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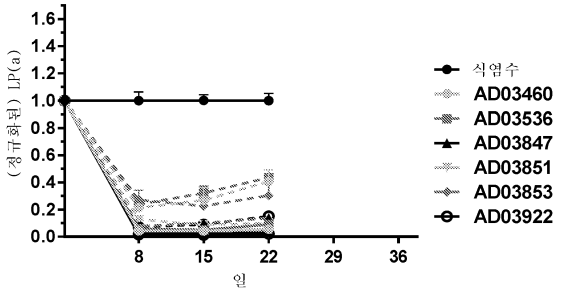
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(54) 발명의 명칭 **LPA의 유전자 발현을 저해하기 위한 조성물 및 방법**

(57) 요 약

LPA(아포(a)) 유전자의 발현을 저해하기 위한 RNA 간섭(RNAi) 물질 및 RNAi 물질 접합체가 기재되어 있다. 임의로 하나 이상의 추가 치유제와 함께 하나 이상의 LPA RNAi 물질을 포함하는 약제학적 조성물이 또한 기재되어 있다. 생체내 간 세포로의 기재된 LPA RNAi 물질의 전달은 LPA 유전자 발현의 저해 및 심혈관 및 심혈관 관련 질환의 치료를 제공한다.

대 표 도



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명 세 서

청구범위

청구항 1

센스 가닥 및 안티센스 가닥을 포함하는 LPA RNA 간섭(RNAi) 물질이며,

상기 안티센스 가닥이 서열 번호 1280, 서열 번호 1282, 서열 번호 1246, 서열 번호 1242, 서열 번호 1244, 또는 서열 번호 1254 중 임의의 하나의 서열을 포함하고, 상기 센스 가닥이 상기 안티센스 가닥의 서열에 상보성인 서열을 포함하는 것인 LPA RNAi 물질.

청구항 2

제1항에 있어서, 상기 센스 가닥 및 안티센스 가닥이 각각 19개 내지 26개의 뉴클레오타이드 길이인 LPA RNAi 물질.

청구항 3

제2항에 있어서, 상기 센스 가닥 및 안티센스 가닥이 각각 21개의 뉴클레오타이드 길이인 LPA RNAi 물질.

청구항 4

제1항에 있어서, 1개 또는 2개의 오버행(overhang)을 포함하는 LPA RNAi 물질.

청구항 5

제4항에 있어서, 안티센스 가닥의 3' 말단에 오버행을 포함하는 LPA RNAi 물질.

청구항 6

제4항에 있어서, 안티센스 가닥의 3' 말단에 오버행 및 센스 가닥의 3' 말단에 오버행을 포함하는 LPA RNAi 물질.

청구항 7

제1항에 있어서, 1개 또는 2개의 무딘 말단(blunt end)을 포함하는 LPA RNAi 물질.

청구항 8

제7항에 있어서, 2개의 무딘 말단을 포함하는 LPA RNAi 물질.

청구항 9

제1항에 있어서, 상기 센스 가닥, 상기 안티센스 가닥, 또는 상기 센스 가닥 및 안티센스 가닥 둘 다가 하나 이상의 변형된 뉴클레오타이드를 포함하는 것인 LPA RNAi 물질.

청구항 10

제9항에 있어서, 상기 하나 이상의 변형된 뉴클레오타이드가 독립적으로 2'-변형된 뉴클레오타이드, 잠긴(locked) 뉴클레오타이드, 비염기성 뉴클레오타이드, 인버티드(inverted) 데옥시뉴클레오타이드, 모르폴리노 뉴클레오타이드, 2',3'-세코 뉴클레오타이드 모방체, 또는 비천연 염기 포함 뉴클레오타이드로부터 선택된 것인 LPA RNAi 물질.

청구항 11

제10항에 있어서, 상기 2'-변형된 뉴클레오타이드가 2'-O-메틸 뉴클레오타이드, 2'-데옥시-2'-플루오로 뉴클레오타이드, 2'-데옥시뉴클레오타이드, 2'-메톡시에틸 뉴클레오타이드, 2'-아미노 뉴클레오타이드, 또는 2'-알킬 뉴클레오타이드인 LPA RNAi 물질.

청구항 12

제1항에 있어서, 하나 이상의 포스포로티오에이트 뉴클레오사이드간 연결을 포함하는 LPA RNAi 물질.

청구항 13

제12항에 있어서, 상기 센스 및 안티센스 가닥 둘 다가 독립적으로 1개, 2개, 3개 또는 4개의 포스포로티오에이트 뉴클레오사이드간 연결을 포함하는 것인 LPA RNAi 물질.

청구항 14

제1항에 있어서, 표적화기를 추가로 포함하는 LPA RNAi 물질.

청구항 15

제14항에 있어서, 상기 표적화기가 아시알로당단백질 수용체 리간드를 포함하는 것인 LPA RNAi 물질.

청구항 16

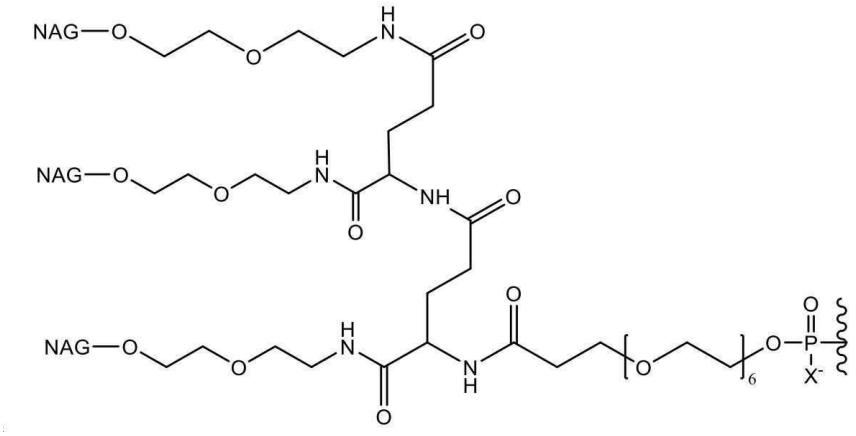
제15항에 있어서, 상기 아시알로당단백질 수용체 리간드가 갈락토스, 갈락토스아민, N-아세틸-갈락토스아민, 또는 갈락토스 유도체를 포함하는 것인 LPA RNAi 물질.

청구항 17

제14항에 있어서, 상기 표적화기가 (Chol-TEG), (TEG-Chol), (C11-PEG3-NAG3), (C6-PEG4-NAG3), (NAG3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 또는 (NAG37)인 LPA RNAi 물질.

청구항 18

제17항에 있어서, 상기 표적화기가 하기 구조를 포함하는 것인 LPA RNAi 물질.



여기서, NAG는 N-아세틸-갈락토스아민이고, X는 O 및 S로 이루어진 군으로부터 선택된다.

청구항 19

제14항에 있어서, 상기 표적화기가 상기 센스 가닥의 3' 말단에 접합된 것인 LPA RNAi 물질.

청구항 20

제14항에 있어서, 상기 표적화기가 상기 센스 가닥의 5' 말단에 접합된 것인 LPA RNAi 물질.

청구항 21

제1항에 있어서,

a) 상기 안티센스 가닥이 서열 번호 1280의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1284의 서열을 포함하거나,

b) 상기 안티센스 가닥이 서열 번호 1246의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1247의 서열을 포함하거나,

c) 상기 안티센스 가닥이 서열 번호 1242의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1243의 서열을 포함하거나,

d) 상기 안티센스 가닥이 서열 번호 1244의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1245의 서열을 포함하거나,

e) 상기 안티센스 가닥이 서열 번호 1254의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1255의 서열을 포함하거나,

f) 상기 안티센스 가닥이 서열 번호 1280의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1260의 서열을 포함하거나,

g) 상기 안티센스 가닥이 서열 번호 1282의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1259의 서열을 포함

하는 것인 LPA RNAi 물질.

청구항 22

제21항에 있어서, 상기 안티센스 가닥이 서열 번호 1280의 서열을 포함하고, 상기 센스 가닥이 서열 번호 1284의 서열을 포함하는 것인 LPA RNAi 물질.

청구항 23

제1항에 있어서,

a) 상기 안티센스 가닥이 서열 번호 188의 서열을 포함하고, 상기 센스 가닥이 서열 번호 384의 서열을 포함하거나,

b) 상기 안티센스 가닥이 서열 번호 156의 서열을 포함하고, 상기 센스 가닥이 서열 번호 310의 서열을 포함하거나,

c) 상기 안티센스 가닥이 서열 번호 164의 서열을 포함하고, 상기 센스 가닥이 서열 번호 357의 서열을 포함하거나,

d) 상기 안티센스 가닥이 서열 번호 164의 서열을 포함하고, 상기 센스 가닥이 서열 번호 376의 서열을 포함하거나,

e) 상기 안티센스 가닥이 서열 번호 164의 서열을 포함하고, 상기 센스 가닥이 서열 번호 384의 서열을 포함

하는 것인 LPA RNAi 물질.

청구항 24

제23항에 있어서, 상기 안티센스 가닥이 서열 번호 188의 서열을 포함하고 , 상기 센스 가닥이 서열 번호 384의 서열을 포함하는 것인 LPA RNAi 물질.

청구항 25

제1항에 있어서,

a) 상기 안티센스 가닥이 서열 번호 790에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서열 번호 1189에 따른 변형된 뉴클레오타이드 서열을 포함하거나,

b) 상기 안티센스 가닥이 서열 번호 637에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서열 번호 1132에 따른 변형된 뉴클레오타이드 서열을 포함하거나,

c) 상기 안티센스 가닥이 서열 번호 709에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서

열 번호 1135에 따른 변형된 뉴클레오타이드 서열을 포함하거나,

d) 상기 안티센스 가닥이 서열 번호 787에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서열 번호 1191에 따른 변형된 뉴클레오타이드 서열을 포함하거나,

e) 상기 안티센스 가닥이 서열 번호 788에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서열 번호 1189에 따른 변형된 뉴클레오타이드 서열을 포함

하는 것인 LPA RNAi 물질.

청구항 26

제25항에 있어서, 상기 안티센스 가닥이 서열번호 790에 따른 변형된 뉴클레오타이드 서열을 포함하고, 상기 센스 가닥이 서열 번호 1189에 따른 변형된 뉴클레오타이드 서열을 포함하는 것인 LPA RNAi 물질.

청구항 27

제26항에 있어서, 센스 가닥의 5' 말단에 접합된 (NAG25)s의 표적화기를 추가로 포함하는 것인 LPA RNAi 물질.

청구항 28

제1항 내지 제27항 중 어느 한 항의 LPA RNAi 물질을 포함하는, 관상동맥 질환의 치료를 요하는 대상체에서 관상동맥 질환을 치료하기 위한 약제학적 조성물.

청구항 29

제1항 내지 제27항 중 어느 한 항의 LPA RNAi 물질을 포함하는, 말초 동맥 질환의 치료를 요하는 대상체에서 말초 동맥 질환을 치료하기 위한 약제학적 조성물.

청구항 30

제1항 내지 제27항 중 어느 한 항의 LPA RNAi 물질을 포함하는, 심혈관 질환의 치료를 요하는 대상체에서 심혈관 질환을 치료하기 위한 약제학적 조성물.

청구항 31

제1항 내지 제27항 중 어느 한 항의 LPA RNAi 물질을 포함하는, 급성 관상동맥 증후군의 치료를 요하는 대상체에서 급성 관상동맥 증후군을 치료하기 위한 약제학적 조성물.

청구항 32

제1항 내지 제27항 중 어느 한 항의 LPA RNAi 물질을 포함하는, 질환의 치료를 요하는 대상체에서 질환을 치료하기 위한 약제학적 조성물이며,

상기 질환은 베르거(Berger) 질환, 대사 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환, 또는 정맥성 혈전증인, 약제학적 조성물.

발명의 설명

배 경 기 술

[0001] 지단백(a)[Lp(a)]은, 지질 코어 및 아포지단백 B(아포B-100)를, 다이설파이드 결합을 통해 아포B-100에 부착된, 아포지단백(a)(아포(a))인 독특한 성분과 함께, 함유하는 불균일 저밀도 지단백(low density lipoprotein: LDL) 유사 입자이다.

[0002] 아포(a) 유전자(*LPA*)는 주로 간에서 발현되고, 발현은 인간 및 비인간 영장류로 제한된다. 인간에서의 Lp(a) 수준은 유전적으로 한정되고, 식이, 운동 또는 다른 라이프사이클 변화에 의해 상당히 변하지 않는다. *LPA*는 존재하는 Kringle KIV2 도메인의 수에 따라 길이가 변하고, 이의 발현은 존재하는 도메인의 수와 역으로 상관된다. 정상 Lp(a) 수준은 0.1 내지 25㎎/㎗의 범위이고, 미합중국에서의 집단의 약 25%는 30㎎/㎗ 이상의 Lp(a) 수준

을 가진다.

[0003] 다수의 연구에서의 Lp(a) 수준의 분석은 심혈관 질환, 뇌졸중 및 다른 관련 장애, 예컨대 죽상동맥경화성 협착증에 대한 독리적 위험 인자로서 높은 Lp(a) 수준을 시사하였다. 또한, 게놈형 회합 분석은 또한 죽상동맥경화성 협착증과 같은 질환에 대한 유전적 위험 인자로서 LPA를 시사하였다.

[0004] 고지혈증 환자에서 Lp(a) 및 LDL 수준 둘 다를 낮추기 위해 치료학적 지단백 성분채집술을 이용할 때, 심혈관 사건의 상당한 감소가 관찰되었다. 따라서, 이들 및 다른 LPA 관련 질환에 관한 치유제 및 치료제에 대한 수요가 존재한다.

발명의 내용

[0005] *LPA* 유전자의 발현을 선택적으로 및 효율적으로 저해하기 위한, LPA(또한 아포(a)라 칭함) RNA 간섭(RNAi) 물질(또한 RNAi 트리거 또는 트리거라 칭함) 및 LPA RNAi 물질을 함유하는 조성물이 본 명세서에 기재되어 있다. *LPA*는 지단백(a) 입자(Lp(a))의 중요한 성분인 아포지단백(a)(아포(a))을 코딩하는 유전자의 명칭이다. 본 명세서에 기재된 LPA RNAi 물질은, 베르거(Berger) 질환, 말초 동맥 질환, 관상동맥 질환, 대사 증후군, 급성 관상동맥 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 뇌혈관 질환, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 급성 관상동맥 증후군, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환 및 정맥성 혈전증(이들로 제한되지는 않음)을 포함하는, 질환의 예방 또는 치료 또는 이 질환의 예방 또는 치료를 위한 약제의 제조시 사용될 수 있다.

[0006] 각각의 LPA RNAi 물질은 적어도 센스 가닥 및 안티센스 가닥을 포함한다. 센스 가닥 및 안티센스 가닥은 서로에 부분적으로, 실질적으로 또는 완전히 상보성이다. 본 명세서에 기재된 RNAi 물질 센스 및 안티센스 가닥의 길이는 각각 17개 내지 30개의 뉴클레오타이드 길이일 수 있다. 몇몇 실시형태에서, 센스 및 안티센스 가닥은 독립적으로 17개 내지 26개의 뉴클레오타이드 길이이다. 센스 및 안티센스 가닥은 동일한 길이 또는 상이한 길이일 수 있다. 본 명세서에 기재된 RNAi 물질은, LPA 유전자를 발현하는 세포에 전달 시, 시험관내 또는 생체내 LPA 유전자의 발현을 저해한다.

[0007] LPA RNAi 물질의 센스 가닥은 *LPA* mRNA에서의 서열에 적어도 17개의 연속적 뉴클레오타이드의 코어 스트레치에 걸쳐 적어도 90%의 동일성을 가지는 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, *LPA* mRNA에서의 서열에 적어도 90%의 동일성을 가지는 센스 가닥 뉴클레오타이드 서열은 17개, 18개, 19개, 20개, 21개, 22개 또는 23개의 뉴클레오타이드 길이이다. LPA RNAi 물질의 안티센스 가닥은 *LPA* mRNA에서의 서열에 적어도 16개의 연속적 뉴클레오타이드의 코어 스트레치 및 상응하는 센스 가닥에 걸쳐 적어도 90%의 상보성을 가지는 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, *LPA* mRNA에서의 서열에 적어도 90%의 상보성을 가지는 안티센스 가닥 뉴클레오타이드 서열 또는 상응하는 센스 가닥은 17개, 18개, 19개, 20개, 21개, 22개 또는 23개의 뉴클레오타이드 길이이다.

[0008] 몇몇 실시형태에서, 하나 이상의 LPA RNAi 물질은 당해 분야에 공지된 임의의 올리고뉴클레오타이드 전달 기법을 이용하여 표적 세포 또는 조직으로 전달된다. 핵산 전달 방법은 리포솜에서의 캡슐화에 의한, 이온도입법에 의한, 또는 다른 비히클, 예컨대 하이드로겔, 사이클로덱스트린, 생분해성 나노캡슐 및 생접착성 마이크로구, 단백질성 벡터 또는 Dynamic Polyconjugates(상표명)(DPC)로의 혼입에 의한 것을 포함하지만, 이들로 제한되지는 않는다(예를 들어, WO 제2000/053722호, WO 제2008/0022309호, WO 제2011/104169호 및 WO 제2012/083185호(이들은 각각 본 명세서에 참고로 포함됨) 참조). 몇몇 실시형태에서, LPA RNAi 물질은 표적화기에 접합된다. 몇몇 실시형태에서, 표적화기는 세포 수용체 리간드, 예컨대 갈락토스 클러스터, 예컨대 N-아세틸-갈락토스아민 삼합체를 포함하는 갈락토스 클러스터를 포함할 수 있다.

[0009] 몇몇 실시형태에서, 하나 이상의 LPA RNAi 물질을 포함하는 약제학적 조성물이 기재되어 있다. 몇몇 실시형태에서, LPA RNAi 물질은 하나 이상의 추가(즉, 제2, 제3 등) 치유제와 임의로 조합된다. 추가 치료제는 또 다른 LPA RNAi 물질(예를 들어, LPA 표적 내에 상이한 서열을 표적화하는 LPA RNAi 물질)일 수 있다. 추가 치료제는 또한 소분자 약물, 항체, 항체 단편 및/또는 백신일 수 있다. 하나 이상의 추가 치유제와 함께 또는 이것 없이 LPA RNAi 물질은 하나 이상의 부형제와 조합되어 약제학적 조성물을 형성할 수 있다.

[0010] 몇몇 실시형태에서, 표적화기에 접합된, LPA RNAi 물질을 포함하는, 간 세포, 특히 간세포로 LPA RNAi 물질을 전달하기 위한 조성물이 생체내 기재되어 있다. 몇몇 실시형태에서, 표적화기는 아시알로당단백질 리간드이다.

[0011] 적어도 부분적으로 LPA 발현에 의해 매개된 병리학적 상태를 가지거나 이 병리학적 상태를 발생시킬 위험에 있는 인간 대상체를 치료하는 방법이 또한 기재되어 있고, 상기 방법은 치료학적 유효량의 LPA RNAi 물질 또는 LPA RNAi 물질 함유 조성물을 대상체에게 투여하는 단계(들)를 포함한다. LPA RNAi 물질 또는 LPA RNAi 물질 함유 조성물에 의해 대상체를 치료하는 방법은 하나 이상의 추가(즉, 제2) 치유제 또는 치료를 투여하는 하나 이상의 단계와 임의로 조합될 수 있다. LPA RNAi 물질 및 추가 치유제는 단일 조성물로 투여될 수 있거나, 별개로 투여될 수 있다. 추가 치유제의 예는 HMg Co-A 환원효소 저해제(스타틴), 에제티미브, PCSK-9 저해제, CTEP 저해제, ANGPTL3을 표적화하는 치료제, APOC3을 표적화하는 치료제 및 니아신을 포함하지만, 이들로 제한되지는 않는다.

[0012] 기재된 LPA RNAi 물질의 사용은 베르거 질환, 말초 동맥 질환, 관상동맥 동맥 질환, 대사 증후군, 급성 관상동맥 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 뇌혈관 질환, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 급성 관상동맥 증후군, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환 및 정맥성 혈전증(이들로 제한되지는 않음)을 포함하는 질환의 치료학적 예방 또는 치료를 위한 방법에서 사용될 수 있다. 이러한 방법은 대상체, 예를 들어, 인간 또는 동물 대상체에 대한 본 명세서에 기재된 바와 같은 LPA RNAi 물질의 투여를 포함한다.

[0013] 약제학적 조성물은 국소 또는 전신 치료가 원해지는지 및 치료되는 부위에 따라 다수의 방식으로 투여될 수 있다. 투여는 당해 분야에 흔히 공지된 임의의 방식, 예컨대 국소(예를 들어, 경피 패치에 의해), 폐(예를 들어, 분무기에 의한 것을 포함하여, 분말 또는 에어로졸의 흡입 또는 통기법에 의해, 기관내, 비강내), 표피, 경피, 경구 또는 비경구(이들로 제한되지는 않음)에 의해 이루어질 수 있다. 비경구 투여는 정맥내, 동맥내, 피하, 복강내 또는 근육내 주사 또는 점적주사; (예를 들어, 이식 장치를 통한) 피하, 두개내, 뇌실질내, 척추강내 및 심실내 투여를 포함하지만, 이들로 제한되지는 않는다. 몇몇 실시형태에서, 본 명세서에 기재된 약제학적 조성물은 피하 주사에 의해 투여된다.

[0014] 기재된 LPA RNAi 물질 및/또는 조성물은 베르거 질환, 말초 동맥 질환, 관상동맥 동맥 질환, 대사 증후군, 급성 관상동맥 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 뇌혈관 질환, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 급성 관상동맥 증후군, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환 및 정맥성 혈전증(이들로 제한되지는 않음)을 포함하는 질환의 치료학적 치료를 위한 방법에서 사용될 수 있다. 이러한 방법은 대상체, 예를 들어, 인간 또는 동물 대상체에 대한 본 명세서에 기재된 바와 같은 LPA RNAi 물질의 투여를 포함한다.

[0015] 다르게 정의되지 않은 한, 본 명세서에 사용된 모든 기술 용어 및 과학 용어는 본 발명이 속하는 분야의 숙련자에 의해 흔히 이해되는 것과 동일한 의미를 가진다. 본 명세서에 기재된 것과 유사하거나 동등한 방법 및 재료가 본 발명의 실행 또는 교시에서 사용될 수 있지만, 적합한 방법 및 재료가 하기 기재되어 있다. 본 명세서에 언급된 모든 공보, 특허 출원, 특허 및 다른 문헌은 그 전문이 참고로 포함된다. 상충의 경우에, 정의를 포함하는 본 명세서가 지배할 것이다. 또한, 재료, 방법 및 예는 오직 예시적이고 제한되도록 의도되지 않는다.

[0016] 본 발명의 다른 특징 및 이점은 하기 상세한 설명 및 청구항으로부터 명확할 것이다.

도면의 간단한 설명

[0017] 도 1. 0.5㎎/㎏(파선) 또는 2㎎/㎏(실선)의 표시된 LPA RNAi 물질의 단일 피하 투여 후 Lp(a) 형질전환(Tg) 마우스에서의 혈청 Lp(a) 단백질 수준을 예시하는 그래프. Lp(a) 수준을 1일 및 식염수 대조군으로 정규화하였다.

도 2. 3주 동안 주 1회 투여된(1일, 8일 및 15일에 투약), 1㎎/㎏(파선) 또는 3㎎/㎏(실선)의 표시된 LPA RNAi 물질의 3의 피하 용량의 투여 후 Lp(a) Tg 마우스에서의 혈청 Lp(a) 단백질 수준을 예시하는 그래프. Lp(a) 수준을 1일 및 식염수 대조군으로 정규화하였다.

도 3. 1일에 전달 중합체와 함께 1:1(중량/중량) 투약된 단일 2㎎/㎏의 AD01196 LPA RNAi 물질의 투여 후 사이노몰거스 원숭이 혈청에서의 Lp(a) 입자 수준을 예시하는 그래프. Lp(a) 수준을 (0일로 표시된) 2의 투약전 값으로 정규화하였다.

도 4. 1일 및 71일에 전달 중합체와 함께 1:1(중량/중량) 투약된 4㎎/㎏ 또는 6㎎/㎏의 LPA RNAi 물질의 투여 후 사이노몰거스 원숭이 혈청에서의 Lp(a) 입자 수준을 예시하는 그래프. Lp(a) 수준을 (0일로 표시된) 2의 투

약전 값으로 정규화하였다. 4㎎/㎏ 용량 = 검정 원; 6㎎/㎏ 용량 = 회색 정사각형.

도 5. 1일, 8일 및 15일에 3㎎/㎏의 AD02819 LPA RNAi 물질의 3의 주마다의 피하 용량 후 사이노몰거스 원숭이 혈청에서의 Lp(a) 입자 수준을 예시하는 그래프. Lp(a) 수준을 (0일로 표시된) 3의 투약전 값으로 정규화하였다.

도 6. 1일에 3㎎/㎏의 LPA RNAi 물질의 단일 피하 투여 후 사이노몰거스 원숭이 혈청에서의 Lp(a) 입자 수준을 예시하는 그래프. AD03460 및 AD03536 군은 48일에 추가 1㎎/㎏의 LPA RNAi 물질의 용량을 받았다. Lp(a) 수준을 (0일로 표시된) 3의 투약전 값으로 정규화하였다.

발명을 실시하기 위한 구체적인 내용

[0018] LPA 유전자의 발현을 저해하기 위한 RNAi 물질(본 명세서에서 LPA RNAi 물질이라 칭함)이 본 명세서에 기재되어 있다. 본 명세서에 기재된 RNAi 물질은, *LPA* 유전자를 발현하는 세포로의 전달 시, RNA 간섭(RNAi)의 생물학적 과정을 통해 *시험관내* 및/또는 생체내 LPA의 발현을 저해하거나 넉다운시킨다. 본 명세서에 사용된 바대로, 구체적으로 달리 기재되지 않은 한, LPA는 적절한 경우 *LPA* 유전자, *LPA* mRNA 또는 LP(a) 단백질을 의미할 수 있다.

[0019] LPA RNAi 물질은 센스 가닥 및 안티센스 가닥을 포함한다. 센스 가닥 및 안티센스 가닥은 각각 코어 서열 17개 내지 23개의 핵염기 길이를 함유한다. 안티센스 가닥 코어 서열은 *LPA* mRNA에 존재하는 뉴클레오타이드 서열(때때로 예를 들어 표적 서열이라 칭해짐)에 100%(완전히) 상보성 또는 적어도 90%(실질적으로) 상보성이다. 센스 가닥 코어 서열은 안티센스 가닥에서의 서열에 100%(완전히) 상보성 또는 적어도 90%(실질적으로) 상보성이고, 이에 따라 센스 가닥 코어 서열은 LPA mRNA에 존재하는 뉴클레오타이드 서열(표적 서열)에 완전히 동일하거나 적어도 90% 동일하다. 센스 가닥 코어 서열은 상응하는 안티센스 코어 서열과 동일한 길이일 수 있거나, 이것은 상이한 길이일 수 있다. 몇몇 실시형태에서, 안티센스 가닥 코어 서열은 17개, 18개, 19개, 20개, 21개, 22개 또는 23개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 가닥 코어 서열은 17개, 18개, 19개, 20개, 21개, 22개 또는 23개의 뉴클레오타이드 길이이다.

[0020] LPA RNAi 물질 센스 및 안티센스 가닥은 어닐링하여 듀플렉스를 형성한다. LPA RNAi 물질의 센스 가닥 및 안티센스 가닥은 서로에 부분적으로, 실질적으로 또는 완전히 상보성이다. 상보성 듀플렉스 영역 내에, 센스 가닥 코어 서열은 안티센스 코어 서열에 적어도 90% 상보성 또는 100% 상보성이다. 몇몇 실시형태에서, 센스 가닥 코어 서열은 안티센스 가닥 코어 서열의 상응하는 17개, 18개, 19개, 20개 또는 21개의 뉴클레오타이드 서열에 적어도 90% 또는 100% 상보성인 적어도 17개, 적어도 18개, 적어도 19개, 적어도 20개 또는 적어도 21개의 뉴클레오타이드의 서열을 함유한다(즉, LPA RNAi 물질의 센스 가닥 및 안티센스 코어 서열은 적어도 90%의 쌍지은 염기 또는 100%의 쌍지은 염기인 적어도 17개, 적어도 18개, 적어도 19개, 적어도 20개 또는 적어도 21개의 뉴클레오타이드의 영역을 가진다.)

[0021] 다르게 표시되지 않은 한, 본 명세서에 사용된 바와 같은, 용어 "상보성"은, 제2 뉴클레오타이드 서열(예를 들어, RNAi 물질 안티센스 가닥)과 관련하여 제1 뉴클레오타이드 서열(예를 들어, RNAi 물질 센스 가닥 또는 LPA mRNA)을 기재하도록 사용될 때, 혼성화하고(염기 쌍 수소 결합을 형성하고), 제2 뉴클레오타이드 서열을 포함하는 올리고뉴클레오타이드 또는 폴리뉴클레오타이드와 소정의 조건 하에 듀플렉스 또는 이중 나선 구조를 형성하는, 제1 뉴클레오타이드 서열을 포함하는 올리고뉴클레오타이드 또는 폴리뉴클레오타이드의 능력을 의미한다. 상보성 서열은 왓슨-클릭(Watson-Crick) 염기 쌍 또는 비-왓슨-클릭 염기 쌍을 포함하고, 혼성화하는 이의 능력과 관련하여 상기 요건이 충족되는 한, 천연 또는 변형된 뉴클레오타이드 또는 뉴클레오타이드 모방체를 포함한다. "완벽히 상보성" 또는 "완전히 상보성"은 제1 폴리뉴클레오타이드의 인접한 서열에서의 모든(100%) 염기가 제2 폴리뉴클레오타이드의 인접한 서열에서의 동일한 수의 염기와 혼성화한다는 것을 의미한다. 인접한 서열은 제1 또는 제2 뉴클레오타이드 서열의 전부 또는 일부를 포함할 수 있다. 본 명세서에 사용된 바와 같은, "부분 상보성"은, 핵염기 서열의 혼성화된 쌍에서, 제1 폴리뉴클레오타이드의 인접한 서열에서의 적어도 70%의 염기가 제2 폴리뉴클레오타이드의 인접한 서열에서의 동일한 수의 염기와 혼성화한다는 것을 의미한다. 본 명세서에 사용된 바와 같은, "실질적인 상보성"은, 핵염기 서열의 혼성화된 쌍에서, 제1 폴리뉴클레오타이드의 인접한 서열에서의 적어도 85%의 염기가 제2 폴리뉴클레오타이드의 인접한 서열에서의 동일한 수의 염기와 혼성화한다는 것을 의미한다. 본 명세서에 사용된 바와 같은, 용어 "상보성", "완전히 상보성" 및 "실질적으로 상보성"은 RNAi 물질의 센스 가닥 및 안티센스 가닥 사이, 또는 RNAi 물질의 안티센스 가닥과 LPA mRNA의 서열 사이의 염기 미스매칭과 관련하여 사용될 수 있다. 서열 동일성 또는 상보성은 변형에 독립적이다. 동일성 또는 상보성을 결정

할 목적을 위해, 예를 들어 a 및 Af는 U(또는 T)에 상보성이고, A와 동일하다.

[0022] 본 명세서에 기재된 LPA RNAi 물질 센스 및 안티센스 가닥의 길이는 독립적으로 17개 내지 30개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 및 안티센스 가닥은 독립적으로 17개 내지 26개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 및 안티센스 가닥은 19개 내지 26개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 기재된 RNAi 물질 센스 및 안티센스 가닥은 독립적으로 17개, 18개, 19개, 20개, 21개, 22개, 23개, 24개, 25개 또는 26개의 뉴클레오타이드 길이이다. 센스 및 안티센스 가닥은 동일한 길이일 수 있거나, 상이한 길이일 수 있다. 몇몇 실시형태에서, 센스 가닥 및 안티센스 가닥은 각각 26개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 가닥은 23개의 뉴클레오타이드 길이이고, 안티센스 가닥은 21개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 가닥은 22개의 뉴클레오타이드 길이이고, 안티센스 가닥은 21개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 가닥은 21개의 뉴클레오타이드 길이이고, 안티센스 가닥은 21개의 뉴클레오타이드 길이이다. 몇몇 실시형태에서, 센스 가닥은 19개의 뉴클레오타이드 길이이고, 안티센스 가닥은 21개의 뉴클레오타이드 길이이다.

[0023] 센스 가닥 및/또는 안티센스 가닥은 임의로 및 독립적으로 코어 서열의 3' 말단, 5' 말단, 또는 3' 및 5' 말단 둘 다에서 추가 1개, 2개, 3개, 4개, 5개 또는 6개의 뉴클레오타이드(연장)를 함유할 수 있다. 존재하는 경우, 안티센스 가닥 추가 뉴클레오타이드는 LPA mRNA에서의 상응하는 서열에 상보성이거나 아닐 수 있다. 존재하는 경우, 센스 가닥 추가 뉴클레오타이드는 LPA mRNA에서의 상응하는 서열에 동일하거나 동일하지 않을 수 있다. 존재하는 경우, 안티센스 가닥 추가 뉴클레오타이드는, 존재하는 경우, 상응하는 센스 가닥의 추가 뉴클레오타이드에 상보성이거나 아닐 수 있다.

[0024] 본 명세서에 사용된 바와 같은, 연장은 센스 가닥 코어 서열 및/또는 안티센스 가닥 코어 서열의 5' 및/또는 3' 말단에서 1개, 2개, 3개, 4개, 5개 또는 6개의 뉴클레오타이드를 포함한다. 센스 가닥에서의 연장 뉴클레오타이드는 상응하는 안티센스 가닥에서 코어 서열 뉴클레오타이드 또는 연장 뉴클레오타이드 중 어느 하나인 뉴클레오타이드에 상보성이거나 아닐 수 있다. 반대로, 안티센스 가닥에서의 연장 뉴클레오타이드는 상응하는 센스 가닥에서 코어 서열 뉴클레오타이드 또는 연장 뉴클레오타이드 중 어느 하나인 뉴클레오타이드에 상보성이거나 아닐 수 있다. 몇몇 실시형태에서, RNAi 물질의 센스 가닥 및 안티센스 가닥은 둘 다 3' 및 5' 연장을 함유한다. 몇몇 실시형태에서, 하나의 가닥 염기의 하나 이상의 3' 연장 뉴클레오타이드는 다른 가닥의 하나 이상의 5' 연장 뉴클레오타이드와 쌍을 이룬다. 다른 실시형태에서, 하나의 가닥의 하나 이상의 3' 연장 뉴클레오타이드는 다른 가닥의 하나 이상의 5' 연장 뉴클레오타이드와 쌍을 이루지 않는다. 몇몇 실시형태에서, LPA RNAi 물질은 3' 연장을 가지는 안티센스 가닥 및 5' 연장을 가지는 센스 가닥을 가진다.

[0025] 몇몇 실시형태에서, LPA RNAi 물질은 1개, 2개, 3개, 4개, 5개 또는 6개의 뉴클레오타이드 길이의 3' 연장을 가지는 안티센스 가닥을 포함한다. 다른 실시형태에서, LPA RNAi 물질은 1개, 2개 또는 3개의 뉴클레오타이드 길이의 3' 연장을 가지는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 안티센스 가닥 연장 뉴클레오타이드는 우라실 또는 타이미딘 뉴클레오타이드 또는 상응하는 LPA mRNA 서열에 상보성인 뉴클레오타이드를 포함한다. 몇몇 실시형태에서, 3' 안티센스 가닥 연장은 Ab, AbAb, AUA, UGCUU, CUG, UG, UGCC, CUGCC, CGU, CUU, UGCCUA, CUGCCU, UGCCU, UGAUU, GCCUAU, T, TT(각각 5'에서 3'로 기재됨)를 포함하거나 이들로 이루어지지만, 이들로 제한되지는 않는다.

[0026] 몇몇 실시형태에서, LPA RNAi 물질은 1개, 2개, 3개, 4개 또는 5개의 뉴클레오타이드 길이의 5' 연장을 가지는 안티센스 가닥을 포함한다. 다른 실시형태에서, LPA RNAi 물질은 1개 또는 2개의 뉴클레오타이드 길이의 5' 연장을 가지는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 안티센스 가닥 연장 뉴클레오타이드는 우라실 또는 타이미딘 뉴클레오타이드 또는 상응하는 LPA mRNA 서열에 상보성인 뉴클레오타이드를 포함한다. 몇몇 실시형태에서, 5' 안티센스 가닥 연장은 UA, TU, U, T, CUC(각각 5'에서 3'로 기재됨)를 포함하거나 이들로 이루어지지만, 이들로 제한되지는 않는다. 안티센스 가닥은, 존재하는 경우, 기재된 임의의 5' 안티센스 가닥 연장과 조합되어 상기 기재된 임의의 3' 연장을 가질 수 있다.

[0027] 몇몇 실시형태에서, LPA RNAi 물질은 1개, 2개, 3개, 4개 또는 5개의 뉴클레오타이드 길이의 3' 연장을 가지는 센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 센스 가닥 연장 뉴클레오타이드는 아데노신, 우라실, 또는 타이미딘 뉴클레오타이드, AT 다이뉴클레오타이드, 또는 LPA mRNA 서열에서의 뉴클레오타이드에 상응하는 뉴클레오타이드를 포함한다. 몇몇 실시형태에서, 3' 센스 가닥 연장은 T, UUAb, UAb, Ab, UT, TT, UUT, TTT 또는 TTTT(각각 5'에서 3'로 기재됨)를 포함하거나 이들로 이루어지지만, 이들로 제한되지는 않는다.

[0028] 몇몇 실시형태에서, LPA RNAi 물질은 1개, 2개, 3개, 4개, 5개 또는 6개의 뉴클레오타이드 길이의 5' 연장을 가

지는 센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 센스 가닥 연장 뉴클레오타이드는 우라실 또는 아데노신 뉴클레오타이드 또는 LPA mRNA 서열에서의 뉴클레오타이드에 상응하는 뉴클레오타이드를 포함한다. 몇몇 실시형태에서, 센스 가닥 5' 연장은 CA, AUAGGC, AUAGG, AUAG, AUA, A, AA, AC, GCA, GGCA, GGC, UAUCA, UAUC, Ab, UCA, UAU(각각 5'에서 3'로 기재됨)일 수 있지만, 이들로 제한되지는 않는다. 센스 가닥은 3' 연장 및/또는 5' 연장을 가질 수 있다.

[0029] LPA RNAi 물질을 형성하는 데 사용되는 뉴클레오타이드 서열의 예는 표 1, 표 2A, 표 2B, 표 3A 및 표 3B에 제공된다. 본 명세서에 사용된 바와 같은, 용어 "서열" 또는 "뉴클레오타이드 서열"은 표준 뉴클레오타이드 명명법 및 본 명세서에 기재된 변형된 뉴클레오타이드에 대한 키를 이용하여 철자의 연속에 의해 기재된, 변형되든 또는 변형되지 않든, 핵염기, 뉴클레오타이드, 및/또는 뉴클레오사이드의 연속 또는 순서를 의미한다.

[0030] RNAi 물질은 짧은 간섭 RNA(siRNA), 이중 가닥 RNA(dsRNA), 마이크로 RNA(miRNA), 짧은 헤어핀 RNA(shRNA) 및 다이서(dicer) 기질(예를 들어, 미국 특허 제8084599호, 제8349809호 및 제8513207호)를 포함하지만, 이들로 제한되지는 않는다.

[0031] 비변형된 LPA RNAi 물질 센스 가닥 및 안티센스 가닥 서열은 표 1에 제공된다. LPA RNAi 물질을 형성하는 데 있어서, 표 1에 기재된 각각의 서열에서의 각각의 뉴클레오타이드는 변형된 뉴클레오타이드일 수 있다.

표 1. 비변형된 LPA RNAi 물질 안티센스 가닥 및 센스 가닥 서열.

안티센스 가닥 염기 서열 5' → 3'	서열 번호	센스 가닥 염기 서열 5' → 3'	서열 번호
TCGGCAGUCCCUUCUGCGUTT	1	ACGCAGAAGGGACUGCCGAT	190
TGUAGCACUCCUGCACCCCTT	2	GGGGUGCAGGAGUGCUACAT	191
TAAUAAGGGGCUGCCACAGTT	3	CUGUGGCAGCCCCUUAUUAT	192
TUAACAAUAAGGGGCUGCCTT	4	GGCAGCCCCUUAUUGUUAAT	193
TGUAUAACAAUAAGGGGCUTT	5	AGCCCCUUAUUGUUAUACAT	194
TCGUAUAACAAUAAGGGGCTT	6	GCCCCUUAUUGUUAUACGAT	195
TCGUCUGAGCAUUGUGUCATT	7	UGACACAAUGCUCAGACGAT	196
TGCGUCUGAGCAUUGUGUCTT	8	GACACAAUGCUCAGACGCAT	197
TUGCGUCUGAGCAUUGUGUTT	9	ACACAAUGCUCAGACGCAAT	198
TUCUGCGUCUGAGCAUUGUTT	10	ACAAUGCUCAGACGCAGAAT	199
TGGAUCUGGAUUUCGGCAGTT	11	CUGCCGAAAUCCAGAUCCAT	200
TCAGGAUCUGGAUUUCGGCTT	12	GCCGAAAUCCAGAUCCUGAT	201
TCAUCUGAGCAUCGUGUCATT	13	UGACACGAUGCUCAGAUGAT	202
TGCAUCUGAGCAUCGUGUCTT	14	GACACGAUGCUCAGAUGCAT	203
TUGCAUCUGAGCAUCGUGUTT	15	ACACGAUGCUCAGAUGCAAT	204
TUCUGCAUCUGAGCAUCGUTT	16	ACGAUGCUCAGAUGCAGAAT	205
TAAAGCCUCUAGGCUUGGATT	17	UCCAAGCCUAGAGGCUUUAT	206
TGUACCCCGGGGGUUUCCUTT	18	AGGAAACCCCCGGGGUACAT	207
TUGUACCCCGGGGGUUUCCTT	19	GGAAACCCCCGGGGUACAAT	208
TCUGUACCCCGGGGGUUUCTT	20	GAAACCCCCGGGGUACAGAT	209
TUCCAUAAUGGUAGUAGCATT	21	UGCUACUACCAUUAUGGAAT	210
TGUCCAUAAUGGUAGUAGCTT	22	GCUACUACCAUUAUGGACAT	211
TCUCUGUCCAUAAUGGUAGTT	23	CUACCAUUAUGGACAGAGAT	212
TCGACUAUGCUGGUGUGGUTT	24	ACCACACCAGCAUAGUCGAT	213
TCCGACUAUGCUGGUGUGGTT	25	CCACACCAGCAUAGUCGGAT	214

[0032]

TUCCGACUAUGCUGGUGUGTT	26	CACACCAGCAUAGUCGGAAT	215
TGGUCCGACUAUGCUGGUGTT	27	CACCAGCAUAGUCGGACCAT	216
TUUUCUGGGGUCCGACUAUTT	28	AUAGUCGGACCCCAGAAAAT	217
TUUUUCUGGGGUCCGACUATT	29	UAGUCGGACCCCAGAAAAAT	218
TGCGAAUCUCAGCAUCUGGTT	30	CCAGAUGCUGAGAUUCGCAT	219
TCCAAGGGCGAAUCUCAGCTT	31	GCUGAGAUUCGCCCUUGGAT	220
TACCAAGGGCGAAUCUCAGTT	32	CUGAGAUUCGCCCUUGGUAT	221
TCACCAAGGGCGAAUCUCATT	33	UGAGAUUCGCCCUUGGUGAT	222
TACACCAAGGGCGAAUCUCTT	34	GAGAUUCGCCCUUGGUGUAT	223
TCCUGACACUGGGAUCCAUTT	35	AUGGAUCCCAGUGUCAGGAT	224
TUGCAAGGACACUUGAUUCTT	36	GAAUCAAGUGUCCUUGCAAT	225
TUUGCAAGGACACUUGAUUTT	37	AAUCAAGUGUCCUUGCAAAT	226
TUUGCUCCGUUGGUGCUUCTT	38	GAAGCACCAACGGAGCAAAT	227
TAAUGAGCCUCGAUAACUCTT	39	GAGUUAUCGAGGCUCAUUAT	228
TGAAUGAGCCUCGAUAACUTT	40	AGUUAUCGAGGCUCAUUCAT	229
TGGAUAAUAUUCUGUUGUCTT	41	GACAACAGAAUAUUAUCCAT	230
TCCAUGGUAUAACACCAAGTT	42	CUUGGUGUUAUACCAUGGAT	231
TGAUCCAUGGUAUAACACCTT	43	GGUGUUAUACCAUGGAUCAT	232
TAUUGGGAUCCAUGGUAUATT	44	UAUACCAUGGAUCCCAAUAT	233
TCAUUGGGAUCCAUGGUAUTT	45	AUACCAUGGAUCCCAAUGAT	234
TACAUUGGGAUCCAUGGUATT	46	UACCAUGGAUCCCAAUGUAT	235
TGACAUUGGGAUCCAUGGUTT	47	ACCAUGGAUCCCAAUGUCAT	236
TGACAUUGUGUCAGGUUGCTT	48	GCAACCUGACACAAUGUCAT	237
TCACUGGACAUUGUGUCAGTT	49	CUGACACAAUGUCCAGUGAT	238
TACUUGAUUCUGUCACUGGTT	50	CCAGUGACAGAAUCAAGUAT	239
TGAGAAUGAGCCUCGAUAATT	51	UUAUCGAGGCUCAUUCUCAT	240
TCCAUUUGGGUAGUAUUCUTT	52	AGAAUACUACCCAAAUGGAT	241
TCACCAUUUGGGUAGUAUUTT	53	AAUACUACCCAAAUGGUGAT	242

[0033]

TCCACCAUUUGGGUAGUAUTT	54	AUACUACCCAAAUGGUGGAT	243
TAUAACACCAAGGGCGAAUTT	55	AUUCGCCCUUGGUGUUAUAT	244
TACUGGGAUCCAUGGUAUATT	56	UAUACCAUGGAUCCCAGUAT	245
TCACUGGGAUCCAUGGUAUTT	57	AUACCAUGGAUCCCAGUGAT	246
TACCACCGUGGGAGUUGUGTT	58	CACAACUCCCACGGUGGUAT	247
TCAAGACUGACAUGUUCUUTT	59	AAGAACAUGUCAGUCUUGAT	248
TGGGAGUUGUGAGGACACUTT	60	AGUGUCCUCACAACUCCCAT	249
TUCUCAGGUGGUGCUUGUUTT	61	AACAAGCACCACCUGAGAAT	250
TCACAGGGCUUUUCUCAGGTT	62	CCUGAGAAAAGCCCUGUGAT	251
TGAUGCCAGUGUGGUAUCATT	63	UGAUACCACACUGGCAUCAT	252
TUGAUGCCAGUGUGGUAUCTT	64	GAUACCACACUGGCAUCAAT	253
TGACACCUGAUUCUGUUUCTT	65	GAAACAGAAUCAGGUGUCAT	254
TGGACACCUGAUUCUGUUUTT	66	AAACAGAAUCAGGUGUCCAT	255
TCUAGGACACCUGAUUCUGTT	67	CAGAAUCAGGUGUCCUAGAT	256
TAUAAGGGGCUGCCACAGGTT	68	CCUGUGGCAGCCCCUUAUAT	257
TAACAAUAAGGGGCUGCCATT	69	UGGCAGCCCCUUAUUGUUAT	258
TGUCCGACUAUGCUGGUGUTT	70	ACACCAGCAUAGUCGGACAT	259
TUCUCAGCAUCUGGAUUCCTT	71	GGAAUCCAGAUGCUGAGAAT	260
TCGAAUCUCAGCAUCUGGATT	72	UCCAGAUGCUGAGAUUCGAT	261
TAAGGGCGAAUCUCAGCAUTT	73	AUGCUGAGAUUCGCCCUUAT	262
TUGACACUGGGAUCCAUGGTT	74	CCAUGGAUCCCAGUGUCAAT	263
TCCGUUGGUGCUUCUUCAGTT	75	CUGAAGAAGCACCAACGGAT	264
TCUUGAUUCUGUCACUGGATT	76	UCCAGUGACAGAAUCAAGAT	265
TCACCGUGGGAGUUGUGAGTT	77	CUCACAACUCCCACGGUGAT	266
TUCUAGGACACCUGAUUCUTT	78	AGAAUCAGGUGUCCUAGAAT	267
TAGUCUCUAGGACACCUGATT	79	UCAGGUGUCCUAGAGACUAT	268
TCAAUAAGGGGCUGCCACATT	80	UAUAGCCCCUUAUUGUUAUACAT	269
TCUGCGUCUGAGCAUUGUGTT	81	UAUGCCCCUUAUUGUUAUACGAT	270

[0034]

TACAGGAUCUGGAUUUCGGTT	82	UAUGACACAAUGCUCAGACGCAT	271
TCCGGGGGUUUCCUCAGUCTT	83	UAUACACAAUGCUCAGACGCAAT	272
TUGUCCAUAAUGGUAGUAGTT	84	UAUUUAUCGAGGCUCAUUCUCAT	273
TUCUGUCCAUAAUGGUAGUTT	85	UAUGAAACAGAAUCAGGUGUCAT	274
TACUCUGUCCAUAAUGGUATT	86	UAUACACCAGCAUAGUCGGACAT	275
TAACUCUGUCCAUAAUGGUTT	87	UAUUCCAGAUGCUGAGAUUCGAT	276
TGGGCGAAUCUCAGCAUCUTT	88	UAUAUGCUGAGAUUCGCCCUUAT	277
TAGGGCGAAUCUCAGCAUCTT	89	UAUCCAUGGAUCCCAGUGUCAAT	278
TAACACCAAGGGCGAAUCUTT	90	UGUGGCAGCCCCUUAUUGAT	279
TAGGACACUUGAUUCUGUCTT	91	CACAAUGCUCAGACGCAGAT	280
TGGACCAAGACUGACAUGUTT	92	CCGAAAUCCAGAUCCUGUAT	281
TGGUCAGGCCACCAUUUGGTT	93	GACUGAGGAAACCCCCGGAT	282
TAUCCAUGGUAUAACACCATT	94	CUACUACCAUUAUGGACAAT	283
TGGGAUCCAUGGUAUAACATT	95	ACUACCAUUAUGGACAGAAT	284
TUGGACAUUGUGUCAGGUUTT	96	UACCAUUAUGGACAGAGUAT	285
TAUUCUGUCACUGGACAUUTT	97	ACCAUUAUGGACAGAGUUAT	286
TGGUGCUUGUUCAGAAACATT	98	AGAUGCUGAGAUUCGCCCAT	287
TGGAGAAUGAGCCUCGAUATT	99	GAUGCUGAGAUUCGCCCUAT	288
TGUGGAGAAUGAGCCUCGATT	100	AGAUUCGCCCUUGGUGUUAT	289
TCCGUGGGAGUUGUGAGGATT	101	GACAGAAUCAAGUGUCCUAT	290
TGGACCACCGUGGGAGUUGTT	102	ACAUGUCAGUCUUGGUCCAT	291
TUGCUUGUUCAGAAGGAGCTT	103	CCAAAUGGUGGCCUGACCAT	292
TCUGAUGCCAGUGUGGUAUTT	104	UGGUGUUAUACCAUGGAUAT	293
TUAGGACACCUGAUUCUGUTT	105	UGUUAUACCAUGGAUCCCAT	294
TCUCUAGGACACCUGAUUCTT	106	AACCUGACACAAUGUCCAAT	295
TUCUCUAGGACACCUGAUUTT	107	AAUGUCCAGUGACAGAAUAT	296
TGUCUCUAGGACACCUGAUTT	108	UGUUUCUGAACAAGCACCAT	297
TGAGAAUGAGCCUCGAUAACUCUUAU	109	UAUCGAGGCUCAUUCUCCAT	298

[0035]

TGACACCUGAUUCUGUUUCUGAGUAU	110	UCGAGGCUCAUUCUCCACAT	299
TCGUAUAACAAUAAGGGGCUGCCUAU	111	UCCUCACAACUCCCACGGAT	300
TGCGUCUGAGCAUUGUGUCAGGUUAU	112	CAACUCCCACGGUGGUCCAT	301
TUGCGUCUGAGCAUUGUGUCAGGUAU	113	GCUCCUUCUGAACAAGCAAT	302
TAAGGGCGAAUCUCAGCAUCUGGUAU	114	AUACCACACUGGCAUCAGAT	303
UUAACAAUAAGGGGCUGCAb	115	ACAGAAUCAGGUGUCCUAAT	304
UGUAUAACAAUAAGGGGCAb	116	GAAUCAGGUGUCCUAGAGAT	305
UCGUAUAACAAUAAGGGGAb	117	AAUCAGGUGUCCUAGAGAAT	306
UGCGUCUGAGCAUUGUGUAb	118	AUCAGGUGUCCUAGAGACAT	307
UUGCGUCUGAGCAUUGUGAb	119	UAUAUAGUUAUCGAGGCUCAUUCUCA	308
UCAGGAUCUGGAUUUCGGAb	120	UAUAUCAGAAACAGAAUCAGGUGUCA	309
UUGCAUCUGAGCAUCGUGAb	121	UAUAUCAGCCCCUUAUUGUUAUACGA	310
UCGACUAUGCUGGUGUGGAb	122	UAUAUCUGACACAAUGCUCAGACGCA	311
UUUUCUGGGGUCCGACUAAb	123	UAUAUUGACACAAUGCUCAGACGCAA	312
UGCGAAUCUCAGCAUCUGAb	124	UAUAUAGAUGCUGAGAUUCGCCCUUA	313
UUGCAAGGACACUUGAUUAb	125	GCAGCCCCUUAUUGUUAA	314
UAAUGAGCCUCGAUAACUAb	126	GCCCCUUAUUGUUAUACA	315
UGAAUGAGCCUCGAUAACAb	127	CCCCUUAUUGUUAUACGA	316
UGACAUUGUGUCAGGUUGAb	128	ACACAAUGCUCAGACGCA	317
UGAGAAUGAGCCUCGAUAAb	129	CACAAUGCUCAGACGCAA	318
UCCAUUUGGGUAGUAUUCAb	130	CCGAAAUCCAGAUCCUGA	319
UCACCAUUUGGGUAGUAUAb	131	CACGAUGCUCAGAUGCAA	320
UGACACCUGAUUCUGUUUAb	132	CCACACCAGCAUAGUCGA	321
UGGACACCUGAUUCUGUUAb	133	UAGUCGGACCCCAGAAAA	322
UUAACAAUAAGGGGCUGAbAb	134	CAGAUGCUGAGAUUCGCA	323
UGUAUAACAAUAAGGGGAbAb	135	AAUCAAGUGUCCUUGCAA	324
UCGUAUAACAAUAAGGGAbAb	136	AGUUAUCGAGGCUCAUUA	325
UGCGUCUGAGCAUUGUGAbAb	137	GUUAUCGAGGCUCAUUCA	326

[0036]

UUGCGUCUGAGCAUUGUAbAb	138	CAACCUGACACAAUGUCA	327
UCAGGAUCUGGAUUUCGAbAb	139	UAUCGAGGCUCAUUCUCA	328
UUGCAUCUGAGCAUCGUAbAb	140	GAAUACUACCCAAAUGGA	329
UCGACUAUGCUGGUGUGAbAb	141	AUACUACCCAAAUGGUGA	330
UUUUCUGGGGUCCGACUAbAb	142	AAACAGAAUCAGGUGUCA	331
UGCGAAUCUCAGCAUCUAbAb	143	AACAGAAUCAGGUGUCCA	332
UUGCAAGGACACUUGAUAbAb	144	CAGCCCCUUAUUGUUAA	333
UAAUGAGCCUCGAUAACAbAb	145	CCCCUUAUUGUUAUACA	334
UGAAUGAGCCUCGAUAAAbAb	146	CCCUUAUUGUUAUACGA	335
UGACAUUGUGUCAGGUUAbAb	147	CACAAUGCUCAGACGCA	336
UGAGAAUGAGCCUCGAUAbAb	148	ACAAUGCUCAGACGCAA	337
UCCAUUUGGGUAGUAUUAbAb	149	CGAAAUCCAGAUCCUGA	338
UCACCAUUUGGGUAGUAAbAb	150	ACGAUGCUCAGAUGCAA	339
UGACACCUGAUUCUGUUAbAb	151	CACACCAGCAUAGUCGA	340
UGGACACCUGAUUCUGUAbAb	152	AGUCGGACCCCAGAAAA	341
UGAGAAUGAGCCUCGAUAACUCUUAU	153	AGAUGCUGAGAUUCGCA	342
UGACACCUGAUUCUGUUUCUGAGUAU	154	AUCAAGUGUCCUUGCAA	343
UGAGAAUGAGCCUCGAUAACUCTUAU	155	GUUAUCGAGGCUCAUUA	344
UCGUAUAACAAUAAGGGGCUGCCUAU	156	UUAUCGAGGCUCAUUCA	345
UGAGAAUGAGCCUCGAUAATT	157	AACCUGACACAAUGUCA	346
UCGUAUAACAAUAAGGCGCUGCCUAU	158	AUCGAGGCUCAUUCUCA	347
UGAGAAUGAGCCUCGATAbAb	159	AAUACUACCCAAAUGGA	348
UGACACCUGAUUCUGTTAbAb	160	UACUACCCAAAUGGUGA	349
UCGUAUAACAAUAAGGGGCUGAUU	161	AACAGAAUCAGGUGUCA	350
UCGUAUAACAAUAAGGGGCUGCUU	162	ACAGAAUCAGGUGUCCA	351
UGAGAAUGAGCCUCGAUAACUCUU	163	UAUAUCAGCGCCUUAUUGUUAUACGA	352
UCGUAUAACAAUAAGGGGCUU	164	ATCGAGGCUCAUUCUCA	353
UGUAUAACAAUAAGGGG	165	UCAGCCCCUUAUUGUUAUACGAUUAb	354

[0037]

UCGUAUAACAAUAAGGG	166	UCAGCCCCUUAUUGUUAUACGAAb	355
UGAGAAUGAGCCUCGAT	167	UAGUUAUCGAGGCUCAUUCUCAUUAb	356
UGACACCUGAUUCUGTT	168	AbGCCCCUUAUUGUUAUACGAUUAb	357
TUCGUAUAACAAUAAGGGGCUGCCUA	169	AUAUCAGCCCCUUAUUGUUAUACGAT	358
UAUCGUAUAACAAUAAGGGGCUGCCU	170	UAUCAGCCCCUUAUUGUUAUACGAUT	359
TCCGUAUAACAAUAAGGGGCUGCCUA	171	AUAUAGUUAUCGAGGCUCAUUCUCAT	360
CUCCGUAUAACAAUAAGGGGCUGCCU	172	UAUAGUUAUCGAGGCUCAUUCUCAUT	361
TUGAGAAUGAGCCUCGAUAACUCUUA	173	AbUUAUCGAGGCUCAUUCUCAUUAb	362
UAUGAGAAUGAGCCUCGAUAACUCUU	174	UAUAUAAUUAUCGAGGCUCAUUCUCAAb	363
TGGAGAAUGAGCCUCGAUAACUCUUA	175	GGCAGCCCCUUAUUGUUAUACGATT	364
GUGGAGAAUGAGCCUCGAUAACUCUU	176	GGCAGCCCCUUAUUGUUAUACGAUUT	365
UGAGAAUGAGCCUCGAUAAUU	177	CAGCCCCUUAUUGUUAUACGATTTT	366
TCGUAUAACAAUAAGGGGCUU	178	GCGAUAGUUAUCGAGGCUCAUUCUCA	367
UGAGAAUGAGCCUCGAUAAUUAUAUA	179	UGAAUAGUUAUCGAGGCUCAUUCUCA	368
UCGUAUAACAAUAAGGGGCUGCC	180	AUCGUAGUUAUCGAGGCUCAUUCUCA	369
TUCGUAUAACAAUAAGGGGCUGCC	181	UAUAAAGUUAUCGAGGCUCAUUCUCA	370
TUCGUAUAACAAUAAGGGGCUG	182	AGCCCCUUAUUGUUAUACGAAb	371
UGAGAAUGAGCCUCGAUAACUAUCGC	183	AAGCCCCUUAUUGUUAUACGAAb	372
UGAGAAUGAGCCUCGAUAACUAUUCA	184	GCAGCCCCUUAUUGUUAUACGAAb	373
UGAGAAUGAGCCUCGAUAACUACGAU	185	UAUAUAGUUAUCGAGGCUCAUUCUCAAb	374
UCGUAUAACAAUAAGGGGCGU	186	ACGCCCCUUAUUGUUAUACGAAb	375
UCGUAUAACAAUAAGGGGCUGCCU	187	GCCCCUUAUUGUUAUACGAUUAb	376
UCGUAUAACAAUAAGGGGCUG	188	AGCCCCUUAUUGUUAUACGAUUAb	377
TCGUAUAACAAUAAGGGGCUGCUU	189	AAGCCCCUUAUUGUUAUACGAUUAb	378
TCGUAUAACAAUAAGGGGC	1242	UAUCAGCCCCUUAUUGUUAUACGA	379
UCGUAUAACAAUAAGGGG	1244	UAGCAGCCCCUUAUUGUUAUACGA	380
UCGUAUAACAAUAAGGG	1246	GCAGCCCCUUAUUGUUAUACGA	381
TGAGAAUGAGCCUCGAUAA	1248	AUAAGAGUUAUCGAGGCUCAUUCUCA	382

[0038]

UGAGAAUGAGCCUCGAUA	1250	AUAGGCAGCCCCUUAUUGUUAUACGA	383
UGAGAAUGAGCCUCGAU	1252	CAGCCCCUUAUUGUUAUACGA	384
UGUAUAACAAUAAGGGG	1254	UAUAUCAGCCCCTUAUUGUUAUACGA	385
CGUAUAACAAUAAGGGGC	1280	AbGCCCCTUAUUGUUAUACGAUUAb	1241
GAGAAUGAGCCUCGAUAA	1281	GCCCCUUAUUGUUAUACGA	1243
UCGUAUAACAAUAAGGGGC	1282	CCCCUUAUUGUUAUACGA	1245
UGAGAAUGAGCCUCGAUAA	1283	CCCUUAUUGUUAUACGA	1247
		UUAUCGAGGCUCAUUCUCA	1249
		UAUCGAGGCUCAUUCUCA	1251
		AUCGAGGCUCAUUCUCA	1253
		CCCCUUAUUGUUAUACA	1255
		UUAUCGAGGCUCAUUCUCA	1258
		GCCCCUUAUUGUUAUACGA	1259
		ACAGCCCCUUAUUGUUAUACGA	1260
		AAAGCCCCUUAUUGUUAUACGA	1261
		GCCCCUUAUUGUUAUACG	1284
		UUAUCGAGGCUCAUUCUC	1285

Ab = 비염기성 뉴클레오타이드

[0039]

[0040] 본 명세서에 기재된 LPA RNAi 물질은 안티센스 가닥을 센스 가닥에 의해 어닐링함으로써 형성된다. 표 1 또는 표 2B에 기재된 서열을 함유하는 센스 가닥은 표 1 또는 표 2A에 기재된 서열을 함유하는 임의의 안티센스 가닥에 혼성화될 수 있고, 단 2개의 서열은 인접한 16개, 17개, 18개, 19개, 20개 또는 21개의 뉴클레오타이드 서열에 대해 적어도 90% 상보성의 영역을 가진다.

[0041] 몇몇 실시형태에서, LPA RNAi 물질 안티센스 가닥은 표 1에서의 임의의 서열의 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질 안티센스 가닥은 표 1에서의 임의의 서열의 1-17번, 2-17번, 1-18번, 2-18번, 1-19번, 2-19번, 1-20번, 2-20번, 1-21번, 2-21번, 1-22번, 2-22번, 1-23번, 2-23번, 1-24번, 2-24번, 1-25번, 2-25번, 1-26번 또는 2-26번 뉴클레오타이드의 서열을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질 센스 가닥은 표 1에서의 임의의 서열의 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질 센스 가닥은 표 1에서의 임의의 서열의 1-17번, 2-17번, 1-18번, 2-18번, 1-19번, 2-19번, 1-20번, 2-20번, 1-21번, 2-21번, 1-22번, 2-22번, 1-23번, 2-23번, 1-24번, 2-24번, 1-25번, 2-25번, 1-26번 또는 2-26번 뉴클레오타이드의 서열을 포함한다.

