUUUCUUCcAUGCGGACCC	1222	1956
AD-26753	ucAcAuccuAGcucGGGAu	564	AUCCCGAGCuAGGAUGUGA	1223	1999

AD-26754	cAuccuAGcucGGGAuGuu	565	AAcAUCCCGAGCuAGGAUG	1224	2002
AD-26755	uAGcucGGGAuGuucAcAA	566	UUGUGAAcAUCCCGAGCuA	1225	2007
AD-26756	GGGAuGuucAcAAccGAAu	567	AUUCGGUUGUGAAcAUCCC	1226	2013
AD-26757	GGAuGuucAcAAccGAAuu	568	AAUUCGGUUGUGAAcAUCC	1227	2014
AD-26758	cAGAGGAcuAAAuAccAuu	569	AAUGGuAUUuAGUCCUCUG	1228	2038
AD-26759	GGAcuAAAuAccAuuccAu	570	AUGGAAUGGuAUUuAGUCC	1229	2042
AD-26760	uAAAuAccAuuccAuuGuu	571	AAcAAUGGAAUGGuAUUuA	1230	2046
AD-26761	AAAuAccAuuccAuuGuuu	572	AAAcAAUGGAAUGGuAUUU	1231	2047
AD-26762	AuuGuuuGuGcAGcuGcuu	573	AAGcAGCUGcAcAAAcAAU	1232	2059
AD-26763	uuGuuuGuGcAGcuGcuuu	574	AAAGcAGCUGcAcAAAcAA	1233	2060
AD-26764	uGuuuGuGcAGcuGcuuuA	575	uAAAGcAGCUGcAcAAAcA	1234	2061
AD-26765	GuuuGuGcAGcuGcuuuAu	576	AuAAAGcAGCUGcAcAAAC	1235	2062
AD-26766	uuuGuGcAGcuGcuuuAuu	577	AAuAAAGcAGCUGcAcAAA	1236	2063
AD-26767	AGcuGcuuuAuucucccAu	578	AUGGGAGAAuAAAGcAGCU	1237	2070
AD-26768	GcuGcuuuAuucucccAuu	579	AAUGGGAGAAuAAAGcAGC	1238	2071
AD-26769	uuuAuucucccAuuGAAAA	580	UUUUcAAUGGGAGAAuAAA	1239	2076
AD-26770	AuucucccAuuGAAAAcAu	581	AUGUUUUcAAUGGGAGAAU	1240	2079
AD-26771	ucccAuuGAAAAcAuccAA	582	UUGGAUGUUUUcAAUGGGA	1241	2083
AD-26772	uGcAGGGGuccucuGuGAA	583	UUcAcAGAGGACCCCUGcA	1242	2110
AD-26773	AcuuGcucAGGAcAAGGAA	584	UUCCUUGUCCUGAGcAAGU	1243	2128
AD-26774	cAGcuccucuGAcAGAGuu	585	AACUCUGUcAGAGGAGCUG	1244	2178
AD-26775	AGcuccucuGAcAGAGuuA	586	uAACUCUGUcAGAGGAGCU	1245	2179
AD-26776	uccucuGAcAGAGuuAcuu	587	AAGuAACUCUGUcAGAGGA	1246	2182
AD-26777	AcAGAGuuAcuucAcucuA	588	uAGAGUGAAGuAACUCUGU	1247	2189
AD-26778	AGuuAcuucAcucuAGGAA	589	UUCCuAGAGUGAAGuAACU	1248	2193
AD-26779	GuuAcuucAcucuAGGAAu	590	AUUCCuAGAGUGAAGuAAC	1249	2194
AD-26780	AcuucAcucuAGGAAuGAA	591	UUcAUUCCuAGAGUGAAGU	1250	2197
AD-26781	GcuGcuGuuuuGuuccGAA	592	UUCGGAAcAAAAcAGcAGC	1251	2234
AD-26782	cuGcuGuuuuGuuccGAAu	593	AUUCGGAAcAAAAcAGcAG	1252	2235
AD-26783	GucuGAGGAcAAGccAcAA	594	UUGUGGCUUGUCCUcAGAC	1253	2254
AD-26784	uGAGGAcAAGccAcAAGAu	595	AUCUUGUGGCUUGUCCUcA	1254	2257
AD-26785	AcAAGccAcAAGAuuAcAA	596	UUGuAAUCUUGUGGCUUGU	1255	2262
AD-26786	AGccAcAAGAuuAcAAGAA	597	UUCUUGuAAUCUUGUGGCU	1256	2265
AD-26787	AGAuuAcAAGAAAcGGcuu	598	AAGCCGUUUCUUGuAAUCU	1257	2272
AD-26788	cAAGAAAcGGcuuucAGuu	599	AACUGAAAGCCGUUUCUUG	1258	2278
AD-26789	AGcuGAccAGcucucucuu	600	AAGAGAGAGCUGGUcAGCU	1259	2298
AD-26790	AccAGcucucucuucAGAA	601	UUCUGAAGAGAGAGCUGGU	1260	2303
AD-26791	uAuuGGuGcccAGGGAGAA	602	UUCUCCCUGGGcACcAAuA	1261	2365
AD-26792	cAGGGAGAAccccuuGGAu	603	AUCcAAGGGGUUCUCCCUG	1262	2375
AD-26793	AGGGAGAAccccuuGGAuA	604	uAUCcAAGGGGUUCUCCCU	1263	2376
AD-26794	ccuuGGAuAucGccAGGAu	605	AUCCUGGCGAuAUCcAAGG	1264	2386
AD-26795	uAucGccAGGAuGAuccuA	606	uAGGAUcAUCCUGGCGAuA	1265	2393
AD-26796	GccAGGAuGAuccuAGcuA	607	uAGCuAGGAUcAUCCUGGC	1266	2397
AD-26797	ccAGGAuGAuccuAGcuAu	608	AuAGCuAGGAUcAUCCUGG	1267	2398
AD-26798	GAuGAuccuAGcuAucGuu	609	AACGAuAGCuAGGAUcAUC	1268	2402

AD-26799	AuccuAGcuAucGuucuuu	610	AAAGAACGAuAGCuAGGAU	1269	2406
AD-26800	uccuAGcuAucGuucuuuu	611	AAAAGAACGAuAGCuAGGA	1270	2407
AD-26801	ucuuuucAcucuGGuGGAu	612	AUCcACcAGAGUGAAAAGA	1271	2420
AD-26802	cuuuucAcucuGGuGGAuA	613	uAUCcACcAGAGUGAAAAG	1272	2421
AD-26803	uuuucAcucuGGuGGAuAu	614	AuAUCcACcAGAGUGAAAA	1273	2422
AD-26804	uGGuGGAuAuGGccAGGAu	615	AUCCUGGCcAuAUCcACcA	1274	2431
AD-26805	GAuAuGGccAGGAuGccuu	616	AAGGcAUCCUGGCcAuAUC	1275	2436
AD-26806	ccuuGGGuAuGGAccccAu	617	AUGGGGUCcAuACCcAAGG	1276	2451
AD-26807	uGGGuAuGGAccccAuGAu	618	AUcAUGGGGUCcAuACCcA	1277	2454
AD-26808	uuGuAAAcuuGAuuAAcuA	619	uAGUuAAUcAAGUUuAcAA	1278	675
AD-26809	uGuAAAcuuGAuuAAcuAu	620	AuAGUuAAUcAAGUUuAcA	1279	676
AD-26810	AAAcuuGAuuAAcuAucAA	621	UUGAuAGUuAAUcAAGUUU	1280	679
AD-26811	uAuGGAccccAuGAuGGAA	622	UUCcAUcAUGGGGUCcAuA	1281	2458
AD-26812	GGAccccAuGAuGGAAcAu	623	AUGUUCcAUcAUGGGGUCC	1282	2461
AD-26813	ccAuGAuGGAAcAuGAGAu	624	AUCUcAUGUUCcAUcAUGG	1283	2466
AD-26814	AccAccccuGGuGcuGAcuA	625	uAGUcAGcACcAGGGUGGU	1284	2493
AD-26815	ccAccccuGGuGcuGAcuAu	626	AuAGUcAGcACcAGGGUGG	1285	2494
AD-26816	uGcuGAcuAuccAGuuGAu	627	AUcAACUGGAuAGUcAGcA	1286	2503
AD-26817	AGuuGAuGGGcuGccAGAu	628	AUCUGGcAGCCcAUcAACU	1287	2515
AD-26818	uGcccAGGAccucAuGGAu	629	AUCcAUGAGGUCCUGGGcA	1288	2542
AD-26819	GcAAucAGcuGGccuGGuu	630	AACcAGGCcAGCUGAUUGC	1289	2580
AD-26820	cAAucAGcuGGccuGGuuu	631	AAACcAGGCcAGCUGAUUG	1290	2581
AD-26821	GGuuuGAuAcuGAccuGuA	632	uAcAGGUcAGuAUcAAACC	1291	2595
AD-26822	AuAcuGAccuGuAAAucAu	633	AUGAUUuAcAGGUcAGuAU	1292	2601
AD-26823	uGAccuGuAAAucAuccuu	634	AAGGAUGAUUuAcAGGUcA	1293	2605
AD-26824	GAccuGuAAAucAuccuuu	635	AAAGGAUGAUUuAcAGGUC	1294	2606
AD-26825	AccuGuAAAucAuccuuuA	636	uAAAGGAUGAUUuAcAGGU	1295	2607
AD-26826	AAuAcAAAuGAuGuAGAAA	637	UUUCuAcAUcAUUUGuAUU	1296	878
AD-26900	uuuuAAGAAuAucuGuAAu	638	AUuAcAGAuAUUCUuAAAA	1297	2745
AD-26901	uAcAGcAAuuucuAAuuuu	639	AAAAUuAGAAAUUGCUGuA	1298	2872
AD-26902	cAcuAAuucAuAAucAcuc	640	GAGUGAUuAUGAAUuAGUG	1299	2915
AD-26903	AcuAAuucAuAAucAcucu	641	AGAGUGAUuAUGAAUuAGU	1300	2916
AD-26904	uAAuucAuAAucAcucuAA	642	UuAGAGUGAUuAUGAAUuA	1301	2918
AD-26905	AAuucAuAAucAcucuAAu	643	AUuAGAGUGAUuAUGAAUU	1302	2919
AD-26906	AAuuGuAAucuGAAuAAAG	644	CUUuAUUcAGAUuAcAAUU	1303	2939
AD-26907	uuuGuAuAAAAuAGAcAAA	645	UUUGUCuAUUUuAuAcAAA	1304	2978
AD-26908	uuGuAuAAAAuAGAcAAAu	646	AUUUGUCuAUUUuAuAcAA	1305	2979
AD-26909	uGuAuAAAAuAGAcAAAuA	647	uAUUUGUCuAUUUuAuAcA	1306	2980
AD-26910	GuAuAAAAuAGAcAAAuAG	648	CuAUUUGUCuAUUUuAuAC	1307	2981
AD-26911	AuAAAAuAGAcAAAuAGAA	649	UUCuAUUUGUCuAUUUuAU	1308	2983
AD-26912	uAAAAuAGAcAAAuAGAAA	650	UUUCuAUUUGUCuAUUUuA	1309	2984
AD-26913	AAAuAGAcAAAuAGAAAAu	651	AUUUUCuAUUUGUCuAUUU	1310	2986
AD-26914	uGGGAuAuGuAuGGGuAGG	652	CCuACCcAuAcAuAUCCcA	1311	3081
AD-26915	GGGAuAuGuAuGGGuAGGG	653	CCCuACCcAuAcAuAUCCC	1312	3082
AD-26916	cuAAuucAuAAucAcucuA	654	uAGAGUGAUuAUGAAUuAG	1313	2917

AD-26917	AAAuAGAAAAuGGuccAAu	655	AUUGGACcAUUUUCuAUUU	1314	2994
AD-26918	AAuAGAAAAuGGuccAAuu	656	AAUUGGACcAUUUUCuAUU	1315	2995
AD-26919	uuuGGAcAGuuuAccAGuu	657	AACUGGuAAACUGUCcAAA	1316	3134
AD-26920	AuucuuucuAAccucAcuu	658	AAGUGAGGUuAGAAAGAAU	1317	1535
AD-26921	uGGAuuGAuucGAAAucuu	659	AAGAUUUCGAAUcAAUCcA	1318	1801
Set1 254 A22 S26	ccAtAcAActGttttGAAA	6141	TTTcAAAAcAGTTGtATGG	6309	236
Set1 703 A22 S26	GAttAActAtcAAGAtGAt	6142	ATcATCTTGAtAGTtAATC	6310	685
Set1 709 A22 S26	ctAtcAAGAtGAtGcAGAA	6143	TTCTGcATcATCTTGAtAG	6311	691
Set1 895 A22 S26	GAAtAcAAAtGAtGtAGAA	6144	TTCtAcATcATTTGtATTC	6312	877
Set1 1816 A22 S26	tGttGGAttGAttcGAAAt	6145	ATTTCGAATcAATCcAAcA	6313	1798
Set1 1974 A22 S26	GGGtccGcAtGGAAGAAAt	6146	ATTTCTTCcATGCGGACCC	6314	1956
Set1 2425 A22 S26	tcctAGctAtcGttctttt	6147	AAAAGAACGAtAGCtAGGA	6315	2407
Set1 3146 A22 S26	AAGtGAAGAAtGcAcAAGA	6148	TCTTGTGcATTCTTcACTT	6316	3128
Set1 889 A22 S26	cAtGcAGAAtAcAAAtGAt	6149	ATcATTTGtATTCTGcATG	6317	871
Set1 1814 A22 S26	ActGttGGAttGAttcGAA	6150	TTCGAATcAATCcAAcAGT	6318	1796
Set1 1245 A22 S26	GAccccAAGctttAGtAAA	6151	TTtACtAAAGCTTGGGGTC	6319	1227
Set1 3196 A22 S26	AGccttGcttGttAAAttt	6152	AAATTtAAcAAGcAAGGCT	6320	3178
Set1 1450 A22 S26	ttcAGAtGctGcAActAAA	6153	TTtAGTTGcAGcATCTGAA	6321	1432
Set1 3169 A22 S26	AtcAcAAGAtGGAAtttAt	6154	AtAAATTCcATCTTGTGAT	6322	3151
Set1 3477 A22 S26	AAtAGAAAAtGGtccAAtt	6155	AATTGGACcATTTTCtATT	6323	3459
Set1 865 A22 S26	GAtGGtGtctGctAttGtA	6156	tAcAAtAGcAGAcACcATC	6324	847
Set1 1249 A22 S26	ccAAGctttAGtAAAtAtA	6157	tAtATTtACtAAAGCTTGG	6325	1231
Set1 1250 A22 S26	cAAGctttAGtAAAtAtAA	6158	TtAtATTtACtAAAGCTTG	6326	1232
Set1 2202 A22 S26	ctctGAcAGAGttActtcA	6159	TGAAGtAAcTcTGTcAGAG	6327	2184
Set1 1545 A22 S26	cAGctGGAAttctttctAA	6160	TtAGAAAGAATTCcAGCTG	6328	1527
Set1 1755 A22 S26	GActAccAGttGtGGttAA	6161	TtAACcAcAACTGGtAGTC	6329	1737
Set1 254 A25 S27	CCATACAACTGTTTTGAAA	6162	TTTCAAAACAGTTGTATGG	6330	236
Set1 703 A25 S27	GATTAACTATCAAGATGAT	6163	ATCATCTTGATAGTTAATC	6331	685
Set1 709 A25 S27	CTATCAAGATGATGCAGAA	6164	TTCTGCATCATCTTGATAG	6332	691
Set1 895 A25 S27	GAATACAAATGATGTAGAA	6165	TTCTACATCATTTGTATTC	6333	877
Set1 1816 A25 S27	TGTTGGATTGATTCGAAAT	6166	ATTTCGAATCAATCCAACA	6334	1798
Set1 1974 A25 S27	GGGTCCGCATGGAAGAAAT	6167	ATTTCTTCCATGCGGACCC	6335	1956

Set1 2425 A25 S27	TCCTAGCTATCGTTCTTTT	6168	AAAAGAACGATAGCTAGGA	6336	2407
Set1 3146 A25 S27	AAGTGAAGAATGCACAAGA	6169	TCTTGTGCATTCTTCACTT	6337	3128
Set1 889 A25 S27	CATGCAGAATACAAATGAT	6170	ATCATTTGTATTCTGCATG	6338	871
Set1 1814 A25 S27	ACTGTTGGATTGATTCGAA	6171	TTCGAATCAATCCAACAGT	6339	1796
Set1 1245 A25 S27	GACCCCAAGCTTTAGTAAA	6172	TTTACTAAAGCTTGGGGTC	6340	1227
Set1 3196 A25 S27	AGCCTTGCTTGTTAAATTT	6173	AAATTTAACAAGCAAGGCT	6341	3178
Set1 1450 A25 S27	TTCAGATGCTGCAACTAAA	6174	TTTAGTTGCAGCATCTGAA	6342	1432
Set1 3169 A25 S27	ATCACAAGATGGAATTTAT	6175	ATAAATTCCATCTTGTGAT	6343	3151
Set1 3477 A25 S27	AATAGAAAATGGTCCAATT	6176	AATTGGACCATTTTCTATT	6344	3459
Set1 865 A25 S27	GATGGTGTCTGCTATTGTA	6177	TACAATAGCAGACACCATC	6345	847
Set1 1249 A25 S27	CCAAGCTTTAGTAAATATA	6178	TATATTTACTAAAGCTTGG	6346	1231
Set1 1250 A25 S27	CAAGCTTTAGTAAATATAA	6179	TTATATTTACTAAAGCTTG	6347	1232
Set1 2202 A25 S27	CTCTGACAGAGTTACTTCA	6180	TGAAGTAACTCTGTCAGAG	6348	2184
Set1 1545 A25 S27	CAGCTGGAATTCTTTCTAA	6181	TTAGAAAGAATTCCAGCTG	6349	1527
Set1 1755 A25 S27	GACTACCAGTTGTGGTTAA	6182	TTAACCACAACTGGTAGTC	6350	1737
Set1 254 A LO V1 S26	ccAtAcAActGttttGAAA	6183	TTtcAAAAcAGttGtAtGG	6351	236
Set1 703 A LO V1 S26	GAttAActAtcAAGAtGAt	6184	ATcAtcttGAtAGTtAAtc	6352	685
Set1 709 A LO V1 S26	ctAtcAAGAtGAtGcAGAA	6185	TTctGcAtcAtctTGAtAG	6353	691
Set1 895 A LO V1 S26	GAAtAcAAAtGAtGtAGAA	6186	TTctAcAtcAtttGtAttc	6354	877
Set1 1816 A LO V1 S26	tGttGGAttGAttcGAAAt	6187	ATttcGAAtcAAtCcAAcA	6355	1798
Set1 1974 A LO V1 S26	GGGtccGcAtGGAAGAAAt	6188	ATttcttccAtGcGGAccc	6356	1956
Set1 2425 A LO V1 S26	tcctAGctAtcGttctttt	6189	AAAAGAAcGAtAGCtAGGA	6357	2407
Set1 3146 A LO V1 S26	AAGtGAAGAAtGcAcAAGA	6190	TCttGtGcAttctTcActt	6358	3128
Set1 889 A LO V1 S26	cAtGcAGAAtAcAAAtGAt	6191	ATcAtttGtAttcTGcAtG	6359	871
Set1 1814 A LO V1 S26	ActGttGGAttGAttcGAA	6192	TTcGAAtcAAtccAAcAGt	6360	1796
Set1 1245 A LO V1 S26	GAccccAAGctttAGtAAA	6193	TTtActAAAGcttGGGGtc	6361	1227
Set1 3196 A LO V1 S26	AGccttGcttGttAAAttt	6194	AAAtttAAcAAGcAAGGct	6362	3178
Set1 1450 A LO V1 S26	ttcAGAtGctGcAActAAA	6195	TTtAGttGcAGcATctGAA	6363	1432
Set1 3169 A LO V1 S26	AtcAcAAGAtGGAAtttAt	6196	ATAAAttccAtctTGtGAt	6364	3151
Set1 3477 A LO V1 S26	AAtAGAAAAtGGtccAAtt	6197	AAttGGAccAtttTctAtt	6365	3459
Set1 865 A	GAtGGtGtctGctAttGtA	6198	TAcAAtAGcAGAcAccAtc	6366	847

LO V1 S26					
Set1 1249 A LO V1 S26	ccAAGctttAGtAAAtAtA	6199	TAtAtttActAAAGcttGG	6367	1231
Set1 1250 A LO V1 S26	cAAGctttAGtAAAtAtAA	6200	TTAtAtttActAAAGcttG	6368	1232
Set1 2202 A LO V1 S26	ctctGAcAGAGttActtcA	6201	TGAAGtAActctGTcAGAG	6369	2184
Set1 1545 A LO V1 S26	cAGctGGAAttctttctAA	6202	TTAGAAAGAAttcCAGctG	6370	1527
Set1 1755 A LO V1 S26	GActAccAGttGtGGttAA	6203	TTAAccAcAActGGtAGtc	6371	1737
Set1 254 A LOV2 SLOV1	ccAtACAaCTGtTTtGAaa	6204	TTtCAAaACaGTtGTATgg	6372	236
Set1 703 A LOV2 SLOV1	gaTtAACtATCaAGaTGat	6205	ATcATCtTGaTAgTTAAtc	6373	685
Set1 709 A LOV2 SLOV1	ctAtCAAgATGaTGcAGaa	6206	TTcTGCaTCaTCtTGATag	6374	691
Set1 895 A LOV2 SLOV1	gaAtACAaATGaTGtAGaa	6207	TTcTACaTCaTTtGTATtc	6375	877
Set1 1816 A LOV2 SLOV1	tgTtGGAtTGAtTCgAAat	6208	ATtTCGaATcAAtCCAAca	6376	1798
Set1 1974 A LOV2 SLOV1	ggGtCCGcATGgAAgAAat	6209	ATtTCTtCCaTGcGGACcc	6377	1956
Set1 2425 A LOV2 SLOV1	tcCtAGCtATCgTTcTTtt	6210	AAaAGAaCGaTAgCTAGga	6378	2407
Set1 3146 A LOV2 SLOV1	aaGtGAAgAATgCAcAAga	6211	TCtTGTgCAtTCtTCACtt	6379	3128
Set1 889 A LOV2 SLOV1	caTgCAGaATAcAAaTGat	6212	ATcATTtGTaTTcTGCAtg	6380	871
Set1 1814 A LOV2 SLOV1	acTgTTGgATTgATtCGaa	6213	TTcGAAtCAaTCcAACAgt	6381	1796
Set1 1245 A LOV2 SLOV1	gaCcCCAaGCTtTAgTAaa	6214	TTtACTaAAgCTtGGGGtc	6382	1227
Set1 3196 A LOV2 SLOV1	agCcTTGcTTGtTAaATtt	6215	AAaTTTaACaAGcAAGGct	6383	3178
Set1 1450 A LOV2 SLOV1	ttCaGATgCTGcAAcTAaa	6216	TTtAGTtGCaGCaTCTGaa	6384	1432
Set1 3169 A LOV2 SLOV1	atCaCAAgATGgAAtTTat	6217	ATaAATtCCaTCtTGTGat	6385	3151
Set1 3477 A LOV2 SLOV1	aaTaGAAaATGgTCcAAtt	6218	AAtTGGaCCaTTtTCTAtt	6386	3459
Set1 865 A LOV2 SLOV1	gaTgGTGtCTGcTAtTGta	6219	TAcAATaGCaGAcACCAtc	6387	847
Set1 1249 A LOV2 SLOV1	ccAaGCTtTAGtAAaTAta	6220	TAtATTtACtAAaGCTTgg	6388	1231
Set1 1250 A LOV2 SLOV1	caAgCTTtAGTaAAtATaa	6221	TTaTATtTAcTAaAGCTtg	6389	1232
Set1 2202 A LOV2 SLOV1	ctCtGACaGAGtTAcTTca	6222	TGaAGTaACtCTgTCAGag	6390	2184
Set1 1545 A LOV2 SLOV1	caGcTGGaATTcTTtCTaa	6223	TTaGAAaGAaTTcCAGCtg	6391	1527
Set1 1755 A LOV2 SLOV1	gaCtACCaGTTgTGgTTaa	6224	TTaACCaCAaCTgGTAGtc	6392	1737
Set2 254 A LOV3 SLOV2	ccAtACAaCTGtTTtGAaa	6225	TTtCAAaACaGTtGTATgg	6393	236
Set2 703 A LOV3 SLOV2	gaTtAACtATCaAGaTGat	6226	ATcATCtTGaTAgTTAAtc	6394	685
Set2 709 A LOV3 SLOV2	ctAtCAAgATGaTGcAGaa	6227	TTcTGCaTCaTCtTGATag	6395	691
Set2 895 A LOV3 SLOV2	gaAtACAaATGaTGtAGaa	6228	TTcTACaTCaTTtGTATtc	6396	877

Set2 1816 A LOV3 SLOV2	tgTtGGAtTGAtTCgAAat	6229	ATtTCGaATcAAtCCAAca	6397	1798
Set2 1974 A LOV3 SLOV2	ggGtCCGcATGgAAgAAat	6230	ATtTCTtCCaTGcGGACcc	6398	1956
Set2 2425 A LOV3 SLOV2	tcCtAGCtATCgTTcTTtt	6231	AAaAGAaCGaTAgCTAGga	6399	2407
Set2 3146 A LOV3 SLOV2	aaGtGAAgAATgCAcAAga	6232	TCtTGTgCAtTCtTCACtt	6400	3128
Set2 889 A LOV3 SLOV2	caTgCAGaATAcAAaTGat	6233	ATcATTtGTaTTcTGCAtg	6401	871
Set2 1814 A LOV3 SLOV2	acTgTTGgATTgATtCGaa	6234	TTcGAAtCAaTCcAACAgt	6402	1796
Set2 1245 A LOV3 SLOV2	gaCcCCAaGCTtTAgTAaa	6235	TTtACTaAAgCTtGGGGtc	6403	1227
Set2 3196 A LOV3 SLOV2	agCcTTGcTTGtTAaATtt	6236	AAaTTTaACaAGcAAGGct	6404	3178
Set2 1450 A LOV3 SLOV2	ttCaGATgCTGcAAcTAaa	6237	TTtAGTtGCaGCaTCTGaa	6405	1432
Set2 3169 A LOV3 SLOV2	atCaCAAgATGgAAtTTat	6238	ATaAATtCCaTCtTGTGat	6406	3151
Set2 3477 A LOV3 SLOV2	aaTaGAAaATGgTCcAAtt	6239	AAtTGGaCCaTTtTCTAtt	6407	3459
Set2 865 A LOV3 SLOV2	gaTgGTGtCTGcTAtTGta	6240	TAcAATaGCaGAcACCAtc	6408	847
Set2 1249 A LOV3 SLOV2	ccAaGCTtTAGtAAaTAta	6241	TAtATTtACtAAaGCTTgg	6409	1231
Set2 1250 A LOV3 SLOV2	caAgCTTtAGTaAAtATaa	6242	TTaTATtTAcTAaAGCTtg	6410	1232
Set2 2202 A LOV3 SLOV2	ctCtGACAGAGTTAcTTca	6243	TGaAGTaACtCTgTCAGag	6411	2184
Set2 1545 A LOV3 SLOV2	caGcTGGaATTcTTtCTaa	6244	TTaGAAaGAaTTcCAGCtg	6412	1527
Set2 1755 A LOV3 SLOV2	gaCtACCaGTTgTGgTTaa	6245	TTaACCaCAaCTgGTAGtc	6413	1737
Set2 254 A LOV4 SLOV1	ccAtACAaCTGtTTtGAaa	6246	tTtCAAaACaGTtGTATgg	6414	236
Set2 703 A LOV4 SLOV1	gaTtAACtATCaAGaTGat	6247	aTcATCtTGaTAgTTAAtc	6415	685
Set2 709 A LOV4 SLOV1	ctAtCAAgATGaTGcAGaa	6248	tTcTGCaTCaTCtTGATag	6416	691
Set2 895 A LOV4 SLOV1	gaAtACAaATGaTGtAGaa	6249	tTcTACaTCaTTtGTATtc	6417	877
Set2 1816 A LOV4 SLOV1	tgTtGGAtTGAtTCgAAat	6250	aTtTCGaATcAAtCCAAca	6418	1798
Set2 1974 A LOV4 SLOV1	ggGtCCGcATGgAAgAAat	6251	aTtTCTtCCaTGcGGACcc	6419	1956
Set2 2425 A LOV4 SLOV1	tcCtAGCtATCgTTcTTtt	6252	aAaAGAaCGaTAgCTAGga	6420	2407
Set2 3146 A LOV4 SLOV1	aaGtGAAgAATgCAcAAga	6253	tCtTGTgCAtTCtTCACtt	6421	3128
Set2 889 A LOV4 SLOV1	caTgCAGaATAcAAaTGat	6254	aTcATTtGTaTTcTGCAtg	6422	871
Set2 1814 A LOV4 SLOV1	acTgTTGgATTgATtCGaa	6255	tTcGAAtCAaTCcAACAgt	6423	1796
Set2 1245 A LOV4 SLOV1	gaCcCCAaGCTtTAgTAaa	6256	tTtACTaAAgCTtGGGGtc	6424	1227
Set2 3196 A LOV4 SLOV1	agCcTTGcTTGtTAaATtt	6257	aAaTTTaACaAGcAAGGct	6425	3178
Set2 1450 A LOV4 SLOV1	ttCaGATgCTGcAAcTAaa	6258	tTtAGTtGCaGCaTCTGaa	6426	1432
Set2 3169 A	atCaCAAgATGgAAtTTat	6259	aTaAATtCCaTCtTGTGat	6427	3151

LOV4 S LOV1					
Set2 3477 A LOV4 S LOV1	aaTaGAAaATGgTCcAAtt	6260	aAtTGGaCCaTTtTCTAtt	6428	3459
Set2 865 A LOV4 S LOV1	gaTgGTGtCTGcTAtTGta	6261	tAcAATaGCaGAcACCAtc	6429	847
Set2 1249 A LOV4 S LOV1	ccAaGCTtTAGtAAaTAta	6262	tAtATTtACtAAaGCTTgg	6430	1231
Set2 1250 A LOV4 S LOV1	caAgCTTtAGTaAAtATaa	6263	tTaTATtTAcTAaAGCTtg	6431	1232
Set2 2202 A LOV4 S LOV1	ctCtGACaGAGtTAcTTca	6264	tGaAGTaACtCTgTCAGag	6432	2184
Set2 1545 A LOV4 S LOV1	caGcTGGaATTcTTtCTaa	6265	tTaGAAaGAaTTcCAGCtg	6433	1527
Set2 1755 A LOV4 S LOV1	gaCtACCaGTTgTGgTTaa	6266	tTaACCaCAaCTgGTAGtc	6434	1737
Set2 254 A LOV5 S LOV1	ccAtACAaCTGtTTtGAaa	6267	tTtCAAaACaGTtGTATgg	6435	236
Set2 703 A LOV5 S LOV1	gaTtAACtATCaAGaTGat	6268	aTcATCtTGaTAgTTAAtc	6436	685
Set2 709 A LOV5 S LOV1	ctAtCAAgATGaTGcAGaa	6269	tTcTGCaTCaTCtTGATag	6437	691
Set2 895 A LOV5 S LOV1	gaAtACAaATGaTGtAGaa	6270	tTcTACaTCaTTtGTATtc	6438	877
Set2 1816 A LOV5 S LOV1	tgTtGGAtTGAtTCgAAat	6271	aTtTCGaATcAAtCCAAca	6439	1798
Set2 1974 A LOV5 S LOV1	ggGtCCGcATGgAAgAAat	6272	aTtTCTtCCaTGcGGACcc	6440	1956
Set2 2425 A LOV5 S LOV1	tcCtAGCtATCgTTcTTtt	6273	aAaAGAaCGaTAgCTAGga	6441	2407
Set2 3146 A LOV5 S LOV1	aaGtGAAgAATgCAcAAga	6274	tCtTGTgCAtTCtTCACtt	6442	3128
Set2 889 A LOV5 S LOV1	caTgCAGaATAcAAaTGat	6275	aTcATTtGTaTTcTGCAtg	6443	871
Set2 1814 A LOV5 S LOV1	acTgTTGgATTgATtCGaa	6276	tTcGAAtCAaTCcAACAgt	6444	1796
Set2 1245 A LOV5 S LOV1	gaCcCCAaGCTtTAgTAaa	6277	tTtACTaAAgCTtGGGGtc	6445	1227
Set2 3196 A LOV5 S LOV1	agCcTTGcTTGtTAaATtt	6278	aAaTTTaACaAGcAAGGct	6446	3178
Set2 1450 A LOV5 S LOV1	ttCaGATgCTGcAAcTAaa	6279	tTtAGTtGCaGCaTCTGaa	6447	1432
Set2 3169 A LOV5 S LOV1	atCaCAAgATGgAAtTTat	6280	aTaAATtCCaTCtTGTGat	6448	3151
Set2 3477 A LOV5 S LOV1	aaTaGAAaATGgTCcAAtt	6281	aAtTGGaCCaTTtTCTAtt	6449	3459
Set2 865 A LOV5 S LOV1	gaTgGTGtCTGcTAtTGta	6282	tAcAATaGCaGAcACCAtc	6450	847
Set2 1249 A LOV5 S LOV1	ccAaGCTtTAGtAAaTAta	6283	tAtATTtACtAAaGCTTgg	6451	1231
Set2 1250 A LOV5 S LOV1	caAgCTTtAGTaAAtATaa	6284	tTaTATtTAcTAaAGCTtg	6452	1232
Set2 2202 A LOV5 S LOV1	ctCtGACaGAGtTAcTTca	6285	tGaAGTaACtCTgTCAGag	6453	2184
Set2 1545 A LOV5 S LOV1	caGcTGGaATTcTTtCTaa	6286	tTaGAAaGAaTTcCAGCtg	6454	1527
Set2 1755 A LOV5 S LOV1	gaCtACCaGTTgTGgTTaa	6287	tTaACCaCAaCTgGTAGtc	6455	1737
Set2 254 A48 S26	ccAtAcAActGttttGAAA	6288	tTTcAAAAcAGTTGtATGG	6456	236
Set2 703 A48 S26	GAttAActAtcAAGAtGAt	6289	aTcATCTTGAtAGTtAATC	6457	685

Set2 709 A48 S26	ctAtcAAGAtGAtGcAGAA	6290	tTCTGcATcATCTTGAtAG	6458	691
Set2 895 A48 S26	GAAtAcAAAtGAtGtAGAA	6291	tTCtAcATcATTTGtATTC	6459	877
Set2 1816 A48 S26	tGttGGAttGAttcGAAAt	6292	aTTTCGAATcAATCcAAcA	6460	1798
Set2 1974 A48 S26	GGGtccGcAtGGAAGAAAt	6293	aTTTCTTCcATGCGGACCC	6461	1956
Set2 2425 A48 S26	tcctAGctAtcGttctttt	6294	aAAAGAACGAtAGCtAGGA	6462	2407
Set2 3146 A48 S26	AAGtGAAGAAtGcAcAAGA	6295	tCTTGTGcATTCTTcACTT	6463	3128
Set2 889 A48 S26	cAtGcAGAAtAcAAAtGAt	6296	aTcATTTGtATTCTGcATG	6464	871
Set2 1814 A48 S26	ActGttGGAttGAttcGAA	6297	tTCGAATcAATCcAAcAGT	6465	1796
Set2 1245 A48 S26	GAccccAAGctttAGtAAA	6298	tTtACtAAAGCTTGGGGTC	6466	1227
Set2 3196 A48 S26	AGccttGcttGttAAAttt	6299	aAATTtAAcAAGcAAGGCT	6467	3178
Set2 1450 A48 S26	ttcAGAtGctGcAActAAA	6300	tTtAGTTGcAGcATCTGAA	6468	1432
Set2 3169 A48 S26	AtcAcAAGAtGGAAtttAt	6301	atAAATTCcATCTTGTGAT	6469	3151
Set2 3477 A48 S26	AAtAGAAAAtGGtccAAtt	6302	aATTGGACcATTTTCtATT	6470	3459
Set2 865 A48 S26	GAtGGtGtctGctAttGtA	6303	tAcAAtAGcAGAcACcATC	6471	847
Set2 1249 A48 S26	ccAAGctttAGtAAAtAtA	6304	tAtATTtACtAAAGCTTGG	6472	1231
Set2 1250 A48 S26	cAAGctttAGtAAAtAtAA	6305	ttAtATTtACtAAAGCTTG	6473	1232
Set2 2202 A48 S26	ctctGAcAGAGttActtcA	6306	tGAAGtAAcTcTGTcAGAG	6474	2184
Set2 1545 A48 S26	cAGctGGAAttctttctAA	6307	ttAGAAAGAATTCcAGCTG	6475	1527
Set2 1755 A48 S26	GActAccAGttGtGGttAA	6308	ttAACcAcAACTGGtAGTC	6476	1737

名称	第一链序列	SEQ ID NO:	第二链序列	SEQ ID NO:
hs_CTNNB1_1816_AD26740_A22S26	uGuuGGAuuGAuucGAAAuuu	6477	AUUUCGAAUcAAUCcAAcAuu	6486
hs_CTNNB1_3477_AD-26918-A22S26	AAuAGAAAAuGGuccAAuuuu	6478	AAUUGGACcAUUUUCuAUUuu	6487
hs_CTNNB1_1814_AD18983_A22S26	AcuGuuGGAuuGAuucGAAuu	6479	UUCGAAUcAAUCcAAcAGUuu	6488
hs_CTNNB1_709_AD26109_A22S26	cuAucAAGAuGAuGcAGAAuu	6480	UUCUGcAUcAUCUUGAuAGuu	6489

hs_CTNNB1_254_AD-26034-A22S26	ccAuAcAAcuGuuuuGAAAuu	6481	UUUcAAAAcAGUUGuAUGGuu	6490
hs_CTNNB1_3169_AD-25944-A22S26	AucAcAAGAuGGAAuuuAuuu	6482	AuAAAUUCcAUCUUGUGAUuu	6491
hs_CTNNB1_703_AD-26108-A22S26	AUcAUCUUGAuAGUuAAUCuu	6483	uccuAGcuAucGuucuuuuuu	6492
hs_CTNNB1_2425_AD-26800-A22S26	uccuAGcuAucGuucuuuuuu	6484	AAAAGAACGAuAGCuAGGAuu	6493
hs_CTNNB1_1974_AD-26752-A22S26	GGGuccGcAuGGAAGAAAuuu	6485	AUUUCUUCcAUGCGGACCCuu	6494

[00783] “位置”表示 RNAi 剂在人 β-联蛋白序列 NM_001098210.1 中的位置。

[00784] 表 3 中的序列由表 3A 中的缩写代表：

表 3A. 缩写

缩写[a]	核苷酸
A	腺苷-5’-磷酸
C	胞苷-5’-磷酸
G	鸟苷-5’-磷酸
dT	2’-脱氧胸苷-5’-磷酸
U	尿苷-5’-磷酸
c	2’-O-甲基胞苷-5’-磷酸
u	2’-O-甲基尿苷-5’-磷酸
sdT	2’-脱氧胸苷 5’-硫代磷酸酯