[0042] 몇몇 실시형태에서, 본 명세서에 기재된 RNAi 물질의 센스 및 안티센스 가닥은 동일한 수의 뉴클레오타이드를 함유한다. 몇몇 실시형태에서, 본 명세서에 기재된 RNAi 물질의 센스 및 안티센스 가닥은 상이한 수의 뉴클레오타이드를 함유한다. 몇몇 실시형태에서, RNAi 물질의 센스 가닥 5' 말단 및 안티센스 가닥 3' 말단은 무딘 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 센스 가닥 3' 말단 및 안티센스 가닥 5' 말단은 무딘 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 말단 둘 다는 무딘 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 말단 중 어느 것도 무딘 말단이 아니다. 본 명세서에 사용된 바와 같은, 무딘 말단은, 2개의 어닐링된 가닥의 말단 뉴클레오타이드가 상보성인(상보성 염기 쌍을 형성하는), 이중 가닥 RNAi 물질의 말단을 의미한다. 몇몇 실시형태에서, RNAi 물질의 센스 가닥 5' 말단 및 안티센스 가닥 3' 말단은 날카로운 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 센스 가닥 3' 말단 및 안티센스 가닥 5' 말단은 날카로운 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 말단 둘 다는 날카로운 말단을 형성한다. 몇몇 실시형태에서, RNAi 물질의 말단 중 어느 것도 날카로운 말단이 아니다. 본 명세서에 사용된 바와 같은, 날카로운 말단은, 2개의 어닐링된 가닥의 말단 뉴클레오타이드가 쌍을 형성하지만(즉, 오버행(overhang)을 형성하지 않음), 상보성이 아닌(즉, 비상보성 쌍을 형성함), 이중 가닥 RNAi 물질의 말단을 의미한다. 본 명세서에 사용된 바와 같은, 오버행은 이중 가닥 RNAi 물질의 하나의 가닥의 말단에서의 하나 이상의 쌍 짓지 않은 뉴클레오타이드의 스트레치이다. 쌍 짓지 않은 뉴클레오타이드는 센스 가닥 또는 안티센스 가닥에 있을 수 있어서, 3' 또는 5' 오버행을 생성한다. 몇몇 실시형태

에서, RNAi 물질은 무딘 말단 및 날카로운 말단, 무딘 말단 및 5' 오버행 말단, 무딘 말단 및 3' 오버행 말단, 날카로운 말단 및 5' 오버행 말단, 날카로운 말단 및 3' 오버행 말단, 2개의 5' 오버행 말단, 2개의 3' 오버행 말단, 5' 오버행 말단 및 3' 오버행 말단, 2개의 날카로운 말단, 또는 2개의 무딘 말단을 함유한다.

[0043] 뉴클레오타이드 염기(또는 핵염기)는 모든 핵산의 구성성분인 헤테로사이클릭 피리미딘 또는 퓨린 화합물이고, 아데닌(A), 구아닌(G), 시토신(C), 타이민(T) 및 우라실(U)을 포함한다. 본 명세서에 사용된 바와 같은, 용어 "뉴클레오타이드"는 변형된 뉴클레오타이드 또는 뉴클레오타이드 모방체, 비염기성 부위(Ab 또는 X), 또는 대리 대체 모이어티를 포함할 수 있다.

[0044] 몇몇 실시형태에서, LPA RNAi 물질은 염, 혼합 염 또는 유리 산으로서 제조되거나 제공된다.

[0045] 변형된 뉴클레오타이드

[0046] 몇몇 실시형태에서, LPA RNAi 물질은 하나 이상의 변형된 뉴클레오타이드를 함유한다. 본 명세서에 사용된 바대로, "변형된 뉴클레오타이드"는 리보뉴클레오타이드(2'-하이드록실 뉴클레오타이드) 이외의 뉴클레오타이드이다. 몇몇 실시형태에서, 적어도 50%, 적어도 60%, 적어도 70%, 적어도 80%, 적어도 90%, 적어도 95%, 또는 100%의 뉴클레오타이드는 변형된다. 변형된 뉴클레오타이드는 데옥시뉴클레오타이드, 뉴클레오타이드 모방체, 비염기성 뉴클레오타이드(X, Ab로서 본 명세서에서 표시됨), 2' 변형된 뉴클레오타이드, 3' 내지 3' 연결(인버티드) 뉴클레오타이드(invdN, invN, invn, invX, invAb로서 본 명세서에서 표시됨), 비천연 염기 포함 뉴클레오타이드, 브릿징된 뉴클레오타이드, 펩타이드 핵산(PNA), 2',3'-세코 뉴클레오타이드 모방체(잠기지 않은 핵염기 유사체, N_{UNA} 또는 NUNA로서 본 명세서에서 표시됨), 잠긴 뉴클레오타이드(N_{LNA} 또는 NLNA로서 본 명세서에서 표시됨), 3'-O-메톡시(2' 뉴클레오사이드간 연결된) 뉴클레오타이드(3'-OMen으로서 본 명세서에서 표시됨), 2'-F-아라비노 뉴클레오타이드(NfANA 또는 Nf_{ANA}로서 본 명세서에서 표시됨), 5'-Me,2'-플루오로 뉴클레오타이드(5Me-Nf로서 본 명세서에서 표시됨), 모르폴리노 뉴클레오타이드, 비닐 포스포네이트 데옥시리보뉴클레오타이드(vpdN으로서 본 명세서에서 표시됨), 비닐 포스포네이트 함유 뉴클레오타이드 및 사이클로프로필 포스포네이트 함유 뉴클레오타이드(cPrpN)를 포함하지만, 이들로 제한되지는 않는다. 2' 변형된 뉴클레오타이드(즉, 5원 당 고리의 2'번 위치에서의 하이드록실기 이외의 기를 가지는 뉴클레오타이드)는 2'-O-메틸 뉴클레오타이드(뉴클레오타이드 서열에서 소문자 'n'으로서 본 명세서에서 표시됨), 2'-데옥시-2'-플루오로 뉴클레오타이드(Nf로서 본 명세서에서 표시됨, 또한 2'-플루오로 뉴클레오타이드로서 본 명세서에서 표시됨), 2'-데옥시 뉴클레오타이드(dN으로서 본 명세서에서 표시됨), 2'-메톡시에틸(2'-O-2-메톡실에틸) 뉴클레오타이드(NM 또는 2'-MOE로서 본 명세서에서 표시됨), 2'-아미노 뉴클레오타이드 및 2'-알킬 뉴클레오타이드를 포함하지만, 이들로 제한되지는 않는다. 균일하게 변형된 소정의 화합물에서 모든 위치에 이것이 필요하지 않다. 반대로, 하나 초과의 변형이 단일 LPA RNAi 물질에서 또는 심지어 이의 단일 뉴클레오타이드에서 혼입될 수 있다. LPA RNAi 물질 센스 가닥 및 안티센스 가닥은 당해 분야에 공지된 방법에 의해 합성되고/되거나 변형될 수 있다. 하나의 뉴클레오타이드에서의 변형은 또 다른 뉴클레오타이드에서의 변형에 독립적이다.

[0047] 변형된 뉴클레오타이드는 또한 변형된 핵염기를 가지는 뉴클레오타이드를 포함한다. 변형된 핵염기는 합성 및 천연 핵염기, 5-치환된 피리미딘, 6-아자피리미딘 및 N-2, N-6 및 O-6 치환된 퓨린, 예컨대 2-아미노프로필아데닌, 5-프로피닐우라실 및 5-프로피닐시토신, 5-메틸시토신(5-me-C), 5-하이드록시메틸 시토신, 잔틴, 하이포잔틴, 2-아미노아데닌, 아데닌 및 구아닌의 6-메틸 및 다른 알킬 유도체, 아데닌 및 구아닌의 2-프로필 및 다른 알킬 유도체, 2-티오우라실, 2-티오타이민 및 2-티오시토신, 5-할로우라실 및 시토신, 5-프로피닐 우라실 및 시토신, 6-아조 우라실, 시토신 및 타이민, 5-우라실(슈도우라실), 4-티오우라실, 8-할로, 8-아미노, 8-티올, 8-티오알킬, 8-하이드록실 및 다른 8-치환된 아데닌 및 구아닌, 5-할로 특히 5-브로모, 5-트라이플루오로메틸 및 다른 5-치환된 우라실 및 시토신, 7-메틸구아닌 및 7-메틸아데닌, 8-아자구아닌 및 8-아자아데닌, 7-데아자구아닌 및 7-데아자아데닌 및 3-데아자구아닌 및 3-데아자아데닌을 포함하지만, 이들로 제한되지는 않는다.

[0048] 변형된 뉴클레오사이드간 연결

[0049] 몇몇 실시형태에서, LPA RNAi 물질의 하나 이상의 뉴클레오타이드는 비표준 연결 또는 골격(즉 변형된 뉴클레오사이드간 연결 또는 변형된 골격)에 의해 연결된다. 몇몇 실시형태에서, 변형된 뉴클레오사이드간 연결은 비포스페이트 함유 공유 뉴클레오사이드간 연결이다. 변형된 뉴클레오사이드간 연결 또는 골격은 5'-포스포로티오에이트기(sN, sn, sNf 또는 sdN에서처럼 뉴클레오타이드 앞에 소문자 's'로서 본 명세서에서 표시됨), 키랄 포스포로티오에이트, 티오포스페이트, 포스포로다이티오에이트, 포스포트라이에스터, 아미노알킬-포스포트라이에스터, 메틸 및 다른 알킬 포스포네이트, 예컨대 3'-알킬렌 포스포네이트 및 키랄 포스포네이트, 포스피네이트, 포

스포르아미데이트, 예컨대 3'-아미노 포스포르아미데이트 및 아미노알킬포스포르아미데이트, 티오노포스포르아미데이트, 티오노알킬-포스포네이트, 티오노알킬포스포트라이에스터, 모르폴리노 연결, 및 일반 3'-5' 연결을 가지는 보라노포스페이트, 이들의 2'-5' 연결된 유사체, 및 반전 극성을 가지는 것(여기서, 뉴클레오사이드 단위의 인접한 쌍은 3'-5' 내지 5'-3' 또는 2'-5' 내지 5'-2' 연결됨)을 포함하지만, 이들로 제한되지는 않는다. 다른 실시형태에서, 변형된 뉴클레오사이드간 연결 또는 골격은 인 원자가 결여된다. 인 원자가 결여된 변형된 뉴클레오사이드간 연결은 짧은 사슬 알킬 또는 사이클로알킬 당간 연결, 혼합된 이종원자 및 알킬 또는 사이클로알킬 당간 연결, 또는 하나 이상의 짧은 사슬 이종원자 또는 헤테로사이클 당간 연결을 포함하지만, 이들로 제한되지는 않는다. 몇몇 실시형태에서, 변형된 뉴클레오사이드간 골격은 실록산 골격, 설파이드, 설폭사이드 및 설폰 골격; 폼아세틸 및 티오폼아세틸 골격, 메틸렌 폼아세틸 및 티오폼아세틸 골격, 알켄 함유 골격, 설파메이트 골격, 메틸렌이미노 및 메틸렌하이드라지노 골격, 설포네이트 및 설폰아미드 골격, 아미드 골격; 및 혼합된 N, O, S, 및 CH_2 성분 파트를 가지는 기타를 포함하지만, 이들로 제한되지는 않는다.

[0050] 몇몇 실시형태에서, LPA RNAi 물질의 센스 가닥은 1개, 2개, 3개 또는 4개의 포스포로티오에이트 연결을 함유할 수 있고, LPA RNAi 물질의 안티센스 가닥은 1개, 2개, 3개 또는 4개의 포스포로티오에이트 연결을 함유할 수 있거나, 센스 가닥 및 안티센스 가닥 둘 다는 독립적으로 1개, 2개, 3개 또는 4개의 포스포로티오에이트 연결을 함유할 수 있다.

[0051] 몇몇 실시형태에서, LPA RNAi 물질 센스 가닥은 2개의 포스포로티오에이트 뉴클레오사이드간 연결을 함유한다. 몇몇 실시형태에서, 2개의 포스포로티오에이트 뉴클레오사이드간 연결은 센스 가닥의 3' 말단으로부터 1-3번 위치에서의 뉴클레오타이드 사이이다. 몇몇 실시형태에서, 2개의 포스포로티오에이트 뉴클레오사이드간 연결은 센스 가닥의 5' 말단으로부터 1-3번, 2-4번, 3-5번, 4-6번, 4-5번 또는 6-8번 위치에서의 뉴클레오타이드 사이이다. 몇몇 실시형태에서, LPA RNAi 물질 안티센스 가닥은 4개의 포스포로티오에이트 뉴클레오사이드간 연결을 함유한다. 몇몇 실시형태에서, 4개의 포스포로티오에이트 뉴클레오사이드간 연결은 센스 가닥의 5' 말단으로부터의 1-3번 위치에서의 뉴클레오타이드 사이 및 5' 말단으로부터의 19-21번, 20-22번, 21-23번, 22-24번, 23-25번 또는 24-26번 위치에서의 뉴클레오타이드 사이이다. 몇몇 실시형태에서, LPA RNAi 물질은 센스 가닥에서의 2개의 포스포로티오에이트 뉴클레오사이드간 연결 및 안티센스 가닥에서의 4개의 포스포로티오에이트 뉴클레오사이드간 연결을 함유한다.

[0052] 몇몇 실시형태에서, LPA RNAi 물질은 하나 이상의 변형된 뉴클레오타이드 및 하나 이상의 변형된 뉴클레오사이드간 연결을 함유한다. 몇몇 실시형태에서, 2'-변형된 뉴클레오타이드는 변형된 뉴클레오사이드간 연결과 조합된다.

[0053] 변형된 뉴클레오타이드를 가지는 LPA RNAi 물질

[0054] 변형된 뉴클레오타이드를 함유하는 안티센스 가닥의 예는 표 2A에 제공된다. 변형된 뉴클레오타이드를 함유하는 센스 가닥의 예는 표 2B에 제공된다. 표 2A 및 2B에서, 하기 주석은 변형된 뉴클레오타이드를 표시하도록 사용된다:

[0055] N = 2'-OH (비변형된) 리보뉴클레오타이드(f 또는 d 표시가 없는 대문자)

[0056] n = 2'-OMe 변형된 뉴클레오타이드

[0057] Nf = 2'-플루오로 변형된 뉴클레오타이드

[0058] dN = 2'-데옥시 뉴클레오타이드

[0059] N_{UNA} = 2',3'-세코 뉴클레오타이드 모방체(잠기지 않은 핵염기 유사체)

[0060] N_{LNA} = 잠긴 뉴클레오타이드

[0061] Nf_{ANA} = 2'-F-아라비노 뉴클레오타이드

[0062] NM = 2'-메톡시에틸 뉴클레오타이드

[0063] Ab = 비염기성 리보스

[0064] (invdN) = 인버티드 데옥시리보뉴클레오타이드(3'-3' 연결된 뉴클레오타이드)

[0065] (invAb) = 인버티드 비염기성 뉴클레오타이드

[0066] (invn) = 인버티드 2'-OMe 뉴클레오타이드

[0067] s = 포스포로티오에이트 연결된 뉴클레오타이드

[0068] p = 포스페이트

[0069] vpdN = 비닐 포스포네이트 데옥시리보뉴클레오타이드

[0070] (3'OMen) = 3'-OMe 뉴클레오타이드

[0071] (5Me-Nf) = 5'-Me, 2'-플루오로 뉴클레오타이드

[0072] cPrp = 사이클로프로필 포스포네이트

[0073] epTcPr = 표 4 참조

[0074] epTM = 표 4 참조

[0075] 또한, 하기 표적화기 및 연결기는 표 2A 및 2B에 기재되어 있다: (Alk-PEG5-C6), (C11-PEG3-NAG3), (C12), (C6-PEG4-NAG3), (C6-SS-Alk-Me), (Chol-TEG), (Dy540), (NAG13), (NAG18), (NAG24), (NAG25), (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG31), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36), (NAG37), (NAG4), (PAZ), (Sp18), (Steryl), (Alk-SMPT-C6). 각각의 센스 가닥 및/또는 안티센스 가닥은 임의의 상기 표시된 표적화기 또는 연결기, 및 서열의 5' 및 또는 3' 말단에 접합된 다른 표적화 또는 연결기를 가질 수 있다. 이 기에 대한 화학 구조는 표 4에 제공된다.

표 2A. 변형된 뉴클레오타이드를 가지는 LPA RNAi 물질 안티센스 가닥.

안티센스 가닥 번호	안티센스 가닥 서열 5' → 3'	서열 번호	서열 번호
AM01240-AS	dTCfgGfcAfgUfcCfcUfuCfuGfcGfudTsdT	386	1
AM01241-AS	dTGfuAfgCfaCfuCfcUfgCfaCfcCfcdTsdT	387	2
AM01242-AS	dTAfaUfaAfgGfgGfcUfgCfcAfcAfgdTsdT	388	3
AM01243-AS	dTUfaAfcAfaUfaAfgGfgGfcUfgCfcdTsdT	389	4
AM01244-AS	dTGfuAfuAfaCfaAfuAfaGfgGfgCfudTsdT	390	5
AM01245-AS	dTCfgUfaUfaAfcAfaUfaAfgGfgGfcdTsdT	391	6
AM01246-AS	dTCfgUfcUfgAfgCfaUfuGfuGfuCfadTsdT	392	7
AM01247-AS	dTGfcGfuCfuGfaGfcAfuUfgUfgUfcdTsdT	393	8
AM01248-AS	dTUfgCfgUfcUfgAfgCfaUfuGfuGfudTsdT	394	9
AM01249-AS	dTUfcUfgCfgUfcUfgAfgCfaUfuGfudTsdT	395	10
AM01250-AS	dTGfgAfuCfuGfgAfuUfuCfgGfcAfgdTsdT	396	11
AM01251-AS	dTCfaGfgAfuCfuGfgAfuUfuCfgGfcdTsdT	397	12
AM01252-AS	dTCfaUfcUfgAfgCfaUfcGfuGfuCfadTsdT	398	13
AM01253-AS	dTGfcAfuCfuGfaGfcAfuCfgUfgUfcdTsdT	399	14
AM01254-AS	dTUfgCfaUfcUfgAfgCfaUfcGfuGfudTsdT	400	15
AM01255-AS	dTUfcUfgCfaUfcUfgAfgCfaUfcGfudTsdT	401	16
AM01256-AS	dTAfaAfgCfcUfcUfaGfgCfuUfgGfadTsdT	402	17
AM01257-AS	dTGfuAfcCfcCfgGfgGfgUfuUfcCfudTsdT	403	18
AM01258-AS	dTUfgUfaCfcCfcGfgGfgGfuUfuCfcdTsdT	404	19
AM01259-AS	dTCfuGfuAfcCfcCfgGfgGfgUfuUfcdTsdT	405	20
AM01260-AS	dTUfcCfaUfaAfuGfgUfaGfuAfgCfadTsdT	406	21
AM01261-AS	dTGfuCfcAfuAfaUfgGfuAfgUfaGfcdTsdT	407	22
AM01262-AS	dTCfuCfuGfuCfcAfuAfaUfgGfuAfgdTsdT	408	23
AM01263-AS	dTCfgAfcUfaUfgCfuGfgUfgUfgGfudTsdT	409	24
AM01264-AS	dTCfcGfaCfuAfuGfcUfgGfuGfuGfgdTsdT	410	25

[0076]

AM01265-AS	dTUfcCfgAfcUfaUfgCfuGfgUfgUfgdTsdT	411	26
AM01266-AS	dTGfgUfcCfgAfcUfaUfgCfuGfgUfgdTsdT	412	27
AM01267-AS	dTUfuUfcUfgGfgGfuCfcGfaCfuAfudTsdT	413	28
AM01268-AS	dTUfuUfuCfuGfgGfgUfcCfgAfcUfadTsdT	414	29
AM01269-AS	dTGfcGfaAfuCfuCfaGfcAfuCfuGfgdTsdT	415	30
AM01270-AS	dTCfcAfaGfgGfcGfaAfuCfuCfaGfcdTsdT	416	31
AM01271-AS	dTAfcCfaAfgGfgCfgAfaUfcUfcAfgdTsdT	417	32
AM01272-AS	dTCfaCfcAfaGfgGfcGfaAfuCfuCfadTsdT	418	33
AM01273-AS	dTAfcAfcCfaAfgGfgCfgAfaUfcUfcdTsdT	419	34
AM01274-AS	dTCfcUfgAfcAfcUfgGfgAfuCfcAfudTsdT	420	35
AM01275-AS	dTUfgCfaAfgGfaCfaCfuUfgAfuUfcdTsdT	421	36
AM01276-AS	dTUfuGfcAfaGfgAfcAfcUfuGfaUfudTsdT	422	37
AM01277-AS	dTUfuGfcUfcCfgUfuGfgUfgCfuUfcdTsdT	423	38
AM01278-AS	dTAfaUfgAfgCfcUfcGfaUfaAfcUfcdTsdT	424	39
AM01279-AS	dTGfaAfuGfaGfcCfuCfgAfuAfaCfudTsdT	425	40
AM01280-AS	dTGfgAfuAfaUfaUfuCfuGfuUfgUfcdTsdT	426	41
AM01281-AS	dTCfcAfuGfgUfaUfaAfcAfcCfaAfgdTsdT	427	42
AM01282-AS	dTGfaUfcCfaUfgGfuAfuAfaCfaCfcdTsdT	428	43
AM01283-AS	dTAfuUfgGfgAfuCfcAfuGfgUfaUfadTsdT	429	44
AM01284-AS	dTCfaUfuGfgGfaUfcCfaUfgGfuAfudTsdT	430	45
AM01285-AS	dTAfcAfuUfgGfgAfuCfcAfuGfgUfadTsdT	431	46
AM01286-AS	dTGfaCfaUfuGfgGfaUfcCfaUfgGfudTsdT	432	47
AM01287-AS	dTGfaCfaUfuGfuGfuCfaGfgUfuGfcdTsdT	433	48
AM01288-AS	dTCfaCfuGfgAfcAfuUfgUfgUfcAfgdTsdT	434	49
AM01289-AS	dTAfcUfuGfaUfuCfuGfuCfaCfuGfgdTsdT	435	50
AM01290-AS	dTGfaGfaAfuGfaGfcCfuCfgAfuAfadTsdT	436	51
AM01291-AS	dTCfcAfuUfuGfgGfuAfgUfaUfuCfudTsdT	437	52
AM01292-AS	dTCfaCfcAfuUfuGfgGfuAfgUfaUfudTsdT	438	53

[0077]

AM01293-AS	dTCfcAfcCfaUfuUfgGfgUfaGfuAfudTsdT	439	54
AM01294-AS	dTAfuAfaCfaCfcAfaGfgGfcGfaAfudTsdT	440	55
AM01295-AS	dTAfcUfgGfgAfuCfcAfuGfgUfaUfadTsdT	441	56
AM01296-AS	dTCfaCfuGfgGfaUfcCfaUfgGfuAfudTsdT	442	57
AM01297-AS	dTAfcCfaCfcGfuGfgGfaGfuUfgUfgdTsdT	443	58
AM01298-AS	dTCfaAfgAfcUfgAfcAfuGfuUfcUfudTsdT	444	59
AM01299-AS	dTGfgGfaGfuUfgUfgAfgGfaCfaCfudTsdT	445	60
AM01300-AS	dTUfcUfcAfgGfuGfgUfgCfuUfgUfudTsdT	446	61
AM01301-AS	dTCfaCfaGfgGfcUfuUfuCfuCfaGfgdTsdT	447	62
AM01302-AS	dTGfaUfgCfcAfgUfgUfgGfuAfuCfadTsdT	448	63
AM01303-AS	dTUfgAfuGfcCfaGfuGfuGfgUfaUfcdTsdT	449	64
AM01304-AS	dTGfaCfaCfcUfgAfuUfcUfgUfuUfcdTsdT	450	65
AM01305-AS	dTGfgAfcAfcCfuGfaUfuCfuGfuUfudTsdT	451	66
AM01306-AS	dTCfuAfgGfaCfaCfcUfgAfuUfcUfgdTsdT	452	67
AM01796-AS	dTAfuAfaGfgGfgCfuGfcCfaCfaGfgdTsdT	453	68
AM01798-AS	dTAfaCfaAfuAfaGfgGfgCfuGfcCfadTsdT	454	69
AM01800-AS	dTGfuCfcGfaCfuAfuGfcUfgGfuGfudTsdT	455	70
AM01802-AS	dTUfcUfcAfgCfaUfcUfgGfaUfuCfcdTsdT	456	71
AM01804-AS	dTCfgAfaUfcUfcAfgCfaUfcUfgGfadTsdT	457	72
AM01806-AS	dTAfaGfgGfcGfaAfuCfuCfaGfcAfudTsdT	458	73
AM01808-AS	dTUfgAfcAfcUfgGfgAfuCfcAfuGfgdTsdT	459	74
AM01810-AS	dTCfcGfuUfgGfuGfcUfuCfuUfcAfgdTsdT	460	75
AM01812-AS	dTCfuUfgAfuUfcUfgUfcAfcUfgGfadTsdT	461	76
AM01814-AS	dTCfaCfcGfuGfgGfaGfuUfgUfgAfgdTsdT	462	77
AM01816-AS	dTUfcUfaGfgAfcAfcCfuGfaUfuCfudTsdT	463	78
AM01818-AS	dTAfgUfcUfcUfaGfgAfcAfcCfuGfadTsdT	464	79
AM02003-AS	dTGfuAfuAfaCfaAfuaaGfgGfgCfudTsdT	465	5
AM02004-AS	dTGfuAfuA_{UNA}aCfaAfuaaGfgGfgCfudTsdT	466	5

[0078]

AM02005-AS	dTGfuAfuAfA$_{UNA}$CfaAfuaaGfgGfgCfudTsdT	467	5
AM02007-AS	dTCfgUfaUfaAfcAfauaAfgGfgGfcdTsdT	468	6
AM02008-AS	dTCfgUfaU$_{UNA}$aAfcAfauaAfgGfgGfcdTsdT	469	6
AM02009-AS	dTCfgUfaUfA$_{UNA}$AfcAfauaAfgGfgGfcdTsdT	470	6
AM02011-AS	dTGfcGfuCfuGfaGfcauUfgUfgUfcdTsdT	471	8
AM02012-AS	dTGfcGfuC$_{UNA}$uGfaGfcauUfgUfgUfcdTsdT	472	8
AM02013-AS	dTGfcGfuCfU$_{UNA}$GfaGfcauUfgUfgUfcdTsdT	473	8
AM02015-AS	dTUfgCfgUfcUfgAfgcaUfuGfuGfudTsdT	474	9
AM02016-AS	dTUfgCfgU$_{UNA}$cUfgAfgcaUfuGfuGfudTsdT	475	9
AM02017-AS	dTUfgCfgUfC$_{UNA}$UfgAfgcaUfuGfuGfudTsdT	476	9
AM02019-AS	dTGfaGfaAfuGfaGfccuCfgAfuAfadTsdT	477	51
AM02020-AS	dTGfaGfaA$_{UNA}$uGfaGfccuCfgAfuAfadTsdT	478	51
AM02021-AS	dTGfaGfaAfU$_{UNA}$GfaGfccuCfgAfuAfadTsdT	479	51
AM02023-AS	dTGfaCfaCfcUfgAfuucUfgUfuUfcdTsdT	480	65
AM02024-AS	dTGfaCfaC$_{UNA}$cUfgAfuucUfgUfuUfcdTsdT	481	65
AM02025-AS	dTGfaCfaCfC$_{UNA}$UfgAfuucUfgUfuUfcdTsdT	482	65
AM02027-AS	dTGfuCfcGfaCfuAfugcUfgGfuGfudTsdT	483	70
AM02028-AS	dTGfuCfcG$_{UNA}$aCfuAfugcUfgGfuGfudTsdT	484	70
AM02029-AS	dTGfuCfcGfA$_{UNA}$CfuAfugcUfgGfuGfudTsdT	485	70
AM02031-AS	dTCfgAfaUfcUfcAfgcaUfcUfgGfadTsdT	486	72
AM02032-AS	dTCfgAfaU$_{UNA}$cUfcAfgcaUfcUfgGfadTsdT	487	72
AM02033-AS	dTCfgAfaUfC$_{UNA}$UfcAfgcaUfcUfgGfadTsdT	488	72
AM02035-AS	dTAfaGfgGfcGfaAfucuCfaGfcAfudTsdT	489	73
AM02036-AS	dTAfaGfgG$_{UNA}$cGfaAfucuCfaGfcAfudTsdT	490	73
AM02037-AS	dTAfaGfgGfC$_{UNA}$GfaAfucuCfaGfcAfudTsdT	491	73
AM02039-AS	dTUfgAfcAfcUfgGfgauCfcAfuGfgdTsdT	492	74
AM02040-AS	dTUfgAfcA$_{UNA}$cUfgGfgauCfcAfuGfgdTsdT	493	74
AM02041-AS	dTUfgAfcAfC$_{UNA}$UfgGfgauCfcAfuGfgdTsdT	494	74

[0079]

AM02240-AS	dTCfaAfuAfaGfgGfgcuGfcCfaCfadTsdT	495	80
AM02241-AS	dTCfuGfcGfuCfuGfagcAfuUfgUfgdTsdT	496	81
AM02242-AS	dTAfcAfgGfaUfcUfggaUfuUfcGfgdTsdT	497	82
AM02243-AS	dTCfcGfgGfgGfuUfuccUfcAfgUfcdTsdT	498	83
AM02244-AS	dTUfgUfcCfaUfaAfuggUfaGfuAfgdTsdT	499	84
AM02245-AS	dTUfcUfgUfcCfaUfaauGfgUfaGfudTsdT	500	85
AM02246-AS	dTAfcUfcUfgUfcCfauaAfuGfgUfadTsdT	501	86
AM02247-AS	dTAfaCfuCfuGfuCfcauAfaUfgGfudTsdT	502	87
AM02248-AS	dTGfgGfcGfaAfuCfucaGfcAfuCfudTsdT	503	88
AM02249-AS	dTAfgGfgCfgAfaUfcucAfgCfaUfcdTsdT	504	89
AM02250-AS	dTAfaCfaCfcAfaGfggcGfaAfuCfudTsdT	505	90
AM02251-AS	dTAfgGfaCfaCfuUfgauUfcUfgUfcdTsdT	506	91
AM02252-AS	dTGfgAfcCfaAfgAfcugAfcAfuGfudTsdT	507	92
AM02253-AS	dTGfgUfcAfgGfcCfaccAfuUfuGfgdTsdT	508	93
AM02254-AS	dTAfuCfcAfuGfgUfauaAfcAfcCfadTsdT	509	94
AM02255-AS	dTGfgGfaUfcCfaUfgguAfuAfaCfadTsdT	510	95
AM02256-AS	dTUfgGfaCfaUfuGfuguCfaGfgUfudTsdT	511	96
AM02257-AS	dTAfuUfcUfgUfcAfcugGfaCfaUfudTsdT	512	97
AM02258-AS	dTGfgUfgCfuUfgUfucaGfaAfaCfadTsdT	513	98
AM02259-AS	dTGfgAfgAfaUfgAfgccUfcGfaUfadTsdT	514	99
AM02260-AS	dTGfuGfgAfgAfaUfgagCfcUfcGfadTsdT	515	100
AM02261-AS	dTCfcGfuGfgGfaGfuugUfgAfgGfadTsdT	516	101
AM02262-AS	dTGfgAfcCfaCfcGfuggGfaGfuUfgdTsdT	517	102
AM02263-AS	dTUfgCfuUfgUfuCfagaAfgGfaGfcdTsdT	518	103
AM02264-AS	dTCfuGfaUfgCfcAfgugUfgGfuAfudTsdT	519	104
AM02265-AS	dTUfaGfgAfcAfcCfugaUfuCfuGfudTsdT	520	105
AM02266-AS	dTCfuCfuAfgGfaCfaccUfgAfuUfcdTsdT	521	106
AM02267-AS	dTUfcUfcUfaGfgAfcacCfuGfaUfudTsdT	522	107

[0080]

AM02268-AS	dTGfuCfuCfuAfgGfacaCfcUfgAfudTsdT	523	108
AM02404-AS	dTsGfsaGfaAfuGfaGfcCfuCfgAfuAfaCfuCfsusuAu	524	109
AM02406-AS	dTsGfsaGfaAfuGfaGfccUfCfgAfuAfaCfuCfsusuAu	525	109
AM02408-AS	dTsGfsaGfaAfuGfaGfccUfcgAfuAfaCfuCfsusuAu	526	109
AM02410-AS	dTsGfsaGfaAfuGfaGfcCfUfcGfaUfaAfcUfcsUfsuAu	527	109
AM02412-AS	dTsGfsaCfaCfcUfgAfuUfcUfgUfuUfcUfgAfsgsuAu	528	110
AM02414-AS	dTsGfsaCfaCfcUfgAfuuCfUfgUfuUfcUfgAfsgsuAu	529	110
AM02416-AS	dTsGfsaCfaCfcUfgAfuuCfugUfuUfcUfgAfsgsuAu	530	110
AM02418-AS	dTsGfsaCfaCfcUfgAfuUfCfuGfuUfuCfuGfasGfsuAu	531	110
AM02531-AS	dTsCfsgUfaUfaAfcAfauaAfgGfgGfcUfgCfscsuAu	532	111
AM02532-AS	dTsGfscGfuCfuGfaGfcauUfgUfgUfcAfgGfsusuAu	533	112
AM02533-AS	dTsUfsgCfgUfcUfgAfgcaUfuGfuGfuCfaGfsgsuAu	534	113
AM02534-AS 1532-AS00	dTsGfsaGfaAfuGfaGfccuCfgAfuAfaCfuCfsusuAu	535	109
AM02535-AS 1533-AS00	dTsGfsaCfaCfcUfgAfuucUfgUfuUfcUfgAfsgsuAu	536	110
AM02536-AS	dTsAfsaGfgGfcGfaAfucuCfaGfcAfuCfuGfsgsuAu	537	114
AM02755-AS	usUfsaAfcAfaUfaAfgGfgGfcUfgCfAbs(PAZ)	538	115
AM02756-AS	usGfsuAfuAfaCfaAfuAfaGfgGfgCfAbs(PAZ)	539	116
AM02757-AS	usCfsgUfaUfaAfcAfaUfaAfgGfgGfAbs(PAZ)	540	117
AM02758-AS	usGfscGfuCfuGfaGfcAfuUfgUfgUfAbs(PAZ)	541	118
AM02759-AS	usUfsgCfgUfcUfgAfgCfaUfuGfuGfAbs(PAZ)	542	119
AM02760-AS	usCfsaGfgAfuCfuGfgAfuUfuCfgGfAbs(PAZ)	543	120
AM02761-AS	usUfsgCfaUfcUfgAfgCfaUfcGfuGfAbs(PAZ)	544	121
AM02762-AS	usCfsgAfcUfaUfgCfuGfgUfgUfgGfAbs(PAZ)	545	122
AM02763-AS	usUfsuUfcUfgGfgGfuCfcGfaCfuAfAbs(PAZ)	546	123
AM02764-AS	usGfscGfaAfuCfuCfaGfcAfuCfuGfAbs(PAZ)	547	124
AM02765-AS	usUfsgCfaAfgGfaCfaCfuUfgAfuUfAbs(PAZ)	548	125

[0081]

AM02766-AS	usAfsaUfgAfgCfcUfcGfaUfaAfcUfAbs(PAZ)	549	126
AM02767-AS	usGfsaAfuGfaGfcCfuCfgAfuAfaCfAbs(PAZ)	550	127
AM02768-AS	usGfsaCfaUfuGfuGfuCfaGfgUfuGfAbs(PAZ)	551	128
AM02769-AS	usGfsaGfaAfuGfaGfcCfuCfgAfuAfAbs(PAZ)	552	129
AM02770-AS	usCfscAfuUfuGfgGfuAfgUfaUfuCfAbs(PAZ)	553	130
AM02771-AS	usCfsaCfcAfuUfuGfgGfuAfgUfaUfAbs(PAZ)	554	131
AM02772-AS	usGfsaCfaCfcUfgAfuUfcUfgUfuUfAbs(PAZ)	555	132
AM02773-AS	usGfsgAfcAfcCfuGfaUfuCfuGfuUfAbs(PAZ)	556	133
AM02774-AS	usUfsaAfcAfaUfaAfgGfgGfcUfgAbAbs(PAZ)	557	134
AM02775-AS	usGfsuAfuAfaCfaAfuAfaGfgGfgAbAbs(PAZ)	558	135
AM02776-AS	usCfsgUfaUfaAfcAfaUfaAfgGfgAbAbs(PAZ)	559	136
AM02777-AS	usGfscGfuCfuGfaGfcAfuUfgUfgAbAbs(PAZ)	560	137
AM02778-AS	usUfsgCfgUfcUfgAfgCfaUfuGfuAbAbs(PAZ)	561	138
AM02779-AS	usCfsaGfgAfuCfuGfgAfuUfuCfgAbAbs(PAZ)	562	139
AM02780-AS	usUfsgCfaUfcUfgAfgCfaUfcGfuAbAbs(PAZ)	563	140
AM02781-AS	usCfsgAfcUfaUfgCfuGfgUfgUfgAbAbs(PAZ)	564	141
AM02782-AS	usUfsuUfcUfgGfgGfuCfcGfaCfuAbAbs(PAZ)	565	142
AM02783-AS	usGfscGfaAfuCfuCfaGfcAfuCfuAbAbs(PAZ)	566	143
AM02784-AS	usUfsgCfaAfgGfaCfaCfuUfgAfuAbAbs(PAZ)	567	144
AM02785-AS	usAfsaUfgAfgCfcUfcGfaUfaAfcAbAbs(PAZ)	568	145
AM02786-AS	usGfsaAfuGfaGfcCfuCfgAfuAfaAbAbs(PAZ)	569	146
AM02787-AS	usGfsaCfaUfuGfuGfuCfaGfgUfuAbAbs(PAZ)	570	147
AM02788-AS	usGfsaGfaAfuGfaGfcCfuCfgAfuAbAbs(PAZ)	571	148
AM02789-AS	usCfscAfuUfuGfgGfuAfgUfaUfuAbAbs(PAZ)	572	149
AM02790-AS	usCfsaCfcAfuUfuGfgGfuAfgUfaAbAbs(PAZ)	573	150
AM02791-AS	usGfsaCfaCfcUfgAfuUfcUfgUfuAbAbs(PAZ)	574	151
AM02792-AS	usGfsgAfcAfcCfuGfaUfuCfuGfuAbAbs(PAZ)	575	152
AM02857-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuCfsusuAu	576	153

[0082]

1532-AS14			
AM02858-AS	usgsaGfaAfuGfaGfccuCfgAfuAfaCfuCfsusuAu	577	153
AM02859-AS	usgsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	578	153
AM02860-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	579	153
AM02863-AS 1533-AS15	usGfsaCfaCfcUfgAfuucUfgUfuUfcUfgAfsgsuAu	580	154
AM02864-AS	usgsaCfaCfcUfgAfuucUfgUfuUfcUfgAfsgsuAu	581	154
AM02865-AS	usgsaCfaCfcUfgAfuucUfgUfuUfcUfgasgsuAu	582	154
AM02866-AS	usGfsaCfaCfcUfgAfuucUfgUfuUfcUfgasgsuAu	583	154
AM02943-AS	usgsagaAfugaGfccuCfgAfuaaCfuCfsusuAu	584	153
AM02944-AS	usgsagaauGfagccuCfgauAfaCfuCfsusuAu	585	153
AM02945-AS	usgsagaauGfagccuCfgauAfacucsusuAu	586	153
AM02950-AS	usgsaCfaCfcUfgAfuucUfgUfuucUfgasgsuAu	587	154
AM02951-AS	usgsaCfaCfcUfgAfuucUfguuUfcugasgsuAu	588	154
AM02952-AS	usgsacaccugAfuucUfgUfuucUfgasgsuAu	589	154
AM03040-AS	usGfsAfcAfcCfUfgAfuucUfgUfuUfcUfgAfsgsuAu	590	154
AM03041-AS	usGfsAfcAfccUfgAfuucUfgUfuUfcUfgAfsgsuAu	591	154
AM03043-AS	usGfsaCfaCfCfUfgAfuucUfgUfuUfcUfgAfsgsuAu	592	154
AM03065-AS 1533-AS18	dTsGfsaCfaCfcugauucUfgUfuUfcUfgAfsgsuAu	593	110
AM03066-AS 1533-AS03	usGfsaCfaCfcugauucUfgUfuUfcUfgAfsgsuAu	594	154
AM03067-AS	dTsGfsaCfaCfcugauucUfgUfuucugasgsuAu	595	110
AM03068-AS	usGfsaCfaCfcugauucUfgUfuucugasgsuAu	596	154
AM03069-AS 1533-AS14	dTsGfsaCfaCfcUfgAfuucUfgUfuucugasgsuAu	597	110
AM03070-AS 1533-AS29	usGfsaCfaCfcUfgAfuucUfgUfuucugasgsuAu	598	154

[0083]

AM03107-AS	usCfsgUfaUfaAfcAfauaAfgGfgGfcUfgCfscsuAu	599	156
AM03108-AS	usCfsgUfaUfaAfcAfauaAfgGfgGfcUfgcscsuAu	600	156
AM03119-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuCMsTMsuAu	601	155
AM03120-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuCMTMuAu	602	155
AM03121-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfucuuAu	603	153
AM03127-AS	usCfsgUfaUfaAfCfAfauaAfgGfgGfcUfgCfscsuAu	604	156
AM03129-AS	usCfsgUfaUfaAfCfAfauaAfgGfgGfcUfgcscsuAu	605	156
AM03130-AS	usGfsaGfaAfuGfaGfCfcuCfgAfuAfaCfuCfsusuAu	606	153
AM03131-AS	usGfsaGfaAfuGfaGfCfCfuCfgAfuAfaCfuCfsusuAu	607	153
AM03149-AS	usGfsagaAfugaGfccuCfgAfuaaCfuCfsusuAu	608	153
AM03150-AS	usGfsagaauGfagccuCfgauAfaCfuCfsusuAu	609	153
AM03151-AS	usGfsagaauGfagccuCfgauAfacucsusuAu	610	153
AM03255-AS 1532-AS26	usGfsaGfaAfugaGfccuCfgauaaCfuCfsusuAu	611	153
AM03256-AS	usGfsagaaugagccuCfgauaaCfuCfsusuAu	612	153
AM03257-AS	usGfsagaaugagccuCfgauaacuCfsusuAu	613	153
AM03258-AS	usGfsagaaugagccuCfgauaaCfucsusuAu	614	153
AM03259-AS	usGfsagaaugagccuCfgauaacucsusuAu	615	153
AM03260-AS	usGfsaGfaAfugaGfccUfCfgauaaCfuCfsusuAu	616	153
AM03261-AS	usGfsagaaugagccUfCfgauaaCfuCfsusuAu	617	153
AM03262-AS	usGfsagaaugagccUfCfgauaacuCfsusuAu	618	153
AM03263-AS	usGfsagaaugagccUfCfgauaaCfucsusuAu	619	153
AM03264-AS	usGfsagaaugagccUfCfgauaacucsusuAu	620	153
AM03265-AS	usGfsaGfaAfugaGfcCfuCfgauaaCfuCfsusuAu	621	153
AM03266-AS	usGfsagaaugagcCfuCfgauaaCfuCfsusuAu	622	153
AM03267-AS	usGfsagaaugagcCfuCfgauaacuCfsusuAu	623	153
AM03268-AS	usGfsagaaugagcCfuCfgauaaCfucsusuAu	624	153
AM03269-AS	usGfsagaaugagcCfuCfgauaacucsusuAu	625	153

[0084]

AM03270-AS	usGfsaGfaAfugaGfCfcuCfgauaaCfuCfsusuAu	626	153
AM03271-AS	usGfsagaaugagCfcuCfgauaaCfuCfsusuAu	627	153
AM03272-AS	usGfsagaaugagCfcuCfgauaacuCfsusuAu	628	153
AM03273-AS	usGfsagaaugagCfcuCfgauaaCfucsusuAu	629	153
AM03274-AS	usGfsagaaugagCfcuCfgauaacucsusuAu	630	153
AM03279-AS	usCfsgUfaUfaacaauaAfgGfgGfcUfgCfscsuAu	631	156
AM03280-AS	usCfsgUfaUfaAfcAfauaAfggggcUfgCfscsuAu	632	156
AM03281-AS	usCfsguauaAfcAfauaAfgGfgGfcUfgCfscsuAu	633	156
AM03282-AS	usCfsgUfaUfaAfcAfauaAfgGfgGfcugcscsuAu	634	156
AM03283-AS	usCfsgUfaUfaacaauaAfgGfgGfcugcscsuAu	635	156
AM03284-AS	usCfsguauaAfcAfauaAfggggcUfgCfscsuAu	636	156
AM03300-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsuAu	637	156
AM03301-AS	usCfsguauaAfcAfaUfaAfggggcUfgCfscsuAu	638	156
AM03331-AS	usGfsaGfaAfuGfaGfcCfuCfgAfuAfasdTsdT	639	157
AM03375-AS	usCfsguauaAfcAfauaAfggggcugcscsuAu	640	156
AM03376-AS	usCfsguauaacaauaAfggggcugcscsuAu	641	156
AM03377-AS	usGfsagaauGfaGfccuCfgauaacucsusuAu	642	153
AM03427-AS	dTsGfaGfaAfuGfaGfccuCfgAfuAfaCfuCfuuAu	643	109
AM03486-AS	vpdTGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	644	109
AM03487-AS	vpdTsGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	645	109
AM03488-AS	dTsGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	646	109
AM03490-AS	vpdTCfsgUfaUfaAfcAfauaAfgGfgGfcUfgCfscsuAu	647	111
AM03491-AS	vpdTsCfsgUfaUfaAfcAfauaAfgGfgGfcUfgCfscsuAu	648	111
AM03655-AS	usGfsAfgaaugagccuCfgauaacucsusuAu	649	153
AM03656-AS	usGfsaGfaaugagccuCfgauaacucsusuAu	650	153
AM03657-AS	usGfsagAfaugagccuCfgauaacucsusuAu	651	153
AM03658-AS	usGfsagaAfugagccuCfgauaacucsusuAu	652	153
AM03659-AS	usGfsagaaUfgagccuCfgauaacucsusuAu	653	153

[0085]

AM03660-AS	usGfsagaauGfagccuCfgauaacucsusuAu	654	153
AM03661-AS	usGfsagaaugaGfccuCfgauaacucsusuAu	655	153
AM03671-AS	usCfsgUfaUfaAfcAfauaAfgGfcGfcUfgCfscsuAu	656	158
AM03672-AS	usCfsgUfaUfaAfcAfauaAfggggCfugCfscsuAu	657	156
AM03673-AS	usCfsgUfaUfaAfcAfauaAfggggcugcscsuAu	658	156
AM03674-AS	usCfsGfuauaAfcAfauaAfggggcugcscsuAu	659	156
AM03675-AS	usCfsgUfaUfaAfcaauaAfggggcugcscsuAu	660	156
AM03676-AS	usCfsgUfaUfaaCfaauaAfggggcugcscsuAu	661	156
AM03677-AS	usCfsGfuauAfaCfaauaAfggggcugcscsuAu	662	156
AM03678-AS	usGfsaGfaAfuGfaGfccuCfgauaacucsusuAu	663	153
AM03679-AS	usGfsAfgaAfuGfaGfccuCfgauaacucsusuAu	664	153
AM03680-AS	usGfsAfgAfauGfaGfcCfuCfgauaacucsusuAu	665	153
AM03681-AS	usGfsAfgAfauGfagCfCfuCfgauaacucsusuAu	666	153
AM03682-AS	usGfsaGfaAfuGfagccuCfgauaacucsusuAu	667	153
AM03744-AS	usGfsuauaaCfaAfuaaGfgggAbAbs(PAZ)	668	135
AM03745-AS	usGfsuAfuAfaCfaAfuAfaGfgGMGMAbAbs(PAZ)	669	135
AM03749-AS	usCfsguauaAfcAfauaAfgggAbAbs(PAZ)	670	136
AM03750-AS	usCfsgUfaUfaAfcAfaUfaAfgGMGMAbAbs(PAZ)	671	136
AM03754-AS	usGfsagaauGfaGfccuCfgauAbAbs(PAZ)	672	148
AM03755-AS	usGfsagaaugagcCfuCfgauAbAbs(PAZ)	673	148
AM03756-AS	usGfsaGfaAfuGfaGfcCfuCfgAMTMAbAbs(PAZ)	674	159
AM03760-AS	usGfsacaccUfgAfuucUfguuAbAbs(PAZ)	675	151
AM03761-AS	usGfsaCfaCfcugauucUfguuAbAbs(PAZ)	676	151
AM03762-AS	usGfsaCfaCfcUfgAfuUfcUfgTMTMAbAbs(PAZ)	677	160
AM03823-AS	usCf$_{ANA}$sgUfaUfaAfCfAfauaAfgGfgGfcUfgcscsuAu	678	156
AM03824-AS	usCfsgUf$_{ANA}$aUfaAfCfAfauaAfgGfgGfcUfgcscsuAu	679	156
AM03825-AS	usCfsgUfaUf$_{ANA}$aAfCfAfauaAfgGfgGfcUfgcscsuAu	680	156
AM03826-AS	usCfsgUfaUfaAf$_{ANA}$CfAfauaAfgGfgGfcUfgcscsuAu	681	156

[0086]

AM03827-AS	usGf$_{ANA}$sagaauGfaGfccuCfgauaacucsusuAu	682	153
AM03828-AS	usGfsagaauGf$_{ANA}$aGfccuCfgauaacucsusuAu	683	153
AM03856-AS	TMsGfsagaauGfaGfccuCfgauaacucsusuAu	684	109
AM03857-AS	TMsCfsgUfaUfaAfCfAfauaAfgGfgGfcUfgcscsuAu	685	111
AM03862-AS	TMsGfsagaaugagccuCfgauaacucsusuAu	686	109
AM03866-AS	usCfsgUfaUfaacaauaAfggggcugcscsuAu	687	156
AM03867-AS	usCfsgUfauaAfcaauaAfggggcugcscsuAu	688	156
AM03868-AS	usCfsgUfauaacAfauaAfggggcugcscsuAu	689	156
AM03869-AS	usCfsgUfauaacaaUfaAfggggcugcscsuAu	690	156
AM03870-AS	usCfsguaUfaAfcaauaAfggggcugcscsuAu	691	156
AM03871-AS	usCfsguaUfaacAfauaAfggggcugcscsuAu	692	156
AM03872-AS	usCfsguaUfaacaaUfaAfggggcugcscsuAu	693	156
AM03873-AS	usCfsguauaAfcaaUfaAfggggcugcscsuAu	694	156
AM03874-AS	usCfsguauaacAfaUfaAfggggcugcscsuAu	695	156
AM03875-AS	usCfsgUfaUfaAfcAfaUfaAfgggGfcUfgCfscsuAu	696	156
AM03876-AS	usCfsgUfaUfaAfcAfaUfaAfgGfggcUfgCfscsuAu	697	156
AM03877-AS	usCfsgUfaUfaAfcAfaUfaAfgGfgGfcugCfscsuAu	698	156
AM03878-AS	usCfsgUfaUfaAfcAfaUfaAfgGfgGfcUfgcscsuAu	699	156
AM03883-AS	vpusCfsgsUfaUfaAfCfAfauaAfgGfgGfcUfgasusu	700	161
AM03884-AS	vpusCfsgsUfaUfaAfCfAfauaAfgGfgGfcUfgcsusu	701	162
AM03885-AS	vpusGfsasgaauGfaGfccuCfgauaacucsusu	702	163
AM03929-AS	usCfsguaUfaAfcaauaAfgGfggcugcscsuAu	703	156
AM03930-AS	usCfsguaUfaAfCfaauaAfgGfggcugcscsuAu	704	156
AM03932-AS	usGfsagaAfuGfagccuCfgAfuaacucsusuAu	705	153
AM03933-AS	usGfsagaAfuGfAfgccuCfgAfuaacucsusuAu	706	153
AM03969-AS	vpusCfsgUfaUfaAfCfAfauaAfgGfgGfcUfgcscsuAu	707	156
AM03971-AS	vpusCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	708	164
AM03972-AS	usCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	709	164

[0087]

AM03973-AS	U_{UNA}sCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	710	164
AM04132-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuau	711	153
AM04133-AS	usGfsagaauGfaGfccuCfgauaacucsusuau	712	153
AM04134-AS	usGfsaGfaAfuGfAfGfccuCfgAfuAfaCfucsusuau	713	153
AM04135-AS	usGfsagaauGfAfGfccuCfgauaacucsusuau	714	153
AM04136-AS	usGfsaGfaAfuGfAfgccuCfgAfuAfaCfucsusuau	715	153
AM04137-AS	usGfsagaauGfAfgccuCfgauaacucsusuau	716	153
AM04150-AS	usGfsagaauGfaGfccuCfgauaacucsusuau(Dy540)	717	153
AM04215-AS	usCfsgUfaUfaaCfaaUfaAfgGfgGfcUfgCfscsuAu	718	156
AM04216-AS	usCfsguauaAfcaaUfaAfggggcugCfscsuAu	719	156
AM04217-AS	usCfsguauaaCfaaUfaAfggggcugCfscsuAu	720	156
AM04218-AS	usCfsguauaaCfaaUfaAfggggCfugCfscsuAu	721	156
AM04219-AS	usCfsguaUfaaCfaaUfaAfggggCfugCfscsuAu	722	156
AM04250-AS	usGfsuAfuAfaCfaAfuAfaGfgGMGMsAbsAbs(PAZ)	723	135
AM04251-AS	usGfsuAfuAfaCfaAfuAfaGfgGMGM(Sp18)s(PAZ)	724	165
AM04252-AS	usGfsuAfuAfaCfaAfuAfaGfgGMGM(C12)s(PAZ)	725	165
AM04253-AS	usCfsgUfaUfaAfcAfaUfaAfgGMGMsAbsAbs(PAZ)	726	136
AM04254-AS	usCfsgUfaUfaAfcAfaUfaAfgGMGM(Sp18)s(PAZ)	727	166
AM04255-AS	usCfsgUfaUfaAfcAfaUfaAfgGMGM(C12)s(PAZ)	728	166
AM04256-AS	usGfsaGfaAfuGfaGfcCfuCfgAMTMsAbsAbs(PAZ)	729	159
AM04257-AS	usGfsaGfaAfuGfaGfcCfuCfgAMTM(Sp18)s(PAZ)	730	167
AM04258-AS	usGfsaGfaAfuGfaGfcCfuCfgAMTM(C12)s(PAZ)	731	167
AM04259-AS	usGfsaCfaCfcUfgAfuUfcUfgTMTMsAbsAbs(PAZ)	732	160
AM04260-AS	usGfsaCfaCfcUfgAfuUfcUfgTMTM(Sp18)s(PAZ)	733	168
AM04261-AS	usGfsaCfaCfcUfgAfuUfcUfgTMTM(C12)s(PAZ)	734	168
AM04377-AS	dTusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsua	735	169
AM04378-AS	uAusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsu	736	170
AM04379-AS	dTcsCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsua	737	171

[0088]

AM04380-AS	cUcsCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsu	738	172
AM04383-AS	dTusGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusua	739	173
AM04384-AS	uAusGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusu	740	174
AM04385-AS	dTgsGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusua	741	175
AM04386-AS	gUgsGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusu	742	176
AM04387-AS	dTusGfsagaauGfaGfccuCfgauaacucsusua	743	173
AM04388-AS	uAusGfsagaauGfaGfccuCfgauaacucsusu	744	174
AM04389-AS	dTgsGfsagaauGfaGfccuCfgauaacucsusua	745	175
AM04390-AS	gUgsGfsagaauGfaGfccuCfgauaacucsusu	746	176
AM04413-AS	usCfsgsUfaUfaacaaUfaAfgGfgGfcusu	747	164
AM04415-AS	usGfsasGfaAfuGfaGfccuCfgAfuAfausu	748	177
AM04437-AS	usGfsuAfuAfaCfaAfuAfaGfgGMGMs(C12)s(PAZ)	749	165
AM04438-AS	usCfsgUfaUfaAfcAfaUfaAfgGMGMs(C12)s(PAZ)	750	166
AM04439-AS	usGfsaGfaAfuGfaGfcCfuCfgAMTMs(C12)s(PAZ)	751	167
AM04440-AS	usGfsaCfaCfcUfgAfuUfcUfgTMTMs(C12)s(PAZ)	752	168
AM04501-AS	cPrpTMsCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	753	178
AM04507-AS	usGfsasGfaAfuGfaGfccuCfgAfuAfausuAUAUA	754	179
AM04539-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgsCfscuAu	755	156
AM04540-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgsCfcuAu	756	156
AM04541-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuscsuuAu	757	153
AM04542-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuscuuAu	758	153
AM04544-AS	usCfsgsUfaUfaAfCfAfauaAfgGfgGfcUfgcsusu	759	162
AM04545-AS	usCfsgsUfaUfaAfCfAfauaagGfgGfcusu	760	164
AM04546-AS	usCfsgsUfaUfaAfCfAfaUfaagGfgGfcusu	761	164
AM04582-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgsCfsc	762	180
AM04583-AS	dTusCfsgUfaUfaacaaUfaAfgGfgGfcUfgsCfsc	763	181
AM04584-AS	dTusCfsgUfaUfaacaaUfaAfgGfgGfcUfgscsc	764	181
AM04585-AS	dTusCfsgsUfaUfaacaaUfaAfgGfgGfcUfgscsc	765	181

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AM04586-AS	dTusCfsgsUfaUfaacaaUfaAfgGfgGfcUfgcsc	766	181
AM04587-AS	dTusCfsgsUfaUfaacaaUfaAfgGfgGfcusg	767	182
AM04609-AS	epTcPrsCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	768	178
AM04610-AS	epTMsCfsgsUfaUfaAfCfAfauaAfgGfgGfcusu	769	178
AM04677-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfsuscuuAu	770	153
AM04678-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfasCfsucuuAu	771	153
AM04679-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuasuscGc	772	183
AM04680-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuasusuCa	773	184
AM04681-AS	usGfsaGfaAfuGfaGfccuCfgAfuAfaCfuascsgAu	774	185
AM04733-AS	us(5Me-Gf)saGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	775	153
AM04734-AS	usGfsa(5Me-Gf)aAfuGfaGfccuCfgAfuAfaCfucsusuAu	776	153
AM04735-AS	usGfsaGfaAfu(5Me-Gf)aGfccuCfgAfuAfaCfucsusuAu	777	153
AM04736-AS	usGfsaGfaAfuGfa(5Me-Gf)ccuCfgAfuAfaCfucsusuAu	778	153
AM04805-AS	vpusCfsgsUfaUfaAfCfAfauaAfgGfgGfcgsu	779	186
AM04821-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsu	780	187
AM04822-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfsusu	781	162
AM04823-AS	vpusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsu	782	187
AM04824-AS	vpusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfsusu	783	162
AM04871-AS	usGfsaGfaAfuGfAfgccuCfgAfuAfaCfusCfsuuAu	784	153
AM04872-AS	cPrpusGfsaGfaAfuGfaGfccuCfgAfuAfaCfucsusuAu	785	153
AM04873-AS	cPrpusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsuAu	786	156
AM04874-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcsusu	787	164
AM04875-AS	cPrpusCfsgUfaUfaacaaUfaAfgGfgGfcsusu	788	164
AM04876-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcsusg	789	188
AM04877-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcsUfsg	790	188
AM04878-AS	cPrpusCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfsusu	791	162
AM04879-AS	usGfsaGfaAfuGfaGfcCfuCfgAfuAfaCfucsusuAu	792	153
AM04880-AS	cPrpusGfsaGfaAfuGfaGfcCfuCfgAfuAfaCfucsusuAu	793	153

[0090]

AM04969-AS	cPrpTMsGfsaGfaAfuGfaGfcCfuCfgAfuAfaCfucsusuAu	794	109
AM04970-AS	cPrpTMsCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfscsuAu	795	111
AM04971-AS	cPrpTMsCfsgUfaUfaacaaUfaAfgGfgGfcsusu	796	178
AM04972-AS	cPrpTMsCfsgUfaUfaacaaUfaAfgGfgGfcUfgCfsusu	797	189
AM04979-AS	usCfsgsUfaUfaAfcAfaUfaAfgGfgGfcusu	798	164
1532-AS01	usgsagaaugaGfccuCfgAfuAfaCfuCfsusuAu	799	153
1532-AS02	usgsagaauGfagccuCfgAfuAfaCfuCfsusuAu	800	153
1532-AS03	usgsagaAfugagccuCfgAfuAfaCfuCfsusuAu	801	153
1532-AS04	usgsaGfaaugagccuCfgAfuAfaCfuCfsusuAu	802	153
1532-AS05	usGfsagaaugagccuCfgAfuAfaCfuCfsusuAu	803	153
1532-AS06	dTsgsagaaugagccuCfgAfuAfaCfuCfsusuAu	804	109
1532-AS07	dTsGfsaGfaAfugagccuCfgAfuAfaCfuCfsusuAu	805	109
1532-AS08	dTsGfsaGfaAfugaGfccuCfgauAfaCfuCfsusuAu	806	109
1532-AS09	dTsGfsaGfaAfuGfagccuCfgauAfaCfuCfsusuAu	807	109
1532-AS10	dTsGfsaGfaAfugagccuCfgauAfaCfuCfsusuAu	808	109
1532-AS11	dTsGfsaGfaAfugagccuCfgAfuaaCfuCfsusuAu	809	109
1532-AS12	dTsGfsaGfaAfugaGfccuCfgauaaCfuCfsusuAu	810	109
1532-AS13	dTsGfsaGfaAfuGfagccuCfgauaaCfuCfsusuAu	811	109
1532-AS15	dTsgsagaaugaGfccuCfgAfuAfaCfuCfsusuAu	812	109
1532-AS16	dTsgsagaauGfagccuCfgAfuAfaCfuCfsusuAu	813	109
1532-AS17	dTsgsagaAfugagccuCfgAfuAfaCfuCfsusuAu	814	109
1532-AS18	dTsgsaGfaaugagccuCfgAfuAfaCfuCfsusuAu	815	109
1532-AS19	dTsGfsagaaugagccuCfgAfuAfaCfuCfsusuAu	816	109
1532-AS20	usgsagaaugagccuCfgAfuAfaCfuCfsusuAu	817	153
1532-AS21	usGfsaGfaAfugagccuCfgAfuAfaCfuCfsusuAu	818	153
1532-AS22	usGfsaGfaAfugaGfccuCfgauAfaCfuCfsusuAu	819	153
1532-AS23	usGfsaGfaAfuGfagccuCfgauAfaCfuCfsusuAu	820	153
1532-AS24	usGfsaGfaAfugagccuCfgauAfaCfuCfsusuAu	821	153

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1532-AS25	usGfsaGfaAfugagccuCfgAfuaaCfuCfsusuAu	822	153
1532-AS27	usGfsaGfaAfuGfagccuCfgauaaCfuCfsusuAu	823	153
1533-AS01	usgsaCfaCfcugAfuucUfgUfuUfcUfgAfsgsuAu	824	154
1533-AS02	usgsaCfaCfcUfgauucUfgUfuUfcUfgAfsgsuAu	825	154
1533-AS04	dTsgsaCfaCfcugauucUfgUfuUfcUfgAfsgsuAu	826	110
1533-AS05	dTsGfsaCfaCfcugAfuucUfguuUfcUfgAfsgsuAu	827	110
1533-AS06	dTsGfsaCfaCfcUfgauucUfguuUfcUfgAfsgsuAu	828	110
1533-AS07	dTsGfsaCfaCfcUfgauucUfgUfuucUfgAfsgsuAu	829	110
1533-AS08	dTsGfsaCfaCfcUfgAfuucUfguuucUfgAfsgsuAu	830	110
1533-AS09	dTsGfsaCfaCfcUfgAfuucUfguuUfcugAfsgsuAu	831	110
1533-AS10	dTsGfsaCfaCfcUfgAfuucUfgUfuucugAfsgsuAu	832	110
1533-AS11	dTsGfsaCfaCfcUfgAfuucUfguuucugAfsgsuAu	833	110
1533-AS12	dTsGfsaCfaCfcUfgAfuucUfguuucUfgasgsuAu	834	110
1533-AS13	dTsGfsaCfaCfcUfgAfuucUfguuUfcugasgsuAu	835	110
1533-AS16	dTsgsaCfaCfcugAfuucUfgUfuUfcUfgAfsgsuAu	836	110
1533-AS17	dTsgsaCfaCfcUfgauucUfgUfuUfcUfgAfsgsuAu	837	110
1533-AS19	usgsaCfaCfcugauucUfgUfuUfcUfgAfsgsuAu	838	154
1533-AS20	usGfsaCfaCfcugAfuucUfguuUfcUfgAfsgsuAu	839	154
1533-AS21	usGfsaCfaCfcUfgauucUfguuUfcUfgAfsgsuAu	840	154
1533-AS22	usGfsaCfaCfcUfgauucUfgUfuucUfgAfsgsuAu	841	154
1533-AS23	usGfsaCfaCfcUfgAfuucUfguuucUfgAfsgsuAu	842	154
1533-AS24	usGfsaCfaCfcUfgAfuucUfguuUfcugAfsgsuAu	843	154
1533-AS25	usGfsaCfaCfcUfgAfuucUfgUfuucugAfsgsuAu	844	154
1533-AS26	usGfsaCfaCfcUfgAfuucUfguuucugAfsgsuAu	845	154
1533-AS27	usGfsaCfaCfcUfgAfuucUfguuucUfgasgsuAu	846	154
1533-AS28	usGfsaCfaCfcUfgAfuucUfguuUfcugasgsuAu	847	154
1533-CfinAS	dTsGfsacaccUfgAfuucUfgUfuUfcUfgAfsgsuAu	848	110
AM05490-AS	usGfsasGfaAfuGfaGfcCfuCfgAfuAfausu	1262	177

[0092]

AM05492-AS	cPrpTMsCfsgsUfaUfaAfCfAfaUfaAfgGfgGfcusu	1263	178
AM05493-AS	cPrpTMsCfsgsUfaUfaAfcAfaUfaAfgGfgGfcusu	1264	178
AM05495-AS	usCfsguauaaCfaaUfaAfgggGfcugCfscsuAu	1265	156
AM05496-AS	usCfsguaUfaaCfaaUfaAfgggGfcugCfscsuAu	1266	156
AM05497-AS	usCfsgUfaUfaacaaUfaAfgGfgGfcsUfsu	1267	164
AM05498-AS	usCfsgsUfaUfaAfCfAfaUfaAfgGfgGfcusu	1268	164

[0093]

표 2B. 변형된 뉴클레오타이드를 가지는 LPA RNAi 물질 센스 가닥.

센스 가닥 번호	SS 서열 5' → 3'	서열 번호	서열 번호
AM01173-SS	AfcGfcAfgAfaGfgGfaCfuGfcCfgAf(invdT)	849	190
AM01174-SS	GfgGfgUfgCfaGfgAfgUfgCfuAfcAf(invdT)	850	191
AM01175-SS	CfuGfuGfgCfaGfcCfcCfuUfaUfuAf(invdT)	851	192
AM01176-SS	GfgCfaGfcCfcCfuUfaUfuGfuUfaAf(invdT)	852	193
AM01177-SS	AfgCfcCfcUfuAfuUfgUfuAfuAfcAf(invdT)	853	194
AM01178-SS	GfcCfcCfuUfaUfuGfuUfaUfaCfgAf(invdT)	854	195
AM01179-SS	UfgAfcAfcAfaUfgCfuCfaGfaCfgAf(invdT)	855	196
AM01180-SS	GfaCfaCfaAfuGfcUfcAfgAfcGfcAf(invdT)	856	197
AM01181-SS	AfcAfcAfaUfgCfuCfaGfaCfgCfaAf(invdT)	857	198
AM01182-SS	AfcAfaUfgCfuCfaGfaCfgCfaGfaAf(invdT)	858	199
AM01183-SS	CfuGfcCfgAfaAfuCfcAfgAfuCfcAf(invdT)	859	200
AM01184-SS	GfcCfgAfaAfuCfcAfgAfuCfcUfgAf(invdT)	860	201
AM01185-SS	UfgAfcAfcGfaUfgCfuCfaGfaUfgAf(invdT)	861	202
AM01186-SS	GfaCfaCfgAfuGfcUfcAfgAfuGfcAf(invdT)	862	203
AM01187-SS	AfcAfcGfaUfgCfuCfaGfaUfgCfaAf(invdT)	863	204
AM01188-SS	AfcGfaUfgCfuCfaGfaUfgCfaGfaAf(invdT)	864	205
AM01189-SS	UfcCfaAfgCfcUfaGfaGfgCfuUfuAf(invdT)	865	206
AM01190-SS	AfgGfaAfaCfcCfcCfgGfgGfuAfcAf(invdT)	866	207
AM01191-SS	GfgAfaAfcCfcCfcGfgGfgUfaCfaAf(invdT)	867	208
AM01192-SS	GfaAfaCfcCfcCfgGfgGfuAfcAfgAf(invdT)	868	209
AM01193-SS	UfgCfuAfcUfaCfcAfuUfaUfgGfaAf(invdT)	869	210
AM01194-SS	GfcUfaCfuAfcCfaUfuAfuGfgAfcAf(invdT)	870	211
AM01195-SS	CfuAfcCfaUfuAfuGfgAfcAfgAfgAf(invdT)	871	212
AM01196-SS	AfcCfaCfaCfcAfgCfaUfaGfuCfgAf(invdT)	872	213
AM01197-SS	CfcAfcAfcCfaGfcAfuAfgUfcGfgAf(invdT)	873	214

[0094]

AM01198-SS	CfaCfaCfcAfgCfaUfaGfuCfgGfaAf(invdT)	874	215
AM01199-SS	CfaCfcAfgCfaUfaGfuCfgGfaCfcAf(invdT)	875	216
AM01200-SS	AfuAfgUfcGfgAfcCfcCfaGfaAfaAf(invdT)	876	217
AM01201-SS	UfaGfuCfgGfaCfcCfcAfgAfaAfaAf(invdT)	877	218
AM01202-SS	CfcAfgAfuGfcUfgAfgAfuUfcGfcAf(invdT)	878	219
AM01203-SS	GfcUfgAfgAfuUfcGfcCfcUfuGfgAf(invdT)	879	220
AM01204-SS	CfuGfaGfaUfuCfgCfcCfuUfgGfuAf(invdT)	880	221
AM01205-SS	UfgAfgAfuUfcGfcCfcUfuGfgUfgAf(invdT)	881	222
AM01206-SS	GfaGfaUfuCfgCfcCfuUfgGfuGfuAf(invdT)	882	223
AM01207-SS	AfuGfgAfuCfcCfaGfuGfuCfaGfgAf(invdT)	883	224
AM01208-SS	GfaAfuCfaAfgUfgUfcCfuUfgCfaAf(invdT)	884	225
AM01209-SS	AfaUfcAfaGfuGfuCfcUfuGfcAfaAf(invdT)	885	226
AM01210-SS	GfaAfgCfaCfcAfaCfgGfaGfcAfaAf(invdT)	886	227
AM01211-SS	GfaGfuUfaUfcGfaGfgCfuCfaUfuAf(invdT)	887	228
AM01212-SS	AfgUfuAfuCfgAfgGfcUfcAfuUfcAf(invdT)	888	229
AM01213-SS	GfaCfaAfcAfgAfaUfaUfuAfuCfcAf(invdT)	889	230
AM01214-SS	CfuUfgGfuGfuUfaUfaCfcAfuGfgAf(invdT)	890	231
AM01215-SS	GfgUfgUfuAfuAfcCfaUfgGfaUfcAf(invdT)	891	232
AM01216-SS	UfaUfaCfcAfuGfgAfuCfcCfaAfuAf(invdT)	892	233
AM01217-SS	AfuAfcCfaUfgGfaUfcCfcAfaUfgAf(invdT)	893	234
AM01218-SS	UfaCfcAfuGfgAfuCfcCfaAfuGfuAf(invdT)	894	235
AM01219-SS	AfcCfaUfgGfaUfcCfcAfaUfgUfcAf(invdT)	895	236
AM01220-SS	GfcAfaCfcUfgAfcAfcAfaUfgUfcAf(invdT)	896	237
AM01221-SS	CfuGfaCfaCfaAfuGfuCfcAfgUfgAf(invdT)	897	238
AM01222-SS	CfcAfgUfgAfcAfgAfaUfcAfaGfuAf(invdT)	898	239
AM01223-SS	UfuAfuCfgAfgGfcUfcAfuUfcUfcAf(invdT)	899	240
AM01224-SS	AfgAfaUfaCfuAfcCfcAfaAfuGfgAf(invdT)	900	241
AM01225-SS	AfaUfaCfuAfcCfcAfaAfuGfgUfgAf(invdT)	901	242

[0095]

AM01226-SS	AfuAfcUfaCfcCfaAfaUfgGfuGfgAf(invdT)	902	243
AM01227-SS	AfuUfcGfcCfcUfuGfgUfgUfuAfuAf(invdT)	903	244
AM01228-SS	UfaUfaCfcAfuGfgAfuCfcCfaGfuAf(invdT)	904	245
AM01229-SS	AfuAfcCfaUfgGfaUfcCfcAfgUfgAf(invdT)	905	246
AM01230-SS	CfaCfaAfcUfcCfcAfcGfgUfgGfuAf(invdT)	906	247
AM01231-SS	AfaGfaAfcAfuGfuCfaGfuCfuUfgAf(invdT)	907	248
AM01232-SS	AfgUfgUfcCfuCfaCfaAfcUfcCfcAf(invdT)	908	249
AM01233-SS	AfaCfaAfgCfaCfcAfcCfuGfaGfaAf(invdT)	909	250
AM01234-SS	CfcUfgAfgAfaAfaGfcCfcUfgUfgAf(invdT)	910	251
AM01235-SS	UfgAfuAfcCfaCfaCfuGfgCfaUfcAf(invdT)	911	252
AM01236-SS	GfaUfaCfcAfcAfcUfgGfcAfuCfaAf(invdT)	912	253
AM01237-SS	GfaAfaCfaGfaAfuCfaGfgUfgUfcAf(invdT)	913	254
AM01238-SS	AfaAfcAfgAfaUfcAfgGfuGfuCfcAf(invdT)	914	255
AM01239-SS	CfaGfaAfuCfaGfgUfgUfcCfuAfgAf(invdT)	915	256
AM01795-SS	CfcUfgUfgGfcAfgCfcCfcUfuAfuAf(invdT)	916	257
AM01797-SS	UfgGfcAfgCfcCfcUfuAfuUfgUfuAf(invdT)	917	258
AM01799-SS	AfcAfcCfaGfcAfuAfgUfcGfgAfcAf(invdT)	918	259
AM01801-SS	GfgAfaUfcCfaGfaUfgCfuGfaGfaAf(invdT)	919	260
AM01803-SS	UfcCfaGfaUfgCfuGfaGfaUfuCfgAf(invdT)	920	261
AM01805-SS	AfuGfcUfgAfgAfuUfcGfcCfcUfuAf(invdT)	921	262
AM01807-SS	CfcAfuGfgAfuCfcCfaGfuGfuCfaAf(invdT)	922	263
AM01809-SS	CfuGfaAfgAfaGfcAfcCfaAfcGfgAf(invdT)	923	264
AM01811-SS	UfcCfaGfuGfaCfaGfaAfuCfaAfgAf(invdT)	924	265
AM01813-SS	CfuCfaCfaAfcUfcCfcAfcGfgUfgAf(invdT)	925	266
AM01815-SS	AfgAfaUfcAfgGfuGfuCfcUfaGfaAf(invdT)	926	267
AM01817-SS	UfcAfgGfuGfuCfcUfaGfaGfaCfuAf(invdT)	927	268
AM02006-SS	(Chol-TEG)uAuAfgCfcCfcUfUfAfuUfgUfuAfuAfcAf(invdT)	928	269
AM02010-SS	(Chol-TEG)uAuGfcCfcCfuUfAfUfuGfuUfaUfaCfgAf(invdT)	929	270

[0096]

AM02014-SS	(Chol-TEG)uAuGfaCfaCfaAfUfGfcUfcAfgAfcGfcAf(invdT)	930	271
AM02018-SS	(Chol-TEG)uAuAfcAfcAfaUfGfCfuCfaGfaCfgCfaAf(invdT)	931	272
AM02022-SS	(Chol-TEG)uAuUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf(invdT)	932	273
AM02026-SS	(Chol-TEG)uAuGfaAfaCfaGfAfAfuCfaGfgUfgUfcAf(invdT)	933	274
AM02030-SS	(Chol-TEG)uAuAfcAfcCfaGfCfAfuAfgUfcGfgAfcAf(invdT)	934	275
AM02034-SS	(Chol-TEG)uAuUfcCfaGfaUfGfCfuGfaGfaUfuCfgAf(invdT)	935	276
AM02038-SS	(Chol-TEG)uAuAfuGfcUfgAfgAfuUfcGfcCfcUfuAf(invdT)	936	277
AM02042-SS	(Chol-TEG)uAuCfcAfuGfgAfUfCfcCfaGfuGfuCfaAf(invdT)	937	278
AM02211-SS	UfgUfgGfcAfGfCfcCfcUfuAfuUfgAf(invdT)	938	279
AM02212-SS	CfaCfaAfuGfCfUfcAfgAfcGfcAfgAf(invdT)	939	280
AM02213-SS	CfcGfaAfaUfCfCfaGfaUfcCfuGfuAf(invdT)	940	281
AM02214-SS	GfaCfuGfaGfGfAfaAfcCfcCfcGfgAf(invdT)	941	282
AM02215-SS	CfuAfcUfaCfCfAfuUfaUfgGfaCfaAf(invdT)	942	283
AM02216-SS	AfcUfaCfcAfUfUfaUfgGfaCfaGfaAf(invdT)	943	284
AM02217-SS	UfaCfcAfuUfAfUfgGfaCfaGfaGfuAf(invdT)	944	285
AM02218-SS	AfcCfaUfuAfUfGfgAfcAfgAfgUfuAf(invdT)	945	286
AM02219-SS	AfgAfuGfcUfGfAfgAfuUfcGfcCfcAf(invdT)	946	287
AM02220-SS	GfaUfgCfuGfAfGfaUfuCfgCfcCfuAf(invdT)	947	288
AM02221-SS	AfgAfuUfcGfCfCfcUfuGfgUfgUfuAf(invdT)	948	289
AM02222-SS	GfaCfaGfaAfUfCfaAfgUfgUfcCfuAf(invdT)	949	290
AM02223-SS	AfcAfuGfuCfAfGfuCfuUfgGfuCfcAf(invdT)	950	291
AM02224-SS	CfcAfaAfuGfGfUfgGfcCfuGfaCfcAf(invdT)	951	292
AM02225-SS	UfgGfuGfuUfAfUfaCfcAfuGfgAfuAf(invdT)	952	293
AM02226-SS	UfgUfuAfuAfCfCfaUfgGfaUfcCfcAf(invdT)	953	294
AM02227-SS	AfaCfcUfgAfCfAfcAfaUfgUfcCfaAf(invdT)	954	295
AM02228-SS	AfaUfgUfcCfAfGfuGfaCfaGfaAfuAf(invdT)	955	296
AM02229-SS	UfgUfuUfcUfGfAfaCfaAfgCfaCfcAf(invdT)	956	297
AM02230-SS	UfaUfcGfaGfGfCfuCfaUfuCfuCfcAf(invdT)	957	298

[0097]

AM02231-SS	UfcGfaGfgCfUfCfaUfuCfuCfcAfcAf(invdT)	958	299
AM02232-SS	UfcCfuCfaCfAfAfcUfcCfcAfcGfgAf(invdT)	959	300
AM02233-SS	CfaAfcUfcCfCfAfcGfgUfgGfuCfcAf(invdT)	960	301
AM02234-SS	GfcUfcCfuUfCfUfgAfaCfaAfgCfaAf(invdT)	961	302
AM02235-SS	AfuAfcCfaCfAfCfuGfgCfaUfcAfgAf(invdT)	962	303
AM02236-SS	AfcAfgAfaUfCfAfgGfuGfuCfcUfaAf(invdT)	963	304
AM02237-SS	GfaAfuCfaGfGfUfgUfcCfuAfgAfgAf(invdT)	964	305
AM02238-SS	AfaUfcAfgGfUfGfuCfcUfaGfaGfaAf(invdT)	965	306
AM02239-SS	AfuCfaGfgUfGfUfcCfuAfgAfgAfcAf(invdT)	966	307
AM02441-SS	uAuAusAfsgUfuAfuCfgAfgGfcUfcAfuUfcUfcAf(C6-SS-Alk-Me)	967	308
AM02442-SS	uAuAusAfsgUfuAfuCfgaGfGfcUfcAfuUfcUfcAf(C6-SS-Alk-Me)	968	308
AM02443-SS	uAuAusAfsgUfuAfuCfGfaGfGfcUfcAfuUfcUfcAf(C6-SS-Alk-Me)	969	308
AM02444-SS	uAuAusasGfuUfaUfcGfaGfGfcUfcAfuUfcUfcAf(C6-SS-Alk-Me)	970	308
AM02445-SS	uAuAusCfsaGfaAfaCfaGfaAfuCfaGfgUfgUfcAf(C6-SS-Alk-Me)	971	309
AM02446-SS	uAuAusCfsaGfaAfaCfagAfAfuCfaGfgUfgUfcAf(C6-SS-Alk-Me)	972	309
AM02447-SS	uAuAusCfsaGfaAfaCfAfgAfAfuCfaGfgUfgUfcAf(C6-SS-Alk-Me)	973	309
AM02448-SS	uAuAuscsAfgAfaAfcAfgAfAfuCfaGfgUfgUfcAf(C6-SS-Alk-Me)	974	309
AM02537-SS	uAuAusCfsaGfcCfcCfuUfAfUfuGfuUfaUfaCfgAf (C11-PEG3-NAG3)	975	310
AM02538-SS	uAuAusCfsuGfaCfaCfaAfUfGfcUfcAfgAfcGfcAf (C11-PEG3-NAG3)	976	311
AM02539-SS	uAuAusUfsgAfcAfcAfaUfGfCfuCfaGfaCfgCfaAf (C11-PEG3-NAG3)	977	312
AM02540-SS	uAuAusAfsgUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf (C11-PEG3-NAG3)	978	308
AM02541-SS	uAuAusCfsaGfaAfaCfaGfAfAfuCfaGfgUfgUfcAf (C11-PEG3-NAG3)	979	309
AM02542-SS	uAuAusAfsgAfuGfcUfgAfGfAfuUfcGfcCfcUfuAf	980	313

[0098]

	(C11-PEG3-NAG3)		
AM02793-SS	gsCfsaGfcCfcCfuUfaUfuGfuUfa(invdA)	981	314
AM02794-SS	gsCfscCfcUfuAfuUfgUfuAfuAfc(invdA)	982	315
AM02795-SS	csCfscCfuUfaUfuGfuUfaUfaCfg(invdA)	983	316
AM02796-SS	asCfsaCfaAfuGfcUfcAfgAfcGfc(invdA)	984	317
AM02797-SS	csAfscAfaUfgCfuCfaGfaCfgCfa(invdA)	985	318
AM02798-SS	csCfsgAfaAfuCfcAfgAfuCfcUfg(invdA)	986	319
AM02799-SS	csAfscGfaUfgCfuCfaGfaUfgCfa(invdA)	987	320
AM02800-SS	csCfsaCfaCfcAfgCfaUfaGfuCfg(invdA)	988	321
AM02801-SS	usAfsgUfcGfgAfcCfcCfaGfaAfa(invdA)	989	322
AM02802-SS	csAfsgAfuGfcUfgAfgAfuUfcGfc(invdA)	990	323
AM02803-SS	asAfsuCfaAfgUfgUfcCfuUfgCfa(invdA)	991	324
AM02804-SS	asGfsuUfaUfcGfaGfgCfuCfaUfu(invdA)	992	325
AM02805-SS	gsUfsuAfuCfgAfgGfcUfcAfuUfc(invdA)	993	326
AM02806-SS	csAfsaCfcUfgAfcAfcAfaUfgUfc(invdA)	994	327
AM02807-SS	usAfsuCfgAfgGfcUfcAfuUfcUfc(invdA)	995	328
AM02808-SS	gsAfsaUfaCfuAfcCfcAfaAfuGfg(invdA)	996	329
AM02809-SS	asUfsaCfuAfcCfcAfaAfuGfgUfg(invdA)	997	330
AM02810-SS	asAfsaCfaGfaAfuCfaGfgUfgUfc(invdA)	998	331
AM02811-SS	asAfscAfgAfaUfcAfgGfuGfuCfc(invdA)	999	332
AM02812-SS	CfsasGfcCfcCfuUfaUfuGfuUfa(invdA)	1000	333
AM02813-SS	CfscsCfcUfuAfuUfgUfuAfuAfc(invdA)	1001	334
AM02814-SS	CfscsCfuUfaUfuGfuUfaUfaCfg(invdA)	1002	335
AM02815-SS	CfsasCfaAfuGfcUfcAfgAfcGfc(invdA)	1003	336
AM02816-SS	AfscsAfaUfgCfuCfaGfaCfgCfa(invdA)	1004	337
AM02817-SS	CfsgsAfaAfuCfcAfgAfuCfcUfg(invdA)	1005	338
AM02818-SS	AfscsGfaUfgCfuCfaGfaUfgCfa(invdA)	1006	339
AM02819-SS	CfsasCfaCfcAfgCfaUfaGfuCfg(invdA)	1007	340

[0099]

AM02820-SS	AfsgsUfcGfgAfcCfcCfaGfaAfa(invdA)	1008	341
AM02821-SS	AfsgsAfuGfcUfgAfgAfuUfcGfc(invdA)	1009	342
AM02822-SS	AfsusCfaAfgUfgUfcCfuUfgCfa(invdA)	1010	343
AM02823-SS	GfsusUfaUfcGfaGfgCfuCfaUfu(invdA)	1011	344
AM02824-SS	UfsusAfuCfgAfgGfcUfcAfuUfc(invdA)	1012	345
AM02825-SS	AfsasCfcUfgAfcAfcAfaUfgUfc(invdA)	1013	346
AM02826-SS	AfsusCfgAfgGfcUfcAfuUfcUfc(invdA)	1014	347
AM02827-SS	AfsasUfaCfuAfcCfcAfaAfuGfg(invdA)	1015	348
AM02828-SS	UfsasCfuAfcCfcAfaAfuGfgUfg(invdA)	1016	349
AM02829-SS	AfsasCfaGfaAfuCfaGfgUfgUfc(invdA)	1017	350
AM02830-SS	AfscsAfgAfaUfcAfgGfuGfuCfc(invdA)	1018	351
AM02861-SS	uAuAusAfsgUfuauCfgAfGfGfcUfcAfuUfcUfcAf (C11-PEG3-NAG3)	1019	308
AM02941-SS	uAuAusasguuaucgAfgGfcucauucuca(C11-PEG3-NAG3)	1020	308
AM02942-SS	uAuAusasguuaucgaGfGfcucauucuca(C11-PEG3-NAG3)	1021	308
AM02946-SS	uAuAuscsagaaaCfagAfAfuCfagguguca(C11-PEG3-NAG3)	1022	309
AM02947-SS	uAuAuscsagaaaCfaGfaAfuCfagguguca(C11-PEG3-NAG3)	1023	309
AM02948-SS	uAuAuscsagaaacaGfaAfucagguguca(C11-PEG3-NAG3)	1024	309
AM02949-SS	uAuAuscsagaaacagAfAfucagguguca(C11-PEG3-NAG3)	1025	309
AM03030-SS	(Stearyl)uAuAusCfsaGfaAfaCfaGfAfAfuCfaGfgUfgUfcAf (C11-PEG3-NAG3)	1026	309
AM03036-SS	uAuAusCfsagaAfaCfaGfAfAfuCfaGfgUfgUfcAf (C11-PEG3-NAG3)	1027	309
AM03037-SS	uAuAusCfsagaaaCfaGfAfAfuCfaGfgUfgUfcAf(C11-PEG3-NAG3)	1028	309
AM03038-SS	uAuAusCfsagaaaCfagaAfuCfaggUfgUfcAf(C11-PEG3-NAG3)	1029	309
AM03039-SS	uAuAusCfsaGfaAfaCfaGfAfAfuCfagGfuGfucAf (C11-PEG3-NAG3)	1030	309
AM03042-SS	uAuAusCfsaGfaAfaCfaGfAfAfucagguguca(C11-PEG3-NAG3)	1031	309

[0100]

AM03060-SS	uAuAusCfsaGfaAfaCfaGfAfAfuCfaggugUfca(C11-PEG3-NAG3)	1032	309
AM03061-SS	uAuAusCfsaGfaAfaCfaGfAfAfuCfagguguca(C11-PEG3-NAG3)	1033	309
AM03062-SS	uAuAusCfsagaaaCfaGfAfAfuCfaggugUfca(C11-PEG3-NAG3)	1034	309
AM03064-SS	uAuAusCfsaGfaAfaCfaGfaAfuCfaGfgugucAf(C11-PEG3-NAG3)	1035	309
AM03122-SS	uAuAusAfsgUfuAfuCfgAfGfGfcUfcAfuUfcUfCMAM (C11-PEG3-NAG3)	1036	308
AM03123-SS	uAuAU$_{UNA}$AfsgsUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf (C11-PEG3-NAG3)	1037	308
AM03124-SS	uAuAuAfsgsUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf (C11-PEG3-NAG3)	1038	308
AM03125-SS	uAuAusCfsaGfcCfcCfuUfAfUfuGfuUfaUfaCfga (C11-PEG3-NAG3)	1039	310
AM03126-SS	uAuAuscsaGfcCfcCfuUfAfUfuGfuUfaUfaCfgAf (C11-PEG3-NAG3)	1040	310
AM03128-SS	uAuAuscsaGfcCfcCfuUfAfUfuGfuUfaUfaCfga (C11-PEG3-NAG3)	1041	310
AM03144-SS	uAuAusAfsgUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf (C6-PEG4-NAG3)	1042	308
AM03220-SS 1532-SS01	uAuAusAfsgUfuAfuCfgAfGfGfcUfcauucuca	1043	308
AM03221-SS	uAuAusAfsgUfuAfuCfgAfGfGfcucauucuca	1044	308
AM03222-SS	uAuAusAfsguuauCfgAfGfGfcUfcauucuca	1045	308
AM03223-SS	uAuAusAfsguuauCfgAfGfGfcucauucuca	1046	308
AM03224-SS	uAuAusasguuauCfgAfGfGfcucauucuca	1047	308
AM03225-SS	uAuAusasguuaucgAfGfGfcucauucuca	1048	308
AM03226-SS	uAuAusAfsgUfuAfuCfgAfGfdGcUfcauucuca	1049	308
AM03227-SS	uAuAusAfsgUfuAfuCfgAfGfdGcucauucuca	1050	308
AM03228-SS	uAuAusAfsguuauCfgAfGfdGcUfcauucuca	1051	308

[0101]

AM03229-SS	uAuAusAfsguuauCfgAfGfdGcucauucuca	1052	308
AM03230-SS	uAuAusasguuauCfgAfGfdGcucauucuca	1053	308
AM03231-SS	uAuAusasguuaucgAfGfdGcucauucuca	1054	308
AM03232-SS	uAuAusAfsgUfuAfuCfgaGfGfcUfcauucuca	1055	308
AM03233-SS	uAuAusAfsgUfuAfuCfgaGfGfcucauucuca	1056	308
AM03234-SS	uAuAusAfsguuauCfgaGfGfcUfcauucuca	1057	308
AM03235-SS	uAuAusAfsguuauCfgaGfGfcucauucuca	1058	308
AM03236-SS	uAuAusasguuauCfgaGfGfcucauucuca	1059	308
AM03237-SS	uAuAusasguuaucgaGfGfcucauucuca	1060	308
AM03238-SS	uAuAusAfsgUfuAfuCfgAfGfGfcUfcauucuca(C11-PEG3-NAG3)	1061	308
AM03240-SS	uAuAusAfsguuauCfgAfGfGfcUfcauucuca(C11-PEG3-NAG3)	1062	308
AM03330-SS 1532-SS00	uAuAusAfsgUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf	1063	308
AM03291-SS	uAuAusCfsaGfcCfcCfuUfAfUfuGfuUfaUfaCfgAf	1064	310
AM03292-SS	uAuAusCfsagcCfcCfuUfaUfuguUfaUfaCfga	1065	310
AM03293-SS	uAuAusCfsagcCfcCfuUfaUfuguuauaCfga	1066	310
AM03294-SS	uAuAuscsagccccuUfaUfuguuauacga	1067	310
AM03295-SS	uAuAuscsagccccuuAfUfuguuauacga	1068	310
AM03296-SS	uAuAusCfsagcCfcCfuUfAfUfuguUfaUfaCfga	1069	310
AM03297-SS	uAuAusCfsagcCfcCfuUfAfUfuguuauaCfga	1070	310
AM03298-SS	uAuAuscsagccccuUfAfUfuguuauacga	1071	310
AM03299-SS	uAuAusCfsagcCfcCfuuAfUfuguuauaCfga	1072	310
AM03277-SS	uAuAuscsagccccuUfaUfuguuauacga(C11-PEG3-NAG3)	1073	310
AM03275-SS	uAuAusCfsagcCfcCfuUfaUfuguUfaUfaCfga(C11-PEG3-NAG3)	1074	310
AM03276-SS	uAuAusCfsagcCfcCfuUfaUfuguuauaCfga(C11-PEG3-NAG3)	1075	310
AM03278-SS	uAuAuscsagccccuuAfUfuguuauacga(C11-PEG3-NAG3)	1076	310
AM03287-SS	uAuAusCfsagcCfcCfuUfAfUfuguUfaUfaCfga(C11-PEG3-NAG3)	1077	310
AM03288-SS	uAuAusCfsagcCfcCfuUfAfUfuguuauaCfga(C11-PEG3-NAG3)	1078	310

[0102]

AM03289-SS	uAuAuscsagccccuUfAfUfuguuauacga(C11-PEG3-NAG3)	1079	310
AM03290-SS	uAuAusCfsagcCfcCfuuAfUfuguuauaCfga(C11-PEG3-NAG3)	1080	310
AM03243-SS	uAuAusasguuaucgAfGfGfcucauucuca(C11-PEG3-NAG3)	1081	308
AM03424-SS	(Chol-TEG)uAuAusasguuaucgaGfGfcucauucuc(invdA)	1082	308
AM03425-SS	(Chol-TEG)uAuAusasguuaucgaGfGfcucauucuca	1083	308
AM03426-SS	(Chol-TEG)uAuAusAfgUfuAfuCfgAfGfGfcUfcAfuUfcUfc (invdA)	1084	308
AM03457-SS	CfscsCfcUfuAfuUfgUfuAfuAfca(NAG13)	1085	334
AM03458-SS	CfscsCfuUfaUfuGfuUfaUfaCfga(NAG13)	1086	335
AM03459-SS	AfsgsAfuGfcUfgAfgAfuUfcGfca(NAG13)	1087	342
AM03460-SS	GfsusUfaUfcGfaGfgCfuCfaUfua(NAG13)	1088	344
AM03461-SS	AfsusCfgAfgGfcUfcAfuUfcUfca(NAG13)	1089	347
AM03462-SS	AfsasCfaGfaAfuCfaGfgUfgUfca(NAG13)	1090	350
AM03489-SS	uAuAusasguuaucgaGfGfcucauucuca(NAG13)	1091	308
AM03492-SS	uAuAusCfsaGfcCfcCfuUfAfUfuGfuUfaUfaCfga(NAG13)	1092	310
AM03544-SS	uAuAuscsagcccCfuUfaUfuguuauacga(NAG13)	1093	310
AM03545-SS	uAuAuscsagccccuuAfUfuGfuuauacga(NAG13)	1094	310
AM03546-SS	uAuAuscsagccccuUfAfUfuguuauacga(NAG13)	1095	310
AM03547-SS	uAuAusAfsgUfuAfuCfgAfGfGfcUfcAfuUfcUfcAf(NAG13)	1096	308
AM03650-SS	uAuAusasguuaucgAfGfGfcucauucuca(NAG13)	1097	308
AM03651-SS	uAuAuscsaGfcCfcCfuUfAfUfuGfuUfaUfaCfga(NAG13)	1098	310
AM03670-SS	uAuAuscsagcgccuUfAfUfuguuauacga(NAG13)	1099	352
AM03683-SS	uAuAuscsaGfcCfcCfuUfAfUfuGfuUfaUfaCfga	1100	310
AM03741-SS	cscsccUfUfAfuuguuauaca(NAG13)	1101	334
AM03742-SS	cscsccUfUfAfuuguuauaCMAM(NAG13)	1102	334
AM03743-SS	CMsCMsccUfUfAfuuguuauaCMAM(NAG13)	1103	334
AM03746-SS	cscscuUfAfUfuguuauacga(NAG13)	1104	335
AM03747-SS	cscscuUfAfUfuguuauacGMAM(NAG13)	1105	335
AM03748-SS	CMsCMscuUfAfUfuguuauacGMAM(NAG13)	1106	335

[0103]

AM03751-SS	asuscgAfGfGfcucauucuca(NAG13)	1107	347
AM03752-SS	asuscgAfGfGfcucauucuCMAM(NAG13)	1108	347
AM03753-SS	AMsTMscgAfGfGfcucauucuCMAM(NAG13)	1109	353
AM03757-SS	asascaGfAfAfucagguguca(NAG13)	1110	350
AM03758-SS	asascaGfAfAfucagguguCMAM(NAG13)	1111	350
AM03759-SS	AMsAMscaGfAfAfucagguguCMAM(NAG13)	1112	350
AM03859-SS	(NAG18)uauausasguuaucgAfGfGfcucauucuc(invdA)	1113	308
AM03861-SS	(NAG18)uauauscsaGfcCfcCfuUfAfUfuGfuUfaUfaCfg(invdA)	1114	310
AM03879-SS	(NAG4)uscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1115	354
AM03880-SS	(NAG4)uscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1116	355
AM03881-SS	(NAG24)uscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1117	354
AM03882-SS	(NAG4)usaguuaucgAfGfGfcucauucucausu(invAb)	1118	356
AM03928-SS	uAuAuscsagcccCfuUfAfUfuguuauacga(NAG13)	1119	310
AM03931-SS	uAuAusasguuauCfgAfGfGfcucauucuca(NAG13)	1120	308
AM03968-SS	(NAG4)uauauscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgs(invdA)	1121	310
AM03970-SS	(NAG4)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1122	357
AM04138-SS	(NAG25)uauausasguuaucgAfGfGfcucauucuc(invdA)	1123	308
AM04152-SS	(Alk-PEG5-C6)uauausasguuaucgAfGfGfcucauucuCM(invdA)	1124	308
AM04214-SS	(Alk-SMPT-C6)uauausasguuaucgAfGfGfcucauucuCM(invdA)	1125	308
AM04233-SS	(NAG26)uauausasguuaucgAfGfGfcucauucuCM(invdA)	1126	308
AM04372-SS	(NAG27)uauausasguuaucgAfGfGfcucauucuCM(invdA)	1127	308
AM04381-SS	(NAG25)auauscsagccccuUfAfUfuguuauacga(invdT)	1128	358
AM04382-SS	(NAG25)uauscsagccccuUfAfUfuguuauacgau(invdT)	1129	359
AM04391-SS	(NAG25)auausasguuaucgAfGfGfcucauucuca(invdT)	1130	360
AM04392-SS	(NAG25)uausasguuaucgAfGfGfcucauucucau(invdT)	1131	361
AM04412-SS	(NAG25)uauauscsagccccuUfAfUfuguuauacg(invdA)	1132	310
AM04414-SS	(NAG25)(invAb)gccccuUfAfUfuguuauacgauus(invAb)	1133	357
AM04416-SS	(NAG25)(invAb)uuaucgAfGfGfcucauucucausu(invAb)	1134	362

[0104]

AM04496-SS	(NAG25)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1135	357
AM04497-SS	(NAG29)uauausasguuaucgAfGfGfcucauucuc(invdA)	1136	308
AM04499-SS	(NAG28)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1137	357
AM04498-SS	(NAG29)uauauaasuuaucgaGfGfcucauucucsa(invAb)	1138	363
AM04500-SS	(NAG30)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1139	357
AM04502-SS	(NAG25)uauauaasuuaucgaGfGfcucauucucsa(invAb)	1140	363
AM04535-SS	(NAG25)uauaucsasgccccuUfAfUfuguuauacg(invdA)	1141	310
AM04536-SS	(NAG25)uauaucasgccccuUfAfUfuguuauacg(invdA)	1142	310
AM04537-SS	(NAG25)uauauasgsuuaucgAfGfGfcucauucuc(invdA)	1143	308
AM04538-SS	(NAG25)uauauagsuuaucgAfGfGfcucauucuc(invdA)	1144	308
AM04543-SS	(NAG30)uscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1145	355
AM04578-SS	(NAG25)ggcsagccccuUfAfUfuguuauacgAMs(invdT)dT	1146	364
AM04588-SS	(NAG25)ggcsagccccuUfAfUfuguuauacgAMsuu(invdT)	1147	365
AM04579-SS	(NAG25)G_{UNA}gcsagccccuUfAfUfuguuauacgAMs(invdT)dT	1148	364
AM04580-SS	(NAG25)ggcs(invdA)gccccuUfAfUfuguuauacgAMs(invdT)dT	1149	364
AM04581-SS	(NAG25)csagccccuUfAfUfuguuauacgAMs(invdT)dTdTdT	1150	366
AM04611-SS	(NAG31)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1151	357
AM04612-SS	(NAG32)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1152	357
AM04669-SS	(NAG25)uauauagsusuaucgAfGfGfcucauucuc(invdA)	1153	308
AM04670-SS	(NAG25)uauauagususaucgAfGfGfcucauucuc(invdA)	1154	308
AM04671-SS	(NAG25)gcgausasguuaucgAfGfGfcucauucuc(invdA)	1155	367
AM04672-SS	(NAG25)ugaausasguuaucgAfGfGfcucauucuc(invdA)	1156	368
AM04673-SS	(NAG25)aucgusasguuaucgAfGfGfcucauucuc(invdA)	1157	369
AM04674-SS	(NAG25)u(invdA)uausasguuaucgAfGfGfcucauucuc(invdA)	1158	308
AM04675-SS	(NAG25)uaua(invdA)sasguuaucgAfGfGfcucauucuc(invdA)	1159	370
AM04676-SS	(NAG25)uauaus(invdA)sguuaucgAfGfGfcucauucuc(invdA)	1160	308
AM04726-SS	(NAG30)aGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1161	371
AM04727-SS	(NAG30)aaGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1162	372

[0105]

AM04728-SS	(NAG30)sasGfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1163	371
AM04729-SS	(NAG30)gscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1164	373
AM04737-SS	(NAG25)uauauagsuuaucgaGfGfcucauucucsa(invAb)	1165	374
AM04741-SS	(NAG30)sgscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1166	373
AM04742-SS	(NAG33)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1167	357
AM04743-SS	(NAG34)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1168	357
AM04744-SS	(NAG35)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1169	357
AM04803-SS	(NAG30)acGfcCfcCfuUfAfUfuGfuUfaUfaCfgsa(invAb)	1170	375
AM04804-SS	(NAG30)sasaGfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1171	372
AM04807-SS	(NAG30)sascGfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1172	375
AM04806-SS	(NAG30)sgscaGfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1173	373
AM04808-SS	(NAG31)sGfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1174	376
AM04809-SS	(NAG31)saGfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1175	377
AM04810-SS	(NAG31)sasaGfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1176	372
AM04811-SS	(NAG31)sasaGfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1177	378
AM04812-SS	(NAG31)sasaGfcCfcCfuUfAfUfuGfuUfaUfaCfg(invdA)usu(invAb)	1178	378
AM04813-SS	(NAG31)uauausasguuaucgAfGfGfcucauucuc(invdA)	1179	308
AM04816-SS	(NAG31)uauscsagccccuUfAfUfuguuauacgs(invdA)	1180	379
AM04817-SS	(NAG31)uagscsagccccuUfAfUfuguuauacgs(invdA)	1181	380
AM04835-SS	(NAG31)uaucagccccuUfAfUfuguuauacgs(invdA)	1182	379
AM04819-SS	(NAG31)sgscagccccuUfAfUfuguuauacgs(invdA)	1183	381
AM04820-SS	(NAG31)sgscagccccuUfAfUfuguuauacgsa(invAb)	1184	373
AM04862-SS	(NAG25)auaagasguuaucgAfGfGfcucauucuc(invdA)	1185	382
AM04863-SS	(NAG25)auaagsasguuaucgAfGfGfcucauucuc(invdA)	1186	382
AM04864-SS	(NAG25)auaggcsagccccuUfAfUfuguuauacg(invdA)	1187	383
AM04865-SS	(NAG25)auaggscsagccccuUfAfUfuguuauacg(invdA)	1188	383
AM04866-SS	(NAG25)scsagccccuUfAfUfuguuauacgs(invdA)	1189	384

[0106]

AM04867-SS	(NAG31)scsagccccuUfAfUfuguuauacgs(invdA)	1190	384
AM04868-SS	(NAG25)sgsccccuUfAfUfuguuauacgauus(invAb)	1191	376
AM04869-SS	(NAG31)sgsccccuUfAfUfuguuauacgauus(invAb)	1192	376
AM04870-SS	(NAG25)sGfsccccuUfAfUfuguuauacgauus(invAb)	1193	376
AM04978-SS	(NAG31)sGfscCfcCfuUfAfUfuGfuUfaUfaCfgauus(invAb)	1194	376
AM05070-SS	(NAG25)uauauscsagcccc(NOTA-dT)UfAfUfuguuauacg(invdA)	1195	385
AM05072-SS	(NAG25)(invAb)GfcCfcCf(NOTA-dT) UfAfUfuGfuUfaUfaCfgausu(invAb)	1196	1241
1532-SS02	uAuAusAfsgUfuAfuCfgAfGfGfcucAfuucuca	1197	308
1532-SS03	uAuAusAfsgUfuAfuCfgAfGfGfcucauUfcuca	1198	308
1532-SS04	uAuAusAfsgUfuAfuCfgAfGfGfcucauucUfca	1199	308
1532-SS05	uAuAusAfsgUfuAfuCfgAfGfGfcucauucucAf	1200	308
1532-SS06	uAuAusAfsgUfuAfuCfgAfgGfcUfcauucucAf	1201	308
1532-SS07	uAuAusAfsgUfuAfuCfgAfgGfcucAfuucucAf	1202	308
1532-SS08	uAuAusAfsgUfuAfuCfgAfgGfcucauUfcucAf	1203	308
1532-SS09	uAuAusAfsgUfuAfuCfgAfgGfcucauucUfcAf	1204	308
1532-SS10	uAuAusAfsgUfuAfuCfgAfgGfcucauucucAf	1205	308
1532-SS11	uAuAusAfsgUfuAfuCfgaGfGfcucauucucAf	1206	308
1532-SS12	uAuAusAfsgUfuAfuCfgagGfcUfcauucucAf	1207	308
1532-SS13	uAuAusAfsgUfuAfuCfgagGfcucAfuucucAf	1208	308
1532-SS14	uAuAusAfsgUfuAfuCfgagGfcucauUfcucAf	1209	308
1532-SS15	uAuAusAfsgUfuAfuCfgagGfcucauucUfcAf	1210	308
1532-SS16	uAuAusAfsgUfuAfuCfgagGfcucauUfcUfcAf	1211	308
1532-SS17	uAuAusAfsgUfuauCfgAfgGfcucauUfcUfcAf	1212	308
1532-SS18	uAuAusAfsgUfuauCfgaGfGfcucauUfcUfcAf	1213	308
1532-SS19	uAuAusAfsgUfuauCfgagGfcUfcauUfcUfcAf	1214	308
1532-SS20	uAuAusAfsgUfuauCfgagGfcucAfuUfcUfcAf	1215	308
1532-SS21	uAuAusAfsgUfuauCfgagGfcUfcAfuUfcUfcAf	1216	308

[0107]

1532-SS22	uAuAusAfsguuAfuCfgagGfcUfcAfuUfcUfcAf	1217	308
1532-SS23	uAuAusAfsguuauCfgAfgGfcUfcAfuUfcUfcAf	1218	308
1532-SS24	uAuAusAfsguuauCfgaGfGfcUfcAfuUfcUfcAf	1219	308
1533-CfinSS	uAuAuscsaGfaAfacaGfAfAfucaGfgUfgUfcAf	1220	309
1533-SS00	uAuAusCfsaGfaAfaCfaGfAfAfuCfaGfgUfgUfcAf	1221	309
1533-SS01	uAuAusCfsaGfaAfaCfaGfAfAfuCfaGfguguca	1222	309
1533-SS02	uAuAusCfsaGfaAfaCfaGfAfAfuCfaggugUfca	1223	309
1533-SS03	uAuAusCfsaGfaAfaCfaGfAfAfuCfaggugucAf	1224	309
1533-SS04	uAuAusCfsaGfaAfaCfaGfAfAfuCfaggUfguca	1225	309
1533-SS05	uAuAusCfsaGfaAfaCfaGfaAfuCfaGfgugucAf	1226	309
1533-SS06	uAuAusCfsaGfaAfaCfaGfaAfuCfaggugUfcAf	1227	309
1533-SS07	uAuAusCfsaGfaAfaCfaGfaAfuCfaggUfgucAf	1228	309
1533-SS08	uAuAusCfsaGfaAfaCfagAfAfuCfaggugUfcAf	1229	309
1533-SS09	uAuAusCfsaGfaAfaCfagaAfuCfaggUfgUfcAf	1230	309
1533-SS10	uAuAusCfsaGfaAfaCfagaAfuCfaGfgugUfcAf	1231	309
1533-SS11 1533-SS20	uAuAusCfsaGfaaaCfagAfAfuCfaGfgUfgUfcAf	1232	309
1533-SS12	uAuAusCfsaGfaaaCfaGfaAfuCfaGfgUfgUfcAf	1233	309
1533-SS13	uAuAusCfsaGfaAfaCfagaAfuCfaGfgUfgUfcAf	1234	309
1533-SS14	uAuAusCfsaGfaaaCfagaAfuCfaGfgUfgUfcAf	1235	309
1533-SS15	uAuAusCfsagaAfaCfagaAfuCfaGfgUfgUfcAf	1236	309
1533-SS16	uAuAusCfsagaaaCfagAfAfuCfaGfgUfgUfcAf	1237	309
1533-SS17	uAuAusCfsagaaaCfaGfaAfuCfaGfgUfgUfcAf	1238	309
1533-SS18	uAuAusCfsagaaaCfaGfAfAfuCfaGfgUfgUfcAf	1239	309
1533-SS19	uAuAusCfsagaAfaCfagAfAfuCfaGfgUfgUfcAf	1240	309
AM05341-SS	(NAG37)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgausu(invAb)	1256	357
AM05342-SS	(NAG37)scsagcccccuUfAfUfuguuauacgs(invdA)	1257	381
AM05489-SS	(NAG25)uauausasguuaucgAfGfGfcucauucucas(invAb)	1269	308

[0108]

AM05491-SS	(NAG25)(invAb)uuaucgAfGfGfcucauucucas(invAb)	1270	1258
AM05494-SS	(NAG25)(invAb)GfcCfcCfuUfAfUfuGfuUfaUfaCfgas(invAb)	1271	1259
AM05499-SS	(NAG25)(invAb)gccccuUfAfUfuguuauacgausu(invAb)	1272	357
AM05500-SS	(NAG25)uauauscsagccccuUfAfUfuguuauacgas(invAb)	1273	310
AM05501-SS	(NAG25)(invAb)gccccuUfAfUfuguuauacgas(invAb)	1274	1259
AM05502-SS	(NAG25)sasagccccuUfAfUfuguuauacgs(invdA)	1275	1261
AM05503-SS	(NAG25)scsagccccuUfAfUfuguuauacgas(invAb)	1276	1260
AM05504-SS	(NAG25)sgsccccuUfAfUfuguuauacgas(invAb)	1277	371
AM05505-SS	(NAG25)sgsccccuUfAfUfuguuauacgs(invdA)	1278	371
AM05506-SS	(NAG25)sasagccccuUfAfUfuguuauacgas(invAb)	1279	1261

[0109]

[0110] 표 2B에 기재된 서열을 함유하는 센스 가닥은 표 2A에 기재된 서열을 함유하는 임의의 안티센스 가닥에 혼성화될 수 있고, 단 2개의 서열은 인접한 16개, 17개, 18개, 19개, 20개 또는 21개의 뉴클레오타이드 서열에 걸쳐

적어도 90% 상보성의 영역을 가진다. 대표적인 LPA RNAi 물질은 표 3A 및 3B에 기재된 듀플렉스 번호로 표시된다.

[0111] 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호를 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호로 이루어진다. 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호의 센스 가닥 및 안티센스 가닥 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호의 센스 가닥 및 안티센스 가닥 뉴클레오타이드 서열 및 표적화기 및/또는 연결기를 포함하고, 표적화기 및/또는 연결기는 센스 가닥 또는 안티센스 가닥에 공유로 연결(즉, 접합)된다. 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호의 센스 가닥 및 안티센스 가닥 변형된 뉴클레오타이드 서열을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 본 명세서에 제시된 임의의 듀플렉스 번호의 센스 가닥 및 안티센스 가닥 변형된 뉴클레오타이드 서열 및 표적화기 및/또는 연결기를 포함하고, 표적화기 및/또는 연결기는 센스 가닥 또는 안티센스 가닥에 공유로 연결된다.

표 3A. 듀플렉스 번호를 가지는 LPA RNAi 물질 듀플렉스.

듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호	듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호	듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호
AD00571	AM01240-AS	AM01173-SS	AD02120	AM03257-AS	AM03229-SS	AD02500	AM03107-AS	AM03205-SS
AD00572	AM01241-AS	AM01174-SS	AD02121	AM03257-AS	AM03230-SS	AD02501	AM03279-AS	AM03205-SS
AD00573	AM01242-AS	AM01175-SS	AD02122	AM03257-AS	AM03231-SS	AD02502	AM03280-AS	AM03205-SS
AD00574	AM01243-AS	AM01176-SS	AD02123	AM03257-AS	AM03232-SS	AD02503	AM03281-AS	AM03205-SS
AD00575	AM01244-AS	AM01177-SS	AD02124	AM03257-AS	AM03233-SS	AD02504	AM03282-AS	AM03205-SS
AD00576	AM01245-AS	AM01178-SS	AD02125	AM03257-AS	AM03234-SS	AD02505	AM03283-AS	AM03205-SS
AD00577	AM01246-AS	AM01179-SS	AD02126	AM03257-AS	AM03235-SS	AD02506	AM03284-AS	AM03205-SS
AD00578	AM01247-AS	AM01180-SS	AD02127	AM03257-AS	AM03236-SS	AD02507	AM03300-AS	AM03205-SS
AD00579	AM01248-AS	AM01181-SS	AD02128	AM03257-AS	AM03237-SS	AD02508	AM03301-AS	AM03205-SS
AD00580	AM01249-AS	AM01182-SS	AD02129	AM03258-AS	AM03220-SS	AD02509	AM03107-AS	AM03206-SS
AD00581	AM01250-AS	AM01183-SS	AD02130	AM03258-AS	AM03221-SS	AD02510	AM03279-AS	AM03206-SS
AD00582	AM01251-AS	AM01184-SS	AD02131	AM03258-AS	AM03222-SS	AD02511	AM03280-AS	AM03206-SS
AD00583	AM01252-AS	AM01185-SS	AD02132	AM03258-AS	AM03223-SS	AD02512	AM03281-AS	AM03206-SS
AD00584	AM01253-AS	AM01186-SS	AD02133	AM03258-AS	AM03224-SS	AD02513	AM03282-AS	AM03206-SS
AD00585	AM01254-AS	AM01187-SS	AD02134	AM03258-AS	AM03225-SS	AD02514	AM03283-AS	AM03206-SS
AD00586	AM01255-AS	AM01188-SS	AD02135	AM03258-AS	AM03226-SS	AD02515	AM03284-AS	AM03206-SS

[0112]

AD00587	AM01256-AS	AM01180-SS	AD02136	AM03258-AS	AM03227-SS	AD02516	AM03300-AS	AM03296-SS	
AD00588	AM01257-AS	AM01190-SS	AD02137	AM03258-AS	AM03228-SS	AD02517	AM03301-AS	AM03296-SS	
AD00589	AM01258-AS	AM01191-SS	AD02138	AM03258-AS	AM03229-SS	AD02518	AM03107-AS	AM03297-SS	
AD00590	AM01259-AS	AM01192-SS	AD02139	AM03258-AS	AM03230-SS	AD02519	AM03279-AS	AM03297-SS	
AD00591	AM01260-AS	AM01193-SS	AD02140	AM03258-AS	AM03231-SS	AD02520	AM03280-AS	AM03297-SS	
AD00592	AM01261-AS	AM01194-SS	AD02141	AM03258-AS	AM03232-SS	AD02521	AM03281-AS	AM03297-SS	
AD00593	AM01262-AS	AM01195-SS	AD02142	AM03258-AS	AM03233-SS	AD02522	AM03282-AS	AM03297-SS	
AD00594	AM01263-AS	AM01196-SS	AD02143	AM03258-AS	AM03234-SS	AD02523	AM03283-AS	AM03297-SS	
AD00595	AM01264-AS	AM01197-SS	AD02144	AM03258-AS	AM03235-SS	AD02524	AM03284-AS	AM03297-SS	
AD00596	AM01265-AS	AM01198-SS	AD02145	AM03258-AS	AM03236-SS	AD02525	AM03300-AS	AM03297-SS	
AD00597	AM01266-AS	AM01199-SS	AD02146	AM03258-AS	AM03237-SS	AD02526	AM03301-AS	AM03297-SS	
AD00598	AM01267-AS	AM01200-SS	AD02147	AM03259-AS	AM03220-SS	AD02527	AM03107-AS	AM03298-SS	
AD00599	AM01268-AS	AM01201-SS	AD02148	AM03259-AS	AM03221-SS	AD02528	AM03279-AS	AM03298-SS	
AD00600	AM01269-AS	AM01202-SS	AD02149	AM03259-AS	AM03222-SS	AD02529	AM03280-AS	AM03298-SS	
AD00601	AM01270-AS	AM01203-SS	AD02150	AM03259-AS	AM03223-SS	AD02530	AM03281-AS	AM03298-SS	
AD00602	AM01271-AS	AM01204-SS	AD02151	AM03259-AS	AM03224-SS	AD02531	AM03282-AS	AM03298-SS	
AD00603	AM01272-AS	AM01205-SS	AD02152	AM03259-AS	AM03225-SS	AD02532	AM03283-AS	AM03298-SS	
AD00604	AM01273-AS	AM01206-SS	AD02153	AM03259-AS	AM03226-SS	AD02533	AM03284-AS	AM03298-SS	
AD00605	AM01274-AS	AM01207-SS	AD02154	AM03259-AS	AM03227-SS	AD02534	AM03300-AS	AM03298-SS	

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[0114]

AD00606	AM01275-AS	AM01208-SS	AD02155	AM03250-AS	AM03228-SS	AD02535	AM03301-AS	AM03298-SS
AD00607	AM01276-AS	AM01209-SS	AD02156	AM03250-AS	AM03229-SS	AD02536	AM03107-AS	AM03299-SS
AD00608	AM01277-AS	AM01210-SS	AD02157	AM03250-AS	AM03230-SS	AD02537	AM03279-AS	AM03299-SS
AD00609	AM01278-AS	AM01211-SS	AD02158	AM03250-AS	AM03231-SS	AD02538	AM03280-AS	AM03299-SS
AD00610	AM01279-AS	AM01212-SS	AD02159	AM03250-AS	AM03232-SS	AD02539	AM03281-AS	AM03299-SS
AD00611	AM01280-AS	AM01213-SS	AD02160	AM03250-AS	AM03233-SS	AD02540	AM03282-AS	AM03299-SS
AD00612	AM01281-AS	AM01214-SS	AD02161	AM03250-AS	AM03234-SS	AD02541	AM03283-AS	AM03299-SS
AD00613	AM01282-AS	AM01215-SS	AD02162	AM03250-AS	AM03235-SS	AD02542	AM03284-AS	AM03299-SS
AD00614	AM01283-AS	AM01216-SS	AD02163	AM03250-AS	AM03236-SS	AD02543	AM03300-AS	AM03299-SS
AD00615	AM01284-AS	AM01217-SS	AD02164	AM03250-AS	AM03237-SS	AD02544	AM03301-AS	AM03299-SS
AD00616	AM01285-AS	AM01218-SS	AD02165	AM03260-AS	AM03220-SS	AD02545	AM03301-AS	AM03277-SS
AD00617	AM01286-AS	AM01219-SS	AD02166	AM03260-AS	AM03221-SS	AD02546	AM03107-AS	AM03275-SS
AD00618	AM01287-AS	AM01220-SS	AD02167	AM03260-AS	AM03222-SS	AD02547	AM03107-AS	AM03276-SS
AD00619	AM01288-AS	AM01221-SS	AD02168	AM03260-AS	AM03223-SS	AD02548	AM03107-AS	AM03277-SS
AD00620	AM01289-AS	AM01222-SS	AD02169	AM03260-AS	AM03224-SS	AD02549	AM03107-AS	AM03278-SS
AD00621	AM01290-AS	AM01223-SS	AD02170	AM03260-AS	AM03225-SS	AD02550	AM03107-AS	AM03287-SS
AD00622	AM01291-AS	AM01224-SS	AD02171	AM03260-AS	AM03226-SS	AD02551	AM03107-AS	AM03288-SS
AD00623	AM01292-AS	AM01225-SS	AD02172	AM03260-AS	AM03227-SS	AD02552	AM03107-AS	AM03289-SS
AD00624	AM01293-AS	AM01226-SS	AD02173	AM03260-AS	AM03228-SS	AD02553	AM03107-AS	AM03290-SS

AD00625	AM01294-AS	AM01227-SS	AD02174	AM03260-AS	AM03229-SS	AD02554	AM03279-AS	AM02537-SS	
AD00626	AM01295-AS	AM01228-SS	AD02175	AM03260-AS	AM03230-SS	AD02555	AM03280-AS	AM02537-SS	
AD00627	AM01296-AS	AM01229-SS	AD02176	AM03260-AS	AM03231-SS	AD02556	AM03281-AS	AM02537-SS	
AD00628	AM01297-AS	AM01230-SS	AD02177	AM03260-AS	AM03232-SS	AD02557	AM03282-AS	AM02537-SS	
AD00629	AM01298-AS	AM01231-SS	AD02178	AM03260-AS	AM03233-SS	AD02558	AM03283-AS	AM02537-SS	
AD00630	AM01299-AS	AM01232-SS	AD02179	AM03260-AS	AM03234-SS	AD02559	AM03284-AS	AM02537-SS	
AD00631	AM01300-AS	AM01233-SS	AD02180	AM03260-AS	AM03235-SS	AD02560	AM03300-AS	AM02537-SS	
AD00632	AM01301-AS	AM01234-SS	AD02181	AM03260-AS	AM03236-SS	AD02561	AM03301-AS	AM02537-SS	
AD00633	AM01302-AS	AM01235-SS	AD02182	AM03260-AS	AM03237-SS	AD02609	AM03375-AS	AM03277-SS	
AD00634	AM01303-AS	AM01236-SS	AD02183	AM03261-AS	AM03220-SS	AD02610	AM03376-AS	AM03277-SS	
AD00635	AM01304-AS	AM01237-SS	AD02184	AM03261-AS	AM03221-SS	AD02611	AM03375-AS	AM03278-SS	
AD00636	AM01305-AS	AM01238-SS	AD02185	AM03261-AS	AM03222-SS	AD02612	AM03376-AS	AM03278-SS	
AD00637	AM01306-AS	AM01239-SS	AD02186	AM03261-AS	AM03223-SS	AD02613	AM03375-AS	AM03289-SS	
AD01068	AM01796-AS	AM01795-SS	AD02187	AM03261-AS	AM03224-SS	AD02614	AM03376-AS	AM03289-SS	
AD01069	AM01798-AS	AM01797-SS	AD02188	AM03261-AS	AM03225-SS	AD02615	AM03377-AS	AM02941-SS	
AD01070	AM01800-AS	AM01799-SS	AD02189	AM03261-AS	AM03226-SS	AD02616	AM03250-AS	AM02941-SS	
AD01071	AM01802-AS	AM01801-SS	AD02190	AM03261-AS	AM03227-SS	AD02617	AM03377-AS	AM02942-SS	
AD01072	AM01804-AS	AM01803-SS	AD02191	AM03261-AS	AM03228-SS	AD02618	AM03250-AS	AM02942-SS	
AD01073	AM01806-AS	AM01805-SS	AD02192	AM03261-AS	AM03229-SS	AD02619	AM03377-AS	AM03243-SS	

[0115]

AD01074	AM01808-AS	AM01807-SS	AD02193	AM03261-AS	AM03230-SS	AD02620	AM03250-AS	AM03243-SS	
AD01075	AM01810-AS	AM01809-SS	AD02194	AM03261-AS	AM03231-SS	AD02662	AM02860-AS	AM03424-SS	
AD01076	AM01812-AS	AM01811-SS	AD02195	AM03261-AS	AM03232-SS	AD02663	AM02860-AS	AM03425-SS	
AD01077	AM01814-AS	AM01813-SS	AD02196	AM03261-AS	AM03233-SS	AD02664	AM03427-AS	AM03426-SS	
AD01078	AM01816-AS	AM01815-SS	AD02197	AM03261-AS	AM03234-SS	AD02682	AM02775-AS	AM03457-SS	
AD01079	AM01818-AS	AM01817-SS	AD02198	AM03261-AS	AM03235-SS	AD02683	AM02776-AS	AM03458-SS	
AD01184	AM02003-AS	AM02006-SS	AD02199	AM03261-AS	AM03236-SS	AD02684	AM02783-AS	AM03459-SS	
AD01185	AM02004-AS	AM02006-SS	AD02200	AM03261-AS	AM03237-SS	AD02685	AM02785-AS	AM03460-SS	
AD01186	AM02005-AS	AM02006-SS	AD02201	AM03262-AS	AM03220-SS	AD02686	AM02788-AS	AM03461-SS	
AD01187	AM02007-AS	AM02010-SS	AD02202	AM03262-AS	AM03221-SS	AD02687	AM02791-AS	AM03462-SS	
AD01188	AM02008-AS	AM02010-SS	AD02203	AM03262-AS	AM03222-SS	AD02696	AM02860-AS	AM03243-SS	
AD01189	AM02009-AS	AM02010-SS	AD02204	AM03262-AS	AM03223-SS	AD02697	AM03107-AS	AM03277-SS	
AD01190	AM02011-AS	AM02014-SS	AD02205	AM03262-AS	AM03224-SS	AD02698	AM03107-AS	AM03278-SS	
AD01191	AM02012-AS	AM02014-SS	AD02206	AM03262-AS	AM03225-SS	AD02699	AM03107-AS	AM03289-SS	
AD01192	AM02013-AS	AM02014-SS	AD02207	AM03262-AS	AM03226-SS	AD02710	AM03486-AS	AM03480-SS	
AD01193	AM02015-AS	AM02018-SS	AD02208	AM03262-AS	AM03227-SS	AD02711	AM03487-AS	AM03489-SS	
AD01194	AM02016-AS	AM02018-SS	AD02209	AM03262-AS	AM03228-SS	AD02712	AM03488-AS	AM03489-SS	
AD01195	AM02017-AS	AM02018-SS	AD02210	AM03262-AS	AM03229-SS	AD02713	AM02860-AS	AM03489-SS	
AD01196	AM02019-AS	AM02022-SS	AD02211	AM03262-AS	AM03230-SS	AD02714	AM03490-AS	AM03492-SS	

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AD01197	AM02020-AS	AM02022-SS	AD02212	AM03262-AS	AM03231-SS	AD02715	AM03491-AS	AM03492-SS	
AD01198	AM02021-AS	AM02022-SS	AD02213	AM03262-AS	AM03232-SS	AD02716	AM02531-AS	AM03492-SS	
AD01199	AM02023-AS	AM02026-SS	AD02214	AM03262-AS	AM03233-SS	AD02717	AM03107-AS	AM03492-SS	
AD01200	AM02024-AS	AM02026-SS	AD02215	AM03262-AS	AM03234-SS	AD02745	AM03107-AS	AM03544-SS	
AD01201	AM02025-AS	AM02026-SS	AD02216	AM03262-AS	AM03235-SS	AD02746	AM03283-AS	AM03544-SS	
AD01202	AM02027-AS	AM02030-SS	AD02217	AM03262-AS	AM03236-SS	AD02747	AM03300-AS	AM03544-SS	
AD01203	AM02028-AS	AM02030-SS	AD02218	AM03262-AS	AM03237-SS	AD02748	AM03107-AS	AM03545-SS	
AD01204	AM02029-AS	AM02030-SS	AD02219	AM03263-AS	AM03220-SS	AD02749	AM03283-AS	AM03545-SS	
AD01205	AM02031-AS	AM02034-SS	AD02220	AM03263-AS	AM03221-SS	AD02750	AM03300-AS	AM03545-SS	
AD01206	AM02032-AS	AM02034-SS	AD02221	AM03263-AS	AM03222-SS	AD02751	AM03107-AS	AM03546-SS	
AD01207	AM02033-AS	AM02034-SS	AD02222	AM03263-AS	AM03223-SS	AD02752	AM03283-AS	AM03546-SS	
AD01208	AM02035-AS	AM02038-SS	AD02223	AM03263-AS	AM03224-SS	AD02753	AM03300-AS	AM03546-SS	
AD01209	AM02036-AS	AM02038-SS	AD02224	AM03263-AS	AM03225-SS	AD02754	AM02534-AS	AM03547-SS	
AD01210	AM02037-AS	AM02038-SS	AD02225	AM03263-AS	AM03226-SS	AD02755	AM02857-AS	AM03547-SS	
AD01211	AM02039-AS	AM02042-SS	AD02226	AM03263-AS	AM03227-SS	AD02819	AM03377-AS	AM03650-SS	
AD01212	AM02040-AS	AM02042-SS	AD02227	AM03263-AS	AM03228-SS	AD02820	AM03250-AS	AM03650-SS	
AD01213	AM02041-AS	AM02042-SS	AD02228	AM03263-AS	AM03229-SS	AD02821	AM03129-AS	AM03651-SS	
AD01328	AM02240-AS	AM02211-SS	AD02229	AM03263-AS	AM03230-SS	AD02825	AM03655-AS	AM03650-SS	
AD01329	AM02241-AS	AM02212-SS	AD02230	AM03263-AS	AM03231-SS	AD02826	AM03656-AS	AM03650-SS	