[00785] 表 1、表 2 和表 3 的 RNAi 剂的修饰变体和未修饰变体由本领域技术人员容易地构思。未修饰的变体包括不包含碱基修饰的那些（如表 3 中提供）。在几种情况下，修饰有义链中的嘧啶；和/或修饰反义链中位于“A”碱基之前的嘧啶。容易构思涉及其他位置的修饰（或在特定碱基处不存在修饰）。

[00786] 通常而言，深度修饰有义链，并且略微修饰反义链。将一些修饰置于据预测对核酸内切酶敏感的位点处。一些修饰设计成消除针对 RNAi 剂的免疫反应，同时保留活性。一些修饰起到不止一种目的。

[00787]RNAi 剂还偶尔由“ND”前缀而非“AD”提及；因此例如命名为 AD-18892 和 ND-18892 的 RNAi 剂是相同的并且包含相同序列。

[00788] 本文中列出的 RNAi 剂当中，许多如实施例 2 中所述那样合成并且如实施例 3 中所述那样测试。

[00789] 实施例 1A

[00790] 重叠性 siRNA

[00791] 上文所列的一些 siRNA 在序列中彼此重叠。以下表展示 RNAi 剂群组的汇编，其中群组的每个成员与相同群组的每个其他成员重叠至少 12 个核苷酸。提出了有义链的 12 个核苷酸重叠部分和反义链的 12 个核苷酸重叠部分。因此，例如，AD-26022 和 AD-26204 在有义链中共有 CCUGUUCCCCUG(SEQ ID NO:1319) 的序列的共同技术特征并且在反义链中分享 CAGGGGAACAGG(SEQ ID NO:2714) 的序列的共同技术特征。当然应指出，仅显示重叠的 12 核苷酸部分；许多组的 RNAi 剂将重叠超过 12 个核苷酸。还指示在基因内部的位置。

[00792] 本公开还涵盖重叠性 RNAi 剂的公开群组的亚组。例如，本公开包含 AD-26027、AD-26024、AD-26028、AD-26026、AD-26025 的群组，它们均共有 SEQ ID NOs:1334 和 2729 的序列。然而，本公开还包含了这个群组内部的全部亚组或部分组，例如，AD-26027 和 AD-26024；AD-26027、AD-26024、AD-26028 和 AD-26026；AD-26028、AD-26026 和 AD-26025；AD-26027 和 AD-26028；AD-26028 和 AD-26025 等。本公开因此涵在重叠性 RNAi 剂的公开群组内部的任何亚组。这些亚组的成员的序列可以与本文中公开的任何其他要素（例如，修饰、修饰群组、5' 和 / 或 3' 末端帽、平末端、突出端、配体、额外的治疗或方法、药用载体、额外的 RNAi 剂等）组合，条件是这类组合不相互排斥（例如，包含两条链的 RNAi 剂按定义不能同时具有两个平末端和两个突出端）。

表 4. 针对 β - 联蛋白的重叠性 RNAi 剂的群组

位置	有义重叠	SEQ ID NO:	反义重叠	SEQ ID NO:	RNAi剂的重叠性群组
206	CCUGUUCCCCUG	1319	CAGGGGAACAGG	2714	AD-26022、AD-26204
207	CUGUUCCCCUGA	1320	UCAGGGGAACAG	2715	AD-26022、AD-26204
208	UGUUCCCCUGAG	1321	CUCAGGGGAACA	2716	AD-26022、AD-26023
209	GUUCCCCUGAGG	1322	CCUCAGGGGAAC	2717	AD-26022、AD-26023、AD-26204
210	UUCCCCUGAGGG	1323	CCCUCAGGGGAA	2718	AD-26022、AD-26023、AD-26204
211	UCCCCUGAGGGU	1324	ACCCUCAGGGGA	2719	AD-26022、AD-26023、AD-26204
212	CCCCUGAGGGUA	1325	UACCCUCAGGGG	2720	AD-26022、AD-26023、AD-26204
213	CCCUGAGGGUAU	1326	AUACCCUCAGGG	2721	AD-26022、AD-26023
214	CCUGAGGGUAUU	1327	AAUACCCUCAGG	2722	AD-26024、AD-26023
215	CUGAGGGUAUUU	1328	AAAUACCCUCAG	2723	AD-26024、AD-26025
216	UGAGGGUAUUUG	1329	CAAAUACCCUCA	2724	AD-26024、AD-26026
217	GAGGGUAUUUGA	1330	UCAAAUACCCUC	2725	AD-26024、AD-26025
218	AGGGUAUUUGAA	1331	UUCAAAUACCCU	2726	AD-26024、AD-26026、AD-26025
219	GGGUAUUUGAAG	1332	CUUCAAAUACCC	2727	AD-26024、AD-26026、AD-26025
220	GGUAUUUGAAGU	1333	ACUUCAAAUACC	2728	AD-26027、AD-26024、AD-26026、AD-26025
221	GUAUUUGAAGUA	1334	UACUUCAAAUAC	2729	AD-26027、AD-26024、AD-26028、AD-26026、AD-26025
222	UAUUUGAAGUAU	1335	AUACUUCAAAUA	2730	AD-26027、AD-26028、AD-26026、AD-26025
223	AUUUGAAGUAUA	1336	UAUACUUCAAAU	2731	AD-26027、AD-26028
224	UUUGAAGUAUAC	1337	GUAUACUUCAAA	2732	AD-26027、AD-26029
225	UUGAAGUAUACC	1338	GGUAUACUUCAA	2733	AD-26029、AD-26028
226	UGAAGUAUACCA	1339	UGGUAUACUUCA	2734	AD-26027、AD-26029、AD-26028
227	GAAGUAUACCAU	1340	AUGGUAUACUUC	2735	AD-26027、AD-26029、AD-26028
228	AAGUAUACCAUA	1341	UAUGGUAUACUU	2736	AD-26029、AD-26028

229	AGUAUACCAUAC	1342	GUAUGGUAUACU	2737	AD-26029、AD-26030
230	GUAUACCAUACA	1343	UGUAUGGUAUAC	2738	AD-26031、AD-26029、AD-26030
231	UAUACCAUACAA	1344	UUGUAUGGUAUA	2739	AD-26032、AD-26031、AD-26029、AD-26030
232	AUACCAUACAAC	1345	GUUGUAUGGUAU	2740	AD-26032、AD-26031
233	UACCAUACAACU	1346	AGUUGUAUGGUA	2741	AD-26032、AD-26031、AD-26030
234	ACCAUACAACUG	1347	CAGUUGUAUGGU	2742	AD-26032、AD-26031、AD-26033、AD-26030
235	CCAUACAACUGU	1348	ACAGUUGUAUGG	2743	AD-26032、AD-26034、AD-26031、AD-26033、AD-26030
236	CAUACAACUGUU	1349	AACAGUUGUAUG	2744	AD-26032、AD-26034、AD-26031、AD-26033、AD-26030
237	AUACAACUGUUU	1350	AAACAGUUGUAU	2745	AD-26032、AD-26034、AD-26031、AD-26033
238	UACAACUGUUUU	1351	AAAACAGUUGUA	2746	AD-26032、AD-26034、AD-26033
239	ACAACUGUUUUG	1352	CAAAACAGUUGU	2747	AD-26034、AD-26033
240	CAACUGUUUUGA	1353	UCAAAACAGUUG	2748	AD-26034、AD-26033
241	AACUGUUUUGAA	1354	UUCAAAACAGUU	2749	AD-26034、AD-26033
250	GAAAAUCCAGCG	1355	CGCUGGAUUUUC	2750	AD-19763、AD-26035
251	AAAAUCCAGCGU	1356	ACGCUGGAUUUU	2751	AD-26036、AD-19763、AD-26035
252	AAAUCCAGCGUG	1357	CACGCUGGAUUU	2752	AD-26036、AD-19763、AD-26035
253	AAUCCAGCGUGG	1358	CCACGCUGGAUU	2753	AD-26036、AD-26035
254	AUCCAGCGUGGA	1359	UCCACGCUGGAU	2754	AD-26036、AD-26035
255	UCCAGCGUGGAC	1360	GUCCACGCUGGA	2755	AD-26036、AD-26035
256	CCAGCGUGGACA	1361	UGUCCACGCUGG	2756	AD-26036、AD-26035、AD-26037
257	CAGCGUGGACAA	1362	UUGUCCACGCUG	2757	AD-26036、AD-26035、AD-26037
258	AGCGUGGACAAU	1363	AUUGUCCACGCU	2758	AD-26036、AD-26037
261	GUGGACAAUGGC	1364	GCCAUUGUCCAC	2759	AD-26038、AD-26037
262	UGGACAAUGGCU	1365	AGCCAUUGUCCA	2760	AD-26038、AD-26037
263	GGACAAUGGCUA	1366	UAGCCAUUGUCC	2761	AD-26038、AD-26037
264	GACAAUGGCUAC	1367	GUAGCCAUUGUC	2762	AD-18896、AD-26038
265	ACAAUGGCUACU	1368	AGUAGCCAUUGU	2763	AD-18896、AD-26038、AD-18953
266	CAAUGGCUACUC	1369	GAGUAGCCAUUG	2764	AD-18896、AD-26038、AD-18953

267	AAUGGCUACUCA	1370	UGAGUAGCCAUU	2765	AD-18896、AD-26038、AD-18953
268	AUGGCUACUCAA	1371	UUGAGUAGCCAU	2766	AD-18896、AD-26038、AD-18953、AD-26040
269	UGGCUACUCAAG	1372	CUUGAGUAGCCA	2767	AD-18896、AD-26041、AD-18953、AD-26040
270	GGCUACUCAAGC	1373	GCUUGAGUAGCC	2768	AD-18896、AD-26041、AD-26039、AD-18953、AD-26040
271	GCUACUCAAGCU	1374	AGCUUGAGUAGC	2769	AD-18896、AD-26041、AD-18953、AD-26040
272	CUACUCAAGCUG	1375	CAGCUUGAGUAG	2770	AD-26041、AD-26042、AD-18953、AD-26040
273	UACUCAAGCUGA	1376	UCAGCUUGAGUA	2771	AD-26041、AD-26042、AD-26040
274	ACUCAAGCUGAU	1377	AUCAGCUUGAGU	2772	AD-26041、AD-26042、AD-26039、AD-26040
275	CUCAAGCUGAUU	1378	AAUCAGCUUGAG	2773	AD-26041、AD-26042、AD-26040
276	UCAAGCUGAUUU	1379	AAAUCAGCUUGA	2774	AD-26041、AD-26042
290	UGGAGUUGGACA	1380	UGUCCAACUCCA	2775	AD-26043、AD-26044
291	GGAGUUGGACAU	1381	AUGUCCAACUCC	2776	AD-26043、AD-26044
294	GUUGGACAUGGC	1382	GCCAUGUCCAAC	2777	AD-26045、AD-26044
295	UUGGACAUGGCC	1383	GGCCAUGUCCAA	2778	AD-26045、AD-26044
296	UGGACAUGGCCA	1384	UGGCCAUGUCCA	2779	AD-26045、AD-26044
297	GGACAUGGCCAU	1385	AUGGCCAUGUCC	2780	AD-26045、AD-26044
306	CAUGGAACCAGA	1386	UCUGGUUCCAUG	2781	AD-26047、AD-26046
307	AUGGAACCAGAC	1387	GUCUGGUUCCAU	2782	AD-26047、AD-26046
308	UGGAACCAGACA	1388	UGUCUGGUUCCA	2783	AD-26047、AD-26046
309	GGAACCAGACAG	1389	CUGUCUGGUUCC	2784	AD-26047、AD-26046
310	GAACCAGACAGA	1390	UCUGUCUGGUUC	2785	AD-26047、AD-26046
311	AACCAGACAGAA	1391	UUCUGUCUGGUU	2786	AD-26047、AD-26046
316	GACAGAAAAGCG	1392	CGCUUUUCUGUC	2787	AD-26050、AD-26049
317	ACAGAAAAGCGG	1393	CCGCUUUUCUGU	2788	AD-26050、AD-26049
318	CAGAAAAGCGGC	1394	GCCGCUUUUCUG	2789	AD-26050、AD-26049
319	AGAAAAGCGGCU	1395	AGCCGCUUUUCU	2790	AD-26050、AD-26049
320	GAAAAGCGGCUG	1396	CAGCCGCUUUUC	2791	AD-26050、AD-26049
321	AAAAGCGGCUGU	1397	ACAGCCGCUUUU	2792	AD-26050、AD-26049
322	AAAGCGGCUGUU	1398	AACAGCCGCUUU	2793	AD-26050、AD-26049
323	AAGCGGCUGUUA	1399	UAACAGCCGCUU	2794	AD-26050、AD-19743
330	UGUUAGUCACUG	1400	CAGUGACUAACA	2795	AD-26051、AD-19743
337	CACUGGCAGCAA	1401	UUGCUGCCAGUG	2796	AD-26051、AD-26052
338	ACUGGCAGCAAC	1402	GUUGCUGCCAGU	2797	AD-26053、AD-26052
339	CUGGCAGCAACA	1403	UGUUGCUGCCAG	2798	AD-26053、AD-26052

340	UGGCAGCAACAG	1404	CUGUUGCUGCCA	2799	AD-26053、AD-26052
341	GGCAGCAACAGU	1405	ACUGUUGCUGCC	2800	AD-26053、AD-26052
342	GCAGCAACAGUC	1406	GACUGUUGCUGC	2801	AD-26053、AD-26052
343	CAGCAACAGUCU	1407	AGACUGUUGCUG	2802	AD-26053、AD-26052
344	AGCAACAGUCUU	1408	AAGACUGUUGCU	2803	AD-26053、AD-26052
353	CUUACCUGGACU	1409	AGUCCAGGUAAG	2804	AD-26054、AD-26055
354	UUACCUGGACUC	1410	GAGUCCAGGUAA	2805	AD-26054、AD-26055
355	UACCUGGACUCU	1411	AGAGUCCAGGUA	2806	AD-26054、AD-26055
356	ACCUGGACUCUG	1412	CAGAGUCCAGGU	2807	AD-26054、AD-26055
357	CCUGGACUCUGG	1413	CCAGAGUCCAGG	2808	AD-26056、AD-26055
358	CUGGACUCUGGA	1414	UCCAGAGUCCAG	2809	AD-26054、AD-26056、AD-26055
359	UGGACUCUGGAA	1415	UUCCAGAGUCCA	2810	AD-26054、AD-26056、AD-26055
360	GGACUCUGGAAU	1416	AUUCCAGAGUCC	2811	AD-26056、AD-26055
366	UGGAAUCCAUUC	1417	GAAUGGAUUCCA	2812	AD-19072、AD-18925
367	GGAAUCCAUUCU	1418	AGAAUGGAUUCC	2813	AD-19072、AD-18925
368	GAAUCCAUUCUG	1419	CAGAAUGGAUUC	2814	AD-19072、AD-18925
369	AAUCCAUUCUGG	1420	CCAGAAUGGAUU	2815	AD-19072、AD-18925
370	AUCCAUUCUGGU	1421	ACCAGAAUGGAU	2816	AD-19072、AD-18925
371	UCCAUUCUGGUG	1422	CACCAGAAUGGA	2817	AD-19072、AD-18925
372	CCAUUCUGGUGC	1423	GCACCAGAAUGG	2818	AD-19072、AD-18925
401	CUCUGAGUGGUA	1424	UACCACUCAGAG	2819	AD-26060、AD-26059
402	UCUGAGUGGUAA	1425	UUACCACUCAGA	2820	AD-26060、AD-26059
403	CUGAGUGGUAAA	1426	UUUACCACUCAG	2821	AD-26060、AD-26059
417	CAAUCCUGAGGA	1427	UCCUCAGGAUUG	2822	AD-26062、AD-26061
418	AAUCCUGAGGAA	1428	UUCCUCAGGAUU	2823	AD-26062、AD-26061
423	UGAGGAAGAGGA	1429	UCCUCUUCCUCA	2824	AD-26062、AD-26063
424	GAGGAAGAGGAU	1430	AUCCUCUUCCUC	2825	AD-26062、AD-26063
441	UACCUCCCAAGU	1431	ACUUGGGAGGUA	2826	AD-26065、AD-26064
442	ACCUCCCAAGUC	1432	GACUUGGGAGGU	2827	AD-26065、AD-26064
443	CCUCCCAAGUCC	1433	GGACUUGGGAGG	2828	AD-26065、AD-26064
444	CUCCCAAGUCCU	1434	AGGACUUGGGAG	2829	AD-26065、AD-26064
445	UCCCAAGUCCUG	1435	CAGGACUUGGGA	2830	AD-26065、AD-26064
446	CCCAAGUCCUGU	1436	ACAGGACUUGGG	2831	AD-26065、AD-26064
447	CCAAGUCCUGUA	1437	UACAGGACUUGG	2832	AD-26065、AD-26064
457	UAUGAGUGGGAA	1438	UUCCCACUCAUA	2833	AD-26066、AD-26067
459	UGAGUGGGAACA	1439	UGUUCCCACUCA	2834	AD-26070、AD-26067
460	GAGUGGGAACAG	1440	CUGUUCCCACUC	2835	AD-26071、AD-26070、AD-26067
461	AGUGGGAACAGG	1441	CCUGUUCCCACU	2836	AD-26071、AD-26070、AD-26067
462	GUGGGAACAGGG	1442	CCCUGUUCCCAC	2837	AD-26071、AD-26070、AD-26067

463	UGGGAACAGGGA	1443	UCCCUGUUCCCA	2838	AD-26071、AD-26070、AD-26067
464	GGGAACAGGGAU	1444	AUCCCUGUUCCC	2839	AD-26071、AD-26070、AD-26067
465	GGAACAGGGAUU	1445	AAUCCCUGUUCC	2840	AD-26071、AD-26070
466	GAACAGGGAUUU	1446	AAAUCCCUGUUC	2841	AD-26071、AD-26070
477	UUCUCAGUCCUU	1447	AAGGACUGAGAA	2842	AD-26073、AD-26072
480	UCAGUCCUUCAC	1448	GUGAAGGACUGA	2843	AD-26074、AD-26073
481	CAGUCCUUCACU	1449	AGUGAAGGACUG	2844	AD-26074、AD-26073
482	AGUCCUUCACUC	1450	GAGUGAAGGACU	2845	AD-26074、AD-26073
483	GUCCUUCACUCA	1451	UGAGUGAAGGAC	2846	AD-26074、AD-26073
484	UCCUUCACUCAA	1452	UUGAGUGAAGGA	2847	AD-26074、AD-26073
486	CUUCACUCAAGA	1453	UCUUGAGUGAAG	2848	AD-26074、AD-26075
487	UUCACUCAAGAA	1454	UUCUUGAGUGAA	2849	AD-26074、AD-26075
492	UCAAGAACAAGU	1455	ACUUGUUCUUGA	2850	AD-26076、AD-26075
493	CAAGAACAAGUA	1456	UACUUGUUCUUG	2851	AD-26076、AD-26075
511	AUUGAUGGACAG	1457	CUGUCCAUCAAU	2852	AD-26077、AD-26078
512	UUGAUGGACAGU	1458	ACUGUCCAUCAA	2853	AD-26077、AD-26078
513	UGAUGGACAGUA	1459	UACUGUCCAUCA	2854	AD-26077、AD-26078
523	UAUGCAAUGACU	1460	AGUCAUUGCAUA	2855	AD-19757、AD-19756
524	AUGCAAUGACUC	1461	GAGUCAUUGCAU	2856	AD-19757、AD-19756
525	UGCAAUGACUCG	1462	CGAGUCAUUGCA	2857	AD-19757、AD-19756
526	GCAAUGACUCGA	1463	UCGAGUCAUUGC	2858	AD-19757、AD-19756
534	UCGAGCUCAGAG	1464	CUCUGAGCUCGA	2859	AD-19744、AD-26079
535	CGAGCUCAGAGG	1465	CCUCUGAGCUCG	2860	AD-19744、AD-26079
536	GAGCUCAGAGGG	1466	CCCUCUGAGCUC	2861	AD-19744、AD-26079
537	AGCUCAGAGGGU	1467	ACCCUCUGAGCU	2862	AD-19744、AD-26079
538	GCUCAGAGGGUA	1468	UACCCUCUGAGC	2863	AD-19744、AD-26079
541	CAGAGGGUACGA	1469	UCGUACCCUCUG	2864	AD-26080、AD-19744
542	AGAGGGUACGAG	1470	CUCGUACCCUCU	2865	AD-26080、AD-26081
543	GAGGGUACGAGC	1471	GCUCGUACCCUC	2866	AD-26080、AD-26081
544	AGGGUACGAGCU	1472	AGCUCGUACCCU	2867	AD-26080、AD-26081
545	GGGUACGAGCUG	1473	CAGCUCGUACCC	2868	AD-26080、AD-26081
546	GGUACGAGCUGC	1474	GCAGCUCGUACC	2869	AD-26080、AD-26082
547	GUACGAGCUGCU	1475	AGCAGCUCGUAC	2870	AD-26080、AD-26081、AD-26082
548	UACGAGCUGCUA	1476	UAGCAGCUCGUA	2871	AD-26080、AD-26081、AD-26082
549	ACGAGCUGCUAU	1477	AUAGCAGCUCGU	2872	AD-26081、AD-26082
558	UAUGUUCCCUGA	1478	UCAGGGAACAUA	2873	AD-26084、AD-26083
559	AUGUUCCCUGAG	1479	CUCAGGGAACAU	2874	AD-26084、AD-26083
560	UGUUCCCUGAGA	1480	UCUCAGGGAACA	2875	AD-26084、AD-26083
561	GUUCCCUGAGAC	1481	GUCUCAGGGAAC	2876	AD-26084、AD-26085、AD-26083

562	UUCCCUGAGACA	1482	UGUCUCAGGGAA	2877	AD-26084、AD-26085、AD-26083
563	UCCCUGAGACAU	1483	AUGUCUCAGGGA	2878	AD-26084、AD-26085、AD-26083
564	CCCUGAGACAUU	1484	AAUGUCUCAGGG	2879	AD-26084、AD-26085、AD-26083
565	CCUGAGACAUUA	1485	UAAUGUCUCAGG	2880	AD-26084、AD-26085
576	AGAUGAGGGCAU	1486	AUGCCCUCAUCU	2881	AD-26086、AD-18911
577	GAUGAGGGCAUG	1487	CAUGCCCUCAUC	2882	AD-26086、AD-18911
578	AUGAGGGCAUGC	1488	GCAUGCCCUCAU	2883	AD-19011、AD-18911
579	UGAGGGCAUGCA	1489	UGCAUGCCCUCA	2884	AD-26086、AD-19011、AD-18911
580	GAGGGCAUGCAG	1490	CUGCAUGCCCUC	2885	AD-18911、AD-26087
581	AGGGCAUGCAGA	1491	UCUGCAUGCCCU	2886	AD-18959、AD-26086、AD-18911、AD-26087
582	GGGCAUGCAGAU	1492	AUCUGCAUGCCC	2887	AD-18911、AD-26087
583	GGCAUGCAGAUC	1493	GAUCUGCAUGCC	2888	AD-26088、AD-18911、AD-26087
584	GCAUGCAGAUCC	1494	GGAUCUGCAUGC	2889	AD-26088、AD-26087
585	CAUGCAGAUCCC	1495	GGGAUCUGCAUG	2890	AD-26088、AD-18959、AD-19011、AD-26087
586	AUGCAGAUCCCA	1496	UGGGAUCUGCAU	2891	AD-26088、AD-26087
587	UGCAGAUCCCAU	1497	AUGGGAUCUGCA	2892	AD-26088、AD-18959
588	GCAGAUCCCAUC	1498	GAUGGGAUCUGC	2893	AD-26088、AD-18959
590	AGAUCCCAUCUA	1499	UAGAUGGGAUCU	2894	AD-26088、AD-26089
594	CCCAUCUACACA	1500	UGUGUAGAUGGG	2895	AD-26089、AD-26090
595	CCAUCUACACAG	1501	CUGUGUAGAUGG	2896	AD-26089、AD-26090
596	CAUCUACACAGU	1502	ACUGUGUAGAUG	2897	AD-26089、AD-26090
597	AUCUACACAGUU	1503	AACUGUGUAGAU	2898	AD-26089、AD-26090
610	GAUGCUGCUCAU	1504	AUGAGCAGCAUC	2899	AD-26091、AD-26092
611	AUGCUGCUCAUC	1505	GAUGAGCAGCAU	2900	AD-26092、AD-26093
612	UGCUGCUCAUCC	1506	GGAUGAGCAGCA	2901	AD-26092、AD-26094
613	GCUGCUCAUCCC	1507	GGGAUGAGCAGC	2902	AD-26092、AD-26093
614	CUGCUCAUCCCA	1508	UGGGAUGAGCAG	2903	AD-26092、AD-26093、AD-26094
615	UGCUCAUCCCAC	1509	GUGGGAUGAGCA	2904	AD-26092、AD-26093、AD-26094
616	GCUCAUCCCACU	1510	AGUGGGAUGAGC	2905	AD-26092、AD-26093、AD-26094
617	CUCAUCCCACUA	1511	UAGUGGGAUGAG	2906	AD-26092、AD-26094
618	UCAUCCCACUAA	1512	UUAGUGGGAUGA	2907	AD-19070、AD-18949、AD-26093、AD-26094
619	CAUCCCACUAAU	1513	AUUAGUGGGAUG	2908	AD-18949、AD-19048、AD-18954、AD-26094

620	AUCCCACUAAUG	1514	CAUUAGUGGGAU	2909	AD-19070、AD-18918、AD-19048、AD-18954
621	UCCCACUAAUGU	1515	ACAUUAGUGGGA	2910	AD-19070、AD-18949、AD-18918、AD-19048、AD-18954
622	CCCACUAAUGUC	1516	GACAUUAGUGGG	2911	AD-26095、AD-19070、AD-18918、AD-19048、AD-18954
623	CCACUAAUGUCC	1517	GGACAUUAGUGG	2912	AD-26095、AD-18949、AD-18918、AD-19048、AD-18954
624	CACUAAUGUCCA	1518	UGGACAUUAGUG	2913	AD-26095、AD-18949、AD-18918、AD-19048、AD-18954
625	ACUAAUGUCCAG	1519	CUGGACAUUAGU	2914	AD-26095、AD-18918、AD-19048
626	CUAAUGUCCAGC	1520	GCUGGACAUUAG	2915	AD-26095、AD-18918、AD-19048
627	UAAUGUCCAGCG	1521	CGCUGGACAUUA	2916	AD-26095、AD-18918
636	GCGUUUGGCUGA	1522	UCAGCCAAACGC	2917	AD-26096、AD-19765
637	CGUUUGGCUGAA	1523	UUCAGCCAAACG	2918	AD-26096、AD-19765
638	GUUUGGCUGAAC	1524	GUUCAGCCAAAC	2919	AD-26096、AD-19765
639	UUUGGCUGAACC	1525	GGUUCAGCCAAA	2920	AD-26096、AD-19765
640	UUGGCUGAACCA	1526	UGGUUCAGCCAA	2921	AD-26096、AD-18974、AD-19765
641	UGGCUGAACCAU	1527	AUGGUUCAGCCA	2922	AD-26096、AD-19765、AD-26097
642	GGCUGAACCAUC	1528	GAUGGUUCAGCC	2923	AD-18974、AD-19000、AD-19765、AD-26097
643	GCUGAACCAUCA	1529	UGAUGGUUCAGC	2924	AD-18974、AD-19765、AD-26097
644	CUGAACCAUCAC	1530	GUGAUGGUUCAG	2925	AD-18974、AD-19000
645	UGAACCAUCACA	1531	UGUGAUGGUUCA	2926	AD-18974、AD-26097
646	GAACCAUCACAG	1532	CUGUGAUGGUUC	2927	AD-18974、AD-19000、AD-26097
647	AACCAUCACAGA	1533	UCUGUGAUGGUU	2928	AD-18974、AD-19000、AD-26098、AD-26097
648	ACCAUCACAGAU	1534	AUCUGUGAUGGU	2929	AD-19000、AD-26098、AD-26099、AD-26097
649	CCAUCACAGAUG	1535	CAUCUGUGAUGG	2930	AD-19000、AD-26098、AD-26099
650	CAUCACAGAUGC	1536	GCAUCUGUGAUG	2931	AD-26098、AD-26099
651	AUCACAGAUGCU	1537	AGCAUCUGUGAU	2932	AD-26100、AD-26098
652	UCACAGAUGCUG	1538	CAGCAUCUGUGA	2933	AD-26100、AD-26099

653	CACAGAUGCUGA	1539	UCAGCAUCUGUG	2934	AD-26100、AD-26098、AD-26099
654	ACAGAUGCUGAA	1540	UUCAGCAUCUGU	2935	AD-26100、AD-26099
655	CAGAUGCUGAAA	1541	UUUCAGCAUCUG	2936	AD-26100、AD-26099
657	GAUGCUGAAACA	1542	UGUUUCAGCAUC	2937	AD-26100、AD-26101
658	AUGCUGAAACAU	1543	AUGUUUCAGCAU	2938	AD-26100、AD-26101
661	CUGAAACAUGCA	1544	UGCAUGUUUCAG	2939	AD-26101、AD-26102
662	UGAAACAUGCAG	1545	CUGCAUGUUUCA	2940	AD-26101、AD-26102
663	GAAACAUGCAGU	1546	ACUGCAUGUUUC	2941	AD-26101、AD-26102
664	AAACAUGCAGUU	1547	AACUGCAUGUUU	2942	AD-26101、AD-26102
665	AACAUGCAGUUG	1548	CAACUGCAUGUU	2943	AD-26103、AD-26102
666	ACAUGCAGUUGU	1549	ACAACUGCAUGU	2944	AD-26103、AD-26102
667	CAUGCAGUUGUA	1550	UACAACUGCAUG	2945	AD-26103、AD-26102
668	AUGCAGUUGUAA	1551	UUACAACUGCAU	2946	AD-26104、AD-26103、AD-26102
669	UGCAGUUGUAAA	1552	UUUACAACUGCA	2947	AD-26105、AD-26103
670	GCAGUUGUAAAC	1553	GUUUACAACUGC	2948	AD-26105、AD-26104、AD-26103
671	CAGUUGUAAACU	1554	AGUUUACAACUG	2949	AD-26105、AD-26104、AD-26103、AD-26106
672	AGUUGUAAACUU	1555	AAGUUUACAACU	2950	AD-26105、AD-26103、AD-26106
673	GUUGUAAACUUG	1556	CAAGUUUACAAC	2951	AD-26105、AD-26104、AD-26106
674	UUGUAAACUUGA	1557	UCAAGUUUACAA	2952	AD-26105、AD-26808、AD-26104、AD-26106
675	UGUAAACUUGAU	1558	AUCAAGUUUACA	2953	AD-26105、AD-26808、AD-26104、AD-26106、AD-26809
676	GUAAACUUGAUU	1559	AAUCAAGUUUAC	2954	AD-26105、AD-26808、AD-26106、AD-26809
677	UAAACUUGAUUA	1560	UAAUCAAGUUUA	2955	AD-26808、AD-26106、AD-26809
678	AAACUUGAUUAA	1561	UUAAUCAAGUUU	2956	AD-26808、AD-26810、AD-26106、AD-26809
679	AACUUGAUUAAC	1562	GUUAAUCAAGUU	2957	AD-26808、AD-26810、AD-26809
680	ACUUGAUUAACU	1563	AGUUAAUCAAGU	2958	AD-26808、AD-26809
681	CUUGAUUAACUA	1564	UAGUUAAUCAAG	2959	AD-26107、AD-26808、AD-26810、AD-26809
682	UUGAUUAACUAU	1565	AUAGUUAAUCAA	2960	AD-26107、AD-26810、AD-26809
683	UGAUUAACUAUC	1566	GAUAGUUAAUCA	2961	AD-26107、AD-26810
684	GAUUAACUAUCA	1567	UGAUAGUUAAUC	2962	AD-26107、AD-26810、

					AD-26108
685	AUUAACUAUCAA	1568	UUGAUAGUUAAU	2963	AD-26107、AD-26108
686	UUAACUAUCAAG	1569	CUUGAUAGUUAA	2964	AD-26107、AD-26108
687	UAACUAUCAAGA	1570	UCUUGAUAGUUA	2965	AD-26107、AD-26108
688	AACUAUCAAGAU	1571	AUCUUGAUAGUU	2966	AD-26107、AD-26108
690	CUAUCAAGAUGA	1572	UCAUCUUGAUAG	2967	AD-26109、AD-26108
691	UAUCAAGAUGAU	1573	AUCAUCUUGAUA	2968	AD-26109、AD-26108
707	AACUUGCCACAC	1574	GUGUGGCAAGUU	2969	AD-26110、AD-26111
708	ACUUGCCACACG	1575	CGUGUGGCAAGU	2970	AD-26110、AD-26111
709	CUUGCCACACGU	1576	ACGUGUGGCAAG	2971	AD-26110、AD-26111
710	UUGCCACACGUG	1577	CACGUGUGGCAA	2972	AD-26110、AD-26111
711	UGCCACACGUGC	1578	GCACGUGUGGCA	2973	AD-26110、AD-26111
712	GCCACACGUGCA	1579	UGCACGUGUGGC	2974	AD-26110、AD-26111
713	CCACACGUGCAA	1580	UUGCACGUGUGG	2975	AD-26110、AD-26111
714	CACACGUGCAAU	1581	AUUGCACGUGUG	2976	AD-26112、AD-26111
721	GCAAUCCCUGAA	1582	UUCAGGGAUUGC	2977	AD-26112、AD-26123
722	CAAUCCCUGAAC	1583	GUUCAGGGAUUG	2978	AD-26124、AD-26123
723	AAUCCCUGAACU	1584	AGUUCAGGGAUU	2979	AD-26124、AD-26125
724	AUCCCUGAACUG	1585	CAGUUCAGGGAU	2980	AD-26124、AD-26123
725	UCCCUGAACUGA	1586	UCAGUUCAGGGA	2981	AD-26124、AD-26125
726	CCCUGAACUGAC	1587	GUCAGUUCAGGG	2982	AD-26124、AD-26123
727	CCUGAACUGACA	1588	UGUCAGUUCAGG	2983	AD-26124、AD-26123、AD-26125
728	CUGAACUGACAA	1589	UUGUCAGUUCAG	2984	AD-26124、AD-26123、AD-26125
729	UGAACUGACAAA	1590	UUUGUCAGUUCA	2985	AD-26124、AD-26125、AD-26126
730	GAACUGACAAAA	1591	UUUUGUCAGUUC	2986	AD-26125、AD-26126
731	AACUGACAAAAC	1592	GUUUUGUCAGUU	2987	AD-26128、AD-26126、AD-26127
732	ACUGACAAAACU	1593	AGUUUUGUCAGU	2988	AD-26128、AD-26126、AD-26129
733	CUGACAAAACUG	1594	CAGUUUUGUCAG	2989	AD-26128、AD-26126、AD-26129
734	UGACAAAACUGC	1595	GCAGUUUUGUCA	2990	AD-26128、AD-26127、AD-26129
735	GACAAAACUGCU	1596	AGCAGUUUUGUC	2991	AD-26128、AD-26126、AD-26129
736	ACAAAACUGCUA	1597	UAGCAGUUUUGU	2992	AD-26128、AD-26126、AD-26127、AD-26129
737	CAAAACUGCUAA	1598	UUAGCAGUUUUG	2993	AD-26128、AD-26127、AD-26129
738	AAAACUGCUAAA	1599	UUUAGCAGUUUU	2994	AD-26128、AD-26129
755	AGGACCAGGUGG	1600	CCACCUGGUCCU	2995	AD-26131、AD-26130

756	GGACCAGGUGGU	1601	ACCACCUGGUCC	2996	AD-26132、AD-26131、AD-26130
757	GACCAGGUGGUG	1602	CACCACCUGGUC	2997	AD-26132、AD-26133、AD-26131、AD-26130
758	ACCAGGUGGUGG	1603	CCACCACCUGGU	2998	AD-26132、AD-26133、AD-26131、AD-26130、AD-26136
759	CCAGGUGGUGGU	1604	ACCACCACCUGG	2999	AD-26132、AD-26131、AD-26136
760	CAGGUGGUGGUU	1605	AACCACCACCUG	3000	AD-26132、AD-26133、AD-26131、AD-26136
761	AGGUGGUGGUUA	1606	UAACCACCACCU	3001	AD-26132、AD-26131、AD-26130、AD-26136
762	GGUGGUGGUUAA	1607	UUAACCACCACC	3002	AD-26132、AD-26131
763	GUGGUGGUUAAU	1608	AUUAACCACCAC	3003	AD-26132、AD-26133、AD-26136
764	UGGUGGUUAAUA	1609	UAUUAACCACCA	3004	AD-26133、AD-26136
784	GUUAUGGUCCAU	1610	AUGGACCAUAAC	3005	AD-26138、AD-26137
787	AUGGUCCAUCAG	1611	CUGAUGGACCAU	3006	AD-26138、AD-26139
788	UGGUCCAUCAGC	1612	GCUGAUGGACCA	3007	AD-26138、AD-26139、AD-26140
789	GGUCCAUCAGCU	1613	AGCUGAUGGACC	3008	AD-26142、AD-26140
790	GUCCAUCAGCUU	1614	AAGCUGAUGGAC	3009	AD-26143、AD-26142、AD-26140
791	UCCAUCAGCUUU	1615	AAAGCUGAUGGA	3010	AD-26139、AD-26143、AD-26142、AD-26140
792	CCAUCAGCUUUC	1616	GAAAGCUGAUGG	3011	AD-26143、AD-26142、AD-26140
793	CAUCAGCUUUCU	1617	AGAAAGCUGAUG	3012	AD-26139、AD-26143、AD-26142、AD-26140
794	AUCAGCUUUCUA	1618	UAGAAAGCUGAU	3013	AD-26143、AD-26142、AD-26140
795	UCAGCUUUCUAA	1619	UUAGAAAGCUGA	3014	AD-26143、AD-26142
796	CAGCUUUCUAAA	1620	UUUAGAAAGCUG	3015	AD-26143、AD-26142
811	GAAGCUUCCAGA	1621	UCUGGAAGCUUC	3016	AD-26144、AD-18950
812	AAGCUUCCAGAC	1622	GUCUGGAAGCUU	3017	AD-26144、AD-18950
813	AGCUUCCAGACA	1623	UGUCUGGAAGCU	3018	AD-26145、AD-26144、AD-18950
814	GCUUCCAGACAC	1624	GUGUCUGGAAGC	3019	AD-26145、AD-26144
815	CUUCCAGACACG	1625	CGUGUCUGGAAG	3020	AD-26145、AD-26144
816	UUCCAGACACGC	1626	GCGUGUCUGGAA	3021	AD-26146、AD-26144
817	UCCAGACACGCU	1627	AGCGUGUCUGGA	3022	AD-26145、AD-26146、AD-26144
818	CCAGACACGCUA	1628	UAGCGUGUCUGG	3023	AD-26145、AD-26146