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AD01330	AM02242-AS	AM02213-SS	AD02231	AM03263-AS	AM03232-SS	AD02827	AM03657-AS	AM03650-SS
AD01331	AM02243-AS	AM02214-SS	AD02232	AM03263-AS	AM03233-SS	AD02828	AM03658-AS	AM03650-SS
AD01332	AM02244-AS	AM02215-SS	AD02233	AM03263-AS	AM03234-SS	AD02829	AM03659-AS	AM03650-SS
AD01333	AM02245-AS	AM02216-SS	AD02234	AM03263-AS	AM03235-SS	AD02830	AM03660-AS	AM03650-SS
AD01334	AM02246-AS	AM02217-SS	AD02235	AM03263-AS	AM03236-SS	AD02831	AM03661-AS	AM03650-SS
AD01335	AM02247-AS	AM02218-SS	AD02236	AM03263-AS	AM03237-SS	AD02832	AM03260-AS	AM03650-SS
AD01336	AM02248-AS	AM02219-SS	AD02237	AM03264-AS	AM03220-SS	AD02841	AM03671-AS	AM03670-SS
AD01337	AM02249-AS	AM02220-SS	AD02238	AM03264-AS	AM03221-SS	AD02842	AM03672-AS	AM03546-SS
AD01338	AM02250-AS	AM02221-SS	AD02239	AM03264-AS	AM03222-SS	AD02843	AM03673-AS	AM03546-SS
AD01339	AM02251-AS	AM02222-SS	AD02240	AM03264-AS	AM03223-SS	AD02844	AM03674-AS	AM03546-SS
AD01340	AM02252-AS	AM02223-SS	AD02241	AM03264-AS	AM03224-SS	AD02845	AM03675-AS	AM03546-SS
AD01341	AM02253-AS	AM02224-SS	AD02242	AM03264-AS	AM03225-SS	AD02846	AM03676-AS	AM03546-SS
AD01342	AM02254-AS	AM02225-SS	AD02243	AM03264-AS	AM03226-SS	AD02847	AM03677-AS	AM03546-SS
AD01343	AM02255-AS	AM02226-SS	AD02244	AM03264-AS	AM03227-SS	AD02848	AM03678-AS	AM03650-SS
AD01344	AM02256-AS	AM02227-SS	AD02245	AM03264-AS	AM03228-SS	AD02849	AM03679-AS	AM03650-SS
AD01345	AM02257-AS	AM02228-SS	AD02246	AM03264-AS	AM03229-SS	AD02850	AM03680-AS	AM03650-SS
AD01346	AM02258-AS	AM02229-SS	AD02247	AM03264-AS	AM03230-SS	AD02851	AM03681-AS	AM03650-SS
AD01347	AM02259-AS	AM02230-SS	AD02248	AM03264-AS	AM03231-SS	AD02852	AM03682-AS	AM03650-SS
AD01348	AM02260-AS	AM02231-SS	AD02249	AM03264-AS	AM03232-SS	AD02853	AM02860-AS	AM03237-SS

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AD01349	AM02261-AS	AM02232-SS	AD02250	AM03264-AS	AM03233-SS	AD02854	AM03377-AS	AM03225-SS
AD01350	AM02262-AS	AM02233-SS	AD02251	AM03264-AS	AM03234-SS	AD02855	AM03120-AS	AM03683-SS
AD01351	AM02263-AS	AM02234-SS	AD02252	AM03264-AS	AM03235-SS	AD02907	AM02775-AS	AM03741-SS
AD01352	AM02264-AS	AM02235-SS	AD02253	AM03264-AS	AM03236-SS	AD02908	AM02775-AS	AM03742-SS
AD01353	AM02265-AS	AM02236-SS	AD02254	AM03264-AS	AM03237-SS	AD02909	AM02775-AS	AM03743-SS
AD01354	AM02266-AS	AM02237-SS	AD02255	AM03265-AS	AM03220-SS	AD02910	AM03744-AS	AM03457-SS
AD01355	AM02267-AS	AM02238-SS	AD02256	AM03265-AS	AM03221-SS	AD02911	AM03745-AS	AM03457-SS
AD01356	AM02268-AS	AM02239-SS	AD02257	AM03265-AS	AM03222-SS	AD02912	AM03745-AS	AM03742-SS
AD01462	AM02404-AS	AM02441-SS	AD02258	AM03265-AS	AM03223-SS	AD02913	AM02776-AS	AM03746-SS
AD01463	AM02406-AS	AM02442-SS	AD02259	AM03265-AS	AM03224-SS	AD02914	AM02776-AS	AM03747-SS
AD01464	AM02408-AS	AM02443-SS	AD02260	AM03265-AS	AM03225-SS	AD02915	AM02776-AS	AM03748-SS
AD01465	AM02410-AS	AM02444-SS	AD02261	AM03265-AS	AM03226-SS	AD02916	AM03740-AS	AM03458-SS
AD01466	AM02412-AS	AM02445-SS	AD02262	AM03265-AS	AM03227-SS	AD02917	AM03750-AS	AM03458-SS
AD01467	AM02414-AS	AM02446-SS	AD02263	AM03265-AS	AM03228-SS	AD02918	AM03750-AS	AM03747-SS
AD01468	AM02416-AS	AM02447-SS	AD02264	AM03265-AS	AM03229-SS	AD02919	AM02788-AS	AM03751-SS
AD01469	AM02418-AS	AM02448-SS	AD02265	AM03265-AS	AM03230-SS	AD02920	AM02788-AS	AM03752-SS
AD01529	AM02531-AS	AM02537-SS	AD02266	AM03265-AS	AM03231-SS	AD02921	AM02788-AS	AM03753-SS
AD01530	AM02532-AS	AM02538-SS	AD02267	AM03265-AS	AM03232-SS	AD02922	AM03754-AS	AM03461-SS
AD01531	AM02533-AS	AM02539-SS	AD02268	AM03265-AS	AM03233-SS	AD02923	AM03755-AS	AM03461-SS

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AD01532	AM02534-AS	AM02540-SS	AD02269	AM03265-AS	AM03234-SS	AD02924	AM03756-AS	AM03461-SS	
AD01533	AM02535-AS	AM02541-SS	AD02270	AM03265-AS	AM03235-SS	AD02925	AM03756-AS	AM03752-SS	
AD01534	AM02536-AS	AM02542-SS	AD02271	AM03265-AS	AM03236-SS	AD02926	AM02791-AS	AM03757-SS	
AD01708	AM02755-AS	AM02703-SS	AD02272	AM03265-AS	AM03237-SS	AD02927	AM02791-AS	AM03758-SS	
AD01709	AM02756-AS	AM02794-SS	AD02273	AM03266-AS	AM03220-SS	AD02928	AM02791-AS	AM03759-SS	
AD01710	AM02757-AS	AM02795-SS	AD02274	AM03266-AS	AM03221-SS	AD02929	AM03760-AS	AM03462-SS	
AD01711	AM02758-AS	AM02706-SS	AD02275	AM03266-AS	AM03222-SS	AD02930	AM03761-AS	AM03462-SS	
AD01712	AM02759-AS	AM02797-SS	AD02276	AM03266-AS	AM03223-SS	AD02931	AM03762-AS	AM03462-SS	
AD01713	AM02760-AS	AM02708-SS	AD02277	AM03266-AS	AM03224-SS	AD02932	AM03762-AS	AM03758-SS	
AD01714	AM02761-AS	AM02709-SS	AD02278	AM03266-AS	AM03225-SS	AD03049	AM03856-AS	AM03650-SS	
AD01715	AM02762-AS	AM02800-SS	AD02279	AM03266-AS	AM03226-SS	AD03050	AM03857-AS	AM03651-SS	
AD01716	AM02763-AS	AM02801-SS	AD02280	AM03266-AS	AM03227-SS	AD03051	AM03377-AS	AM03859-SS	
AD01717	AM02764-AS	AM02802-SS	AD02281	AM03266-AS	AM03228-SS	AD03052	AM03129-AS	AM03861-SS	
AD01718	AM02765-AS	AM02803-SS	AD02282	AM03266-AS	AM03229-SS	AD03053	AM03862-AS	AM03650-SS	
AD01719	AM02766-AS	AM02804-SS	AD02283	AM03266-AS	AM03230-SS	AD03054	AM03259-AS	AM03859-SS	
AD01720	AM02767-AS	AM02805-SS	AD02284	AM03266-AS	AM03231-SS	AD03058	AM03866-AS	AM03546-SS	
AD01721	AM02768-AS	AM02806-SS	AD02285	AM03266-AS	AM03232-SS	AD03059	AM03867-AS	AM03546-SS	
AD01722	AM02769-AS	AM02807-SS	AD02286	AM03266-AS	AM03233-SS	AD03060	AM03868-AS	AM03546-SS	
AD01723	AM02770-AS	AM02808-SS	AD02287	AM03266-AS	AM03234-SS	AD03061	AM03869-AS	AM03546-SS	

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AD01724	AM02771-AS	AM02809-SS	AD02288	AM03266-AS	AM03235-SS	AD03062	AM03870-AS	AM03546-SS	
AD01725	AM02772-AS	AM02810-SS	AD02289	AM03266-AS	AM03236-SS	AD03063	AM03871-AS	AM03546-SS	
AD01726	AM02773-AS	AM02811-SS	AD02290	AM03266-AS	AM03237-SS	AD03064	AM03872-AS	AM03546-SS	
AD01727	AM02774-AS	AM02793-SS	AD02291	AM03267-AS	AM03220-SS	AD03065	AM03873-AS	AM03546-SS	
AD01728	AM02775-AS	AM02794-SS	AD02292	AM03267-AS	AM03221-SS	AD03066	AM03874-AS	AM03546-SS	
AD01729	AM02776-AS	AM02795-SS	AD02293	AM03267-AS	AM03222-SS	AD03067	AM03875-AS	AM03546-SS	
AD01730	AM02777-AS	AM02796-SS	AD02294	AM03267-AS	AM03223-SS	AD03068	AM03876-AS	AM03546-SS	
AD01731	AM02778-AS	AM02797-SS	AD02295	AM03267-AS	AM03224-SS	AD03069	AM03877-AS	AM03546-SS	
AD01732	AM02779-AS	AM02798-SS	AD02296	AM03267-AS	AM03225-SS	AD03070	AM03878-AS	AM03546-SS	
AD01733	AM02780-AS	AM02799-SS	AD02297	AM03267-AS	AM03226-SS	AD03071	AM03883-AS	AM03879-SS	
AD01734	AM02781-AS	AM02800-SS	AD02298	AM03267-AS	AM03227-SS	AD03072	AM03884-AS	AM03880-SS	
AD01735	AM02782-AS	AM02801-SS	AD02299	AM03267-AS	AM03228-SS	AD03073	AM03883-AS	AM03881-SS	
AD01736	AM02783-AS	AM02802-SS	AD02300	AM03267-AS	AM03229-SS	AD03074	AM03885-AS	AM03882-SS	
AD01737	AM02784-AS	AM02803-SS	AD02301	AM03267-AS	AM03230-SS	AD03075	AM03129-AS	AM03546-SS	
AD01738	AM02785-AS	AM02804-SS	AD02302	AM03267-AS	AM03231-SS	AD03114	AM03929-AS	AM03651-SS	
AD01739	AM02786-AS	AM02805-SS	AD02303	AM03267-AS	AM03232-SS	AD03115	AM03930-AS	AM03651-SS	
AD01740	AM02787-AS	AM02806-SS	AD02304	AM03267-AS	AM03233-SS	AD03116	AM03129-AS	AM03928-SS	
AD01741	AM02788-AS	AM02807-SS	AD02305	AM03267-AS	AM03234-SS	AD03117	AM03929-AS	AM03928-SS	
AD01742	AM02789-AS	AM02808-SS	AD02306	AM03267-AS	AM03235-SS	AD03118	AM03930-AS	AM03928-SS	

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AD01743	AM02790-AS	AM02809-SS	AD02307	AM03267-AS	AM03236-SS	AD03119	AM03932-AS	AM03650-SS	
AD01744	AM02791-AS	AM02810-SS	AD02308	AM03267-AS	AM03237-SS	AD03120	AM03933-AS	AM03650-SS	
AD01745	AM02792-AS	AM02811-SS	AD02309	AM03268-AS	AM03220-SS	AD03121	AM03377-AS	AM03931-SS	
AD01746	AM02774-AS	AM02812-SS	AD02310	AM03268-AS	AM03221-SS	AD03122	AM03932-AS	AM03931-SS	
AD01747	AM02775-AS	AM02813-SS	AD02311	AM03268-AS	AM03222-SS	AD03123	AM03933-AS	AM03931-SS	
AD01748	AM02776-AS	AM02814-SS	AD02312	AM03268-AS	AM03223-SS	AD03156	AM03969-AS	AM03968-SS	
AD01749	AM02777-AS	AM02815-SS	AD02313	AM03268-AS	AM03224-SS	AD03157	AM03971-AS	AM03970-SS	
AD01750	AM02778-AS	AM02816-SS	AD02314	AM03268-AS	AM03225-SS	AD03158	AM03972-AS	AM03970-SS	
AD01751	AM02779-AS	AM02817-SS	AD02315	AM03268-AS	AM03226-SS	AD03159	AM03973-AS	AM03970-SS	
AD01752	AM02780-AS	AM02818-SS	AD02316	AM03268-AS	AM03227-SS	AD03170	AM03823-AS	AM03651-SS	
AD01753	AM02781-AS	AM02819-SS	AD02317	AM03268-AS	AM03228-SS	AD03171	AM03824-AS	AM03651-SS	
AD01754	AM02782-AS	AM02820-SS	AD02318	AM03268-AS	AM03229-SS	AD03172	AM03825-AS	AM03651-SS	
AD01755	AM02783-AS	AM02821-SS	AD02319	AM03268-AS	AM03230-SS	AD03173	AM03826-AS	AM03651-SS	
AD01756	AM02784-AS	AM02822-SS	AD02320	AM03268-AS	AM03231-SS	AD03174	AM03827-AS	AM03650-SS	
AD01757	AM02785-AS	AM02823-SS	AD02321	AM03268-AS	AM03232-SS	AD03175	AM03828-AS	AM03650-SS	
AD01758	AM02786-AS	AM02824-SS	AD02322	AM03268-AS	AM03233-SS	AD03272	AM02860-AS	AM04138-SS	
AD01759	AM02787-AS	AM02825-SS	AD02323	AM03268-AS	AM03234-SS	AD03273	AM03377-AS	AM04138-SS	
AD01760	AM02788-AS	AM02826-SS	AD02324	AM03268-AS	AM03235-SS	AD03274	AM04132-AS	AM04138-SS	
AD01761	AM02789-AS	AM02827-SS	AD02325	AM03268-AS	AM03236-SS	AD03275	AM04133-AS	AM04138-SS	

AD01762	AM02790-AS	AM02828-SS	AD02326	AM03268-AS	AM03237-SS	AD03276	AM04134-AS	AM04138-SS	
AD01763	AM02791-AS	AM02829-SS	AD02327	AM03269-AS	AM03220-SS	AD03277	AM04135-AS	AM04138-SS	
AD01764	AM02792-AS	AM02830-SS	AD02328	AM03269-AS	AM03221-SS	AD03278	AM04136-AS	AM04138-SS	
AD01765	AM02857-AS	AM02540-SS	AD02329	AM03269-AS	AM03222-SS	AD03279	AM04137-AS	AM04138-SS	
AD01766	AM02858-AS	AM02540-SS	AD02330	AM03269-AS	AM03223-SS	AD03291	AM04150-AS	AM04152-SS	
AD01767	AM02859-AS	AM02540-SS	AD02331	AM03269-AS	AM03224-SS	AD03327	AM04150-AS	AM04214-SS	
AD01768	AM02860-AS	AM02540-SS	AD02332	AM03269-AS	AM03225-SS	AD03341	AM04133-AS	AM04233-SS	
AD01769	AM02859-AS	AM02861-SS	AD02333	AM03269-AS	AM03226-SS	AD03351	AM04250-AS	AM03742-SS	
AD01770	AM02860-AS	AM02861-SS	AD02334	AM03269-AS	AM03227-SS	AD03352	AM04251-AS	AM03742-SS	
AD01772	AM02863-AS	AM02541-SS	AD02335	AM03269-AS	AM03228-SS	AD03353	AM04252-AS	AM03742-SS	
AD01773	AM02864-AS	AM02541-SS	AD02336	AM03269-AS	AM03229-SS	AD03354	AM04253-AS	AM03747-SS	
AD01774	AM02865-AS	AM02541-SS	AD02337	AM03269-AS	AM03230-SS	AD03355	AM04254-AS	AM03747-SS	
AD01780	AM02866-AS	AM02541-SS	AD02338	AM03269-AS	AM03231-SS	AD03356	AM04255-AS	AM03747-SS	
AD01803	AM02534-AS	AM02941-SS	AD02339	AM03269-AS	AM03232-SS	AD03357	AM04256-AS	AM03752-SS	
AD01804	AM02534-AS	AM02942-SS	AD02340	AM03269-AS	AM03233-SS	AD03358	AM04257-AS	AM03752-SS	
AD01805	AM02943-AS	AM02540-SS	AD02341	AM03269-AS	AM03234-SS	AD03359	AM04258-AS	AM03752-SS	
AD01806	AM02943-AS	AM02941-SS	AD02342	AM03269-AS	AM03235-SS	AD03360	AM04259-AS	AM03758-SS	
AD01807	AM02943-AS	AM02942-SS	AD02343	AM03269-AS	AM03236-SS	AD03361	AM04260-AS	AM03758-SS	
AD01808	AM02944-AS	AM02540-SS	AD02344	AM03269-AS	AM03237-SS	AD03362	AM04261-AS	AM03758-SS	

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AD01809	AM02944-AS	AM02941-SS	AD02345	AM03270-AS	AM03220-SS	AD03421	AM04133-AS	AM04372-SS
AD01810	AM02944-AS	AM02942-SS	AD02346	AM03270-AS	AM03221-SS	AD03424	AM04215-AS	AM03546-SS
AD01811	AM02945-AS	AM02540-SS	AD02347	AM03270-AS	AM03222-SS	AD03425	AM04216-AS	AM03546-SS
AD01812	AM02945-AS	AM02941-SS	AD02348	AM03270-AS	AM03223-SS	AD03426	AM04217-AS	AM03546-SS
AD01813	AM02945-AS	AM02942-SS	AD02349	AM03270-AS	AM03224-SS	AD03427	AM04218-AS	AM03546-SS
AD01814	AM02535-AS	AM02946-SS	AD02350	AM03270-AS	AM03225-SS	AD03428	AM04219-AS	AM03546-SS
AD01815	AM02535-AS	AM02947-SS	AD02351	AM03270-AS	AM03226-SS	AD03430	AM04377-AS	AM04381-SS
AD01816	AM02535-AS	AM02948-SS	AD02352	AM03270-AS	AM03227-SS	AD03431	AM04378-AS	AM04382-SS
AD01817	AM02535-AS	AM02949-SS	AD02353	AM03270-AS	AM03228-SS	AD03432	AM04379-AS	AM04381-SS
AD01818	AM02950-AS	AM02541-SS	AD02354	AM03270-AS	AM03229-SS	AD03433	AM04380-AS	AM04382-SS
AD01819	AM02950-AS	AM02946-SS	AD02355	AM03270-AS	AM03230-SS	AD03434	AM04383-AS	AM04391-SS
AD01820	AM02950-AS	AM02947-SS	AD02356	AM03270-AS	AM03231-SS	AD03435	AM04384-AS	AM04392-SS
AD01821	AM02950-AS	AM02948-SS	AD02357	AM03270-AS	AM03232-SS	AD03436	AM04385-AS	AM04391-SS
AD01822	AM02950-AS	AM02949-SS	AD02358	AM03270-AS	AM03233-SS	AD03437	AM04386-AS	AM04392-SS
AD01823	AM02951-AS	AM02541-SS	AD02359	AM03270-AS	AM03234-SS	AD03438	AM04387-AS	AM04391-SS
AD01824	AM02951-AS	AM02946-SS	AD02360	AM03270-AS	AM03235-SS	AD03439	AM04388-AS	AM04392-SS
AD01825	AM02951-AS	AM02947-SS	AD02361	AM03270-AS	AM03236-SS	AD03440	AM04389-AS	AM04391-SS
AD01826	AM02951-AS	AM02948-SS	AD02362	AM03270-AS	AM03237-SS	AD03441	AM04390-AS	AM04392-SS
AD01827	AM02951-AS	AM02949-SS	AD02363	AM03271-AS	AM03220-SS	AD03460	AM03300-AS	AM04412-SS

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AD01828	AM02952-AS	AM02541-SS	AD02364	AM03271-AS	AM03221-SS	AD03461	AM04413-AS	AM04414-SS	
AD01829	AM02952-AS	AM02946-SS	AD02365	AM03271-AS	AM03222-SS	AD03462	AM04415-AS	AM04416-SS	
AD01830	AM02952-AS	AM02947-SS	AD02366	AM03271-AS	AM03223-SS	AD03463	AM04417-AS	AM04412-SS	
AD01831	AM02952-AS	AM02948-SS	AD02367	AM03271-AS	AM03224-SS	AD03494	AM04437-AS	AM03742-SS	
AD01832	AM02952-AS	AM02940-SS	AD02368	AM03271-AS	AM03225-SS	AD03495	AM04438-AS	AM03747-SS	
AD01895	AM02863-AS	AM03030-SS	AD02369	AM03271-AS	AM03226-SS	AD03496	AM04439-AS	AM03752-SS	
AD01896	AM02865-AS	AM03036-SS	AD02370	AM03271-AS	AM03227-SS	AD03497	AM04440-AS	AM03758-SS	
AD01897	AM02865-AS	AM03037-SS	AD02371	AM03271-AS	AM03228-SS	AD03536	AM03972-AS	AM04496-SS	
AD01898	AM02865-AS	AM03038-SS	AD02372	AM03271-AS	AM03229-SS	AD03537	AM02860-AS	AM04497-SS	
AD01899	AM03040-AS	AM03039-SS	AD02373	AM03271-AS	AM03230-SS	AD03538	AM03972-AS	AM04499-SS	
AD01900	AM03041-AS	AM03039-SS	AD02374	AM03271-AS	AM03231-SS	AD03539	AM04415-AS	AM04498-SS	
AD01901	AM03041-AS	AM03042-SS	AD02375	AM03271-AS	AM03232-SS	AD03540	AM03972-AS	AM04500-SS	
AD01902	AM02863-AS	AM03042-SS	AD02376	AM03271-AS	AM03233-SS	AD03541	AM04501-AS	AM03970-SS	
AD01903	AM03043-AS	AM03042-SS	AD02377	AM03271-AS	AM03234-SS	AD03542	AM02860-AS	AM04502-SS	
AD01912	AM03065-AS	AM03060-SS	AD02378	AM03271-AS	AM03235-SS	AD03547	AM04507-AS	AM04498-SS	
AD01913	AM03066-AS	AM03060-SS	AD02379	AM03271-AS	AM03236-SS	AD03548	AM02860-AS	AM04498-SS	
AD01914	AM03067-AS	AM03060-SS	AD02380	AM03271-AS	AM03237-SS	AD03549	AM04507-AS	AM04502-SS	
AD01915	AM03068-AS	AM03060-SS	AD02381	AM03272-AS	AM03220-SS	AD03573	AM04539-AS	AM04535-SS	
AD01916	AM03069-AS	AM03060-SS	AD02382	AM03272-AS	AM03221-SS	AD03574	AM04540-AS	AM04536-SS	

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AD01917	AM03070-AS	AM03060-SS	AD02383	AM03272-AS	AM03222-SS	AD03575	AM04541-AS	AM04537-SS	
AD01918	AM03065-AS	AM03061-SS	AD02384	AM03272-AS	AM03223-SS	AD03576	AM04542-AS	AM04538-SS	
AD01919	AM03066-AS	AM03061-SS	AD02385	AM03272-AS	AM03224-SS	AD03577	AM04544-AS	AM04543-SS	
AD01920	AM03067-AS	AM03061-SS	AD02386	AM03272-AS	AM03225-SS	AD03578	AM04545-AS	AM04500-SS	
AD01921	AM03068-AS	AM03061-SS	AD02387	AM03272-AS	AM03226-SS	AD03579	AM04546-AS	AM04500-SS	
AD01922	AM03069-AS	AM03061-SS	AD02388	AM03272-AS	AM03227-SS	AD03603	AM04582-AS	AM04578-SS	
AD01923	AM03070-AS	AM03061-SS	AD02389	AM03272-AS	AM03228-SS	AD03604	AM04583-AS	AM04578-SS	
AD01924	AM03065-AS	AM03062-SS	AD02390	AM03272-AS	AM03229-SS	AD03605	AM04584-AS	AM04578-SS	
AD01925	AM03066-AS	AM03062-SS	AD02391	AM03272-AS	AM03230-SS	AD03606	AM04585-AS	AM04578-SS	
AD01926	AM03067-AS	AM03062-SS	AD02392	AM03272-AS	AM03231-SS	AD03607	AM04586-AS	AM04578-SS	
AD01927	AM03068-AS	AM03062-SS	AD02393	AM03272-AS	AM03232-SS	AD03608	AM04587-AS	AM04578-SS	
AD01928	AM03069-AS	AM03062-SS	AD02394	AM03272-AS	AM03233-SS	AD03609	AM04584-AS	AM04588-SS	
AD01929	AM03070-AS	AM03062-SS	AD02395	AM03272-AS	AM03234-SS	AD03610	AM04584-AS	AM04579-SS	
AD01930	AM03065-AS	AM03037-SS	AD02396	AM03272-AS	AM03235-SS	AD03611	AM04584-AS	AM04580-SS	
AD01931	AM03066-AS	AM03037-SS	AD02397	AM03272-AS	AM03236-SS	AD03612	AM04584-AS	AM04581-SS	
AD01932	AM03067-AS	AM03037-SS	AD02398	AM03272-AS	AM03237-SS	AD03627	AM04609-AS	AM03970-SS	
AD01933	AM03068-AS	AM03037-SS	AD02399	AM03273-AS	AM03220-SS	AD03628	AM04610-AS	AM03970-SS	
AD01934	AM03069-AS	AM03037-SS	AD02400	AM03273-AS	AM03221-SS	AD03629	AM03972-AS	AM04611-SS	
AD01935	AM03070-AS	AM03037-SS	AD02401	AM03273-AS	AM03222-SS	AD03630	AM03972-AS	AM04612-SS	

AD01936	AM03065-AS	AM03064-SS	AD02402	AM03273-AS	AM03223-SS	AD03668	AM04501-AS	AM04500-SS	
AD01937	AM03066-AS	AM03064-SS	AD02403	AM03273-AS	AM03224-SS	AD03671	AM04677-AS	AM04669-SS	
AD01938	AM03067-AS	AM03064-SS	AD02404	AM03273-AS	AM03225-SS	AD03672	AM04678-AS	AM04670-SS	
AD01939	AM03068-AS	AM03064-SS	AD02405	AM03273-AS	AM03226-SS	AD03673	AM04679-AS	AM04671-SS	
AD01940	AM03069-AS	AM03064-SS	AD02406	AM03273-AS	AM03227-SS	AD03674	AM04680-AS	AM04672-SS	
AD01941	AM03070-AS	AM03064-SS	AD02407	AM03273-AS	AM03228-SS	AD03675	AM04681-AS	AM04673-SS	
AD01976	AM03119-AS	AM02540-SS	AD02408	AM03273-AS	AM03229-SS	AD03676	AM02860-AS	AM04674-SS	
AD01977	AM03120-AS	AM02540-SS	AD02409	AM03273-AS	AM03230-SS	AD03677	AM02860-AS	AM04675-SS	
AD01978	AM03121-AS	AM02540-SS	AD02410	AM03273-AS	AM03231-SS	AD03678	AM02860-AS	AM04676-SS	
AD01979	AM02857-AS	AM03122-SS	AD02411	AM03273-AS	AM03232-SS	AD03705	AM04501-AS	AM04726-SS	
AD01980	AM02857-AS	AM03123-SS	AD02412	AM03273-AS	AM03233-SS	AD03706	AM04501-AS	AM04727-SS	
AD01981	AM03119-AS	AM03122-SS	AD02413	AM03273-AS	AM03234-SS	AD03707	AM04501-AS	AM04728-SS	
AD01982	AM02857-AS	AM03124-SS	AD02414	AM03273-AS	AM03235-SS	AD03708	AM04544-AS	AM04729-SS	
AD01983	AM03107-AS	AM02537-SS	AD02415	AM03273-AS	AM03236-SS	AD03713	AM04733-AS	AM04138-SS	
AD01984	AM03108-AS	AM02537-SS	AD02416	AM03273-AS	AM03237-SS	AD03714	AM04734-AS	AM04138-SS	
AD01985	AM03107-AS	AM03125-SS	AD02417	AM03274-AS	AM03220-SS	AD03715	AM04735-AS	AM04138-SS	
AD01986	AM03107-AS	AM03126-SS	AD02418	AM03274-AS	AM03221-SS	AD03716	AM04736-AS	AM04138-SS	
AD01987	AM03127-AS	AM02537-SS	AD02419	AM03274-AS	AM03222-SS	AD03717	AM02860-AS	AM04737-SS	
AD01988	AM03129-AS	AM03128-SS	AD02420	AM03274-AS	AM03223-SS	AD03720	AM03884-AS	AM04741-SS	

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AD01989	AM03130-AS	AM02540-SS	AD02421	AM03274-AS	AM03224-SS	AD03721	AM03972-AS	AM04742-SS	
AD01990	AM03131-AS	AM02540-SS	AD02422	AM03274-AS	AM03225-SS	AD03722	AM03972-AS	AM04743-SS	
AD02001	AM02860-AS	AM02942-SS	AD02423	AM03274-AS	AM03226-SS	AD03723	AM03972-AS	AM04744-SS	
AD02002	AM02857-AS	AM03144-SS	AD02424	AM03274-AS	AM03227-SS	AD03760	AM04805-AS	AM04803-SS	
AD02003	AM03149-AS	AM02540-SS	AD02425	AM03274-AS	AM03228-SS	AD03761	AM04501-AS	AM04804-SS	
AD02004	AM03149-AS	AM02941-SS	AD02426	AM03274-AS	AM03229-SS	AD03762	AM04805-AS	AM04807-SS	
AD02005	AM03149-AS	AM02942-SS	AD02427	AM03274-AS	AM03230-SS	AD03763	AM03884-AS	AM04729-SS	
AD02006	AM03150-AS	AM02540-SS	AD02428	AM03274-AS	AM03231-SS	AD03764	AM03884-AS	AM04806-SS	
AD02007	AM03150-AS	AM02941-SS	AD02429	AM03274-AS	AM03232-SS	AD03765	AM04501-AS	AM04611-SS	
AD02008	AM03150-AS	AM02942-SS	AD02430	AM03274-AS	AM03233-SS	AD03766	AM04501-AS	AM04808-SS	
AD02009	AM03151-AS	AM02540-SS	AD02431	AM03274-AS	AM03234-SS	AD03767	AM04501-AS	AM04809-SS	
AD02010	AM03151-AS	AM02941-SS	AD02432	AM03274-AS	AM03235-SS	AD03768	AM04501-AS	AM04810-SS	
AD02011	AM03151-AS	AM02942-SS	AD02433	AM03274-AS	AM03236-SS	AD03769	AM04501-AS	AM04811-SS	
AD02075	AM03255-AS	AM03220-SS	AD02434	AM03274-AS	AM03237-SS	AD03770	AM04501-AS	AM04812-SS	
AD02076	AM03256-AS	AM03221-SS	AD02435	AM03255-AS	AM03238-SS	AD03771	AM02860-AS	AM04813-SS	
AD02077	AM03256-AS	AM03222-SS	AD02436	AM03256-AS	AM03238-SS	AD03801	AM04821-AS	AM04816-SS	
AD02078	AM03255-AS	AM03223-SS	AD02437	AM03255-AS	AM03240-SS	AD03802	AM04822-AS	AM04817-SS	
AD02079	AM03255-AS	AM03224-SS	AD02438	AM03256-AS	AM03240-SS	AD03803	AM04823-AS	AM04816-SS	
AD02080	AM03255-AS	AM03225-SS	AD02439	AM03255-AS	AM02942-SS	AD03804	AM04821-AS	AM04835-SS	

AD02081	AM03255-AS	AM03226-SS	AD02440	AM03256-AS	AM02942-SS	AD03805	AM04824-AS	AM04819-SS
AD02082	AM03255-AS	AM03227-SS	AD02462	AM02857-AS	AM03330-SS	AD03806	AM04824-AS	AM04820-SS
AD02083	AM03255-AS	AM03228-SS	AD02463	AM03331-AS	AM01223-SS	AD03841	AM04871-AS	AM04862-SS
AD02084	AM03255-AS	AM03229-SS	AD02464	AM03107-AS	AM03291-SS	AD03842	AM02860-AS	AM04863-SS
AD02085	AM03255-AS	AM03230-SS	AD02465	AM03279-AS	AM03291-SS	AD03843	AM04872-AS	AM04138-SS
AD02086	AM03255-AS	AM03231-SS	AD02466	AM03280-AS	AM03291-SS	AD03844	AM04539-AS	AM04864-SS
AD02087	AM03255-AS	AM03232-SS	AD02467	AM03281-AS	AM03291-SS	AD03845	AM03300-AS	AM04865-SS
AD02088	AM03255-AS	AM03233-SS	AD02468	AM03282-AS	AM03291-SS	AD03846	AM04873-AS	AM04412-SS
AD02089	AM03255-AS	AM03234-SS	AD02469	AM03283-AS	AM03291-SS	AD03847	AM04874-AS	AM04866-SS
AD02090	AM03255-AS	AM03235-SS	AD02470	AM03284-AS	AM03291-SS	AD03848	AM04874-AS	AM04867-SS
AD02091	AM03255-AS	AM03236-SS	AD02471	AM03300-AS	AM03291-SS	AD03849	AM04875-AS	AM04867-SS
AD02092	AM03255-AS	AM03237-SS	AD02472	AM03301-AS	AM03291-SS	AD03850	AM04876-AS	AM04866-SS
AD02093	AM03256-AS	AM03220-SS	AD02473	AM03107-AS	AM03292-SS	AD03851	AM04877-AS	AM04866-SS
AD02094	AM03256-AS	AM03221-SS	AD02474	AM03279-AS	AM03292-SS	AD03852	AM04877-AS	AM04867-SS
AD02095	AM03256-AS	AM03222-SS	AD02475	AM03280-AS	AM03292-SS	AD03853	AM04874-AS	AM04868-SS
AD02096	AM03256-AS	AM03223-SS	AD02476	AM03281-AS	AM03292-SS	AD03854	AM04874-AS	AM04869-SS
AD02097	AM03256-AS	AM03224-SS	AD02477	AM03282-AS	AM03292-SS	AD03855	AM04875-AS	AM04869-SS
AD02098	AM03256-AS	AM03225-SS	AD02478	AM03283-AS	AM03292-SS	AD03856	AM04874-AS	AM04870-SS
AD02099	AM03256-AS	AM03226-SS	AD02479	AM03284-AS	AM03292-SS	AD03857	AM03972-AS	AM04808-SS

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AD02100	AM03256-AS	AM03227-SS	AD02480	AM03300-AS	AM03292-SS	AD03858	AM03972-AS	AM04811-SS	
AD02101	AM03256-AS	AM03228-SS	AD02481	AM03301-AS	AM03292-SS	AD03859	AM04822-AS	AM04819-SS	
AD02102	AM03256-AS	AM03229-SS	AD02482	AM03107-AS	AM03293-SS	AD03860	AM04878-AS	AM04819-SS	
AD02103	AM03256-AS	AM03230-SS	AD02483	AM03279-AS	AM03293-SS	AD03861	AM04878-AS	AM04820-SS	
AD02104	AM03256-AS	AM03231-SS	AD02484	AM03280-AS	AM03293-SS	AD03862	AM04879-AS	AM04138-SS	
AD02105	AM03256-AS	AM03232-SS	AD02485	AM03281-AS	AM03293-SS	AD03863	AM04879-AS	AM04863-SS	
AD02106	AM03256-AS	AM03233-SS	AD02486	AM03282-AS	AM03293-SS	AD03864	AM04880-AS	AM04138-SS	
AD02107	AM03256-AS	AM03234-SS	AD02487	AM03283-AS	AM03293-SS	AD03920	AM04960-AS	AM04138-SS	
AD02108	AM03256-AS	AM03235-SS	AD02488	AM03284-AS	AM03293-SS	AD03921	AM04970-AS	AM04412-SS	
AD02109	AM03256-AS	AM03236-SS	AD02489	AM03300-AS	AM03293-SS	AD03922	AM04971-AS	AM04867-SS	
AD02110	AM03256-AS	AM03237-SS	AD02490	AM03301-AS	AM03293-SS	AD03923	AM04971-AS	AM04869-SS	
AD02111	AM03257-AS	AM03220-SS	AD02491	AM03107-AS	AM03294-SS	AD03924	AM04972-AS	AM04820-SS	
AD02112	AM03257-AS	AM03221-SS	AD02492	AM03279-AS	AM03294-SS	AD03925	AM04972-AS	AM04819-SS	
AD02113	AM03257-AS	AM03222-SS	AD02493	AM03280-AS	AM03294-SS	AD03931	AM04979-AS	AM04978-SS	
AD02114	AM03257-AS	AM03223-SS	AD02494	AM03281-AS	AM03294-SS	AD03932	AM04979-AS	AM04811-SS	
AD02115	AM03257-AS	AM03224-SS	AD02495	AM03282-AS	AM03294-SS	AD03933	AM04979-AS	AM04869-SS	
AD02116	AM03257-AS	AM03225-SS	AD02496	AM03283-AS	AM03294-SS	AD04017	AM03300-AS	AM05070-SS	
AD02117	AM03257-AS	AM03226-SS	AD02497	AM03284-AS	AM03294-SS	AD04018	AM03972-AS	AM05072-SS	
AD02118	AM03257-AS	AM03227-SS	AD02498	AM03300-AS	AM03294-SS	AD04017	AM03300-AS	AM05070-SS	

AD02119	AM03257-AS	AM03228-SS	AD02499	AM03301-AS	AM03294-SS	AD04018	AM03972-AS	AM05072-SS
AD04170	AM03972-AS	AM05341-SS	AD04171	AM04877-AS	AM05342-SS	AD04110	AM04875-AS	AM04866-SS
AD04263	AM04879-AS	AM05480-SS	AD04272	AM04970-AS	AM05490-SS	AD04281	AM05496-AS	AM04412-SS
AD04264	AM05490-AS	AM04416-SS	AD04273	AM03972-AS	AM05494-SS	AD04282	AM04874-AS	AM05503-SS
AD04265	AM05490-AS	AM05491-SS	AD04274	AM05498-AS	AM05494-SS	AD04283	AM04874-AS	AM05502-SS
AD04266	AM05492-AS	AM04496-SS	AD04275	AM04970-AS	AM05494-SS	AD04284	AM04874-AS	AM05506-SS
AD04267	AM05493-AS	AM04496-SS	AD04276	AM03972-AS	AM05501-SS	AD04285	AM04877-AS	AM05503-SS
AD04268	AM05498-AS	AM04496-SS	AD04277	AM05498-AS	AM05501-SS	AD04286	AM05497-AS	AM05502-SS
AD04269	AM04979-AS	AM04496-SS	AD04278	AM04970-AS	AM05501-SS	AD04287	AM05497-AS	AM05506-SS
AD04270	AM03972-AS	AM05490-SS	AD04279	AM03300-AS	AM05500-SS	AD04288	AM04874-AS	AM05504-SS
AD04271	AM05498-AS	AM05499-SS	AD04280	AM05495-AS	AM04412-SS	AD04289	AM04874-AS	AM05505-SS

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표 3B. 듀플렉스 번호를 가지는 LPA RNAi 물질 듀플렉스.

듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호	듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호	듀플렉스 번호	안티센스 가닥 번호	센스 가닥 번호
SD0001	1533-AS00	1533-SS00	SD0240	1533-AS08	1533-SS12	SD0479	1532-AS01	1532-SS09
SD0002	1533-AS01	1533-SS00	SD0241	1533-AS09	1533-SS12	SD0480	1532-AS02	1532-SS09
SD0003	1533-AS02	1533-SS00	SD0242	1533-AS10	1533-SS12	SD0481	1532-AS03	1532-SS09
SD0004	1533-AS03	1533-SS00	SD0243	1533-AS11	1533-SS12	SD0482	1532-AS04	1532-SS09
SD0005	1533-AS04	1533-SS00	SD0244	1533-AS12	1533-SS12	SD0483	1532-AS05	1532-SS09
SD0006	1533-AS05	1533-SS00	SD0245	1533-AS13	1533-SS12	SD0484	1532-AS06	1532-SS09
SD0007	1533-AS06	1533-SS00	SD0246	1533-AS14	1533-SS12	SD0485	1532-AS07	1532-SS09
SD0008	1533-AS07	1533-SS00	SD0247	1533-AS00	1533-SS13	SD0486	1532-AS08	1532-SS09
SD0009	1533-AS08	1533-SS00	SD0248	1533-AS01	1533-SS13	SD0487	1532-AS09	1532-SS09
SD0010	1533-AS09	1533-SS00	SD0249	1533-AS02	1533-SS13	SD0488	1532-AS10	1532-SS09
SD0011	1533-AS10	1533-SS00	SD0250	1533-AS03	1533-SS13	SD0489	1532-AS11	1532-SS09
SD0012	1533-AS11	1533-SS00	SD0251	1533-AS04	1533-SS13	SD0490	1532-AS12	1532-SS09
SD0013	1533-AS12	1533-SS00	SD0252	1533-AS05	1533-SS13	SD0491	1532-AS13	1532-SS09
SD0014	1533-AS13	1533-SS00	SD0253	1533-AS06	1533-SS13	SD0492	1532-AS00	1532-SS10
SD0015	1533-AS14	1533-SS00	SD0254	1533-AS07	1533-SS13	SD0493	1532-AS01	1532-SS10
SD0016	1533-AS00	1533-SS01	SD0255	1533-AS08	1533-SS13	SD0494	1532-AS02	1532-SS10

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SD0017	1533-AS01	1533-SS01	SD0256	1533-AS09	1533-SS13	SD0495	1532-AS03	1532-SS10
SD0018	1533-AS02	1533-SS01	SD0257	1533-AS10	1533-SS13	SD0496	1532-AS04	1532-SS10
SD0019	1533-AS03	1533-SS01	SD0258	1533-AS11	1533-SS13	SD0497	1532-AS05	1532-SS10
SD0020	1533-AS04	1533-SS01	SD0259	1533-AS12	1533-SS13	SD0498	1532-AS06	1532-SS10
SD0021	1533-AS05	1533-SS01	SD0260	1533-AS13	1533-SS13	SD0499	1532-AS07	1532-SS10
SD0022	1533-AS06	1533-SS01	SD0261	1533-AS14	1533-SS13	SD0500	1532-AS08	1532-SS10
SD0023	1533-AS07	1533-SS01	SD0262	1533-AS00	1533-SS14	SD0501	1532-AS09	1532-SS10
SD0024	1533-AS08	1533-SS01	SD0263	1533-AS01	1533-SS14	SD0502	1532-AS10	1532-SS10
SD0025	1533-AS09	1533-SS01	SD0264	1533-AS02	1533-SS14	SD0503	1532-AS11	1532-SS10
SD0026	1533-AS10	1533-SS01	SD0265	1533-AS03	1533-SS14	SD0504	1532-AS12	1532-SS10
SD0027	1533-AS11	1533-SS01	SD0266	1533-AS04	1533-SS14	SD0505	1532-AS13	1532-SS10
SD0028	1533-AS12	1533-SS01	SD0267	1533-AS05	1533-SS14	SD0506	1532-AS00	1532-SS11
SD0029	1533-AS13	1533-SS01	SD0268	1533-AS06	1533-SS14	SD0507	1532-AS01	1532-SS11
SD0030	1533-AS14	1533-SS01	SD0269	1533-AS07	1533-SS14	SD0508	1532-AS02	1532-SS11
SD0031	1533-AS00	1533-SS02	SD0270	1533-AS08	1533-SS14	SD0509	1532-AS03	1532-SS11
SD0032	1533-AS01	1533-SS02	SD0271	1533-AS09	1533-SS14	SD0510	1532-AS04	1532-SS11
SD0033	1533-AS02	1533-SS02	SD0272	1533-AS10	1533-SS14	SD0511	1532-AS05	1532-SS11
SD0034	1533-AS03	1533-SS02	SD0273	1533-AS11	1533-SS14	SD0512	1532-AS06	1532-SS11
SD0035	1533-AS04	1533-SS02	SD0274	1533-AS12	1533-SS14	SD0513	1532-AS07	1532-SS11

SD0036	1533-AS05	1533-SS02	SD0275	1533-AS13	1533-SS14	SD0514	1532-AS08	1532-SS11	
SD0037	1533-AS06	1533-SS02	SD0276	1533-AS14	1533-SS14	SD0515	1532-AS09	1532-SS11	
SD0038	1533-AS07	1533-SS02	SD0277	1533-AS00	1533-SS15	SD0516	1532-AS10	1532-SS11	
SD0039	1533-AS08	1533-SS02	SD0278	1533-AS01	1533-SS15	SD0517	1532-AS11	1532-SS11	
SD0040	1533-AS09	1533-SS02	SD0279	1533-AS02	1533-SS15	SD0518	1532-AS12	1532-SS11	
SD0041	1533-AS10	1533-SS02	SD0280	1533-AS03	1533-SS15	SD0519	1532-AS13	1532-SS11	
SD0042	1533-AS11	1533-SS02	SD0281	1533-AS04	1533-SS15	SD0520	1532-AS00	1532-SS12	
SD0043	1533-AS12	1533-SS02	SD0282	1533-AS05	1533-SS15	SD0521	1532-AS01	1532-SS12	
SD0044	1533-AS13	1533-SS02	SD0283	1533-AS06	1533-SS15	SD0522	1532-AS02	1532-SS12	
SD0045	1533-AS14	1533-SS02	SD0284	1533-AS07	1533-SS15	SD0523	1532-AS03	1532-SS12	
SD0046	1533-AS00	1533-SS03	SD0285	1533-AS08	1533-SS15	SD0524	1532-AS04	1532-SS12	
SD0047	1533-AS01	1533-SS03	SD0286	1533-AS09	1533-SS15	SD0525	1532-AS05	1532-SS12	
SD0048	1533-AS02	1533-SS03	SD0287	1533-AS10	1533-SS15	SD0526	1532-AS06	1532-SS12	
SD0049	1533-AS03	1533-SS03	SD0288	1533-AS11	1533-SS15	SD0527	1532-AS07	1532-SS12	
SD0050	1533-AS04	1533-SS03	SD0289	1533-AS12	1533-SS15	SD0528	1532-AS08	1532-SS12	
SD0051	1533-AS05	1533-SS03	SD0290	1533-AS13	1533-SS15	SD0529	1532-AS09	1532-SS12	
SD0052	1533-AS06	1533-SS03	SD0291	1533-AS14	1533-SS15	SD0530	1532-AS10	1532-SS12	
SD0053	1533-AS07	1533-SS03	SD0292	1533-AS00	1533-SS16	SD0531	1532-AS11	1532-SS12	
SD0054	1533-AS08	1533-SS03	SD0293	1533-AS01	1533-SS16	SD0532	1532-AS12	1532-SS12	

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SD0055	1533-AS09	1533-SS03	SD0294	1533-AS02	1533-SS16	SD0533	1532-AS13	1532-SS12
SD0056	1533-AS10	1533-SS03	SD0295	1533-AS03	1533-SS16	SD0534	1532-AS00	1532-SS13
SD0057	1533-AS11	1533-SS03	SD0296	1533-AS04	1533-SS16	SD0535	1532-AS01	1532-SS13
SD0058	1533-AS12	1533-SS03	SD0297	1533-AS05	1533-SS16	SD0536	1532-AS02	1532-SS13
SD0059	1533-AS13	1533-SS03	SD0298	1533-AS06	1533-SS16	SD0537	1532-AS03	1532-SS13
SD0060	1533-AS14	1533-SS03	SD0299	1533-AS07	1533-SS16	SD0538	1532-AS04	1532-SS13
SD0061	1533-AS00	1533-SS04	SD0300	1533-AS08	1533-SS16	SD0539	1532-AS05	1532-SS13
SD0062	1533-AS01	1533-SS04	SD0301	1533-AS09	1533-SS16	SD0540	1532-AS06	1532-SS13
SD0063	1533-AS02	1533-SS04	SD0302	1533-AS10	1533-SS16	SD0541	1532-AS07	1532-SS13
SD0064	1533-AS03	1533-SS04	SD0303	1533-AS11	1533-SS16	SD0542	1532-AS08	1532-SS13
SD0065	1533-AS04	1533-SS04	SD0304	1533-AS12	1533-SS16	SD0543	1532-AS09	1532-SS13
SD0066	1533-AS05	1533-SS04	SD0305	1533-AS13	1533-SS16	SD0544	1532-AS10	1532-SS13
SD0067	1533-AS06	1533-SS04	SD0306	1533-AS14	1533-SS16	SD0545	1532-AS11	1532-SS13
SD0068	1533-AS07	1533-SS04	SD0307	1533-AS00	1533-SS17	SD0546	1532-AS12	1532-SS13
SD0069	1533-AS08	1533-SS04	SD0308	1533-AS01	1533-SS17	SD0547	1532-AS13	1532-SS13
SD0070	1533-AS09	1533-SS04	SD0309	1533-AS02	1533-SS17	SD0548	1532-AS00	1532-SS14
SD0071	1533-AS10	1533-SS04	SD0310	1533-AS03	1533-SS17	SD0549	1532-AS01	1532-SS14
SD0072	1533-AS11	1533-SS04	SD0311	1533-AS04	1533-SS17	SD0550	1532-AS02	1532-SS14
SD0073	1533-AS12	1533-SS04	SD0312	1533-AS05	1533-SS17	SD0551	1532-AS03	1532-SS14

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SD0074	1533-AS13	1533-SS04	SD0313	1533-AS06	1533-SS17	SD0552	1532-AS04	1532-SS14	
SD0075	1533-AS14	1533-SS04	SD0314	1533-AS07	1533-SS17	SD0553	1532-AS05	1532-SS14	
SD0076	1533-AS00	1533-SS05	SD0315	1533-AS08	1533-SS17	SD0554	1532-AS06	1532-SS14	
SD0077	1533-AS01	1533-SS05	SD0316	1533-AS09	1533-SS17	SD0555	1532-AS07	1532-SS14	
SD0078	1533-AS02	1533-SS05	SD0317	1533-AS10	1533-SS17	SD0556	1532-AS08	1532-SS14	
SD0079	1533-AS03	1533-SS05	SD0318	1533-AS11	1533-SS17	SD0557	1532-AS09	1532-SS14	
SD0080	1533-AS04	1533-SS05	SD0319	1533-AS12	1533-SS17	SD0558	1532-AS10	1532-SS14	
SD0081	1533-AS05	1533-SS05	SD0320	1533-AS13	1533-SS17	SD0559	1532-AS11	1532-SS14	
SD0082	1533-AS06	1533-SS05	SD0321	1533-AS14	1533-SS17	SD0560	1532-AS12	1532-SS14	
SD0083	1533-AS07	1533-SS05	SD0322	1533-AS00	1533-SS18	SD0561	1532-AS13	1532-SS14	
SD0084	1533-AS08	1533-SS05	SD0323	1533-AS01	1533-SS18	SD0562	1532-AS00	1532-SS15	
SD0085	1533-AS09	1533-SS05	SD0324	1533-AS02	1533-SS18	SD0563	1532-AS01	1532-SS15	
SD0086	1533-AS10	1533-SS05	SD0325	1533-AS03	1533-SS18	SD0564	1532-AS02	1532-SS15	
SD0087	1533-AS11	1533-SS05	SD0326	1533-AS04	1533-SS18	SD0565	1532-AS03	1532-SS15	
SD0088	1533-AS12	1533-SS05	SD0327	1533-AS05	1533-SS18	SD0566	1532-AS04	1532-SS15	
SD0089	1533-AS13	1533-SS05	SD0328	1533-AS06	1533-SS18	SD0567	1532-AS05	1532-SS15	
SD0090	1533-AS14	1533-SS05	SD0329	1533-AS07	1533-SS18	SD0568	1532-AS06	1532-SS15	
SD0091	1533-AS00	1533-SS06	SD0330	1533-AS08	1533-SS18	SD0569	1532-AS07	1532-SS15	
SD0092	1533-AS01	1533-SS06	SD0331	1533-AS09	1533-SS18	SD0570	1532-AS08	1532-SS15	

SD0093	1533-AS02	1533-SS06	SD0332	1533-AS10	1533-SS18	SD0571	1532-AS09	1532-SS15
SD0094	1533-AS03	1533-SS06	SD0333	1533-AS11	1533-SS18	SD0572	1532-AS10	1532-SS15
SD0095	1533-AS04	1533-SS06	SD0334	1533-AS12	1533-SS18	SD0573	1532-AS11	1532-SS15
SD0096	1533-AS05	1533-SS06	SD0335	1533-AS13	1533-SS18	SD0574	1532-AS12	1532-SS15
SD0097	1533-AS06	1533-SS06	SD0336	1533-AS14	1533-SS18	SD0575	1532-AS13	1532-SS15
SD0098	1533-AS07	1533-SS06	SD0337	1533-AS00	1533-SS19	SD0576	1532-AS00	1532-SS16
SD0099	1533-AS08	1533-SS06	SD0338	1533-AS01	1533-SS19	SD0577	1532-AS01	1532-SS16
SD0100	1533-AS09	1533-SS06	SD0339	1533-AS02	1533-SS19	SD0578	1532-AS02	1532-SS16
SD0101	1533-AS10	1533-SS06	SD0340	1533-AS03	1533-SS19	SD0579	1532-AS03	1532-SS16
SD0102	1533-AS11	1533-SS06	SD0341	1533-AS04	1533-SS19	SD0580	1532-AS04	1532-SS16
SD0103	1533-AS12	1533-SS06	SD0342	1533-AS05	1533-SS19	SD0581	1532-AS05	1532-SS16
SD0104	1533-AS13	1533-SS06	SD0343	1533-AS06	1533-SS19	SD0582	1532-AS06	1532-SS16
SD0105	1533-AS14	1533-SS06	SD0344	1533-AS07	1533-SS19	SD0583	1532-AS07	1532-SS16
SD0106	1533-AS00	1533-SS07	SD0345	1533-AS08	1533-SS19	SD0584	1532-AS08	1532-SS16
SD0107	1533-AS01	1533-SS07	SD0346	1533-AS09	1533-SS19	SD0585	1532-AS09	1532-SS16
SD0108	1533-AS02	1533-SS07	SD0347	1533-AS10	1533-SS19	SD0586	1532-AS10	1532-SS16
SD0109	1533-AS03	1533-SS07	SD0348	1533-AS11	1533-SS19	SD0587	1532-AS11	1532-SS16
SD0110	1533-AS04	1533-SS07	SD0349	1533-AS12	1533-SS19	SD0588	1532-AS12	1532-SS16
SD0111	1533-AS05	1533-SS07	SD0350	1533-AS13	1533-SS19	SD0589	1532-AS13	1532-SS16

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SD0112	1533-AS06	1533-SS07	SD0351	1533-AS14	1533-SS19	SD0590	1532-AS00	1532-SS17
SD0113	1533-AS07	1533-SS07	SD0352	1532-AS00	1532-SS00	SD0591	1532-AS01	1532-SS17
SD0114	1533-AS08	1533-SS07	SD0353	1532-AS01	1532-SS00	SD0592	1532-AS02	1532-SS17
SD0115	1533-AS09	1533-SS07	SD0354	1532-AS02	1532-SS00	SD0593	1532-AS03	1532-SS17
SD0116	1533-AS10	1533-SS07	SD0355	1532-AS03	1532-SS00	SD0594	1532-AS04	1532-SS17
SD0117	1533-AS11	1533-SS07	SD0356	1532-AS04	1532-SS00	SD0595	1532-AS05	1532-SS17
SD0118	1533-AS12	1533-SS07	SD0357	1532-AS05	1532-SS00	SD0596	1532-AS06	1532-SS17
SD0119	1533-AS13	1533-SS07	SD0358	1532-AS06	1532-SS00	SD0597	1532-AS07	1532-SS17
SD0120	1533-AS14	1533-SS07	SD0359	1532-AS07	1532-SS00	SD0598	1532-AS08	1532-SS17
SD0121	1533-AS00	1533-SS08	SD0360	1532-AS08	1532-SS00	SD0599	1532-AS09	1532-SS17
SD0122	1533-AS01	1533-SS08	SD0361	1532-AS09	1532-SS00	SD0600	1532-AS10	1532-SS17
SD0123	1533-AS02	1533-SS08	SD0362	1532-AS10	1532-SS00	SD0601	1532-AS11	1532-SS17
SD0124	1533-AS03	1533-SS08	SD0363	1532-AS11	1532-SS00	SD0602	1532-AS12	1532-SS17
SD0125	1533-AS04	1533-SS08	SD0364	1532-AS12	1532-SS00	SD0603	1532-AS13	1532-SS17
SD0126	1533-AS05	1533-SS08	SD0365	1532-AS13	1532-SS00	SD0604	1532-AS00	1532-SS18
SD0127	1533-AS06	1533-SS08	SD0366	1532-AS00	1532-SS01	SD0605	1532-AS01	1532-SS18
SD0128	1533-AS07	1533-SS08	SD0367	1532-AS01	1532-SS01	SD0606	1532-AS02	1532-SS18
SD0129	1533-AS08	1533-SS08	SD0368	1532-AS02	1532-SS01	SD0607	1532-AS03	1532-SS18
SD0130	1533-AS09	1533-SS08	SD0369	1532-AS03	1532-SS01	SD0608	1532-AS04	1532-SS18

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SD0131	1533-AS10	1533-SS08	SD0370	1532-AS04	1532-SS01	SD0609	1532-AS05	1532-SS18	
SD0132	1533-AS11	1533-SS08	SD0371	1532-AS05	1532-SS01	SD0610	1532-AS06	1532-SS18	
SD0133	1533-AS12	1533-SS08	SD0372	1532-AS06	1532-SS01	SD0611	1532-AS07	1532-SS18	
SD0134	1533-AS13	1533-SS08	SD0373	1532-AS07	1532-SS01	SD0612	1532-AS08	1532-SS18	
SD0135	1533-AS14	1533-SS08	SD0374	1532-AS08	1532-SS01	SD0613	1532-AS09	1532-SS18	
SD0136	1533-AS00	1533-SS09	SD0375	1532-AS09	1532-SS01	SD0614	1532-AS10	1532-SS18	
SD0137	1533-AS01	1533-SS09	SD0376	1532-AS10	1532-SS01	SD0615	1532-AS11	1532-SS18	
SD0138	1533-AS02	1533-SS09	SD0377	1532-AS11	1532-SS01	SD0616	1532-AS12	1532-SS18	
SD0139	1533-AS03	1533-SS09	SD0378	1532-AS12	1532-SS01	SD0617	1532-AS13	1532-SS18	
SD0140	1533-AS04	1533-SS09	SD0379	1532-AS13	1532-SS01	SD0618	1532-AS00	1532-SS19	
SD0141	1533-AS05	1533-SS09	SD0380	1532-AS00	1532-SS02	SD0619	1532-AS01	1532-SS19	
SD0142	1533-AS06	1533-SS09	SD0381	1532-AS01	1532-SS02	SD0620	1532-AS02	1532-SS19	
SD0143	1533-AS07	1533-SS09	SD0382	1532-AS02	1532-SS02	SD0621	1532-AS03	1532-SS19	
SD0144	1533-AS08	1533-SS09	SD0383	1532-AS03	1532-SS02	SD0622	1532-AS04	1532-SS19	
SD0145	1533-AS09	1533-SS09	SD0384	1532-AS04	1532-SS02	SD0623	1532-AS05	1532-SS19	
SD0146	1533-AS10	1533-SS09	SD0385	1532-AS05	1532-SS02	SD0624	1532-AS06	1532-SS19	
SD0147	1533-AS11	1533-SS09	SD0386	1532-AS06	1532-SS02	SD0625	1532-AS07	1532-SS19	
SD0148	1533-AS12	1533-SS09	SD0387	1532-AS07	1532-SS02	SD0626	1532-AS08	1532-SS19	
SD0149	1533-AS13	1533-SS09	SD0388	1532-AS08	1532-SS02	SD0627	1532-AS09	1532-SS19	

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SD0150	1533-AS14	1533-SS09	SD0389	1532-AS09	1532-SS02	SD0628	1532-AS10	1532-SS19
SD0151	1533-AS00	1533-SS01	SD0390	1532-AS10	1532-SS02	SD0629	1532-AS11	1532-SS19
SD0152	1533-AS01	1533-SS01	SD0391	1532-AS11	1532-SS02	SD0630	1532-AS12	1532-SS19
SD0153	1533-AS02	1533-SS01	SD0392	1532-AS12	1532-SS02	SD0631	1532-AS13	1532-SS19
SD0154	1533-AS03	1533-SS01	SD0393	1532-AS13	1532-SS02	SD0632	1532-AS00	1532-SS20
SD0155	1533-AS04	1533-SS01	SD0394	1532-AS00	1532-SS03	SD0633	1532-AS01	1532-SS20
SD0156	1533-AS05	1533-SS01	SD0395	1532-AS01	1532-SS03	SD0634	1532-AS02	1532-SS20
SD0157	1533-AS06	1533-SS01	SD0396	1532-AS02	1532-SS03	SD0635	1532-AS03	1532-SS20
SD0158	1533-AS07	1533-SS01	SD0397	1532-AS03	1532-SS03	SD0636	1532-AS04	1532-SS20
SD0159	1533-AS08	1533-SS01	SD0398	1532-AS04	1532-SS03	SD0637	1532-AS05	1532-SS20
SD0160	1533-AS09	1533-SS01	SD0399	1532-AS05	1532-SS03	SD0638	1532-AS06	1532-SS20
SD0161	1533-AS10	1533-SS01	SD0400	1532-AS06	1532-SS03	SD0639	1532-AS07	1532-SS20
SD0162	1533-AS11	1533-SS01	SD0401	1532-AS07	1532-SS03	SD0640	1532-AS08	1532-SS20
SD0163	1533-AS12	1533-SS01	SD0402	1532-AS08	1532-SS03	SD0641	1532-AS09	1532-SS20
SD0164	1533-AS13	1533-SS01	SD0403	1532-AS09	1532-SS03	SD0642	1532-AS10	1532-SS20
SD0165	1533-AS14	1533-SS01	SD0404	1532-AS10	1532-SS03	SD0643	1532-AS11	1532-SS20
SD0166	1533-AS00	1533-SS01	SD0405	1532-AS11	1532-SS03	SD0644	1532-AS12	1532-SS20
SD0167	1533-AS01	1533-SS01	SD0406	1532-AS12	1532-SS03	SD0645	1532-AS13	1532-SS20
SD0168	1533-AS02	1533-SS01	SD0407	1532-AS13	1532-SS03	SD0646	1532-AS00	1532-SS21

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SD0169	1533-AS03	1533-SS01	SD0408	1532-AS00	1532-SS04	SD0647	1532-AS01	1532-SS21	
SD0170	1533-AS04	1533-SS01	SD0409	1532-AS01	1532-SS04	SD0648	1532-AS02	1532-SS21	
SD0171	1533-AS05	1533-SS01	SD0410	1532-AS02	1532-SS04	SD0649	1532-AS03	1532-SS21	
SD0172	1533-AS06	1533-SS01	SD0411	1532-AS03	1532-SS04	SD0650	1532-AS04	1532-SS21	
SD0173	1533-AS07	1533-SS01	SD0412	1532-AS04	1532-SS04	SD0651	1532-AS05	1532-SS21	
SD0174	1533-AS08	1533-SS01	SD0413	1532-AS05	1532-SS04	SD0652	1532-AS06	1532-SS21	
SD0175	1533-AS09	1533-SS01	SD0414	1532-AS06	1532-SS04	SD0653	1532-AS07	1532-SS21	
SD0176	1533-AS10	1533-SS01	SD0415	1532-AS07	1532-SS04	SD0654	1532-AS08	1532-SS21	
SD0177	1533-AS11	1533-SS01	SD0416	1532-AS08	1532-SS04	SD0655	1532-AS09	1532-SS21	
SD0178	1533-AS12	1533-SS01	SD0417	1532-AS09	1532-SS04	SD0656	1532-AS10	1532-SS21	
SD0179	1533-AS13	1533-SS01	SD0418	1532-AS10	1532-SS04	SD0657	1532-AS11	1532-SS21	
SD0180	1533-AS14	1533-SS01	SD0419	1532-AS11	1532-SS04	SD0658	1532-AS12	1532-SS21	
SD0181	1533-AS00	1533-SS02	SD0420	1532-AS12	1532-SS04	SD0659	1532-AS13	1532-SS21	
SD0182	1533-AS01	1533-SS02	SD0421	1532-AS13	1532-SS04	SD0660	1532-AS00	1532-SS22	
SD0183	1533-AS02	1533-SS02	SD0422	1532-AS00	1532-SS05	SD0661	1532-AS01	1532-SS22	
SD0184	1533-AS03	1533-SS02	SD0423	1532-AS01	1532-SS05	SD0662	1532-AS02	1532-SS22	
SD0185	1533-AS04	1533-SS02	SD0424	1532-AS02	1532-SS05	SD0663	1532-AS03	1532-SS22	
SD0186	1533-AS05	1533-SS02	SD0425	1532-AS03	1532-SS05	SD0664	1532-AS04	1532-SS22	
SD0187	1533-AS06	1533-SS02	SD0426	1532-AS04	1532-SS05	SD0665	1532-AS05	1532-SS22	

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SD0188	1533-AS07	1533-SS02	SD0427	1532-AS05	1532-SS05	SD0666	1532-AS06	1532-SS22	
SD0189	1533-AS08	1533-SS02	SD0428	1532-AS06	1532-SS05	SD0667	1532-AS07	1532-SS22	
SD0190	1533-AS09	1533-SS02	SD0429	1532-AS07	1532-SS05	SD0668	1532-AS08	1532-SS22	
SD0191	1533-AS10	1533-SS02	SD0430	1532-AS08	1532-SS05	SD0669	1532-AS09	1532-SS22	
SD0192	1533-AS11	1533-SS02	SD0431	1532-AS09	1532-SS05	SD0670	1532-AS10	1532-SS22	
SD0193	1533-AS12	1533-SS02	SD0432	1532-AS10	1532-SS05	SD0671	1532-AS11	1532-SS22	
SD0194	1533-AS13	1533-SS02	SD0433	1532-AS11	1532-SS05	SD0672	1532-AS12	1532-SS22	
SD0195	1533-AS14	1533-SS02	SD0434	1532-AS12	1532-SS05	SD0673	1532-AS13	1532-SS22	
SD0196	1533-AS00	1533-CfinSS	SD0435	1532-AS13	1532-SS05	SD0674	1532-AS00	1532-SS23	
SD0197	1533-AS01	1533-CfinSS	SD0436	1532-AS00	1532-SS06	SD0675	1532-AS01	1532-SS23	
SD0198	1533-AS02	1533-CfinSS	SD0437	1532-AS01	1532-SS06	SD0676	1532-AS02	1532-SS23	
SD0199	1533-AS03	1533-CfinSS	SD0438	1532-AS02	1532-SS06	SD0677	1532-AS03	1532-SS23	
SD0200	1533-AS04	1533-CfinSS	SD0439	1532-AS03	1532-SS06	SD0678	1532-AS04	1532-SS23	
SD0201	1533-AS05	1533-CfinSS	SD0440	1532-AS04	1532-SS06	SD0679	1532-AS05	1532-SS23	
SD0202	1533-AS06	1533-CfinSS	SD0441	1532-AS05	1532-SS06	SD0680	1532-AS06	1532-SS23	
SD0203	1533-AS07	1533-CfinSS	SD0442	1532-AS06	1532-SS06	SD0681	1532-AS07	1532-SS23	
SD0204	1533-AS08	1533-CfinSS	SD0443	1532-AS07	1532-SS06	SD0682	1532-AS08	1532-SS23	
SD0205	1533-AS09	1533-CfinSS	SD0444	1532-AS08	1532-SS06	SD0683	1532-AS09	1532-SS23	
SD0206	1533-AS10	1533-CfinSS	SD0445	1532-AS09	1532-SS06	SD0684	1532-AS10	1532-SS23	

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SD0207	1533-AS11	1533-CfinSS	SD0446	1532-AS10	1532-SS06	SD0685	1532-AS11	1532-SS23
SD0208	1533-AS12	1533-CfinSS	SD0447	1532-AS11	1532-SS06	SD0686	1532-AS12	1532-SS23
SD0209	1533-AS13	1533-CfinSS	SD0448	1532-AS12	1532-SS06	SD0687	1532-AS13	1532-SS23
SD0210	1533-AS14	1533-CfinSS	SD0449	1532-AS13	1532-SS06	SD0688	1532-AS00	1532-SS24
SD0211	1533-CfinAS	1533-SS00	SD0450	1532-AS00	1532-SS07	SD0689	1532-AS01	1532-SS24
SD0212	1533-CfinAS	1533-SS01	SD0451	1532-AS01	1532-SS07	SD0690	1532-AS02	1532-SS24
SD0213	1533-CfinAS	1533-SS02	SD0452	1532-AS02	1532-SS07	SD0691	1532-AS03	1532-SS24
SD0214	1533-CfinAS	1533-SS03	SD0453	1532-AS03	1532-SS07	SD0692	1532-AS04	1532-SS24
SD0215	1533-CfinAS	1533-SS04	SD0454	1532-AS04	1532-SS07	SD0693	1532-AS05	1532-SS24
SD0216	1533-CfinAS	1533-SS05	SD0455	1532-AS05	1532-SS07	SD0694	1532-AS06	1532-SS24
SD0217	1533-CfinAS	1533-SS06	SD0456	1532-AS06	1532-SS07	SD0695	1532-AS07	1532-SS24
SD0218	1533-CfinAS	1533-SS07	SD0457	1532-AS07	1532-SS07	SD0696	1532-AS08	1532-SS24
SD0219	1533-CfinAS	1533-SS08	SD0458	1532-AS08	1532-SS07	SD0697	1532-AS09	1532-SS24
SD0220	1533-CfinAS	1533-SS09	SD0459	1532-AS09	1532-SS07	SD0698	1532-AS10	1532-SS24
SD0221	1533-CfinAS	1533-SS10	SD0460	1532-AS10	1532-SS07	SD0699	1532-AS11	1532-SS24
SD0222	1533-CfinAS	1533-SS11	SD0461	1532-AS11	1532-SS07	SD0700	1532-AS12	1532-SS24
SD0223	1533-CfinAS	1533-SS12	SD0462	1532-AS12	1532-SS07	SD0701	1532-AS13	1532-SS24
SD0224	1533-CfinAS	1533-SS13	SD0463	1532-AS13	1532-SS07	SD0702	1532-AS14	1532-SS00
SD0225	1533-CfinAS	1533-SS14	SD0464	1532-AS00	1532-SS08	SD0703	1532-AS15	1532-SS00

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SD0226	1533-CfinAS	1533-SS15	SD0465	1532-AS01	1532-SS08	SD0704	1532-AS16	1532-SS00
SD0227	1533-CfinAS	1533-SS16	SD0466	1532-AS02	1532-SS08	SD0705	1532-AS17	1532-SS00
SD0228	1533-CfinAS	1533-SS17	SD0467	1532-AS03	1532-SS08	SD0706	1532-AS18	1532-SS00
SD0229	1533-CfinAS	1533-SS18	SD0468	1532-AS04	1532-SS08	SD0707	1532-AS19	1532-SS00
SD0230	1533-CfinAS	1533-SS19	SD0469	1532-AS05	1532-SS08	SD0708	1532-AS20	1532-SS00
SD0231	1533-CfinAS	1533-SS20	SD0470	1532-AS06	1532-SS08	SD0709	1532-AS21	1532-SS00
SD0232	1533-AS00	1533-SS12	SD0471	1532-AS07	1532-SS08	SD0710	1532-AS22	1532-SS00
SD0233	1533-AS01	1533-SS12	SD0472	1532-AS08	1532-SS08	SD0711	1532-AS23	1532-SS00
SD0234	1533-AS02	1533-SS12	SD0473	1532-AS09	1532-SS08	SD0712	1532-AS24	1532-SS00
SD0235	1533-AS03	1533-SS12	SD0474	1532-AS10	1532-SS08	SD0713	1532-AS25	1532-SS00
SD0236	1533-AS04	1533-SS12	SD0475	1532-AS11	1532-SS08	SD0714	1532-AS26	1532-SS00
SD0237	1533-AS05	1533-SS12	SD0476	1532-AS12	1532-SS08	SD0715	1532-AS27	1532-SS00
SD0238	1533-AS06	1533-SS12	SD0477	1532-AS13	1532-SS08			
SD0239	1533-AS07	1533-SS12	SD0478	1532-AS00	1532-SS09			

[0144]

[0145] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1242(TCGUAUAACAAUAAGGGGC)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1244(UCGUAUAACAAUAAGGGG)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1246(UCGUAUAACAAUAAGGG)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1248(TGAGAAUGAGCCUCGAUAA)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1250(UGAGAAUGAGCCUCGAUA)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1252(UGAGAAUGAGCCUCGAU)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1254(UGUAUAACAAUAAGGGG)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1280(CGUAUAACAAUAAGGGGC)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1281(GAGAAUGAGCCUCGAUAA)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1282(UCGUAUAACAAUAAGGGGC)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1283(UGAGAAUGAGCCUCGAUAA)의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 뉴클레오타이드는 변형된다.