819	CAGACACGCUAU	1629	AUAGCGUGUCUG	3024	AD-26145、AD-26146
820	AGACACGCUAUC	1630	GAUAGCGUGUCU	3025	AD-26146、AD-26147
821	GACACGCUAUCA	1631	UGAUAGCGUGUC	3026	AD-19745、AD-26146
822	ACACGCUAUCAU	1632	AUGAUAGCGUGU	3027	AD-19745、AD-26146、AD-26147
823	CACGCUAUCAUG	1633	CAUGAUAGCGUG	3028	AD-19745、AD-26147
824	ACGCUAUCAUGC	1634	GCAUGAUAGCGU	3029	AD-19745、AD-19739、AD-26147
825	CGCUAUCAUGCG	1635	CGCAUGAUAGCG	3030	AD-19745、AD-19746、AD-19739
826	GCUAUCAUGCGU	1636	ACGCAUGAUAGC	3031	AD-19766、AD-19739、AD-26147
827	CUAUCAUGCGUU	1637	AACGCAUGAUAG	3032	AD-19766、AD-19745、AD-19739、AD-26147
828	UAUCAUGCGUUC	1638	GAACGCAUGAUA	3033	AD-19766、AD-19745、AD-19739
829	AUCAUGCGUUCU	1639	AGAACGCAUGAU	3034	AD-19766、AD-19746、AD-19739
830	UCAUGCGUUCUC	1640	GAGAACGCAUGA	3035	AD-19739、AD-26148
831	CAUGCGUUCUCC	1641	GGAGAACGCAUG	3036	AD-19739、AD-26148
832	AUGCGUUCUCCU	1642	AGGAGAACGCAU	3037	AD-19746、AD-26148
842	CUCAGAUGGUGU	1643	ACACCAUCUGAG	3038	AD-26150、AD-26149
843	UCAGAUGGUGUC	1644	GACACCAUCUGA	3039	AD-26150、AD-26149
844	CAGAUGGUGUCU	1645	AGACACCAUCUG	3040	AD-26150、AD-26149
845	AGAUGGUGUCUG	1646	CAGACACCAUCU	3041	AD-26150、AD-26149
846	GAUGGUGUCUGC	1647	GCAGACACCAUC	3042	AD-26150、AD-26149
847	AUGGUGUCUGCU	1648	AGCAGACACCAU	3043	AD-26150、AD-26149
848	UGGUGUCUGCUA	1649	UAGCAGACACCA	3044	AD-26150、AD-26149
854	CUGCUAUUGUAC	1650	GUACAAUAGCAG	3045	AD-26151、AD-26152
855	UGCUAUUGUACG	1651	CGUACAAUAGCA	3046	AD-26151、AD-26152
856	GCUAUUGUACGU	1652	ACGUACAAUAGC	3047	AD-26151、AD-26152
857	CUAUUGUACGUA	1653	UACGUACAAUAG	3048	AD-26151、AD-26152
860	UUGUACGUACCA	1654	UGGUACGUACAA	3049	AD-26153、AD-26152
861	UGUACGUACCAU	1655	AUGGUACGUACA	3050	AD-26154、AD-26153、AD-26152
862	GUACGUACCAUG	1656	CAUGGUACGUAC	3051	AD-26154、AD-26153
863	UACGUACCAUGC	1657	GCAUGGUACGUA	3052	AD-26154、AD-26153
864	ACGUACCAUGCA	1658	UGCAUGGUACGU	3053	AD-26154、AD-26153
865	CGUACCAUGCAG	1659	CUGCAUGGUACG	3054	AD-26154、AD-26153
866	GUACCAUGCAGA	1660	UCUGCAUGGUAC	3055	AD-26154、AD-26155
867	UACCAUGCAGAA	1661	UUCUGCAUGGUA	3056	AD-26154、AD-26155、AD-26153
868	ACCAUGCAGAAU	1662	AUUCUGCAUGGU	3057	AD-26154、AD-26155
870	CAUGCAGAAUAC	1663	GUAUUCUGCAUG	3058	AD-26155、AD-26156

871	AUGCAGAAUACA	1664	UGUAUUCUGCAU	3059	AD-26155、AD-26156
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873	GCAGAAUACAAA	1666	UUUGUAUUCUGC	3061	AD-26156、AD-26157
874	CAGAAUACAAAU	1667	AUUUGUAUUCUG	3062	AD-19068、AD-26157
875	AGAAUACAAAUG	1668	CAUUUGUAUUCU	3063	AD-19068、AD-26156
876	GAAUACAAAUGA	1669	UCAUUUGUAUUC	3064	AD-19068、AD-26156、AD-26157
877	AAUACAAAUGAU	1670	AUCAUUUGUAUU	3065	AD-19068、AD-26158、AD-26826、AD-26157
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880	ACAAAUGAUGUA	1673	UACAUCAUUUGU	3068	AD-19068、AD-26158、AD-26826、AD-26157
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882	AAAUGAUGUAGA	1675	UCUACAUCAUUU	3070	AD-26158、AD-26826
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907	ACCGCUGGGACC	1678	GGUCCCAGCGGU	3073	AD-26161、AD-26160
908	CCGCUGGGACCU	1679	AGGUCCCAGCGG	3074	AD-26161、AD-26162
909	CGCUGGGACCUU	1680	AAGGUCCCAGCG	3075	AD-26162、AD-26160
910	GCUGGGACCUUG	1681	CAAGGUCCCAGC	3076	AD-26161、AD-26162
911	CUGGGACCUUGC	1682	GCAAGGUCCCAG	3077	AD-26161、AD-26162
912	UGGGACCUUGCA	1683	UGCAAGGUCCCA	3078	AD-26161、AD-26162、AD-26163
913	GGGACCUUGCAU	1684	AUGCAAGGUCCC	3079	AD-26161、AD-26162、AD-26163、AD-26164
914	GGACCUUGCAUA	1685	UAUGCAAGGUCC	3080	AD-26162、AD-26163、AD-26164
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917	CCUUGCAUAACC	1688	GGUUAUGCAAGG	3083	AD-19759、AD-26164
918	CUUGCAUAACCU	1689	AGGUUAUGCAAG	3084	AD-19759、AD-26163、AD-26164、AD-26165
919	UUGCAUAACCUU	1690	AAGGUUAUGCAA	3085	AD-19759、AD-26163、AD-26164、AD-26165
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921	GCAUAACCUUUC	1692	GAAAGGUUAUGC	3087	AD-19759、AD-26165
922	CAUAACCUUUCC	1693	GGAAAGGUUAUG	3088	AD-19759、AD-26165

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976	AUUCCUGCCCUG	1697	CAGGGCAGGAAU	3092	AD-26167、AD-26168、AD-26169
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978	UCCUGCCCUGGU	1699	ACCAGGGCAGGA	3094	AD-26170、AD-26168、AD-26169
979	CCUGCCCUGGUG	1700	CACCAGGGCAGG	3095	AD-26170、AD-26168
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982	GCCCUGGUGAAA	1703	UUUCACCAGGGC	3098	AD-26170、AD-26171、AD-26168、AD-26169
983	CCCUGGUGAAAA	1704	UUUUCACCAGGG	3099	AD-26170、AD-26171、AD-26169
984	CCUGGUGAAAAU	1705	AUUUUCACCAGG	3100	AD-26170、AD-26171
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986	UGGUGAAAAUGC	1707	GCAUUUUCACCA	3102	AD-26172、AD-26171
987	GGUGAAAAUGCU	1708	AGCAUUUUCACC	3103	AD-26172、AD-26171
988	GUGAAAAUGCUU	1709	AAGCAUUUUCAC	3104	AD-26172、AD-26171
997	CUUGGUUCACCA	1710	UGGUGAACCAAG	3105	AD-26173、AD-26174
998	UUGGUUCACCAG	1711	CUGGUGAACCAA	3106	AD-26173、AD-26174
999	UGGUUCACCAGU	1712	ACUGGUGAACCA	3107	AD-26173、AD-26174
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1001	GUUCACCAGUGG	1714	CCACUGGUGAAC	3109	AD-26173、AD-26174
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1003	UCACCAGUGGAU	1716	AUCCACUGGUGA	3111	AD-26173、AD-26174
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1007	CAGUGGAUUCUG	1718	CAGAAUCCACUG	3113	AD-26177、AD-26178
1008	AGUGGAUUCUGU	1719	ACAGAAUCCACU	3114	AD-26177、AD-26178、AD-26179
1009	GUGGAUUCUGUG	1720	CACAGAAUCCAC	3115	AD-26177、AD-26178、AD-26179、AD-26180
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1011	GGAUUCUGUGUU	1722	AACACAGAAUCC	3117	AD-26177、AD-26181、AD-26178、AD-26179、AD-26182、AD-26180
1012	GAUUCUGUGUUG	1723	CAACACAGAAUC	3118	AD-26181、AD-26178、

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1013	AUUCUGUGUUGU	1724	ACAACACAGAAU	3119	AD-26181、AD-26178、AD-26179、AD-26182
1014	UUCUGUGUUGUU	1725	AACAACACAGAA	3120	AD-26181、AD-26179、AD-26182、AD-26180
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1018	GUGUUGUUUUAU	1729	AUAAAACAACAC	3124	AD-26183、AD-26182、AD-26185
1019	UGUUGUUUUAUG	1730	CAUAAAACAACA	3125	AD-26183、AD-26185
1020	GUUGUUUUAUGC	1731	GCAUAAAACAAC	3126	AD-26183、AD-26185
1021	UUGUUUUAUGCC	1732	GGCAUAAAACAA	3127	AD-26183、AD-26186
1022	UGUUUUAUGCCA	1733	UGGCAUAAAACA	3128	AD-26183、AD-26185
1023	GUUUUAUGCCAU	1734	AUGGCAUAAAAC	3129	AD-26183、AD-26185、AD-26186
1024	UUUUAUGCCAUU	1735	AAUGGCAUAAAA	3130	AD-26183、AD-26185、AD-26186
1025	UUUAUGCCAUUA	1736	UAAUGGCAUAAA	3131	AD-26185、AD-26186
1027	UAUGCCAUUACA	1737	UGUAAUGGCAUA	3132	AD-26186、AD-19767
1028	AUGCCAUUACAA	1738	UUGUAAUGGCAU	3133	AD-26186、AD-19767
1031	CCAUUACAACUC	1739	GAGUUGUAAUGG	3134	AD-26187、AD-19767
1032	CAUUACAACUCU	1740	AGAGUUGUAAUG	3135	AD-26187、AD-19767
1033	AUUACAACUCUC	1741	GAGAGUUGUAAU	3136	AD-26187、AD-19767
1034	UUACAACUCUCC	1742	GGAGAGUUGUAA	3137	AD-26187、AD-19767
1035	UACAACUCUCCA	1743	UGGAGAGUUGUA	3138	AD-26188、AD-26187
1036	ACAACUCUCCAC	1744	GUGGAGAGUUGU	3139	AD-26188、AD-26189、AD-26187
1037	CAACUCUCCACA	1745	UGUGGAGAGUUG	3140	AD-26190、AD-26188、AD-26189、AD-26187
1038	AACUCUCCACAA	1746	UUGUGGAGAGUU	3141	AD-26190、AD-26191、AD-26188、AD-26189、AD-26187
1039	ACUCUCCACAAC	1747	GUUGUGGAGAGU	3142	AD-26190、AD-26192、AD-26191、AD-26188、AD-26189
1040	CUCUCCACAACC	1748	GGUUGUGGAGAG	3143	AD-26190、AD-26192、AD-26193、AD-26191、AD-26188、AD-26189
1041	UCUCCACAACCU	1749	AGGUUGUGGAGA	3144	AD-26190、AD-26192、

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1042	CUCCACAACCUU	1750	AAGGUUGUGGAG	3145	AD-26190、AD-26192、AD-26193、AD-26194、AD-26191、AD-26189
1043	UCCACAACCUUU	1751	AAAGGUUGUGGA	3146	AD-26190、AD-26192、AD-26193、AD-26194、AD-26189
1044	CCACAACCUUUU	1752	AAAAGGUUGUGG	3147	AD-26190、AD-26192、AD-26193、AD-26194、AD-26191
1045	CACAACCUUUUA	1753	UAAAAGGUUGUG	3148	AD-26192、AD-26193、AD-26194、AD-26191
1046	ACAACCUUUUAU	1754	AUAAAAGGUUGU	3149	AD-26192、AD-26193、AD-26194
1047	CAACCUUUUAUU	1755	AAUAAAAGGUUG	3150	AD-26193、AD-26194、AD-26195
1048	AACCUUUUAUUA	1756	UAAUAAAAGGUU	3151	AD-26194、AD-26195
1050	CCUUUUAUUACA	1757	UGUAAUAAAAGG	3152	AD-26196、AD-26195
1051	CUUUUAUUACAU	1758	AUGUAAUAAAAG	3153	AD-26196、AD-26195
1052	UUUUAUUACAUC	1759	GAUGUAAUAAAA	3154	AD-26196、AD-26195
1053	UUUAUUACAUCA	1760	UGAUGUAAUAAA	3155	AD-26196、AD-26195
1054	UUAUUACAUCAA	1761	UUGAUGUAAUAA	3156	AD-26196、AD-26195
1057	UUACAUCAAGAA	1762	UUCUUGAUGUAA	3157	AD-26197、AD-26196
1058	UACAUCAAGAAG	1763	CUUCUUGAUGUA	3158	AD-26198、AD-26197
1059	ACAUCAAGAAGG	1764	CCUUCUUGAUGU	3159	AD-26198、AD-26197
1060	CAUCAAGAAGGA	1765	UCCUUCUUGAUG	3160	AD-26198、AD-26199、AD-26197
1061	AUCAAGAAGGAG	1766	CUCCUUCUUGAU	3161	AD-26198、AD-26199、AD-26197、AD-26200
1062	UCAAGAAGGAGC	1767	GCUCCUUCUUGA	3162	AD-26198、AD-26199、AD-26200
1063	CAAGAAGGAGCU	1768	AGCUCCUUCUUG	3163	AD-26198、AD-26197、AD-26200
1064	AAGAAGGAGCUA	1769	UAGCUCCUUCUU	3164	AD-26198、AD-26199、AD-26197、AD-26200
1065	AGAAGGAGCUAA	1770	UUAGCUCCUUCU	3165	AD-26198、AD-26199、AD-26200
1066	GAAGGAGCUAAA	1771	UUUAGCUCCUUC	3166	AD-26199、AD-26200
1067	AAGGAGCUAAAA	1772	UUUUAGCUCCUU	3167	AD-26199、AD-26200
1068	AGGAGCUAAAAU	1773	AUUUUAGCUCCU	3168	AD-26200、AD-18977
1072	GCUAAAAUGGCA	1774	UGCCAUUUUAGC	3169	AD-26201、AD-18977
1073	CUAAAAUGGCAG	1775	CUGCCAUUUUAG	3170	AD-26201、AD-18977

1074	UAAAAUGGCAGU	1776	ACUGCCAUUUUA	3171	AD-26201、AD-26202、AD-18977
1075	AAAAUGGCAGUG	1777	CACUGCCAUUUU	3172	AD-26201、AD-18977
1076	AAAUGGCAGUGC	1778	GCACUGCCAUUU	3173	AD-26201、AD-26202
1077	AAUGGCAGUGCG	1779	CGCACUGCCAUU	3174	AD-26201、AD-26202
1078	AUGGCAGUGCGU	1780	ACGCACUGCCAU	3175	AD-26201、AD-26202
1079	UGGCAGUGCGUU	1781	AACGCACUGCCA	3176	AD-26201、AD-26202
1112	UGGUUGCCUUGC	1782	GCAAGGCAACCA	3177	AD-26205、AD-26203
1113	GGUUGCCUUGCU	1783	AGCAAGGCAACC	3178	AD-26206、AD-26205、AD-26203
1114	GUUGCCUUGCUC	1784	GAGCAAGGCAAC	3179	AD-26206、AD-26205、AD-26203、AD-26207
1115	UUGCCUUGCUCA	1785	UGAGCAAGGCAA	3180	AD-26206、AD-26205、AD-26203
1116	UGCCUUGCUCAA	1786	UUGAGCAAGGCA	3181	AD-26206、AD-26203、AD-26207
1117	GCCUUGCUCAAC	1787	GUUGAGCAAGGC	3182	AD-26205、AD-26208、AD-26207
1118	CCUUGCUCAACA	1788	UGUUGAGCAAGG	3183	AD-26206、AD-26205、AD-26208、AD-26207、AD-26209
1119	CUUGCUCAACAA	1789	UUGUUGAGCAAG	3184	AD-26206、AD-26205、AD-26208、AD-26207、AD-26209
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1121	UGCUCAACAAAA	1791	UUUUGUUGAGCA	3186	AD-26208、AD-26207、AD-26209
1122	GCUCAACAAAAC	1792	GUUUUGUUGAGC	3187	AD-26208、AD-26209
1123	CUCAACAAAACA	1793	UGUUUUGUUGAG	3188	AD-26208、AD-26209
1124	UCAACAAAACAA	1794	UUGUUUUGUUGA	3189	AD-26208、AD-26209
1219	AGUGGUGGACCC	1795	GGGUCCACCACU	3190	AD-26057、AD-26213
1220	GUGGUGGACCCC	1796	GGGGUCCACCAC	3191	AD-26057、AD-26213、AD-26214
1221	UGGUGGACCCCA	1797	UGGGGUCCACCA	3192	AD-26215、AD-26057、AD-26213、AD-26214
1222	GGUGGACCCCAA	1798	UUGGGGUCCACC	3193	AD-26215、AD-26057、AD-26213
1223	GUGGACCCCAAG	1799	CUUGGGGUCCAC	3194	AD-26215、AD-26213、AD-26214
1224	UGGACCCCAAGC	1800	GCUUGGGGUCCA	3195	AD-26215、AD-26216、AD-26213、AD-26214
1225	GGACCCCAAGCU	1801	AGCUUGGGGUCC	3196	AD-26215、AD-26217、AD-26216、AD-26213、

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1226	GACCCCAAGCUU	1802	AAGCUUGGGGUC	3197	AD-26215、AD-26217、AD-26216、AD-26213、AD-26214、AD-26218
1227	ACCCCAAGCUUU	1803	AAAGCUUGGGGU	3198	AD-26215、AD-26651、AD-26217、AD-26216、AD-26218
1228	CCCCAAGCUUUA	1804	UAAAGCUUGGGG	3199	AD-26215、AD-26652、AD-26217、AD-26216、AD-26218
1229	CCCAAGCUUUAG	1805	CUAAAGCUUGGG	3200	AD-26651、AD-26652、AD-26217、AD-26216、AD-26653、AD-26218
1230	CCAAGCUUUAGU	1806	ACUAAAGCUUGG	3201	AD-26654、AD-26651、AD-26652、AD-26217、AD-26216、AD-26653、AD-26218
1231	CAAGCUUUAGUA	1807	UACUAAAGCUUG	3202	AD-26654、AD-26651、AD-26652、AD-26217、AD-26068、AD-26216、AD-26653、AD-26218
1232	AAGCUUUAGUAA	1808	UUACUAAAGCUU	3203	AD-26654、AD-26651、AD-26652、AD-26217、AD-26068、AD-26653、AD-26069、AD-26218
1233	AGCUUUAGUAAA	1809	UUUACUAAAGCU	3204	AD-26654、AD-26651、AD-26652、AD-26068、AD-26653、AD-26069、AD-26218
1234	GCUUUAGUAAAU	1810	AUUUACUAAAGC	3205	AD-26654、AD-26651、AD-26652、AD-26068、AD-26653、AD-26069
1235	CUUUAGUAAAUA	1811	UAUUUACUAAAG	3206	AD-26654、AD-26652、AD-26068、AD-26653、AD-26069
1236	UUUAGUAAAUAU	1812	AUAUUUACUAAA	3207	AD-26654、AD-26068、AD-26653、AD-26069
1237	UUAGUAAAUAUA	1813	UAUAUUUACUAA	3208	AD-26654、AD-26068、AD-26069
1238	UAGUAAAUAUAA	1814	UUAUAUUUACUA	3209	AD-26068、AD-26069
1242	AAAUAUAAUGAG	1815	CUCAUUAUAUUU	3210	AD-26655、AD-26656
1243	AAUAUAAUGAGG	1816	CCUCAUUAUAUU	3211	AD-26655、AD-26657
1244	AUAUAAUGAGGA	1817	UCCUCAUUAUAU	3212	AD-26655、AD-26656、AD-26657
1245	UAUAAUGAGGAC	1818	GUCCUCAUUAUA	3213	AD-26655、AD-26656、

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1246	AUAAUGAGGACC	1819	GGUCCUCAUUAU	3214	AD-26655、AD-26656、AD-26657
1247	UAAUGAGGACCU	1820	AGGUCCUCAUUA	3215	AD-26658、AD-26655、AD-26656、AD-26657
1248	AAUGAGGACCUA	1821	UAGGUCCUCAUU	3216	AD-26658、AD-26655、AD-26657
1249	AUGAGGACCUAU	1822	AUAGGUCCUCAU	3217	AD-26658、AD-26656、AD-26657
1250	UGAGGACCUAUA	1823	UAUAGGUCCUCA	3218	AD-26658、AD-26657
1285	ACAAGCAGAGUG	1824	CACUCUGCUUGU	3219	AD-18945、AD-26660
1286	CAAGCAGAGUGC	1825	GCACUCUGCUUG	3220	AD-18945、AD-26660
1287	AAGCAGAGUGCU	1826	AGCACUCUGCUU	3221	AD-18945、AD-26660
1288	AGCAGAGUGCUG	1827	CAGCACUCUGCU	3222	AD-18945、AD-19046
1289	GCAGAGUGCUGA	1828	UCAGCACUCUGC	3223	AD-18945、AD-26660、AD-19046
1290	CAGAGUGCUGAA	1829	UUCAGCACUCUG	3224	AD-18945、AD-26660、AD-19046、AD-26661
1291	AGAGUGCUGAAG	1830	CUUCAGCACUCU	3225	AD-18945、AD-19046、AD-26661、AD-26662
1292	GAGUGCUGAAGG	1831	CCUUCAGCACUC	3226	AD-18945、AD-19046、AD-26662
1293	AGUGCUGAAGGU	1832	ACCUUCAGCACU	3227	AD-19046、AD-26661、AD-26662
1294	GUGCUGAAGGUG	1833	CACCUUCAGCAC	3228	AD-19046、AD-26662
1295	UGCUGAAGGUGC	1834	GCACCUUCAGCA	3229	AD-26661、AD-26662
1296	GCUGAAGGUGCU	1835	AGCACCUUCAGC	3230	AD-26661、AD-26662
1297	CUGAAGGUGCUA	1836	UAGCACCUUCAG	3231	AD-26661、AD-26662
1313	UCUGCUCUAGUA	1837	UACUAGAGCAGA	3232	AD-19768、AD-19748
1314	CUGCUCUAGUAA	1838	UUACUAGAGCAG	3233	AD-19768、AD-19748
1315	UGCUCUAGUAAU	1839	AUUACUAGAGCA	3234	AD-19768、AD-19748
1316	GCUCUAGUAAUA	1840	UAUUACUAGAGC	3235	AD-19768、AD-19748
1317	CUCUAGUAAUAA	1841	UUAUUACUAGAG	3236	AD-19768、AD-19748
1318	UCUAGUAAUAAG	1842	CUUAUUACUAGA	3237	AD-19768、AD-19748
1319	CUAGUAAUAAGC	1843	GCUUAUUACUAG	3238	AD-19768、AD-19748
1337	UUGUAGAAGCUG	1844	CAGCUUCUACAA	3239	AD-26664、AD-26663
1338	UGUAGAAGCUGG	1845	CCAGCUUCUACA	3240	AD-26664、AD-26663
1339	GUAGAAGCUGGU	1846	ACCAGCUUCUAC	3241	AD-26664、AD-26663
1340	UAGAAGCUGGUG	1847	CACCAGCUUCUA	3242	AD-26664、AD-26663
1341	AGAAGCUGGUGG	1848	CCACCAGCUUCU	3243	AD-26664、AD-26663
1342	GAAGCUGGUGGA	1849	UCCACCAGCUUC	3244	AD-26664、AD-26663
1343	AAGCUGGUGGAA	1850	UUCCACCAGCUU	3245	AD-26664、AD-26663
1346	CUGGUGGAAUGC	1851	GCAUUCCACCAG	3246	AD-26665、AD-26666
1347	UGGUGGAAUGCA	1852	UGCAUUCCACCA	3247	AD-26665、AD-26666

1348	GGUGGAAUGCAA	1853	UUGCAUUCCACC	3248	AD-26665、AD-26666
1349	GUGGAAUGCAAG	1854	CUUGCAUUCCAC	3249	AD-26665、AD-26666
1350	UGGAAUGCAAGC	1855	GCUUGCAUUCCA	3250	AD-26665、AD-26666
1351	GGAAUGCAAGCU	1856	AGCUUGCAUUCC	3251	AD-26665、AD-26666
1352	GAAUGCAAGCUU	1857	AAGCUUGCAUUC	3252	AD-26665、AD-26666
1369	CUUCACCUGACA	1858	UGUCAGGUGAAG	3253	AD-26667、AD-26668
1370	UUCACCUGACAG	1859	CUGUCAGGUGAA	3254	AD-26667、AD-26668
1371	UCACCUGACAGA	1860	UCUGUCAGGUGA	3255	AD-26667、AD-26668
1372	CACCUGACAGAU	1861	AUCUGUCAGGUG	3256	AD-26667、AD-26668
1374	CCUGACAGAUCC	1862	GGAUCUGUCAGG	3257	AD-26669、AD-26668
1375	CUGACAGAUCCA	1863	UGGAUCUGUCAG	3258	AD-26669、AD-26668
1376	UGACAGAUCCAA	1864	UUGGAUCUGUCA	3259	AD-26669、AD-26668
1380	AGAUCCAAGUCA	1865	UGACUUGGAUCU	3260	AD-26669、AD-26670
1381	GAUCCAAGUCAA	1866	UUGACUUGGAUC	3261	AD-26669、AD-26670
1383	UCCAAGUCAACG	1867	CGUUGACUUGGA	3262	AD-26671、AD-26670
1384	CCAAGUCAACGU	1868	ACGUUGACUUGG	3263	AD-26671、AD-26670
1385	CAAGUCAACGUC	1869	GACGUUGACUUG	3264	AD-26671、AD-26670
1386	AAGUCAACGUCU	1870	AGACGUUGACUU	3265	AD-26671、AD-26670
1387	AGUCAACGUCUU	1871	AAGACGUUGACU	3266	AD-26671、AD-26670
1396	CUUGUUCAGAAC	1872	GUUCUGAACAAG	3267	AD-26672、AD-26673
1397	UUGUUCAGAACU	1873	AGUUCUGAACAA	3268	AD-26672、AD-26673
1398	UGUUCAGAACUG	1874	CAGUUCUGAACA	3269	AD-26672、AD-26673
1399	GUUCAGAACUGU	1875	ACAGUUCUGAAC	3270	AD-26672、AD-26673
1400	UUCAGAACUGUC	1876	GACAGUUCUGAA	3271	AD-26672、AD-26673
1401	UCAGAACUGUCU	1877	AGACAGUUCUGA	3272	AD-26672、AD-26673
1402	CAGAACUGUCUU	1878	AAGACAGUUCUG	3273	AD-26672、AD-26673
1406	ACUGUCUUUGGA	1879	UCCAAAGACAGU	3274	AD-19056、AD-19079
1407	CUGUCUUUGGAC	1880	GUCCAAAGACAG	3275	AD-19056、AD-19079
1408	UGUCUUUGGACU	1881	AGUCCAAAGACA	3276	AD-19056、AD-19079
1409	GUCUUUGGACUC	1882	GAGUCCAAAGAC	3277	AD-26674、AD-19056、AD-19079
1410	UCUUUGGACUCU	1883	AGAGUCCAAAGA	3278	AD-26674、AD-26675、AD-19056、AD-19079
1411	CUUUGGACUCUC	1884	GAGAGUCCAAAG	3279	AD-26674、AD-19056、AD-19079
1412	UUUGGACUCUCA	1885	UGAGAGUCCAAA	3280	AD-26674、AD-26675、AD-19079
1413	UUGGACUCUCAG	1886	CUGAGAGUCCAA	3281	AD-26675、AD-26676、AD-19079
1414	UGGACUCUCAGG	1887	CCUGAGAGUCCA	3282	AD-26674、AD-26675、AD-26676、AD-26678
1415	GGACUCUCAGGA	1888	UCCUGAGAGUCC	3283	AD-26674、AD-26676、AD-26678
1416	GACUCUCAGGAA	1889	UUCCUGAGAGUC	3284	AD-26674、AD-26675、

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1417	ACUCUCAGGAAU	1890	AUUCCUGAGAGU	3285	AD-26675、AD-26676、AD-26678
1418	CUCUCAGGAAUC	1891	GAUUCCUGAGAG	3286	AD-26676、AD-26678
1419	UCUCAGGAAUCU	1892	AGAUUCCUGAGA	3287	AD-26679、AD-26676、AD-26678
1420	CUCAGGAAUCUU	1893	AAGAUUCCUGAG	3288	AD-26679、AD-26678
1421	UCAGGAAUCUUU	1894	AAAGAUUCCUGA	3289	AD-26679、AD-26678
1426	AAUCUUUCAGAU	1895	AUCUGAAAGAUU	3290	AD-26679、AD-26680
1429	CUUUCAGAUGCU	1896	AGCAUCUGAAAG	3291	AD-26681、AD-26680
1430	UUUCAGAUGCUG	1897	CAGCAUCUGAAA	3292	AD-26681、AD-26680
1431	UUCAGAUGCUGC	1898	GCAGCAUCUGAA	3293	AD-26682、AD-26680
1432	UCAGAUGCUGCA	1899	UGCAGCAUCUGA	3294	AD-26682、AD-26681
1433	CAGAUGCUGCAA	1900	UUGCAGCAUCUG	3295	AD-26682、AD-26681、AD-26680
1434	AGAUGCUGCAAC	1901	GUUGCAGCAUCU	3296	AD-26682、AD-26681
1435	GAUGCUGCAACU	1902	AGUUGCAGCAUC	3297	AD-26682、AD-26681
1436	AUGCUGCAACUA	1903	UAGUUGCAGCAU	3298	AD-26682、AD-26681
1437	UGCUGCAACUAA	1904	UUAGUUGCAGCA	3299	AD-26682、AD-26683
1438	GCUGCAACUAAA	1905	UUUAGUUGCAGC	3300	AD-26682、AD-26683
1467	UCUCCUUGGGAC	1906	GUCCCAAGGAGA	3301	AD-26687、AD-26686
1468	CUCCUUGGGACU	1907	AGUCCCAAGGAG	3302	AD-26687、AD-26686
1469	UCCUUGGGACUC	1908	GAGUCCCAAGGA	3303	AD-26687、AD-26686
1470	CCUUGGGACUCU	1909	AGAGUCCCAAGG	3304	AD-26687、AD-26686
1471	CUUGGGACUCUU	1910	AAGAGUCCCAAG	3305	AD-26687、AD-26686
1473	UGGGACUCUUGU	1911	ACAAGAGUCCCA	3306	AD-26688、AD-26687
1474	GGGACUCUUGUU	1912	AACAAGAGUCCC	3307	AD-26688、AD-26687
1480	CUUGUUCAGCUU	1913	AAGCUGAACAAG	3308	AD-26689、AD-26688
1485	UCAGCUUCUGGG	1914	CCCAGAAGCUGA	3309	AD-26689、AD-26690
1486	CAGCUUCUGGGU	1915	ACCCAGAAGCUG	3310	AD-26689、AD-26690
1487	AGCUUCUGGGUU	1916	AACCCAGAAGCU	3311	AD-26689、AD-26690
1488	GCUUCUGGGUUC	1917	GAACCCAGAAGC	3312	AD-26691、AD-26690
1489	CUUCUGGGUUCA	1918	UGAACCCAGAAG	3313	AD-26692、AD-26691、AD-26690
1490	UUCUGGGUUCAG	1919	CUGAACCCAGAA	3314	AD-26692、AD-26691、AD-26694、AD-26690
1491	UCUGGGUUCAGA	1920	UCUGAACCCAGA	3315	AD-26692、AD-26694、AD-26690
1492	CUGGGUUCAGAU	1921	AUCUGAACCCAG	3316	AD-26692、AD-26691、AD-26694、AD-26695、AD-26690
1493	UGGGUUCAGAUG	1922	CAUCUGAACCCA	3317	AD-26692、AD-26691、AD-26696、AD-26694、AD-26695

1494	GGGUUCAGAUGA	1923	UCAUCUGAACCC	3318	AD-26692、AD-26691、AD-26696、AD-26694
1495	GGUUCAGAUGAU	1924	AUCAUCUGAACC	3319	AD-26692、AD-26691、AD-26694、AD-26695
1496	GUUCAGAUGAUA	1925	UAUCAUCUGAAC	3320	AD-26696、AD-26694、AD-26695
1497	UUCAGAUGAUAU	1926	AUAUCAUCUGAA	3321	AD-26696、AD-26694、AD-26695
1498	UCAGAUGAUAUA	1927	UAUAUCAUCUGA	3322	AD-26696、AD-26695
1499	CAGAUGAUAUAA	1928	UUAUAUCAUCUG	3323	AD-26696、AD-26695
1503	UGAUAUAAAUGU	1929	ACAUUUAUAUCA	3324	AD-18994、AD-18927
1504	GAUAUAAAUGUG	1930	CACAUUUAUAUC	3325	AD-19045、AD-18994
1505	AUAUAAAUGUGG	1931	CCACAUUUAUAU	3326	AD-19045、AD-18927
1506	UAUAAAUGUGGU	1932	ACCACAUUUAUA	3327	AD-18994、AD-18927
1507	AUAAAUGUGGUC	1933	GACCACAUUUAU	3328	AD-19045、AD-18994、AD-18927
1508	UAAAUGUGGUCA	1934	UGACCACAUUUA	3329	AD-19045、AD-18994、AD-18927
1509	AAAUGUGGUCAC	1935	GUGACCACAUUU	3330	AD-19045、AD-18994
1510	AAUGUGGUCACC	1936	GGUGACCACAUU	3331	AD-19045、AD-18994
1517	UCACCUGUGCAG	1937	CUGCACAGGUGA	3332	AD-26697、AD-26698
1518	CACCUGUGCAGC	1938	GCUGCACAGGUG	3333	AD-26697、AD-26698
1519	ACCUGUGCAGCU	1939	AGCUGCACAGGU	3334	AD-26697、AD-26699
1520	CCUGUGCAGCUG	1940	CAGCUGCACAGG	3335	AD-26697、AD-26699、AD-26698
1521	CUGUGCAGCUGG	1941	CCAGCUGCACAG	3336	AD-26700、AD-26697、AD-26699、AD-26698
1522	UGUGCAGCUGGA	1942	UCCAGCUGCACA	3337	AD-26700、AD-26697、AD-26699、AD-26701、AD-26698
1523	GUGCAGCUGGAA	1943	UUCCAGCUGCAC	3338	AD-26700、AD-26699、AD-26701、AD-26698
1524	UGCAGCUGGAAU	1944	AUUCCAGCUGCA	3339	AD-26700、AD-26699、AD-26701、AD-26698
1525	GCAGCUGGAAUU	1945	AAUUCCAGCUGC	3340	AD-26700、AD-26699、AD-26701、AD-26702
1526	CAGCUGGAAUUC	1946	GAAUUCCAGCUG	3341	AD-26700、AD-26701、AD-26702
1527	AGCUGGAAUUCU	1947	AGAAUUCCAGCU	3342	AD-26700、AD-26703、AD-26702
1528	GCUGGAAUUCUU	1948	AAGAAUUCCAGC	3343	AD-26700、AD-26703、AD-26701、AD-26702
1529	CUGGAAUUCUUU	1949	AAAGAAUUCCAG	3344	AD-26703、AD-26701、AD-26702

1530	UGGAAUUCUUUC	1950	GAAAGAAUUCCA	3345	AD-26703、AD-26702
1531	GGAAUUCUUUCU	1951	AGAAAGAAUUCC	3346	AD-26703、AD-26702
1532	GAAUUCUUUCUA	1952	UAGAAAGAAUUC	3347	AD-26703、AD-26702
1538	UUUCUAACCUCA	1953	UGAGGUUAGAAA	3348	AD-26704、AD-26920
1539	UUCUAACCUCAC	1954	GUGAGGUUAGAA	3349	AD-26704、AD-26920、AD-26705
1540	UCUAACCUCACU	1955	AGUGAGGUUAGA	3350	AD-26704、AD-26920、AD-26705、AD-18899
1541	CUAACCUCACUU	1956	AAGUGAGGUUAG	3351	AD-26704、AD-26920、AD-26705、AD-18899、AD-18917
1542	UAACCUCACUUG	1957	CAAGUGAGGUUA	3352	AD-26704、AD-26705、AD-18899、AD-18917
1543	AACCUCACUUGC	1958	GCAAGUGAGGUU	3353	AD-26704、AD-19074、AD-26705、AD-18899、AD-18917
1544	ACCUCACUUGCA	1959	UGCAAGUGAGGU	3354	AD-26704、AD-26706、AD-19074、AD-26705、AD-18899、AD-18917
1545	CCUCACUUGCAA	1960	UUGCAAGUGAGG	3355	AD-26704、AD-26706、AD-26707、AD-19074、AD-26705、AD-18899、AD-18917
1546	CUCACUUGCAAU	1961	AUUGCAAGUGAG	3356	AD-26706、AD-26707、AD-19074、AD-26708、AD-26705、AD-18899、AD-18917
1547	UCACUUGCAAUA	1962	UAUUGCAAGUGA	3357	AD-26706、AD-26134、AD-26707、AD-19074、AD-26708、AD-18899、AD-18917
1548	CACUUGCAAUAA	1963	UUAUUGCAAGUG	3358	AD-26706、AD-26134、AD-26707、AD-19074、AD-26708、AD-18917
1549	ACUUGCAAUAAU	1964	AUUAUUGCAAGU	3359	AD-26706、AD-26134、AD-26707、AD-19074、AD-26708
1550	CUUGCAAUAAUU	1965	AAUUAUUGCAAG	3360	AD-26706、AD-26134、AD-26707、AD-19074、AD-26708、AD-26135
1551	UUGCAAUAAUUA	1966	UAAUUAUUGCAA	3361	AD-26706、AD-26134、AD-26707、AD-26708、AD-26135
1552	UGCAAUAAUUAU	1967	AUAAUUAUUGCA	3362	AD-26134、AD-26707、AD-26708、AD-26135

1553	GCAAUAAUUAUA	1968	UAUAAUUAUUGC	3363	AD-26134、AD-26708、AD-26135
1554	CAAUAAUUAUAA	1969	UUAUAAUUAUUG	3364	AD-26134、AD-26135
1580	UCUGCCAAGUGG	1970	CCACUUGGCAGA	3365	AD-26710、AD-26709
1581	CUGCCAAGUGGG	1971	CCCACUUGGCAG	3366	AD-26710、AD-26709
1582	UGCCAAGUGGGU	1972	ACCCACUUGGCA	3367	AD-26710、AD-26709
1583	GCCAAGUGGGUG	1973	CACCCACUUGGC	3368	AD-26710、AD-26709
1584	CCAAGUGGGUGG	1974	CCACCCACUUGG	3369	AD-26710、AD-26709
1585	CAAGUGGGUGGU	1975	ACCACCCACUUG	3370	AD-26710、AD-26709
1586	AAGUGGGUGGUA	1976	UACCACCCACUU	3371	AD-26710、AD-26709
1597	AUAGAGGCUCUU	1977	AAGAGCCUCUAU	3372	AD-26712、AD-26711
1628	CUGGUGACAGGG	1978	CCCUGUCACCAG	3373	AD-26714、AD-26141
1629	UGGUGACAGGGA	1979	UCCCUGUCACCA	3374	AD-26714、AD-26141
1630	GGUGACAGGGAA	1980	UUCCCUGUCACC	3375	AD-26714、AD-26141
1637	GGGAAGACAUCA	1981	UGAUGUCUUCCC	3376	AD-18938、AD-19064
1638	GGAAGACAUCAC	1982	GUGAUGUCUUCC	3377	AD-18938、AD-18937
1639	GAAGACAUCACU	1983	AGUGAUGUCUUC	3378	AD-18938、AD-19064
1640	AAGACAUCACUG	1984	CAGUGAUGUCUU	3379	AD-19064、AD-18937
1641	AGACAUCACUGA	1985	UCAGUGAUGUCU	3380	AD-18938、AD-19064、AD-18937
1642	GACAUCACUGAG	1986	CUCAGUGAUGUC	3381	AD-18938、AD-19064、AD-18937
1643	ACAUCACUGAGC	1987	GCUCAGUGAUGU	3382	AD-18938、AD-19064、AD-18937、AD-26715
1644	CAUCACUGAGCC	1988	GGCUCAGUGAUG	3383	AD-18938、AD-18937、AD-26715
1645	AUCACUGAGCCU	1989	AGGCUCAGUGAU	3384	AD-18937、AD-26715
1654	CCUGCCAUCUGU	1990	ACAGAUGGCAGG	3385	AD-26716、AD-18990
1655	CUGCCAUCUGUG	1991	CACAGAUGGCAG	3386	AD-26716、AD-18990
1656	UGCCAUCUGUGC	1992	GCACAGAUGGCA	3387	AD-26716、AD-18990
1657	GCCAUCUGUGCU	1993	AGCACAGAUGGC	3388	AD-26716、AD-18990、AD-19061
1658	CCAUCUGUGCUC	1994	GAGCACAGAUGG	3389	AD-26716、AD-18990、AD-18893、AD-19061
1659	CAUCUGUGCUCU	1995	AGAGCACAGAUG	3390	AD-26716、AD-18946、AD-18990、AD-18893、AD-19061
1660	AUCUGUGCUCUU	1996	AAGAGCACAGAU	3391	AD-26716、AD-18946、AD-18990、AD-19082、AD-18893、AD-19061
1661	UCUGUGCUCUUC	1997	GAAGAGCACAGA	3392	AD-18946、AD-18990、AD-19082、AD-18893、AD-19061
1662	CUGUGCUCUUCG	1998	CGAAGAGCACAG	3393	AD-18946、AD-19082、

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1663	UGUGCUCUUCGU	1999	ACGAAGAGCACA	3394	AD-18946、AD-19082、AD-18893、AD-19061
1664	GUGCUCUUCGUC	2000	GACGAAGAGCAC	3395	AD-18946、AD-18904、AD-19082、AD-18893、AD-19061
1665	UGCUCUUCGUCA	2001	UGACGAAGAGCA	3396	AD-18946、AD-18904、AD-19082、AD-18893
1666	GCUCUUCGUCAU	2002	AUGACGAAGAGC	3397	AD-18946、AD-18932、AD-18904、AD-19082
1667	CUCUUCGUCAUC	2003	GAUGACGAAGAG	3398	AD-18932、AD-19082、AD-18943
1668	UCUUCGUCAUCU	2004	AGAUGACGAAGA	3399	AD-18932、AD-18904、AD-18943
1669	CUUCGUCAUCUG	2005	CAGAUGACGAAG	3400	AD-18904、AD-19002、AD-18943
1670	UUCGUCAUCUGA	2006	UCAGAUGACGAA	3401	AD-18932、AD-18904、AD-19002、AD-18943
1671	UCGUCAUCUGAC	2007	GUCAGAUGACGA	3402	AD-18904、AD-18943
1672	CGUCAUCUGACC	2008	GGUCAGAUGACG	3403	AD-18932、AD-19002、AD-18943
1673	GUCAUCUGACCA	2009	UGGUCAGAUGAC	3404	AD-18932、AD-18943
1674	UCAUCUGACCAG	2010	CUGGUCAGAUGA	3405	AD-19002、AD-18943
1677	UCUGACCAGCCG	2011	CGGCUGGUCAGA	3406	AD-26717、AD-19761
1678	CUGACCAGCCGA	2012	UCGGCUGGUCAG	3407	AD-26717、AD-19761
1679	UGACCAGCCGAC	2013	GUCGGCUGGUCA	3408	AD-26717、AD-19761
1680	GACCAGCCGACA	2014	UGUCGGCUGGUC	3409	AD-26717、AD-19761
1681	ACCAGCCGACAC	2015	GUGUCGGCUGGU	3410	AD-26717、AD-26718
1682	CCAGCCGACACC	2016	GGUGUCGGCUGG	3411	AD-26717、AD-26718、AD-19761
1683	CAGCCGACACCA	2017	UGGUGUCGGCUG	3412	AD-26717、AD-26718、AD-19761
1684	AGCCGACACCAA	2018	UUGGUGUCGGCU	3413	AD-26717、AD-26718
1704	GAUGGCCCAGAA	2019	UUCUGGGCCAUC	3414	AD-26721、AD-26720
1705	AUGGCCCAGAAU	2020	AUUCUGGGCCAU	3415	AD-26721、AD-26720
1710	CCAGAAUGCAGU	2021	ACUGCAUUCUGG	3416	AD-26721、AD-26722
1711	CAGAAUGCAGUU	2022	AACUGCAUUCUG	3417	AD-26721、AD-26722
1713	GAAUGCAGUUCG	2023	CGAACUGCAUUC	3418	AD-26722、AD-19741
1714	AAUGCAGUUCGC	2024	GCGAACUGCAUU	3419	AD-26722、AD-19741
1715	AUGCAGUUCGCC	2025	GGCGAACUGCAU	3420	AD-26722、AD-19741、AD-26723
1716	UGCAGUUCGCCU	2026	AGGCGAACUGCA	3421	AD-26724、AD-26722、AD-19741、AD-26723
1717	GCAGUUCGCCUU	2027	AAGGCGAACUGC	3422	AD-26724、AD-19741、

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1718	CAGUUCGCCUUC	2028	GAAGGCGAACUG	3423	AD-26724、AD-26723
1719	AGUUCGCCUUCA	2029	UGAAGGCGAACU	3424	AD-26724、AD-19741
1720	GUUCGCCUUCAC	2030	GUGAAGGCGAAC	3425	AD-19741、AD-26723
1721	UUCGCCUUCACU	2031	AGUGAAGGCGAA	3426	AD-26724、AD-26723
1722	UCGCCUUCACUA	2032	UAGUGAAGGCGA	3427	AD-26724、AD-26725、AD-26723
1723	CGCCUUCACUAU	2033	AUAGUGAAGGCG	3428	AD-26724、AD-26725
1728	UCACUAUGGACU	2034	AGUCCAUAGUGA	3429	AD-26725、AD-26726
1729	CACUAUGGACUA	2035	UAGUCCAUAGUG	3430	AD-26725、AD-26726
1734	UGGACUACCAGU	2036	ACUGGUAGUCCA	3431	AD-26727、AD-26726
1735	GGACUACCAGUU	2037	AACUGGUAGUCC	3432	AD-26727、AD-26728
1736	GACUACCAGUUG	2038	CAACUGGUAGUC	3433	AD-26728、AD-26729
1737	ACUACCAGUUGU	2039	ACAACUGGUAGU	3434	AD-26727、AD-26729
1738	CUACCAGUUGUG	2040	CACAACUGGUAG	3435	AD-26727、AD-26728、AD-26729
1739	UACCAGUUGUGG	2041	CCACAACUGGUA	3436	AD-26727、AD-26728、AD-26729
1740	ACCAGUUGUGGU	2042	ACCACAACUGGU	3437	AD-26727、AD-26728、AD-26729
1741	CCAGUUGUGGUU	2043	AACCACAACUGG	3438	AD-26727、AD-26728、AD-26729
1742	CAGUUGUGGUUA	2044	UAACCACAACUG	3439	AD-26728、AD-26730、AD-26729
1743	AGUUGUGGUUAA	2045	UUAACCACAACU	3440	AD-26731、AD-26730、AD-26729
1744	GUUGUGGUUAAG	2046	CUUAACCACAAC	3441	AD-26731、AD-26730
1745	UUGUGGUUAAGC	2047	GCUUAACCACAA	3442	AD-26731、AD-26730
1746	UGUGGUUAAGCU	2048	AGCUUAACCACA	3443	AD-26731、AD-26730
1747	GUGGUUAAGCUC	2049	GAGCUUAACCAC	3444	AD-26731、AD-26730
1748	UGGUUAAGCUCU	2050	AGAGCUUAACCA	3445	AD-26731、AD-26730
1749	GGUUAAGCUCUU	2051	AAGAGCUUAACC	3446	AD-26731、AD-26730
1770	AUCCCACUGGCC	2052	GGCCAGUGGGAU	3447	AD-26734、AD-26733
1771	UCCCACUGGCCU	2053	AGGCCAGUGGGA	3448	AD-26734、AD-26733、AD-26735
1772	CCCACUGGCCUG	2054	GAGGCCAGUGGG	3449	AD-26734、AD-18963、AD-26733、AD-26735
1773	CCACUGGCCUCU	2055	AGAGGCCAGUGG	3450	AD-26734、AD-18930、AD-18963、AD-26733、AD-26735
1774	CACUGGCCUCUG	2056	CAGAGGCCAGUG	3451	AD-26734、AD-18930、AD-18963、AD-26733、AD-26735、AD-19078
1775	ACUGGCCUCUGA	2057	UCAGAGGCCAGU	3452	AD-26734、AD-18930、

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1776	CUGGCCUCUGAU	2058	AUCAGAGGCCAG	3453	AD-26734、AD-18963、AD-26733、AD-26735、AD-18948、AD-19078
1777	UGGCCUCUGAUA	2059	UAUCAGAGGCCA	3454	AD-26734、AD-18930、AD-26736、AD-18963、AD-26735、AD-18948、AD-19078
1778	GGCCUCUGAUAA	2060	UUAUCAGAGGCC	3455	AD-18930、AD-26736、AD-18963、AD-26735、AD-18948、AD-19078
1779	GCCUCUGAUAAA	2061	UUUAUCAGAGGC	3456	AD-18930、AD-26736、AD-18963、AD-18948、AD-19078
1780	CCUCUGAUAAAG	2062	CUUUAUCAGAGG	3457	AD-18930、AD-26736、AD-18948、AD-19078
1781	CUCUGAUAAAGG	2063	CCUUUAUCAGAG	3458	AD-26736、AD-18948、AD-19078
1782	UCUGAUAAAGGC	2064	GCCUUUAUCAGA	3459	AD-26736、AD-18948、AD-26737
1783	CUGAUAAAGGCU	2065	AGCCUUUAUCAG	3460	AD-26736、AD-26737
1784	UGAUAAAGGCUA	2066	UAGCCUUUAUCA	3461	AD-26736、AD-26737
1786	AUAAAGGCUACU	2067	AGUAGCCUUUAU	3462	AD-26738、AD-26737
1787	UAAAGGCUACUG	2068	CAGUAGCCUUUA	3463	AD-26738、AD-26737
1788	AAAGGCUACUGU	2069	ACAGUAGCCUUU	3464	AD-26738、AD-26737
1789	AAGGCUACUGUU	2070	AACAGUAGCCUU	3465	AD-26738、AD-26737
1791	GGCUACUGUUGG	2071	CCAACAGUAGCC	3466	AD-26738、AD-26739
1792	GCUACUGUUGGA	2072	UCCAACAGUAGC	3467	AD-26738、AD-26739
1793	CUACUGUUGGAU	2073	AUCCAACAGUAG	3468	AD-26738、AD-26739
1795	ACUGUUGGAUUG	2074	CAAUCCAACAGU	3469	AD-18983、AD-26739
1796	CUGUUGGAUUGA	2075	UCAAUCCAACAG	3470	AD-18983、AD-26739、AD-18897
1797	UGUUGGAUUGAU	2076	AUCAAUCCAACA	3471	AD-26740、AD-18983、AD-26739、AD-18897
1798	GUUGGAUUGAUU	2077	AAUCAAUCCAAC	3472	AD-26740、AD-26739、AD-18897
1799	UUGGAUUGAUUC	2078	GAAUCAAUCCAA	3473	AD-26740、AD-18983、AD-18897
1800	UGGAUUGAUUCG	2079	CGAAUCAAUCCA	3474	AD-26740、AD-18897、AD-26921
1801	GGAUUGAUUCGA	2080	UCGAAUCAAUCC	3475	AD-26740、AD-18983、AD-18897、AD-26921
1802	GAUUGAUUCGAA	2081	UUCGAAUCAAUC	3476	AD-18983、AD-18897、

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1803	AUUGAUUCGAAA	2082	UUUCGAAUCAAU	3477	AD-26740、AD-18897、AD-26921
1804	UUGAUUCGAAAU	2083	AUUUCGAAUCAA	3478	AD-26740、AD-26921
1848	GCGUGAGCAGGG	2084	CCCUGCUCACGC	3479	AD-26175、AD-26176
1849	CGUGAGCAGGGU	2085	ACCCUGCUCACG	3480	AD-26175、AD-26176
1850	GUGAGCAGGGUG	2086	CACCCUGCUCAC	3481	AD-26175、AD-26176
1851	UGAGCAGGGUGC	2087	GCACCCUGCUCA	3482	AD-26175、AD-26176
1852	GAGCAGGGUGCC	2088	GGCACCCUGCUC	3483	AD-26175、AD-26176
1853	AGCAGGGUGCCA	2089	UGGCACCCUGCU	3484	AD-26175、AD-26176
1854	GCAGGGUGCCAU	2090	AUGGCACCCUGC	3485	AD-26175、AD-26176
1859	GUGCCAUUCCAC	2091	GUGGAAUGGCAC	3486	AD-19742、AD-19749
1860	UGCCAUUCCACG	2092	CGUGGAAUGGCA	3487	AD-26741、AD-19749
1861	GCCAUUCCACGA	2093	UCGUGGAAUGGC	3488	AD-26741、AD-19742
1862	CCAUUCCACGAC	2094	GUCGUGGAAUGG	3489	AD-26741、AD-19742、AD-19749
1863	CAUUCCACGACU	2095	AGUCGUGGAAUG	3490	AD-26741、AD-19742、AD-19749、AD-19762
1864	AUUCCACGACUA	2096	UAGUCGUGGAAU	3491	AD-26741、AD-19742、AD-19749
1865	UUCCACGACUAG	2097	CUAGUCGUGGAA	3492	AD-26742、AD-26741、AD-19742、AD-19749、AD-19762
1866	UCCACGACUAGU	2098	ACUAGUCGUGGA	3493	AD-26742、AD-26741、AD-19749、AD-19762
1867	CCACGACUAGUU	2099	AACUAGUCGUGG	3494	AD-26742、AD-26741、AD-19751、AD-19762
1868	CACGACUAGUUC	2100	GAACUAGUCGUG	3495	AD-26742、AD-19751、AD-19762、AD-19752
1869	ACGACUAGUUCA	2101	UGAACUAGUCGU	3496	AD-26742、AD-26743、AD-19751、AD-19762
1870	CGACUAGUUCAG	2102	CUGAACUAGUCG	3497	AD-26742、AD-26743、AD-19751、AD-19762、AD-19752
1871	GACUAGUUCAGU	2103	ACUGAACUAGUC	3498	AD-26742、AD-26743、AD-19751、AD-19752
1872	ACUAGUUCAGUU	2104	AACUGAACUAGU	3499	AD-26742、AD-26743、AD-19751、AD-19752、AD-26744
1873	CUAGUUCAGUUG	2105	CAACUGAACUAG	3500	AD-26743、AD-19752、AD-26744
1874	UAGUUCAGUUGC	2106	GCAACUGAACUA	3501	AD-26743、AD-19751、AD-19752、AD-26744
1875	AGUUCAGUUGCU	2107	AGCAACUGAACU	3502	AD-26743、AD-19753、

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1876	GUUCAGUUGCUU	2108	AAGCAACUGAAC	3503	AD-26743、AD-19753、AD-26744
1877	UUCAGUUGCUUG	2109	CAAGCAACUGAA	3504	AD-19753、AD-26744
1878	UCAGUUGCUUGU	2110	ACAAGCAACUGA	3505	AD-19753、AD-26744
1879	CAGUUGCUUGUU	2111	AACAAGCAACUG	3506	AD-19753、AD-26744
1881	GUUGCUUGUUCG	2112	CGAACAAGCAAC	3507	AD-19753、AD-26745
1882	UUGCUUGUUCGU	2113	ACGAACAAGCAA	3508	AD-19753、AD-26745
1887	UGUUCGUGCACA	2114	UGUGCACGAACA	3509	AD-26746、AD-26745
1888	GUUCGUGCACAU	2115	AUGUGCACGAAC	3510	AD-26746、AD-26747、AD-26745
1889	UUCGUGCACAUC	2116	GAUGUGCACGAA	3511	AD-26746、AD-26747
1890	UCGUGCACAUCA	2117	UGAUGUGCACGA	3512	AD-26746、AD-26747
1891	CGUGCACAUCAG	2118	CUGAUGUGCACG	3513	AD-26746、AD-26747
1892	GUGCACAUCAGG	2119	CCUGAUGUGCAC	3514	AD-26746、AD-26747
1893	UGCACAUCAGGA	2120	UCCUGAUGUGCA	3515	AD-26746、AD-26747
1894	GCACAUCAGGAU	2121	AUCCUGAUGUGC	3516	AD-26746、AD-26747
1907	CCCAGCGCCGUA	2122	UACGGCGCUGGG	3517	AD-19738、AD-19754
1908	CCAGCGCCGUAC	2123	GUACGGCGCUGG	3518	AD-19738、AD-19754
1909	CAGCGCCGUACG	2124	CGUACGGCGCUG	3519	AD-19738、AD-19754
1910	AGCGCCGUACGU	2125	ACGUACGGCGCU	3520	AD-19738、AD-19754
1911	GCGCCGUACGUC	2126	GACGUACGGCGC	3521	AD-19738、AD-19754
1912	CGCCGUACGUCC	2127	GGACGUACGGCG	3522	AD-19738、AD-19754
1927	GGUGGGACACAG	2128	CUGUGUCCCACC	3523	AD-26184、AD-26748
1928	GUGGGACACAGC	2129	GCUGUGUCCCAC	3524	AD-26749、AD-26184、AD-26748
1929	UGGGACACAGCA	2130	UGCUGUGUCCCA	3525	AD-26749、AD-26750、AD-26184、AD-26748
1930	GGGACACAGCAG	2131	CUGCUGUGUCCC	3526	AD-26749、AD-26750、AD-26184
1931	GGACACAGCAGC	2132	GCUGCUGUGUCC	3527	AD-26749、AD-26184、AD-26748
1932	GACACAGCAGCA	2133	UGCUGCUGUGUC	3528	AD-26749、AD-26750、AD-26184、AD-26748
1933	ACACAGCAGCAA	2134	UUGCUGCUGUGU	3529	AD-26750、AD-26184、AD-26748
1934	CACAGCAGCAAU	2135	AUUGCUGCUGUG	3530	AD-26749、AD-26750、AD-26748
1935	ACAGCAGCAAUU	2136	AAUUGCUGCUGU	3531	AD-26749、AD-26750
1955	GGGUCCGCAUGG	2137	CCAUGCGGACCC	3532	AD-26751、AD-26752
1956	GGUCCGCAUGGA	2138	UCCAUGCGGACC	3533	AD-26751、AD-26752
1957	GUCCGCAUGGAA	2139	UUCCAUGCGGAC	3534	AD-26751、AD-26752
1958	UCCGCAUGGAAG	2140	CUUCCAUGCGGA	3535	AD-26751、AD-26752
1959	CCGCAUGGAAGA	2141	UCUUCCAUGCGG	3536	AD-26751、AD-26752

1960	CGCAUGGAAGAA	2142	UUCUUCCAUGCG	3537	AD-26751、AD-26752
1961	GCAUGGAAGAAA	2143	UUUCUUCCAUGC	3538	AD-26751、AD-26752
2001	CAUCCUAGCUCG	2144	CGAGCUAGGAUG	3539	AD-26753、AD-26754
2002	AUCCUAGCUCGG	2145	CCGAGCUAGGAU	3540	AD-26753、AD-26754
2003	UCCUAGCUCGGG	2146	CCCGAGCUAGGA	3541	AD-26753、AD-26754
2004	CCUAGCUCGGGA	2147	UCCCGAGCUAGG	3542	AD-26753、AD-26754
2005	CUAGCUCGGGAU	2148	AUCCCGAGCUAG	3543	AD-26753、AD-26754
2006	UAGCUCGGGAUG	2149	CAUCCCGAGCUA	3544	AD-26755、AD-26754
2007	AGCUCGGGAUGU	2150	ACAUCCCGAGCU	3545	AD-26755、AD-26754
2008	GCUCGGGAUGUU	2151	AACAUCCCGAGC	3546	AD-26755、AD-26754
2011	CGGGAUGUUCAC	2152	GUGAACAUCCCG	3547	AD-26755、AD-20124
2012	GGGAUGUUCACA	2153	UGUGAACAUCCC	3548	AD-26756、AD-26755、AD-20124
2013	GGAUGUUCACAA	2154	UUGUGAACAUCC	3549	AD-26756、AD-26755、AD-26757、AD-20124
2014	GAUGUUCACAAC	2155	GUUGUGAACAUC	3550	AD-26756、AD-26757、AD-20124
2015	AUGUUCACAACC	2156	GGUUGUGAACAU	3551	AD-26756、AD-26757、AD-20124
2016	UGUUCACAACCG	2157	CGGUUGUGAACA	3552	AD-26756、AD-19750、AD-20124
2017	GUUCACAACCGA	2158	UCGGUUGUGAAC	3553	AD-19750、AD-26757、AD-20124
2018	UUCACAACCGAA	2159	UUCGGUUGUGAA	3554	AD-26756、AD-19750、AD-26757、AD-20124
2019	UCACAACCGAAU	2160	AUUCGGUUGUGA	3555	AD-26756、AD-19750、AD-26757
2020	CACAACCGAAUU	2161	AAUUCGGUUGUG	3556	AD-19750、AD-26757
2041	GGACUAAAUACC	2162	GGUAUUUAGUCC	3557	AD-26758、AD-26759
2042	GACUAAAUACCA	2163	UGGUAUUUAGUC	3558	AD-26758、AD-26759
2043	ACUAAAUACCAU	2164	AUGGUAUUUAGU	3559	AD-26758、AD-26759
2044	CUAAAUACCAUU	2165	AAUGGUAUUUAG	3560	AD-26758、AD-26759
2045	UAAAUACCAUUC	2166	GAAUGGUAUUUA	3561	AD-26760、AD-26759
2046	AAAUACCAUUCC	2167	GGAAUGGUAUUU	3562	AD-26760、AD-26761、AD-26759
2047	AAUACCAUUCCA	2168	UGGAAUGGUAUU	3563	AD-26760、AD-26759
2048	AUACCAUUCCAU	2169	AUGGAAUGGUAU	3564	AD-26760、AD-26761、AD-26759、AD-18982
2049	UACCAUUCCAUU	2170	AAUGGAAUGGUA	3565	AD-26760、AD-19062、AD-18982
2050	ACCAUUCCAUUG	2171	CAAUGGAAUGGU	3566	AD-26760、AD-26761、AD-19062、AD-18982
2051	CCAUUCCAUUGU	2172	ACAAUGGAAUGG	3567	AD-26761、AD-19062、AD-18982

2052	CAUUCCAUUGUU	2173	AACAAUGGAAUG	3568	AD-26760、AD-26761、AD-19062
2053	AUUCCAUUGUUU	2174	AAACAAUGGAAU	3569	AD-26761、AD-19062、AD-18982
2054	UUCCAUUGUUUG	2175	CAAACAAUGGAA	3570	AD-19062、AD-18982
2055	UCCAUUGUUUGU	2176	ACAAACAAUGGA	3571	AD-19062、AD-18982
2059	UUGUUUGUGCAG	2177	CUGCACAAACAA	3572	AD-26763、AD-26762
2060	UGUUUGUGCAGC	2178	GCUGCACAAACA	3573	AD-26764、AD-26763、AD-26762
2061	GUUUGUGCAGCU	2179	AGCUGCACAAAC	3574	AD-26764、AD-26765、AD-26763、AD-26762
2062	UUUGUGCAGCUG	2180	CAGCUGCACAAA	3575	AD-26764、AD-26765、AD-26766、AD-26763、AD-26762
2063	UUGUGCAGCUGC	2181	GCAGCUGCACAA	3576	AD-26764、AD-26765、AD-26766、AD-26763
2064	UGUGCAGCUGCU	2182	AGCAGCUGCACA	3577	AD-26764、AD-26766、AD-26763、AD-26762
2065	GUGCAGCUGCUU	2183	AAGCAGCUGCAC	3578	AD-26765、AD-26766、AD-26763、AD-26762
2066	UGCAGCUGCUUU	2184	AAAGCAGCUGCA	3579	AD-26764、AD-26765、AD-26766、AD-26763
2067	GCAGCUGCUUUA	2185	UAAAGCAGCUGC	3580	AD-26764、AD-26765、AD-26766
2068	CAGCUGCUUUAU	2186	AUAAAGCAGCUG	3581	AD-26765、AD-26766
2069	AGCUGCUUUAUU	2187	AAUAAAGCAGCU	3582	AD-26766、AD-26767
2070	GCUGCUUUAUUC	2188	GAAUAAAGCAGC	3583	AD-26768、AD-26767
2071	CUGCUUUAUUCU	2189	AGAAUAAAGCAG	3584	AD-26768、AD-26767
2072	UGCUUUAUUCUC	2190	GAGAAUAAAGCA	3585	AD-26768、AD-26767
2073	GCUUUAUUCUCC	2191	GGAGAAUAAAGC	3586	AD-26768、AD-18928
2074	CUUUAUUCUCCC	2192	GGGAGAAUAAAG	3587	AD-26768、AD-18928、AD-26767
2075	UUUAUUCUCCCA	2193	UGGGAGAAUAAA	3588	AD-26769、AD-18928、AD-26767
2076	UUAUUCUCCCAU	2194	AUGGGAGAAUAA	3589	AD-26769、AD-26768、AD-18928、AD-26767
2077	UAUUCUCCCAUU	2195	AAUGGGAGAAUA	3590	AD-26769、AD-26768、AD-18928
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2080	UCUCCCAUUGAA	2198	UUCAAUGGGAGA	3593	AD-26769、AD-26770
2081	CUCCCAUUGAAA	2199	UUUCAAUGGGAG	3594	AD-26769、AD-26770
2082	UCCCAUUGAAAA	2200	UUUUCAAUGGGA	3595	AD-26771、AD-26769、AD-26770

2083	CCCAUUGAAAAC	2201	GUUUUCAAUGGG	3596	AD-26771、AD-26770
2084	CCAUUGAAAACA	2202	UGUUUUCAAUGG	3597	AD-26771、AD-26770
2085	CAUUGAAAACAU	2203	AUGUUUUCAAUG	3598	AD-26771、AD-26770
2100	AAGAGUAGCUGC	2204	GCAGCUACUCUU	3599	AD-18962、AD-18895
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2102	GAGUAGCUGCAG	2206	CUGCAGCUACUC	3601	AD-18962、AD-18895
2104	GUAGCUGCAGGG	2207	CCCUGCAGCUAC	3602	AD-18962、AD-18976
2105	UAGCUGCAGGGG	2208	CCCCUGCAGCUA	3603	AD-19003、AD-18962
2106	AGCUGCAGGGGU	2209	ACCCCUGCAGCU	3604	AD-19003、AD-18962、AD-18976
2107	GCUGCAGGGGUC	2210	GACCCCUGCAGC	3605	AD-18962、AD-18976
2108	CUGCAGGGGUCC	2211	GGACCCCUGCAG	3606	AD-19003、AD-18976
2109	UGCAGGGGUCCU	2212	AGGACCCCUGCA	3607	AD-19003、AD-26772、AD-18976
2110	GCAGGGGUCCUC	2213	GAGGACCCCUGC	3608	AD-19003、AD-26772、AD-18976
2111	CAGGGGUCCUCU	2214	AGAGGACCCCUG	3609	AD-18923、AD-19003、AD-26772、AD-18976
2112	AGGGGUCCUCUG	2215	CAGAGGACCCCU	3610	AD-18923、AD-19003、AD-18955、AD-26772
2113	GGGGUCCUCUGU	2216	ACAGAGGACCCC	3611	AD-18923、AD-18955、AD-26772
2114	GGGUCCUCUGUG	2217	CACAGAGGACCC	3612	AD-18923、AD-18934、AD-18955、AD-26772
2115	GGUCCUCUGUGA	2218	UCACAGAGGACC	3613	AD-18923、AD-18934、AD-19052、AD-18912、AD-18955
2116	GUCCUCUGUGAA	2219	UUCACAGAGGAC	3614	AD-18923、AD-19052、AD-18912、AD-18955、AD-26772
2117	UCCUCUGUGAAC	2220	GUUCACAGAGGA	3615	AD-18923、AD-18934、AD-19052、AD-18912、AD-18955
2118	CCUCUGUGAACU	2221	AGUUCACAGAGG	3616	AD-18923、AD-18934、AD-18973、AD-19052、AD-18912、AD-18955
2119	CUCUGUGAACUU	2222	AAGUUCACAGAG	3617	AD-18934、AD-18973、AD-19052、AD-18912、AD-18955
2120	UCUGUGAACUUG	2223	CAAGUUCACAGA	3618	AD-18934、AD-18973、AD-19052、AD-18912
2121	CUGUGAACUUGC	2224	GCAAGUUCACAG	3619	AD-18973、AD-19052、AD-18912
2122	UGUGAACUUGCU	2225	AGCAAGUUCACA	3620	AD-18973、AD-19047

2123	GUGAACUUGCUC	2226	GAGCAAGUUCAC	3621	AD-18973、AD-19047、AD-18971
2124	UGAACUUGCUCA	2227	UGAGCAAGUUCA	3622	AD-18973、AD-19047、AD-18971、AD-18961
2125	GAACUUGCUCAG	2228	CUGAGCAAGUUC	3623	AD-18973、AD-19047、AD-18971、AD-18961
2126	AACUUGCUCAGG	2229	CCUGAGCAAGUU	3624	AD-19047、AD-18984、AD-18971、AD-18961
2127	ACUUGCUCAGGA	2230	UCCUGAGCAAGU	3625	AD-19047、AD-18984、AD-26773、AD-18971、AD-18961
2128	CUUGCUCAGGAC	2231	GUCCUGAGCAAG	3626	AD-19047、AD-18984、AD-26773、AD-18971
2129	UUGCUCAGGACA	2232	UGUCCUGAGCAA	3627	AD-19047、AD-18984、AD-26773、AD-18971、AD-18961
2130	UGCUCAGGACAA	2233	UUGUCCUGAGCA	3628	AD-18984、AD-26773、AD-18971、AD-18961
2131	GCUCAGGACAAG	2234	CUUGUCCUGAGC	3629	AD-18984、AD-26773、AD-18961
2132	CUCAGGACAAGG	2235	CCUUGUCCUGAG	3630	AD-18984、AD-26773
2133	UCAGGACAAGGA	2236	UCCUUGUCCUGA	3631	AD-18984、AD-26773
2178	AGCUCCUCUGAC	2237	GUCAGAGGAGCU	3632	AD-26775、AD-26774
2179	GCUCCUCUGACA	2238	UGUCAGAGGAGC	3633	AD-26775、AD-26774
2180	CUCCUCUGACAG	2239	CUGUCAGAGGAG	3634	AD-26775、AD-26774
2181	UCCUCUGACAGA	2240	UCUGUCAGAGGA	3635	AD-26775、AD-26774
2182	CCUCUGACAGAG	2241	CUCUGUCAGAGG	3636	AD-26775、AD-26776
2183	CUCUGACAGAGU	2242	ACUCUGUCAGAG	3637	AD-26776、AD-26774
2184	UCUGACAGAGUU	2243	AACUCUGUCAGA	3638	AD-26775、AD-26776、AD-26774
2185	CUGACAGAGUUA	2244	UAACUCUGUCAG	3639	AD-26775、AD-26776
2188	ACAGAGUUACUU	2245	AAGUAACUCUGU	3640	AD-26777、AD-26776
2191	GAGUUACUUCAC	2246	GUGAAGUAACUC	3641	AD-26777、AD-19755
2192	AGUUACUUCACU	2247	AGUGAAGUAACU	3642	AD-26777、AD-26778、AD-19755
2193	GUUACUUCACUC	2248	GAGUGAAGUAAC	3643	AD-26777、AD-26779、AD-26778、AD-19755
2194	UUACUUCACUCU	2249	AGAGUGAAGUAA	3644	AD-26777、AD-26779、AD-19755
2195	UACUUCACUCUA	2250	UAGAGUGAAGUA	3645	AD-26777、AD-26778、AD-19755
2196	ACUUCACUCUAG	2251	CUAGAGUGAAGU	3646	AD-26780、AD-26778、AD-19755
2197	CUUCACUCUAGG	2252	CCUAGAGUGAAG	3647	AD-26779、AD-26780、

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2198	UUCACUCUAGGA	2253	UCCUAGAGUGAA	3648	AD-26779、AD-26780、AD-26778、AD-19755
2199	UCACUCUAGGAA	2254	UUCCUAGAGUGA	3649	AD-26779、AD-26780、AD-26778
2200	CACUCUAGGAAU	2255	AUUCCUAGAGUG	3650	AD-26779、AD-26780
2234	CUGCUGUUUUGU	2256	ACAAAACAGCAG	3651	AD-26782、AD-26781
2235	UGCUGUUUUGUU	2257	AACAAAACAGCA	3652	AD-26782、AD-26781
2236	GCUGUUUUGUUC	2258	GAACAAAACAGC	3653	AD-26782、AD-26781
2237	CUGUUUUGUUCC	2259	GGAACAAAACAG	3654	AD-26782、AD-26781
2238	UGUUUUGUUCCG	2260	CGGAACAAAACA	3655	AD-26782、AD-26781
2239	GUUUUGUUCCGA	2261	UCGGAACAAAAC	3656	AD-26782、AD-26781
2240	UUUUGUUCCGAA	2262	UUCGGAACAAAA	3657	AD-26782、AD-26781
2256	UGAGGACAAGCC	2263	GGCUUGUCCUCA	3658	AD-26783、AD-26784
2257	GAGGACAAGCCA	2264	UGGCUUGUCCUC	3659	AD-26783、AD-26784
2258	AGGACAAGCCAC	2265	GUGGCUUGUCCU	3660	AD-26783、AD-26784
2259	GGACAAGCCACA	2266	UGUGGCUUGUCC	3661	AD-26783、AD-26784
2260	GACAAGCCACAA	2267	UUGUGGCUUGUC	3662	AD-26783、AD-26784
2261	ACAAGCCACAAG	2268	CUUGUGGCUUGU	3663	AD-26784、AD-26785
2262	CAAGCCACAAGA	2269	UCUUGUGGCUUG	3664	AD-26784、AD-26785
2263	AAGCCACAAGAU	2270	AUCUUGUGGCUU	3665	AD-26784、AD-26785
2264	AGCCACAAGAUU	2271	AAUCUUGUGGCU	3666	AD-26786、AD-26785
2265	GCCACAAGAUUA	2272	UAAUCUUGUGGC	3667	AD-26786、AD-26785
2266	CCACAAGAUUAC	2273	GUAAUCUUGUGG	3668	AD-26786、AD-26785
2267	CACAAGAUUACA	2274	UGUAAUCUUGUG	3669	AD-26786、AD-26785
2268	ACAAGAUUACAA	2275	UUGUAAUCUUGU	3670	AD-26786、AD-26785
2271	AGAUUACAAGAA	2276	UUCUUGUAAUCU	3671	AD-26786、AD-26787
2277	CAAGAAACGGCU	2277	AGCCGUUUCUUG	3672	AD-26788、AD-26787
2278	AAGAAACGGCUU	2278	AAGCCGUUUCUU	3673	AD-26788、AD-26787
2302	ACCAGCUCUCUC	2279	GAGAGAGCUGGU	3674	AD-26790、AD-26789
2303	CCAGCUCUCUCU	2280	AGAGAGAGCUGG	3675	AD-26790、AD-26789
2304	CAGCUCUCUCUU	2281	AAGAGAGAGCUG	3676	AD-26790、AD-26789
2325	GCCAAUGGCUUG	2282	CAAGCCAUUGGC	3677	AD-18909、AD-18910
2326	CCAAUGGCUUGG	2283	CCAAGCCAUUGG	3678	AD-18909、AD-18910、AD-19080
2327	CAAUGGCUUGGA	2284	UCCAAGCCAUUG	3679	AD-18909、AD-18947、AD-18910、AD-19080
2328	AAUGGCUUGGAA	2285	UUCCAAGCCAUU	3680	AD-18909、AD-19051、AD-18947、AD-18910、AD-19080
2329	AUGGCUUGGAAU	2286	AUUCCAAGCCAU	3681	AD-18909、AD-19051、AD-18947、AD-18978、AD-18910
2330	UGGCUUGGAAUG	2287	CAUUCCAAGCCA	3682	AD-18909、AD-19051、