[0146] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1243(GCCCCUUAUUGUUAUACGA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1245(CCCCUUAUUGUUAUACGA)의 뉴클레오타

이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1247(CCCUUAUUGUUAUACGA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1249(UUAUCGAGGCUCAUUCUCA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1251(UAUCGAGGCUCAUUCUCA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1253(AUCGAGGCUCAUUCUCA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1255(CCCCUUAUUGUUAUACA)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1284(GCCCCUUAUUGUUAUACG)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1285(UUAUCGAGGCUCAUUCUC)의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 뉴클레오타이드는 변형된다.

[0147] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1242의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1243의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1244의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1245의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1246의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1247의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1248의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1249의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1250의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1251의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1252의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1253의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1254의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1255의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1280의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1284의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1281의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1285의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1282의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1259의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1283의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 서열 번호 1249의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 뉴클레오타이드는 변형된다.

[0148] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 156, 164 또는 188의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 310, 357, 384 또는 376의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 156/310, 서열 번호 164/357, 서열 번호 188/384, 서열 번호 164/376 또는 서열 번호 164/384의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 센스 가닥을 포함한다. 몇몇 실시형태에서, 하나 이상의 뉴클레오타이드는 변형된다.

[0149] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637, 709, 790, 787 또는 788의 뉴클레오타이드 서열을 포함하는 안티센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1132, 1135, 1189, 1191 또는 1186의 뉴클레오타이드 서열을 포함하는 센스 가닥을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637/1132, 서열 번호 709/1135, 서열 번호 790/1189, 서열 번호 787/1191 또는 서열 번호 788/1186의 뉴클레오타이드 서열을 포함하는 안티센스 가닥 및 센스 가닥을 포함한다.

[0150] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637, 709, 790, 787 또는 788을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1132, 1135, 1189, 1191 또는 1186을 포함한다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637/1132, 서열 번호 709/1135, 서열 번호 790/1189, 서열 번호 787/1191 또는 서열 번호 788/1186을 포함한다.

[0151] 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637, 709, 790, 787 또는 788로 이루어진다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 1132, 1135, 1189, 1191 또는 1186으로 이루어진다. 몇몇 실시형태에서, LPA RNAi 물질은 서열 번호 637/1132, 서열 번호 709/1135, 서열 번호 790/1189, 서열 번호 787/1191, 또는 서열 번호 788/1186으로 이루어진다.

[0152] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 뉴클레오

타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함한다.

[0153] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 뉴클레오타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, 아시알로당단백질 수용체 리간드 표적화기를 추가로 포함한다.

[0154] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 뉴클레오타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, (C11-PEG3-NAG3), (C11-PEG3-NAG3), (C6-PEG4-NAG3), (NAG 3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG13), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 및 (NAG37)로 이루어진 군으로부터 선택된 표적화기를 추가로 포함한다.

[0155] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 변형된 뉴클레오타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함한다.

[0156] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 변형된 뉴클레오타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, 아시알로당단백질 수용체 리간드 표적화기를 추가로 포함한다.

[0157] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 안티센스 가닥/센스 가닥 듀플렉스의 변형된 뉴클레오타이드 서열을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, (C11-PEG3-NAG3), (C11-PEG3-NAG3), (C6-PEG4-NAG3), (NAG 3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG13), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 및 (NAG37)로 이루어진 군으로부터 선택된 표적화기를 추가로 포함한다.

[0158] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 듀플렉스를 포함한다.

[0159] 몇몇 실시형태에서, LPA RNAi 물질은 표 3A 또는 표 3B의 임의의 듀플렉스로 이루어진다.

[0160] 몇몇 실시형태에서, LPA RNAi 물질은 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함한다.

[0161] 몇몇 실시형태에서, LPA RNAi 물질은 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, 아시알로당단백질 수용체 리간드 표적화기를 추가로 포함한다.

[0162] 몇몇 실시형태에서, LPA RNAi 물질은 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, (C11-PEG3-NAG3), (C11-PEG3-NAG3), (C6-PEG4-NAG3), (NAG 3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG13), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 및 (NAG37)로 이루어진 군으로부터 선택된 표적화기를 추가로 포함한다.

[0163] 몇몇 실시형태에서, LPA RNAi 물질은 변형된 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함한다.

[0164] 몇몇 실시형태에서, LPA RNAi 물질은 변형된 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, 아시알로당단백질 수용체 리간드 표적화기를 추가로 포함한다.

[0165] 몇몇 실시형태에서, LPA RNAi 물질은 변형된 뉴클레오타이드 서열 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 가지는 안티센스 가닥 및 센스 가닥을 포함하고, (C11-PEG3-NAG3), (C11-PEG3-NAG3), (C6-PEG4-NAG3), (NAG3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG13), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 및 (NAG37)로 이루어진 군으로부터 선택된 표적화기를 추가로 포함한다.

[0166] 몇몇 실시형태에서, LPA RNAi 물질은 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110을 포함한다.

[0167] 몇몇 실시형태에서, LPA RNAi 물질은 AD03460, AD03536, AD03851, AD03853, AD3847 또는 AD04110으로 이루어진다.

[0168] 비뉴클레오타이드기

[0169] 몇몇 실시형태에서, LPA RNAi 물질은 표적화기, 연결기, 전달 중합체, 또는 전달 비히클(이들로 제한되지는 않음)을 포함하는 하나 이상의 비뉴클레오타이드기를 함유하거나 이에 접합된다. 비뉴클레오타이드기는 RNAi 물질의 표적화, 전달 또는 부착을 증대시킬 수 있다. 표적화기 및 연결기의 예는 표 4에 제공된다. 비뉴클레오타이드기는 센스 가닥 및/또는 안티센스 가닥 중 어느 하나의 3' 및/또는 5' 말단에 공유로 연결될 수 있다. 몇몇 실시형태에서, LPA RNAi 물질은 센스 가닥의 3' 및/또는 5' 말단에 연결된 비뉴클레오타이드기를 함유한다. 몇몇 실시형태에서, 비뉴클레오타이드기는 LPA RNAi 물질 센스 가닥의 5' 말단에 연결된다. 비뉴클레오타이드기는 RNAi 물질에 직접적으로 또는 간접적으로 링커/연결기를 통해 연결될 수 있다. 몇몇 실시형태에서, 비뉴클레오타이드기는 불안정한, 절단 가능한 또는 가역적 결합 또는 링커를 통해 RNAi 물질에 연결된다.

[0170] 몇몇 실시형태에서, 비뉴클레오타이드기는 세포 또는 조직 특이적 분포 및 접합체의 세포 특이적 흡수를 개선하도록 RNAi 물질 또는 이것이 부착된 접합체의 약동학적 또는 생물분포 특성을 증대시킨다. 몇몇 실시형태에서, 비뉴클레오타이드기는 RNAi 물질의 내포작용을 증대시킨다.

[0171] 표적화기

[0172] 표적화기는 1가, 2가, 3가, 4가 또는 더 고차의 원자가일 수 있다. 대표적인 표적화기는, 제한 없이, 세포 표면 분자에 대한 친화도를 가지는 화합물, 세포 수용체 리간드, 합텐, 항체, 단일클론 항체, 항체 단편, 및 세포 표면 분자에 대한 친화도를 가지는 항체 모방체를 포함한다. 몇몇 실시형태에서, 표적화기는 링커, 예컨대 PEG 링커 또는 1개, 2개 또는 3개의 비염기성 및/또는 리비톨기를 사용하여 RNAi 물질에 연결된다. 몇몇 실시형태에서, 표적화기는 갈락토스 클러스터를 포함한다.

[0173] 5'-말단에서 반응성 기, 예컨대 아민기를 가지는, 본 명세서에 기재된 LPA RNAi 물질은 합성될 수 있다. 반응성 기는 후속하여 당해 분야에서 통상적인 방법을 이용하여 표적화 모이어티에 부착하도록 사용될 수 있다.

[0174] 몇몇 실시형태에서, 표적화기는 아시알로당단백질 수용체 리간드를 포함한다. 몇몇 실시형태에서, 아시알로당단백질 수용체 리간드는 하나 이상의 갈락토스 유도체 또는 갈락토스 클러스터를 포함하거나, 이것으로 이루어진다. 본 명세서에 사용된 바대로, 용어 갈락토스 유도체는 갈락토스와 동일하거나 이보다 큰 아시알로당단백질 수용체에 대한 친화도를 가지는 갈락토스 및 갈락토스의 유도체 둘 다를 포함한다. 갈락토스 유도체는 갈락토스, 갈락토스아민, N-폼일갈락토스아민, N-아세틸-갈락토스아민, N-프로피오닐-갈락토스아민, N-n-뷰타노일-갈락토스아민 및 N-아이소-뷰타노일갈락토스-아민을 포함하지만, 이들로 제한되지는 않는다(예를 들어, 문헌[Iobst, S.T. and Drickamer, K. *J.B.C.* 1996, *271*, 6686] 참조). 간에 대한 올리고뉴클레오타이드 및 다른 분자의 생체내 표적화에 유용한 갈락토스 유도체 및 갈락토스 클러스터는 당해 분야에 공지되어 있다(예를 들어, 문헌[Baenziger and Fiete, 1980, Cell, 22, 611-620; Connolly et al., 1982, J. Biol. Chem., 257, 939-945] 참조). 갈락토스 유도체는 간세포의 표면에서 발현된 아시알로당단백질 수용체(ASGPr)에 대한 이의 결합을 통해 생체내 간세포로 분자를 표적화하도록 사용된다. ASGPr(들)로의 ASGPr 리간드의 결합은 간세포에 대한 세포 특이적 표적화 및 간세포로의 분자의 내포작용을 촉진한다. 갈락토스 클러스터는 당해 분야에 공지된 방법을 이용하여 RNAi 폴리뉴클레오타이드의 3' 또는 5' 말단에 부착될 수 있다.

[0175] 본 명세서에 사용된 바대로, 갈락토스 클러스터는 2개 내지 4개의 말단 갈락토스 유도체를 가지는 분자를 포함한다. 말단 갈락토스 유도체는 이의 C-1 탄소를 통해 분자에 부착된다. 몇몇 실시형태에서, 갈락토스 클러스터는 갈락토스 유도체 삼합체, 트라이-안테너리(tri-antennary) 갈락토스 유도체 또는 3가 갈락토스 유도체이다. 몇몇 실시형태에서, 갈락토스 클러스터는 N-아세틸갈락토스아민(GalNAc)을 포함한다. 몇몇 실시형태에서, 갈락토스 클러스터는 3가 N-아세틸-갈락토스아민을 포함한다. 몇몇 실시형태에서, 갈락토스 클러스터는 갈락토스 유도체 사합체, 테트라-안테너리 갈락토스 유도체 또는 4가 갈락토스 유도체이다. 몇몇 실시형태에서, 갈락토스 클러스터는 4가 N-아세틸-갈락토스아민을 포함한다.

[0176] 본 명세서에 사용된 바대로, 갈락토스 삼합체는 중앙 분지점에 각각 연결된 3개의 갈락토스 유도체를 함유한다. 본 명세서에 사용된 바대로, 갈락토스 유도체 사합체는 중앙 분지점에 각각 연결된 4개의 갈락토스 유도체를 함유한다. 갈락토스 유도체는 사카라이드의 C-1 탄소를 통해 중앙 분지점에 부착될 수 있다. 몇몇 실시형태에서, 갈락토스 유도체는 링커 또는 스페이서를 통해 분지점에 연결된다. 몇몇 실시형태에서, 링커 또는 스페이서는 가요성 친수성 스페이서, 예컨대 PEG 기이다(예를 들어, 문헌[미국 특허 제5885968호; Biessen et al. J. Med. Chem. 1995 Vol. 39 p. 1538-1546] 참조). 몇몇 실시형태에서, PEG 스페이서는 PEG_3 스페이서이다. 분지점은 3개의 갈락토스 유도체의 부착을 허용하는 임의의 소분자일 수 있고, RNAi 물질에 대한 분지점의 부착을 추가로

허용한다. 분지점 기의 예는 다이라이신 또는 다이글루타메이트이다. RNAi 물질에 대한 분지점의 부착은 링커 또는 스페이서를 통해 발생할 수 있다. 몇몇 실시형태에서, 링커 또는 스페이서는 가요성 친수성 스페이서, 예컨대 PEG 스페이서(이들로 제한되지는 않음)를 포함한다. 몇몇 실시형태에서, PEG 스페이서는 PEG_3 스페이서(3개의 에틸렌 단위)이다. 다른 실시형태에서, PEG 스페이서는 1개 내지 20개의 에틸렌 단위(PEG_1 내지 PEG_{20})를 가진다. 몇몇 실시형태에서, 갈락토스 유도체는 N-아세틸갈락토스아민(GalNAc 또는 NAG)을 포함한다. 몇몇 실시형태에서, 갈락토스 클러스터는 갈락토스 유도체 사합체로 이루어지고, 이것은 예를 들어, N-아세틸-갈락토스아민 사합체일 수 있다.

[0177] 몇몇 실시형태에서, 생체내 간 세포로 LPA RNAi 물질을 전달하기 위한 약제학적 조성물이 기재되어 있다. 이러한 약제학적 조성물은 예를 들어 갈락토스 클러스터에 접합된 LPA RNAi 물질을 포함할 수 있다. 몇몇 실시형태에서, 갈락토스 클러스터는 갈락토스 유도체 삼합체(예를 들어, N-아세틸-갈락토스아민 삼합체일 수 있음) 또는 갈락토스 유도체 사합체(이것은 예를 들어, N-아세틸-갈락토스아민 사합체일 수 있음)로 이루어진다.

[0178] 표적화기는 (Chol-TEG), (TEG-Chol), (C11-PEG3-NAG3), (C_m-PEG_n-NAG3), (C_x-PEG_z-NAG3), (NAG 3), (NAG4), (NAG3-AA2), (NAG3-Palm), (NAG13), (NAG18), (NAG24), (NAG25), (NAG25)s, (NAG26), (NAG27), (NAG28), (NAG29), (NAG30), (NAG30)s, (NAG31), (NAG13), (NAG31s), (NAG32), (NAG33), (NAG34), (NAG35), (NAG36) 및 (NAG37)을 포함하지만, 이들로 제한되지는 않는다.

[0179] 연결기

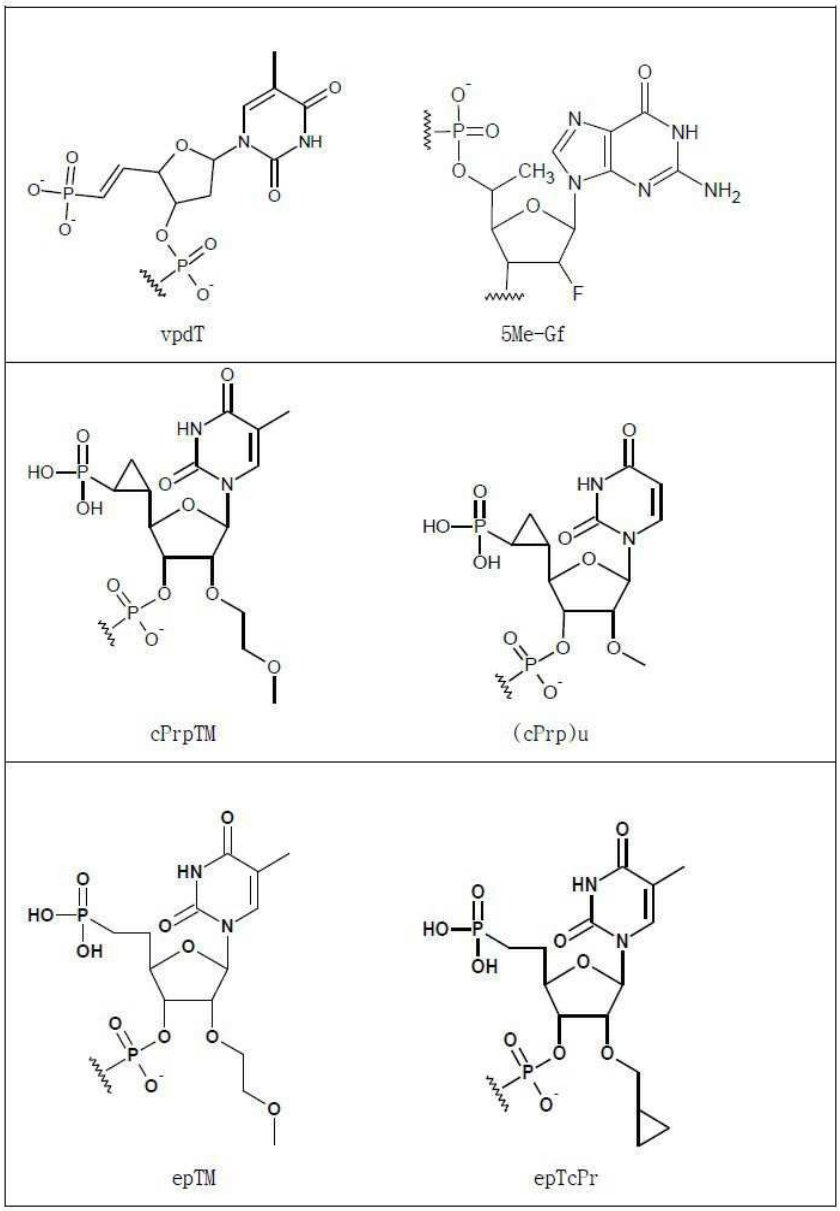
[0180] 몇몇 실시형태에서, 연결기는 RNAi 물질에 접합된다. 연결기는 표적화기 기 또는 전달 중합체 또는 전달 비히클에 대한 상기 물질의 공유 연결을 촉진한다. 연결기는 RNAi 물질 센스 가닥 또는 안티센스 가닥의 3' 또는 5' 말단에 연결될 수 있다. 몇몇 실시형태에서, 연결기는 RNAi 물질 센스 가닥에 연결된다. 몇몇 실시형태에서, 연결기는 RNAi 물질 센스 가닥의 5' 또는 3' 말단에 접합된다. 몇몇 실시형태에서, 연결기는 RNAi 물질 센스 가닥의 5' 말단에 접합된다. 연결기의 예는 Alk-SMPT-C6, Alk-SS-C6, DBCO-TEG, Me-Alk-SS-C6, 및 C6-SS-Alk-Me, 반응성 기, 예컨대 1차 아민 및 알킨, 알킬기, 비염기성 리보스, 리비톨, 및/또는 PEG 기를 포함하지만, 이들로 제한되지는 않는다.

[0181] 링커 또는 연결기는 하나 이상의 공유 결합을 통해 1개의 화학 기(예컨대 RNAi 물질) 또는 관심 있는 분절을 또 다른 화학 기(예컨대 표적화기 또는 전달 중합체) 또는 관심 있는 분절에 연결하는 2개의 원자 사이의 연결이다. 불안정한 연결은 불안정한 결합을 함유한다. 연결은 2개의 연결된 원자 사이의 거리를 증가시키는 스페이서를 임의로 포함할 수 있다. 스페이서는 추가로 연결에 가요성 및/또는 길이를 추가할 수 있다. 스페이서는 알킬기, 알켄일기, 알킨일기, 아릴기, 아르알킬기, 아르알켄일기 및 아르알킨일기를 포함할 수 있지만, 이들로 제한되지는 않고, 이들은 각각 하나 이상의 이종원자, 헤테로사이클, 아미노산, 뉴클레오타이드 및 사카라이드를 함유할 수 있다. 스페이서기는 당해 분야에 널리 공지되어 있고, 이전의 목록은 설명의 범위를 제한하도록 의도되지 않는다.

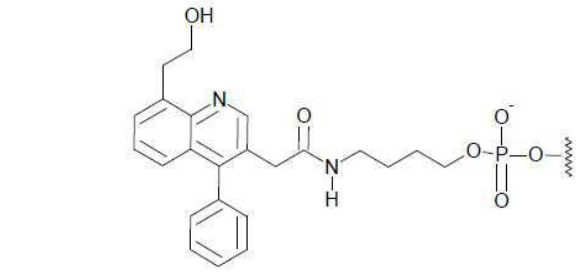
[0182] 연결기는 알킬, PEG, (C6-PEG_n-Alk), (C_n-SMPT-Alk) 및 (C_n-SS-Alk-Me)를 포함하지만, 이들로 제한되지는 않는다.

[0183] 3' 또는 5' 표적화기 또는 연결기를 함유하는, 표 2A 및 2B에 기재된 임의의 LPA RNAi 물질은 대안적으로 3' 또는 5' 표적화기 또는 연결기를 함유하지 않을 수 있거나, 표 4에 기재된 것(이들로 제한되지는 않음)을 포함하는 상이한 3' 또는 5' 표적화기 또는 연결기를 함유할 수 있다. 표 1, 표 2A 및 표 2B에 기재된 임의의 LPA RNAi 물질 뉴클레오타이드 서열은, 변형되든 또는 변형되지 않든, 표 4에 기재된 것(이들로 제한되지는 않음)을 포함하는 3' 또는 5' 표적화기 또는 연결기를 함유할 수 있다. 표 3A 및 3B에 기재된 임의의 LPA RNAi 물질 듀플렉스는, 변형되든 또는 변형되지 않든, 표 4에 기재된 것(이들로 제한되지는 않음)을 포함하는 표적화기 또는 연결기를 추가로 포함할 수 있고, 표적화기 또는 연결기는 LPA RNAi 물질 듀플렉스의 센스 가닥 또는 안티센스 가닥 중 어느 하나의 3' 또는 5' 말단에 부착될 수 있다.

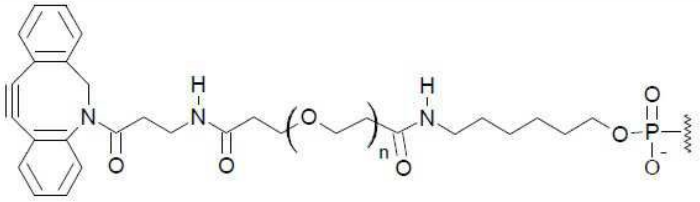
표 4. 다양한 변형된 뉴클레오타이드, 표적화기 및 연결기를 나타내는 구조.



[0184]

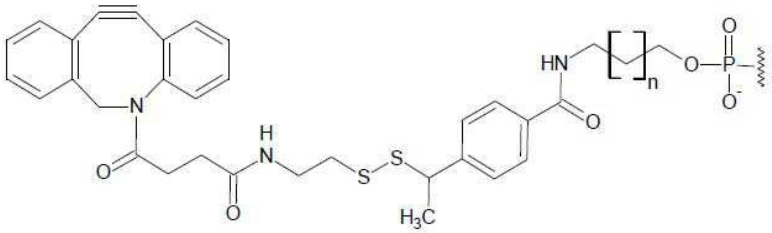


(PAZ)



(Alk-PEG$_n$-C6) 또는 (C6-PEG$_n$-Alk)(식 중, n = 1-12 임)

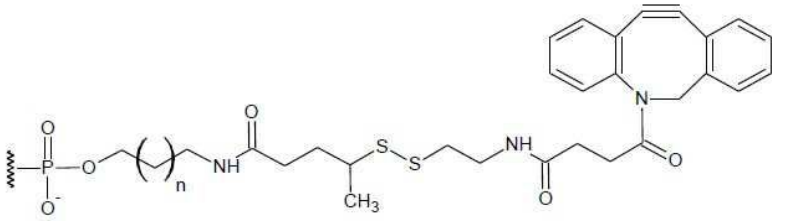
몇몇 실시형태에서, n = 5(예를 들어, (Alk-PEG5-C6)임)이다.



(C$_n$-SMPT-Alk) 또는 (Alk-SMPT-C$_n$)(식 중, n = 1-10 임),

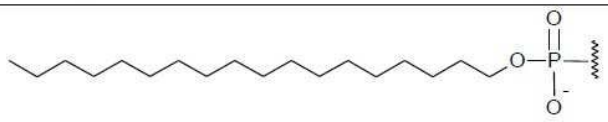
몇몇 실시형태에서, n = 4(예를 들어, (C6-SMPT-Alk)임)이다.

[0185]

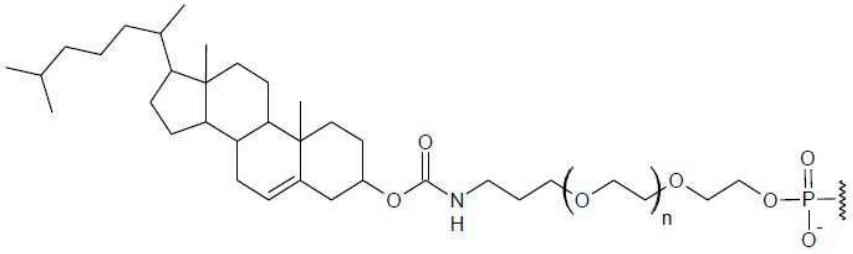


(C_n-SS-Alk-Me) 또는 ((Me-Alk-SS-C_n)(식 중, n = 1-10 임)

몇몇 실시형태에서, n = 4(예를 들어, (C6-SS-Alk-Me)임)이다.

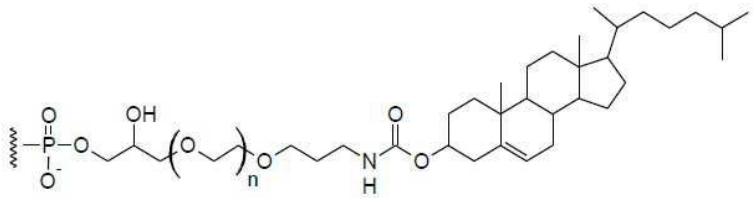


(스테아릴)



(Chol-TEG)(식 중, n = 1-10 임)

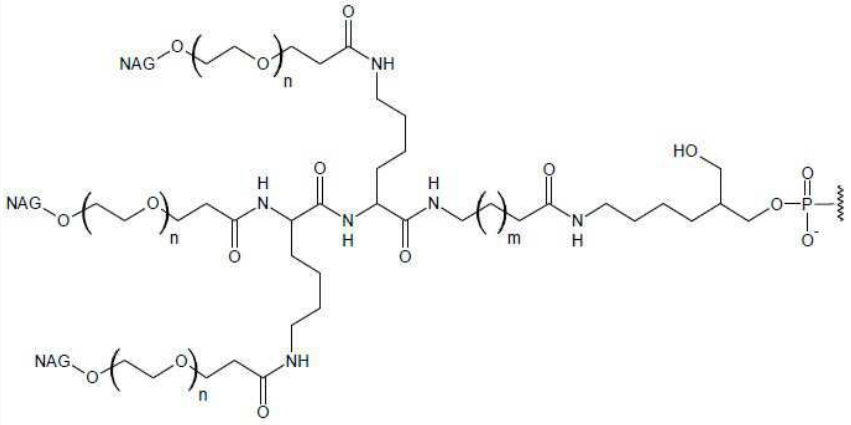
몇몇 실시형태에서, n = 2 이다.



(TEG-Chol)(식 중, n = 1-10 임)

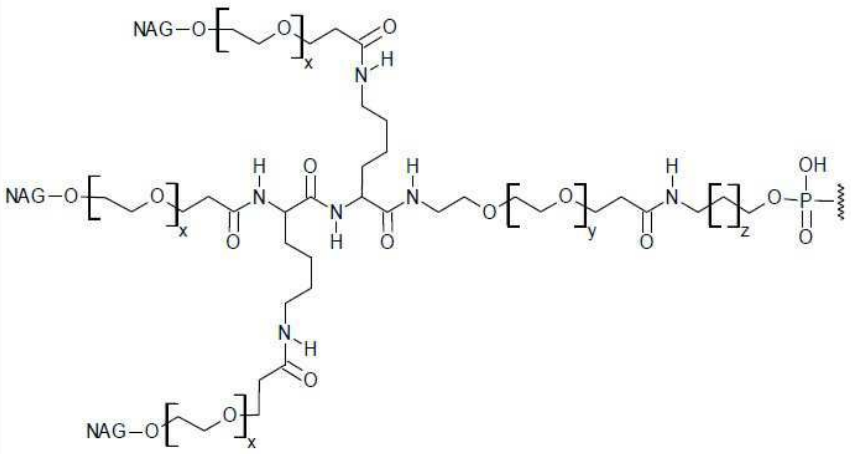
몇몇 실시형태에서, n = 3 이다.

[0186]



(NAG3-PEG$_n$-C$_m$) 또는 (C$_m$-PEG$_n$-NAG3)(식 중, n =1-6 이고, m = 1-12 임)

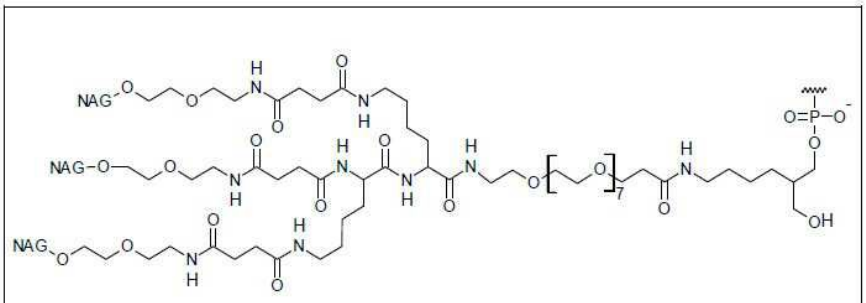
몇몇 실시형태에서, n = 3 이고, m = 9(예를 들어, (C11-PEG3-NAG3))이다



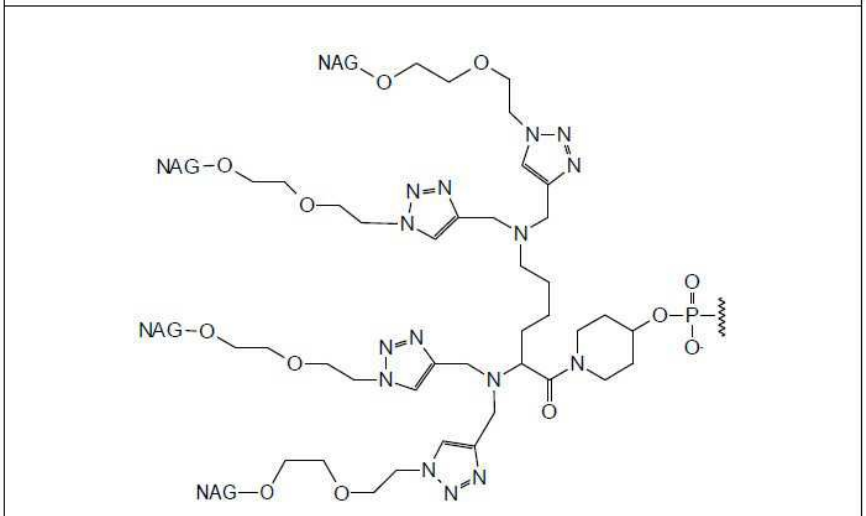
(C$_x$-PEG$_z$-NAG3)(식 중, x = 1-10 이고, y - 1-10 이고, z = 1-10 임)

몇몇 실시형태에서, x = 3 이고, y = 3 이고, z = 4(C6-PEG4-NAG3)이다

[0187]

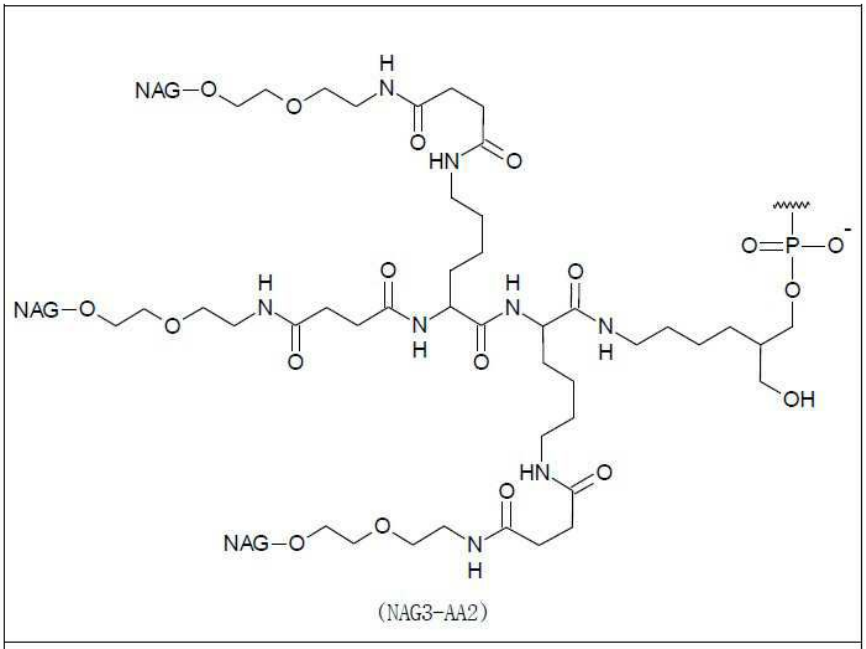


(NAG 3)

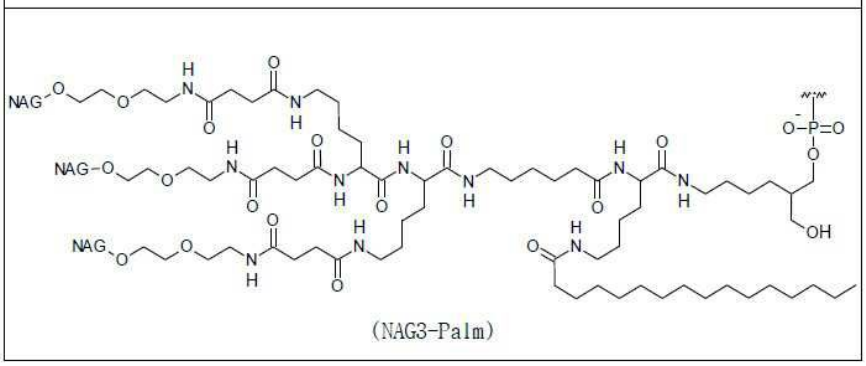


(NAG4)

[0188]

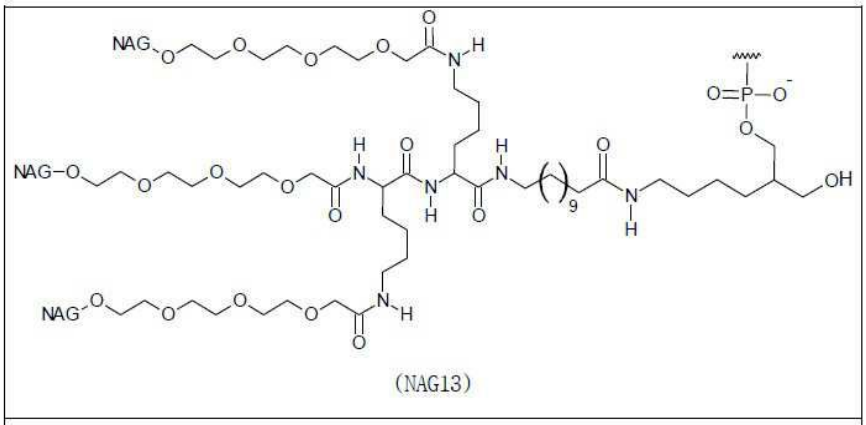


(NAG3-AA2)

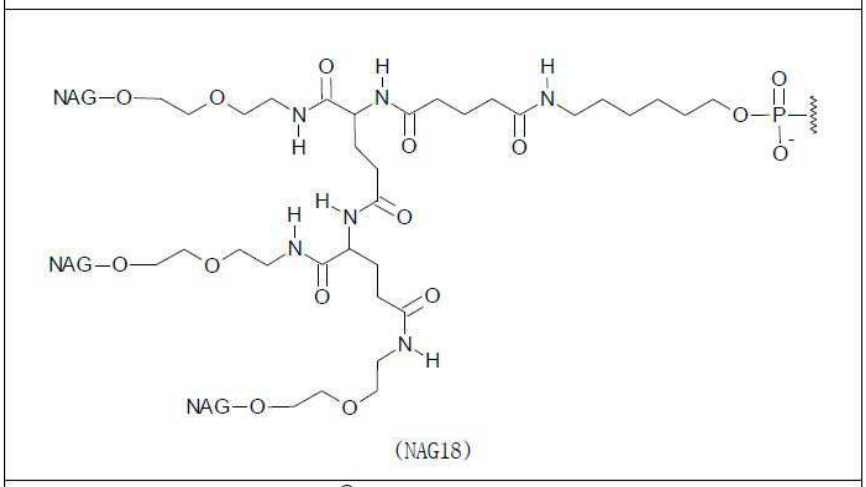


(NAG3-Palm)

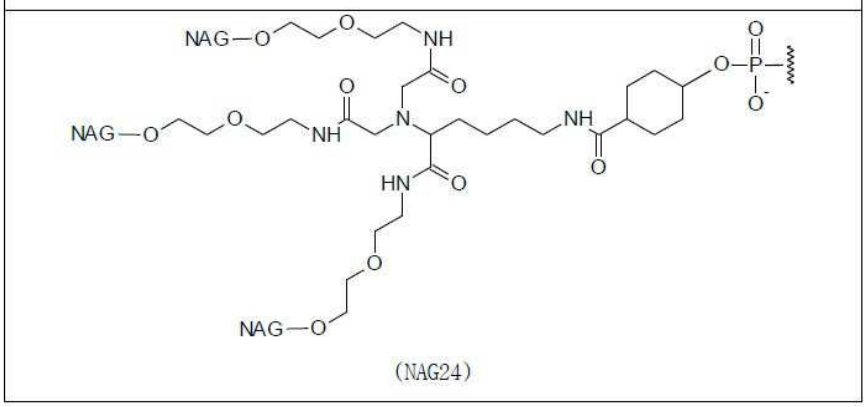
[0189]



(NAG13)

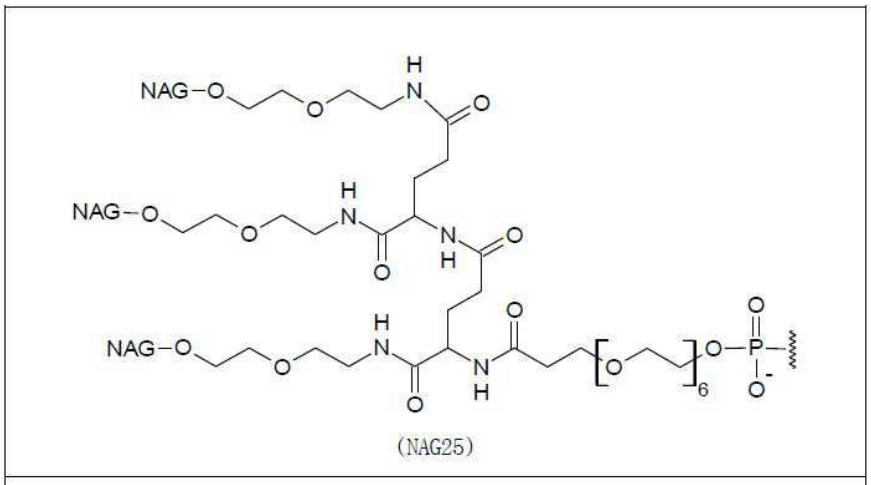


(NAG18)

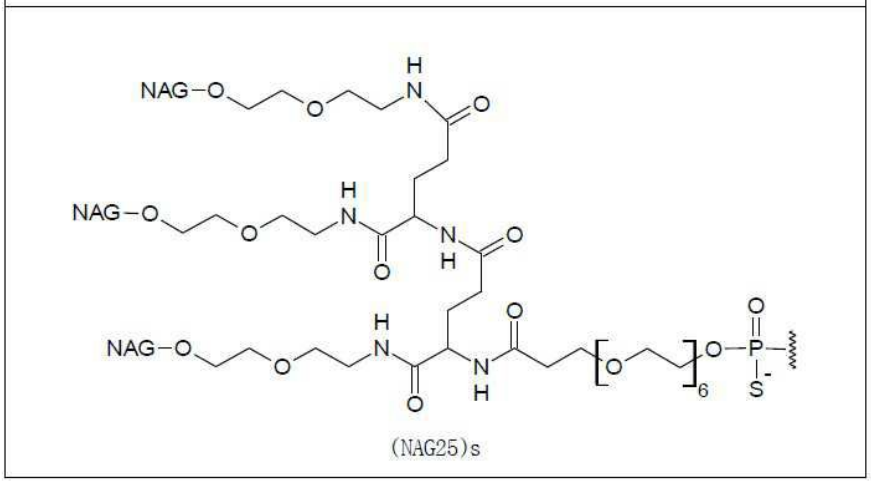


(NAG24)

[0190]

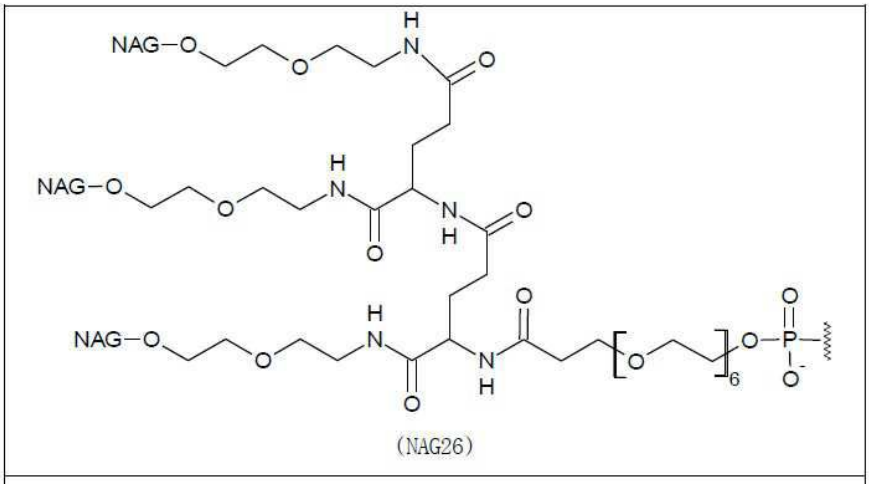


(NAG25)

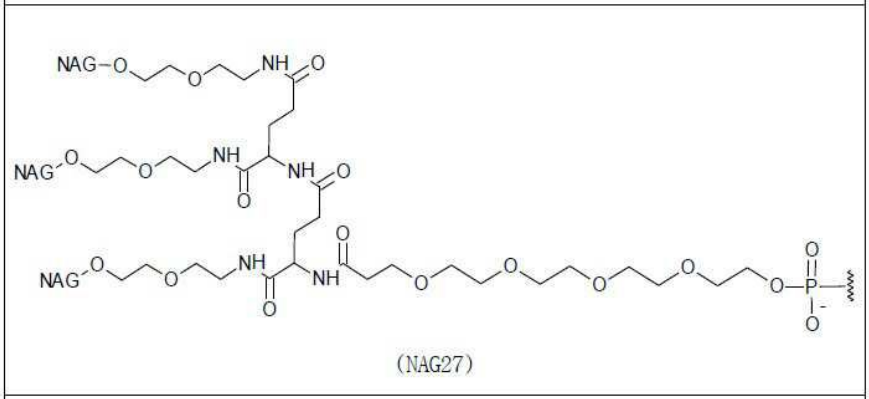


(NAG25)s

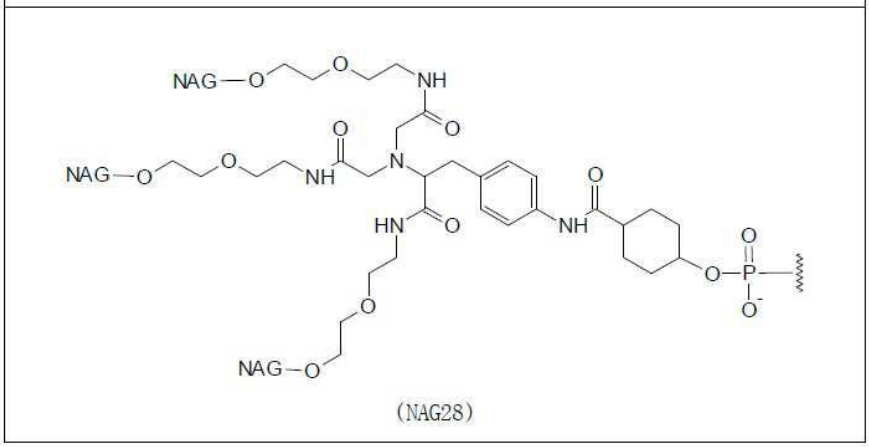
[0191]



(NAG26)

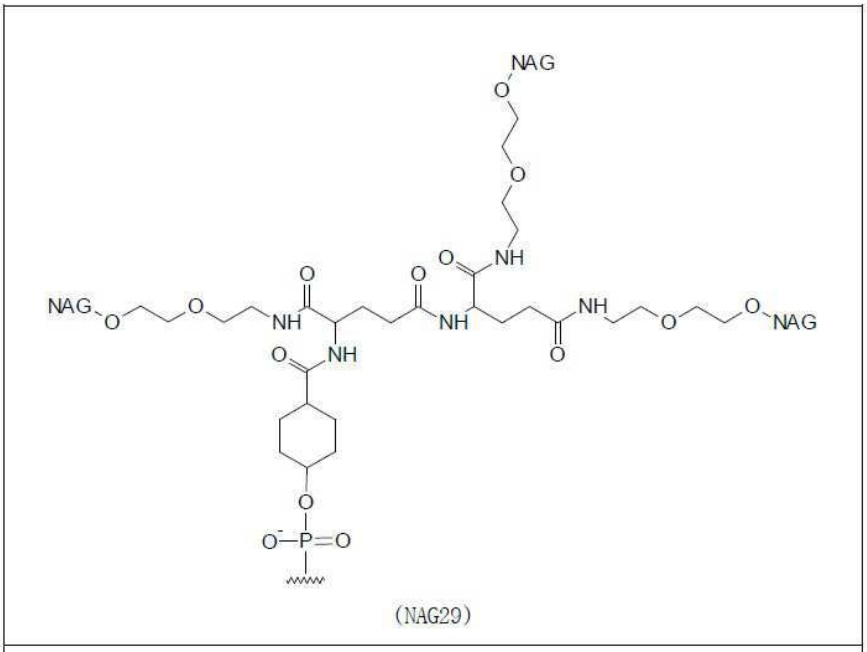


(NAG27)

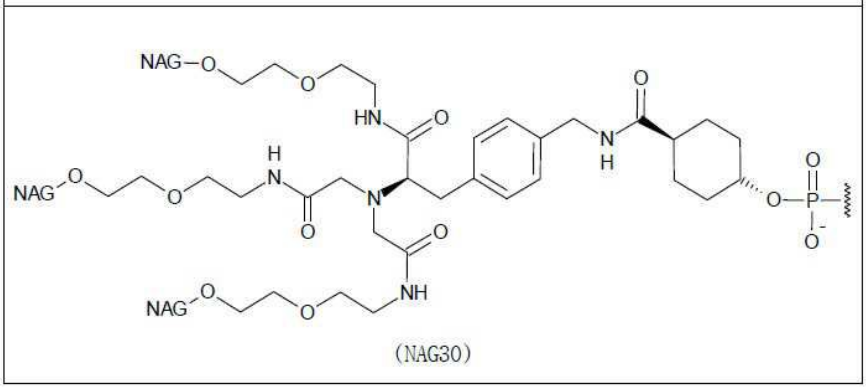


(NAG28)

[0192]

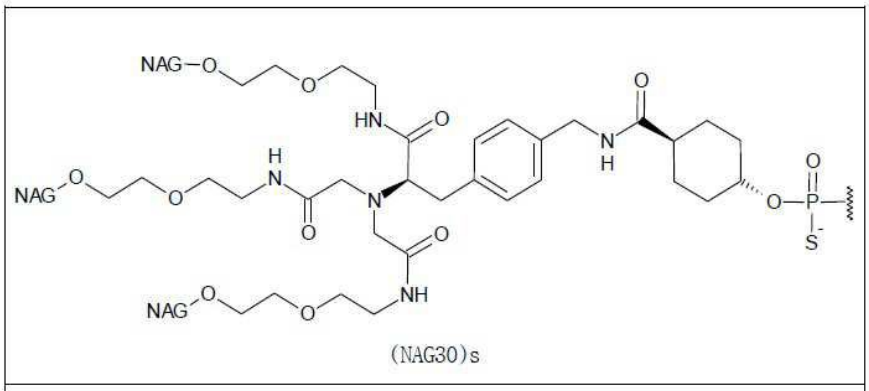


(NAG29)

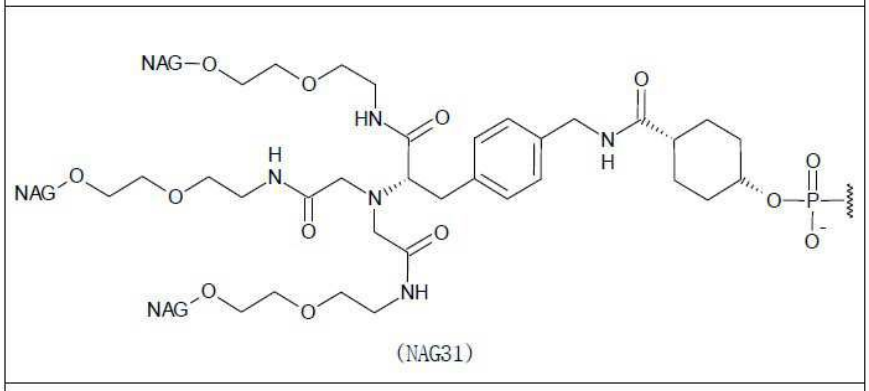


(NAG30)

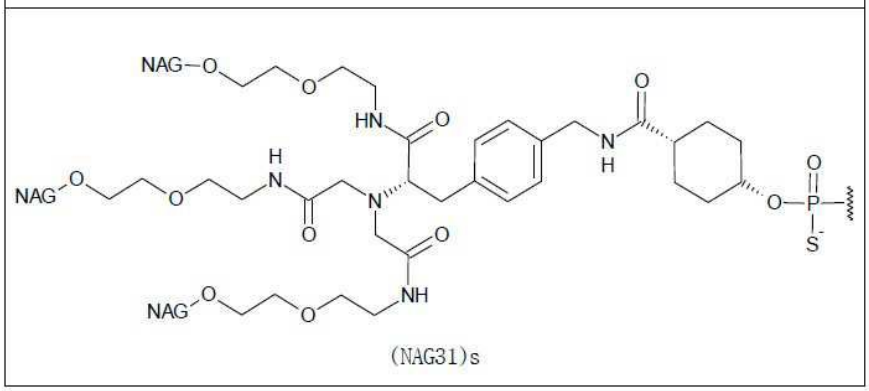
[0193]



(NAG30)s

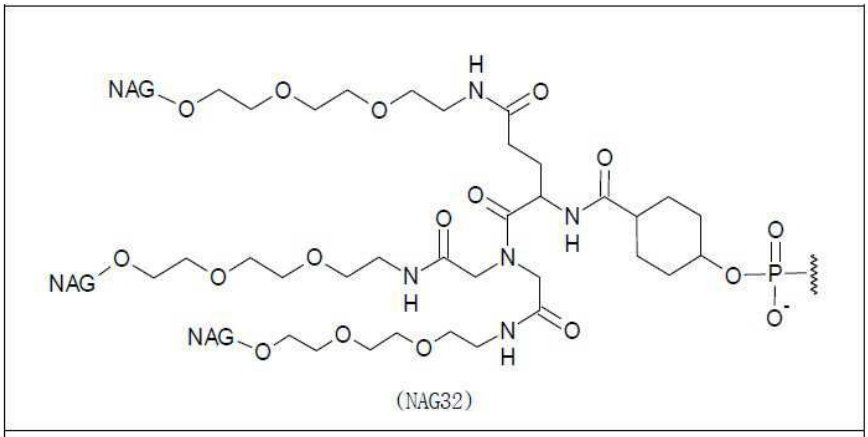


(NAG31)

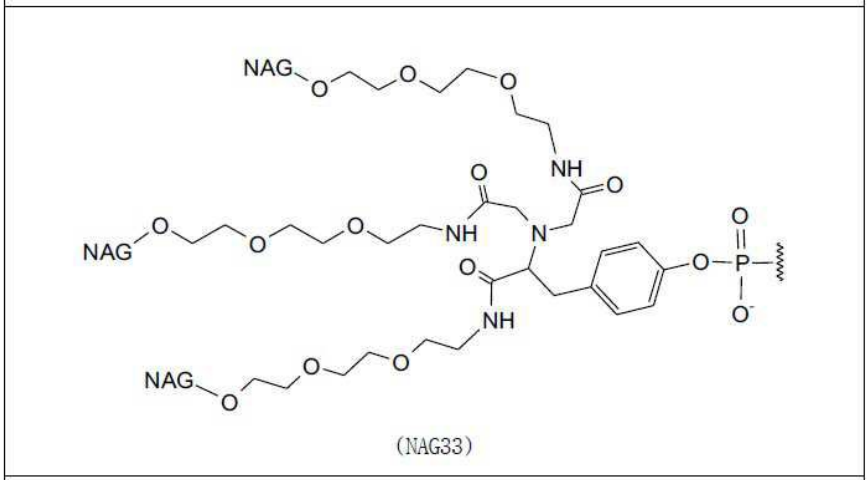


(NAG31)s

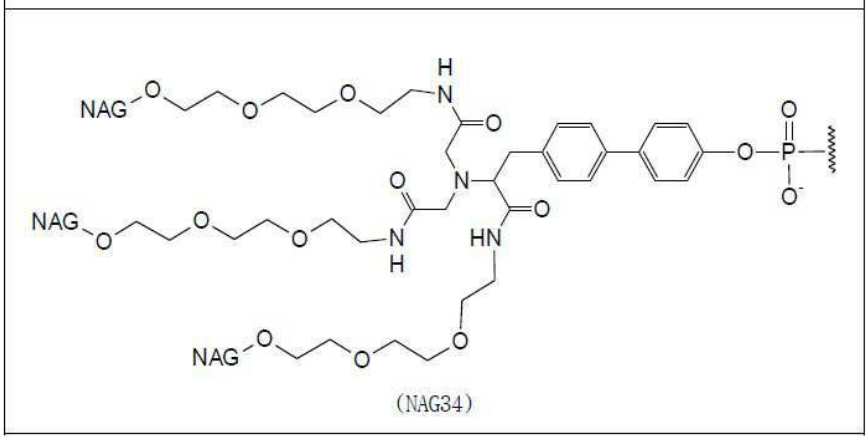
[0194]



(NAG32)

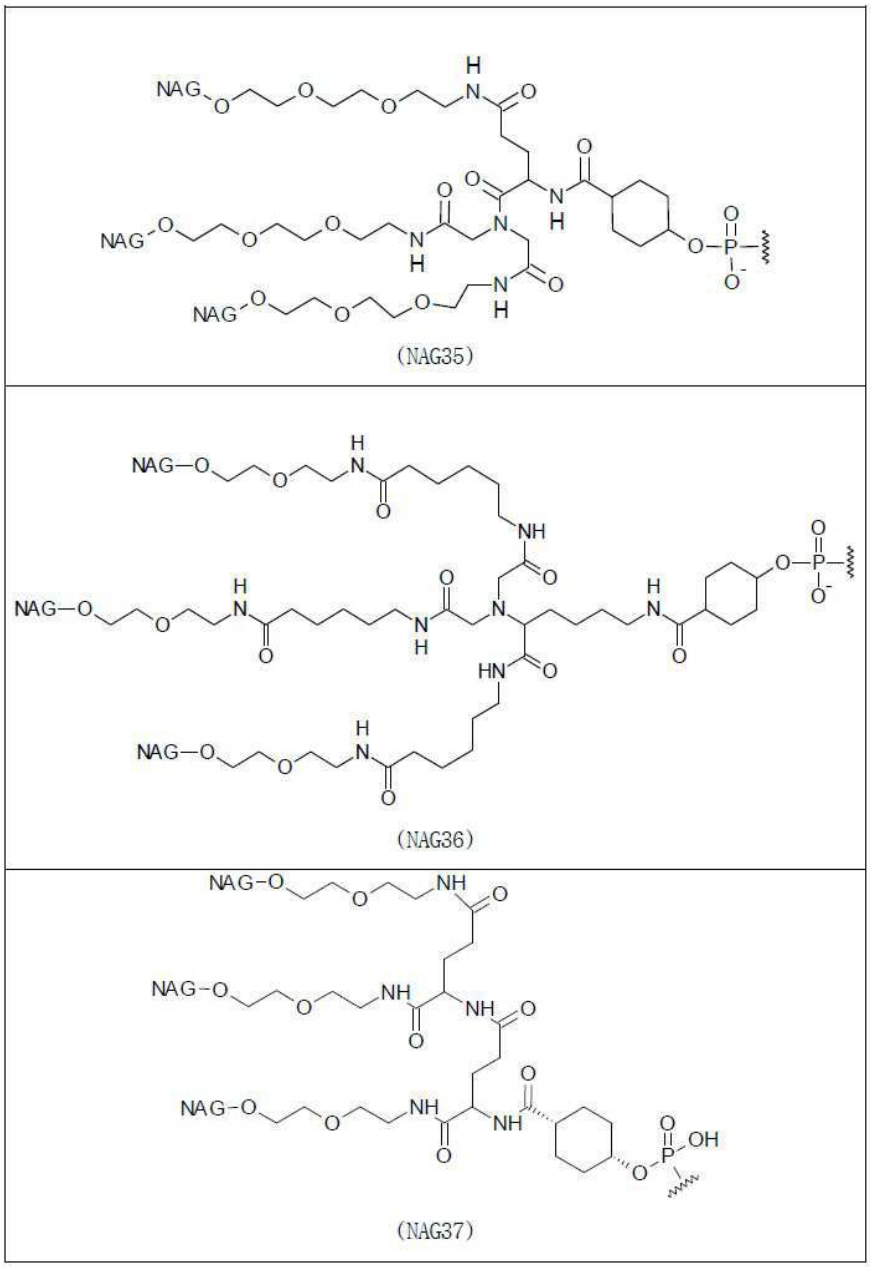


(NAG33)



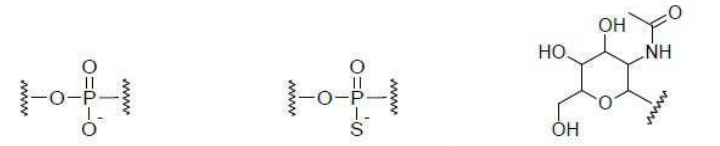
(NAG34)

[0195]



[0196]

[0197] 각각의 상기 구조에서, NAG는 N-아세틸-갈락토스아민 또는 또 다른 ASGPR 리간드를 포함한다. 각각의 (NAGx)는 포스페이트기((NAG25), (NAG30) 및 (NAG31)에서처럼), 또는 포스포로티오에이트기((NAG25)s, (NAG30)s 및 (NAG31)s에서처럼) 또는 또 다른 연결기를 통해 LPA RNAi 물질에 부착될 수 있다. 대안적으로, 당해 분야에 공지된 다른 연결기를 사용할 수 있다.