					AD-18947、AD-18978、AD-19080
2331	GGCUUGGAAUGA	2288	UCAUUCCAAGCC	3683	AD-18909、AD-19051、AD-18947、AD-18978、AD-18910、AD-19080
2332	GCUUGGAAUGAG	2289	CUCAUUCCAAGC	3684	AD-19051、AD-18947、AD-18978、AD-18910、AD-19080
2333	CUUGGAAUGAGA	2290	UCUCAUUCCAAG	3685	AD-19051、AD-18947、AD-18978、AD-19080
2334	UUGGAAUGAGAC	2291	GUCUCAUUCCAA	3686	AD-19051、AD-18947、AD-18978
2335	UGGAAUGAGACU	2292	AGUCUCAUUCCA	3687	AD-19051、AD-18978
2370	UGCCCAGGGAGA	2293	UCUCCCUGGGCA	3688	AD-26677、AD-26791
2371	GCCCAGGGAGAA	2294	UUCUCCCUGGGC	3689	AD-26677、AD-26791
2374	CAGGGAGAACCC	2295	GGGUUCUCCCUG	3690	AD-26792、AD-26677
2375	AGGGAGAACCCC	2296	GGGGUUCUCCCU	3691	AD-26793、AD-26677
2376	GGGAGAACCCCU	2297	AGGGGUUCUCCC	3692	AD-26793、AD-26792
2377	GGAGAACCCCUU	2298	AAGGGGUUCUCC	3693	AD-26793、AD-26792、AD-26677
2378	GAGAACCCCUUG	2299	CAAGGGGUUCUC	3694	AD-26793、AD-26792
2379	AGAACCCCUUGG	2300	CCAAGGGGUUCU	3695	AD-26793、AD-26792
2380	GAACCCCUUGGA	2301	UCCAAGGGGUUC	3696	AD-26793、AD-26792
2381	AACCCCUUGGAU	2302	AUCCAAGGGGUU	3697	AD-26793、AD-26792
2385	CCUUGGAUAUCG	2303	CGAUAUCCAAGG	3698	AD-26794、AD-19063
2386	CUUGGAUAUCGC	2304	GCGAUAUCCAAG	3699	AD-26794、AD-19063
2387	UUGGAUAUCGCC	2305	GGCGAUAUCCAA	3700	AD-18979、AD-26794、AD-19063
2388	UGGAUAUCGCCA	2306	UGGCGAUAUCCA	3701	AD-18979、AD-19001、AD-26794、AD-19063
2389	GGAUAUCGCCAG	2307	CUGGCGAUAUCC	3702	AD-18979、AD-18941、AD-19001、AD-26794、AD-19063
2390	GAUAUCGCCAGG	2308	CCUGGCGAUAUC	3703	AD-18979、AD-18941、AD-19001、AD-18900、AD-26794、AD-19063
2391	AUAUCGCCAGGA	2309	UCCUGGCGAUAU	3704	AD-18979、AD-18941、AD-19001、AD-18900、AD-26794
2392	UAUCGCCAGGAU	2310	AUCCUGGCGAUA	3705	AD-18979、AD-18941、AD-19001、AD-18900、AD-26794、AD-26795
2393	AUCGCCAGGAUG	2311	CAUCCUGGCGAU	3706	AD-18979、AD-18941、AD-19001、AD-26795

2394	UCGCCAGGAUGA	2312	UCAUCCUGGCGA	3707	AD-18979、AD-18941、AD-19001、AD-18900、AD-26795
2395	CGCCAGGAUGAU	2313	AUCAUCCUGGCG	3708	AD-18941、AD-19001、AD-18900、AD-26795
2396	GCCAGGAUGAUC	2314	GAUCAUCCUGGC	3709	AD-18941、AD-26796、AD-26795
2397	CCAGGAUGAUCC	2315	GGAUCAUCCUGG	3710	AD-26796、AD-18900、AD-26795、AD-26797
2398	CAGGAUGAUCCU	2316	AGGAUCAUCCUG	3711	AD-26796、AD-26795、AD-26797
2399	AGGAUGAUCCUA	2317	UAGGAUCAUCCU	3712	AD-26796、AD-26795
2400	GGAUGAUCCUAG	2318	CUAGGAUCAUCC	3713	AD-26796、AD-26797
2401	GAUGAUCCUAGC	2319	GCUAGGAUCAUC	3714	AD-26796、AD-26798、AD-26797
2402	AUGAUCCUAGCU	2320	AGCUAGGAUCAU	3715	AD-26796、AD-26797
2403	UGAUCCUAGCUA	2321	UAGCUAGGAUCA	3716	AD-26796、AD-26798、AD-26797
2404	GAUCCUAGCUAU	2322	AUAGCUAGGAUC	3717	AD-26798、AD-26797
2405	AUCCUAGCUAUC	2323	GAUAGCUAGGAU	3718	AD-26799、AD-26798
2406	UCCUAGCUAUCG	2324	CGAUAGCUAGGA	3719	AD-26799、AD-26800
2407	CCUAGCUAUCGU	2325	ACGAUAGCUAGG	3720	AD-26799、AD-26798
2408	CUAGCUAUCGUU	2326	AACGAUAGCUAG	3721	AD-26799、AD-26798、AD-26800
2409	UAGCUAUCGUUC	2327	GAACGAUAGCUA	3722	AD-26799、AD-26800
2410	AGCUAUCGUUCU	2328	AGAACGAUAGCU	3723	AD-26799、AD-26800
2411	GCUAUCGUUCUU	2329	AAGAACGAUAGC	3724	AD-26799、AD-26800
2412	CUAUCGUUCUUU	2330	AAAGAACGAUAG	3725	AD-26799、AD-26800
2419	UCUUUUCACUCU	2331	AGAGUGAAAAGA	3726	AD-18951、AD-26801
2420	CUUUUCACUCUG	2332	CAGAGUGAAAAG	3727	AD-18951、AD-26802、AD-26801
2421	UUUUCACUCUGG	2333	CCAGAGUGAAAA	3728	AD-18951、AD-26803、AD-26802、AD-26801
2422	UUUCACUCUGGU	2334	ACCAGAGUGAAA	3729	AD-18951、AD-26802、AD-26801
2423	UUCACUCUGGUG	2335	CACCAGAGUGAA	3730	AD-18951、AD-26803、AD-26801
2424	UCACUCUGGUGG	2336	CCACCAGAGUGA	3731	AD-26803、AD-26802
2425	CACUCUGGUGGA	2337	UCCACCAGAGUG	3732	AD-26803、AD-26801
2426	ACUCUGGUGGAU	2338	AUCCACCAGAGU	3733	AD-26803、AD-26802、AD-26801
2427	CUCUGGUGGAUA	2339	UAUCCACCAGAG	3734	AD-26803、AD-26802
2435	GAUAUGGCCAGG	2340	CCUGGCCAUAUC	3735	AD-26805、AD-26804
2436	AUAUGGCCAGGA	2341	UCCUGGCCAUAU	3736	AD-26805、AD-26804

2437	UAUGGCCAGGAU	2342	AUCCUGGCCAUA	3737	AD-26805、AD-26804
2440	GGCCAGGAUGCC	2343	GGCAUCCUGGCC	3738	AD-26693、AD-26805
2441	GCCAGGAUGCCU	2344	AGGCAUCCUGGC	3739	AD-26693、AD-26805
2442	CCAGGAUGCCUU	2345	AAGGCAUCCUGG	3740	AD-26693、AD-26805
2453	UGGGUAUGGACC	2346	GGUCCAUACCCA	3741	AD-26806、AD-26807
2454	GGGUAUGGACCC	2347	GGGUCCAUACCC	3742	AD-26806、AD-26807
2455	GGUAUGGACCCC	2348	GGGGUCCAUACC	3743	AD-26806、AD-26807
2456	GUAUGGACCCCA	2349	UGGGGUCCAUAC	3744	AD-26806、AD-26807
2457	UAUGGACCCCAU	2350	AUGGGGUCCAUA	3745	AD-26806、AD-26811、AD-26807
2458	AUGGACCCCAUG	2351	CAUGGGGUCCAU	3746	AD-26811、AD-26807
2459	UGGACCCCAUGA	2352	UCAUGGGGUCCA	3747	AD-26811、AD-26807
2460	GGACCCCAUGAU	2353	AUCAUGGGGUCC	3748	AD-26811、AD-26807、AD-26812
2461	GACCCCAUGAUG	2354	CAUCAUGGGGUC	3749	AD-26811、AD-26812
2462	ACCCCAUGAUGG	2355	CCAUCAUGGGGU	3750	AD-26811、AD-26812
2463	CCCCAUGAUGGA	2356	UCCAUCAUGGGG	3751	AD-26811、AD-26812
2464	CCCAUGAUGGAA	2357	UUCCAUCAUGGG	3752	AD-26811、AD-26812
2465	CCAUGAUGGAAC	2358	GUUCCAUCAUGG	3753	AD-26813、AD-26812
2466	CAUGAUGGAACA	2359	UGUUCCAUCAUG	3754	AD-26813、AD-26812
2467	AUGAUGGAACAU	2360	AUGUUCCAUCAU	3755	AD-26813、AD-26812
2493	CCACCCUGGUGC	2361	GCACCAGGGUGG	3756	AD-26814、AD-26815
2494	CACCCUGGUGCU	2362	AGCACCAGGGUG	3757	AD-26814、AD-26815
2495	ACCCUGGUGCUG	2363	CAGCACCAGGGU	3758	AD-26814、AD-26815
2496	CCCUGGUGCUGA	2364	UCAGCACCAGGG	3759	AD-26814、AD-26815、AD-19057
2497	CCUGGUGCUGAC	2365	GUCAGCACCAGG	3760	AD-19071、AD-26814、AD-26815、AD-19057
2498	CUGGUGCUGACU	2366	AGUCAGCACCAG	3761	AD-19071、AD-26814、AD-26815、AD-18970、AD-19057
2499	UGGUGCUGACUA	2367	UAGUCAGCACCA	3762	AD-19071、AD-26814、AD-26815、AD-18970、AD-19057、AD-18892
2500	GGUGCUGACUAU	2368	AUAGUCAGCACC	3763	AD-19071、AD-26815、AD-18970、AD-19057、AD-18892
2501	GUGCUGACUAUC	2369	GAUAGUCAGCAC	3764	AD-19071、AD-18970、AD-19057、AD-18892
2502	UGCUGACUAUCC	2370	GGAUAGUCAGCA	3765	AD-19071、AD-26816、AD-18970、AD-19057、AD-18892
2503	GCUGACUAUCCA	2371	UGGAUAGUCAGC	3766	AD-19071、AD-19042、AD-26816、AD-18970、

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2504	CUGACUAUCCAG	2372	CUGGAUAGUCAG	3767	AD-19071、AD-19042、AD-26816、AD-18970、AD-18919、AD-18892
2505	UGACUAUCCAGU	2373	ACUGGAUAGUCA	3768	AD-19042、AD-18944、AD-18970、AD-18919、AD-18892
2506	GACUAUCCAGUU	2374	AACUGGAUAGUC	3769	AD-19042、AD-26816、AD-18944、AD-18908、AD-18919、AD-18892
2507	ACUAUCCAGUUG	2375	CAACUGGAUAGU	3770	AD-19042、AD-26816、AD-18967、AD-18944、AD-18908、AD-18919
2508	CUAUCCAGUUGA	2376	UCAACUGGAUAG	3771	AD-19042、AD-26816、AD-18967、AD-18944、AD-18908、AD-19077、AD-18919
2509	UAUCCAGUUGAU	2377	AUCAACUGGAUA	3772	AD-19042、AD-26816、AD-18967、AD-18944、AD-18908、AD-19077、AD-18919
2510	AUCCAGUUGAUG	2378	CAUCAACUGGAU	3773	AD-19042、AD-18967、AD-18944、AD-18908、AD-19077、AD-18919
2511	UCCAGUUGAUGG	2379	CCAUCAACUGGA	3774	AD-18967、AD-18944、AD-18908、AD-19077、AD-18919
2512	CCAGUUGAUGGG	2380	CCCAUCAACUGG	3775	AD-18967、AD-18944、AD-18908、AD-19077
2513	CAGUUGAUGGGC	2381	GCCCAUCAACUG	3776	AD-18967、AD-18908、AD-19077
2514	AGUUGAUGGGCU	2382	AGCCCAUCAACU	3777	AD-26817、AD-18967、AD-19077
2515	GUUGAUGGGCUG	2383	CAGCCCAUCAAC	3778	AD-26817、AD-19077
2544	CGAGGACCUCAU	2384	AUGAGGUCCUGG	3779	AD-19073、AD-26818
2545	CAGGACCUCAUG	2385	CAUGAGGUCCUG	3780	AD-19073、AD-26818
2546	AGGACCUCAUGG	2386	CCAUGAGGUCCU	3781	AD-19073、AD-26818
2547	GGACCUCAUGGA	2387	UCCAUGAGGUCC	3782	AD-19073、AD-26818
2548	GACCUCAUGGAU	2388	AUCCAUGAGGUC	3783	AD-19073、AD-26818
2580	CAAUCAGCUGGC	2389	GCCAGCUGAUUG	3784	AD-26819、AD-26820
2581	AAUCAGCUGGCC	2390	GGCCAGCUGAUU	3785	AD-26819、AD-26820
2582	AUCAGCUGGCCU	2391	AGGCCAGCUGAU	3786	AD-26819、AD-18989、AD-26820
2583	UCAGCUGGCCUG	2392	CAGGCCAGCUGA	3787	AD-18975、AD-26819、

					AD-18989、AD-26820
2584	CAGCUGGCCUGG	2393	CCAGGCCAGCUG	3788	AD-18975、AD-26819、AD-18989、AD-26820
2585	AGCUGGCCUGGU	2394	ACCAGGCCAGCU	3789	AD-18975、AD-19060、AD-26819、AD-18989、AD-26820
2586	GCUGGCCUGGUU	2395	AACCAGGCCAGC	3790	AD-18975、AD-18898、AD-26819、AD-18989、AD-26820
2587	CUGGCCUGGUUU	2396	AAACCAGGCCAG	3791	AD-18975、AD-19060、AD-18898、AD-18989、AD-26820
2588	UGGCCUGGUUUG	2397	CAAACCAGGCCA	3792	AD-18975、AD-19059、AD-19060、AD-18964、AD-18898、AD-18989
2589	GGCCUGGUUUGA	2398	UCAAACCAGGCC	3793	AD-18920、AD-19059、AD-19060、AD-18964、AD-18898、AD-18989
2590	GCCUGGUUUGAU	2399	AUCAAACCAGGC	3794	AD-18975、AD-18920、AD-19059、AD-19060、AD-18964、AD-18898
2591	CCUGGUUUGAUA	2400	UAUCAAACCAGG	3795	AD-18922、AD-19059、AD-19060、AD-18907、AD-18964、AD-18898
2592	CUGGUUUGAUAC	2401	GUAUCAAACCAG	3796	AD-18922、AD-18920、AD-19060、AD-18907、AD-18964、AD-18898
2593	UGGUUUGAUACU	2402	AGUAUCAAACCA	3797	AD-18905、AD-18922、AD-18920、AD-18907、AD-18964
2594	GGUUUGAUACUG	2403	CAGUAUCAAACC	3798	AD-18905、AD-18920、AD-26821、AD-18907、AD-18964
2595	GUUUGAUACUGA	2404	UCAGUAUCAAAC	3799	AD-18922、AD-18920、AD-19059、AD-26821、AD-18986
2596	UUUGAUACUGAC	2405	GUCAGUAUCAAA	3800	AD-18905、AD-18922、AD-18920、AD-26821、AD-18907、AD-19066、AD-18986
2597	UUGAUACUGACC	2406	GGUCAGUAUCAA	3801	AD-18905、AD-26821、AD-18907、AD-18986
2598	UGAUACUGACCU	2407	AGGUCAGUAUCA	3802	AD-18905、AD-18999、AD-18907、AD-18965、AD-19066

2599	GAUACUGACCUG	2408	CAGGUCAGUAUC	3803	AD-18905、AD-26821、AD-18999、AD-18965、AD-19066、AD-18986
2600	AUACUGACCUGU	2409	ACAGGUCAGUAU	3804	AD-26822、AD-18905、AD-18965、AD-19066、AD-18986
2601	UACUGACCUGUA	2410	UACAGGUCAGUA	3805	AD-26822、AD-26821、AD-18999、AD-18965、AD-19066、AD-18986
2602	ACUGACCUGUAA	2411	UUACAGGUCAGU	3806	AD-26822、AD-18999、AD-18965、AD-19066、AD-18986
2603	CUGACCUGUAAA	2412	UUUACAGGUCAG	3807	AD-26822、AD-18999、AD-18965、AD-19066
2604	UGACCUGUAAAU	2413	AUUUACAGGUCA	3808	AD-26822、AD-18999、AD-18965、AD-26823
2605	GACCUGUAAAUC	2414	GAUUUACAGGUC	3809	AD-26822、AD-26824、AD-18999、AD-26823
2606	ACCUGUAAAUCA	2415	UGAUUUACAGGU	3810	AD-26822、AD-26824、AD-26825、AD-26823
2607	CCUGUAAAUCAU	2416	AUGAUUUACAGG	3811	AD-26822、AD-26824、AD-26825、AD-26823
2608	CUGUAAAUCAUC	2417	GAUGAUUUACAG	3812	AD-26824、AD-26825、AD-26823
2609	UGUAAAUCAUCC	2418	GGAUGAUUUACA	3813	AD-26824、AD-26823
2610	GUAAAUCAUCCU	2419	AGGAUGAUUUAC	3814	AD-26825、AD-26823
2611	UAAAUCAUCCUU	2420	AAGGAUGAUUUA	3815	AD-26824、AD-26825、AD-26823
2612	AAAUCAUCCUUU	2421	AAAGGAUGAUUU	3816	AD-26824、AD-26825
2628	GUAACAAUACAA	2422	UUGUAUUGUUAC	3817	AD-18933、AD-19053
2629	UAACAAUACAAA	2423	UUUGUAUUGUUA	3818	AD-18933、AD-19053
2630	AACAAUACAAAU	2424	AUUUGUAUUGUU	3819	AD-18933、AD-19053
2631	ACAAUACAAAUG	2425	CAUUUGUAUUGU	3820	AD-18933、AD-19053
2632	CAAUACAAAUGG	2426	CCAUUUGUAUUG	3821	AD-18933、AD-19053、AD-25889
2633	AAUACAAAUGGA	2427	UCCAUUUGUAUU	3822	AD-18933、AD-25889
2634	AUACAAAUGGAU	2428	AUCCAUUUGUAU	3823	AD-18933、AD-25889
2635	UACAAAUGGAUU	2429	AAUCCAUUUGUA	3824	AD-18933、AD-25889
2636	ACAAAUGGAUUU	2430	AAAUCCAUUUGU	3825	AD-25890、AD-25889
2637	CAAAUGGAUUUU	2431	AAAAUCCAUUUG	3826	AD-25890、AD-25889
2638	AAAUGGAUUUUG	2432	CAAAAUCCAUUU	3827	AD-25890、AD-25889
2648	UGGGAGUGACUC	2433	GAGUCACUCCCA	3828	AD-25892、AD-25891
2649	GGGAGUGACUCA	2434	UGAGUCACUCCC	3829	AD-25892、AD-25891
2650	GGAGUGACUCAA	2435	UUGAGUCACUCC	3830	AD-25892、AD-25891

2651	GAGUGACUCAAG	2436	CUUGAGUCACUC	3831	AD-25892、AD-25891
2652	AGUGACUCAAGA	2437	UCUUGAGUCACU	3832	AD-25892、AD-25891
2653	GUGACUCAAGAA	2438	UUCUUGAGUCAC	3833	AD-25892、AD-25891
2654	UGACUCAAGAAG	2439	CUUCUUGAGUCA	3834	AD-25892、AD-25891
2663	AAGUGAAGAAUG	2440	CAUUCUUCACUU	3835	AD-25894、AD-25893
2664	AGUGAAGAAUGC	2441	GCAUUCUUCACU	3836	AD-25894、AD-25938
2665	GUGAAGAAUGCA	2442	UGCAUUCUUCAC	3837	AD-25893、AD-25938
2666	UGAAGAAUGCAC	2443	GUGCAUUCUUCA	3838	AD-25894、AD-25893
2667	GAAGAAUGCACA	2444	UGUGCAUUCUUC	3839	AD-25894、AD-25893、AD-25938
2668	AAGAAUGCACAA	2445	UUGUGCAUUCUU	3840	AD-25894、AD-25893、AD-25938
2669	AGAAUGCACAAG	2446	CUUGUGCAUUCU	3841	AD-25894、AD-25893、AD-25938
2670	GAAUGCACAAGA	2447	UCUUGUGCAUUC	3842	AD-25894、AD-25938
2682	AUGGAUCACAAG	2448	CUUGUGAUCCAU	3843	AD-25940、AD-25939
2683	UGGAUCACAAGA	2449	UCUUGUGAUCCA	3844	AD-25941、AD-25940、AD-25939
2684	GGAUCACAAGAU	2450	AUCUUGUGAUCC	3845	AD-25941、AD-25940、AD-25942、AD-25939
2685	GAUCACAAGAUG	2451	CAUCUUGUGAUC	3846	AD-25941、AD-25940、AD-25942、AD-25939、AD-25943
2686	AUCACAAGAUGG	2452	CCAUCUUGUGAU	3847	AD-25941、AD-25940、AD-25944、AD-25942、AD-25939、AD-25943
2687	UCACAAGAUGGA	2453	UCCAUCUUGUGA	3848	AD-25941、AD-25940、AD-25944、AD-25942、AD-25943
2688	CACAAGAUGGAA	2454	UUCCAUCUUGUG	3849	AD-25941、AD-25944、AD-25942、AD-25939、AD-25943
2689	ACAAGAUGGAAU	2455	AUUCCAUCUUGU	3850	AD-25941、AD-25940、AD-25944、AD-25942、AD-25943
2690	CAAGAUGGAAUU	2456	AAUUCCAUCUUG	3851	AD-25941、AD-25944、AD-25942、AD-25943
2691	AAGAUGGAAUUU	2457	AAAUUCCAUCUU	3852	AD-25944、AD-25942、AD-25943
2692	AGAUGGAAUUUA	2458	UAAAUUCCAUCU	3853	AD-25944、AD-25943
2693	GAUGGAAUUUAU	2459	AUAAAUUCCAUC	3854	AD-25944、AD-25895
2694	AUGGAAUUUAUC	2460	GAUAAAUUCCAU	3855	AD-25895、AD-25896
2695	UGGAAUUUAUCA	2461	UGAUAAAUUCCA	3856	AD-25895、AD-25896、AD-25945

2696	GGAAUUUAUCAA	2462	UUGAUAAAUUCC	3857	AD-25895、AD-25896、AD-25897、AD-25945
2697	GAAUUUAUCAAA	2463	UUUGAUAAAUUC	3858	AD-25895、AD-25896、AD-25898、AD-25897、AD-25945
2698	AAUUUAUCAAAC	2464	GUUUGAUAAAUU	3859	AD-25895、AD-25899、AD-25896、AD-25898、AD-25945
2699	AUUUAUCAAACC	2465	GGUUUGAUAAAU	3860	AD-25895、AD-25896、AD-25898、AD-25897、AD-25945
2700	UUUAUCAAACCC	2466	GGGUUUGAUAAA	3861	AD-25895、AD-25899、AD-25896、AD-25898、AD-25897、AD-25945
2701	UUAUCAAACCCU	2467	AGGGUUUGAUAA	3862	AD-25899、AD-25896、AD-25897、AD-18929、AD-25945
2702	UAUCAAACCCUA	2468	UAGGGUUUGAUA	3863	AD-25899、AD-25898、AD-25897、AD-18929、AD-25945
2703	AUCAAACCCUAG	2469	CUAGGGUUUGAU	3864	AD-18996、AD-25899、AD-18915、AD-25898、AD-25897、AD-18929
2704	UCAAACCCUAGC	2470	GCUAGGGUUUGA	3865	AD-18996、AD-25899、AD-18915、AD-25898、AD-18929
2705	CAAACCCUAGCC	2471	GGCUAGGGUUUG	3866	AD-18935、AD-18996、AD-25899、AD-18915
2706	AAACCCUAGCCU	2472	AGGCUAGGGUUU	3867	AD-18915、AD-18942、AD-18929
2707	AACCCUAGCCUU	2473	AAGGCUAGGGUU	3868	AD-18913、AD-18935、AD-18996、AD-18915
2708	ACCCUAGCCUUG	2474	CAAGGCUAGGGU	3869	AD-18913、AD-18996、AD-18915、AD-18942、AD-18929、AD-25946
2709	CCCUAGCCUUGC	2475	GCAAGGCUAGGG	3870	AD-18913、AD-18935、AD-18996、AD-25947、AD-18915、AD-25946
2710	CCUAGCCUUGCU	2476	AGCAAGGCUAGG	3871	AD-18913、AD-25948、AD-18935、AD-25947、AD-18915、AD-18942、AD-25946
2711	CUAGCCUUGCUU	2477	AAGCAAGGCUAG	3872	AD-18913、AD-25948、AD-18935、AD-25949、AD-25947、AD-18942、

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2712	UAGCCUUGCUUG	2478	CAAGCAAGGCUA	3873	AD-18913、AD-25948、AD-18935、AD-25950、AD-25947、AD-18942、AD-25946
2713	AGCCUUGCUUGU	2479	ACAAGCAAGGCU	3874	AD-18913、AD-25948、AD-25951、AD-25949、AD-25947、AD-18942、AD-25946
2714	GCCUUGCUUGUU	2480	AACAAGCAAGGC	3875	AD-18913、AD-25948、AD-25951、AD-25950、AD-25949、AD-25947、AD-25946
2715	CCUUGCUUGUUA	2481	UAACAAGCAAGG	3876	AD-25948、AD-25951、AD-25950、AD-25949、AD-25947、AD-25946
2716	CUUGCUUGUUAA	2482	UUAACAAGCAAG	3877	AD-25948、AD-25951、AD-25950、AD-25949、AD-25947
2717	UUGCUUGUUAAA	2483	UUUAACAAGCAA	3878	AD-25948、AD-25951、AD-25950、AD-25949
2718	UGCUUGUUAAAU	2484	AUUUAACAAGCA	3879	AD-25951、AD-25950、AD-25949
2719	GCUUGUUAAAUU	2485	AAUUUAACAAGC	3880	AD-25951、AD-25950
2750	GAAUAUCUGUAA	2486	UUACAGAUAUUC	3881	AD-25900、AD-26900
2751	AAUAUCUGUAAU	2487	AUUACAGAUAUU	3882	AD-25900、AD-26900、AD-25901
2752	AUAUCUGUAAUG	2488	CAUUACAGAUAU	3883	AD-25900、AD-25902、AD-25901
2753	UAUCUGUAAUGG	2489	CCAUUACAGAUA	3884	AD-25900、AD-25902、AD-25901
2754	AUCUGUAAUGGU	2490	ACCAUUACAGAU	3885	AD-25900、AD-25901
2755	UCUGUAAUGGUA	2491	UACCAUUACAGA	3886	AD-25902、AD-25901
2756	CUGUAAUGGUAC	2492	GUACCAUUACAG	3887	AD-25900、AD-25902、AD-25901
2757	UGUAAUGGUACU	2493	AGUACCAUUACA	3888	AD-25900、AD-25902
2758	GUAAUGGUACUG	2494	CAGUACCAUUAC	3889	AD-25902、AD-25901
2832	UUUAAGUCUCUC	2495	GAGAGACUUAAA	3890	AD-25903、AD-25904
2833	UUAAGUCUCUCG	2496	CGAGAGACUUAA	3891	AD-25903、AD-25952、AD-25904
2834	UAAGUCUCUCGU	2497	ACGAGAGACUUA	3892	AD-25903、AD-25952、AD-25904、AD-25953
2835	AAGUCUCUCGUA	2498	UACGAGAGACUU	3893	AD-25954、AD-25903、AD-25952、AD-25904、

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2836	AGUCUCUCGUAG	2499	CUACGAGAGACU	3894	AD-25954、AD-25903、AD-25952、AD-25904、AD-25953、AD-25905
2837	GUCUCUCGUAGU	2500	ACUACGAGAGAC	3895	AD-25954、AD-25903、AD-25952、AD-25904、AD-25953
2838	UCUCUCGUAGUG	2501	CACUACGAGAGA	3896	AD-25954、AD-25952、AD-25904、AD-25953、AD-25905
2839	CUCUCGUAGUGU	2502	ACACUACGAGAG	3897	AD-25954、AD-25952、AD-25904、AD-25953、AD-25905
2840	UCUCGUAGUGUU	2503	AACACUACGAGA	3898	AD-25954、AD-25952、AD-25953、AD-25905
2841	CUCGUAGUGUUA	2504	UAACACUACGAG	3899	AD-25954、AD-25955、AD-25953、AD-25905
2842	UCGUAGUGUUAA	2505	UUAACACUACGA	3900	AD-25954、AD-25906、AD-25955、AD-25905
2843	CGUAGUGUUAAG	2506	CUUAACACUACG	3901	AD-25907、AD-25906、AD-25955
2844	GUAGUGUUAAGU	2507	ACUUAACACUAC	3902	AD-25907、AD-25906、AD-25955
2845	UAGUGUUAAGUU	2508	AACUUAACACUA	3903	AD-25907、AD-25908、AD-25906、AD-25955、AD-25909
2846	AGUGUUAAGUUA	2509	UAACUUAACACU	3904	AD-25907、AD-25908、AD-25956、AD-25906、AD-25955、AD-25909
2847	GUGUUAAGUUAU	2510	AUAACUUAACAC	3905	AD-25907、AD-25908、AD-25956、AD-25957、AD-25906、AD-25955、AD-25909
2848	UGUUAAGUUAUA	2511	UAUAACUUAACA	3906	AD-25907、AD-25908、AD-25956、AD-25957、AD-25906、AD-25909
2849	GUUAAGUUAUAG	2512	CUAUAACUUAAC	3907	AD-25907、AD-25908、AD-25956、AD-25957、AD-25906、AD-25909
2850	UUAAGUUAUAGU	2513	ACUAUAACUUAA	3908	AD-25907、AD-25956、AD-25957、AD-25909
2851	UAAGUUAUAGUG	2514	CACUAUAACUUA	3909	AD-25908、AD-25956、AD-25957、AD-25909
2852	AAGUUAUAGUGA	2515	UCACUAUAACUU	3910	AD-25956、AD-25957、AD-25909

2853	AGUUAUAGUGAA	2516	UUCACUAUAACU	3911	AD-25956、AD-25957
2871	UACAGCAAUUUC	2517	GAAAUUGCUGUA	3912	AD-26901、AD-25958
2872	ACAGCAAUUUCU	2518	AGAAAUUGCUGU	3913	AD-26901、AD-25958
2873	CAGCAAUUUCUA	2519	UAGAAAUUGCUG	3914	AD-26901、AD-25958
2874	AGCAAUUUCUAA	2520	UUAGAAAUUGCU	3915	AD-26901、AD-25958
2875	GCAAUUUCUAAU	2521	AUUAGAAAUUGC	3916	AD-26901、AD-25958
2876	CAAUUUCUAAUU	2522	AAUUAGAAAUUG	3917	AD-26901、AD-25958
2877	AAUUUCUAAUUU	2523	AAAUUAGAAAUU	3918	AD-26901、AD-25958
2901	UAAUGGUGUAGA	2524	UCUACACCAUUA	3919	AD-18936、AD-19054
2902	AAUGGUGUAGAA	2525	UUCUACACCAUU	3920	AD-18936、AD-19054
2903	AUGGUGUAGAAC	2526	GUUCUACACCAU	3921	AD-18936、AD-19010、AD-19054
2904	UGGUGUAGAACA	2527	UGUUCUACACCA	3922	AD-18936、AD-19009、AD-19010、AD-19054
2905	GGUGUAGAACAC	2528	GUGUUCUACACC	3923	AD-18936、AD-19009、AD-18939、AD-19054
2906	GUGUAGAACACU	2529	AGUGUUCUACAC	3924	AD-18966、AD-19009、AD-19010、AD-18939、AD-19054
2907	UGUAGAACACUA	2530	UAGUGUUCUACA	3925	AD-18966、AD-19009、AD-18902、AD-19010、AD-18939、AD-19054
2908	GUAGAACACUAA	2531	UUAGUGUUCUAC	3926	AD-18966、AD-19009、AD-18902、AD-19010、AD-18939、AD-19054、AD-19076
2909	UAGAACACUAAU	2532	AUUAGUGUUCUA	3927	AD-18966、AD-19009、AD-18902、AD-19010、AD-18939、AD-19076
2910	AGAACACUAAUU	2533	AAUUAGUGUUCU	3928	AD-18966、AD-19009、AD-19010、AD-18939、AD-19076
2911	GAACACUAAUUC	2534	GAAUUAGUGUUC	3929	AD-18966、AD-18902、AD-18914、AD-18939、AD-19076
2912	AACACUAAUUCA	2535	UGAAUUAGUGUU	3930	AD-18966、AD-18902、AD-18914、AD-25911、AD-19076
2913	ACACUAAUUCAU	2536	AUGAAUUAGUGU	3931	AD-18966、AD-18902、AD-18914、AD-25912、AD-19076
2914	CACUAAUUCAUA	2537	UAUGAAUUAGUG	3932	AD-18902、AD-18914、AD-25912、AD-25911、AD-26902

2915	ACUAAUUCAUAA	2538	UUAUGAAUUAGU	3933	AD-18914、AD-25912、AD-25911、AD-26903、AD-26902、AD-19076
2916	CUAAUUCAUAAU	2539	AUUAUGAAUUAG	3934	AD-18914、AD-25912、AD-25911、AD-26903、AD-26902
2917	UAAUUCAUAAUC	2540	GAUUAUGAAUUA	3935	AD-26916、AD-25911、AD-26903、AD-26902、AD-26904
2918	AAUUCAUAAUCA	2541	UGAUUAUGAAUU	3936	AD-26905、AD-26916、AD-18914、AD-25912、AD-25911、AD-26903、AD-26902、AD-26904
2919	AUUCAUAAUCAC	2542	GUGAUUAUGAAU	3937	AD-26905、AD-26916、AD-25912、AD-25911、AD-26903、AD-26902、AD-26904
2920	UUCAUAAUCACU	2543	AGUGAUUAUGAA	3938	AD-26905、AD-26916、AD-25912、AD-26903、AD-26902、AD-26904
2921	UCAUAAUCACUC	2544	GAGUGAUUAUGA	3939	AD-26905、AD-26916、AD-26903、AD-26902、AD-26904
2922	CAUAAUCACUCU	2545	AGAGUGAUUAUG	3940	AD-26905、AD-26916、AD-26903、AD-26904
2923	AUAAUCACUCUA	2546	UAGAGUGAUUAU	3941	AD-26905、AD-26916、AD-26904
2924	UAAUCACUCUAA	2547	UUAGAGUGAUUA	3942	AD-26905、AD-26904
2938	AAUUGUAAUCUG	2548	CAGAUUACAAUU	3943	AD-25913、AD-26906
2939	AUUGUAAUCUGA	2549	UCAGAUUACAAU	3944	AD-25913、AD-26906、AD-25914
2940	UUGUAAUCUGAA	2550	UUCAGAUUACAA	3945	AD-25913、AD-26906、AD-25915、AD-25914
2941	UGUAAUCUGAAU	2551	AUUCAGAUUACA	3946	AD-25916、AD-25913、AD-26906、AD-25915、AD-25914
2942	GUAAUCUGAAUA	2552	UAUUCAGAUUAC	3947	AD-25916、AD-25913、AD-26906、AD-25914
2943	UAAUCUGAAUAA	2553	UUAUUCAGAUUA	3948	AD-26906、AD-25915、AD-25914
2944	AAUCUGAAUAAA	2554	UUUAUUCAGAUU	3949	AD-25916、AD-25913、AD-26906、AD-25915、AD-25914
2945	AUCUGAAUAAAG	2555	CUUUAUUCAGAU	3950	AD-25916、AD-26906、AD-25915、AD-25914

2946	UCUGAAUAAAGU	2556	ACUUUAUUCAGA	3951	AD-25916、AD-25915、AD-25914
2947	CUGAAUAAAGUG	2557	CACUUUAUUCAG	3952	AD-25916、AD-25915
2978	UUGUAUAAAAUA	2558	UAUUUUAUACAA	3953	AD-26908、AD-26907
2979	UGUAUAAAAUAG	2559	CUAUUUUAUACA	3954	AD-26908、AD-26907、AD-26909
2980	GUAUAAAAUAGA	2560	UCUAUUUUAUAC	3955	AD-26908、AD-26909
2981	UAUAAAAUAGAC	2561	GUCUAUUUUAUA	3956	AD-26908、AD-26910、AD-26907、AD-26909
2982	AUAAAAUAGACA	2562	UGUCUAUUUUAU	3957	AD-26910、AD-26911、AD-26907、AD-26909
2983	UAAAAUAGACAA	2563	UUGUCUAUUUUA	3958	AD-26908、AD-26910、AD-26911、AD-26907、AD-26909
2984	AAAAUAGACAAA	2564	UUUGUCUAUUUU	3959	AD-26908、AD-26910、AD-26912、AD-26911、AD-26907、AD-26909
2985	AAAUAGACAAAU	2565	AUUUGUCUAUUU	3960	AD-26908、AD-26912、AD-26911、AD-26913、AD-26909
2986	AAUAGACAAAUA	2566	UAUUUGUCUAUU	3961	AD-26910、AD-26912、AD-26911、AD-26913、AD-26909
2987	AUAGACAAAUAG	2567	CUAUUUGUCUAU	3962	AD-26910、AD-26912、AD-26911、AD-26913
2988	UAGACAAAUAGA	2568	UCUAUUUGUCUA	3963	AD-26912、AD-26911
2989	AGACAAAUAGAA	2569	UUCUAUUUGUCU	3964	AD-26912、AD-26911、AD-26913
2990	GACAAAUAGAAA	2570	UUUCUAUUUGUC	3965	AD-25917、AD-26913
2991	ACAAAUAGAAAA	2571	UUUUCUAUUUGU	3966	AD-26913、AD-25918
2992	CAAAUAGAAAAU	2572	AUUUUCUAUUUG	3967	AD-25917、AD-25959、AD-25918
2993	AAAUAGAAAAUG	2573	CAUUUUCUAUUU	3968	AD-25917、AD-25959、AD-26917、AD-25918
2994	AAUAGAAAAUGG	2574	CCAUUUUCUAUU	3969	AD-25917、AD-26918、AD-25959、AD-26917
2995	AUAGAAAAUGGU	2575	ACCAUUUUCUAU	3970	AD-25917、AD-26918、AD-25959、AD-26917、AD-25918、AD-25960
2996	UAGAAAAUGGUC	2576	GACCAUUUUCUA	3971	AD-25917、AD-26918、AD-25959、AD-26917、AD-25919、AD-25918、AD-25960
2997	AGAAAAUGGUCC	2577	GGACCAUUUUCU	3972	AD-25917、AD-26918、

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2998	GAAAAUGGUCCA	2578	UGGACCAUUUUC	3973	AD-26918、AD-25920、AD-25959、AD-26917、AD-25919、AD-25918、AD-25960
2999	AAAAUGGUCCAA	2579	UUGGACCAUUUU	3974	AD-26918、AD-25920、AD-25959、AD-26917、AD-25919、AD-25960
3000	AAAUGGUCCAAU	2580	AUUGGACCAUUU	3975	AD-26918、AD-25920、AD-26917、AD-25919、AD-25960
3001	AAUGGUCCAAUU	2581	AAUUGGACCAUU	3976	AD-26918、AD-25920、AD-25919、AD-25960
3002	AUGGUCCAAUUA	2582	UAAUUGGACCAU	3977	AD-25920、AD-25919、AD-25960
3003	UGGUCCAAUUAG	2583	CUAAUUGGACCA	3978	AD-25920、AD-25919
3028	AUGCUUAAAAUA	2584	UAUUUUAAGCAU	3979	AD-18985、AD-18992
3029	UGCUUAAAAUAA	2585	UUAUUUUAAGCA	3980	AD-18985、AD-18992
3030	GCUUAAAAUAAG	2586	CUUAUUUUAAGC	3981	AD-18985、AD-18992
3031	CUUAAAAUAAGC	2587	GCUUAUUUUAAG	3982	AD-18985、AD-18992、AD-19081
3032	UUAAAAUAAGCA	2588	UGCUUAUUUUAA	3983	AD-18985、AD-19081
3033	UAAAAUAAGCAG	2589	CUGCUUAUUUUA	3984	AD-18985、AD-18992、AD-19081、AD-19044
3034	AAAAUAAGCAGG	2590	CCUGCUUAUUUU	3985	AD-18985、AD-18992、AD-19081
3035	AAAUAAGCAGGU	2591	ACCUGCUUAUUU	3986	AD-18985、AD-19044
3036	AAUAAGCAGGUG	2592	CACCUGCUUAUU	3987	AD-18993、AD-19081、AD-19044
3037	AUAAGCAGGUGG	2593	CCACCUGCUUAU	3988	AD-18993、AD-18894、AD-19081、AD-19044
3038	UAAGCAGGUGGA	2594	UCCACCUGCUUA	3989	AD-19043、AD-18993、AD-18894、AD-19044
3039	AAGCAGGUGGAU	2595	AUCCACCUGCUU	3990	AD-19043、AD-18956、AD-18993、AD-18894
3040	AGCAGGUGGAUC	2596	GAUCCACCUGCU	3991	AD-19043、AD-18956、AD-18993、AD-18894、AD-19044、AD-18958
3041	GCAGGUGGAUCU	2597	AGAUCCACCUGC	3992	AD-19043、AD-18956、AD-18993、AD-18894、AD-18958
3042	CAGGUGGAUCUA	2598	UAGAUCCACCUG	3993	AD-19043、AD-18956、

					AD-18894、AD-18969、AD-18958、AD-19058
3043	AGGUGGAUCUAU	2599	AUAGAUCCACCU	3994	AD-19069、AD-19043、AD-18956、AD-18993、AD-18894、AD-18969、AD-18958、AD-19058
3044	GGUGGAUCUAUU	2600	AAUAGAUCCACC	3995	AD-19069、AD-19043、AD-18956、AD-18894、AD-18969、AD-18958、AD-19058
3045	GUGGAUCUAUUU	2601	AAAUAGAUCCAC	3996	AD-19069、AD-19043、AD-18956、AD-18969、AD-18958、AD-19058
3046	UGGAUCUAUUUC	2602	GAAAUAGAUCCA	3997	AD-19069、AD-18956、AD-18969、AD-18958、AD-19058
3047	GGAUCUAUUUCA	2603	UGAAAUAGAUCC	3998	AD-19069、AD-18969、AD-18958、AD-19058
3048	GAUCUAUUUCAU	2604	AUGAAAUAGAUC	3999	AD-19069、AD-18969、AD-19058
3049	AUCUAUUUCAUG	2605	CAUGAAAUAGAU	4000	AD-19069、AD-19058
3077	AUUUGGGAUAUG	2606	CAUAUCCCAAAU	4001	AD-25921、AD-25922
3078	UUUGGGAUAUGU	2607	ACAUAUCCCAAA	4002	AD-25961、AD-25921、AD-25922
3079	UUGGGAUAUGUA	2608	UACAUAUCCCAA	4003	AD-25961、AD-25923、AD-25921、AD-25922
3080	UGGGAUAUGUAU	2609	AUACAUAUCCCA	4004	AD-25961、AD-25923、AD-26914、AD-25921、AD-25922
3081	GGGAUAUGUAUG	2610	CAUACAUAUCCC	4005	AD-25961、AD-25923、AD-26915、AD-26914、AD-25921、AD-25922
3082	GGAUAUGUAUGG	2611	CCAUACAUAUCC	4006	AD-25961、AD-25923、AD-25924、AD-26915、AD-26914、AD-25921、AD-25922
3083	GAUAUGUAUGGG	2612	CCCAUACAUAUC	4007	AD-25961、AD-25923、AD-25924、AD-26915、AD-25962、AD-26914、AD-25921、AD-25922
3084	AUAUGUAUGGGU	2613	ACCCAUACAUAU	4008	AD-25961、AD-25923、AD-25924、AD-26915、AD-25962、AD-26914、AD-25922
3085	UAUGUAUGGGUA	2614	UACCCAUACAUA	4009	AD-25961、AD-25923、

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3086	AUGUAUGGGUAG	2615	CUACCCAUACAU	4010	AD-25923、AD-25924、AD-26915、AD-25962、AD-26914
3087	UGUAUGGGUAGG	2616	CCUACCCAUACA	4011	AD-25924、AD-26915、AD-25962、AD-26914
3088	GUAUGGGUAGGG	2617	CCCUACCCAUAC	4012	AD-25924、AD-26915、AD-25962
3089	UAUGGGUAGGGU	2618	ACCCUACCCAUA	4013	AD-25924、AD-25962
3093	GGUAGGGUAAAU	2619	AUUUACCCUACC	4014	AD-18998、AD-25963
3094	GUAGGGUAAAUC	2620	GAUUUACCCUAC	4015	AD-18998、AD-25963、AD-18995
3095	UAGGGUAAAUCA	2621	UGAUUUACCCUA	4016	AD-18998、AD-25963、AD-18995
3096	AGGGUAAAUCAG	2622	CUGAUUUACCCU	4017	AD-18998、AD-25963、AD-18995
3097	GGGUAAAUCAGU	2623	ACUGAUUUACCC	4018	AD-18998、AD-25963、AD-18981、AD-18995
3098	GGUAAAUCAGUA	2624	UACUGAUUUACC	4019	AD-18921、AD-18998、AD-25963、AD-18981、AD-18995
3099	GUAAAUCAGUAA	2625	UUACUGAUUUAC	4020	AD-18921、AD-18998、AD-18981、AD-18995
3100	UAAAUCAGUAAG	2626	CUUACUGAUUUA	4021	AD-18921、AD-18998、AD-18981、AD-19050、AD-18995
3101	AAAUCAGUAAGA	2627	UCUUACUGAUUU	4022	AD-18921、AD-18968、AD-18981、AD-19050
3102	AAUCAGUAAGAG	2628	CUCUUACUGAUU	4023	AD-18921、AD-18968、AD-18981、AD-19050、AD-19005
3103	AUCAGUAAGAGG	2629	CCUCUUACUGAU	4024	AD-18921、AD-18968、AD-18981、AD-19050、AD-18903、AD-19005
3104	UCAGUAAGAGGU	2630	ACCUCUUACUGA	4025	AD-18921、AD-18968、AD-18972、AD-18981、AD-19050、AD-18903、AD-19005
3105	CAGUAAGAGGUG	2631	CACCUCUUACUG	4026	AD-18921、AD-18968、AD-18972、AD-19050、AD-18903、AD-19005
3106	AGUAAGAGGUGU	2632	ACACCUCUUACU	4027	AD-18968、AD-19050、AD-18903、AD-19005

3107	GUAAGAGGUGUU	2633	AACACCUCUUAC	4028	AD-18972、AD-19050、AD-18903、AD-19005
3108	UAAGAGGUGUUA	2634	UAACACCUCUUA	4029	AD-18968、AD-18972、AD-18903、AD-25964、AD-19005
3109	AAGAGGUGUUAU	2635	AUAACACCUCUU	4030	AD-18972、AD-18903、AD-25964、AD-19005
3110	AGAGGUGUUAUU	2636	AAUAACACCUCU	4031	AD-18972、AD-18903、AD-25925、AD-25926、AD-25964
3111	GAGGUGUUAUUU	2637	AAAUAACACCUC	4032	AD-25925、AD-25926、AD-25964
3112	AGGUGUUAUUUG	2638	CAAAUAACACCU	4033	AD-25927、AD-25925、AD-25926、AD-25964
3113	GGUGUUAUUUGG	2639	CCAAAUAACACC	4034	AD-25927、AD-25926、AD-25964
3114	GUGUUAUUUGGA	2640	UCCAAAUAACAC	4035	AD-25927、AD-25925、AD-25926、AD-25964
3115	UGUUAUUUGGAA	2641	UUCCAAAUAACA	4036	AD-25925、AD-25926、AD-25964
3116	GUUAUUUGGAAC	2642	GUUCCAAAUAAC	4037	AD-25927、AD-25925、AD-25926
3117	UUAUUUGGAACC	2643	GGUUCCAAAUAA	4038	AD-25927、AD-25926
3123	GGAACCUUGUUU	2644	AAACAAGGUUCC	4039	AD-25929、AD-25928
3124	GAACCUUGUUUU	2645	AAAACAAGGUUC	4040	AD-25930、AD-25928
3125	AACCUUGUUUUG	2646	CAAAACAAGGUU	4041	AD-25930、AD-25929、AD-25928
3126	ACCUUGUUUUGG	2647	CCAAAACAAGGU	4042	AD-25930、AD-25929
3127	CCUUGUUUUGGA	2648	UCCAAAACAAGG	4043	AD-25930、AD-25929、AD-25928
3128	CUUGUUUUGGAC	2649	GUCCAAAACAAG	4044	AD-25930、AD-25929、AD-25928
3129	UUGUUUUGGACA	2650	UGUCCAAAACAA	4045	AD-25929、AD-25928
3130	UGUUUUGGACAG	2651	CUGUCCAAAACA	4046	AD-25930、AD-25929
3131	GUUUUGGACAGU	2652	ACUGUCCAAAAC	4047	AD-25930、AD-25931
3132	UUUUGGACAGUU	2653	AACUGUCCAAAA	4048	AD-25932、AD-25931
3133	UUUGGACAGUUU	2654	AAACUGUCCAAA	4049	AD-25932、AD-26919、AD-25931
3134	UUGGACAGUUUA	2655	UAAACUGUCCAA	4050	AD-25933、AD-26919、AD-25931
3135	UGGACAGUUUAC	2656	GUAAACUGUCCA	4051	AD-25933、AD-25932、AD-26919、AD-25931
3136	GGACAGUUUACC	2657	GGUAAACUGUCC	4052	AD-25933、AD-25932、AD-25931

3137	GACAGUUUACCA	2658	UGGUAAACUGUC	4053	AD-25932、AD-26919、AD-25931
3138	ACAGUUUACCAG	2659	CUGGUAAACUGU	4054	AD-25933、AD-25932、AD-26919、AD-25931
3139	CAGUUUACCAGU	2660	ACUGGUAAACUG	4055	AD-25933、AD-25932、AD-26919
3140	AGUUUACCAGUU	2661	AACUGGUAAACU	4056	AD-25933、AD-26919
3145	ACCAGUUGCCUU	2662	AAGGCAACUGGU	4057	AD-18940、AD-18916
3146	CCAGUUGCCUUU	2663	AAAGGCAACUGG	4058	AD-18940、AD-18906、AD-18916
3147	CAGUUGCCUUUU	2664	AAAAGGCAACUG	4059	AD-18940、AD-18906、AD-18916
3148	AGUUGCCUUUUA	2665	UAAAAGGCAACU	4060	AD-18940、AD-19075、AD-18916
3149	GUUGCCUUUUAU	2666	AUAAAAGGCAAC	4061	AD-19075、AD-18906、AD-18916
3150	UUGCCUUUUAUC	2667	GAUAAAAGGCAA	4062	AD-18940、AD-19075、AD-18906、AD-18916
3151	UGCCUUUUAUCC	2668	GGAUAAAAGGCA	4063	AD-18940、AD-19075、AD-18906、AD-18916
3152	GCCUUUUAUCCC	2669	GGGAUAAAAGGC	4064	AD-18906、AD-18916
3153	CCUUUUAUCCCA	2670	UGGGAUAAAAGG	4065	AD-26017、AD-19075、AD-18906、AD-18997
3154	CUUUUAUCCCAA	2671	UUGGGAUAAAAG	4066	AD-26017、AD-19075、AD-18997
3155	UUUUAUCCCAAA	2672	UUUGGGAUAAAA	4067	AD-26017、AD-18997
3156	UUUAUCCCAAAG	2673	CUUUGGGAUAAA	4068	AD-26017、AD-18997
3157	UUAUCCCAAAGU	2674	ACUUUGGGAUAA	4069	AD-26017、AD-18997
3158	UAUCCCAAAGUU	2675	AACUUUGGGAUA	4070	AD-26017、AD-18997、AD-18988
3159	AUCCCAAAGUUG	2676	CAACUUUGGGAU	4071	AD-18997、AD-18988
3160	UCCCAAAGUUGU	2677	ACAACUUUGGGA	4072	AD-19067、AD-18997、AD-18988
3161	CCCAAAGUUGUU	2678	AACAACUUUGGG	4073	AD-19067、AD-19083
3162	CCAAAGUUGUUG	2679	CAACAACUUUGG	4074	AD-19083、AD-18988
3163	CAAAGUUGUUGU	2680	ACAACAACUUUG	4075	AD-19067、AD-19083、AD-19049、AD-18988
3164	AAAGUUGUUGUA	2681	UACAACAACUUU	4076	AD-19067、AD-19083、AD-18952、AD-19049、AD-18988
3165	AAGUUGUUGUAA	2682	UUACAACAACUU	4077	AD-19067、AD-19083、AD-18957、AD-18952、AD-19049、AD-18988
3166	AGUUGUUGUAAC	2683	GUUACAACAACU	4078	AD-19067、AD-19083、

					AD-18957、AD-18952、AD-19049
3167	GUUGUUGUAACC	2684	GGUUACAACAAC	4079	AD-19067、AD-19083、AD-18957、AD-25934、AD-18952、AD-19049
3168	UUGUUGUAACCU	2685	AGGUUACAACAA	4080	AD-19083、AD-18957、AD-25934、AD-18952、AD-25935、AD-19049
3169	UGUUGUAACCUG	2686	CAGGUUACAACA	4081	AD-18957、AD-25934、AD-18952、AD-26018、AD-25935、AD-19049
3170	GUUGUAACCUGC	2687	GCAGGUUACAAC	4082	AD-26019、AD-18957、AD-25934、AD-18952、AD-26018、AD-25935、AD-19049
3171	UUGUAACCUGCU	2688	AGCAGGUUACAA	4083	AD-26019、AD-18957、AD-25936、AD-25934、AD-18952、AD-26018、AD-25935
3172	UGUAACCUGCUG	2689	CAGCAGGUUACA	4084	AD-26019、AD-18957、AD-25936、AD-25934、AD-26018、AD-25935
3173	GUAACCUGCUGU	2690	ACAGCAGGUUAC	4085	AD-26019、AD-25936、AD-25934、AD-26018
3174	UAACCUGCUGUG	2691	CACAGCAGGUUA	4086	AD-26019、AD-25936、AD-25934、AD-26018、AD-25935
3175	AACCUGCUGUGA	2692	UCACAGCAGGUU	4087	AD-26019、AD-25936、AD-26018、AD-25935
3176	ACCUGCUGUGAU	2693	AUCACAGCAGGU	4088	AD-26019、AD-25936、AD-26018
3177	CCUGCUGUGAUA	2694	UAUCACAGCAGG	4089	AD-26019、AD-25936
3197	CAAGAGAAAAUG	2695	CAUUUUCUCUUG	4090	AD-26020、AD-25937
3198	AAGAGAAAAUGC	2696	GCAUUUUCUCUU	4091	AD-26020、AD-26021、AD-25937
3199	AGAGAAAAUGCG	2697	CGCAUUUUCUCU	4092	AD-26020、AD-26021
3200	GAGAAAAUGCGG	2698	CCGCAUUUUCUC	4093	AD-26020、AD-26021
3201	AGAAAAUGCGGU	2699	ACCGCAUUUUCU	4094	AD-26020、AD-26021
3202	GAAAAUGCGGUU	2700	AACCGCAUUUUC	4095	AD-26020、AD-26021
3203	AAAAUGCGGUUA	2701	UAACCGCAUUUU	4096	AD-26020、AD-26021
3204	AAAUGCGGUUAU	2702	AUAACCGCAUUU	4097	AD-26020、AD-26021
3220	AAUGGUUCAGAA	2703	UUCUGAACCAUU	4098	AD-18960、AD-18987
3221	AUGGUUCAGAAU	2704	AUUCUGAACCAU	4099	AD-18960、AD-18987、AD-19008

3222	UGGUUCAGAAUU	2705	AAUUCUGAACCA	4100	AD-18960、AD-18987、AD-19008
3223	GGUUCAGAAUUA	2706	UAAUUCUGAACC	4101	AD-18980、AD-18987、AD-19008
3224	GUUCAGAAUUAA	2707	UUAAUUCUGAAC	4102	AD-18960、AD-18987、AD-19008
3225	UUCAGAAUUAAA	2708	UUUAAUUCUGAA	4103	AD-18960、AD-18980、AD-19008
3226	UCAGAAUUAAAC	2709	GUUUAAUUCUGA	4104	AD-18960、AD-18980、AD-18987、AD-19008
3227	CAGAAUUAAACU	2710	AGUUUAAUUCUG	4105	AD-18980、AD-18987、AD-19008
3228	AGAAUUAAACUU	2711	AAGUUUAAUUCU	4106	AD-18980、AD-19008
3229	GAAUUAAACUUU	2712	AAAGUUUAAUUC	4107	AD-18980、AD-19007
3230	AAUUAAACUUUU	2713	AAAAGUUUAAUU	4108	AD-18980、AD-19007

[00793] 实施例 2

[00794] β-联蛋白 RNAi 剂序列的合成

[00795] β-联蛋白 RNAi 剂序列选择

[00796] 合成了本文中列出的 CTNNB1 衍生的 479 种有义和 479 种反义 RNAi 剂寡聚物并形成双链体。

[00797] β-联蛋白序列的合成

[00798] 合成：

[00799] 在 MerMade 192 合成仪上以 1μmol 规模合成 β-联蛋白序列。

[00800] 合成用于人 β-联蛋白基因的 958 个单链序列（对应于 479 种 RNAi 剂双链体）。对于全部序列，如下文详述那样实施‘endolight’化学。

•将有义链中的全部嘧啶（胞嘧啶和尿苷）均替换为相应的 2'-O-甲基碱基（2'O-甲基 C 和 2'-O-甲基 U）

• 在反义链中，将毗邻（指向 5'位置）核糖 A 核苷的嘧啶（C 和 U）替换为它们相应的 2-O-甲基核苷

• 在有义序列和反义序列的 3'末端引入双碱基 dTdT 延长。这个双碱基突出端具有磷酸二酯键

• 序列文件转换成文本文件，以便使其相容于在 MerMade 192 合成软件中加载。

[00801] 利用磷酰亚胺化学品，使用固相支持的寡核苷酸合成仪合成 β-联蛋白序列。

[00802] 上述序列的合成以 1μm 规模在 96 孔板中进行并且每轮产生 192 个序列。以 0.1M 浓度制备 amidite 溶液并且使用乙基硫代四唑（乙腈中的 0.6M）作为活化剂。

[00803] 切割和去保护：

[00804] 在 96 孔平板中，在第一步骤中使用甲胺并在第二步骤中使用三乙胺 ^{3}HF，切下合成的序列并使其去保护。使用丙酮：乙醇混合物沉淀如此获得的粗制序列并将沉淀物重悬于 0.02M 乙酸钠缓冲液中。通过 LC-MS 分析来自每个序列的样品并且所得的质量数据证实序列的身份。还通过 IEX 色谱分析所选择的样品集合。

[00805] 纯化：

[00806] 该过程中的下一个步骤过程是纯化。全部序列均在 AKTA 探索者纯化系统上，使用 Source 15Q 柱纯化。使用柱和设定在 60℃的内嵌缓冲液加热器进行纯化。将对应于全长序列的单峰收集在洗脱剂中并随后通过离子交换层析分析纯度。

[00807] 使用 AKTA 纯化仪，在 SephadexG25 柱上使纯化的序列脱盐。对脱盐的 β-联蛋白序列分析浓度和纯度。随后使单链复性以形成 RNAi 剂双链体。每种双链体以 1x PBS 中的 10μM 浓度产生。

[00808] 在本文上述实施例 1 中显示 β-联蛋白单链和双链体的详细清单。在体外筛选中使用双链体来测试它们敲减 β-联蛋白基因水平的能力，下文实施例 3。

[00809] 实施例 3

[00810] 体外筛选 β-联蛋白 RNAi 剂

[00811] 在体外筛选：

[00812] 对本文中（实施例 1）列出并如实施例 2 中所述合成的 RNAi 剂测试体外活性。

[00813] 细胞培养物和转染：

[00814] 将 HeLa 细胞 (ATCC，马纳萨斯，VA) 在 37℃在 5% CO_2 气氛下，在补充有 10% FBS、链霉素和谷氨酰胺 (ATCC) 的 Eagle's 极限基本培养基 (EMEM，ATCC) 中培育至接近汇合，之后，通过胰蛋白酶消化法从平板释放。通过将每孔 5μl Opti-MEM 对 5μl RNAi 剂双链体连同每孔 10μl Opti-MEM 外加 0.2μl 脂质转染胺 (lipofectamine) RNAiMax(Invitrogen，Carlsbad，CA. 目录号 13778-150) 一起添加至 96 孔板中并且在室温温育 15 分钟，实施反向转染。对于按 24 小时进行的测定法，随后将 80μl 不含抗生素，含有约 $2x10^4$ 个 HeLa 细胞的完全生长培养基添加至 RNAi 剂混合物。对于按 120 小时进行的测定法，随后将 80μl 不含抗生素，含有约 $2x10^4$ 个 HeLa 细胞的完全生长培养基添加至 RNAi 剂混合物。在 RNA 纯化之前，将细胞温育 24 小时或 48 小时。单剂量实验以 10nM 和并且在一些情况下 0.1nM 双链体终浓度进行并且剂量反应实验以 10、1、0.5、0.1、0.05、0.01、0.005、0.001、0.0005、0.0001、0.00005、0.00001nM 双链体终浓度进行。

[00815] 使用 MagMAX-96 总 RNA 分离试剂盒 (Applied Biosystem，Foster City CA，产品编号：AM1830) 分离总 RNA：

[00816] 收获细胞并使其在 140μl 裂解 / 结合溶液中裂解，随后使用 Eppendorf 热混合仪以 850 转 / 分钟混合 1 分钟（混合速度在整个过程至始至终相同）。将 20 微升磁珠和裂解 / 结合增强混合物添加至细胞 - 裂解物中并混合 5 分钟。使用磁力支座捕获磁珠并且在不扰动磁珠的情况下除去上清液。在移除上清液后，将磁珠用（添加异丙醇的）洗涤液 1 洗涤并且混合 1 分钟。再次捕获磁珠并移除上清液。随后将磁珠用（添加乙醇的）150μl 洗涤液 2 洗涤，捕获并且移除上清液。随后将 50μl DNA 酶混合物 (MagMax turbo DNA 酶缓冲液和 Turbo DNA 酶）添加至磁珠并将它们混合 10 至 15 分钟。在混合后，添加 100μl RNA 再结合溶液并混合 3 分钟。移除上清液并将磁珠用 150μl 洗涤液 2 再次洗涤并混合 1 分钟，并且彻底移除上清液。将磁珠混合 2 分钟以干燥，随后将 RNA 用 50μl 水洗脱。

[00817] 使用 ABI 高容量 cDNA 逆转录试剂盒 (Applied Biosystems，Foster City，CA，目录号 4368813) 合成 cDNA：

[00818] 按每个反应添加主混合物：2μl 10X 缓冲液，0.8μl 25XdNTP，2μl 随机引

物，1μl 逆转录酶，1μl RNA 酶抑制剂和 3.2μl H_2O 至中 10μl 总 RNA。使用 Bio-Rad C-1000 或 S-1000 热循环仪 (Hercules，CA) 通过以下步骤：25℃ 10 分钟，37℃ 120 分钟，85℃ 5 秒，4℃保持，产生 cDNA。

[00819] 实时 PCR：

[00820] 在 MicroAmp Optical 96 孔平板 (Applied Biosystems 目录号 #4326659) 中，将 2μl cDNA 添加至每孔含有 1μl 18S TaqMan 探针 (Applied Biosystems 目录号 #4319413E)、1ul β-联蛋白 TaqMan 探针 (Applied Biosystems 目录号 #HS00170025_m1) 和 10μl TaqMan 通用 PCR 主混合物 (Applied Biosystems 目录号 #4324018) 的主混合物。在 ABI7900HT 实时 PCR 系统 (Applied Biosystems) 中使用 ΔΔCt(RQ) 测定法进行实时 PCR。除非在总结表中另外指出，否则在两次独立转染中测试每种双链体并且重复分析每次转染。

[00821] 将实时数据利用 ΔΔCt 方法分析并且针对采用细胞进行的测定法归一化以计算相对倍数变化，其中所述细胞用 10nM AD-1955(与 β-联蛋白不结合的对照 RNAi 剂) 转染。

[00822] 下文显示结果。表 5 显示在 0.1nM 或 10nM 双链体终浓度，采用每个 β-联蛋白双链体针对单剂量筛选所进行的实验的结果。“残余基因活性”(倍数变化) 表示在 10nM 或 0.1nM 时的残余基因水平。因而，对于 AD-18892，在 10nM 在 24 小时 0.054 的“残余基因活性”表示 5.4%的残余基因活性，或 94.6%基因敲减。平均 EC_{50}(nM) 表示估计的 EC_{50}(在 HeLa 细胞中产生 50%基因敲减所估计的浓度)，如从 10nM、1nM、0.1nM、0.01nM 和 0.001_{nM} 时所采集的可用数据算出。“NA”表示数据不可获得。

表 5. 分析针对 β-联蛋白的 RNAi 剂：

双链体	有义 SEQ ID NO:	反义 SEQ ID NO:	残余基因活性 10 nM 24 小时	残余基因活性 0.1 nM 120 小时	平均 EC_{50}(nM)
AD-18892	1	660	0.054	0.47	NA
AD-18893	2	661	0.026	NA	0.008
AD-18894	3	662	0.068	NA	0.005
AD-18895	4	663	0.466	NA	NA
AD-18896	5	664	0.244	NA	NA
AD-18897	6	665	0.054	NA	0.028
AD-18898	7	666	0.903	NA	NA
AD-18899	8	667	0.301	NA	NA
AD-18900	9	668	1.157	NA	NA
AD-18901	10	669	0.359	NA	NA
AD-18902	11	670	0.058	NA	0.005
AD-18903	12	671	0.052	NA	0.002
AD-18904	13	672	0.690	NA	NA
AD-18905	14	673	0.198	NA	1.260
AD-18906	15	674	0.248	NA	NA
AD-18907	16	675	0.379	NA	NA
AD-18908	17	676	0.157	NA	NA
AD-18909	18	677	0.441	NA	NA
AD-18910	19	678	0.385	NA	NA
AD-18911	20	679	0.186	NA	1.664
AD-18912	21	680	0.221	NA	NA
AD-18913	22	681	0.124	NA	0.018
AD-18914	23	682	0.058	NA	0.002
AD-18915	24	683	0.242	NA	NA
AD-18916	25	684	0.530	NA	NA
AD-18917	26	685	0.527	0.66	NA

AD-18918	27	686	1.161	NA	NA
AD-18919	28	687	0.387	NA	NA
AD-18920	29	688	1.124	NA	NA
AD-18921	30	689	0.752	NA	NA
AD-18922	31	690	0.587	NA	NA
AD-18923	32	691	0.773	NA	NA
AD-18925	33	692	0.738	NA	NA
AD-18926	34	693	0.193	NA	0.033
AD-18927	35	694	0.091	NA	0.764
AD-18928	36	695	0.228	NA	NA
AD-18929	37	696	0.069	NA	NA
AD-18930	38	697	0.428	NA	NA
AD-18931	39	698	1.195	NA	NA
AD-18932	40	699	0.876	NA	NA
AD-18933	41	700	0.047	NA	0.001
AD-18934	42	701	0.651	NA	NA
AD-18935	43	702	0.419	NA	NA
AD-18936	44	703	0.125	NA	0.158
AD-18937	45	704	0.839	NA	NA
AD-18938	46	705	0.436	NA	NA
AD-18939	47	706	0.068	NA	0.011
AD-18940	48	707	0.515	NA	NA
AD-18941	49	708	0.421	NA	NA
AD-18942	50	709	1.397	NA	NA
AD-18943	51	710	0.990	NA	NA
AD-18944	52	711	0.550	NA	NA
AD-18945	53	712	0.193	NA	0.780
AD-18946	54	713	0.086	0.47	NA
AD-18947	55	714	0.397	NA	NA
AD-18948	56	715	0.885	NA	NA
AD-18949	57	716	0.863	NA	NA
AD-18950	58	717	0.103	NA	0.145
AD-18951	59	718	0.184	NA	0.519
AD-18952	60	719	0.382	NA	NA
AD-18953	61	720	1.349	NA	NA
AD-18954	62	721	0.766	NA	NA
AD-18955	63	722	0.649	0.64	NA
AD-18956	64	723	0.240	NA	NA
AD-18957	65	724	1.198	NA	NA
AD-18958	66	725	0.083	NA	0.012
AD-18959	67	726	0.713	NA	NA
AD-18960	68	727	0.188	NA	0.310
AD-18961	69	728	0.105	NA	0.209
AD-18962	70	729	0.942	NA	NA

AD-18963	71	730	0.037	0.37	0.049
AD-18964	72	731	0.907	NA	NA
AD-18965	73	732	0.440	0.48	NA
AD-18966	74	733	0.042	NA	0.000
AD-18967	75	734	0.695	NA	NA
AD-18968	76	735	0.158	NA	0.134
AD-18969	77	736	0.073	NA	0.004
AD-18970	78	737	0.810	NA	NA
AD-18971	79	738	0.336	NA	NA
AD-18972	80	739	0.332	NA	NA
AD-18973	81	740	0.707	NA	NA
AD-18974	82	741	0.038	NA	0.007
AD-18975	83	742	0.184	0.73	NA
AD-18976	84	743	0.094	NA	0.118
AD-18977	85	744	0.965	NA	NA
AD-18978	86	745	0.848	NA	NA
AD-18979	87	746	0.375	NA	NA
AD-18980	88	747	0.052	NA	NA
AD-18981	89	748	0.090	NA	0.004
AD-18982	90	749	0.156	NA	0.156
AD-18983	91	750	0.026	0.23	0.070
AD-18984	92	751	0.913	NA	NA
AD-18985	93	752	0.578	NA	NA
AD-18986	94	753	0.073	NA	0.003
AD-18987	95	754	0.626	NA	NA
AD-18988	96	755	0.379	NA	NA
AD-18989	97	756	0.879	NA	NA
AD-18990	98	757	0.299	NA	NA
AD-18991	99	758	0.112	NA	0.454
AD-18992	100	759	1.171	NA	NA
AD-18993	101	760	0.802	NA	NA
AD-18994	102	761	0.071	NA	0.313
AD-18995	103	762	0.096	NA	0.006
AD-18996	104	763	0.450	NA	NA
AD-18997	105	764	0.226	NA	NA
AD-18998	106	765	0.279	NA	NA
AD-18999	107	766	0.337	NA	NA
AD-19000	108	767	0.134	NA	0.347
AD-19001	109	768	0.470	0.71	NA
AD-19002	110	769	0.619	NA	NA
AD-19003	111	770	0.610	NA	NA
AD-19004	112	771	0.066	NA	0.007
AD-19005	113	772	0.274	NA	NA
AD-19006	114	773	0.139	NA	0.994

AD-19007	115	774	0.655	NA	NA
AD-19008	116	775	0.088	NA	0.001
AD-19009	117	776	0.066	NA	0.000
AD-19010	118	777	0.227	NA	NA
AD-19011	119	778	0.721	NA	NA
AD-19012	120	779	0.175	NA	0.181
AD-19042	121	780	0.283	NA	NA
AD-19043	122	781	0.131	NA	0.006
AD-19044	123	782	0.333	NA	NA
AD-19045	124	783	0.553	NA	NA
AD-19046	125	784	0.947	NA	NA
AD-19047	126	785	0.774	NA	NA
AD-19048	127	786	0.838	NA	NA
AD-19049	128	787	0.938	NA	NA
AD-19050	129	788	0.070	NA	0.001
AD-19051	130	789	0.551	NA	NA
AD-19052	131	790	0.818	NA	NA
AD-19053	132	791	0.364	NA	NA
AD-19054	133	792	0.075	NA	0.002
AD-19055	134	793	0.210	NA	NA
AD-19056	135	794	0.085	NA	0.019
AD-19057	136	795	0.599	NA	NA
AD-19058	137	796	0.577	NA	NA
AD-19059	138	797	0.728	NA	NA
AD-19060	139	798	1.072	NA	NA
AD-19061	140	799	0.885	NA	NA
AD-19062	141	800	0.810	NA	NA
AD-19063	142	801	0.741	NA	NA
AD-19064	143	802	0.591	NA	NA
AD-19065	144	803	0.323	NA	NA
AD-19066	145	804	0.086	0.48	NA
AD-19067	146	805	0.138	NA	NA
AD-19068	147	806	0.321	NA	NA
AD-19069	148	807	0.135	NA	1.403
AD-19070	149	808	0.892	NA	NA
AD-19071	150	809	0.658	NA	NA
AD-19072	151	810	0.704	NA	NA
AD-19073	152	811	0.838	NA	NA
AD-19074	153	812	0.042	NA	0.008
AD-19075	154	813	0.841	NA	NA
AD-19076	155	814	0.037	NA	0.002
AD-19077	156	815	0.226	NA	NA
AD-19078	157	816	0.719	NA	NA
AD-19079	158	817	0.545	NA	NA

AD-19080	159	818	0.092	NA	0.172
AD-19081	160	819	0.203	NA	8.936
AD-19082	161	820	0.055	NA	0.090
AD-19083	162	821	0.404	NA	NA
AD-19738	163	822	1.361	NA	NA
AD-19739	164	823	0.970	NA	NA
AD-19740	165	824	0.679	NA	NA
AD-19741	166	825	0.168	NA	NA
AD-19742	167	826	0.958	NA	NA
AD-19743	168	827	0.839	NA	NA
AD-19744	169	828	0.978	NA	NA
AD-19745	170	829	0.852	NA	NA
AD-19746	171	830	0.086	NA	NA
AD-19747	172	831	0.187	NA	NA
AD-19748	173	832	0.794	NA	NA
AD-19749	174	833	0.115	NA	NA
AD-19750	175	834	0.317	NA	NA
AD-19751	176	835	0.591	NA	NA
AD-19752	177	836	0.089	NA	NA
AD-19753	178	837	0.091	NA	NA
AD-19754	179	838	0.756	NA	NA
AD-19755	180	839	0.443	NA	NA
AD-19756	181	840	0.529	NA	NA
AD-19757	182	841	0.265	NA	NA
AD-19758	183	842	0.139	NA	NA
AD-19759	184	843	0.465	NA	NA
AD-19760	185	844	0.213	NA	NA
AD-19761	186	845	1.234	NA	NA
AD-19762	187	846	0.085	NA	NA
AD-19763	188	847	0.593	NA	NA
AD-19765	189	848	0.031	NA	NA
AD-19766	190	849	0.469	NA	NA
AD-19767	191	850	0.587	NA	NA
AD-19768	192	851	0.780	NA	NA
AD-20124	193	852	0.123	0.44	NA
AD-25889	194	853	0.605	0.73	NA
AD-25890	195	854	0.034	0.49	NA
AD-25891	196	855	0.041	0.16	0.050
AD-25892	197	856	0.099	0.34	NA
AD-25893	198	857	0.062	0.23	0.040
AD-25894	199	858	0.033	0.13	0.004
AD-25895	200	859	0.113	0.60	NA
AD-25896	201	860	0.276	0.74	NA
AD-25897	202	861	0.213	0.82	NA

AD-25898	203	862	0.127	0.79	NA
AD-25899	204	863	0.729	0.61	NA
AD-25900	205	864	0.094	0.64	NA
AD-25901	206	865	0.842	0.91	NA
AD-25902	207	866	0.054	0.24	NA
AD-25903	208	867	0.646	0.96	NA
AD-25904	209	868	0.681	0.83	NA
AD-25905	210	869	0.680	1.61	NA
AD-25906	211	870	0.413	0.96	NA
AD-25907	212	871	0.091	0.90	NA
AD-25908	213	872	0.355	0.72	NA
AD-25909	214	873	0.189	0.76	NA
AD-25910	215	874	0.048	0.48	0.070
AD-25911	216	875	0.134	0.81	NA
AD-25912	217	876	0.095	0.66	NA
AD-25913	218	877	0.291	0.94	NA
AD-25914	219	878	0.057	0.47	0.054
AD-25915	220	879	0.453	0.79	NA
AD-25916	221	880	0.219	0.79	NA
AD-25917	222	881	0.143	0.73	NA
AD-25918	223	882	0.075	0.29	0.013
AD-25919	224	883	0.123	0.68	NA
AD-25920	225	884	0.255	0.69	NA
AD-25921	226	885	0.637	0.81	NA
AD-25922	227	886	0.283	0.83	NA
AD-25923	228	887	0.575	0.64	NA
AD-25924	229	888	0.118	0.52	NA
AD-25925	230	889	0.242	0.96	NA
AD-25926	231	890	0.150	0.67	NA
AD-25927	232	891	0.394	0.72	NA
AD-25928	233	892	0.138	0.62	NA
AD-25929	234	893	0.073	0.50	NA
AD-25930	235	894	0.095	0.71	NA
AD-25931	236	895	0.076	0.77	NA
AD-25932	237	896	0.073	0.61	NA
AD-25933	238	897	0.113	0.79	NA
AD-25934	239	898	0.223	0.46	NA
AD-25935	240	899	0.288	0.78	NA
AD-25936	241	900	0.413	0.78	NA
AD-25937	242	901	0.838	0.77	NA
AD-25938	243	902	0.038	0.08	0.006
AD-25939	244	903	0.078	0.21	NA
AD-25940	245	904	0.063	0.31	NA
AD-25941	246	905	0.025	0.19	0.008