[0198]

[0199] 전달 비히클

[0200] 몇몇 실시형태에서, 전달 비히클은 RNAi 물질을 세포 또는 조직으로 전달하도록 사용될 수 있다. 전달 비히클은 세포 또는 조직으로의 RNAi 물질의 전달을 개선하는 화합물이다. 전달 비히클은 중합체, 예컨대 양친매성 중합체, 막 활성 중합체, 펩타이드, 멜리틴 펩타이드, 멜리틴 유사 펩타이드(melittin-like peptide: MLP), 지질, 가역적으로 변형된 중합체 또는 펩타이드 또는 가역적으로 변형된 막 활성 폴리아민을 포함하거나 이들로 이루

어지지만, 이들로 제한되지는 않는다.

[0201] 몇몇 실시형태에서, RNAi 물질은 지질, 나노입자, 중합체, 리포솜, 미셀, DPC 또는 당해 분야에서 이용 가능한 다른 전달 시스템과 조합될 수 있다. RNAi 물질은 표적화기, 지질(콜레스테롤 및 콜레스테릴 유도체를 포함하지만, 이들로 제한되지는 않음), 나노입자, 중합체, 리포솜, 미셀, DPC(예를 들어, WO 제2000/053722호, WO 제2008/0022309호, WO 제2011/104169호 및 WO 제2012/083185호, WO 제2013/032829호, WO 제2013/158141호(이들은 각각 본 명세서에서 참고로 포함됨) 참조), 또는 당해 분야에서 이용 가능한 다른 전달 시스템에 또한 화학적으로 접합될 수 있다.

[0202] 약제학적 조성물

[0203] 포유류에서 생체내 간 세포로 LPA RNAi 물질을 전달하는 방법이 본 명세서에 기재되어 있다. 몇몇 실시형태에서, 전달 비히클을 사용할 수 있다. 전달 비히클은 세포로의 RNAi 물질의 전달을 개선하는 화합물이다. 전달 비히클은 중합체, 예컨대 양친매성 중합체, 막 활성 중합체, 펩타이드, 예컨대 멜리틴 또는 멜리틴 유사 펩타이드, 가역적으로 변형된 중합체 또는 펩타이드, 또는 지질일 수 있지만, 이들로 제한되지는 않는다. 몇몇 실시형태에서, LPA RNAi 물질은 아시알로당단백질 리간드를 포함하는 표적화 리간드에 연결된다. 몇몇 실시형태에서, LPA RNAi 물질은 갈락토스 클러스터를 포함하거나 이것으로 이루어진 표적화 리간드에 연결된다.

[0204] LPA RNAi 물질은 예를 들어 대상체에서 세포, 세포의 군 또는 조직에서 LPA의 발현을 저해하도록 사용될 수 있다. 몇몇 실시형태에서, LPA RNAi 물질은 대상체에 대한 투여를 위해 조성물, 즉 약제학적 조성물 또는 약제를 제제화하도록 사용된다. 본 명세서에 사용된 바대로, 약제학적 조성물 또는 약제는 적어도 하나의 기재된 LPA RNAi 물질 및 하나 이상의 약제학적으로 허용가능한 부형제의 약물학적 유효량을 포함한다. 약제학적으로 허용가능한 부형제(부형제들)는 안전성을 위해 적절하게 평가되고 약물 전달 시스템에서 의도적으로 포함된 활성 약제 성분(API, 치료 제품, 예를 들어, LPA RNAi 물질) 이외의 물질이다. 부형제는 의도되는 투약량에서 치료 효과를 발휘하지 않거나 발휘하도록 의도되지 않는다. 부형제는 a) 제조 동안 약물 전달 시스템의 프로세싱의 보조, b) API의 안정성, 생체이용성 또는 환자 수용성의 보호, 지원 또는 향상, c) 생성물 식별의 보조, 및/또는 d) 저장 또는 사용 동안 API의 전달의 전체 안정성, 유효성의 임의의 다른 속성의 증대에 작용할 수 있다. 약제학적으로 허용가능한 부형제는 불활성 물질이거나 아닐 수 있다.

[0205] 부형제는 흡수 향상제, 피착방지제(anti-adherent), 소포제, 항산화제, 결합제, 완충제, 캐리어, 코팅제, 색상, 전달 향상제, 전달 중합체, 덱스트란, 덱스트로스, 희석제, 붕괴제, 유화제, 증량제, 필러, 향료, 유동화제, 습윤제, 활택제, 오일, 중합체, 보존제, 식염수, 염, 용매, 당, 현탁제, 서방 매트릭스, 감미료, 증점제, 등장화제, 비히클, 방수제 및 습윤제를 포함하지만, 이들로 제한되지는 않는다.

[0206] 약제학적 조성물은 약제학적 조성물에서 흔히 발견되는 다른 추가 성분을 함유할 수 있다. 이러한 추가 성분은 항소양제, 수렴제, 국소 마취제 또는 소염제(예를 들어, 항히스타민제, 다이펜하이드라민 등)을 이들로 제한되지는 않는다. 본 명세서에서 정의된 RNAi 물질을 발현하거나 포함하는 세포, 조직 또는 단리된 장기가 "약제학적 조성물"로서 사용될 수 있다는 것이 또한 고안된다. 본 명세서에 사용된 바와 같은, "약리학적 유효량", "치료학적 유효량", 또는 단순히 "유효량"은 의도된 약리학적, 치료학적 또는 예방학적 결과를 생성하는 RNAi 물질의 양을 의미한다.

[0207] 몇몇 실시형태에서, 기재된 LPA RNAi 물질은 제2 LPA RNAi 물질 또는 다른 RNAi 물질, 소분자 약물, 항체, 항체 단편, 및/또는 백신(이들로 제한되지는 않음)을 포함하는 하나 이상의 추가 치유제 또는 치료와 조합된다. 추가 치유제의 예는 HMg Co-A 환원효소 저해제(스타틴), 에제티미브, PCSK-9 저해제, CTEP 저해제, ANGPTL3을 표적화하는 치료제, APOC3을 표적화하는 치료제 및 니아신을 포함하지만, 이들로 제한되지는 않는다.

[0208] 기재된 RNAi 물질 및 본 명세서에 개시된 LPA RNAi 물질을 포함하는 약제학적 조성물은 키트, 용기, 팩 또는 분배기에 포장되거나 포함될 수 있다. LPA RNAi 물질 및 상기 LPA RNAi 물질을 포함하는 약제학적 조성물은 프리필드 주사기 또는 바이알에서 포장될 수 있다.

[0209] 몇몇 실시형태에서, 적어도 하나의 기재된 LPA RNAi 물질을 포함하는 약제학적 조성물이 고려된다. 이 약제학적 조성물은 세포, 조직 또는 유기체에서의 LPA 유전자의 발현의 저해에서 유용하다. 몇몇 실시형태에서, 기재된 약제학적 조성물은, LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환, 병태 또는 장애를 가지는 대상체를 치료하기 위해 사용된다. 몇몇 실시형태에서, 기재된 약제학적 조성물은, LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환, 병태 또는 장애를 발생시킬 위험에 있는 대상체를 치료하기 위해 사용된다. LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환, 병태 또는 장애는 베르거 질환, 말초 동맥 질환, 관상동맥 동맥 질환, 대

사 증후군, 급성 관상동맥 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 뇌혈관 질환, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 급성 관상동맥 증후군, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환 및 정맥성 혈전증을 포함하지만, 이들로 제한되지는 않는다. 몇몇 실시형태에서, 대상체는 인간 환자(이들로 제한되지는 않음)를 포함하는 포유류이다.

[0210] 본 명세서에 기재된 적어도 하나의 LPA RNAi 물질을 포함하는 세포, 조직 및 비인간 유기체가 고려된다. 세포, 조직 또는 비인간 유기체는 당해 분야에서 이용 가능한 임의의 수단에 의해 세포, 조직 또는 비인간 유기체로 RNAi 물질을 전달함으로써 만들어진다. 몇몇 실시형태에서, 세포는 인간 세포(이들로 제한되지는 않음)를 포함하는 포유류 세포이다. 세포, 조직 또는 비인간 유기체는 조사에 또는 조사 도구(예를 들어, 약물 시험 또는 진단)로서 유용하다.

[0211] 치료 방법

[0212] 몇몇 실시형태에서, 본 명세서에 기재된 LPA RNAi 물질은, LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환, 병태 또는 장애를 가지거나 가질 위험에 있는 대상체를 치료하기 위해 사용된다. LPA 유전자 발현의 감소 및/또는 저해로부터 이익을 얻는, 대상체의 치료는 치료학적 및/또는 예방학적 치료를 포함한다. 질환, 병태 또는 장애의 예는 베르거 질환, 말초 동맥 질환, 관상동맥 동맥 질환, 대사 증후군, 급성 관상동맥 증후군, 대동맥판막 협착증, 대동맥판막 역류, 대동맥 박리, 망막 동맥 폐쇄, 뇌혈관 질환, 장간막 허혈, 견상장간막 동맥 폐쇄, 신동맥 협착증, 안정/불안정 협심증, 급성 관상동맥 증후군, 이형접합 또는 동형접합 가족성 고콜레스테롤혈증, 고아포베타지단백혈증, 뇌혈관 죽상동맥경화증, 뇌혈관 질환 및 정맥성 혈전증을 포함하지만, 이들로 제한되지는 않는다. 몇몇 실시형태에서, 상기 방법은 치료하고자 하는 포유류에게 본 명세서에 기재된 LPA RNAi 물질을 포함는 조성물, 예컨대 약제학적 조성물을 투여하는 단계를 포함한다.

[0213] 몇몇 실시형태에서, 치료학적 유효량(예를 들어, 대상체에서의 LPA의 발현을 저해하기에 효과적인 양)의 하나 이상의 기재된 LPA RNAi 물질은 대상체에게 투여되어서, 대상체에서의 LPA의 발현을 저해한다. 몇몇 실시형태에서, 본 명세서에 기재된 하나 이상의 LPA RNAi 물질은, LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환 또는 장애를 가지는 대상체를 치료하기 위해 사용된다. 몇몇 실시형태에서, 기재된 LPA RNAi 물질은, LPA 발현의 감소 또는 저해로부터 이익을 얻는, 질환 또는 장애를 가지는 대상체에서 적어도 하나의 증상을 치료하거나 예방하도록 사용된다. 대상체는 치료학적 유효량의 임의의 하나 이상의 기재된 RNAi 물질이 투여되어서 증상을 치료한다. 몇몇 실시형태에서, 대상체는 예방학적 유효량의 임의의 하나 이상의 기재된 RNAi 물질이 투여되어서 하나 이상의 증상을 예방한다.

[0214] 몇몇 실시형태에서, LPA RNAi 물질은 임상 제시를 치료하거나 관리하도록 사용되고, 여기서 이러한 치료, 예방 또는 관리를 요하는 대상체는 치료학적 또는 예방학적 유효량의 본 명세서에 기재된 하나 이상의 LPA RNAi 물질 또는 LPA RNAi 물질 함유 조성물이 투여된다. 몇몇 실시형태에서, 상기 방법은 치료하고자 하는 포유류에게 본 명세서에 기재된 LPA RNAi 물질을 포함하는 조성물을 투여하는 단계를 포함한다.

[0215] 몇몇 실시형태에서, 상기 방법은 제2 치료제 또는 치료를 투여하는 단계를 추가로 포함한다. 몇몇 실시형태에서, 제2 치료제는 또 다른 LPA RNAi 물질(예를 들어, *LPA* 표적 내의 상이한 서열을 표적화하는 *LPA* RNAi 물질)이다. 다른 실시형태에서, 제2 치료제는 소분자 약물, 항체, 항체 단편 및 백신을 포함하는 군으로부터 선택될 수 있다.

[0216] 투여 경로는 RNAi 물질이 신체와 접촉하는 경로이다. 일반적으로, 대상체의 치료를 위해 약물 및 핵산을 전달하는 방법이 당해 분야에 널리 공지되어 있고, 본 명세서에 기재된 조성물의 투여에 적용 가능하다. 본 명세서에 기재된 화합물은 특정한 경로에 적절히 맞춰진 제제에서 임의의 적합한 경로를 통해 투여될 수 있다. 따라서, 본 명세서에 기재된 화합물은 주사에 의해, 예를 들어, 정맥내로, 근육내, 피내로, 피하로 또는 복강내로 투여될 수 있다.

[0217] 몇몇 실시형태에서, 본 명세서에 기재된 LPA RNAi 물질 또는 조성물은 당해 분야에 공지된 올리고뉴클레오타이드 전달 기법을 이용하여 세포, 세포의 군, 조직 또는 대상체에게 전달될 수 있다. 일반적으로, (시험관내 또는 생체내) 핵산 분자를 전달하기 위해 당해 분야에 인식된 임의의 적합한 방법은 본 명세서에 기재된 LPA RNAi 물질에 의한 사용에 적응될 수 있다. 예를 들어, 전달은 국부 투여(예를 들어, 직접 주사, 이식 또는 국소 투여), 전신 투여, 또는 피하, 정맥내, 경구, 복강내 또는 비경구 경로, 예컨대 두개내(예를 들어, 심실내, 뇌실질내 및 척추강내), 근육내, 경피, 기도(에어로졸), 비강, 직장 또는 국소(협측 및 설하 포함) 투여에 의할 수 있다.

소정의 실시형태에서, 조성물은 피하 또는 정맥내 점적주사 또는 주사에 의해 투여될 수 있다.

[0218] 몇몇 실시형태에서, RNAi 물질은 지질, 나노입자, 중합체, 리포솜, 미셀, DPC 또는 당해 분야에서 이용 가능한 다른 전달 시스템과 조합될 수 있다. RNAi 물질은 또한 표적화기, 지질(콜레스테롤 및 콜레스테릴 유도체(이들로 제한되지는 않음) 포함), 나노입자, 중합체, 리포솜, 미셀, DPC(예를 들어, WO 2000/053722, WO 2008/0022309, WO 2011/104169 및 WO 2012/083185(이들은 각각 본 명세서에 참고로 포함됨) 참조), 또는 당해 분야에서 이용 가능한 다른 전달 시스템에 화학적으로 접합될 수 있다. LPA RNAi 물질은 전달 중합체에 접합될 수 있다. 몇몇 실시형태에서, 전달 중합체는 가역적으로 마스킹된/변형된 양친매성 막 활성 폴리아민이다.

[0219] 발현의 저해

[0220] 본 명세서에 사용된 바와 같은, 용어 "침묵시킨다", "감소시킨다", "저해한다", "하향조절한다" 또는 "유전자 발현을 넉다운시킨다"는, LPA 유전자를 말할 때, LPA 유전자가 전사되는 세포, 세포의 군 또는 조직에서, 유전자로부터 전사된 RNA의 수준 또는 mRNA로부터 전사된 폴리펩타이드, 단백질 또는 단백질 하위단위의 수준에 의해 측정되는, 유전자의 발현이, 세포, 세포의 군 또는 조직이 이렇게 치료되거나 치료되지 않은 제2 세포, 세포의 군 또는 조직, 또는 LPA RNAi 물질의 투여 전의 동일한 세포, 세포의 군 또는 조직과 비교하여, 기재된 LPA RNAi 물질에 의해 치료될 때 감소한다는 것을 의미한다.

[0221] 몇몇 실시형태에서, 기재된 LPA RNAi 물질이 투여되는 대상체에서의 유전자 발현 수준 및/또는 LPA의 mRNA 수준은 LPA RNAi 물질이 투여되기 전의 대상체 또는 LPA RNAi 물질을 받지 않는 대상체에 비해 적어도 약 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% 또는 98% 감소한다. 대상체에서의 유전자 발현 수준 및/또는 mRNA 수준은 대상체의 세포, 세포의 군, 및/또는 조직에서 감소할 수 있다. 몇몇 실시형태에서, 기재된 LPA RNAi 물질이 투여되는 대상체에서의 LPA의 단백질 수준은 LPA RNAi 물질이 투여되기 전의 대상체 또는 LPA RNAi 물질을 받지 않는 대상체에 비해 적어도 약 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% 또는 98% 감소한다. 대상체에서의 단백질 수준은 대상체의 세포, 세포의 군, 조직, 혈액, 및/또는 다른 유체에서 감소할 수 있다. 유전자 발현, mRNA 또는 단백질 수준의 감소는 당해 분야에 공지된 임의의 방법에 의해 평가될 수 있다. LPA mRNA 수준 및/또는 단백질 수준의 감소 또는 저하는 본 명세서에서 총체적으로 LPA에서의 감소 또는 저하 또는 LPA의 발현의 저해 또는 감소로 칭해진다.

[0222] 세포로의 도입은, RNAi 물질을 의미할 때, 세포로 RNAi 물질을 기능적으로 전달하는 것을 의미한다. 기능적 전달이란, RNAi 물질이 세포로 전달되고, 생물학적 활성(예를 들어, 유전자 발현의 서열 특이적 저해)을 가진다는 것을 의미한다.

[0223] 세포 및 조직 및 비인간 유기체

[0224] 본 명세서에 기재된 LPA RNAi 물질의 적어도 하나를 포함하는 세포, 조직 및 비인간 유기체가 고려된다. 세포, 조직 또는 비인간 유기체는 세포, 조직, 또는 비인간 유기체로 RNAi 물질을 전달함으로써 만들어진다.

[0225] 상기 제공된 실시형태 및 항목은 하기 비제한적인 실시예에 의해 이제 예시된다.

[0226] 실시예

[0227] 실시예 1. *RNAi 물질 합성.*

[0228] A) *합성*. LPA RNAi 물질을 올리고뉴클레오타이드 합성에서 사용된 고상에서 포스포르아미다이트 기법에 따라 합성하였다. 스케일에 따라, MerMade96E(Bioautomation) 또는 MerMade12(Bioautomation)를 사용하였다. 제어 기공 유리(CPG, 500Å 또는 600Å, Prime Synthesis(미국 펜실베니아주 아스톤)로부터 얻음)로 제조된 고체 지지체에서 합성을 수행하였다. 모든 DNA, 2' 변형된 RNA, 및 UNA 포스포르아미다이트를 Thermo Fisher Scientific(미국 위스콘신주 밀워키))으로부터 구입하였다. 구체적으로, 하기 2'-O-메틸 포스포르아미다이트를 사용하였다: (5'-O-다이메톡시트리틸-N^6-(벤조일)-2'-O-메틸-아데노신-3'-O-(2-사이아노에틸-N,N-다이아이소프로필-1아미노) 포스포르아미다이트, 5'-O-다이메톡시-트리틸-N^4-(아세틸)-2'-O-메틸-사이티딘-3'-O-(2-사이아노에틸-N,N-다이아이소프로필-아미노) 포스포르아미다이트, (5'-O-다이메톡시트리틸-N^2-(아이소뷰티릴)-2'-O-메틸-구아노신-3'-O-(2-사이아노-에틸-N,N-다이아이소프로필아미노)포스포르아미다이트 및 5'-O-다이메톡시-트리틸-2'-O-메틸-우리딘-3'-O-(2-사이아노에틸-N,N-다이아이소프로필아미노)포스포르아미다이트. 2'-데옥시-2'-플루오로-포스포르-아미다이트는 2'-O-메틸 RNA 아미다이트와 동일한 보호기를 보유하였다. 하기 UNA 포스포르아미다

이트를 사용하였다: 5'-(4,4'-다이메톡시트리틸)-N-벤조일-2',3'-세코-아데노신, 2'-벤조일-3'-[(2-사이아노에틸)-(N,N-다이아이소프로필)]-포스포르-아미다이트, 5'-(4,4'-다이메톡시트리틸)-N-아세틸-2',3'-세코-시토신, 2'-벤조일-3'-[(2-사이아노에틸)-(N,N-다이아이소-프로필)]-포스포르아미다이트, 5'-(4,4'-다이메톡시트리틸)-N-아이소뷰티릴-2',3'-세코-구아노신, 2'-벤조일-3'-[(2-사이아노에틸)-(N,N-다이아이소프로필)]-포스포르아미다이트 및 5'-(4,4'-다이메톡시-트리틸)-2',3'-세코-우리딘, 2'-벤조일-3'-[(2-사이아노에틸)-(N,N- 다이아이소-프로필)]-포스포르아미다이트. 모든 아미다이트를 무수 아세토나이트릴(50mM) 중에 용해시키고, 분자체(3Å)를 첨가하였다. 올리고머의 5' 말단에서 TEG-콜레스테롤을 도입하기 위해, Glen Research(미국 버지니아주 스털링))로부터의 1-다이메톡시트리틸옥시-3-O-(N-콜레스테릴-3-아미노프로필)-트라이에틸렌글라이콜-글라이세릴-2-O-(2-사이아노에틸)-(N,N,-다이아이소프로필)-포스포르아미다이트를 사용하였다. 합성 사이클의 어떤 변형 없이 5'-변형을 도입하였다. 5-벤질티오-1H-테트라졸(BTT, 아세토나이트릴 중의 250mM)을 활성제 용액으로서 사용하였다. 커플링 시간은 10분(RNA), 180초(콜레스테롤), 90초(2'OMe 및 UNA) 및 60초(2'F 및 DNA)였다. 포스포로티오에이트 연결을 도입하기 위해, 무수 아세토나이트릴 중의 3-페닐 1,2,4-다이티아졸린-5-온(POS, PolyOrg, Inc.(미국 매사추세츠주 레민스터)로부터 얻음)의 100mM의 용액을 사용하였다. 특정한 서열에 대해 표 1, 표 2A 및 표 2B를 참조한다.

[0229] *B. 지지체 결합된 올리고머의 절단 및 탈보호.* 고상 합성의 마무리 후, 건조된 고체 지지체를 30℃에서 2시간 동안 물 및 28% 수산화암모늄 용액(Aldrich) 중의 40중량% 메틸아민의 1:1 용적 용액에 의해 처리하였다. 용액을 증발시키고, 고체 잔류물을 물 중에 재구성하였다(하기 참조).

[0230] *C. 정제.* Waters XBridge BEH300 C4 5u Prep 컬럼 및 Shimadzu LC-8 시스템을 사용하여 미정제 콜레스테롤 함유 올리고머를 역상 HPLC에 의해 정제하였다. 완충제 A는 100mM의 TEAA(pH 7.5)이고 5% 아세토나이트릴을 함유하였고, 완충제 B는 100mM의 TEAA이고 95% 아세토나이트릴을 함유하였다. 260nm에서의 UV 트레이스를 기록하였다. 이후, 100mM의 중탄산암모늄(pH 6.7) 및 20% 아세토나이트릴의 실행 완충제와 함께 Sephadex G-25 매질이 충전된 GE Healthcare XK 16/40 컬럼을 사용하여 크기 배제 HPLC에서 적절한 분획을 실행하였다. TKSgel SuperQ-5PW 13u 컬럼 및 Shimadzu LC-8 시스템을 사용하여 음이온성 교환 HPLC에 의해 다른 미정제 올리고머를 정제하였다. 완충제 A는 20mM의 Tris, 5mM의 EDTA(pH 9.0)이고, 20% 아세토나이트릴을 함유하고, 완충제 B는 1.5M 염화나트륨의 첨가에 의해 완충제 A와 동일하였다. 260nm에서의 UV 트레이스를 기록하였다. 적절한 분획을 혼주하고, 이후 콜레스테롤 함유 올리고머에 기재된 바대로 크기 배제 HPLC에서 실행하였다.

[0231] *D. 어닐링.* 0.2x PBS(포스페이트 완충 식염수, 1x, Corning, Cellgro) 중의 등몰량 용액(센스 및 안티센스)을 합함으로써 상보성 균주를 혼합하여 RNAi 물질을 형성하였다. 이 용액을 70℃에서 열혼합기(thermomixer)로 위치시키고, 95℃로 가열하고, 95℃에서 5분 동안 유지시키고, 실온으로 천천히 냉각시켰다. 약간의 RNAi 물질을 동결건조시키고, -15 내지 -25℃에서 저장하였다. 0.2x PBS 중의 UV-Vis 분광계에서 용액 흡광도를 측정함으로써 듀플렉스 농도를 결정하였다. 이후, 260nm에서의 용액 흡광도에 전환 인자 및 희석 인자를 곱하여 듀플렉스 농도를 결정하였다. 달리 기재되지 않은 한, 모든 전환 인자는 0.037mg/(㎖·cm)이었다. 약간의 실험을 위해, 실험으로 결정된 흡광 계수로부터 전환 인자를 계산하였다.

[0232] 실시예 2. *LPA RNAi 물질의 1차 시험관내 분석.* 인실리코 분석에 의해 인간 및 비인간 영장류 교차반응성으로 확인된 후보 서열을 스크리닝하였다. 108개의 인실리코 확인된 잠재적인 LPA RNAi 물질을 합성하고, 3개의 그룹에서 시험관내 효율에 대해 스크리닝하였다. 스크리닝 목적을 위해, 인간 LPA cDNA 서열(수탁 번호 NM_005577.1)을 상업적으로 구입 가능한 포유류 발현 벡터(Origene(메릴랜드 로크빌))로부터 상업적으로 구입 가능한 리포터 기반 스크리닝 플라스미드인 psiCHECK2(Promega(미국 위스콘신주 매디슨))로 서브클로닝하고, 이 플라스미드는 레닐라 루시퍼라제/LPA 융합 mRNA를 생성하였다. 인간 배경에서의 LPA RNAi 물질 효율을 위해, 인간 간세포 암종 세포주인 Hep3B 세포를 96웰 포맷에서 웰마다 약 10,000개의 세포로 플레이팅하였다. 각각의 108개의 LPA RNAi 물질을 웰마다 50-100ng의 LPA-psiCHECK2 플라스미드 DNA 및 웰마다 0.2㎕ 리포펙타민(LipoFectamine) 2000과 함께 2 또는 3의 농도(1nM 및 0.1nM, 또는 0.02, 0.2 및 2nM)에서 동시형질감염시켰다. 이중 루시퍼라제 리포터 검정(Promega(미국 위스콘신주 매디슨))을 이용하여 psiCHECK2 플라스미드에 또한 존재하는 구성적으로 발현된 반딧불이 루시퍼라제의 수준으로 정규화된 레닐라 루시퍼라제 수준을 측정함으로써 유전자 넉다운을 결정하였다(표 5A 및 표 5B).

표 5A. LPA RNAi 물질의 시험관내 분석, LPA 발현의 저해.

듀플렉스 번호	상대 R_{luc}-LPA 발현				듀플렉스 번호	상대 R_{luc}-LPA 발현			
	1nM		0.1nM			1nM		0.1nM	
	평균	SD	평균	SD		평균	SD	평균	SD
AD00571	1.012	0.146	1.107	0.174	AD00605	1.006	0.193	1.006	0.146
AD00572	0.776	0.062	1.075	0.089	AD00606	0.509	0.039	0.570	0.054
AD00573	0.708	0.054	0.708	0.134	AD00607	0.816	0.091	0.906	0.068
AD00574	0.441	0.028	0.525	0.056	AD00608	0.883	0.111	1.158	0.054
AD00575	0.242	0.038	0.365	0.035	AD00609	0.515	0.079	0.691	0.137
AD00576	0.166	0.047	0.341	0.073	AD00610	0.628	0.057	0.748	0.090
AD00577	0.702	0.115	0.934	0.036	AD00611	1.320	0.066	1.116	0.046
AD00578	0.272	0.008	0.599	0.200	AD00612	1.103	0.193	1.100	0.052
AD00579	0.290	0.031	0.447	0.066	AD00613	0.910	0.094	0.878	0.040
AD00580	0.825	0.145	0.991	0.123	AD00614	1.101	0.111	1.097	0.043
AD00581	0.654	0.095	0.986	0.127	AD00615	1.051	0.140	0.898	0.161
AD00582	0.610	0.178	0.791	0.244	AD00616	0.898	0.101	1.029	0.042
AD00583	0.824	0.208	0.845	0.240	AD00617	0.715	0.023	0.802	0.150
AD00584	0.800	0.150	0.683	0.077	AD00618	0.434	0.073	0.441	0.199
AD00585	0.387	0.059	0.488	0.151	AD00619	0.758	0.003	0.820	0.165
AD00586	0.754	0.116	0.927	0.103	AD00620	0.984	0.124	0.926	0.080
AD00587	0.921	0.074	0.923	0.052	AD00621	0.308	0.033	0.267	0.044
AD00588	0.763	0.203	0.954	0.169	AD00622	0.493	0.072	0.790	0.009
AD00589	0.838	0.115	1.026	0.216	AD00623	0.641	0.081	0.599	0.014
AD00590	0.959	0.091	0.991	0.285	AD00624	0.795	0.019	0.985	0.123
AD00591	0.970	0.172	0.984	0.244	AD00625	0.768	0.121	0.944	0.117
AD00592	0.600	0.060	0.886	0.069	AD00626	0.981	0.081	1.036	0.036
AD00593	0.555	0.097	0.883	0.130	AD00627	0.943	0.163	0.936	0.038
AD00594	0.645	0.056	0.567	0.008	AD00628	0.765	0.069	0.995	0.090
AD00595	0.812	0.132	1.076	0.285	AD00629	1.001	0.184	1.199	0.064

[0233]

AD00596	0.658	0.116	0.787	0.153	AD00630	0.963	0.149	1.154	0.141
AD00597	0.999	0.120	1.083	0.143	AD00631	0.979	0.084	1.038	0.088
AD00598	0.501	0.067	0.631	0.036	AD00632	0.781	0.048	0.858	0.101
AD00599	0.890	0.098	0.871	0.143	AD00633	0.817	0.072	1.027	0.143
AD00600	0.393	0.018	0.729	0.172	AD00634	0.807	0.087	0.978	0.256
AD00601	0.896	0.180	1.142	0.140	AD00635	0.496	0.073	0.377	0.023
AD00602	0.653	0.134	0.955	0.062	AD00636	0.615	0.102	0.748	0.072
AD00603	0.730	0.118	0.799	0.187	AD00637	0.792	0.056	1.070	0.048
AD00604	0.892	0.058	0.956	0.107					

[0234]

표 5B. LPA RNAi 물질의 시험관내 분석, LPA 발현의 저해.

듀플렉스 번호	상대 R_{luc}-LPA 발현					
	2nM		0.2nM		0.02nM	
	평균	SD	평균	SD	평균	SD
AD01068	0.780	0.110	0.792	0.326	0.861	0.138
AD01069	0.483	0.345	1.062	0.181	0.869	0.112
AD01070	0.747	0.441	1.010	0.015	1.015	0.319
AD01071	1.014	0.254	0.850	0.251	0.857	0.284
AD01072	0.919	0.107	1.137	0.345	0.727	0.124
AD01073	0.539	0.224	1.066	0.195	1.180	0.356
AD01074	0.713	0.545	0.953	0.419	0.841	0.077
AD01075	0.703	0.379	0.913	0.204	0.965	0.216
AD01076	1.145	0.485	1.027	0.287	0.647	0.154
AD01077	0.672	0.074	1.166	0.384	0.703	0.106
AD01078	0.575	0.192	0.847	0.237	0.908	0.071
AD01079	0.863	0.673	1.093	0.187	1.004	0.086
AD01328	0.623	0.089	1.205	0.367	1.238	0.089
AD01329	0.467	0.068	1.161	0.159	1.115	0.102
AD01330	1.158	0.124	0.920	0.143	1.156	0.107
AD01331	1.476	0.225	1.092	0.269	1.304	0.320
AD01332	1.145	0.109	1.100	0.454	0.941	0.510
AD01333	0.829	0.011	1.382	0.252	1.338	0.303
AD01334	0.653	0.122	1.323	0.183	1.095	0.109
AD01335	0.858	0.089	1.632	0.318	1.201	0.159
AD01336	1.019	0.081	1.724	0.353	1.008	0.072
AD01337	0.834	0.143	1.494	0.657	1.130	0.309
AD01338	1.276	0.340	0.719	0.118	0.896	0.118
AD01339	1.240	0.298	1.114	0.287	0.960	0.104
AD01340	1.055	0.423	1.272	0.136	1.338	0.299

[0235]

AD01341	1.206	0.438	1.510	0.315	1.046	0.143
AD01342	1.243	0.324	1.137	0.298	1.159	0.047
AD01343	1.113	0.140	1.045	0.151	1.108	0.094
AD01344	0.931	0.182	1.317	0.244	1.328	0.037
AD01345	0.795	0.233	0.799	0.032	1.418	0.184
AD01346	1.095	0.224	1.045	0.073	1.465	0.109
AD01347	1.122	0.021	1.209	0.161	1.153	0.159
AD01348	1.022	0.068	1.228	0.244	1.097	0.049
AD01349	0.934	0.151	1.217	0.080	1.068	0.149
AD01350	0.871	0.295	1.318	0.225	0.942	0.395
AD01351	1.414	0.065	1.121	0.180	1.029	0.049
AD01352	0.868	0.088	1.024	0.385	1.049	0.176
AD01353	1.150	0.478	1.164	0.276	0.898	0.175
AD01354	0.999	0.119	1.378	0.292	1.507	0.289
AD01355	0.943	0.092	1.066	0.268	1.411	0.113
AD01356	1.116	0.351	1.072	0.196	1.000	0.145

[0236]

표 5C. 10mM LPA RNAi 물질의 시험관내 분석, LPA 발현의 저해.

듀플렉스 번호	LPA 수준	듀플렉스 번호	LPA 수준	듀플렉스 번호	LPA 수준
AD01803	0.77 ± 0.06	AD01827	1.23 ± 0.07	AD01921	0.59 ± 0.06
AD01805	0.77 ± 0.02	AD01828	1.02 ± 0.09	AD01922	0.50 ± 0.04
AD01806	1.01 ± 0.02	AD01829	1.05 ± 0.07	AD01923	0.59 ± 0.04
AD01807	0.97 ± 0.09	AD01830	1.00 ± 0.35	AD01924	0.50 ± 0.02
AD01808	0.78 ± 0.12	AD01831	1.02 ± 0.07	AD01925	0.54 ± 0.05
AD01809	1.06 ± 0.13	AD01832	1.04 ± 0.06	AD01926	0.52 ± 0.05
AD01810	1.06 ± 0.05	AD01896	0.71 ± 0.14	AD01927	0.57 ± 0.04
AD01811	0.86 ± 0.05	AD01897	0.87 ± 0.10	AD01928	0.50 ± 0.06
AD01812	1.08 ± 0.04	AD01898	1.16 ± 0.03	AD01929	0.55 ± 0.04
AD01813	0.99 ± 0.13	AD01899	0.79 ± 0.11	AD01930	0.54 ± 0.06
AD01814	0.57 ± 0.05	AD01900	0.82 ± 0.06	AD01931	0.54 ± 0.07
AD01815	0.65 ± 0.00	AD01901	0.54 ± 0.04	AD01932	0.51 ± 0.01
AD01816	0.84 ± 0.08	AD01902	0.62 ± 0.00	AD01933	0.56 ± 0.06
AD01817	0.75 ± 0.10	AD01903	0.66 ± 0.08	AD01934	0.52 ± 0.08
AD01818	0.94 ± 0.07	AD01912	0.59 ± 0.01	AD01935	0.58 ± 0.03
AD01819	1.21 ± 0.08	AD01913	0.60 ± 0.04	AD01936	0.53 ± 0.02
AD01820	1.22 ± 0.12	AD01914	0.50 ± 0.03	AD01937	0.57 ± 0.04
AD01821	1.16 ± 0.01	AD01915	0.58 ± 0.08	AD01938	0.58 ± 0.03
AD01822	1.22 ± 0.04	AD01916	0.49 ± 0.04	AD01939	0.65 ± 0.05
AD01823	0.91 ± 0.05	AD01917	0.53 ± 0.04	AD01940	0.49 ± 0.03
AD01824	1.22 ± 0.13	AD01918	0.47 ± 0.04	AD01941	0.57 ± 0.02
AD01825	1.25 ± 0.05	AD01919	0.60 ± 0.02		
AD01826	1.18 ± 0.15	AD01920	0.60 ± 0.03		

[0237]

표 5D. 1mM LPA RNAi 물질의 시험관내 분석, LPA 발현의 저해.

듀플렉스 번호	LPA 수준	듀플렉스 번호	LPA 수준	듀플렉스 번호	LPA 수준
AD01760	0.10 ± 0.01	AD02330	0.37 ± 0.01	AD02090	0.68 ± 0.04
AD01722	0.14 ± 0.01	AD02243	0.37 ± 0.02	AD02161	0.68 ± 0.04
AD01757	0.15 ± 0.00	AD02255	0.38 ± 0.02	AD02324	0.68 ± 0.02
AD01719	0.15 ± 0.00	AD02257	0.38 ± 0.00	AD02177	0.69 ± 0.07
AD01738	0.18 ± 0.01	AD02169	0.38 ± 0.02	AD02179	0.69 ± 0.07
AD01755	0.19 ± 0.01	AD02081	0.38 ± 0.00	AD02527	0.69 ± 0.03
AD01741	0.20 ± 0.00	AD02186	0.38 ± 0.02	AD02305	0.69 ± 0.06
AD01759	0.23 ± 0.02	AD01744	0.38 ± 0.03	AD02092	0.70 ± 0.02
AD01747	0.23 ± 0.03	AD02075	0.38 ± 0.01	AD02535	0.70 ± 0.10
AD01752	0.24 ± 0.03	AD02135	0.38 ± 0.03	AD02376	0.71 ± 0.04
AD01736	0.24 ± 0.02	AD02114	0.38 ± 0.04	AD01743	0.71 ± 0.02
AD02311	0.25 ± 0.05	AD02188	0.38 ± 0.04	AD02289	0.71 ± 0.04
AD02201	0.25 ± 0.03	AD02318	0.38 ± 0.02	AD02530	0.71 ± 0.06
AD01750	0.25 ± 0.00	AD02388	0.38 ± 0.02	AD01709	0.71 ± 0.12
AD01756	0.25 ± 0.01	AD02115	0.38 ± 0.04	AD02249	0.71 ± 0.06
AD02291	0.25 ± 0.03	AD02133	0.38 ± 0.00	AD02534	0.71 ± 0.03
AD02292	0.26 ± 0.01	AD02183	0.38 ± 0.04	AD02213	0.71 ± 0.02
AD02266	0.26 ± 0.02	AD02116	0.38 ± 0.02	AD02529	0.71 ± 0.03
AD01763	0.26 ± 0.01	AD02132	0.39 ± 0.03	AD01711	0.71 ± 0.06
AD02259	0.26 ± 0.03	AD02400	0.39 ± 0.02	AD02341	0.72 ± 0.06
AD02327	0.26 ± 0.02	AD02338	0.39 ± 0.04	AD02233	0.72 ± 0.06
AD02274	0.27 ± 0.03	AD02112	0.39 ± 0.01	AD02342	0.73 ± 0.04
AD02297	0.27 ± 0.02	AD02354	0.39 ± 0.05	AD02395	0.73 ± 0.06
AD02147	0.27 ± 0.03	AD01749	0.40 ± 0.06	AD02306	0.73 ± 0.09
AD02365	0.27 ± 0.04	AD02312	0.40 ± 0.02	AD02344	0.73 ± 0.04
AD02260	0.27 ± 0.03	AD02240	0.40 ± 0.00	AD02145	0.74 ± 0.09

[0238]

AD02368	0.27 ± 0.01	AD02313	0.40 ± 0.03	AD02326	0.74 ± 0.06
AD02265	0.28 ± 0.03	AD01710	0.40 ± 0.05	AD02414	0.74 ± 0.04
AD02293	0.28 ± 0.04	AD02301	0.40 ± 0.05	AD02379	0.74 ± 0.06
AD02350	0.28 ± 0.02	AD02425	0.40 ± 0.04	AD02532	0.75 ± 0.04
AD02202	0.28 ± 0.03	AD02099	0.41 ± 0.04	AD02178	0.75 ± 0.11
AD02203	0.28 ± 0.03	AD01723	0.41 ± 0.04	AD02195	0.75 ± 0.05
AD02258	0.28 ± 0.05	AD02391	0.41 ± 0.03	AD02123	0.76 ± 0.07
AD02295	0.28 ± 0.03	AD02392	0.41 ± 0.05	AD02164	0.77 ± 0.09
AD02363	0.28 ± 0.04	AD02083	0.41 ± 0.01	AD01726	0.77 ± 0.01
AD02273	0.28 ± 0.02	AD02155	0.41 ± 0.02	AD02231	0.77 ± 0.05
AD02386	0.28 ± 0.02	AD02082	0.41 ± 0.01	AD02180	0.77 ± 0.04
AD02309	0.28 ± 0.03	AD02336	0.41 ± 0.01	AD02412	0.77 ± 0.05
AD02382	0.29 ± 0.01	AD02101	0.41 ± 0.02	AD02251	0.77 ± 0.02
AD02256	0.29 ± 0.02	AD01728	0.42 ± 0.01	AD02396	0.78 ± 0.13
AD02367	0.29 ± 0.03	AD02424	0.42 ± 0.04	AD02160	0.78 ± 0.04
AD02275	0.29 ± 0.04	AD02175	0.42 ± 0.02	AD02533	0.78 ± 0.05
AD02206	0.29 ± 0.01	AD02225	0.42 ± 0.05	AD02290	0.78 ± 0.03
AD02332	0.29 ± 0.02	AD02086	0.43 ± 0.02	AD02378	0.78 ± 0.07
AD01717	0.29 ± 0.03	AD01725	0.43 ± 0.06	AD02394	0.79 ± 0.04
AD02296	0.29 ± 0.01	AD02374	0.43 ± 0.03	AD02415	0.79 ± 0.05
AD02264	0.29 ± 0.03	AD02390	0.43 ± 0.04	AD02181	0.79 ± 0.08
AD02278	0.29 ± 0.03	AD02227	0.43 ± 0.02	AD02492	0.79 ± 0.06
AD02385	0.29 ± 0.00	AD02137	0.43 ± 0.06	AD02397	0.79 ± 0.05
AD02205	0.29 ± 0.04	AD02085	0.43 ± 0.01	AD02398	0.79 ± 0.09
AD02149	0.29 ± 0.02	AD02407	0.43 ± 0.03	AD02416	0.79 ± 0.04
AD02239	0.30 ± 0.05	AD02100	0.44 ± 0.04	AD02144	0.79 ± 0.09
AD01748	0.30 ± 0.02	AD02406	0.44 ± 0.04	AD02531	0.79 ± 0.06
AD02404	0.30 ± 0.01	AD02136	0.44 ± 0.02	AD02489	0.80 ± 0.04
AD01721	0.30 ± 0.03	AD02209	0.44 ± 0.03	AD02307	0.80 ± 0.10

[0239]

AD02277	0.30 ± 0.05	AD02154	0.44 ± 0.02	AD02308	0.80 ± 0.11
AD02152	0.30 ± 0.01	AD02171	0.44 ± 0.01	AD02182	0.80 ± 0.08
AD02237	0.30 ± 0.02	AD02261	0.45 ± 0.02	AD02198	0.80 ± 0.11
AD02098	0.30 ± 0.03	AD02271	0.45 ± 0.00	AD02199	0.80 ± 0.10
AD02381	0.30 ± 0.02	AD02371	0.45 ± 0.03	AD02200	0.80 ± 0.06
AD02315	0.30 ± 0.02	AD02173	0.45 ± 0.07	AD02125	0.81 ± 0.06
AD02366	0.30 ± 0.01	AD02319	0.45 ± 0.01	AD02141	0.81 ± 0.01
AD02242	0.31 ± 0.03	AD02176	0.46 ± 0.01	AD02516	0.81 ± 0.06
AD02294	0.31 ± 0.02	AD02428	0.46 ± 0.02	AD02127	0.81 ± 0.06
AD02346	0.31 ± 0.04	AD02410	0.46 ± 0.01	AD02380	0.81 ± 0.03
AD02329	0.31 ± 0.02	AD01746	0.46 ± 0.05	AD02124	0.81 ± 0.05
AD02348	0.31 ± 0.01	AD01732	0.46 ± 0.02	AD02197	0.81 ± 0.02
AD01714	0.31 ± 0.05	AD02157	0.47 ± 0.02	AD02159	0.81 ± 0.09
AD01724	0.31 ± 0.01	AD02372	0.47 ± 0.03	AD02485	0.82 ± 0.04
AD02170	0.31 ± 0.02	AD02427	0.47 ± 0.02	AD02142	0.82 ± 0.08
AD02352	0.31 ± 0.02	AD02370	0.47 ± 0.01	AD02126	0.82 ± 0.08
AD02093	0.31 ± 0.01	AD02172	0.47 ± 0.04	AD02254	0.82 ± 0.10
AD02383	0.31 ± 0.02	AD02158	0.47 ± 0.02	AD02232	0.82 ± 0.04
AD02284	0.31 ± 0.04	AD02270	0.48 ± 0.04	AD02146	0.82 ± 0.04
AD02219	0.31 ± 0.04	AD02426	0.48 ± 0.04	AD02490	0.82 ± 0.03
AD02279	0.31 ± 0.03	AD02361	0.48 ± 0.04	AD01745	0.82 ± 0.09
AD02299	0.31 ± 0.05	AD02245	0.48 ± 0.02	AD02162	0.83 ± 0.04
AD01740	0.31 ± 0.02	AD02373	0.48 ± 0.01	AD02471	0.83 ± 0.11
AD02417	0.32 ± 0.01	AD02084	0.48 ± 0.05	AD02487	0.83 ± 0.09
AD02364	0.32 ± 0.02	AD02194	0.48 ± 0.03	AD02523	0.83 ± 0.10
AD02262	0.32 ± 0.03	AD01753	0.48 ± 0.06	AD02483	0.83 ± 0.03
AD02369	0.32 ± 0.01	AD02320	0.48 ± 0.03	AD02128	0.84 ± 0.09
AD01731	0.32 ± 0.02	AD02268	0.48 ± 0.05	AD02143	0.84 ± 0.05
AD02349	0.32 ± 0.01	AD02226	0.49 ± 0.01	AD02214	0.84 ± 0.13

[0240]

AD02095	0.32 ± 0.02	AD02156	0.49 ± 0.01	AD02217	0.84 ± 0.07
AD02281	0.32 ± 0.01	AD02409	0.49 ± 0.03	AD02250	0.84 ± 0.08
AD02224	0.32 ± 0.06	AD02244	0.49 ± 0.02	AD02163	0.85 ± 0.04
AD02148	0.32 ± 0.04	AD02189	0.49 ± 0.06	AD02525	0.85 ± 0.06
AD01718	0.33 ± 0.01	AD01764	0.50 ± 0.02	AD02481	0.85 ± 0.03
AD02333	0.33 ± 0.01	AD02174	0.50 ± 0.04	AD02235	0.85 ± 0.03
AD02403	0.33 ± 0.01	AD02117	0.50 ± 0.01	AD02539	0.86 ± 0.05
AD02317	0.33 ± 0.03	AD02208	0.50 ± 0.05	AD02470	0.86 ± 0.07
AD02399	0.33 ± 0.02	AD02104	0.51 ± 0.03	AD02469	0.86 ± 0.04
AD02222	0.33 ± 0.01	AD02408	0.51 ± 0.06	AD02480	0.86 ± 0.07
AD02310	0.33 ± 0.02	AD02272	0.51 ± 0.04	AD02488	0.87 ± 0.05
AD01733	0.33 ± 0.01	AD02122	0.51 ± 0.06	AD02511	0.87 ± 0.05
AD02131	0.33 ± 0.01	AD02140	0.51 ± 0.04	AD02482	0.87 ± 0.04
AD02353	0.33 ± 0.03	AD02362	0.51 ± 0.04	AD02519	0.87 ± 0.08
AD02263	0.33 ± 0.03	AD01739	0.52 ± 0.04	AD02491	0.88 ± 0.05
AD02204	0.33 ± 0.01	AD02121	0.52 ± 0.06	AD02216	0.88 ± 0.00
AD02080	0.33 ± 0.00	AD02138	0.52 ± 0.04	AD02215	0.88 ± 0.03
AD02298	0.33 ± 0.03	AD02358	0.52 ± 0.02	AD02468	0.88 ± 0.06
AD01737	0.33 ± 0.01	AD01734	0.53 ± 0.06	AD02526	0.88 ± 0.06
AD02220	0.33 ± 0.04	AD01713	0.53 ± 0.04	AD02234	0.88 ± 0.14
AD02302	0.33 ± 0.00	AD02285	0.53 ± 0.03	AD02518	0.89 ± 0.05
AD02097	0.33 ± 0.00	AD02102	0.53 ± 0.07	AD02218	0.89 ± 0.04
AD02328	0.33 ± 0.02	AD02303	0.53 ± 0.03	AD02515	0.89 ± 0.03
AD02221	0.33 ± 0.01	AD02212	0.53 ± 0.01	AD02536	0.89 ± 0.11
AD02421	0.33 ± 0.02	AD02139	0.53 ± 0.03	AD02537	0.89 ± 0.04
AD02420	0.33 ± 0.03	AD02230	0.54 ± 0.08	AD02465	0.89 ± 0.07
AD02347	0.33 ± 0.04	AD02103	0.54 ± 0.04	AD02196	0.90 ± 0.03
AD02134	0.34 ± 0.01	AD02191	0.54 ± 0.03	AD02253	0.90 ± 0.05
AD02078	0.34 ± 0.03	AD02429	0.54 ± 0.02	AD02484	0.90 ± 0.09

[0241]

AD02151	0.34 ± 0.02	AD01716	0.54 ± 0.09	AD02467	0.91 ± 0.00
AD02238	0.34 ± 0.03	AD02360	0.54 ± 0.02	AD02538	0.91 ± 0.10
AD02168	0.34 ± 0.00	AD01762	0.54 ± 0.01	AD02478	0.91 ± 0.01
AD02096	0.34 ± 0.03	AD01735	0.55 ± 0.07	AD02479	0.92 ± 0.05
AD01758	0.34 ± 0.05	AD02248	0.55 ± 0.05	AD02540	0.92 ± 0.08
AD02077	0.34 ± 0.02	AD02193	0.55 ± 0.01	AD02524	0.92 ± 0.03
AD02345	0.34 ± 0.02	AD02119	0.55 ± 0.01	AD02466	0.92 ± 0.05
AD02384	0.34 ± 0.02	AD02287	0.55 ± 0.02	AD02520	0.92 ± 0.06
AD02094	0.34 ± 0.01	AD02357	0.56 ± 0.01	AD02498	0.92 ± 0.06
AD02419	0.34 ± 0.04	AD01708	0.57 ± 0.06	AD02472	0.92 ± 0.05
AD02401	0.34 ± 0.02	AD02247	0.57 ± 0.06	AD02106	0.93 ± 0.08
AD02402	0.34 ± 0.03	AD02430	0.58 ± 0.07	AD02486	0.93 ± 0.02
AD01712	0.34 ± 0.04	AD02339	0.58 ± 0.03	AD02236	0.93 ± 0.04
AD02276	0.34 ± 0.01	AD02321	0.59 ± 0.03	AD02543	0.93 ± 0.12
AD02150	0.34 ± 0.02	AD02269	0.59 ± 0.02	AD02517	0.94 ± 0.05
AD02166	0.34 ± 0.03	AD02210	0.59 ± 0.04	AD02505	0.94 ± 0.10
AD02351	0.34 ± 0.02	AD02211	0.60 ± 0.02	AD02464	0.94 ± 0.06
AD02241	0.35 ± 0.04	AD02091	0.60 ± 0.03	AD02499	0.94 ± 0.16
AD02282	0.35 ± 0.01	AD02120	0.60 ± 0.07	AD02500	0.94 ± 0.05
AD02130	0.35 ± 0.04	AD02229	0.60 ± 0.03	AD02544	0.95 ± 0.07
AD01751	0.35 ± 0.03	AD01727	0.60 ± 0.02	AD02541	0.95 ± 0.15
AD02356	0.35 ± 0.03	AD01730	0.60 ± 0.02	AD02509	0.95 ± 0.09
AD02405	0.35 ± 0.04	AD02190	0.60 ± 0.07	AD02508	0.95 ± 0.10
AD02129	0.35 ± 0.01	AD02411	0.60 ± 0.06	AD02510	0.95 ± 0.03
AD02355	0.35 ± 0.01	AD02322	0.61 ± 0.03	AD02521	0.96 ± 0.16
AD02423	0.35 ± 0.06	AD02433	0.61 ± 0.02	AD02507	0.96 ± 0.03
AD02316	0.35 ± 0.02	AD01761	0.62 ± 0.05	AD02105	0.96 ± 0.09
AD02331	0.35 ± 0.02	AD01720	0.62 ± 0.02	AD02495	0.96 ± 0.05
AD02335	0.35 ± 0.01	AD02228	0.62 ± 0.06	AD02504	0.97 ± 0.04

[0242]

AD02187	0.35 ± 0.03	AD02393	0.62 ± 0.03	AD02493	0.97 ± 0.06
AD02314	0.36 ± 0.04	AD02359	0.62 ± 0.03	AD02542	0.97 ± 0.06
AD02300	0.36 ± 0.03	AD02323	0.62 ± 0.05	AD02503	0.98 ± 0.05
AD02387	0.36 ± 0.06	AD02118	0.63 ± 0.05	AD02107	0.98 ± 0.05
AD02337	0.36 ± 0.04	AD02286	0.63 ± 0.04	AD02477	0.98 ± 0.06
AD01729	0.36 ± 0.01	AD02087	0.63 ± 0.04	AD02501	0.98 ± 0.07
AD02283	0.36 ± 0.02	AD01715	0.63 ± 0.06	AD02497	0.98 ± 0.05
AD02185	0.36 ± 0.01	AD02192	0.63 ± 0.02	AD02494	0.98 ± 0.13
AD02167	0.36 ± 0.01	AD02431	0.64 ± 0.06	AD02475	1.00 ± 0.07
AD02076	0.36 ± 0.04	AD02340	0.64 ± 0.03	AD02514	1.00 ± 0.00
AD02418	0.36 ± 0.01	AD02432	0.64 ± 0.02	AD02474	1.00 ± 0.03
AD02422	0.36 ± 0.03	AD02089	0.65 ± 0.07	AD02502	1.01 ± 0.01
AD02111	0.36 ± 0.02	AD02267	0.65 ± 0.11	AD02522	1.01 ± 0.04
AD02079	0.37 ± 0.02	AD02246	0.65 ± 0.07	AD02476	1.01 ± 0.09
AD01754	0.37 ± 0.04	AD02325	0.65 ± 0.03	AD02513	1.02 ± 0.03
AD02334	0.37 ± 0.02	AD02343	0.66 ± 0.05	AD02109	1.02 ± 0.06
AD02280	0.37 ± 0.05	AD02375	0.66 ± 0.04	AD02252	1.02 ± 0.08
AD02113	0.37 ± 0.03	AD02288	0.66 ± 0.06	AD02496	1.04 ± 0.05
AD02389	0.37 ± 0.03	AD02088	0.66 ± 0.01	AD02473	1.05 ± 0.04
AD02223	0.37 ± 0.04	AD02413	0.66 ± 0.03	AD02506	1.05 ± 0.05
AD02184	0.37 ± 0.02	AD02377	0.67 ± 0.05	AD01742	1.07 ± 0.24
AD02153	0.37 ± 0.02	AD02528	0.67 ± 0.04	AD02110	1.08 ± 0.07
AD02165	0.37 ± 0.02	AD02434	0.67 ± 0.05	AD02512	1.09 ± 0.17
AD02207	0.37 ± 0.01	AD02304	0.67 ± 0.02	AD02108	1.11 ± 0.04

[0243]

[0244] 실시예 3. *LPA RNAi 물질 EC_{50} 결정*. 150fM-3nM의 범위의 LPA RNAi 물질 농도에 의해 동일한 세포 및 형질감염 조건을 이용하여 10점 EC_{50} 곡선을 생성하였다. 그래프패드 프리즘(GraphPad Prism) 소프트웨어를 이용하여 EC_{50}을 결정하였다(표 6).

표 6. 표시된 LPA RNAi 물질에 대한 시험관내 결정된 EC50 값(nM).

듀플렉스 번호	EC_{50}(nM)	듀플렉스 번호	EC_{50}(nM)
AD00575	0.073	AD00635	0.577
AD00576	0.038	AD01070	0.6388
AD00578	0.112	AD01072	0.1068
AD00579	0.083	AD01073	0.1154
AD00621	0.100	AD01074	0.2903

[0245]

[0246] 실시예 4. *구조-활성 관계(Structure-Activity Relationship: SAR) 설계된 LPA RNAi 물질의 시험관내 분석*. LPA RNAi 물질 SAR 세트(AD01532에 기초한 364개의 서열 및 AD01533에 기초한 351개의 서열)를 합성하고, 시험관내 효율에 대해 스크리닝하였다. 스크리닝 목적을 위해, KIV-3으로부터 KIV-9로의 인간 LPA cDNA 서열의 2756bp(수탁 번호 NM_005577.1)를 합성하고, psiCHECK2(Promega(위스콘신주 매디슨))인, 상업적으로 구입 가능한 리포터 기반 스크리닝 플라스미드로 클로닝하고(GeneWiz(뉴저지주 사우스 플레인필드)), 이 플라스미드는 레닐라 루시퍼라제/LPA 융합 mRNA를 생성하였다. 인간 배경에서의 LPA RNAi 물질 효율을 위해, 인간 간세포 암종 세포주인 HuH7 세포를 96웰 포맷에서 웰마다 약 7500개의 세포로 플레이팅하였다. 각각의 LPA RNAi 물질을 웰마

다 25ng의 LPA-psiCHECK2 플라스미드 DNA 및 웰마다 0.2㎕ 리포펙타민 2000과 함께 2의 농도(1nM 및 0.1nM, 또는 10nM 및 1nM)에서 동시형질감염시켰다. 이중 루시퍼라제 리포터 검정(Promega(미국 위스콘신주 매디슨))을 이용하여 psiCHECK2 플라스미드에 또한 존재하는 구성적으로 발현된 반딧불이 루시퍼라제의 수준으로 정규화된 레닐라 루시퍼라제 수준을 측정함으로써 유전자 넉다운을 결정하였다(표 7A 및 표 7B).

표 7A. 이중 루시퍼라제 리포터 검정에 의해 결정된 바와 같은, 시험관내 LPA RNAi 물질의 효율 스크린 결과.

듀플렉스 번호	상대 R_{luc}-LPA 발현		듀플렉스 번호	상대 R_{luc}-LPA 발현	
	1nM	0.1nM		1nM	0.1nM
SD0001	0.570	0.907	SD0117	0.946	1.021
SD0002	0.873	1.061	SD0118	0.879	0.977
SD0003	0.955	1.020	SD0119	0.963	1.016
SD0004	0.845	1.007	SD0120	0.967	0.948
SD0005	0.603	0.891	SD0121	0.651	0.897
SD0006	0.551	0.780	SD0122	1.085	1.111
SD0007	0.510	0.797	SD0123	1.153	1.052
SD0008	0.544	0.892	SD0124	0.955	0.936
SD0009	0.564	0.878	SD0125	0.928	0.928
SD0010	0.542	1.051	SD0126	1.033	0.933
SD0011	0.513	0.873	SD0127	0.637	0.717
SD0012	0.533	0.963	SD0128	0.630	0.653
SD0013	0.541	0.979	SD0129	1.052	1.192
SD0014	0.551	0.987	SD0130	1.025	1.107
SD0015	0.488	0.951	SD0131	1.280	1.059
SD0016	0.588	0.868	SD0132	1.094	1.024
SD0017	1.023	1.005	SD0133	1.113	1.031
SD0018	0.866	0.965	SD0134	0.928	0.991
SD0019	0.792	1.005	SD0135	0.804	1.023
SD0020	0.633	0.860	SD0136	1.028	1.104
SD0021	0.572	0.797	SD0137	0.902	1.149
SD0022	0.610	0.874	SD0138	0.942	1.015
SD0023	0.550	0.836	SD0139	0.984	1.068
SD0024	0.597	0.859	SD0140	0.953	1.091

[0247]

SD0025	0.587	0.899	SD0141	0.925	1.022
SD0026	0.570	0.898	SD0142	0.906	0.994
SD0027	0.580	0.825	SD0143	0.898	0.990
SD0028	0.612	0.885	SD0144	0.858	0.972
SD0029	0.528	0.866	SD0145	0.917	0.947
SD0030	0.657	0.825	SD0146	0.850	0.906
SD0031	0.560	0.914	SD0147	0.933	0.995
SD0032	0.664	0.976	SD0148	0.856	0.994
SD0033	0.787	1.035	SD0149	0.882	0.985
SD0034	0.739	1.002	SD0150	0.810	1.002
SD0035	0.658	0.949	SD0151	0.813	0.909
SD0036	0.554	0.896	SD0152	0.963	1.031
SD0037	0.557	0.873	SD0153	1.058	0.936
SD0038	0.528	0.854	SD0154	0.968	0.944
SD0039	0.511	0.847	SD0155	0.969	0.940
SD0040	0.554	0.976	SD0156	0.933	0.807
SD0041	0.559	0.823	SD0157	0.906	0.913
SD0042	0.496	0.825	SD0158	0.926	0.964
SD0043	0.563	0.851	SD0159	0.805	0.850
SD0044	0.476	0.861	SD0160	0.895	0.965
SD0045	0.542	0.841	SD0161	0.865	1.006
SD0046	0.651	0.980	SD0162	0.935	1.029
SD0047	0.967	0.995	SD0163	0.928	0.985
SD0048	0.694	0.936	SD0164	0.920	0.957
SD0049	0.960	0.946	SD0165	1.039	1.110
SD0050	0.692	0.971	SD0166	1.061	1.023
SD0051	0.611	0.905	SD0167	1.020	0.982
SD0052	0.657	0.849	SD0168	1.053	0.989

[0248]

SD0053	0.642	0.848	SD0169	1.002	1.018
SD0054	0.598	0.852	SD0170	1.078	0.982
SD0055	0.494	0.828	SD0171	0.838	0.923
SD0056	0.524	0.885	SD0172	1.025	0.934
SD0057	0.582	0.816	SD0173	0.864	0.963
SD0058	0.597	0.866	SD0174	1.020	1.043
SD0059	0.560	0.905	SD0175	1.128	1.046
SD0060	0.594	0.849	SD0176	1.009	1.110
SD0061	0.571	1.058	SD0177	0.735	0.975
SD0062	0.871	1.157	SD0178	0.824	1.074
SD0063	0.969	1.138	SD0179	0.690	0.895
SD0064	0.555	1.019	SD0180	0.572	0.914
SD0065	0.671	0.953	SD0181	0.904	1.028
SD0066	0.561	0.951	SD0182	1.176	1.093
SD0067	0.612	0.904	SD0183	1.247	1.090
SD0068	0.573	0.938	SD0184	1.097	0.974
SD0069	0.574	0.975	SD0185	1.045	0.985
SD0070	0.606	1.030	SD0186	0.940	0.943
SD0071	0.494	0.959	SD0187	0.883	0.994
SD0072	0.557	0.892	SD0188	ND	ND
SD0073	0.593	0.984	SD0189	0.872	0.977
SD0074	0.544	0.894	SD0190	0.861	1.166
SD0075	0.552	0.937	SD0191	0.779	1.044
SD0076	0.513	1.058	SD0192	0.796	1.116
SD0077	0.930	1.071	SD0193	0.975	1.112
SD0078	0.984	1.006	SD0194	0.876	1.058
SD0079	0.853	1.031	SD0195	0.747	0.970
SD0080	0.577	0.942	SD0196	0.787	1.086

[0249]

SD0081	0.595	1.044	SD0197	1.276	1.127
SD0082	0.652	0.962	SD0198	1.144	1.140
SD0083	0.583	0.928	SD0199	1.136	1.101
SD0084	0.540	1.049	SD0200	0.814	0.911
SD0085	0.523	0.961	SD0201	0.733	0.915
SD0086	0.536	0.956	SD0202	0.576	0.933
SD0087	0.586	0.987	SD0203	0.593	0.824
SD0088	0.563	0.892	SD0204	0.882	1.038
SD0089	0.555	0.947	SD0205	0.681	1.012
SD0090	0.599	0.928	SD0206	0.600	0.927
SD0091	0.665	0.854	SD0207	0.738	0.974
SD0092	1.002	0.917	SD0208	0.638	0.883
SD0093	1.047	0.880	SD0209	0.641	0.878
SD0094	0.867	0.911	SD0210	0.544	0.886
SD0095	0.919	0.868	SD0211	0.702	0.920
SD0096	0.666	0.887	SD0212	0.704	0.854
SD0097	0.673	0.737	SD0213	0.655	0.887
SD0098	0.567	0.809	SD0214	0.629	0.860
SD0099	0.604	0.909	SD0215	0.598	0.850
SD0100	0.557	0.880	SD0216	0.611	0.782
SD0101	0.545	0.806	SD0217	0.710	0.806
SD0102	0.728	0.900	SD0218	0.738	0.758
SD0103	0.719	0.928	SD0219	0.664	0.809
SD0104	0.766	0.955	SD0220	1.133	0.891
SD0105	0.965	0.927	SD0221	0.940	0.914
SD0106	1.161	1.006	SD0222	0.853	0.882
SD0107	1.048	0.966	SD0223	0.691	0.889
SD0108	1.066	0.985	SD0224	0.997	1.033

[0250]

SD0109	1.111	0.917	SD0225	0.954	0.998
SD0110	1.152	0.954	SD0226	1.202	0.997
SD0111	1.045	0.944	SD0227	0.948	1.017
SD0112	1.089	1.019	SD0228	0.786	0.947
SD0113	0.949	0.935	SD0229	0.620	0.830
SD0114	0.875	1.033	SD0230	0.840	0.972
SD0115	1.022	1.077	SD0231	0.904	0.890
SD0116	0.947	1.028			

[0251]

표 7B. 이중 루시퍼라제 리포터 검정에 의해 결정된 바와 같은, 시험관내 LPA RNAi 물질의 효율 스크린 결과.