AD-25942	247	906	0.029	0.20	0.016
AD-25943	248	907	0.037	0.44	0.080
AD-25944	249	908	0.038	0.23	0.007
AD-25945	250	909	0.045	0.26	NA
AD-25946	251	910	0.107	0.46	NA
AD-25947	252	911	0.100	0.72	NA
AD-25948	253	912	0.159	0.33	NA
AD-25949	254	913	0.104	0.39	NA
AD-25950	255	914	0.026	0.26	0.010
AD-25951	256	915	0.026	0.28	0.007
AD-25952	257	916	0.349	0.80	NA
AD-25953	258	917	0.120	0.65	NA
AD-25954	259	918	0.550	0.92	NA
AD-25955	260	919	0.067	0.53	NA
AD-25956	261	920	0.039	0.40	0.042
AD-25957	262	921	0.105	0.64	NA
AD-25958	263	922	0.044	0.38	0.024
AD-25959	264	923	0.169	0.59	NA
AD-25960	265	924	0.060	0.37	0.044
AD-25961	266	925	0.162	0.67	NA
AD-25962	267	926	0.684	0.76	NA
AD-25963	268	927	0.106	0.48	0.275
AD-25964	269	928	0.033	0.47	0.050
AD-26017	270	929	0.113	0.87	NA
AD-26018	271	930	0.060	0.37	NA
AD-26019	272	931	0.106	0.42	NA
AD-26020	273	932	0.043	0.50	NA
AD-26021	274	933	0.046	0.69	NA
AD-26022	275	934	0.109	0.83	NA
AD-26023	276	935	0.637	0.80	NA
AD-26024	277	936	0.226	0.73	NA
AD-26025	278	937	0.252	0.96	NA
AD-26026	279	938	0.088	0.58	NA
AD-26027	280	939	0.228	0.96	NA
AD-26028	281	940	0.025	0.28	0.050
AD-26029	282	941	0.067	0.76	NA
AD-26030	283	942	0.275	0.52	NA
AD-26031	284	943	0.030	0.25	0.012
AD-26032	285	944	0.078	0.50	NA
AD-26033	286	945	0.353	0.69	NA
AD-26034	287	946	0.022	0.16	0.009
AD-26035	288	947	0.106	0.36	NA
AD-26036	289	948	0.336	0.63	NA
AD-26037	290	949	0.136	0.45	NA

AD-26038	291	950	0.215	0.46	NA
AD-26039	292	951	0.591	0.69	NA
AD-26040	293	952	0.046	0.15	0.099
AD-26041	294	953	0.324	0.67	NA
AD-26042	295	954	0.026	0.38	0.010
AD-26043	296	955	0.026	0.09	0.075
AD-26044	297	956	0.034	0.37	NA
AD-26045	298	957	0.531	0.77	NA
AD-26046	299	958	0.531	0.58	NA
AD-26047	300	959	0.023	0.47	0.058
AD-26048	301	960	0.397	0.95	NA
AD-26049	302	961	0.212	0.65	NA
AD-26050	303	962	0.204	0.95	NA
AD-26051	304	963	0.619	0.57	NA
AD-26052	305	964	0.037	0.55	NA
AD-26053	306	965	0.369	0.71	NA
AD-26054	307	966	0.616	0.78	NA
AD-26055	308	967	0.424	0.64	NA
AD-26056	309	968	0.168	0.81	NA
AD-26057	310	969	0.086	0.28	NA
AD-26058	311	970	0.456	0.67	NA
AD-26059	312	971	0.169	0.47	NA
AD-26060	313	972	0.057	0.19	0.139
AD-26061	314	973	0.050	0.42	NA
AD-26062	315	974	0.110	0.64	NA
AD-26063	316	975	0.021	0.74	NA
AD-26064	317	976	0.785	0.62	NA
AD-26065	318	977	0.678	0.84	NA
AD-26066	319	978	0.035	0.44	NA
AD-26067	320	979	0.305	0.51	NA
AD-26068	321	980	0.028	0.50	0.102
AD-26069	322	981	0.046	0.50	NA
AD-26070	323	982	0.446	0.64	NA
AD-26071	324	983	0.074	0.48	NA
AD-26072	325	984	0.742	0.84	NA
AD-26073	326	985	0.086	0.33	NA
AD-26074	327	986	0.227	0.55	NA
AD-26075	328	987	0.092	0.74	NA
AD-26076	329	988	0.029	0.24	0.159
AD-26077	330	989	0.191	0.70	NA
AD-26078	331	990	0.032	0.32	0.106
AD-26079	332	991	0.131	0.55	NA
AD-26080	333	992	0.589	0.86	NA
AD-26081	334	993	0.538	0.66	NA

AD-26082	335	994	0.021	0.42	0.039
AD-26083	336	995	0.049	0.25	NA
AD-26084	337	996	0.334	0.75	NA
AD-26085	338	997	0.192	0.69	NA
AD-26086	339	998	0.524	0.62	NA
AD-26087	340	999	0.276	0.71	NA
AD-26088	341	1000	0.101	0.83	NA
AD-26089	342	1001	0.821	0.93	NA
AD-26090	343	1002	0.367	0.77	NA
AD-26091	344	1003	0.022	0.32	0.057
AD-26092	345	1004	0.246	0.75	NA
AD-26093	346	1005	0.570	0.70	NA
AD-26094	347	1006	0.145	0.57	NA
AD-26095	348	1007	0.073	0.58	NA
AD-26096	349	1008	0.109	0.51	NA
AD-26097	350	1009	0.145	0.57	NA
AD-26098	351	1010	0.101	0.43	NA
AD-26099	352	1011	0.171	0.68	NA
AD-26100	353	1012	0.058	0.21	NA
AD-26101	354	1013	0.041	0.30	0.030
AD-26102	355	1014	0.169	0.93	NA
AD-26103	356	1015	0.209	0.61	NA
AD-26104	357	1016	0.016	0.22	0.058
AD-26105	358	1017	0.044	0.49	NA
AD-26106	359	1018	0.169	0.75	NA
AD-26107	360	1019	0.290	0.90	NA
AD-26108	361	1020	0.040	0.50	0.030
AD-26109	362	1021	0.024	0.22	0.025
AD-26110	363	1022	0.326	0.79	NA
AD-26111	364	1023	0.798	0.77	NA
AD-26112	365	1024	0.301	0.51	NA
AD-26123	366	1025	0.652	0.84	NA
AD-26124	367	1026	0.277	0.48	NA
AD-26125	368	1027	0.342	0.64	NA
AD-26126	369	1028	0.094	0.46	NA
AD-26127	370	1029	0.455	0.80	NA
AD-26128	371	1030	0.058	0.24	0.066
AD-26129	372	1031	0.409	0.57	NA
AD-26130	373	1032	0.892	0.80	NA
AD-26131	374	1033	0.067	0.41	0.104
AD-26132	375	1034	0.109	0.19	0.060
AD-26133	376	1035	0.790	0.85	NA
AD-26134	377	1036	0.046	0.27	0.103
AD-26135	378	1037	0.069	0.38	NA

AD-26136	379	1038	0.451	0.78	NA
AD-26137	380	1039	0.685	0.64	NA
AD-26138	381	1040	0.579	0.63	NA
AD-26139	382	1041	0.857	0.59	NA
AD-26140	383	1042	0.384	0.71	NA
AD-26141	384	1043	0.104	0.49	NA
AD-26142	385	1044	0.199	0.59	NA
AD-26143	386	1045	0.205	0.61	NA
AD-26144	387	1046	0.821	1.04	NA
AD-26145	388	1047	0.860	0.86	NA
AD-26146	389	1048	0.076	0.34	NA
AD-26147	390	1049	0.559	0.65	NA
AD-26148	391	1050	0.066	0.48	NA
AD-26149	392	1051	0.326	0.50	NA
AD-26150	393	1052	0.396	0.66	NA
AD-26151	394	1053	0.249	0.54	NA
AD-26152	395	1054	0.837	0.74	NA
AD-26153	396	1055	0.119	0.39	NA
AD-26154	397	1056	0.600	0.64	NA
AD-26155	398	1057	0.693	0.69	NA
AD-26156	399	1058	0.033	0.35	0.020
AD-26157	400	1059	0.220	0.74	NA
AD-26158	401	1060	0.031	0.40	0.033
AD-26159	402	1061	0.387	0.49	NA
AD-26160	403	1062	0.836	0.73	NA
AD-26161	404	1063	0.831	0.76	NA
AD-26162	405	1064	0.358	0.50	NA
AD-26163	406	1065	0.817	0.66	NA
AD-26164	407	1066	0.112	0.59	NA
AD-26165	408	1067	0.272	0.67	NA
AD-26166	409	1068	0.300	0.63	NA
AD-26167	410	1069	0.664	0.77	NA
AD-26168	411	1070	0.771	0.78	NA
AD-26169	412	1071	0.480	0.67	NA
AD-26170	413	1072	0.174	0.47	NA
AD-26171	414	1073	0.410	0.75	NA
AD-26172	415	1074	0.294	0.74	NA
AD-26173	416	1075	0.384	0.71	NA
AD-26174	417	1076	0.388	0.79	NA
AD-26175	418	1077	0.611	0.72	NA
AD-26176	419	1078	0.055	0.44	NA
AD-26177	420	1079	0.310	0.67	NA
AD-26178	421	1080	0.038	0.20	0.094
AD-26179	422	1081	0.042	0.33	0.108

AD-26180	423	1082	0.031	0.21	0.036
AD-26181	424	1083	0.041	0.08	0.034
AD-26182	425	1084	0.237	0.79	NA
AD-26183	426	1085	0.028	0.37	0.070
AD-26184	427	1086	0.189	0.54	NA
AD-26185	428	1087	0.357	0.76	NA
AD-26186	429	1088	0.066	0.60	NA
AD-26187	430	1089	0.298	0.60	NA
AD-26188	431	1090	0.159	0.51	NA
AD-26189	432	1091	0.143	0.51	NA
AD-26190	433	1092	0.063	0.34	NA
AD-26191	434	1093	0.674	0.82	NA
AD-26192	435	1094	0.446	0.75	NA
AD-26193	436	1095	0.058	0.36	0.055
AD-26194	437	1096	0.289	0.84	NA
AD-26195	438	1097	0.353	0.81	NA
AD-26196	439	1098	0.055	0.35	NA
AD-26197	440	1099	0.440	0.68	NA
AD-26198	441	1100	0.175	0.53	NA
AD-26199	442	1101	0.055	0.58	NA
AD-26200	443	1102	0.076	0.46	NA
AD-26201	444	1103	0.283	0.48	NA
AD-26202	445	1104	0.052	0.70	NA
AD-26203	446	1105	0.045	0.22	0.162
AD-26204	447	1106	0.660	0.73	NA
AD-26205	448	1107	0.324	0.76	NA
AD-26206	449	1108	0.520	1.12	NA
AD-26207	450	1109	0.367	0.75	NA
AD-26208	451	1110	0.795	0.73	NA
AD-26209	452	1111	0.112	0.54	NA
AD-26210	453	1112	0.030	0.39	NA
AD-26211	454	1113	0.124	0.25	NA
AD-26212	455	1114	0.151	0.45	NA
AD-26213	456	1115	0.223	0.63	NA
AD-26214	457	1116	0.513	0.66	NA
AD-26215	458	1117	0.102	0.29	NA
AD-26216	459	1118	0.496	0.58	NA
AD-26217	460	1119	0.410	0.77	NA
AD-26218	461	1120	0.041	0.15	0.026
AD-26651	462	1121	0.023	0.21	0.041
AD-26652	463	1122	0.025	0.21	0.026
AD-26653	464	1123	0.115	0.76	NA
AD-26654	465	1124	0.068	0.88	NA
AD-26655	466	1125	0.682	0.86	NA

AD-26656	467	1126	0.684	0.91	NA
AD-26657	468	1127	0.468	0.89	NA
AD-26658	469	1128	0.305	0.50	NA
AD-26659	470	1129	0.481	0.50	NA
AD-26660	471	1130	0.041	0.20	0.010
AD-26661	472	1131	0.194	0.77	NA
AD-26662	473	1132	0.717	1.00	NA
AD-26663	474	1133	0.546	1.02	NA
AD-26664	475	1134	0.030	0.36	NA
AD-26665	476	1135	0.037	0.25	0.008
AD-26666	477	1136	0.072	0.57	NA
AD-26667	478	1137	0.587	0.65	NA
AD-26668	479	1138	0.760	0.70	NA
AD-26669	480	1139	0.038	0.64	NA
AD-26670	481	1140	0.033	0.32	0.005
AD-26671	482	1141	0.091	0.71	NA
AD-26672	483	1142	0.084	0.56	NA
AD-26673	484	1143	0.027	0.18	0.012
AD-26674	485	1144	0.044	0.32	0.021
AD-26675	486	1145	0.063	0.67	NA
AD-26676	487	1146	0.617	0.81	NA
AD-26677	488	1147	0.138	0.50	NA
AD-26678	489	1148	0.055	0.34	NA
AD-26679	490	1149	0.052	0.44	NA
AD-26680	491	1150	0.191	0.42	NA
AD-26681	492	1151	0.092	0.57	NA
AD-26682	493	1152	0.035	0.11	0.007
AD-26683	494	1153	0.055	0.87	NA
AD-26684	495	1154	0.035	0.16	0.009
AD-26685	496	1155	0.034	0.37	NA
AD-26686	497	1156	0.821	0.77	NA
AD-26687	498	1157	0.151	0.29	NA
AD-26688	499	1158	0.094	0.69	NA
AD-26689	500	1159	0.086	0.61	NA
AD-26690	501	1160	0.047	0.36	NA
AD-26691	502	1161	0.030	0.24	0.020
AD-26692	503	1162	0.222	0.62	NA
AD-26693	504	1163	0.739	0.76	NA
AD-26694	505	1164	0.331	0.63	NA
AD-26695	506	1165	0.371	0.66	NA
AD-26696	507	1166	0.023	0.37	0.027
AD-26697	508	1167	1.024	0.80	NA
AD-26698	509	1168	0.047	0.22	NA
AD-26699	510	1169	0.145	0.71	NA

AD-26700	511	1170	0.028	0.08	0.005
AD-26701	512	1171	0.028	0.21	0.006
AD-26702	513	1172	0.046	0.43	NA
AD-26703	514	1173	0.193	0.65	NA
AD-26704	515	1174	0.027	0.36	0.010
AD-26705	516	1175	0.054	0.40	NA
AD-26706	517	1176	0.223	0.52	NA
AD-26707	518	1177	0.144	0.70	NA
AD-26708	519	1178	0.160	0.59	NA
AD-26709	520	1179	0.818	0.80	NA
AD-26710	521	1180	0.307	0.84	NA
AD-26711	522	1181	0.209	0.46	NA
AD-26712	523	1182	0.276	0.76	NA
AD-26713	524	1183	0.043	0.23	0.014
AD-26714	525	1184	0.108	0.65	NA
AD-26715	526	1185	0.777	0.67	NA
AD-26716	527	1186	0.551	0.69	NA
AD-26717	528	1187	0.643	0.80	NA
AD-26718	529	1188	0.821	0.70	NA
AD-26719	530	1189	0.053	0.35	NA
AD-26720	531	1190	0.148	0.62	NA
AD-26721	532	1191	0.906	0.92	NA
AD-26722	533	1192	0.042	0.38	0.033
AD-26723	534	1193	0.136	0.69	NA
AD-26724	535	1194	0.472	1.00	NA
AD-26725	536	1195	0.082	0.39	NA
AD-26726	537	1196	0.258	0.70	NA
AD-26727	538	1197	0.043	0.33	NA
AD-26728	539	1198	0.612	0.80	NA
AD-26729	540	1199	0.056	0.15	0.007
AD-26730	541	1200	0.038	0.13	0.007
AD-26731	542	1201	0.034	0.10	0.035
AD-26732	543	1202	0.853	0.74	NA
AD-26733	544	1203	0.805	0.77	NA
AD-26734	545	1204	0.580	0.77	NA
AD-26735	546	1205	0.457	1.02	NA
AD-26736	547	1206	0.701	0.75	NA
AD-26737	548	1207	0.066	0.33	NA
AD-26738	549	1208	0.327	0.79	NA
AD-26739	550	1209	0.102	0.44	NA
AD-26740	551	1210	0.030	0.08	0.006
AD-26741	552	1211	0.128	0.50	NA
AD-26742	553	1212	0.025	0.34	0.057
AD-26743	554	1213	0.033	0.38	0.061

AD-26744	555	1214	0.170	0.74	NA
AD-26745	556	1215	0.304	0.55	NA
AD-26746	557	1216	0.037	0.33	NA
AD-26747	558	1217	0.048	0.43	NA
AD-26748	559	1218	0.081	0.51	NA
AD-26749	560	1219	0.184	0.70	NA
AD-26750	561	1220	0.209	0.64	NA
AD-26751	562	1221	0.570	0.71	NA
AD-26752	563	1222	0.040	0.45	0.042
AD-26753	564	1223	0.153	0.61	NA
AD-26754	565	1224	0.518	0.79	NA
AD-26755	566	1225	0.064	0.27	NA
AD-26756	567	1226	0.146	0.48	NA
AD-26757	568	1227	0.035	0.22	0.047
AD-26758	569	1228	0.053	0.46	NA
AD-26759	570	1229	0.116	0.59	NA
AD-26760	571	1230	0.435	0.60	NA
AD-26761	572	1231	0.088	0.44	NA
AD-26762	573	1232	0.385	0.57	NA
AD-26763	574	1233	0.057	0.22	0.015
AD-26764	575	1234	0.120	0.47	NA
AD-26765	576	1235	0.058	0.43	NA
AD-26766	577	1236	0.183	0.72	NA
AD-26767	578	1237	0.582	0.57	NA
AD-26768	579	1238	0.042	0.39	NA
AD-26769	580	1239	0.071	0.52	NA
AD-26770	581	1240	0.398	0.58	NA
AD-26771	582	1241	0.576	0.71	NA
AD-26772	583	1242	0.784	0.64	NA
AD-26773	584	1243	0.353	0.58	NA
AD-26774	585	1244	0.069	0.55	NA
AD-26775	586	1245	0.506	0.86	NA
AD-26776	587	1246	0.079	0.26	NA
AD-26777	588	1247	0.363	0.73	NA
AD-26778	589	1248	0.101	0.40	NA
AD-26779	590	1249	0.040	0.34	0.109
AD-26780	591	1250	0.069	0.25	NA
AD-26781	592	1251	0.044	0.24	NA
AD-26782	593	1252	0.054	0.53	NA
AD-26783	594	1253	0.053	0.51	NA
AD-26784	595	1254	0.072	0.53	NA
AD-26785	596	1255	0.201	0.51	NA
AD-26786	597	1256	0.134	0.81	NA
AD-26787	598	1257	0.143	0.60	NA

AD-26788	599	1258	0.036	0.57	0.053
AD-26789	600	1259	0.418	0.74	NA
AD-26790	601	1260	0.122	0.62	NA
AD-26791	602	1261	0.305	0.73	NA
AD-26792	603	1262	0.346	0.76	NA
AD-26793	604	1263	0.391	0.63	NA
AD-26794	605	1264	0.077	0.40	NA
AD-26795	606	1265	0.586	0.65	NA
AD-26796	607	1266	0.392	0.70	NA
AD-26797	608	1267	0.063	0.73	NA
AD-26798	609	1268	0.249	0.62	NA
AD-26799	610	1269	0.345	0.66	NA
AD-26800	611	1270	0.034	0.20	0.025
AD-26801	612	1271	0.044	0.46	NA
AD-26802	613	1272	0.096	0.57	NA
AD-26803	614	1273	0.162	0.57	NA
AD-26804	615	1274	0.056	0.35	NA
AD-26805	616	1275	0.742	0.66	NA
AD-26806	617	1276	0.080	0.69	NA
AD-26807	618	1277	0.517	0.62	NA
AD-26808	619	1278	0.043	0.51	NA
AD-26809	620	1279	0.227	0.61	NA
AD-26810	621	1280	0.048	0.22	0.039
AD-26811	622	1281	0.333	0.85	NA
AD-26812	623	1282	0.522	0.84	NA
AD-26813	624	1283	0.044	0.33	0.076
AD-26814	625	1284	0.545	0.72	NA
AD-26815	626	1285	0.594	0.63	NA
AD-26816	627	1286	0.044	0.37	NA
AD-26817	628	1287	0.523	0.68	NA
AD-26818	629	1288	0.575	1.80	NA
AD-26819	630	1289	0.069	0.41	NA
AD-26820	631	1290	0.484	0.76	NA
AD-26821	632	1291	0.245	0.70	NA
AD-26822	633	1292	0.039	0.23	0.037
AD-26823	634	1293	0.062	0.09	0.033
AD-26824	635	1294	0.304	0.60	NA
AD-26825	636	1295	0.038	0.36	NA
AD-26826	637	1296	0.105	0.57	NA
AD-26900	638	1297	0.056	0.73	0.033
AD-26901	639	1298	0.065	0.68	NA
AD-26902	640	1299	0.053	0.42	NA
AD-26903	641	1300	0.075	0.59	NA
AD-26904	642	1301	0.051	0.38	NA

AD-26905	643	1302	0.084	0.45	NA
AD-26906	644	1303	0.186	0.76	NA
AD-26907	645	1304	0.610	0.82	NA
AD-26908	646	1305	0.073	0.78	NA
AD-26909	647	1306	0.235	0.99	NA
AD-26910	648	1307	0.077	0.78	NA
AD-26911	649	1308	0.193	0.96	NA
AD-26912	650	1309	0.074	0.73	NA
AD-26913	651	1310	0.141	0.88	NA
AD-26914	652	1311	0.519	0.64	NA
AD-26915	653	1312	0.587	0.71	NA
AD-26916	654	1313	0.063	0.62	NA
AD-26917	655	1314	0.076	0.55	NA
AD-26918	656	1315	0.069	0.28	0.029
AD-26919	657	1316	0.085	0.55	NA
AD-26920	658	1317	0.042	0.31	NA
AD-26921	659	1318	0.025	0.09	0.014

[00823]NA :数据不可获得或未测定。

[00824] “倍数变化”表示相对于对照在特定时间和浓度（在 HeLa 细胞中）的残余水平。因此，AD-18892 的“倍数变化 10nM 24 小时”为“0.054”表示，在 10nM 浓度，在用该 RNAi 剂处理细胞后 24 小时，HeLa 细胞中存在 5.4%的残余 β-联蛋白水平或 94.6%的基因敲减。

[00825]“倍数变化 0.1nM 120 小时”表示在 120 小时在浓度 0.1nM 时测量的残余 β-联蛋白水平。

[00826]“平均 EC_{50}(nM)”表示基于可用数据，经估计引起 HeLa 细胞中 50%基因敲减的浓度。因此，对于 AD-18893，估计 0.008nM 的浓度敲减 β-联蛋白 50%。为了计算估计的 EC_{50} 平均值，将 HeLa 细胞用 RNAi 剂以 10nM、1nM、0.1nM、0.01nM 和 0.001nM RNAi 剂的浓度处理，并将数据拟合成曲线。所示的 EC_{50} 是从可用数据计算的估计的 EC_{50}，其中预期所述估计的 EC_{50} 在 HeLa 细胞中产生 β-联蛋白的 50%基因敲减。

[00827] 表 1 至表 8 因此公开能够介导 β-联蛋白的基因敲减的多种 RNAi 剂。

[00828] 表 6. 分析针对 β-联蛋白的 RNAi 剂：

[00829] 在体外针对 HeLa 细胞测试（表 3 中列出的）靶向 β-联蛋白的额外双链体。测量 48 小时结果；双链体浓度是 6nM、3nM 和 1.5nM。这个表中的数据表示残余基因活性；因此 Set1254A22S26 在 48 小时在 6nM 在 HeLa 细胞中显示 4.9%残余基因活性（例如，95.1%基因敲减）。

名称	AV HeLa set1-2 d3-6nM	AV HeLa set1-2 3nM	AV HeLa set1-2 1.5nM	SD HeLa set1-2 d3-6nM	SD HeLa set1-2 3nM	SD HeLa set1-2 1.5nM
Set 11 254 A22 S26	4.9	11.1	22.5	1.6	2.1	1.6
Set 11 703 A22 S26	4.8	12.4	29.0	1.5	2.4	7.3
Set 11 709 A22 S26	6.5	13.9	30.7	1.1	2.0	7.1
Set 11 895 A22 S26	5.9	13.1	48.0	0.8	3.9	25.6
Set 11 1816 A22 S26	4.9	12.3	28.6	0.5	2.8	4.3
Set 11 1974 A22 S26	6.6	12.5	36.9	1.0	0.9	0.6
Set 11 2425 A22 S26	5.6	13.6	27.3	0.4	1.7	9.7
Set 11 3146 A22 S26	4.5	9.3	21.0	1.1	1.2	2.9
Set 11 889 A22 S26	8.6	14.2	37.9	3.4	3.7	17.1
Set 11 1814 A22 S26	6.0	11.8	21.3	2.2	3.8	4.6
Set 11 1245 A22 S26	6.7	12.0	28.2	2.6	2.5	8.7
Set 11 3196 A22 S26	4.5	9.1	17.1	0.5	0.0	5.3
Set 11 1450 A22 S26	4.4	12.5	25.4	0.3	3.6	2.7
Set 11 3169 A22 S26	6.3	13.1	29.7	0.9	2.2	9.8
Set 11 3477 A22 S26	9.6	19.8	40.9	2.0	2.6	10.9
Set 11 865 A22 S26	12.0	24.5	57.3	3.3	7.5	14.2
Set 11 1249 A22 S26	34.4	71.2	73.3	7.9	24.7	12.3
Set 11 1250 A22 S26	12.0	30.6	61.6	2.0	8.4	4.2
Set 11 2202 A22 S26	8.3	14.0	45.8	3.1	1.8	12.2
Set 11 1545 A22 S26	34.4	62.0	81.5	11.6	4.1	12.5
Set 11 1755 A22 S26	8.7	21.9	64.9	1.0	6.4	8.0
Set 11 254 A25 S27	6.3	12.3	17.6	1.2	3.4	1.7
Set 11 703 A25 S27	7.0	13.7	32.8	1.2	2.9	8.0
Set 11 709 A25 S27	5.6	11.4	23.4	1.8	0.5	7.7
Set 11 895 A25 S27	6.6	13.5	35.7	1.9	2.5	6.8
Set 11 1816 A25 S27	7.8	15.6	26.4	1.3	1.2	4.8
Set 11 1974 A25 S27	8.1	16.2	34.7	2.6	1.3	3.8
Set 11 2425 A25 S27	7.8	16.5	35.3	1.0	2.2	2.5
Set 11 3146 A25 S27	4.9	11.9	31.0	0.3	1.3	4.2
Set 11 889 A25 S27	9.3	15.0	37.2	1.3	1.9	4.1

Set 11 1814 A25 S27	6.2	13.7	43.2	1.1	0.9	6.1
Set 11 1245 A25 S27	7.2	15.2	36.2	0.3	2.4	11.7
Set 11 3196 A25 S27	5.5	10.3	24.2	1.4	0.8	2.1
Set 11 1450 A25 S27	4.3	10.4	29.9	1.1	1.1	6.4
Set 11 3169 A25 S27	4.3	11.5	22.0	0.4	2.3	2.7
Set 11 3477 A25 S27	7.5	12.8	22.8	1.1	1.3	2.1
Set 11 865 A25 S27	5.1	10.9	18.1	0.7	1.2	2.9
Set 11 1249 A25 S27	8.0	22.9	37.2	1.8	5.1	6.7
Set 11 1250 A25 S27	16.6	28.2	49.1	3.1	2.7	8.9
Set 11 2202 A25 S27	6.1	10.0	29.2	2.3	3.6	4.8
Set 11 1545 A25 S27	9.0	16.6	41.9	1.3	2.2	2.2
Set 11 1755 A25 S27	5.8	15.1	33.8	1.2	2.2	6.1
Set 11 254 A LO V1 S26	6.0	16.4	32.9	0.3	3.8	5.1
Set 11 703 A LO V1 S26	8.1	22.7	50.3	2.8	3.4	16.2
Set 11 709 A LO V1 S26	6.2	14.8	37.1	1.2	1.7	5.1
Set 11 895 A LO V1 S26	42.7	63.9	82.3	7.8	15.5	10.2
Set 11 1816 A LO V1 S26	6.9	16.9	43.4	0.9	1.4	15.1
Set 11 1974 A LO V1 S26	9.0	18.5	36.8	1.4	3.6	6.8
Set 11 2425 A LO V1 S26	5.5	13.9	30.0	0.4	1.6	7.5
Set 11 3146 A LO V1 S26	12.1	27.7	61.2	1.5	2.7	3.8
Set 11 889 A LO V1 S26	24.5	37.8	60.3	3.2	3.2	9.1
Set 11 1814 A LO V1 S26	8.6	20.7	46.5	1.5	2.6	11.1
Set 11 1245 A LO V1 S26	42.0	61.4	85.9	5.8	8.4	10.4
Set 11 3196 A LO V1 S26	6.1	14.0	31.0	0.6	1.2	5.4
Set 11 1450 A LO V1 S26	9.4	21.1	47.6	1.4	1.3	8.0
Set 11 3169 A LO V1 S26	5.3	15.5	30.5	1.3	3.7	1.9
Set 11 3477 A LO V1 S26	8.6	16.9	39.8	1.0	1.0	2.3
Set 11 865 A LO V1 S26	5.5	18.1	34.5	0.9	3.1	11.0
Set 11 1249 A LO V1 S26	61.0	90.3	82.0	5.6	29.0	6.6
Set 11 1250 A LO V1 S26	11.3	23.1	58.2	0.9	3.0	5.1
Set 11 2202 A LO V1 S26	5.7	14.5	45.2	1.0	1.4	1.5
Set 11 1545 A LO V1 S26	5.6	13.1	38.6	0.4	0.9	3.2
Set 11 1755 A LO V1 S26	39.5	53.6	77.5	3.8	3.3	5.0
Set 11 254 A LO V2 S LO V1	8.7	18.6	44.9	2.5	1.4	6.6
Set 11 703 A LO V2 S LO V1	39.9	51.7	75.8	3.9	3.2	9.9
Set 11 709 A LO V2 S LO V1	9.2	20.3	45.0	1.2	0.7	8.7
Set 11 895 A LO V2 S LO V1	33.3	64.9	84.8	1.8	6.5	5.8
Set 11 1816 A LO V2 S LO V1	14.4	33.1	61.2	2.2	2.9	9.3
Set 11 1974 A LO V2 S LO V1	56.7	65.4	91.8	15.4	5.6	6.7
Set 11 2425 A LO V2 S LO V1	13.3	21.4	54.2	1.5	3.6	6.0
Set 11 3146 A LO V2 S LO V1	9.7	16.7	32.7	2.0	1.7	5.0
Set 11 889 A LO V2 S LO V1	18.0	34.6	58.8	1.4	4.2	7.0
Set 11 1814 A LO V2 S LO V1	8.9	18.5	44.1	3.3	5.0	1.0
Set 11 1245 A LO V2 S LO V1	52.2	43.1	93.4	13.1	4.1	6.2

Set 11 3196 A LO V2 S LO V1	7.8	15.1	28.0	2.7	3.1	2.5
Set 11 1450 A LO V2 S LO V1	6.6	14.4	35.0	0.4	2.0	4.0
Set 11 3169 A LO V2 S LO V1	5.3	14.5	26.4	0.5	2.8	2.2
Set 11 3477 A LO V2 S LO V1	9.4	22.0	35.2	1.5	0.8	1.6
Set 11 865 A LO V2 S LO V1	11.2	18.5	45.9	5.4	4.2	18.2
Set 11 1249 A LO V2 S LO V1	65.5	97.0	82.0	19.2	22.0	10.3
Set 11 1250 A LO V2 S LO V1	49.4	62.9	92.4	6.3	19.6	22.4
Set 11 2202 A LO V2 S LO V1	6.7	17.3	34.9	0.8	3.6	1.6
Set 11 1545 A LO V2 S LO V1	17.9	32.6	58.3	1.2	5.0	8.2
Set 11 1755 A LO V2 S LO V1	10.5	23.3	43.1	1.0	3.3	7.3
Set 12 254 A LO V3 S LO V2	15.0	88.6	75.0	3.4	21.7	4.4
Set 12 703 A LO V3 S LO V2	112.0	235.3	135.2	25.2	30.1	22.4
Set 12 709 A LO V3 S LO V2	36.7	93.6	98.4	2.6	7.6	4.8
Set 12 895 A LO V3 S LO V2	80.2	163.3	117.7	9.1	62.4	10.6
Set 12 1816 A LO V3 S LO V2	66.3	113.1	116.6	10.0	22.2	12.6
Set 12 1974 A LO V3 S LO V2	110.7	142.7	134.5	13.1	19.0	12.8
Set 12 2425 A LO V3 S LO V2	50.9	119.3	151.5	13.1	20.2	7.0
Set 12 3146 A LO V3 S LO V2	30.8	73.2	99.6	5.0	13.5	14.3
Set 12 889 A LO V3 S LO V2	72.5	135.6	112.8	12.0	37.8	9.4
Set 12 1814 A LO V3 S LO V2	80.7	129.6	133.9	23.6	13.9	15.2
Set 12 1245 A LO V3 S LO V2	94.9	128.9	129.1	13.2	18.1	13.8
Set 12 3196 A LO V3 S LO V2	20.5	69.2	89.8	1.4	8.7	15.8
Set 12 1450 A LO V3 S LO V2	35.3	95.3	109.0	1.6	15.1	16.1
Set 12 3169 A LO V3 S LO V2	26.2	90.9	85.7	8.9	26.1	7.7
Set 12 3477 A LO V3 S LO V2	16.3	71.8	68.0	3.7	20.3	2.2
Set 12 865 A LO V3 S LO V2	99.3	122.9	115.4	9.0	29.0	14.5
Set 12 1249 A LO V3 S LO V2	62.7	114.9	113.5	7.5	19.6	3.4
Set 12 1250 A LO V3 S LO V2	101.9	112.5	116.1	8.7	12.1	11.1
Set 12 2202 A LO V3 S LO V2	72.2	118.5	129.7	7.1	22.3	7.5
Set 12 1545 A LO V3 S LO V2	65.6	109.5	120.7	12.9	6.5	9.3
Set 12 1755 A LO V3 S LO V2	84.7	140.6	146.9	11.1	52.2	13.5
Set 12 254 A LO V4 S LO V1	11.2	50.5	59.8	1.4	4.6	4.5
Set 12 703 A LO V4 S LO V1	29.1	94.0	100.5	3.4	10.3	6.1
Set 12 709 A LO V4 S LO V1	6.3	25.9	32.9	0.2	2.6	2.2
Set 12 895 A LO V4 S LO V1	26.4	86.4	108.5	1.2	6.5	30.8
Set 12 1816 A LO V4 S LO V1	15.0	94.1	88.1	1.5	13.2	25.2
Set 12 1974 A LO V4 S LO V1	47.3	100.2	126.0	9.1	4.5	21.6
Set 12 2425 A LO V4 S LO V1	13.0	44.3	61.8	3.7	1.7	6.9
Set 12 3146 A LO V4 S LO V1	11.8	36.2	34.8	2.5	2.4	3.6
Set 12 889 A LO V4 S LO V1	28.9	79.6	79.8	9.2	13.4	10.7
Set 12 1814 A LO V4 S LO V1	10.4	50.1	62.9	0.9	17.3	9.2
Set 12 1245 A LO V4 S LO V1	31.7	88.0	105.1	5.3	18.8	14.2
Set 12 3196 A LO V4 S LO V1	9.8	27.2	39.2	1.1	1.4	4.9
Set 12 1450 A LO V4 S LO V1	8.9	27.8	44.0	2.1	7.6	10.9

Set 12 3169 A LO V4 S LO V1	8.1	26.3	29.7	1.4	7.1	6.6
Set 12 3477 A LO V4 S LO V1	7.9	19.2	29.1	0.6	2.5	9.5
Set 12 865 A LO V4 S LO V1	6.2	23.8	33.4	0.6	0.7	5.6
Set 12 1249 A LO V4 S LO V1	69.5	103.4	103.4	19.1	17.3	11.8
Set 12 1250 A LO V4 S LO V1	61.4	90.3	94.6	15.3	12.4	11.7
Set 12 2202 A LO V4 S LO V1	9.3	35.7	42.8	2.9	6.9	5.5
Set 12 1545 A LO V4 S LO V1	32.8	68.0	92.2	6.1	17.1	23.2
Set 12 1755 A LO V4 S LO V1	13.9	50.4	62.0	3.6	4.6	12.5
Set 12 254 A LO V5 S LO V1	11.4	28.3	52.5	1.8	8.2	4.8
Set 12 703 A LO V5 S LO V1	31.1	88.4	97.0	1.4	14.7	6.3
Set 12 709 A LO V5 S LO V1	13.0	34.2	37.9	3.4	8.8	5.7
Set 12 895 A LO V5 S LO V1	25.9	81.1	109.1	3.0	8.2	20.0
Set 12 1816 A LO V5 S LO V1	12.9	42.3	53.7	2.5	7.0	12.1
Set 12 1974 A LO V5 S LO V1	39.5	80.3	93.6	11.6	5.5	10.4
Set 12 2425 A LO V5 S LO V1	11.5	38.8	59.9	1.4	5.4	3.3
Set 12 3146 A LO V5 S LO V1	9.3	32.1	41.6	0.7	5.6	4.3
Set 12 889 A LO V5 S LO V1	26.9	64.9	89.5	5.2	23.5	17.5
Set 12 1814 A LO V5 S LO V1	11.0	47.9	79.5	1.5	9.1	11.6
Set 12 1245 A LO V5 S LO V1	29.5	78.6	127.3	2.2	5.1	16.7
Set 12 3196 A LO V5 S LO V1	8.1	28.6	55.6	0.7	9.8	9.7
Set 12 1450 A LO V5 S LO V1	6.6	27.8	46.3	1.6	12.7	12.4
Set 12 3169 A LO V5 S LO V1	7.8	24.2	32.6	1.5	0.8	5.5
Set 12 3477 A LO V5 S LO V1	11.5	46.6	57.9	2.3	25.4	7.1
Set 12 865 A LO V5 S LO V1	11.4	35.2	40.9	1.6	8.6	6.7
Set 12 1249 A LO V5 S LO V1	52.0	82.3	89.6	3.2	3.0	12.9
Set 12 1250 A LO V5 S LO V1	45.0	75.2	97.3	6.1	4.2	13.0
Set 12 2202 A LO V5 S LO V1	5.8	26.1	35.7	0.8	5.2	4.2
Set 12 1545 A LO V5 S LO V1	23.8	59.7	73.5	3.5	18.3	11.0
Set 12 1755 A LO V5 S LO V1	10.8	40.5	73.9	0.8	10.6	4.8
Set 12 254 A48 S26	7.3	20.0	36.8	0.8	1.5	1.7
Set 12 703 A48 S26	7.4	27.7	48.1	0.7	2.6	5.7
Set 12 709 A48 S26	10.3	35.4	42.0	0.3	12.1	1.3
Set 12 895 A48 S26	8.7	30.7	64.5	0.7	6.6	8.0
Set 12 1816 A48 S26	10.0	29.4	36.0	1.8	6.7	7.5
Set 12 1974 A48 S26	9.3	27.7	45.1	1.3	7.5	2.3
Set 12 2425 A48 S26	8.2	38.6	40.5	1.8	2.5	6.6
Set 12 3146 A48 S26	5.8	22.4	28.5	0.5	2.2	5.6
Set 12 889 A48 S26	7.2	21.9	30.6	0.9	5.9	2.8
Set 12 1814 A48 S26	7.3	19.3	25.2	2.6	7.8	7.6
Set 12 1245 A48 S26	8.3	47.7	58.2	2.0	19.3	10.5
Set 12 3196 A48 S26	8.0	20.2	27.0	0.4	6.9	7.2
Set 12 1450 A48 S26	7.5	27.4	40.4	1.8	9.7	6.6
Set 12 3169 A48 S26	8.4	18.2	30.5	0.8	3.1	7.4
Set 12 3477 A48 S26	12.5	44.1	59.8	2.2	10.3	5.5

Set 12 865 A48 S26	**13.0**	**38.2**	**42.5**	**2.4**	**5.3**	**8.4**
Set 12 1249 A48 S26	**47.7**	**74.5**	**88.6**	**9.0**	**13.3**	**12.3**
Set 12 1250 A48 S26	**11.5**	**56.4**	**66.0**	**2.4**	**7.2**	**7.4**
Set 12 2202 A48 S26	**6.7**	**28.1**	**33.2**	**0.8**	**5.4**	**4.9**
Set 12 1545 A48 S26	**37.0**	**72.7**	**61.7**	**10.9**	**13.6**	**24.3**
Set 12 1755 A48 S26	**8.4**	**25.9**	**39.7**	**2.4**	**4.7**	**6.4**

[00830] 实施例 4

[00831] 在不敏感细胞中的筛选

[00832] 在多种实施方案中，针对 β-联蛋白的优选 RNAi 剂是对 β-联蛋白特异并且在效果方面不显示脱靶效应的那些。因而，为了继续先导选择，将针对 β-联蛋白的各种 RNAi 剂对产生少量或不产生 β-联蛋白的细胞系进行测试。认为不明显降低这些所谓"不敏感细胞系"的生存力的 β-联蛋白 RNAi 剂具有微小脱靶效应或不具有脱靶效应。所用的"不敏感"细胞系是 NCI-H28 和 RKO。NCI-H28 是其中 β-联蛋白基因已经被缺失的间皮瘤细胞系；RKO 是具有低 β-联蛋白表达或无 β-联蛋白表达的结直肠细胞系。

[00833] 已经发现找到的 105 种针对 β-联蛋白的 RNAi 剂在剂量-反应分析中有效。将这些 RNAi 剂针对所用的"不敏感"细胞系 NCI-H28 和 RKO 以 50nM、10nM、1nM、0.1nM 和 0.0001nM 的剂量测试，并且在时间点 3 日、5 日和 7 日测试细胞生存力。

[00834] 在第 5 日在 50nM 或 10nM，以下 RNAi 剂展示 RKO 细胞的至少 80%生存力（不多于 20%生长抑制）和 NCI-H28 细胞的至少 80%生存力。

[00835] 表 7

RNAi 剂	IC50
AD-18963-b2	0.049
AD-25894-b1	0.004
AD-25914-b1	0.054
AD-25956-b1	0.042
AD-26028-b1	0.050
AD-26034-b1	0.009
AD-26108-b1	0.030
AD-26131-b1	0.104
AD-26134-b1	0.103
AD-26158-b1	0.033
AD-26193-b1	0.055

AD-26218-b1	0.026
AD-26652-b1	0.026
AD-26704-b1	0.010
AD-26900-b1	0.033
AD-26918-b1	0.029

[00836] 在第 5 日在 50nM 或 10nM，以下 RNAi 剂展示 RKO 细胞的至少 80％生存力（不多于 20％生长抑制）和 NCI-H28 细胞的约 60％至 80％生存力。

[00837] 表 8

RNAi 剂	IC50
AD-18983-b2	0.070
AD-25893-b1	0.040
AD-25918-b1	0.013
AD-25943-b1	0.080
AD-25944-b1	0.007
AD-25951-b1	0.007
AD-25958-b1	0.024
AD-26068-b1	0.102
AD-26109-b1	0.025
AD-26156-b1	0.020
AD-26673-b1	0.012
AD-26682-b1	0.007
AD-26696-b1	0.027
AD-26740-b1	0.006
AD-26752-b1	0.042
AD-26757-b1	0.047

AD-26779-b1	0.109
AD-26788-b1	0.053
AD-26800-b1	0.025

[00838] 因而,35 种针对 β-联蛋白的 RNAi 剂没有明显减少不依赖于 β-联蛋白的细胞系的生存力;这 35 种针对 β-联蛋白的 RNAi 剂是:AD-18963-b2、AD-18983-b2, AD-25893-b1, AD-25894-b1, AD-25914-b1, AD-25918-b1, AD-25943-b1, AD-25944-b1, AD-25951-b1, AD-25956-b1, AD-25958-b1, AD-26028-b1, AD-26034-b1, AD-26068-b1, AD-26108-b1, AD-26109-b1, AD-26131-b1, AD-26134-b1, AD-26156-b1, AD-26158-b1, AD-26193-b1, AD-26218-b1, AD-26652-b1, AD-26673-b1, AD-26682-b1, AD-26696-b1, AD-26704-b1, AD-26740-b1, AD-26752-b1, AD-26757-b1, AD-26779-b1, AD-26788-b1, AD-26800-b1, AD-26900-b1,和 AD-26918-b1(其中"b1"表示"批次 1")。

[00839] 实施例 5

[00840] 在敏感细胞系中的筛选

[00841] 对 35 种针对 β-联蛋白的 RNAi 剂进行进一步筛选,所述 RNAi 剂能够在体外减少 β-联蛋白表达,并且没有大幅度减少不依赖于 β-联蛋白的细胞系的生存,如先前实施例中所显示。

[00842] 在具有 APC 突变的 4 种结直肠细胞系 (LoVo、DLD-1、LS411N 和 SW403) 上测试这 35 种 RNAi 剂。在野生型 Wnt 途径中,β-联蛋白蛋白质由 GSK-3 磷酸化,并且随后被 APC 降解;因此,β-联蛋白的蛋白质水平不积累。然而,在 APC 突变的情况下,β-联蛋白不降解并且因此该蛋白质积累。实际上,这 4 个细胞系依赖于 β-联蛋白并且如果 β-联蛋白表达下调,则停止生长。

[00843] 将细胞系分别用 35 种针对 β-联蛋白的 RNAi 剂中的每一种以 50nM、10nM、1nM、0.1nM 和 0.0001nM 的剂量处理,并且在第 3、5 和 7 日测试。使用的数据来自以 1nM 处理的 DLD-1、以 1nM 处理的 LoVo 和以 0.1nM 处理的 LS411N,并且在第 7 日采集数据。不使用 SW403 数据,因为这些数据甚至在 0.1nM 时没有在多种 siRNA 之间区分。

[00844] 下文提供了敏感细胞系中针对 β-联蛋白的 RNAi 剂的筛选数据。

[00845] 表 9. 筛选数据

siRNA	Pos	物种	24小时平均IC50 (nM)	DLD1 1nM 第7日	LoVo 1nM 第7日	LS411N 0.1nM 第7日	PBMC
AD-18983	CDS	Hu, Cy, Mo	0.07	0.258	0.150	0.054	Neg
AD-26156	CDS	Hu, Cy, Mo	0.02	0.458	0.194	0.187	Neg
AD-25951	3'UTR	Hu, Cy	0.007	0.659	0.188	0.465	Neg
AD-26109	CDS	Hu, Cy	0.025	0.156	0.172	0.410	Neg
AD-26218	CDS	Hu, Cy	0.026	0.376	0.243	0.566	Neg
AD-25894	3'UTR	Hu, Cy	0.004	0.378	0.293	0.307	Neg
AD-26740	CDS	Hu, Cy	0.006	0.511	0.227	0.330	Neg
AD-26158	CDS	Hu, Cy	0.033	0.347	0.227	0.398	Neg
AD-26682	CDS	Hu, Cy	0.007	0.484	0.297	0.923	Neg
AD-26034	CDS	Hu, Cy	0.009	0.673	0.267	0.656	Neg
AD-25944	3'UTR	Hu, Cy	0.007	0.633	0.264	0.589	Neg
AD-26800	CDS	Hu, Cy	0.025	0.449	0.240	0.815	Neg
AD-26108	CDS	Hu, Cy	0.03	0.437	0.305	0.880	Neg
AD-26752	CDS	Hu, Cy	0.042	0.518	0.396	0.500	Neg
AD-26918	3'UTR	Hu, Cy	0.029	0.371	0.345	0.965	Neg

[00846] 在这个表中，显示出位置，其中 CDS 表示编码区段（或可读框），并且 3'UTR 表示 3' 非翻译区。还显示与 RNAi 剂匹配的 β－联蛋白的物种形式。因此，AD-18983 匹配人 (Hu) 形式、食蟹猴 (Cy) 形式和小鼠 (Mo) 形式 β－联蛋白的每一种。显示估计的 24 小时平均 IC_{50}(nM)。显的 DLD1、LoVo 和 LS411N 细胞中的细胞生存力。对于 AD-18983，"0.258"表示在 1nM 在第 7 日，存在 DLD1 细胞的 25.8％细胞生存力或 74.2％生存力降低。类似地，在 1nM 时存在 LoVo 细胞的 15.0％细胞生存力 (85.5％生存力降低)，并且（在 0.1nM 时）存在 LS411N 细胞的 5.4％细胞生存力 (94.6％生存力降低)。PBMC 表示作为测量 RNAi 剂潜在免疫原性的试验所使用的外周血单核细胞细胞测定法；"Neg"表示 RNAi 剂不激发如 INF-α 和 TNF-α 增加所示的免疫反应。

[00847] 因此，以下针对 β－联蛋白的 RNAi 剂显示在依赖 β－联蛋白而生长的至少一个结直肠细胞系中显著降低细胞生存力：AD-18963-b2，AD-25894-b1，AD-25944-b1，AD-25951-b1，AD-26034-b1，AD-26108-b1，AD-26109-b1，AD-26156-b1，AD-26158-b1，AD-26218-b1，AD-26682-b1，AD-26740-b1，AD-26752-b1，AD-26800-b1，和 AD-26918-b1。

[00848] 等同物

[00849] 实施方案 1 的组合物是包含了含有有义链和反义链的 RNAi 剂的组合物，其中反义链包含与针对表 1 中提供的 β－联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00850] 组合物 1 的组合物，其中组合物还包含针对 β－联蛋白的第二 RNAi 剂。

[00851] 实施方案 1 的组合物，其中反义链具有 30 个或更少的核苷酸长度。

[00852] 实施方案 1 的组合物，其中有义链和反义链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00853] 实施方案 1 的组合物，其中反义链和有义链独立地是 19 至 23 个核苷酸长度。

[00854] 实施方案 1 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00855] 实施方案 1 的组合物，其中 RNAi 剂包含至少一条修饰的主链和 / 或至少一个 2' 修饰的核苷酸。

[00856] 实施方案 1 的组合物，其中 RNAi 剂包含 :

a) 至少一个 5' - 尿苷 - 腺嘌呤 -3' (5' -ua-3') 二核苷酸，其中尿苷是 2' - 修饰的核苷酸 ;和 / 或

b) 至少一个 5' - 尿苷 - 鸟嘌呤 -3' (5' -ug-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸 ;和 / 或

c) 至少一个 5' - 胞苷 - 腺嘌呤 -3' (5' -ca-3') 二核苷酸，其中 5' - 胞苷是 2' - 修饰的核苷酸 ;和 / 或

d) 至少一个 5' - 尿苷 - 尿苷 -3' (5' -uu-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸。

[00857] 实施方案 1 的组合物，其中 RNAi 剂包含选自以下的 2' - 修饰 :2' - 脱氧、2' - 脱氧 -2' - 氟、2' -O- 甲基、2' -O- 甲氧乙基 (2' -O-MOE)、2' -O- 氨基丙基 (2' -O-AP)、2' -O- 二甲基氨基乙基 (2' -O-DMAOE)、2' -O- 二甲氨基丙基 (2' -O-DMAP)、2' -O- 二甲基氨基乙基氧乙基 (2' -O-DMAEOE) 和 2' -O-N- 甲基乙酰氨基 (2' -O-NMA)。

[00858] 实施方案 1 的组合物，其中 RNAi 剂包含平末端。

[00859] 实施方案 1 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[00860] 实施方案 1 的组合物，其中 RNAi 剂在 RNAi 剂的反义链的 3' 末端处包含突出端。

[00861] 实施方案 1 的组合物，其中 RNAi 剂连接至选自以下的一种或多种物质 :一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[00862] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β - 联蛋白基因的表达至少约 60%。

[00863] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β - 联蛋白基因的表达至少约 70%。

[00864] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β - 联蛋白基因的表达至少约 80%。

[00865] 实施方案 1 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β - 联蛋白基因的表达至少约 90%。

[00866] 实施方案 1 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[00867] 实施方案 1 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[00868] 实施方案 1 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[00869] 实施方案 2 的组合物是一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链和第二链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的第一链和第二链分别差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00870] 实施方案 2 的组合物，其中组合物包含针对 β-联蛋白的第二 RNAi 剂。

[00871] 实施方案 2 的组合物，其中第二链具有 30 个或更少的核苷酸长度。

[00872] 实施方案 2 的组合物，其中第一链和第二链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00873] 实施方案 2 的组合物，其中第一链和第二链独立地是 19 至 23 个核苷酸长度。

[00874] 实施方案 2 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00875] 实施方案 2 的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2'-修饰的核苷酸。

[00876] 实施方案 2 的组合物，其中 RNAi 剂包含：

至少一个 5'-尿苷-腺嘌呤-3'(5'-ua-3') 二核苷酸，其中尿苷是 2'-修饰的核苷酸；和 / 或至少一个 5'-尿苷-鸟嘌呤-3'(5'-ug-3') 二核苷酸，其中 5'-尿苷是 2'-修饰的核苷酸；

和 / 或至少一个 5'-胞苷-腺嘌呤-3'(5'-ca-3') 二核苷酸，其中 5'-胞苷是 2'-修饰的核苷酸；

和 / 或至少一个 5'-尿苷-尿苷-3'(5'-uu-3') 二核苷酸，其中 5'-尿苷是 2'-修饰的核苷酸。

实施方案 2 的组合物，其中 RNAi 剂包含选自以下的一个或多个 2'-修饰：

2'-脱氧、2'-脱氧-2'-氟、2'-O-甲基、2'-O-甲氧乙基 (2'-O-MOE)、2'-O-氨基丙基 (2'-O-AP)、2'-O-二甲基氨基乙基 (2'-O-DMAOE)、2'-O-二甲氨基丙基 (2'-O-DMAP)、2'-O-二甲基氨基乙基氧乙基 (2'-O-DMAEOE) 和 2'-O-N-甲基乙酰氨基 (2'-O-NMA)。

[00877] 实施方案 2 的组合物，其中 RNAi 剂包含平末端。

[00878] 实施方案 2 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[00879] 实施方案 2 的组合物，其中 RNAi 剂在反义链的 3' 末端处包含突出端。

[00880] 实施方案 2 的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自：一种或多种诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[00881] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β-联蛋白基因的表达至少约 60%。

[00882] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或

SK-BR-3 细胞中体外抑制 β-联蛋白基因的表达至少约 70%。

[00883] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β-联蛋白基因的表达至少约 80%。

[00884] 实施方案 2 的组合物，其中 RNAi 剂能够以 10nM 浓度在 HeLa、GTL-16 或 SK-BR-3 细胞中体外抑制 β-联蛋白基因的表达至少约 90%。

[00885] 实施方案 2 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[00886] 实施方案 2 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[00887] 实施方案 2 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[00888] 实施方案 3 的方法是一种治疗个体中 β-联蛋白相关疾病的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00889] 实施方案 3 的方法，其中 β-联蛋白相关疾病是癌症、自身免疫或病毒病。

[00890] 实施方案 3 的方法，其中 β-联蛋白相关疾病是癌症。

[00891] 实施方案 3 的方法，其中该方法还包括步骤：施用用于癌症、自身免疫或病毒病的额外治疗。

[00892] 实施方案 3 的方法，其中组合物包含针对 β-联蛋白的第二 RNAi 剂。

[00893] 实施方案 3 的方法，其中方法还包括步骤：施用针对 β-联蛋白的额外 RNAi 剂。

[00894] 实施方案 3 的方法，还包括施用额外的治疗。

[00895] 实施方案 3 的方法，其中额外的治疗是组合物。

[00896] 实施方案 3 的方法，其中额外的治疗是一种方法。

[00897] 实施方案 3 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[00898] 实施方案 4 的方法是一种方法，所述方法包括一种抑制个体中 β-联蛋白基因表达的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00899] 实施方案 4 的方法，其中个体罹患或易患 β-联蛋白相关疾病。

[00900] 实施方案 4 的方法，其中 β-联蛋白相关疾病是癌症、自身免疫或病毒病。

[00901] 实施方案 4 的方法，其中 β-联蛋白相关疾病是癌症。

[00902] 实施方案 4 的方法，还包括施用额外的治疗。

[00903] 实施方案 4 的方法，其中额外的治疗是组合物。

[00904] 实施方案 4 的方法，其中额外的治疗是方法。

[00905] 实施方案 4 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[00906] 实施方案 5 的组合物是一种组合物，所述组合物包含一种用于 RNAi 制剂中的药物，所述 RNAi 制剂包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-联蛋白特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00907] 以上的任何组合物，处于药学有效的制剂中。

[00908] 根据实施方案 5 的组合物，用于治疗个体中 β - 联蛋白相关疾病的方法中，所述方法包括步骤：向所述个体施用治疗有效量的根据实施方案 1 的组合物。

[00909] 根据实施方案 5 的组合物的用途，用于制造治疗 β - 联蛋白相关疾病的药物。

[00910] 实施方案 5 的用途，其中 β - 联蛋白相关疾病是癌症、自身免疫或病毒病。

[00911] 实施方案 5 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[00912] 实施方案 5 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

额外的等同物

[00913] 实施方案 6 的组合物，其包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β -ENaC 特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00914] 组合物 6 的组合物，其中组合物还包含针对 β -ENaC 的第二 RNAi 剂。

[00915] 实施方案 6 的组合物，其中反义链具有 30 个或更少的核苷酸长度。

[00916] 实施方案 6 的组合物，其中有义链和反义链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00917] 实施方案 6 的组合物，其中反义链和有义链独立地是 19 至 23 个核苷酸长度。

[00918] 实施方案 6 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00919] 实施方案 6 的组合物，其中 RNAi 剂包含至少一条修饰的主链和 / 或至少一个 2' 修饰的核苷酸。

[00920] 实施方案 6 的组合物，其中 RNAi 剂包含：

a) 至少一个 5' - 尿苷 - 腺嘌呤 -3' (5' -ua-3') 二核苷酸，其中尿苷是 2' - 修饰的核苷酸；和 / 或

b) 至少一个 5' - 尿苷 - 鸟嘌呤 -3' (5' -ug-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸；和 / 或

c) 至少一个 5' - 胞苷 - 腺嘌呤 -3' (5' -ca-3') 二核苷酸，其中 5' - 胞苷是 2' - 修饰的核苷酸；和 / 或

d) 至少一个 5' - 尿苷 - 尿苷 -3' (5' -uu-3') 二核苷酸，其中 5' - 尿苷是 2' - 修饰的核苷酸。

[00921] 实施方案 6 的组合物，其中 RNAi 剂包含选自以下的 2' - 修饰：2' - 脱氧、2' - 脱氧 -2' - 氟、2' -O- 甲基、2' -O- 甲氧乙基 (2' -O-MOE)、2' -O- 氨基丙基 (2' -O-AP)、2' -O- 二甲基氨基乙基 (2' -O-DMAOE)、2' -O- 二甲氨基丙基 (2' -O-DMAP)、2' -O- 二甲基氨基乙基氧乙基 (2' -O-DMAEOE) 和 2' -O-N- 甲基乙酰氨基 (2' -O-NMA)。

[00922] 实施方案 6 的组合物，其中 RNAi 剂包含平末端。

[00923] 实施方案 6 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[00924] 实施方案 6 的组合物，其中 RNAi 剂在 RNAi 剂的反义链的 3' 末端处包含突出端。

[00925] 实施方案 6 的组合物，其中 RNAi 剂连接至选自以下的一种或多种物质：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁

萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[00926] 实施方案 6 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 60％。

[00927] 实施方案 6 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 70％。

[00928] 实施方案 6 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 80％。

[00929] 实施方案 6 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 90％。

[00930] 实施方案 6 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[00931] 实施方案 6 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[00932] 实施方案 6 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[00933] 实施方案 7 的组合物是一种组合物，其包含了含有第一链和第二链的 RNAi 剂，其中第一链和第二链包含与表 1 中提供的针对 β -ENaC 特异的 RNAi 剂的第一链和第二链分别差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00934] 实施方案 7 的组合物，其中组合物包含针对 β -ENaC 的第二 RNAi 剂。

[00935] 实施方案 7 的组合物，其中第二链具有 30 个或更少的核苷酸长度。

[00936] 实施方案 7 的组合物，其中第一链和第二链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00937] 实施方案 7 的组合物，其中第一链和第二链独立地是 19 至 23 个核苷酸长度。

[00938] 实施方案 7 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00939] 实施方案 7 的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2'- 修饰的核苷酸。

[00940] 实施方案 7 的组合物，其中 RNAi 剂包含：

至少一个 5'- 尿苷 - 腺嘌呤 -3'(5'-ua-3') 二核苷酸，其中尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 鸟嘌呤 -3'(5'-ug-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸；

和 / 或至少一个 5'- 胞苷 - 腺嘌呤 -3'(5'-ca-3') 二核苷酸，其中 5'- 胞苷是 2'- 修饰的核苷酸；

和 / 或至少一个 5'- 尿苷 - 尿苷 -3'(5'-uu-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸。

[00941] 实施方案 7 的组合物，其中 RNAi 剂包含选自以下的一个或多个 2'- 修饰：

2'- 脱氧、2'- 脱氧 -2'- 氟、2'-O- 甲基、2'-O- 甲氧乙基 (2'-O-MOE)、2'-O- 氨基丙基 (2'-O-AP)、2'-O- 二甲基氨基乙基 (2'-O-DMAOE)、2'-O- 二甲氨基丙基 (2'-O-DMAP)、2'-O- 二甲基氨基乙基氧乙基 (2'-O-DMAEOE) 和 2'-O-N- 甲基乙酰氨基 (2'-O-NMA)。

[00942] 实施方案 7 的组合物，其中 RNAi 剂包含平末端。

[00943] 实施方案 7 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[00944] 实施方案 7 的组合物，其中 RNAi 剂在反义链的 3' 末端处包含突出端。

[00945] 实施方案 7 的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[00946] 实施方案 7 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 60％。

[00947] 实施方案 7 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 70％。

[00948] 实施方案 7 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 80％。

[00949] 实施方案 7 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 90％。

[00950] 实施方案 7 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[00951] 实施方案 7 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[00952] 实施方案 7 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[00953] 实施方案 8 的方法是一种治疗个体中 β-ENaC 相关疾病的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-ENaC 特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00954] 实施方案 8 的方法，其中 β-ENaC 相关疾病是囊性纤维化、假性醛固酮减少症 1 型 (PHA1)、Liddle's 综合征、高血压、碱中毒、低钾血症和 / 或肥胖症相关性高血压。

[00955] 实施方案 8 的方法，其中 β-ENaC 相关疾病是囊性纤维化。

[00956] 实施方案 8 的方法，其中该方法还包括步骤：施用用于囊性纤维化、假性醛固酮减少症 1 型 (PHA1)、Liddle's 综合征、高血压、碱中毒、低钾血症和 / 或肥胖症相关性高血压的额外治疗。

[00957] 实施方案 8 的方法，其中组合物包含针对 β-ENaC 的第二 RNAi 剂。

[00958] 实施方案 8 的方法，其中方法还包括步骤：施用针对 β-ENaC 的额外 RNAi 剂。

[00959] 实施方案 8 的方法，还包括施用额外的治疗。

[00960] 实施方案 8 的方法，其中额外的治疗是组合物。

[00961] 实施方案 8 的方法，其中额外的治疗是方法。

[00962] 实施方案 8 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[00963] 实施方案的方法 9 是一种抑制个体中 β-ENaC 基因表达的方法，包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-ENaC 特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核

苷酸的至少 15 个连续核苷酸。

[00964] 实施方案 9 的方法，其中个体罹患或易患 β-ENaC 相关疾病。

[00965] 实施方案 9 的方法，其中 β-ENaC 相关疾病是囊性纤维化、假性醛固酮减少症 1 型 (PHA1)、Liddle's 综合征、高血压、碱中毒、低钾血症和 / 或肥胖症相关性高血压。

[00966] 实施方案 9 的方法，其中 β-ENaC 相关疾病是囊性纤维化。

[00967] 实施方案 9 的方法，还包括施用额外的治疗。

[00968] 实施方案 9 的方法，其中额外的治疗是组合物。

[00969] 实施方案 9 的方法，其中额外的治疗是方法。

[00970] 实施方案 9 的方法，其中额外的治疗和 RNAi 剂可以按任意顺序施用。

[00971] 一种用于 RNAi 制剂中的药物，所述 RNAi 制剂包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-ENaC 特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[00972] 实施方案的组合物 10 是一种组合物，所述组合物包含了含有第一链和第二链的 RNAi 剂，其中第一链的序列包含表 1 中提供的对 β-ENaC 特异的 RNAi 剂的第一链的序列。

[00973] 实施方案 10 的组合物，其中组合物包含针对 β-ENaC 的第二 RNAi 剂。

[00974] 实施方案 10 的组合物，其中第二链具有 30 个或更少的核苷酸长度。

[00975] 实施方案 10 的组合物，其中第一链和第二链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00976] 实施方案 10 的组合物，其中第一链和第二链独立地是 19 至 23 个核苷酸长度。

[00977] 实施方案 10 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00978] 实施方案 10 的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2'- 修饰的核苷酸。

[00979] 实施方案 10 的组合物，其中 RNAi 剂包含：

至少一个 5'- 尿苷 - 腺嘌呤 -3'(5'-ua-3') 二核苷酸，其中尿苷是 2'- 修饰的核苷酸；和 / 或至少一个 5'- 尿苷 - 鸟嘌呤 -3'(5'-ug-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸；

和 / 或至少一个 5'- 胞苷 - 腺嘌呤 -3'(5'-ca-3') 二核苷酸，其中 5'- 胞苷是 2'- 修饰的核苷酸；

和 / 或至少一个 5'- 尿苷 - 尿苷 -3'(5'-uu-3') 二核苷酸，其中 5'- 尿苷是 2'- 修饰的核苷酸。

[00980] 实施方案 10 的组合物，其中 RNAi 剂包含一个或多个 2'- 修饰选自：

2'- 脱氧、2'- 脱氧 -2'- 氟、2'-O- 甲基、2'-O- 甲氧乙基 (2'-O-MOE)、2'-O- 氨基丙基 (2'-O-AP)、2'-O- 二甲基氨基乙基 (2'-O-DMAOE)、2'-O- 二甲氨基丙基 (2'-O-DMAP)、2'-O- 二甲基氨基乙基氧乙基 (2'-O-DMAEOE) 和 2'-O-N- 甲基乙酰氨基 (2'-O-NMA)。

[00981] 实施方案 10 的组合物，其中 RNAi 剂包含平末端。

[00982] 实施方案 10 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[00983] 实施方案 10 的组合物，其中 RNAi 剂在反义链的 3' 末端处包含突出端。

[00984] 实施方案 10 的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[00985] 实施方案 10 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 60％。

[00986] 实施方案 10 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 70％。

[00987] 实施方案 10 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 80％。

[00988] 实施方案 10 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β -ENaC 基因的表达至少约 90％。

[00989] 实施方案 10 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[00990] 实施方案 10 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[00991] 实施方案 10 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[00992] 实施方案的组合物 11 是一种组合物，所述组合物包含了含有第一链和第二链的 RNAi 剂，其中第一链的序列是表 1 中提供的对 β -ENaC 特异的 RNAi 剂的第一链的序列。

[00993] 实施方案 11 的组合物，其中组合物包含针对 β -ENaC 的第二 RNAi 剂。

[00994] 实施方案 11 的组合物，其中第二链具有 30 个或更少的核苷酸长度。

[00995] 实施方案 11 的组合物，其中第一链和第二链形成具有 15 至 30 个核苷酸对长度的双链体区。

[00996] 实施方案 11 的组合物，其中第一链和第二链独立地是 19 至 23 个核苷酸长度。

[00997] 实施方案 11 的组合物，其中 RNAi 剂包含引起 RNAi 剂在生物样品或环境中具有增加的稳定性的修饰。

[00998] 实施方案 11 的组合物，其中 RNAi 剂包含硫代磷酸酯和 / 或 2’ - 修饰的核苷酸。

[00999] 实施方案 11 的组合物，其中 RNAi 剂包含：

至少一个 5’ - 尿苷 - 腺嘌呤 -3’ (5’ -ua-3’) 二核苷酸，其中尿苷是 2’ - 修饰的核苷酸；和 / 或至少一个 5’ - 尿苷 - 鸟嘌呤 -3’ (5’ -ug-3’) 二核苷酸，其中 5’ - 尿苷是 2’ - 修饰的核苷酸；

和 / 或至少一个 5’ - 胞苷 - 腺嘌呤 -3’ (5’ -ca-3’) 二核苷酸，其中 5’ - 胞苷是 2’ - 修饰的核苷酸；

和 / 或至少一个 5’ - 尿苷 - 尿苷 -3’ (5’ -uu-3’) 二核苷酸，其中 5’ - 尿苷是 2’ - 修饰的核苷酸。

[001000] 实施方案 11 的组合物，其中 RNAi 剂包含一个或多个 2’ - 修饰选自：

2’ - 脱氧、2’ - 脱氧 -2’ - 氟、2’ -O- 甲基、2’ -O- 甲氧乙基 (2’ -O-MOE)、2’ -O- 氨基丙

基 (2'-O-AP)、2'-O- 二甲基氨基乙基 (2'-O-DMAOE)、2'-O- 二甲氨基丙基 (2'-O-DMAP)、2'-O- 二甲基氨基乙基氧乙基 (2'-O-DMAEOE) 和 2'-O-N- 甲基乙酰氨基 (2'-O-NMA)。

[001001] 实施方案 11 的组合物，其中 RNAi 剂包含平末端。

[001002] 实施方案 11 的组合物，其中 RNAi 剂包含具有 1 至 4 个非配对核苷酸突出端。

[001003] 实施方案 11 的组合物，其中 RNAi 剂在反义链的 3' 末端处包含突出端。

[001004] 实施方案 11 的组合物，其中 RNAi 剂连接至一种或多种物质，所述物质选自：诊断化合物、报道基团、交联剂、赋予核酸酶抗性的部分、天然或异常核碱基、亲脂分子、胆固醇、脂质、凝集素、类固醇、熊果醇、龙舌兰皂苷配基、薯蓣皂苷配基、萜、三萜、菝葜皂苷元、无羁萜、表木栓醇衍生化的石胆酸、维生素、糖、葡聚糖、普鲁分支葡聚糖、壳多糖、脱乙酰壳多糖、合成糖、低聚乳酸酯 15 聚物、天然聚合物、低分子量或中分子量聚合物、菊糖、环糊精、透明质酸、蛋白质、蛋白质结合剂、整联蛋白靶向分子、聚阳离子、肽、多胺、肽模拟物和 / 或转铁蛋白。

[001005] 实施方案 11 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 60%。

[001006] 实施方案 11 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 70%。

[001007] 实施方案 11 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 80%。

[001008] 实施方案 11 的组合物，其中 RNAi 剂能够以 10nM 浓度在 H441 细胞中体外抑制 β-ENaC 基因的表达至少约 90%。

[001009] 实施方案 11 的组合物，其中 RNAi 具有不多于约 0.1nM 的 EC_{50}。

[001010] 实施方案 11 的组合物，其中 RNAi 具有不多于约 0.01nM 的 EC_{50}。

[001011] 实施方案 11 的组合物，其中 RNAi 具有不多于约 0.001nM 的 EC_{50}。

[001012] 实施方案的组合物 12 是以上在药学有效制剂中的任何组合物。[001013] 根据实施方案 12 的组合物，用在治疗个体中 β-ENaC 相关疾病的方法中，所述方法包括步骤：向所述个体施用治疗有效量的组合物，所述组合物包含了含有有义链和反义链的 RNAi 剂，其中反义链包含与表 1 中提供的针对 β-ENaC 特异的 RNAi 剂的反义链差异 0、1、2 或 3 个核苷酸的至少 15 个连续核苷酸。

[001014] 根据实施方案 12 的组合物的用途，用于制造治疗 β-ENaC 相关疾病的药物。

[001015] 根据实施方案 12 的组合物的用途，其中 β-ENaC 相关疾病是囊性纤维化、假性醛固酮减少症 1 型 (PHA1)、Liddle's 综合征、高血压、碱中毒、低钾血症和 / 或肥胖症相关性高血压。

[001016] 实施方案 12 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[001017] 实施方案 12 的组合物，其中全部嘧啶均是 2' O- 甲基修饰的核苷酸。

[001018] 除非另外定义，否则本文所用的技术术语和科学术语具有与熟悉本公开所属技术领域的专业人员通常所理解的相同意思。

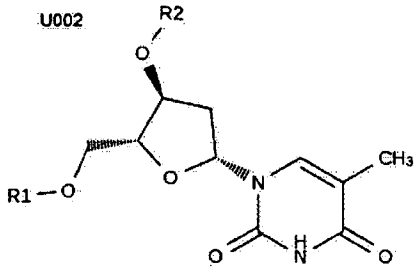
[001019] 除非另外指明，否则如技术人员将显而易见，没有详细描述的全部方法、步骤、技术和操作可以按本身已知的方式进行并且已经按本身已知的方式进行。例如再次参考本文中提到的标准手册和一般背景技术并参考其中所引用的其他参考文献。除非另外指

明，否则通过引用的方式完地并入本文援引的每份参考文献。

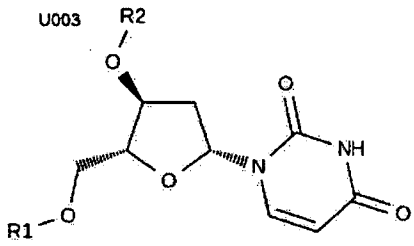
[001020] 对本发明的权利要求是非限制的并且在下文提供。

[001021] 虽然已经在本文中详细公开具体实施方案和权利要求，但是这仅出于说明目的以举例方式进行，并且不意在限制所附权利要求书的范围或任何相应未来应用的权利要求的主题的范围。具体而言，发明人构思了可以对本公开作出各种替换、改变和修改而不脱离如权利要求书所定义的本公开的精神和范围。认为选择核酸起始材料、目的克隆或文库类型是知晓本文所述的实施方案的本领域技术人员的例行工作。其他方面、优点和修改视为处于以下权利要求的范围内。使用不过为例行的实验，本领域技术人员将识别或能够确定本文所述的本发明具体实施方案的许多等同物。此类等同物意在由以下权利要求书涵盖。对稍后提交的相应申请中权利要求书范围的重新起草可以归因于各个国家的专利法的限制并且不应当解读为放弃权利要求的主题。

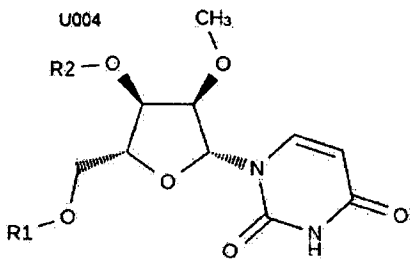
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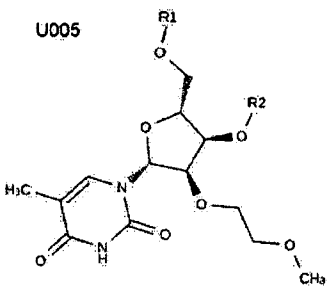
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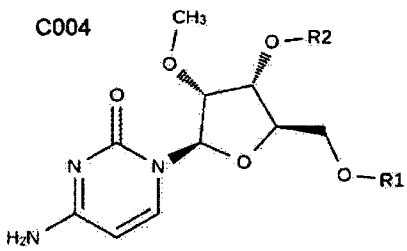
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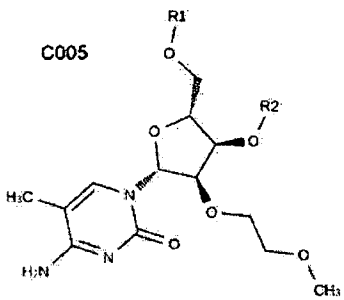
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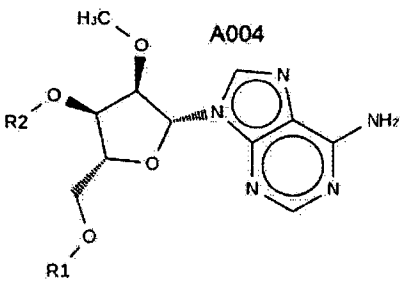
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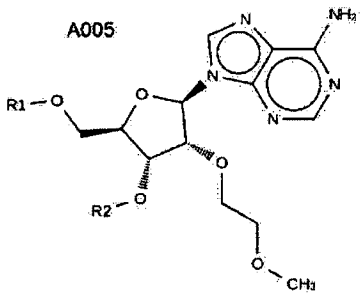
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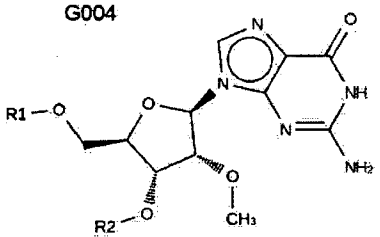
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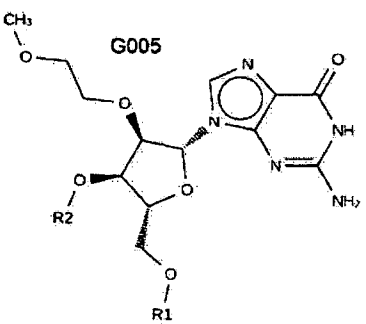
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Abstract

The present disclosure relates to RNAi agents useful in methods of treating Beta-Catenin-related diseases such as adenomatous polyposis of the colon, colorectal cancer, basal cell carcinoma, breast cancer, kidney cancer, Wilms tumors, medulloblastoma, ovarian cancer, adrenocortical tumors, gastric cancer, liver cancer, melanoma, pancreatic cancers, prostate cancer, renal cancer, ectopic teeth and taste papillae, skin cancer, pilomatrixoma, anaplastic thyroid carcinoma, and uterine carcinosarcoma, oligodontia, osteoporosis, ageing, degenerative diseases, bedsores, chronic wounds and impaired wound healing, and similar and related diseases, using a therapeutically effective amount of a RNAi agent to Beta-Catenin.