듀플렉스 번호	상대 R_{luc}-LPA 발현		듀플렉스 번호	상대 R_{luc}-LPA 발현	
	10nM	1nM		10nM	1nM
SD0232	0.659	0.699	SD0474	0.621	0.598
SD0233	0.942	1.252	SD0475	0.564	0.472
SD0234	0.967	1.358	SD0476	0.769	0.631
SD0235	0.910	0.890	SD0477	0.734	0.613
SD0236	0.742	0.822	SD0478	0.460	0.411
SD0237	0.758	0.831	SD0479	0.713	0.802
SD0238	0.700	0.737	SD0480	0.883	0.892
SD0239	0.645	0.765	SD0481	0.926	0.899
SD0240	0.701	0.773	SD0482	1.180	0.937
SD0241	0.770	0.821	SD0483	0.805	0.986
SD0242	0.626	0.719	SD0484	0.920	1.104
SD0243	0.759	0.848	SD0485	0.510	0.524
SD0244	0.798	0.953	SD0486	0.626	0.598
SD0245	0.764	0.821	SD0487	0.628	0.640
SD0246	0.812	0.690	SD0488	0.597	0.637
SD0247	0.786	0.844	SD0489	0.482	0.486
SD0248	1.011	1.167	SD0490	0.685	0.664
SD0249	1.118	1.189	SD0491	0.650	0.662
SD0250	1.021	1.239	SD0492	0.454	0.490
SD0251	1.041	1.151	SD0493	1.006	1.040
SD0252	1.070	1.124	SD0494	0.933	1.024
SD0253	1.044	1.131	SD0495	0.927	1.016
SD0254	0.861	0.948	SD0496	0.921	1.004
SD0255	0.751	0.829	SD0497	0.690	0.846

[0252]

SD0256	0.931	1.037	SD0498	0.970	0.913
SD0257	1.024	1.037	SD0499	0.448	0.399
SD0258	0.935	1.030	SD0500	0.614	0.485
SD0259	1.089	1.081	SD0501	0.609	0.521
SD0260	0.955	1.008	SD0502	0.626	0.526
SD0261	0.923	0.980	SD0503	0.493	0.410
SD0262	0.908	1.107	SD0504	0.727	0.551
SD0263	1.060	1.449	SD0505	0.688	0.541
SD0264	1.041	1.419	SD0506	0.319	0.338
SD0265	1.065	1.373	SD0507	0.927	0.897
SD0266	0.950	1.376	SD0508	0.929	0.972
SD0267	0.963	1.214	SD0509	0.853	0.925
SD0268	1.023	1.299	SD0510	0.755	0.935
SD0269	0.908	1.066	SD0511	0.480	0.559
SD0270	0.963	1.081	SD0512	0.834	0.854
SD0271	1.088	1.189	SD0513	0.440	0.323
SD0272	0.966	1.135	SD0514	0.415	0.414
SD0273	0.953	1.192	SD0515	0.442	0.343
SD0274	1.049	1.217	SD0516	0.422	0.341
SD0275	1.006	1.206	SD0517	0.346	0.320
SD0276	0.969	1.064	SD0518	0.488	0.420
SD0277	0.686	0.796	SD0519	0.435	0.390
SD0278	0.985	1.305	SD0520	0.819	0.737
SD0279	0.985	1.301	SD0521	1.058	0.903
SD0280	0.978	1.237	SD0522	1.088	0.933
SD0281	1.038	1.230	SD0523	1.075	0.948
SD0282	0.933	1.191	SD0524	1.067	0.900
SD0283	0.930	1.152	SD0525	0.917	0.858
SD0284	0.907	1.117	SD0526	1.126	1.055

[0253]

SD0285	0.625	0.870	SD0527	0.832	0.776
SD0286	0.984	1.056	SD0528	0.980	0.886
SD0287	0.906	0.965	SD0529	1.059	0.821
SD0288	1.052	1.123	SD0530	0.934	0.844
SD0289	0.997	1.215	SD0531	0.832	0.883
SD0290	0.892	1.197	SD0532	0.936	0.868
SD0291	0.907	1.065	SD0533	0.900	0.946
SD0292	0.689	0.862	SD0534	1.012	0.984
SD0293	0.955	1.190	SD0535	1.041	1.095
SD0294	1.095	1.157	SD0536	1.113	1.097
SD0295	0.851	1.004	SD0537	1.125	0.957
SD0296	1.018	1.106	SD0538	1.059	1.162
SD0297	0.737	0.760	SD0539	0.901	0.963
SD0298	0.790	0.828	SD0540	0.900	0.924
SD0299	0.721	0.713	SD0541	1.033	0.911
SD0300	0.796	0.869	SD0542	0.958	0.906
SD0301	0.781	0.841	SD0543	0.870	0.816
SD0302	0.621	0.720	SD0544	1.100	0.853
SD0303	0.684	0.852	SD0545	0.881	0.794
SD0304	0.774	0.842	SD0546	0.897	0.813
SD0305	0.778	0.799	SD0547	1.005	0.785
SD0306	0.718	0.793	SD0548	0.972	0.866
SD0307	0.982	0.883	SD0549	1.019	1.121
SD0308	1.297	1.193	SD0550	0.986	1.015
SD0309	1.123	1.208	SD0551	0.966	1.033
SD0310	0.961	1.073	SD0552	0.893	1.028
SD0311	1.168	1.019	SD0553	0.976	0.998
SD0312	0.923	0.824	SD0554	0.938	0.935
SD0313	0.883	0.871	SD0555	0.886	0.875

[0254]

[0255]

SD0314	0.670	0.650	SD0556	1.181	1.142
SD0315	0.988	0.958	SD0557	1.016	0.999
SD0316	0.908	0.880	SD0558	1.026	0.968
SD0317	0.754	0.850	SD0559	0.928	0.844
SD0318	0.963	0.944	SD0560	0.990	0.805
SD0319	0.945	0.862	SD0561	0.836	0.791
SD0320	0.961	0.875	SD0562	1.021	0.772
SD0321	0.841	0.797	SD0563	0.886	0.946
SD0322	0.546	0.521	SD0564	1.194	1.254
SD0323	0.581	0.895	SD0565	1.010	1.033
SD0324	0.692	0.900	SD0566	1.110	0.993
SD0325	0.506	0.796	SD0567	0.995	0.895
SD0326	0.634	0.709	SD0568	0.964	0.901
SD0327	0.522	0.592	SD0569	0.853	0.876
SD0328	0.602	0.632	SD0570	0.832	0.860
SD0329	0.504	0.615	SD0571	1.036	0.959
SD0330	0.445	0.601	SD0572	1.013	0.902
SD0331	0.457	0.579	SD0573	0.948	0.793
SD0332	0.500	0.601	SD0574	0.868	0.812
SD0333	0.447	0.618	SD0575	0.946	0.712
SD0334	0.490	0.528	SD0576	0.922	0.774
SD0335	0.421	0.555	SD0577	0.824	0.800
SD0336	0.488	0.533	SD0578	0.997	0.950
SD0337	1.714	0.978	SD0579	1.048	1.143
SD0338	1.262	1.350	SD0580	1.071	0.935
SD0339	1.259	1.357	SD0581	0.987	0.869
SD0340	0.996	1.277	SD0582	0.946	0.816
SD0341	1.190	1.183	SD0583	0.932	0.789
SD0342	0.818	0.923	SD0584	1.062	0.866

SD0343	0.803	0.855	SD0585	1.155	0.891
SD0344	0.708	0.883	SD0586	0.960	0.819
SD0345	1.132	0.901	SD0587	0.934	0.832
SD0346	0.847	0.890	SD0588	1.033	0.781
SD0347	0.659	0.780	SD0589	0.972	0.798
SD0348	0.730	0.945	SD0590	0.925	0.704
SD0349	0.825	0.886	SD0591	1.061	0.915
SD0350	0.826	0.897	SD0592	1.129	0.996
SD0351	0.730	0.842	SD0593	0.856	0.895
SD0352	0.297	0.276	SD0594	0.840	0.956
SD0353	0.773	0.746	SD0595	0.882	0.857
SD0354	0.663	0.722	SD0596	0.856	0.896
SD0355	0.620	0.626	SD0597	0.869	0.697
SD0356	0.546	0.599	SD0598	0.878	0.700
SD0357	0.298	0.411	SD0599	0.808	0.857
SD0358	0.313	0.318	SD0600	0.856	0.823
SD0359	0.273	0.282	SD0601	0.742	0.713
SD0360	0.256	0.257	SD0602	0.740	0.846
SD0361	0.269	0.276	SD0603	0.808	0.816
SD0362	0.270	0.276	SD0604	0.561	0.527
SD0363	0.350	0.272	SD0605	0.711	0.880
SD0364	0.227	0.243	SD0606	0.852	0.922
SD0365	0.228	0.233	SD0607	0.695	0.887
SD0366	0.264	0.241	SD0608	0.635	0.917
SD0367	0.262	0.252	SD0609	0.655	0.874
SD0368	0.571	0.597	SD0610	0.596	0.765
SD0369	0.539	0.531	SD0611	0.482	0.508
SD0370	0.521	0.545	SD0612	0.629	0.578
SD0371	0.302	0.319	SD0613	0.616	0.503

[0256]

SD0372	0.353	0.335	SD0614	0.716	0.682
SD0373	0.279	0.255	SD0615	0.570	0.491
SD0374	0.266	0.194	SD0616	0.671	0.668
SD0375	0.246	0.238	SD0617	0.713	0.721
SD0376	0.258	0.238	SD0618	0.819	0.862
SD0377	0.246	0.226	SD0619	0.925	0.968
SD0378	0.237	0.226	SD0620	0.859	0.978
SD0379	0.262	0.226	SD0621	0.923	1.075
SD0380	0.247	0.240	SD0622	0.900	0.988
SD0381	0.639	0.657	SD0623	0.908	0.969
SD0382	0.267	0.517	SD0624	0.775	0.889
SD0383	0.473	0.547	SD0625	0.827	0.850
SD0384	0.456	0.563	SD0626	0.832	0.796
SD0385	0.264	0.393	SD0627	0.916	0.796
SD0386	0.329	0.325	SD0628	0.863	0.898
SD0387	0.186	0.231	SD0629	0.915	0.869
SD0388	0.217	0.248	SD0630	0.893	0.856
SD0389	0.230	0.275	SD0631	0.940	0.848
SD0390	0.210	0.270	SD0632	0.878	0.911
SD0391	0.247	0.224	SD0633	0.934	1.074
SD0392	0.257	0.236	SD0634	0.915	1.019
SD0393	0.252	0.253	SD0635	0.911	0.912
SD0394	0.267	0.251	SD0636	0.852	0.911
SD0395	0.594	0.675	SD0637	0.997	0.965
SD0396	0.511	0.678	SD0638	0.983	0.935
SD0397	0.457	0.618	SD0639	0.806	0.823
SD0398	0.516	0.601	SD0640	0.838	0.846
SD0399	0.261	0.389	SD0641	0.906	0.861
SD0400	0.327	0.300	SD0642	0.740	0.836

[0257]

SD0401	0.230	0.250	SD0643	0.739	0.725
SD0402	0.231	0.260	SD0644	0.780	0.762
SD0403	0.237	0.221	SD0645	0.739	0.819
SD0404	0.258	0.243	SD0646	0.734	0.798
SD0405	0.253	0.246	SD0647	0.789	0.913
SD0406	0.228	0.230	SD0648	0.707	0.946
SD0407	0.228	0.215	SD0649	0.943	1.077
SD0408	0.247	0.255	SD0650	0.729	0.872
SD0409	0.565	0.667	SD0651	0.666	0.879
SD0410	0.796	0.863	SD0652	0.704	0.882
SD0411	0.633	0.646	SD0653	0.661	0.726
SD0412	0.613	0.699	SD0654	0.751	0.881
SD0413	0.294	0.439	SD0655	0.727	0.822
SD0414	0.416	0.310	SD0656	0.746	0.839
SD0415	0.275	0.238	SD0657	0.849	0.842
SD0416	0.241	0.290	SD0658	0.835	0.796
SD0417	0.257	0.284	SD0659	0.972	0.830
SD0418	0.267	0.306	SD0660	0.772	0.672
SD0419	0.249	0.229	SD0661	0.883	0.918
SD0420	0.243	0.240	SD0662	0.934	0.952
SD0421	0.250	0.241	SD0663	0.974	0.891
SD0422	0.230	0.237	SD0664	0.939	0.936
SD0423	0.555	0.684	SD0665	1.116	0.919
SD0424	0.614	0.682	SD0666	0.924	0.954
SD0425	0.592	0.733	SD0667	0.780	0.744
SD0426	0.604	0.699	SD0668	0.795	0.726
SD0427	0.281	0.449	SD0669	0.819	0.754
SD0428	0.301	0.330	SD0670	0.856	0.830
SD0429	0.230	0.261	SD0671	0.844	0.758

[0258]

SD0430	0.241	0.273	SD0672	0.978	0.952
SD0431	0.232	0.255	SD0673	0.860	0.845
SD0432	0.247	0.288	SD0674	0.526	0.566
SD0433	0.238	0.280	SD0675	0.661	0.961
SD0434	0.224	0.293	SD0676	0.690	0.916
SD0435	0.249	0.240	SD0677	0.672	0.939
SD0436	0.428	0.445	SD0678	0.821	0.973
SD0437	0.542	0.829	SD0679	0.943	0.952
SD0438	1.106	1.048	SD0680	1.018	0.991
SD0439	0.930	1.096	SD0681	0.561	0.580
SD0440	1.033	1.023	SD0682	0.777	0.688
SD0441	0.630	0.657	SD0683	0.654	0.639
SD0442	0.912	0.913	SD0684	0.691	0.622
SD0443	0.392	0.375	SD0685	0.518	0.555
SD0444	0.552	0.441	SD0686	0.661	0.738
SD0445	0.561	0.514	SD0687	0.722	0.644
SD0446	0.550	0.442	SD0688	0.416	0.385
SD0447	0.415	0.362	SD0689	0.571	0.870
SD0448	0.566	0.503	SD0690	0.697	0.946
SD0449	0.579	0.475	SD0691	0.616	0.840
SD0450	0.463	0.424	SD0692	0.644	0.850
SD0451	0.925	0.929	SD0693	0.781	0.733
SD0452	0.963	0.939	SD0694	1.022	0.902
SD0453	0.967	0.952	SD0695	0.458	0.448
SD0454	0.948	0.883	SD0696	0.500	0.455
SD0455	0.746	0.645	SD0697	0.454	0.444
SD0456	0.840	0.860	SD0698	0.497	0.467
SD0457	0.473	0.402	SD0699	0.369	0.416
SD0458	0.555	0.514	SD0700	0.622	0.552

[0259]

SD0459	0.566	0.472	SD0701	0.542	0.528
SD0460	0.609	0.478	SD0702	0.301	0.423
SD0461	0.408	0.355	SD0703	0.376	0.367
SD0462	0.630	0.532	SD0704	0.373	0.334
SD0463	0.631	0.497	SD0705	0.315	0.347
SD0464	0.549	0.510	SD0706	0.339	0.351
SD0465	0.966	0.809	SD0707	0.245	0.263
SD0466	0.910	0.841	SD0708	0.572	0.703
SD0467	0.904	0.878	SD0709	0.313	0.484
SD0468	0.999	1.009	SD0710	0.297	0.431
SD0469	0.734	0.760	SD0711	0.284	0.397
SD0470	0.925	0.806	SD0712	0.300	0.471
SD0471	0.559	0.482	SD0713	0.297	0.417
SD0472	0.572	0.543	SD0714	0.300	0.438
SD0473	0.652	0.594	SD0715	0.280	0.430

[0260]

[0261] 실시예 5. *일시적 형질전환 및 형질전환 마우스에서의 RNAi 물질 효율의 생체내 분석.*

[0262] *A) 투여 및 샘플 수집.* 생체내 LPA RNAi 물질의 효율을 평가하기 위해, 일시적 형질전환 마우스를 사용하였다. 콜레스테롤 접합된 LPA RNAi 물질 투여 전 적어도 30일에, 야생형 마우스에 마우스 알부민 프로모터의 제어 하에 SEAP 유전자를 함유하는 플라스미드에 의해 수력 꼬리 정맥 주사에 의해 주사하였다. *LPA* 유전자 표적 서열을 플라스미드의 3' UTR에서 클로닝하였다. 이 마우스는 SEAP-LPA HTV 마우스로 기재된다. 1일에 MLP 전달 중합체를 사용하여 마우스에 콜레스테롤 접합된 LPA RNAi 물질을 투여하였다(WO 2012/083185, 본 명세서에 참고로 포함됨; 멜리틴을 합성하고 CDM-NAG에 의해 변형시켜 여기 기재된 바와 같은 MLP 전달 중합체를 생성하였다). 각각의 마우스는 LPA RNAi 물질 + MLP 전달 중합체의 용량을 함유하는 200-250㎕의 용액(대부분의 경우에 1:1 w/w RNAi 물질: MLP 전달 중합체)의 정맥내(IV) 주사를 받았다. 몇몇 실험에서, LPA RNAi 물질을 전달 중합체에 직접적으로 접합하였다. 중합체 접합된 LPA RNAi 물질을 꼬리 정맥에 유사하게 주사하였다. 표시된 LPA RNAi 물질(표 8B)을 54.4% 에폭시 에틸 아미노 아크릴레이트(EEAA) 아민 단량체 및 45.6% 프로필 아크릴레이트 프로필 단량체(MW 41962g/mol, WO 2013/158141에 기재된 바대로 합성된 중합체)를 가지는 ARF1164-106A-5인 폴리아크릴레이트 중합체에 접합하고, 3x ACit-NAG, 6x ACit-PEG(WO 2012/092373 및 PCT/US16/34512에 기재된 바대로 마스킹된 중합체)에 의해 마스킹하였다. -4일 또는 -1일에 주사 전 마우스로부터 대조군 혈청(전처리) 샘플을 취했다. 4일, 8일, 15일, 22일, 29일, 36일 및 43일에 마우스로부터 주사 후 혈청 샘플을 취했다. 몇몇 마우스의 경우, 4일 대신에 3일 또는 5일에 샘플을 수집하였다.

[0263] 추가의 실험에서, 완전 길이 *LPA*를 발현하는 일시적 형질전환 마우스를 사용하여 LPA RNAi 물질을 생체내 평가하였다. 콜레스테롤 표적화된 LPA RNAi 물질 투여 전 적어도 30일에, 면역 손상된(Nod.scid) 마우스에 마우스 알부민 프로모터의 제어 하에 *LPA* cDNA를 함유하는 미니사이클에 의해 수력 꼬리 정맥 주사에 의해 주사하였다. 이 마우스는 LPA mc HTV 마우스로 기재된다. 콜레스테롤 표적화된 또는 NAG(또한 GalNAc라 칭함) 접합된 LPA RNAi 물질을 1일에 마우스에 투여하였다. 콜레스테롤 표적화된 RNAi 물질을 위해, 각각의 마우스는 RNAi 물질 + MLP 전달 중합체의 용량을 함유하는 200-250㎕ 용액(1:1 w/w RNAi 물질:MLP 전달 중합체)의 꼬리 정맥으로 정맥내(IV) 주사를 받았다. NAG 접합된 LPA RNAi 물질에 대해, 마우스는 완충 식염수 중에 RNAi 물질의 용량을 함유하는 300㎕의 용액의 어깨 사이의 등에서 처진 피부로 피하(SC) 주사를 받았다. 몇몇 샘플의 경우, LPA RNAi 물질을 MLP 전달 펩타이드와 함께 또는 이것 없이 투여하였다. MLP 전달 펩타이드에 의해 전달된 RNAi 물질을 용량 of RNAi 물질 + MLP 전달 중합체의 용량을 함유하는 200-250㎕ 용액(대부분의 경우에 1:2 w/w RNAi 물질: MLP 전달 중합체)의 꼬리 정맥으로 정맥내(IV) 주사에 의해 투여하였다. -4일 또는 -1일에 주사 전 마우스로부터 대조군 혈청(전처리) 샘플을 취했다. 4일, 8일, 15일, 22일, 29일, 36일 및 43일에 마우스로부터 주사 후 혈청 샘플을 취했다. 몇몇 마우스의 경우, 4일 대신에 3일 또는 5일에 샘플을 수집하였다.

[0264] 추가의 실험에서, LPA RNAi 물질을 아포(a) 및 Lp(a) 형질전환 마우스에 투여하였다(Frazer KA et al 1995,

Nature Genetics 9:424-431). 이 마우스는, 추가 서열 5' 및 3' 둘 다를 가지는, (아포(a) 단백질을 코딩하는) 완전 *LPA* 유전자를 함유하는 YAC로부터 인간 아포(a)를 발현한다. 아포(a) YAC 함유 마우스를 인간 아포B-100 발현 마우스에 교잡함으로써 Lp(a) 마우스를 교배하였다(Callow MJ et al 1994, PNAS 91:2130-2134). 콜레스테롤 표적화된 RNAi 물질 및 NAG 접합된 RNAi 물질을 상기 기재된 바대로 투여하였다. -1일에 주사 전 마우스로부터 대조군 혈청(전처리) 샘플을 취했다. 4일, 8일, 15일, 22일, 29일, 36일, 43일, 50일, 57일 및 64일에 마우스로부터 주사 후 혈청 샘플을 취했다.

[0265] B) LPA 발현 넉다운 분석. SEAP-LPA HTV 마우스에 대해, Phospha-Light(상표명), 화학발광 리포터 유전자 검정 시스템(Life Technologies)을 사용하여 마우스로부터의 혈청을 평가함으로써 혈청 중의 SEAP 단백질 수준을 모니터링하였다. 정규화를 위해, "전처리로 정규화된" 발현의 비율을 결정하도록 소정의 시점에 각각의 동물에 대한 SEAP 수준을 그 동물에서의 발현의 전처리 수준에 의해 나눴다. 이후, 군 내의 개인 사이에 특정한 시점에서의 발현을 평균하였다.

[0266] LPA mc HTV 마우스 및 형질전환 마우스를 위해, 아포(a)(Abcam)에 대해 ELISA를 이용하여 마우스로부터의 혈청을 평가함으로써 혈청 중의 인간 아포(a) 단백질 수준을 모니터링하였다. 정규화를 위해, "1일로 정규화된" 발현의 비율을 결정하도록 시점에 각각의 동물에 대한 아포(a) 수준을 (이 경우에 1일에) 그 동물에서의 발현의 전처리 수준에 의해 나눴다. 이후, 식염수 대조군에서의 모든 마우스의 평균 "1일로 정규화된" 비율에 의해 개별 동물에 대한 "1일로 정규화된" 비율을 나누어서, 특정한 시점에서의 발현을 식염수 대조군으로 정규화하였다. 이것은 대조군에서의 것에 정규화된 각각의 시점에 대한 발현을 발생시킨다.

[0267] 제조사의 추천에 따라 Cobas Integra 400(Roche Diagnostics)에서 Lp(a) 수준을 결정하였다. 정규화를 위해, "1일로 정규화된" 발현의 비율을 결정하도록 시점에 각각의 동물에 대한 아포(a) 수준을 (이 경우에 1일에) 그 동물에서의 발현의 전처리 수준에 의해 나눴다. 이후, 식염수 대조군에서의 모든 마우스의 평균 "1일로 정규화된" 비율에 의해 개별 동물에 대한 "1일로 정규화된" 비율을 나누어서, 특정한 시점에서의 발현을 식염수 대조군으로 정규화하였다. 이것은 대조군에서의 것에 정규화된 각각의 시점에 대한 발현을 발생시킨다.

표 8A. 콜레스테롤 접합된 LPA RNAi 물질 + MLP 전달 중합체의 정맥내 투여 후 마우스에서의 상대 LPA 수준.

듀플렉스 번호	LPA RNAi 물질 (mg/kg)	MLP (mg/kg)	상대 LPA
AD01184	2	2	0.20
AD01187	2	2	0.18
AD01190	2	2	0.17
AD01193	2	2	0.22
AD01196	2	2	0.02
AD01197	2	2	0.065
AD01198	2	2	0.051
AD01199	2	2	0.070
AD01200	2	2	0.094
AD01201	2	2	0.029
AD01202	8	8	0.14
AD01205	2	2	0.21
AD01206	2	2	0.37
AD01207	2	2	0.19
AD01208	2	2	0.35
AD01209	2	2	0.16
AD01210	2	2	0.18
AD01211	2	2	0.38
AD01212	2	2	0.26
AD01213	2	2	0.30
AD02662	2	2	0.0010
AD02663	2	2	0.010
AD02664	2	2	0.0010

[0268]

표 8B. 전달 중합체 접합된 LPA RNAi 물질의 정맥내 투여 후 마우스에서의 상대 LPA 수준.

듀플렉스 번호	LPA RNAi 물질 (mg/kg)	상대 LPA
AD01462	0.5	0.38
AD01463	0.5	0.41
AD01466	0.5	0.33
AD01467	0.5	0.46

[0269]

표 8C. NAG 접합된 LPA RNAi 물질의 피하 투여 후 마우스에서의 상대 LPA 수준.

듀플렉스 번호	LPA RNAi 물질 (mg/kg)	상대 LPA	듀플렉스 번호	LPA RNAi 물질 (mg/kg)	상대 LPA
AD01529	10	0.068	AD02920	10	0.050
AD01530	10	0.43	AD02921	10	0.040
AD01531	10	0.62	AD02922	10	0.080
AD01532	10	0.18	AD02923	10	0.040
AD01533	10	0.30	AD02924	10	0.050
AD01534	10	0.44	AD02925	10	0.030
AD01765	10	0.14	AD02926	10	0.17
AD01766	10	0.52	AD02927	10	0.31
AD01767	10	0.51	AD02928	10	0.081
AD01768	10	0.15	AD02929	10	0.065
AD01769	10	0.56	AD02930	10	0.15
AD01770	10	0.29	AD02931	10	0.13
AD01772	10	0.25	AD02932	10	0.11
AD01773	10	0.28	AD03049	3	0.20
AD01774	10	0.24	AD03050	3	0.087
AD01780	10	0.34	AD03051	3	0.070
AD01804	10	0.68	AD03052	3	0.080
AD01976	10	0.27	AD03053	3	0.23
AD01977	10	0.27	AD03054	3	0.050
AD01978	10	0.53	AD03058	3	0.27
AD01979	10	0.044	AD03059	3	0.22
AD01980	10	0.087	AD03060	3	0.31
AD01981	10	0.074	AD03061	3	0.16
AD01982	10	0.066	AD03062	3	0.20
AD01983	10	0.078	AD03063	3	0.13
AD01984	10	0.036	AD03064	3	0.21

[0270]

AD01985	10	0.0070	AD03065	3	0.085
AD01986	10	0.019	AD03066	3	0.10
AD01987	10	0.019	AD03067	3	0.094
AD01988	10	0.042	AD03068	3	0.17
AD01989	10	0.053	AD03069	3	0.077
AD01990	10	0.017	AD03070	3	0.36
AD02001	10	0.021	AD03071	3	0.043
AD02003	10	0.050	AD03072	3	0.031
AD02004	10	0.050	AD03073	3	0.019
AD02005	10	0.040	AD03074	3	0.016
AD02006	10	0.11	AD03075	3	0.062
AD02007	10	0.21	AD03114	1	0.33
AD02008	10	0.080	AD03115	1	0.30
AD02009	10	0.090	AD03116	1	0.21
AD02010	10	0.16	AD03117	1	0.14
AD02011	10	0.070	AD03118	1	0.30
AD02435	10	0.038	AD03119	1	0.10
AD02436	10	0.027	AD03120	1	0.080
AD02437	10	0.052	AD03121	1	0.14
AD02438	10	0.063	AD03122	1	0.14
AD02439	10	0.073	AD03123	1	0.34
AD02440	10	0.13	AD03156	1	0.084
AD02545	10	0.079	AD03157	1	0.016
AD02546	10	0.045	AD03158	1	0.037
AD02547	10	0.055	AD03159	1	0.63
AD02548	10	0.13	AD03272	1	0.13
AD02549	10	0.071	AD03273	1	0.20
AD02550	10	0.039	AD03274	1	0.21
AD02551	10	0.057	AD03275	1	0.15

[0271]

AD02552	10	0.033	AD03276	1	0.11
AD02553	10	0.14	AD03277	1	0.13
AD02554	10	0.14	AD03278	1	0.13
AD02555	10	0.18	AD03279	1	0.21
AD02556	10	0.10	AD03341	1	0.13
AD02557	10	0.10	AD03421	1	0.29
AD02558	10	0.071	AD03430	1	0.12
AD02559	10	0.039	AD03432	1	0.16
AD02560	10	0.058	AD03434	1	0.11
AD02561	10	0.12	AD03436	1	0.21
AD02609	3	0.59	AD03438	1	0.25
AD02610	3	0.36	AD03440	1	0.21
AD02611	3	0.35	AD03460	1	0.090
AD02612	3	0.37	AD03462	1	0.40
AD02613	3	0.24	AD03495	1	0.28
AD02614	3	0.24	AD03536	1	0.14
AD02615	3	0.14	AD03538	0.5	0.26
AD02616	3	0.25	AD03539	0.5	0.21
AD02617	3	0.090	AD03540	1	0.15
AD02618	3	0.11	AD03541	0.5	0.10
AD02619	3	0.020	AD03542	1	0.94
AD02620	3	0.11	AD03547	1	0.19
AD02682	10	0.11	AD03548	1	0.73
AD02683	10	0.14	AD03549	1	0.29
AD02684	10	0.79	AD03573	1	0.15
AD02685	10	0.78	AD03574	1	0.15
AD02686	10	0.19	AD03575	1	0.13
AD02687	10	0.27	AD03576	1	0.18
AD02696	3	0.050	AD03577	0.5	0.18

[0272]

AD02710	3	0.040	AD03578	0.5	0.38
AD02711	3	0.040	AD03579	0.5	0.53
AD02712	3	0.49	AD03603	1	0.083
AD02713	3	0.040	AD03604	1	0.091
AD02714	3	0.040	AD03605	1	0.19
AD02715	3	0.070	AD03608	1	0.18
AD02716	3	0.080	AD03609	1	0.16
AD02717	3	0.12	AD03610	1	0.23
AD02745	3	0.25	AD03611	1	0.40
AD02746	3	0.22	AD03612	1	0.21
AD02747	3	0.081	AD03629	1	0.11
AD02748	3	0.17	AD03668	1	0.070
AD02749	3	0.17	AD03705	0.5	0.11
AD02750	3	0.066	AD03707	0.5	0.11
AD02751	3	0.070	AD03720	0.5	0.14
AD02752	3	0.044	AD03721	0.5	0.094
AD02753	3	0.071	AD03722	0.5	0.19
AD02819	1	0.022	AD03723	0.5	0.10
AD02820	1	0.042	AD03765	1	0.080
AD02821	1	0.038	AD03771	1	0.10
AD02825	3	0.050	AD03801	1	0.15
AD02826	3	0.050	AD03802	1	0.18
AD02827	3	0.050	AD03844	1	0.17
AD02828	3	0.050	AD03845	1	0.25
AD02829	3	0.040	AD03848	1	0.10
AD02830	3	0.040	AD03850	1	0.052
AD02831	3	0.030	AD03851	1	0.076
AD02832	3	0.030	AD03852	1	0.13
AD02841	3	0.061	AD03853	1	0.081

[0273]

AD02842	3	0.16	AD03854	1	0.21
AD02843	3	0.10	AD03856	1	0.32
AD02844	3	0.11	AD03859	1	0.15
AD02845	3	0.22	AD03862	1	0.12
AD02846	3	0.16	AD03863	1	0.12
AD02847	3	0.066	AD03921	1	0.17
AD02848	3	0.055	AD03922	1	0.057
AD02849	3	0.083	AD03923	1	0.066
AD02850	3	0.042	AD03924	1	0.14
AD02851	3	0.063	AD03931	1	0.34
AD02852	3	0.11	AD03932	1	0.15
AD02907	10	0.10	AD03933	1	0.34
AD02908	10	0.11	AD03424	1	0.15
AD02909	10	0.049	AD03425	1	0.21
AD02910	10	0.23	AD03426	1	0.21
AD02911	10	0.20	AD03427	1	0.19
AD02912	10	0.10	AD03428	1	0.18
AD02913	10	0.070	AD03760	0.5	0.21
AD02914	10	0.050	AD03762	0.5	0.17
AD02915	10	0.10	AD03763	0.5	0.21
AD02916	10	0.090	AD03764	0.5	0.28
AD02917	10	0.060	AD03766	0.5	0.065
AD02918	10	0.020	AD03847	1	0.15
AD02919	10	0.030	AD04110	1	0.070

[0274]

[0275] 실시예 6. *LPA RNAi 물질의 생체내 스크리닝 및 SEAP 넉다운의 시간 과정*. 콜레스테롤 접합된 LPA RNAi 물질을 상기 기재된 바대로 일시적 형질전환 마우스에 투여하였다. 각각의 마우스는 8mg/kg의 MLP 전달 중합체와 함께 8mg/kg의 LPA RNAi 물질의 단일 정맥내(IV) 용량을 받았다. 36일까지 동안 혈청 중의 SEAP 단백질 수준을 모니터링하였다. 넉다운 수준 및 반응의 기간은 표 9에 기재되어 있다. 시험된 모든 LPA RNAi 물질의 투여 후 85% 초과의 SEAP 혈청 단백질 수준의 감소가 얻어졌고, 시험된 LPA RNAi 물질의 모두가 아닌 2개는 99.4% 넉다운 초과를 나타냈다. AD01196 및 AD01199는 36일에 95% 초과의 넉다운을 나타냈다.

[0276] 실시예 7. *생체내 스크리닝 LPA RNAi 물질 및 더 낮은 LPA RNAi 물질 용량에서의 LPA 넉다운의 시간 과정*. 콜레스테롤 접합된 LPA RNAi 물질을 상기 기재된 바대로 일시적 형질전환 마우스에 투여하였다. 각각의 마우스는 2 mg/kg의 MLP 전달 중합체와 함께 2mg/kg의 LPA RNAi 물질의 단일 정맥내(IV) 용량을 받았다. 43일까지 동안 혈청 중의 SEAP 단백질 수준을 모니터링하였다(표 10).

[0277] 실시예 8. 아포(a) *형질전환(Tg) 마우스에서의 LPA RNAi 물질의 생체내 시험*. AD01196을 상기 기재된 바대로 마우스에 투여하였다. 각각의 마우스는 2mg/kg의 MLP 전달 중합체 또는 식염수와 함께 2mg/kg의 LPA RNAi 물질의 단일 정맥내(IV) 용량을 받았다. 64일까지 동안 혈청 중의 인간 아포(a)(아포(a)) 수준을 모니터링하였다(표 11). 15일에, 식염수 군에서의 동물은 2mg/kg of MLP 전달 중합체와 함께 2mg/kg의 대조군 마우스 VII 인자(F7) RNAi 물질의 단일 IV 용량을 받았다. 22일에, 모든 동물에서 F7 수준을 측정하였다. 혈청 아포(a) 수준에 대한 효과 없이, 투약 후 7일에 99%까지 F7 활성을 넉다운하였다. AD01196은 천저에서 아포(a) 수준의 3 초과의 log10 넉다운을 나타냈고, 3주 후 80% 초과의 넉다운이 관찰되었다(표 11).

표 9. 8 mg/kg의 MLP 전달 펩타이드와 함께 8 mg/kg의 chol-RNAi 올리고 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		4 일		8 일		15 일		22 일		29 일		36 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.24	1.00	0.34	1.00	0.13	1.00	0.33	1.00	0.09	1.00	0.18	1.00	0.44
AD01184	1.00	0.39	0.27	0.10	0.15	0.06	0.01	0.00	0.07	0.04	0.43	0.39	0.98	0.73
AD01187	1.00	0.53	0.24	0.15	0.13	0.10	0.00	0.00	0.01	0.01	0.08	0.06	0.56	0.47
AD01190	1.00	0.77	0.26	0.20	0.14	0.11	0.00	0.00	0.00	0.00	0.00	0.00	0.02	0.01
AD01193	1.00	0.99	0.25	0.26	0.15	0.17	0.01	0.01	0.00	0.00	0.01	0.01	0.02	0.01
AD01196	1.00	0.59	0.24	0.13	0.14	0.08	0.00	0.00	0.00	0.00	0.01	0.01	0.04	0.03
AD01199	1.00	0.52	0.23	0.15	0.13	0.10	0.00	0.00	0.00	0.00	0.01	0.00	0.04	0.02
AD01202	1.00	0.93	0.25	0.24	0.17	0.16	0.14	0.12	0.56	0.55	0.78	0.66	2.09	2.00

[0278]

표 10. 2 mg/kg의 MLP 전달 펩타이드와 함께 2 mg/kg의 chol-RNAi 물질의 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-4 일		4 일		9 일		15 일		22 일		29 일		36 일		43 일	
식염수	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
AD01196	1.00	0.00	1.00	0.72	1.00	0.72	1.00	0.71	1.00	0.43	1.00	0.79	1.00	0.48	1.00	0.54
AD01199	1.00	0.00	0.22	0.08	0.05	0.05	0.02	0.01	0.13	0.04	0.36	0.12	0.69	0.08	1.39	0.91
AD01205	1.00	0.00	0.27	0.28	0.07	0.06	0.17	0.17	0.59	0.51	0.74	0.74	0.83	0.82	1.01	0.58
AD01208	1.00	0.00	0.21	0.13	0.31	0.23	0.45	0.21	1.33	0.68	1.11	0.82	1.55	1.30	1.79	1.09
AD01211	1.00	0.00	0.43	0.20	0.35	0.15	0.68	0.19	1.45	0.44	1.32	0.26	1.39	0.52	0.99	0.12
AD01184	1.00	0.00	0.38	0.14	0.53	0.20	0.94	0.38	1.96	0.93	1.05	0.27	1.44	0.38	0.93	0.28
AD01187	1.00	0.00	0.26	0.07	0.20	0.05	0.61	0.17	1.28	0.14	1.21	0.51	1.39	0.80	ND	ND
AD01190	1.00	0.00	0.37	0.18	0.09	0.07	0.18	0.17	0.86	0.84	0.77	0.33	1.80	0.36	ND	ND
AD01193	1.00	0.00	0.26	0.08	0.17	0.07	0.36	0.13	1.16	0.37	1.39	0.69	1.96	1.64	ND	ND
	1.00	0.00	0.39	0.27	0.22	0.33	0.32	0.37	0.67	0.58	0.84	0.46	1.27	0.23	ND	ND

[0279]

표 11. 2 mg/kg의 MLP 전달 중합체와 함께 2 mg/kg의 콜레스테롤 접합된 LPA RNAi 물질의 투여 후 아포(a) Tg 마우스에서의 혈청 아포(a) 단백질 수준. 아포(a) 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		4 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.06	1.00	0.27	1.00	0.06	1.00	0.17
AD01196	1.00	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.15	0.08
	29 일		36 일		43 일		50 일			
	평균	SD	평균	SD	평균	SD	평균	SD		
식염수	1.00	0.12	1.00	0.04	1.00	0.26	1.00	0.24		
AD01196	0.40	0.23	0.74	0.61	0.75	0.67	0.77	0.52		

[0280]

[0281] 실시예 9. *MLP 전달 중합체에 의한 LPA RNAi 물질 전달 후 비인간 영장류에서의 아포지단백(a)(아포(a)) 넉다운*. MLP 전달 중합체 및 LPA RNAi 물질을 만들고, 상기 기재된 바대로 약제학적으로 허용가능한 완충제 중에 합했다. 1일에, 2마리의 사이노몰거스 마카크(마카카 바스찌쭐라리스(Macaca fascicularis)) 영장류(수컷 둘다, 각각 5.0kg 및 8.15kg)에 2mg/kg의 AD01196 + 2mg/kg의 MLP 전달 중합체에 의해 주사하였다. 각각의 주사를 위해, 22 내지 25 게이지 정맥내 카테터를 사용하여 LPA RNAi 물질 + MLP 전달 중합체(2ml/kg)를 대복제정맥에 주사하였다. (표 12에 표시된) 표시된 시점에, 혈액 샘플을 채혈하고, 아포(a) 수준, 지질 수준 및 독성 마커에 대해 분석하였다. 대퇴 정맥으로부터 혈액을 수집하고, 모든 혈액 수집 전에 영장류를 공복시켰다. Meriter laboratories에서 자동화 화학 분석장치에서 혈액 요소 질소(BUN), 알라닌 아미노기전이효소(ALT), 아스파르테이트 아미노전환효소(AST), 크레아티닌, 총 콜레스테롤(TC) 및 트라이글리세라이드(TG)에 대한 혈액 시험을 수행하였다. 자동화 화학 분석장치에서 지단백(a)(Lp(a)) 및 저밀도 지단백(LDL)에 대한 혈액 시험을 측정하였다. ELISA에 의해 혈청 아포(a) 수준을 측정하였다. 아포(a)의 상당한 넉다운이 22일에 관찰된 94.5%의 평균 최대 넉다운에 의해 관찰되었다. Lp(a)의 평균 최대 넉다운이 15일에 91.5% 관찰되었다(도 3). 치료된 동물에서 용량 관련 독성이 관찰되지 않았다.

표 12. 2 mg/kg의 MLP 전달 중합체와 함께 2 mg/kg의 AD01196 의 투여 후 사이노몰거스 마카크(마카카 바스찌쿨라리스) 영장류에서의 혈청 아포(a) 단백질, 지단백(a)(mg/ dℓ), 저밀도 지단백(LDL), 총 콜레스테롤 및 트라이글리세라이드 수준. 아포(a) 수준을 투약전으로 정규화하였다.

일	혈청 아포(a) 단백질 수준		지단백(a) 수준 (mg/dℓ)		계산된 저밀도 지단백 (mg/dℓ)		총 콜레스테롤 (mg/dℓ)		트라이글리세라이드 (mg/dℓ)	
	동물 1	동물 2	동물 1	동물 2	동물 1	동물 2	동물 1	동물 2	동물 1	동물 2
투약전	1.00	1.00	77.1	126.7	48.4	84.7	95	149	41	36
3	0.47	0.55	46.0	65.0	53.6	83.5	93	143	33	28
8	0.12	0.15	9.3	16.5	53.4	75.9	101	147	36	30
15	0.10	0.10	5.0	7.3	49.8	60.9	106	136	79	34
22	0.05	0.06	7.9	10.3	47.5	63.9	97	136	34	36
29	0.08	0.11	13.4	27.0	55.7	47.5	101	116	20	36
36	0.15	0.25	22.2	50.6	56.8	73.1	-	-	-	-
43	0.19	0.23	31.4	45.5	53.8	55.7	103	138	29	39
50	0.27	0.29	46.1	67.3	52.3	70.9	-	-	-	-
57	0.27	0.3	52.7	69.7	52.1	78.6	104	157	34	39
64	0.33	0.31	68.4	73.7	52.4	75.8	-	-	-	-
71	0.50	0.4	76.8	78.6	62.4	75.0	104	149	43	47
85	0.31	0.34	63.1	75.4	50.3	68.8	102	145	41	49
99	0.27	0.29	67.9	78.8	58.7	72.5	102	150	42	52
120	0.36	0.37	91.7	119.4	53.4	79.8	100	154	43	51

[0282]

표 13. 2 mg/kg의 MLP 전달 중합체와 함께 2 mg/kg의 AD01196 의 투여 후 사이노몰거스 마카크(마카카 바스찌쿨라리스) 영장류에서의 요소 질소, 크레아티닌, 알라닌 아미노기전이효소 및 아스파르테이트 아미노전환효소 수준.

	혈중 요소 질소 (mg/dℓ)		크레아티닌 (mg/dℓ)		알라닌 아미노기전이효소 (U/ℓ)		아스파르테이트 아미노전환효소 (U/ℓ)	
일	동물 1	동물 2	동물 1	동물 2	동물 1	동물 2	동물 1	동물 2
투약 전	16	16	0.79	0.70	37	32	32	33
3	11	14	0.70	0.61	40	42	33	35
8	14	13	0.78	0.58	33	38	25	31
15	15	15	0.67	0.59	51	35	47	32
22	15	15	0.8	0.55	47	35	29	30
29	12	12	0.61	0.59	30	31	23	36
36	-	-	-	-	-	-	-	-
43	12	15	0.64	0.58	29	29	25	30
50	-	-	-	-	-	-	-	-
57	14	15	0.72	0.64	32	35	28	31
64	-	-	-	-	-	-	-	-
71	14	15	0.73	0.69	36	35	29	33
85	14	15	0.60	0.70	126	41	51	40
99	15	18	0.66	0.68	151	40	44	37
120	14	19	0.72	0.60	37	51	28	47

[0283]

[0284] 실시예 10. *NAG 접합된 LPA RNAi 물질의 생체내 스크리닝 및 넉다운의 시간 과정*. NAG 접합된 LPA RNAi 물질을 상기 기재된 바대로 일시적 형질전환 마우스에 투여하였다. 각각의 마우스는 1mg/kg의 MLP 전달 중합체와 함께 2mg/kg의 LPA RNAi 물질의 단일 정맥내(IV) 용량, 또는 10mg/kg의 NAG 접합된 LPA RNAi 물질의 단일 피하(SC) 용량을 받았다. 22일까지 동안 혈청 중의 SEAP 단백질 수준을 모니터링하였다. 넉다운 수준 및 반응의 기간은 표 14-15에 기재되어 있다. AD01529, AD01532 및 AD01533는 MLP 전달 중합체에 의한 IV 투여 후 SEAP 수준의 85% 이상의 넉다운 및 단독의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 SEAP 수준의 60% 이상의 최대 넉다운을 나타냈다.

표 14. 10 mg/kg의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		4 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.14	1.00	0.14	1.00	0.66	1.00	0.27
AD01529	1.00	0.00	0.45	0.07	0.36	0.03	0.60	0.08	0.90	0.37
AD01530	1.00	0.00	0.46	0.15	0.43	0.10	0.79	0.26	0.79	0.32
AD01531	1.00	0.00	0.64	0.13	0.62	0.06	0.99	0.28	1.17	0.29
AD01532	1.00	0.00	0.41	0.12	0.37	0.11	0.99	0.34	1.33	0.11
AD01533	1.00	0.00	0.40	0.03	0.22	0.08	0.37	0.15	0.63	0.13
AD01534	1.00	0.00	0.65	0.19	0.44	0.19	0.74	0.30	1.17	0.55

[0285]

표 15. 1 mg/kg의 NAG 접합된 LPA RNAi 물질 + 2 mg/kg의 MLP 전달 중합체의 IV 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		4 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.33	1.00	0.46	1.00	0.21	1.00	0.39
F7 대조군	1.00	0.00	0.61	0.05	0.71	0.45	1.25	0.44	1.05	0.49
AD01529	1.00	0.00	0.25	0.04	0.15	0.08	0.47	0.24	0.81	0.40
AD01530	1.00	0.00	0.26	0.06	0.28	0.19	0.78	0.60	1.06	0.63
AD01531	1.00	0.00	0.22	0.07	0.26	0.06	0.72	0.21	1.04	0.12
AD01532	1.00	0.00	0.18	0.05	0.06	0.03	0.13	0.08	0.29	0.18
AD01533	1.00	0.00	0.21	0.04	0.13	0.06	0.32	0.15	0.67	0.28
AD01534	1.00	0.00	0.17	0.04	0.22	0.06	0.66	0.24	0.94	0.24

[0286]

[0287] 실시예 11. *변형된 NAG 접합된 LPA RNAi 물질의 생체내 스크리닝 및 넉다운의 시간 과정*. 표시된 NAG 접합된 LPA RNAi 물질을 상기 기재된 바대로 SEAP-LPA HTV 마우스에 투여하였다. 각각의 마우스는 10mg/kg의 NAG 접합된 LPA RNAi 물질의 단일 피하(SC) 용량을 받았다. 22일까지 동안 혈청 중의 SEAP 단백질 수준을 모니터링하였다. 넉다운 수준 및 반응의 기간은 표 16 내지 표 17에 기재되어 있다. AD01765 및 AD01768은 89%의 넉다운 활성을 나타냈다.

표 16. 10 mg/kg의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		3 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.16	1.00	0.16	1.00	0.28	1.00	0.24
AD01533	1.00	0.00	0.41	0.08	0.22	0.02	0.47	0.20	0.66	0.29
AD01772	1.00	0.00	0.46	0.13	0.18	0.00	0.34	0.09	0.61	0.14
AD01773	1.00	0.00	0.47	0.08	0.20	0.08	0.45	0.15	0.83	0.12
AD01774	1.00	0.00	0.49	0.09	0.18	0.03	0.44	0.13	0.68	0.08
AD01780	1.00	0.00	0.52	0.13	0.25	0.09	0.44	0.26	0.65	0.37

[0288]

표 17. 10 mg/kg의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 SEAP-LPA HTV 마우스에서의 혈청 SEAP 단백질 수준. SEAP 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		3 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.27	1.00	0.73	1.00	0.87	1.00	0.80
AD01532	1.00	0.00	0.42	0.19	0.35	0.21	0.85	0.25	1.27	0.57
AD01765	1.00	0.00	0.35	0.02	0.11	0.08	0.25	0.14	0.47	0.19
AD01766	1.00	0.00	0.52	0.10	0.36	0.09	1.05	0.13	1.15	0.08
AD01767	1.00	0.00	0.49	0.03	0.44	0.05	1.43	0.23	1.33	0.71
AD01768	1.00	0.00	0.34	0.15	0.11	0.07	0.39	0.13	0.76	0.19
AD01769	1.00	0.00	0.54	0.17	0.46	0.14	1.32	0.12	1.38	0.37
AD01770	1.00	0.00	0.41	0.07	0.20	0.10	0.80	0.52	1.04	0.67

[0289]

[0290] 실시예 12. 아포(a) *Tg 마우스에서의 NAG 접합된 LPA RNAi 물질의 생체내 시험*. NAG 접합된 LPA RNAi 물질을 상기 기재된 바대로 아포(a) Tg 마우스에 투여하였다. 각각의 마우스는 10mg/kg의 LPA RNAi 물질 또는 식염수의 단일 피하(SC) 용량을 받았다. 최대 22일 동안 혈청 중의 인간 아포(a)(아포(a)) 수준을 모니터링하였다(표 18). AD01765는 8일에 96%의 넉다운으로 아포(a) 수준의 가장 큰 넉다운을 나타내고, 74% 초과의 넉다운이 투약 후 3주에 관찰되었다.

표 18. 10 mg/kg의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 아포(a) Tg 마우스에서의 혈청 아포(a) 단백질 수준. 아포(a) 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	-1 일		4 일		8 일		15 일		22 일	
	평균	SD	평균	SD	평균	SD	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.10	1.00	0.16	1.00	0.42	1.00	0.21
AD01532	1.00	0.00	0.12	0.05	0.22	0.08	0.76	0.30	0.56	0.28
AD01765	1.00	0.00	0.09	0.03	0.04	0.02	0.14	0.02	0.26	0.04
AD01768	1.00	0.00	0.11	0.05	0.09	0.05	0.26	0.12	0.38	0.08

[0291]

[0292] 실시예 13. *LPA mc HTV 마우스에서의 NAG 접합된 LPA RNAi 물질의 생체내 시험*. 표시된 NAG 접합된 LPA RNAi 물질을 상기 기재된 바대로 LPA mc HTV 마우스에 투여하였다. 각각의 마우스는 10mg/kg의 LPA RNAi 물질 또는

식염수의 단일 피하(SC) 용량을 받았다. 4일에 혈청 중의 인간 아포(a)(아포(a)) 수준을 분석하였다(표 19). AD02001, AD01765 및 AD01768은 4일에 90% 초과의 넉다운을 나타냈다.

표 19. 10 mg/kg의 NAG 접합된 LPA RNAi 물질의 SC 투여 후 LPA mc HTV 마우스에서의 혈청 아포(a) 단백질 수준. 아포(a) 수준을 -1 일 및 식염수 대조군에서 정규화하였다.

치료	채혈 전		4 일	
	평균	SD	평균	SD
식염수	1.00	0.00	1.00	0.12
AD01765	1.00	0.00	0.05	0.02
AD01768	1.00	0.00	0.07	0.01
AD01804	1.00	0.00	0.68	0.16
AD02001	1.00	0.00	0.06	0.03

[0293]

[0294] 실시예 14. *MLP 전달 중합체에 의한 LPA RNAi 물질 전달 후 비인간 영장류에서의 아포지단백(a)(아포(a)) 넉다운*. MLP 전달 중합체 및 LPA RNAi 물질을 만들고, 약제학적으로 허용가능한 완충제 중에 합했다. 1일 및 71일에, 2마리의 사이노몰거스 마카크(마카카 바스찌쫄라리스) 영장류에 4mg/kg의 AD01196 + 4mg/kg의 MLP 전달 중합체 또는 6mg/kg의 AD01196 + 6mg/kg의 MLP 전달 중합체를 주사하였다. 각각의 주사를 위해, 22 내지 25 게이지 정맥내 카테터를 사용하여 LPA RNAi 물질 + MLP 전달 중합체를 대복제정맥에 주사하였다. 표시된 시점에(도 4), 혈액 샘플을 채혈하고, 이전에 기재된 바대로 아포(a) 수준, 지질 수준 및 독성 마커에 대해 분석하였다. 아포(a)의 상당한 넉다운이 제1 용량 후 15일에 4mg/kg 용량에 대해 96%의 평균 최대 넉다운에 의해 관찰되고, 15일에 관찰된 6mg/kg 용량에 대해 96%가 관찰되었다. 제1 용량 후 Lp(a)의 평균 최대 넉다운은 29일에 4mg/kg 용량에 대해 98.5% 및 22일에 6mg/kg 용량에 대해 98.5%이었다. 치료된 동물에서 용량 관련 독성이 관찰되지 않았다.

[0295] 실시예 15. *Lp(a) Tg 마우스-용량 반응에서의 NAG 접합된 LPA RNAi 물질의 생체내 시험*. NAG 접합된 LPA RNAi 물질을 상기 기재된 바대로 Lp(a) Tg 마우스에 투여하였다. 각각의 마우스는 0.5mg/kg 또는 2mg/kg의 용량 수준의 LPA RNAi 물질 또는 식염수의 단일 피하(SC) 용량을 받았다. 43일까지 혈청 중의 Lp(a) 수준을 모니터링하였다(도 1, 도 2). 모든 LPA RNAi 물질은 더 높은 용량에 의한 용량-반응을 보여주어서, 15일과 22일 사이의 천저에 의해 더 큰 넉다운을 보여준다.

[0296] 실시예 16. 아포(a) *특이적 LPA RNAi 물질 분자 전달 후 비인간 영장류에서의 아포지단백(a)(아포(a)) 넉다운*. LPA RNAi 물질을 피하(SC) 주사에 대해 본 명세서에 기재된 바대로 약제학적으로 허용가능한 완충제 중에 제조하였다. 1일, 7일 및 15일에, 2마리의 사이노몰거스 마카크(마카카 바스찌쫄라리스) 영장류에 3mg/kg의 AD02713, AD02819, AD02820 또는 AD02821을 피하로 주사하였다. 또한, 57일 및 85일에 AD02819 치료된 원숭이를 3mg/kg의 AD02819에 의해 다시 투약하였다. 혈액 샘플을 채혈하고, 이전에 기재된 바대로 아포(a) 수준, 지질 수준 및 독성 마커에 대해 분석하였다. Lp(a)의 상당한 넉다운이 43일에 AD02713에 대해 89%, 36일에 AD02819에 대해 87%, 36일에 AD02820에 대해 79% 및 29일에 AD02821에 대해 95%의 평균 최대 넉다운에 의해 관찰되었다(도 5). 실험의 시간에 걸쳐 치료된 동물에서 용량 관련 독성이 관찰되지 않았다.

[0297] 실시예 17. *LPA RNAi 물질 전달 후 비인간 영장류에서의 아포지단백(a)(아포(a)) 넉다운*. LPA RNAi 물질을 피하(SC) 주사에 대해 본 명세서에 기재된 바대로 약제학적으로 허용가능한 완충제 중에 제조하였다. 1일에, 2마리의 사이노몰거스 마카크(마카카 바스찌쫄라리스) 영장류에 3mg/kg의 AD03272, AD03462, AD03549, AD03547, AD03668, AD03460 또는 AD03536을 피하로 주사하였다. 또한, 48일에 AD03460 및 AD03536 처리된 원숭이를 1mg/kg의 각각의 LPA RNAi 물질에 의해 다시 투약하였다. 혈액 샘플을 채혈하고, 이전에 기재된 바대로 아포(a) 수준, 지질 수준 및 독성 마커에 대해 분석하였다. Lp(a)의 상당한 넉다운이 15일에 AD03272에 대해 62%, 15일에 AD03462에 대해 28%, 29일에 AD03549에 대해 47%, 15일에 AD03547에 대해 44%, 22일에 AD03668에 대해 53%, 29일에 AD03460에 대해 79% 및 22일에 AD03536에 대해 71%의 평균 최대 넉다운에 의해 관찰되었다(도 6). 실험의 시간에 걸쳐 치료된 동물에서 용량 관련 독성이 관찰되지 않았다.

[0298] 실시예 18. 아포(a) *특이적 LPA RNAi 물질 분자 전달 후 영장류에서의 아포*지단백*(a)(아포(a)) 넉다운*. LPA *RNAi* 물질을 만들고, 피하(SQ) 주사에 대해 상기 기재된 바대로 약제학적으로 허용가능한 완충제 중에 합했다.

1일에, 사이노몰거스 마카크(마카카 바스찌쿨라리스) 영장류에 식염수 또는 2mg/kg의 AD03460, AD03536, AD03851, AD03853 또는 AD04110을 피하로 주사하였다. 혈액 샘플을 채혈하고, 이전에 기재된 바대로 8일 및 15일에 아포(a) 수준, 지질 수준 및 독성 마커에 대해 분석하였다. Lp(a) 수준을 3개의 투약전 값의 평균으로 정규화하였다.

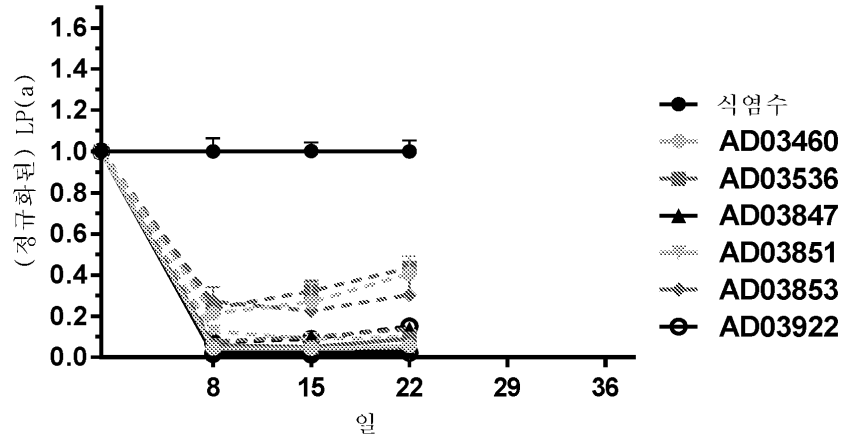
표 20. 식염수 또는 2 mg/kg의 AD03460, AD03536, AD03851, AD03853 또는 AD04110의 투여 후 사이노몰거스 마카크 영장류에서의 지단백(a) 수준.

	정규화된 Lp(a) 8일	정규화된 Lp(a) 15일
식염수	1.01 ± 0.06	1.15 ± 0.07
AD03460	0.68 ± 0.12	0.40 ± 0.13
AD03536	0.54 ± 0.07	0.21 ± 0.06
AD03851	0.41 ± 0.08	0.18 ± 0.08
AD03853	0.50 ± 0.23	0.27 ± 0.17
AD04110	0.59 ± 0.13	0.43 ± 0.10

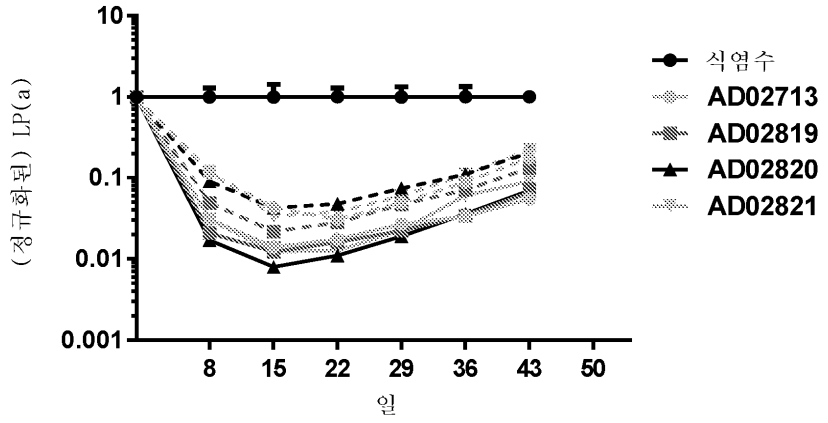
[0299]

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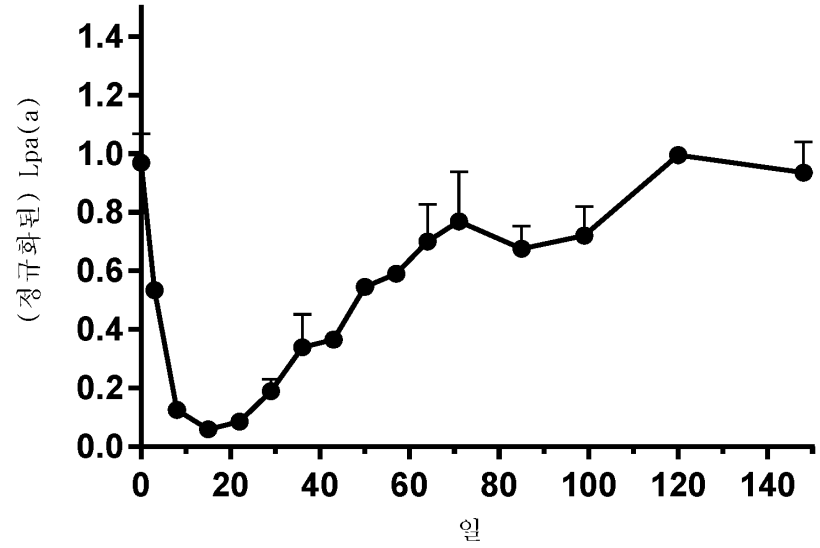
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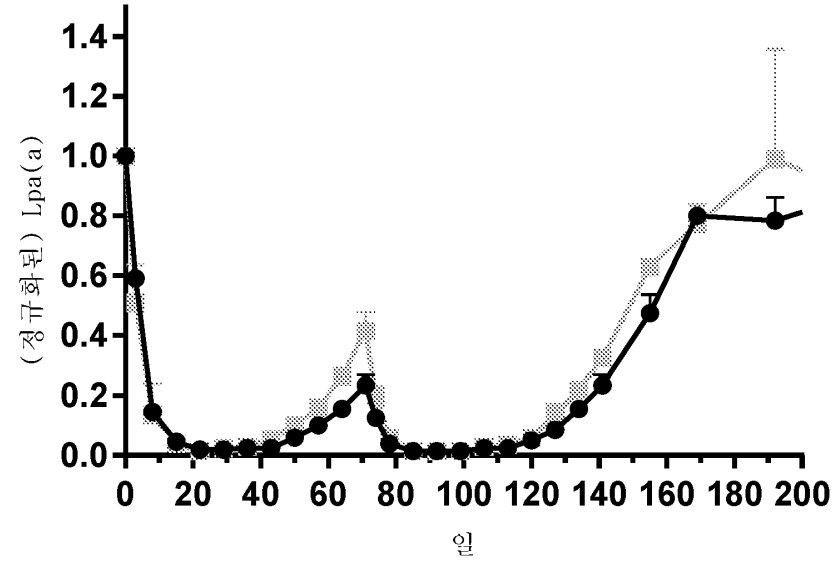
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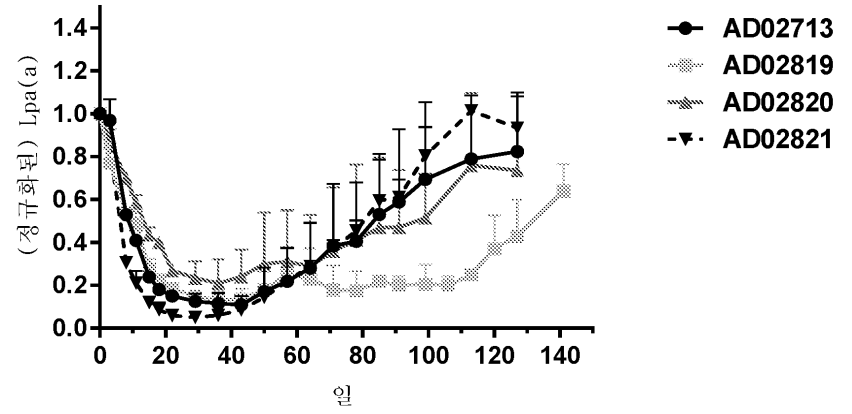
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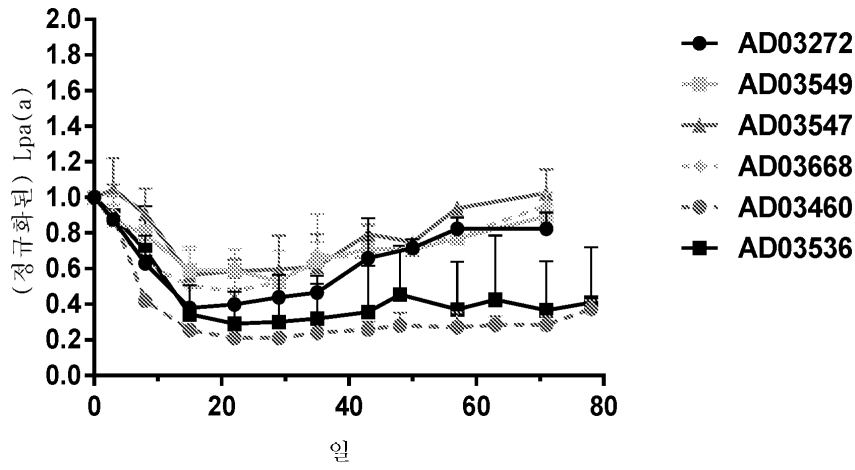
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일

도면5



도면6



서 열 목 록

SEQUENCE LISTING

<110> Arrowhead Pharmaceuticals, Inc.

Stacey Melquist

Steven Kanner

David B. Rozema

David L. Lewis

Lauren J. Almeida

Darren H. Wakefield

Vladimir S. Trubetskoy

Tao Pei

Zhen Li

Aaron Almeida

<120> Compositions and Methods for Inhibiting Gene Expression
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<210> 615

<211> 26

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<400> 615

ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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<210> 618

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ugagaaugag ccucgauaac ucuuau 26

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<400> 619

ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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<400> 628

ugagaaugag ccucgauaac ucuuau 26

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<400> 629

ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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<222> 1,3,5,7,8,9,10,11,12,13,15,17,19,21,23,24,26

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<400> 631

ucguauaaca auaaggggcu gccuau 26

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ucguauaaca auaaggggcu gccuau 26

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ucguauaaca auaaggggcu gccuau 26

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ucguauaaca auaaggggcu gccuau 26

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ucguauaaca auaaggggcu gccuau 26

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<400> 636

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<210> 637

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<400> 637

ucguauaaca auaaggggcu gccuau 26

<210> 638

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<221> modified_base

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<220>

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<400> 638

ucguauaaca auaaggggcu gccuau 26

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<400> 639

ugagaaugag ccucgauaat t 21

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<220>

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<220>

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<400> 640

ucguauaaca auaaggggcu gccuau 26

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<220>

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<220>

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<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<400> 641

ucguauaaca auaaggggcu gccuau 26

<210> 642

<211> 26

<212> DNA

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<220>

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<220>

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<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<220>

<221> modified_base

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<220>

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<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 642

ugagaaugag ccucgauaac ucuuau 26

<210> 643

<211> 26

<212> DNA

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<220

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<220>

<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

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<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 643

tgagaaugag ccucgauaac ucuuau 26

<210> 644

<211> 26

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<220>

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<220>

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<222> 3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

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<220>

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<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

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<220>

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<400> 644

tgagaaugag ccucgauaac ucuuau 26

<210> 645

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<220>

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<222> 3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

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<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

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<222> 26

<223> /mod_base = "3' end Vinyl Phosphonate modification"

<400> 645

tgagaaugag ccucgauaac ucuuau 26

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<400> 646

tgagaaugag ccucgauaac ucuuau 26

<210> 647

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<222> 3,5,7,9,11,12,13,15,17,19,21,23,24,26

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<222> 26

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<400> 647

tcguauaaca auaaggggcu gccuau 26

<210> 648

<211> 26

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<222> 3,5,7,9,11,12,13,15,17,19,21,23,24,26

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<222> 2,3,23,24

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<400> 648

tcguauaaca auaaggggcu gccuau 26

<210> 649

<211> 26

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<400> 649

ugagaaugag ccucgauaac ucuuau 26

<210> 650

<211> 26

<212> DNA

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ugagaaugag ccucgauaac ucuuau 26

<210> 652

<211> 26

<212> DNA

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<220>

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<222> 2,3,23,24

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<400> 652

ugagaaugag ccucgauaac ucuuau 26

<210> 653

<211> 26

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<400> 653

ugagaaugag ccucgauaac ucuuau 26

<210> 654

<211> 26

<212> DNA

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<220>

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<222> 1,3,4,5,6,7,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<400> 654

ugagaaugag ccucgauaac ucuuau 26

<210> 655

<211> 26

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<400> 655

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<222> 1,3,5,7,9,11,12,13,15,17,19,21,23,24,26

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<400> 656

ucguauaaca auaaggcgcu gccuau 26

<210> 657

<211> 26

<212> DNA

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<400> 657

ucguauaaca auaaggggcu gccuau 26

<210> 658

<211> 26

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<400> 658

ucguauaaca auaaggggcu gccuau 26

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<400> 659

ucguauaaca auaaggggcu gccuau 26

<210> 660

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<222> 1,3,5,7,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<222> 2,3,23,24

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<400> 660

ucguauaaca auaaggggcu gccuau 26

<210> 661

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<210> 662

<211> 26

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ucguauaaca auaaggggcu gccuau 26

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ugagaaugag ccucgauaac ucuuau 26

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ugagaaugag ccucgauaac ucuuau 26

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<400> 665

ugagaaugag ccucgauaac ucuuau 26

<210> 666

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ugagaaugag ccucgauaac ucuuau 26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<222> 2,3,23,24

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<400> 667

ugagaaugag ccucgauaac ucuuau 26

<210> 668

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<222> 1,3,4,5,6,7,9,11,12,13,15,16,17

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<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 668

uguauaacaa uaagggg 17

<210> 669

<211> 17

<212> DNA

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<220>

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<222> 16,17

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<220>

<221> modified_base

<222> 2,3

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<400> 669

uguauaacaa uaagggg 17

<210> 670

<211> 17

<212> DNA

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<220>

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<222> 1,3,4,5,6,7,9,11,12,13,15,16,17

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<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 670

ucguauaaca auaaggg 17

<210> 671

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<220>

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<220>

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<400> 671

ucguauaaca auaaggg 17

<210> 672

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<220>

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<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17

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ugagaaugag ccucgau 17

<210> 673

<211> 17

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<220>

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<222> 1,3,4,5,6,7,8,9,10,11,13,15,16,17

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<220>

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<222> 2,3

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ugagaaugag ccucgau 17

<210> 674

<211> 17

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<220>

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<220>

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<222> 16,17

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<222> 2,3

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<400> 674

ugagaaugag ccucgat 17

<210> 675

<211> 17

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<222> 2,3

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<400> 675

ugacaccuga uucuguu 17

<210> 676

<211> 17

<212> DNA

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<220>

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<220>

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<220>

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<222> 1,3,5,7,8,9,10,11,12,13,15,16,17

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 676

ugacaccuga uucuguu 17

<210> 677

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<221> modified_base

<222> 2,4,6,8,10,12,14

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 677

ugacaccuga uucugtt 17

<210> 678

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 678

ucguauaaca auaaggggcu gccuau 26

<210> 679

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 4

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 679

ucguauaaca auaaggggcu gccuau 26

<210> 680

<211> 26

<212> DNA

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<220>

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<221> modified_base

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<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 6

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 680

ucguauaaca auaaggggcu gccuau 26

<210> 681

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 8

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 681

ucguauaaca auaaggggcu gccuau 26

<210> 682

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 8,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 682

ugagaaugag ccucgauaac ucuuau 26

<210> 683

<211> 26

<212> DNA

<213

> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 8

<223> /mod_base = "2'-F-Arabino nucleoside"

<400> 683

ugagaaugag ccucgauaac ucuuau 26

<210> 684

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,8,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 684

tgagaaugag ccucgauaac ucuuau 26

<210> 685

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 685

tcguauaaca auaaggggcu gccuau 26

<210> 686

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,14

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<220>

<221> modified_base

<222> 3,4,5,6,7,8,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 686

tgagaaugag ccucgauaac ucuuau 26

<210> 687

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,14

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<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 687

ucguauaaca auaaggggcu gccuau 26

<210> 688

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,8,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

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<222> 1,3,5,6,7,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 688

ucguauaaca auaaggggcu gccuau 26

<210> 689

<211> 26

<212> DNA

<213> artificial sequence

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<223> LPA RNAi agent antisense strand

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<221

> modified_base

<222> 2,4,10,14

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<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 689

ucguauaaca auaaggggcu gccuau 26

<210> 690

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 690

ucguauaaca auaaggggcu gccuau 26

<210> 691

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,6,8,14

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<220>

<221> modified_base

<222> 1,3,4,5,7,9,10,11,12,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 691

ucguauaaca auaaggggcu gccuau 26

<210> 692

<211> 26

<212> DNA

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<222> 2,6,10,14

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<221> modified_base

<222> 1,3,4,5,7,8,9,11,12,13,15,16,17,18,19,20,21,22,23,24,26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 692

ucguauaaca auaaggggcu gccuau 26

<210> 693

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,6,12,14

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<222> 1,3,4,5,7,8,9,10,11,13,15,16,17,18,19,20,21,22,23,24,26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 693

ucguauaaca auaaggggcu gccuau 26

<210> 694

<211> 26

<212> DNA

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<223> LPA RNAi agent antisense strand

<220>

<221

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<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,10,11,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 694

ucguauaaca auaaggggcu gccuau 26

<210> 695

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<222> 2,10,12,14

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<222> 1,3,4,5,6,7,8,9,11,13,15,16,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 695

ucguauaaca auaaggggcu gccuau 26

<210> 696

<211> 26

<212> DNA

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<220>

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<222> 1,3,5,7,9,11,13,15,16,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 696

ucguauaaca auaaggggcu gccuau 26

<210> 697

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<222> 2,4,6,8,10,12,14,16,20,22

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<220>

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<222> 1,3,5,7,9,11,13,15,17,18,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 697

ucguauaaca auaaggggcu gccuau 26

<210> 698

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> 2,4,6,8,10,12,14,16,18,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220

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<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,19,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 698

ucguauaaca auaaggggcu gccuau 26

<210> 699

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 2,4,6,8,10,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 699

ucguauaaca auaaggggcu gccuau 26

<210> 700

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222

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<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 700

ucguauaaca auaaggggcu gauu 24

<210> 701

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 701

ucguauaaca auaaggggcu gcuu 24

<210> 702

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,8,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221

> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 702

ugagaaugag ccucgauaac ucuu 24

<210> 703

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,6,8,14,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,7,9,10,11,12,13,15,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 703

ucguauaaca auaaggggcu gccuau 26

<210> 704

<211> 26

<212> DNA

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<220>

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<222> 2,6,8,9,14,16

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<220>

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<222> 1,3,4,5,7,10,11,12,13,15,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

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> /mod_base = "phosphorothioate linked nucleoside"

<400> 704

ucguauaaca auaaggggcu gccuau 26

<210> 705

<211> 26

<212> DNA

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<222> 1,3,4,5,7,9,10,11,12,13,15,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 705

ugagaaugag ccucgauaac ucuuau 26

<210> 706

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,6,8,9,14,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,7,10,11,12,13,15,17,18,19,20,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 706

ugagaaugag ccucgauaac ucuuau 26

<210> 707

<211> 26

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<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 707

ucguauaaca auaaggggcu gccuau 26

<210> 708

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 708

ucguauaaca auaaggggcu u 21

<210> 709

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 709

ucguauaaca auaaggggcu u 21

<210> 710

<211> 21

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

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<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 710

ucguauaaca auaaggggcu u 21

<210> 711

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 711

ugagaaugag ccucgauaac ucuuau 26

<210> 712

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,8,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 712

ugagaaugag ccucgauaac ucuuau 26

<210> 713

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 713

ugagaaugag ccucgauaac ucuuau 26

<210> 714

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,8,9,10,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,11,12,13,15,16,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 714

ugagaaugag ccucgauaac ucuuau 26

<210> 715

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<222> 2,4,6,8,9,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,10,11,12,13,15,17,19,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 715

ugagaaugag ccucgauaac ucuuau 26

<210> 716

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,8,9,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,10,11,12,13,15,16,17,18,19,20,21,22,23,24,25,
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<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 716

ugagaaugag ccucgauaac ucuuau 26

<210> 717

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,8,10,14

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<221> modified_base

<222> 1,3,4,5,6,7,9,11,12,13,15,16,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "3' end (Dy540) modification"

<400> 717

ugagaaugag ccucgauaac ucuuau 26

<210> 718

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,9,12,14,16,18,20,22

<223

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<220>

<221> modified_base

<222> 1,3,5,7,8,10,11,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 718

ucguauaaca auaaggggcu gccuau 26

<210> 719

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,8,12,14,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,9,10,11,13,15,16,17,18,19,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 719

ucguauaaca auaaggggcu gccuau 26

<210> 720

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

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<220>

<221> modified_base

<222> 1,3,4,5,6,7,8,10,11,13,15,16,17,18,19,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 720

ucguauaaca auaaggggcu gccuau 26

<210> 721

<211> 26

<212> DNA

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<223> LPA RNAi agent antisense strand

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<220>

<221> modified_base

<222> 1,3,4,5,6,7,8,10,11,13,15,16,17,18,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 721

ucguauaaca auaaggggcu gccuau 26

<210> 722

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,6,9,12,14,19,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

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221> modified_base

<222> 1,3,4,5,7,8,10,11,13,15,16,17,18,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 722

ucguauaaca auaaggggcu gccuau 26

<210> 723

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

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<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 723

uguauaacaa uaagggg 17

<210> 724

<211> 17

<212>

DNA

<213> artificial sequence

<220>

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<220>

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<222> 2,4,6,8,10,12,14

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<222> 1,3,5,7,9,11,13,15

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<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

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<221

> modified_base

<222> 17

<223> /mod_base = "3' end (Sp18)s(PAZ) modification"

<400> 724

uguauaacaa uaagggg 17

<210> 725

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

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<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

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<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end (C12)s(PAZ) modification"

<400> 725

uguauaacaa uaagggg 17

<210> 726

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

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<222> 2,4,6,8,10,12,14

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<220>

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<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 726

ucguauaaca auaaggg 17

<210> 727

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end (Sp18)s(PAZ) modification"

<400> 727

ucguauaaca auaaggg 17

<210> 728

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<222> 2,4,6,8,10,12,14

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<220>

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<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end (C12)s(PAZ) modification"

<400> 728

ucguauaaca auaaggg 17

<210> 729

<211> 17

<212> DNA

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<220>

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<222> 2,4,6,8,10,12,14

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 729

ugagaaugag ccucgat 17

<210> 730

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end (Sp18)s(PAZ) modification"

<400> 730

ugagaaugag ccucgac 17

<210> 731

<211> 17

<212> DNA

<213

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<220>

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<222> 2,4,6,8,10,12,14

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end (C12)s(PAZ) modification"

<400> 731

ugagaaugag ccucgac 17

<210> 732

<211> 17

<212> DNA

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<220>

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<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222>

16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 732

ugacaccuga uucugtt 17

<210> 733

<211> 17

<212> DNA

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<220>

<223> LPA RNAi agent antisense strand

<220>

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<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

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<400> 733

ugacaccuga uucugtc 17

<210> 734

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

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<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

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400> 734

ugacaccuga uucugtc 17

<210> 735

<211> 26

<212> DNA

<213> artificial sequence

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<222> 3,5,7,13,15,17,19,21,23

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 735

tucguauaac aauaaggggc ugccua 26

<210> 736

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,6,8,14,16,18,20,22,24

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,10,11,12,13,15,17,19,21,23,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 736

uaucguauaa caauaagggg cugccu 26

<210> 737

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19,21,23

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 737

tccguauaac aauaaggggc ugccua 26

<210> 738

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,6,8,14,16,18,20,22,24

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,10,11,12,13,15,17,19,21,23,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 738

cuccguauaa caauaagggg cugccu 26

<210> 739

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,9,11,15,17,19,21

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,10,12,13,14,16,18,20,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 739

tugagaauga gccucgauaa cucuua 26

<210> 740

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,6,8,10,12,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,14,15,17,19,21,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 740

uaugagaaug agccucgaua acucuu 26

<210> 741

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,9,11,15,17,19,21

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,10,12,13,14,16,18,20,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 741

tggagaauga gccucgauaa cucuua 26

<210> 742

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223>

LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,6,8,10,12,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,14,15,17,19,21,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 742

guggagaaug agccucgaua acucuu 26

<210> 743

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,9,11,15

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,5,6,7,8,10,12,13,14,16,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 743

tugagaauga gccucgauaa cucuua 26

<210> 744

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,10,12,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,11,13,14,15,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223

> /mod_base = "phosphorothioate linked nucleoside"

<400> 744

uaugagaaug agccucgaua acucuu 26

<210> 745

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,9,11,15

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,5,6,7,8,10,12,13,14,16,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,24,25

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 745

tggagaauga gccucgauaa cucuua 26

<210> 746

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,10,12,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,11,13,14,15,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 4,5,25,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 746

guggagaaug agccucgaua acucuu 26

<210> 747

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221

> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 747

ucguauaaca auaaggggcu u 21

<210> 748

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 748

ugagaaugag ccucgauaau u 21

<210> 749

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end s(C12)s(PAZ) modification"

<400> 749

uguauaacaa uaagggg 17

<210> 750

<211> 17

<212> DNA

<213

> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end s(C12)s(PAZ) modification"

<400> 750

ucguauaaca auaaggg 17

<210> 751

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222

> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end s(C12)s(PAZ) modification"

<400> 751

ugagaaugag ccucgac 17

<210> 752

<211> 17

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 17

<223> /mod_base = "3' end s(C12)s(PAZ) modification"

<400> 752

ugacaccuga uucugtc 17

<210> 753

<211> 21

<212> DNA

<213

> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 753

tcguauaaca auaaggggcu u 21

<210> 754

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 22,23,24,25,26

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 754

ugagaaugag ccucgauaau uauaua 26

<210> 755

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,22,23

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 755

ucguauaaca auaaggggcu gccuau 26

<210> 756

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 756

ucguauaaca auaaggggcu gccuau 26

<210> 757

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,22,23

<223

> /mod_base = "phosphorothioate linked nucleoside"

<400> 757

ugagaaugag ccucgauaac ucuuau 26

<210> 758

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 758

ugagaaugag ccucgauaac ucuuau 26

<210> 759

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 759

ucguauaaca auaaggggcu gcuu 24

<210> 760

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,14,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 760

ucguauaaca auaaggggcu u 21

<210> 761

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,12,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,13,14,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 761

ucguauaaca auaaggggcu u 21

<210> 762

<211> 23

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,22,23

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 762

ucguauaaca auaaggggcu gcc 23

<210> 763

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19,21,23

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 763

tucguauaac aauaaggggc ugcc 24

<210> 764

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19,21

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 764

tucguauaac aauaaggggc ugcc 24

<210> 765

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19,21

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,5,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 765

tucguauaac aauaaggggc ugcc 24

<210> 766

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19,21

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,5,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 766

tucguauaac aauaaggggc ugcc 24

<210> 767

<211> 22

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 3,5,7,13,15,17,19

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,8,9,10,11,12,14,16,18,20,21,22

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 3,4,5,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 767

tucguauaac aauaaggggc ug 22

<210> 768

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end ethyl phosphonate modification"

<400> 768

tcguauaaca auaaggggcu u 21

<210> 769

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end ethyl phosphonate modification"

<400> 769

tcguauaaca auaaggggcu u 21

<210> 770

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,21,22

<223

> /mod_base = "phosphorothioate linked nucleoside"

<400> 770

ugagaaugag ccucgauaac ucuuau 26

<210> 771

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 771

ugagaaugag ccucgauaac ucuuau 26

<210> 772

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 772

ugagaaugag ccucgauaac uaucgc 26

<210> 773

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 773

ugagaaugag ccucgauaac uauuca 26

<210> 774

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 774

ugagaaugag ccucgauaac uacgau 26

<210> 775

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 2

<223> /mod_base = "5'-methyl, 2'-fluoro nucleoside"

<400> 775

ugagaaugag ccucgauaac ucuuau 26

<210> 776

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 4

<223> /mod_base = "5'-methyl, 2'-fluoro nucleoside"

<400> 776

ugagaaugag ccucgauaac ucuuau 26

<210> 777

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 8

<223> /mod_base = "5'-methyl, 2'-fluoro nucleoside"

<400> 777

ugagaaugag ccucgauaac ucuuau 26

<210> 778

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 10

<223> /mod_base = "5'-methyl, 2'-fluoro nucleoside"

<400> 778

ugagaaugag ccucgauaac ucuuau 26

<210> 779

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,10,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,11,12,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

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<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 779

ucguauaaca auaaggggcg u 21

<210> 780

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 780

ucguauaaca auaaggggcu gccu 24

<210> 781

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 781

ucguauaaca auaaggggcu gcuu 24

<210> 782

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 782

ucguauaaca auaaggggcu gccu 24

<210> 783

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end Vinyl Phosphonate modification"

<400> 783

ucguauaaca auaaggggcu gcuu 24

<210> 784

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,9,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,10,11,12,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

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<221

> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,22,23

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 784

ugagaaugag ccucgauaac ucuuau 26

<210> 785

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,12,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 785

ugagaaugag ccucgauaac ucuuau 26

<210> 786

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 786

ucguauaaca auaaggggcu gccuau 26

<210> 787

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 787

ucguauaaca auaaggggcu u 21

<210> 788

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

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<222> 2,4,6,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

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<222> 1,3,5,7,8,9,10,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 788

ucguauaaca auaaggggcu u 21

<210> 789

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 789

ucguauaaca auaaggggcu g 21

<210> 790

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 790

ucguauaaca auaaggggcu g 21

<210> 791

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 791

ucguauaaca auaaggggcu gcuu 24

<210> 792

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 792

ugagaaugag ccucgauaac ucuuau 26

<210> 793

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

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<222> 2,4,6,8,10,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

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<222> 1,3,5,7,9,11,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223

> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 793

ugagaaugag ccucgauaac ucuuau 26

<210> 794

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,8,10,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222>

3,5,7,9,11,13,15,17,19,21,22,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 794

tgagaaugag ccucgauaac ucuuau 26

<210> 795

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,8,9,10,11,13,15,17,19,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 795

tcguauaaca auaaggggcu gccuau 26

<210> 796

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,8,9,10,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 796

tcguauaaca auaaggggcu u 21

<210> 797

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211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2,4,6,12,14,16,18,20,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

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<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

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<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 797

tcguauaaca auaaggggcu gcuu 24

<210> 798

<211> 21

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ucguauaaca auaaggggcu u 21

<210> 799

<211> 26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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ugagaaugag ccucgauaac ucuuau 26

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<400> 800

ugagaaugag ccucgauaac ucuuau 26

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<222> 2,3,23,24

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<400> 801

ugagaaugag ccucgauaac ucuuau 26

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<222> 2,3,23,24

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ugagaaugag ccucgauaac ucuuau 26

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<222> 2,3,23,24

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ugagaaugag ccucgauaac ucuuau 26

<210> 804

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<221> modified_base

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<222> 2,3,23,24

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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tgagaaugag ccucgauaac ucuuau 26

<210> 806

<211> 26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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tgagaaugag ccucgauaac ucuuau 26

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<222> 2,3,23,24

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tgagaaugag ccucgauaac ucuuau 26

<210> 808

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<222> 2,3,23,24

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<400> 808

tgagaaugag ccucgauaac ucuuau 26

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<222> 3,5,7,8,9,10,11,12,13,15,17,18,19,21,23,24,26

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tgagaaugag ccucgauaac ucuuau 26

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<211> 26

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tgagaaugag ccucgauaac ucuuau 26

<210> 811

<211> 26

<212> DNA

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<220>

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<222> 3,5,7,9,10,11,12,13,15,16,17,18,19,21,23,24,26

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tgagaaugag ccucgauaac ucuuau 26

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<222> 2,3,23,24

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<400> 812

tgagaaugag ccucgauaac ucuuau 26

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<400> 813

tgagaaugag ccucgauaac ucuuau 26

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<211> 26

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<222> 25

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tgagaaugag ccucgauaac ucuuau 26

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tgagaaugag ccucgauaac ucuuau 26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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tgagaaugag ccucgauaac ucuuau 26

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,15,17,19,21,23,24,26

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ugagaaugag ccucgauaac ucuuau 26

<210> 818

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<400> 818

ugagaaugag ccucgauaac ucuuau 26

<210> 819

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<222> 2,3,23,24

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<400> 819

ugagaaugag ccucgauaac ucuuau 26

<210> 820

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 820

ugagaaugag ccucgauaac ucuuau 26

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<222> 1,3,5,7,8,9,10,11,12,13,15,16,17,19,21,23,24,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<400> 821

ugagaaugag ccucgauaac ucuuau 26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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ugagaaugag ccucgauaac ucuuau 26

<210> 823

<211> 26

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<220>

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<222> 25

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<222> 2,3,23,24

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<400> 823

ugagaaugag ccucgauaac ucuuau 26

<210> 824

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<222> 1,2,3,5,7,8,9,11,12,13,15,17,19,21,23,24,26

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<222> 25

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<222> 2,3,23,24

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<400> 824

ugacaccuga uucuguuucu gaguau 26

<210> 825

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<212> DNA

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<220>

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<222> 1,2,3,5,7,9,10,11,12,13,15,17,19,21,23,24,26

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ugacaccuga uucuguuucu gaguau 26

<210> 826

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<400> 826

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<220>

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<222> 25

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<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 827

tgacaccuga uucuguuucu gaguau 26

<210> 828

<211> 26

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<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

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<222> 3,5,7,9,10,11,12,13,15,16,17,19,21,23,24,26

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<220>

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<222> 2,3,23,24

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<400> 828

tgacaccuga uucuguuucu gaguau 26

<210> 829

<211> 26

<212> DNA

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<222> 3,5,7,9,10,11,12,13,15,17,18,19,21,23,24,26

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

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<400> 829

tgacaccuga uucuguuucu gaguau 26

<210> 830

<211> 26

<212> DNA

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<222> 3,5,7,9,11,12,13,15,16,17,18,19,21,23,24,26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<222> 2,3,23,24

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<400> 830

tgacaccuga uucuguuucu gaguau 26

<210> 831

<211> 26

<212> DNA

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<222> 3,5,7,9,11,12,13,15,16,17,19,20,21,23,24,26

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 831

tgacaccuga uucuguuucu gaguau 26

<210> 832

<211> 26

<212> DNA

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<222> 3,5,7,9,11,12,13,15,17,18,19,20,21,23,24,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 832

tgacaccuga uucuguuucu gaguau 26

<210> 833

<211> 26

<212> DNA

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<222> 3,5,7,9,11,12,13,15,16,17,18,19,20,21,23,24,26

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<222> 2,3,23,24

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<400> 833

tgacaccuga uucuguuucu gaguau 26

<210> 834

<211> 26

<212> DNA

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<221> modified_base

<222> 3,5,7,9,11,12,13,15,16,17,18,19,21,22,23,24,26

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<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 834

tgacaccuga uucuguuucu gaguau 26

<210> 835

<211> 26

<212> DNA

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<221

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<222> 3,5,7,9,11,12,13,15,16,17,19,20,21,22,23,24,26

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

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<400> 835

tgacaccuga uucuguuucu gaguau 26

<210> 836

<211> 26

<212> DNA

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<221> modified_base

<222> 2,3,5,7,8,9,11,12,13,15,17,19,21,23,24,26

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<222> 25

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<221> modified_base

<222> 2,3,23,24

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<400> 836

tgacaccuga uucuguuucu gaguau 26

<210> 837

<211> 26

<212> DNA

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<223> LPA RNAi agent antisense strand

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<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,3,5,7,9,10,11,12,13,15,17,19,21,23,24,26

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<222> 25

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<221> modified_base

<222> 2,3,23,24

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<400> 837

tgacaccuga uucuguuucu gaguau 26

<210> 838

<211> 26

<212> DNA

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<220>

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<220>

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<222> 1,2,3,5,7,8,9,10,11,12,13,15,17,19,21,23,24,26

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<222> 2,3,23,24

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<400> 838

ugacaccuga uucuguuucu gaguau 26

<210> 839

<211> 26

<212> DNA

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<222> 1,3,5,7,8,9,11,12,13,15,16,17,19,21,23,24,26

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<221> modified_base

<222> 25

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<222> 2,3,23,24

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<400> 839

ugacaccuga uucuguuucu gaguau 26

<210> 840

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent antisense strand

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<222> 1,3,5,7,9,10,11,12,13,15,16,17,19,21,23,24,26

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 840

ugacaccuga uucuguuucu gaguau 26

<210> 841

<211> 26

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<223> LPA RNAi agent antisense strand

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<222> 1,3,5,7,9,10,11,12,13,15,17,18,19,21,23,24,26

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<222> 2,3,23,24

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<400> 841

ugacaccuga uucuguuucu gaguau 26

<210> 842

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent antisense strand

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<220>

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<222> 1,3,5,7,9,11,12,13,15,16,17,18,19,21,23,24,26

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<222> 2,3,23,24

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<400> 842

ugacaccuga uucuguuucu gaguau 26

<210> 843

<211> 26

<212> DNA

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<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 843

ugacaccuga uucuguuucu gaguau 26

<210> 844

<211> 26

<212> DNA

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<220>

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<222> 1,3,5,7,9,11,12,13,15,17,18,19,20,21,23,24,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 2,3,23,24

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<400> 844

ugacaccuga uucuguuucu gaguau 26

<210> 845

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<212> DNA

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<222> 1,3,5,7,9,11,12,13,15,16,17,18,19,20,21,23,24,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<400> 845

ugacaccuga uucuguuucu gaguau 26

<210> 846

<211> 26

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<222> 1,3,5,7,9,11,12,13,15,16,17,18,19,21,22,23,24,26

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<222> 2,3,23,24

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<400> 846

ugacaccuga uucuguuucu gaguau 26

<210> 847

<211> 26

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<400> 847

ugacaccuga uucuguuucu gaguau 26

<210> 848

<211> 26

<212> DNA

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<222> 2,3,23,24

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<400> 848

tgacaccuga uucuguuucu gaguau 26

<210> 849

<211> 20

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<222> 2,4,6,8,10,12,14,16,18

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<222> 20

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<400> 849

acgcagaagg gacugccgat 20

<210> 850

<211> 20

<212> DNA

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<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 850

ggggugcagg agugcuacat 20

<210> 851

<211> 20

<212> DNA

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<220>

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<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 851

cuguggcagc cccuuauuat 20

<210> 852

<211> 20

<212> DNA

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<220>

<221> modified_base

<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 852

ggcagccccu uauuguuaat 20

<210> 853

<211> 20

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<220>

<221> modified_base

<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 853

agccccuuau uguuauacat 20

<210> 854

<211> 20

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<220>

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<221> modified_base

<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 854

gccccuuauu guuauacgat 20

<210> 855

<211> 20

<212> DNA

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<220>

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<221> modified_base

<222> 20

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<400> 855

ugacacaaug cucagacgat 20

<210> 856

<211> 20

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

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<222> 2,4,6,8,10,12,14,16,18

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<221> modified_base

<222> 20

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<400> 856

gacacaaugc ucagacgcat 20

<210> 857

<211> 20

<212> DNA

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<220>

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<222> 2,4,6,8,10,12,14,16,18

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<220>

<221> modified_base

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<400> 857

acacaaugcu cagacgcaat 20

<210> 858

<211> 20

<212> DNA

<213> artificial sequence

<220>

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<222> 2,4,6,8,10,12,14,16,18

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 20

<223> /mod_base = "inverted nucleoside"

<400> 858

acaaugcuca gacgcagaat 20

<210> 859

<211> 20

<212> DNA

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<220>

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<220>

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<222> 20

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<400> 859

cugccgaaau ccagauccat 20

<210> 860

<211> 20

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

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<210> 879

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<400> 884

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<210> 885

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<210> 894

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<210> 896

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uauagccccu uauuguuaua cat 23

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uaugccccuu auuguuauac gat 23

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uauacacaau gcucagacgc aat 23

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uauuuaucga ggcucauucu cat 23

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uaugaaacag aaucaggugu cat 23

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uauacaccag cauagucgga cat 23

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uauccaugga ucccaguguc aat 23

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<210> 943

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ccaaauggug gccugaccat 20

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ugguguuaua ccauggauat 20

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<210> 958

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gcuccuucug aacaagcaat 20

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auaccacacu ggcaucagat 20

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<210> 964

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<400> 964

gaaucaggug uccuagagat 20

<210> 965

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aaucaggugu ccuagagaat 20

<210> 966

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<400> 966

aucagguguc cuagagacat 20

<210> 967

<211> 26

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<222> 1,3,5,7,9,11,13,15,17,19,21,23,25

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<222> 6,7

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<221> modified_base

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<400> 967

uauauaguua ucgaggcuca uucuca 26

<210> 968

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<212> DNA

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<222> 1,3,5,7,9,11,13,14,17,19,21,23,25

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<400> 968

uauauaguua ucgaggcuca uucuca 26

<210> 969

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<212> DNA

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uauauaguua ucgaggcuca uucuca 26

<210> 970

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<212> DNA

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<220>

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<220>

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uauauaguua ucgaggcuca uucuca 26

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<222> 2,4

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<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

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<222> 26

<223> /mod_base = "3' end (C11-PEG3-NAG3) modification"

<400> 1031

uauaucagaa acagaaucag guguca 26

<210> 1032

<211> 26

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<222> 26

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<210> 1033

<211> 26

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<222> 1,3,5,7,9,11,13,17,19,20,21,22,23,24,25,26

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<210> 1034

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<220>

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<222> 1,3,5,7,8,9,10,11,13,17,19,20,21,22,23,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

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<210> 1035

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<222> 1,3,5,7,9,11,13,15,17,19,21,22,23,24,25

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

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<221> modified_base

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<210> 1036

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

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<221> modified_base

<222> 26

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<400> 1036

uauauaguua ucgaggcuca uucuca 26

<210> 1037

<211> 26

<212> DNA

<213> artificial sequence

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<222> 6,8,10,12,14,15,16,18,20,22,24,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 26

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uauauaguua ucgaggcuca uucuca 26

<210> 1038

<211> 26

<212> DNA

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<222> 6,8,10,12,14,15,16,18,20,22,24,26

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<222> 1,3,5,7,9,11,13,17,19,21,23,25

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 7,8

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<222> 26

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<400> 1038

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<210> 1039

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

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<222> 1,3,5,7,9,11,13,17,19,21,23,25,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 26

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<400> 1039

uauaucagcc ccuuauuguu auacga 26

<210> 1040

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

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<400> 1040

uauaucagcc ccuuauuguu auacga 26

<210> 1041

<211> 26

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<400> 1041

uauaucagcc ccuuauuguu auacga 26

<210> 1042

<211> 26

<212> DNA

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<211> 26

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<222> 1,3,5,7,9,11,13,17,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 2,4

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<221> modified_base

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uauauaguua ucgaggcuca uucuca 26

<210> 1044

<211> 26

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<222> 1,3,5,7,9,11,13,17,18,19,20,21,22,23,24,25,26

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<210> 1045

<211> 26

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<222> 1,3,5,7,8,9,10,11,13,17,19,20,21,22,23,24,25,26

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uauauaguua ucgaggcuca uucuca 26

<210> 1046

<211> 26

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<222> 1,3,5,7,8,9,10,11,13,17,18,19,20,21,22,23,24,25,26

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uauauaguua ucgaggcuca uucuca 26

<210> 1047

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uauauaguua ucgaggcuca uucuca 26

<210> 1048

<211> 26

<212> DNA

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uauauaguua ucgaggcuca uucuca 26

<210> 1049

<211> 26

<212> DNA

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uauauaguua ucgaggcuca uucuca 26

<210> 1050

<211> 26

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uauauaguua ucgaggcuca uucuca 26

<210> 1051

<211> 26

<212> DNA

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<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,17,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1051

uauauaguua ucgaggcuca uucuca 26

<210> 1052

<211> 26

<212> DNA

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<222> 1,3,5,7,8,9,10,11,13,17,18,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1052

uauauaguua ucgaggcuca uucuca 26

<210> 1053

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<223> /mod_base = "2'-hydroxy nucleoside"

<220>

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<222> 6,7

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<400> 1053

uauauaguua ucgaggcuca uucuca 26

<210> 1054

<211> 26

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<222> 1,3,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25,26

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<220>

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1054

uauauaguua ucgaggcuca uucuca 26

<210> 1055

<211> 26

<212> DNA

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<222> 1,3,5,7,9,11,13,14,17,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1055

uauauaguua ucgaggcuca uucuca 26

<210> 1056

<211> 26

<212> DNA

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,14,17,18,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1056

uauauaguua ucgaggcuca uucuca 26

<210> 1057

<211> 26

<212>

DNA

<213> artificial sequence

<220>

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<222> 2,4

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<220>

<221> modified_base

<222> 6,7

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<400> 1057

uauauaguua ucgaggcuca uucuca 26

<210> 1058

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> 1,3,5,7,8,9,10,11,13,14,17,18,19,20,21,22,23,24,25,26

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1058

uauauaguua ucgaggcuca uucuca 26

<210> 1059

<211> 26

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<220>

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<222> 2,4

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<220>

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<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1059

uauauaguua ucgaggcuca uucuca 26

<210> 1060

<211> 26

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<222> 15,16

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<220>

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<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,25,26

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<222> 6,7

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<400> 1060

uauauaguua ucgaggcuca uucuca 26

<210> 1061

<211> 26

<212> DNA

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<220>

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,17,19,20,21,22,23,24,25,26

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

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<222> 26

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<400> 1061

uauauaguua ucgaggcuca uucuca 26

<210> 1062

<211> 26

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<220>

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<222> 1,3,5,7,8,9,10,11,13,17,19,20,21,22,23,24,25,26

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<222> 6,7

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<220>

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<222> 26

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<400> 1062

uauauaguua ucgaggcuca uucuca 26

<210> 1063

<211> 26

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1063

uauauaguua ucgaggcuca uucuca 26

<210> 1064

<211> 26

<212> DNA

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<222> 2,4

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<220>

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<222> 6,7

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<400> 1064

uauaucagcc ccuuauuguu auacga 26

<210> 1065

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> 1,3,5,7,8,9,11,13,15,17,18,19,21,23,25,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<400> 1065

uauaucagcc ccuuauuguu auacga 26

<210> 1066

<211> 26

<212> DNA

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<220>

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<222> 1,3,5,7,8,9,11,13,15,17,18,19,20,21,22,23,25,26

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<400> 1066

uauaucagcc ccuuauuguu auacga 26

<210> 1067

<211> 26

<212> DNA

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<222> 14,16

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<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,12,13,15,17,18,19,20,21,22,23,24,25,26

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<400> 1067

uauaucagcc ccuuauuguu auacga 26

<210> 1068

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<222> 15,16

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<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,25,26

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<221> modified_base

<222> 6,7

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<400> 1068

uauaucagcc ccuuauuguu auacga 26

<210> 1069

<211> 26

<212> DNA

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<222> 6,10,12,14,15,16,20,22,24

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<220>

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<222> 1,3,5,7,8,9,11,13,17,18,19,21,23,25,26

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<222> 2,4

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<222> 6,7

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<400> 1069

uauaucagcc ccuuauuguu auacga 26

<210> 1070

<211> 26

<212>

DNA

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<220>

<221> modified_base

<222> 1,3,5,7,8,9,11,13,17,18,19,20,21,22,23,25,26

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<222> 6,7

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<400> 1070

uauaucagcc ccuuauuguu auacga 26

<210> 1071

<211> 26

<212> DNA

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<220>

<221> modified_base

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<222> 6,7

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<400> 1071

uauaucagcc ccuuauuguu auacga 26

<210> 1072

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

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<220>

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<400> 1072

uauaucagcc ccuuauuguu auacga 26

<210> 1073

<211> 26

<212> DNA

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<222> 1,3,5,6,7,8,9,10,11,12,13,15,17,18,19,20,21,22,23,24,25,26

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<221> modified_base

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<400> 1073

uauaucagcc ccuuauuguu auacga 26

<210> 1074

<211> 26

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<221> modified_base

<222> 1,3,5,7,8,9,11,13,15,17,18,19,21,23,25,26

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<400> 1074

uauaucagcc ccuuauuguu auacga 26

<210> 1075

<211> 26

<212> DNA

<213> artificial sequence

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<223> LPA RNAi agent sense strand

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<222> 6,10,12,14,16,24

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<222> 1,3,5,7,8,9,11,13,15,17,18,19,20,21,22,23,25,26

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<400> 1075

uauaucagcc ccuuauuguu auacga 26

<210> 1076

<211> 26

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<221> modified_base

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<222> 26

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<400> 1076

uauaucagcc ccuuauuguu auacga 26

<210> 1077

<211> 26

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<221> modified_base

<222> 26

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<400> 1077

uauaucagcc ccuuauuguu auacga 26

<210> 1078

<211> 26

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<222> 26

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uauaucagcc ccuuauuguu auacga 26

<210> 1079

<211> 26

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<400> 1079

uauaucagcc ccuuauuguu auacga 26

<210> 1080

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<220>

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<222> 1,3,5,7,8,9,11,13,14,17,18,19,20,21,22,23,25,26

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<222> 6,7

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<221> modified_base

<222> 26

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<400> 1080

uauaucagcc ccuuauuguu auacga 26

<210> 1081

<211> 26

<212> DNA

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<220>

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<222> 14,15,16

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<220>

<221> modified_base

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<222> 26

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<400> 1081

uauauaguua ucgaggcuca uucuca 26

<210> 1082

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 15,16

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<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,25

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<221> modified_base

<222> 2,4

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<223> /mod_base = "5' end (Chol-TEG) modification"

<400> 1082

uauauaguua ucgaggcuca uucuca 26

<210> 1083

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

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<222> 15,16

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<220>

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<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,25,26

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 6,7

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<220>

<221> modified_base

<222> 1

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<400>

1083

uauauaguua ucgaggcuca uucuca 26

<210> 1084

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

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<220>

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<222> 26

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<220>

<221> modified_base

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<222> 6

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (Chol-TEG) modification"

<400> 1084

uauauaguua ucgaggcuca uucuca 26

<210> 1085

<211> 17

<212> DNA

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<220>

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<220>

<221> modified_base

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<220>

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<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 17

<223> /mod_base = "3' end (NAG13) modification"

<400> 1085

ccccuuauug uuauaca 17

<210> 1086

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<222> 1,3,5,7,9,11,13,15

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<220>

<221> modified_base

<222> 2,4,6,8,10,12,14,16,17

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<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

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<222> 17

<223> /mod_base = "3' end (NAG13) modification"

<400> 1086

cccuuauugu uauacga 17

<210> 1087

<211> 17

<212> DNA

<213> artificial sequence

<220>

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<220>

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<220>

<221> modified_base

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agaugcugag auucgca 17

<210> 1088

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<222> 2,4,6,8,10,12,14,16,17

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<400> 1088

guuaucgagg cucauua 17

<210> 1089

<211> 17

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<400> 1089

aucgaggcuc auucuca 17

<210> 1090

<211> 17

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<400> 1090

aacagaauca gguguca 17

<210> 1091

<211> 26

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<222> 15,16

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<220>

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<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

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<223> /mod_base = "2'-hydroxy nucleoside"

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<210> 1092

<211> 26

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<222> 1,3,5,7,9,11,13,17,19,21,23,25,26

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<210> 1093

<211> 26

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<220>

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<400> 1093

uauaucagcc ccuuauuguu auacga 26

<210> 1094

<211> 26

<212> DNA

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<222> 1,3,5,6,7,8,9,10,11,12,13,14,17,19,20,21,22,23,24,25,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

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<400> 1094

uauaucagcc ccuuauuguu auacga 26

<210> 1095

<211> 26

<212> DNA

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<222> 14,15,16

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<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25,26

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<223> /mod_base = "2'-hydroxy nucleoside"

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uauaucagcc ccuuauuguu auacga 26

<210> 1096

<211> 26

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<222> 6,8,10,12,14,15,16,18,20,22,24,26

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<222> 1,3,5,7,9,11,13,17,19,21,23,25

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

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<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 26

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<400> 1096

uauauaguua ucgaggcuca uucuca 26

<210> 1097

<211> 26

<212> DNA

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<222> 1,3,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25,26

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<221> modified_base

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<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 6,7

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<221> modified_base

<222> 26

<223> /mod_base = "3' end (NAG13) modification"

<400> 1097

uauauaguua ucgaggcuca uucuca 26

<210> 1098

<211> 26

<212> DNA

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<223> /mod_base = "2'-hydroxy nucleoside"

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<221> modified_base

<222> 6,7

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<400> 1098

uauaucagcc ccuuauuguu auacga 26

<210> 1099

<211> 26

<212> DNA

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<223> /mod_base = "2'-hydroxy nucleoside"

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<400> 1099

uauaucagcg ccuuauuguu auacga 26

<210> 1100

<211> 26

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<222> 1,3,5,6,7,9,11,13,17,19,21,23,25,26

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uauaucagcc ccuuauuguu auacga 26

<210> 1101

<211> 17

<212> DNA

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<220>

<221> modified_base

<222> 1,2,3,4,8,9,10,11,12,13,14,15,16,17

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

<222> 2,3

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<220>

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<400> 1101

ccccuuauug uuauaca 17

<210> 1102

<211> 17

<212> DNA

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<222> 1,2,3,4,8,9,10,11,12,13,14,15

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<400> 1102

ccccuuauug uuauaca 17

<210> 1103

<211> 17

<212> DNA

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ccccuuauug uuauaca 17

<210> 1104

<211> 17

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cccuuauugu uauacga 17

<210> 1105

<211> 17

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cccuuauugu uauacga 17

<210> 1106

<211> 17

<212> DNA

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cccuuauugu uauacga 17

<210> 1107

<211> 17

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<222> 1,2,3,4,8,9,10,11,12,13,14,15,16,17

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aucgaggcuc auucuca 17

<210> 1108

<211> 17

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<222> 1,2,3,4,8,9,10,11,12,13,14,15

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<223> /mod_base = "2'-MOE nucleoside"

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<221> modified_base

<222> 2,3

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<222> 17

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aucgaggcuc auucuca 17

<210> 1109

<211> 17

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<221> modified_base

<222> 3,4,8,9,10,11,12,13,14,15

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<221> modified_base

<222> 1,2,16,17

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<221> modified_base

<222> 2,3

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<222> 17

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<400> 1109

atcgaggcuc auucuca 17

<210> 1110

<211> 17

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<222> 1,2,3,4,8,9,10,11,12,13,14,15,16,17

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<400> 1110

aacagaauca gguguca 17

<210> 1111

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<220>

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<222> 1,2,3,4,8,9,10,11,12,13,14,15

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<222> 16,17

<223> /mod_base = "2'-MOE nucleoside"

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<222> 2,3

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aacagaauca gguguca 17

<210> 1112

<211> 17

<212> DNA

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<220>

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<220>

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<222> 3,4,8,9,10,11,12,13,14,15

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<221> modified_base

<222> 1,2,16,17

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 17

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<400> 1112

aacagaauca gguguca 17

<210> 1113

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 14,15,16

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG18) modification"

<400> 1113

uauauaguua ucgaggcuca uucuca 26

<210> 1114

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 8,10,12,14,15,16,18,20,22,24

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,9,11,13,17,19,21,23,25

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<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

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<400> 1114

uauaucagcc ccuuauuguu auacga 26

<210> 1115

<211> 24

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

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<220>

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<222> 1,2,3,5,7,9,13,15,17,19,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 1

<223> /mod_base = "5' end (NAG4) modification"

<400> 1115

ucagccccuu auuguuauac gauu 24

<210> 1116

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<222> 1,2,3,5,7,9,13,15,17,19,21,22

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG4) modification"

<400> 1116

ucagccccuu auuguuauac ga 22

<210> 1117

<211> 24

<212> DNA

<213> artificial sequence

<220>

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<220>

<221

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<222> 4,6,8,10,11,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,5,7,9,13,15,17,19,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG24) modification"

<400> 1117

ucagccccuu auuguuauac gauu 24

<210> 1118

<211> 24

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 10,11,12

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,13,14,15,16,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG4) modification"

<400> 1118

uaguuaucga ggcucauucu cauu 24

<210> 1119

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 12,14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,13,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "3' end (NAG13) modification"

<400> 1119

uauaucagcc ccuuauuguu auacga 26

<210> 1120

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 12,14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,6,7,8,9,10,11,13,17,18,19,20,21,22,23,24,25,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "3' end (NAG13) modification"

<400> 1120

uauauaguua ucgaggcuca uucuca 26

<210> 1121

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 8,10,12,14,15,16,18,20,22,24

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,9,11,13,17,19,21,23,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 6,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG4) modification"

<400> 1121

uauaucagcc ccuuauuguu auacga 26

<210> 1122

<211> 21

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

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<221> modified_base

<222> 1,3,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,10,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG4) modification"

<400> 1122

gccccuuauu guuauacgau u 21

<210> 1123

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1123

uauauaguua ucgaggcuca uucuca 26

<210> 1124

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (Alk-PEG5-C6) modification"

<400> 1124

uauauaguua ucgaggcuca uucuca 26

<210> 1125

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (Alk-SMPT-C6) modification"

<400> 1125

uauauaguua ucgaggcuca uucuca 26

<210> 1126

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG26) modification"

<400> 1126

uauauaguua ucgaggcuca uucuca 26

<210> 1127

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG27) modification"

<400> 1127

uauauaguua ucgaggcuca uucuca 26

<210> 1128

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 13,14,15

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,16,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 5,6

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1128

auaucagccc cuuauuguua uacgat 26

<210> 1129

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 12,13,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,15,16,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

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modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

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<221> modified_base

<222> 4,5

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1129

uaucagcccc uuauuguuau acgaut 26

<210> 1130

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 13,14,15

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,16,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 5,6

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1130

auauaguuau cgaggcucau ucucat 26

<210> 1131

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 12,13,14

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,15,16,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

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<221> modified_base

<222> 4,5

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1131

uauaguuauc gaggcucauu cucaut 26

<210> 1132

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1132

uauaucagcc ccuuauuguu auacga 26

<210> 1133

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<221> modified_base

<222> 7,8,9

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<400> 1133

gccccuuauu guuauacgau u 21

<210> 1134

<211> 21

<212> DNA

<213> artificial sequence

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<223> LPA RNAi agent sense strand

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<221> modified_base

<222> 7,8,9

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<220>

<221> modified_base

<222

> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1134

uuaucgaggc ucauucucau u 21

<210> 1135

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 1,3,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,10,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 22

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1135

gccccuuauu guuauacgau u 21

<210> 1136

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<221> modified_base

<222> 14,15,16

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<220>

<221

> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG29) modification"

<400> 1136

uauauaguua ucgaggcuca uucuca 26

<210> 1137

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 1,3,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,9,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1137

gccccuuauu guuauacgau u 21

<210> 1138

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 15,16

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,
25,26
<223> /mod_base = "2'-O-methyl nucleoside"
<220>
<221> modified_base
<222> 8,26
<223> /mod_base = "phosphorothioate linked nucleoside"
<220>
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<222> 1
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223> /mod_base = "5' end (NAG29) modification"
<400> 1138
uauauaauua ucgaggcuca uucuca 26
<210> 1139
<211> 21
<212> DNA
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<222> 1,3,5,7,8,9,11,13,15,17
<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"
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<222> 2,4,6,10,12,14,16,18,19,20,21
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<220>
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<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"
<400> 1139
gccccuuauu guuauacgau u 21

<210> 1140

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 15,16

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,14,17,18,19,20,21,22,23,24,
25,26

<223> /mod_base = "2'-o-methyl nucleoside"

<220>

<221> modified_base

<222> 8,26

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1140

uauauaauua ucgaggcuca uucuca 26

<210> 1141

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 7,8

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1141

uauaucagcc ccuuauuguu auacga 26

<210> 1142

<211> 26

<212> DNA

<213

> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 8

<223> /mod_base = "phosphorothioate linked nucleoside"

<220

>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1142

uauaucagcc ccuuauuguu auacga 26

<210> 1143

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 7,8

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1143

uauauaguua ucgaggcuca uucuca 26

<210> 1144

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 8

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 1

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<400> 1144

uauauaguua ucgaggcuca uucuca 26

<210> 1145

<211> 22

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<222> 1,2,3,5,7,9,13,15,17,19,21,22

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<222> 2,22

<223> /mod_base = "phosphorothioate linked nucleoside"

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<222> 1

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<400> 1145

ucagccccuu auuguuauac ga 22

<210> 1146

<211> 25

<212> DNA

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<222> 11,12,13

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,14,15,16,17,18,19,20,21,22

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<222> 24

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<220>

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<220>

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<222> 4,24

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<400> 1146

ggcagccccu uauuguuaua cgatt 25

<210> 1147

<211> 26

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<222> 1

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<400> 1147

ggcagccccu uauuguuaua cgauut 26

<210> 1148

<211> 25

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<220>

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<400> 1148

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<210> 1149

<211> 25

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<220>

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<400> 1149

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<210> 1150

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cagccccuua uuguuauacg atttt 25

<210> 1151

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<220>

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<400> 1151

gccccuuauu guuauacgau u 21

<210> 1152

<211> 21

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<222> 2,4,6,10,12,14,16,18,19,20,21

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<222> 21

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<400> 1152

gccccuuauu guuauacgau u 21

<210> 1153

<211> 26

<212> DNA

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<222> 14,15,16

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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<222> 8,9

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<220>

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<400> 1153

uauauaguua ucgaggcuca uucuca 26

<210> 1154

<211> 26

<212> DNA

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<400> 1154

uauauaguua ucgaggcuca uucuca 26

<210> 1155

<211> 26

<212> DNA

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<221> modified_base

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<222> 6,7

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<400> 1155

gcgauaguua ucgaggcuca uucuca 26

<210> 1156

<211> 26

<212> DNA

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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ugaauaguua ucgaggcuca uucuca 26

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<400> 1157

aucguaguua ucgaggcuca uucuca 26

<210> 1158

<211> 26

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<400> 1158

uauauaguua ucgaggcuca uucuca 26

<210> 1159

<211> 26

<212> DNA

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uauaaaguua ucgaggcuca uucuca 26

<210> 1160

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uauauaguua ucgaggcuca uucuca 26

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aagccccuua uuguuauacg a 21

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<210> 1164

<211> 22

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gcagccccuu auuguuauac ga 22

<210> 1165

<211> 26

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<400> 1165

uauauaguua ucgaggcuca uucuca 26

<210> 1166

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gcagccccuu auuguuauac ga 22

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<400> 1167

gccccuuauu guuauacgau u 21

<210> 1168

<211> 21

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gccccuuauu guuauacgau u 21

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gccccuuauu guuauacgau u 21

<210> 1170

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<210> 1171

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aagccccuua uuguuauacg a 21

<210> 1172

<211> 21

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<222> 1

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<400> 1173

gcagccccuu auuguuauac ga 22

<210> 1174

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 1,3,5,7,8,9,11,13,15,17

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<220>

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<222> 2,4,6,10,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

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<222> 1,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1174

gccccuuauu guuauacgau u 21

<210> 1175

<211> 22

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

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<222> 2,4,6,8,9,10,12,14,16,18

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<220>

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<222> 1,3,5,7,11,13,15,17,19,20,21,22

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

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<222> 1,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

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<400> 1175

agccccuuau uguuauacga uu 22

<210> 1176

<211> 21

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<220>

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<220>

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<222> 1,2,4,6,8,12,14,16,18,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

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<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1176

aagccccuua uuguuauacg a 21

<210> 1177

<211> 23

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

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<220>

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<222> 1,2,4,6,8,12,14,16,18,20,21,22,23

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<220>

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<222> 1,2,23

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1177

aagccccuua uuguuauacg auu 23

<210> 1178

<211> 23

<212> DNA

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<220>

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<220>

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<222> 1,2,4,6,8,12,14,16,18,20,22,23

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<220>

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<222> 21

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 1,2,23

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1178

aagccccuua uuguuauacg auu 23

<210> 1179

<211> 26

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<220>

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

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<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31) modification"

<400> 1179

uauauaguua ucgaggcuca uucuca 26

<210> 1180

<211> 24

<212> DNA

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<220>

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<222> 12,13,14

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,11,15,16,17,18,19,20,21,22,23

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 4,5,24

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<223> /mod_base = "5' end (NAG31) modification"

<400> 1180

uaucagcccc uuauuguuau acga 24

<210> 1181

<211> 24

<212> DNA

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<220>

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<221> modified_base

<222> 12,13,14

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,15,16,17,18,19,20,21,22,23

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<220>

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<222> 4,5,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31) modification"

<400> 1181

uagcagcccc uuauuguuau acga 24

<210> 1182

<211> 24

<212> DNA

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<222> 1,2,3,4,5,6,7,8,9,10,11,15,16,17,18,19,20,21,22,23

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<221> modified_base

<222> 24

<223> /mod_base = "phosphorothioate linked nucleoside"

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<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31) modification"

<400> 1182

uaucagcccc uuauuguuau acga 24

<210> 1183

<211> 22

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 10,11,12

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1183

gcagccccuu auuguuauac ga 22

<210> 1184

<211> 22

<212> DNA

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<220>

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,13,14,15,16,17,18,19,20,21,22

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<222> 1,2,22

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

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<223> /mod_base = "5' end (NAG31)s modification"

<400> 1184

gcagccccuu auuguuauac ga 22

<210> 1185

<211> 26

<212> DNA

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<222> 14,15,16

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1185

auaagaguua ucgaggcuca uucuca 26

<210> 1186

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

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<222> 14,15,16

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

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<221> modified_base

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<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

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<400> 1186

auaagaguua ucgaggcuca uucuca 26

<210> 1187

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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<400> 1187

auaggcagcc ccuuauuguu auacga 26

<210> 1188

<211> 26

<212> DNA

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<223> LPA RNAi agent sense strand

<220>

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<222> 14,15,16

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<220>

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<222> 1,2,3,4,5,6,7,8,9,10,11,12,13,17,18,19,20,21,22,23,24,25

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<223> /mod_base = "inverted nucleoside"

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<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1188

auaggcagcc ccuuauuguu auacga 26

<210> 1189

<211> 21

<212> DNA

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<222> 9,10,11

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1189

cagccccuua uuguuauacg a 21

<210> 1190

<211> 21

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 9,10,11

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

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<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20

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<220>

<221> modified_base

<222> 1,2,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

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<223> /mod_base = "5' end (NAG31)s modification"

<400> 1190

cagccccuua uuguuauacg a 21

<210> 1191

<211> 21

<212> DNA

<213> artificial sequence

<220>

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<221> modified_base

<222> 7,8,9

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1191

gccccuuauu guuauacgau u 21

<210> 1192

<211> 21

<212> DNA

<213> artificial sequence

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<221> modified_base

<222> 7,8,9

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<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

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<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

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<400> 1192

gccccuuauu guuauacgau u 21

<210> 1193

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 1,7,8,9

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<220>

<221> modified_base

<222> 2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

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<223> /mod_base = "5' end (NAG25)s modification"

<400> 1193

gccccuuauu guuauacgau u 21

<210> 1194

<211> 21

<212> DNA

<213> artificial sequence

<220>

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<222> 1,3,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

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<222> 2,4,6,10,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG31)s modification"

<400> 1194

gccccuuauu guuauacgau u 21

<210> 1195

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 14,15,16

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,9,10,11,12,17,18,19,20,21,22,23,24,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 26

<223> /mod_base = "inverted nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 13

<223> /mod_base = "NOTA nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1195

uauaucagcc cctuauuguu auacga 26

<210> 1196

<211> 21

<212> DNA

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<220>

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<222> 2,4,10,12,14,16,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

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<223> /mod_base = "phosphorothioate linked nucleoside"

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<223> /mod_base = "NOTA nucleoside"

<400> 1196

gcccctuauu guuauacgau u 21

<210> 1197

<211> 26

<212> DNA

<213> artificial sequence

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<223> LPA RNAi agent sense strand

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<222> 6,8,10,12,14,15,16,20

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,17,18,19,21,22,23,24,25,26

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1197

uauauaguua ucgaggcuca uucuca 26

<210> 1198

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,17,18,19,20,21,23,24,25,26

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1198

uauauaguua ucgaggcuca uucuca 26

<210> 1199

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> 6,8,10,12,14,15,16,24

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,17,18,19,20,21,22,23,25,26

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1199

uauauaguua ucgaggcuca uucuca 26

<210> 1200

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,17,18,19,20,21,22,23,24,25

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

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<400> 1200

uauauaguua ucgaggcuca uucuca 26

<210> 1201

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

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<222> 6,8,10,12,14,16,18,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,19,20,21,22,23,24,25

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1201

uauauaguua ucgaggcuca uucuca 26

<210> 1202

<211> 26

<212> DNA

<213> artificial sequence

<220>

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<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,18,19,21,22,23,24,25

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<220>

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<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1202

uauauaguua ucgaggcuca uucuca 26

<210> 1203

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 6,8,10,12,14,16,22,26

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<220>

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<222> 6,7

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uauauaguua ucgaggcuca uucuca 26

<210> 1204

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uauauaguua ucgaggcuca uucuca 26

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uauauaguua ucgaggcuca uucuca 26

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uauauaguua ucgaggcuca uucuca 26

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uauauaguua ucgaggcuca uucuca 26

<210> 1208

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uauauaguua ucgaggcuca uucuca 26

<210> 1210

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uauauaguua ucgaggcuca uucuca 26

<210> 1211

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<212> DNA

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uauauaguua ucgaggcuca uucuca 26

<210> 1212

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uauauaguua ucgaggcuca uucuca 26

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<210> 1218

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<210> 1221

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<210> 1232

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<400> 1233

uauaucagaa acagaaucag guguca 26

<210> 1234

<211> 26

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<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 6,8,10,12,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,14,15,17,19,21,23,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1234

uauaucagaa acagaaucag guguca 26

<210> 1235

<211> 26

<212>

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<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

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<222> 6,8,12,16,18,20,22,24,26

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<220>

<221> modified_base

<222> 1,3,5,7,9,10,11,13,14,15,17,19,21,23,25

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1235

uauaucagaa acagaaucag guguca 26

<210> 1236

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 6,10,12,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,11,13,14,15,17,19,21,23,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1236

uauaucagaa acagaaucag guguca 26

<210> 1237

<211> 26

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 6,12,15,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,14,17,19,21,23,25

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<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1237

uauaucagaa acagaaucag guguca 26

<210> 1238

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<222> 6,12,14,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21,23,25

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1238

uauaucagaa acagaaucag guguca 26

<210> 1239

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<221

> modified_base

<222> 6,12,14,15,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,17,19,21,23,25

<223> /mod_base = "2'-O-methyl nucleoside"

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<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1239

uauaucagaa acagaaucag guguca 26

<210> 1240

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 6,10,12,15,16,18,20,22,24,26

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,11,13,14,17,19,21,23,25

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,4

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1240

uauaucagaa acagaaucag guguca 26

<210> 1241

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<222> 1,2,3,4,5,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-hydroxy nucleoside"

<400> 1241

gcccctuauu guuauacgau u 21

<210> 1242

<211> 19

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<222> 2-19

<223> /mod_base = "2'-hydroxy nucleoside"

<400> 1242

tcguauaaca auaaggggc 19

<210> 1243

<211> 19

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1243

gccccuuauu guuauacga 19

<210> 1244

<211> 18

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1244

ucguauaaca auaagggg 18

<210> 1245

<211> 18

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1245

ccccuuauug uuauacga 18

<210> 1246

<211> 17

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1246

ucguauaaca auaaggg 17

<210> 1247

<211> 17

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1247

cccuuauugu uauacga 17

<210> 1248

<211> 19

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

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<221> modified_base

<222> 2-19

<223> /mod_base = "2'-hydroxy nucleoside"

<400> 1248

tgagaaugag ccucgauaa 19

<210> 1249

<211> 19

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1249

uuaucgaggc ucauucuca 19

<210> 1250

<211> 18

<212> RNA

<213

> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1250

ugagaaugag ccucgaua 18

<210> 1251

<211> 18

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1251

uaucgaggcu cauucuca 18

<210> 1252

<211> 17

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1252

ugagaaugag ccucgau 17

<210> 1253

<211> 17

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1253

aucgaggcuc auucuca 17

<210> 1254

<211> 17

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1254

uguauaacaa uaagggg 17

<210> 1255

<211> 17

<212> RNA

<213> artificial sequence

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<223> LPA RNAi agent sense strand

<400> 1255

ccccuuauug uuauaca 17

<210> 1256

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

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<223> 1,3,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,9,10,12,14,16,18,19,21,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1256

gccccuuauu guuauacgau u 21

<210> 1257

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 9,10,11

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG37) modification"

<400> 1257

cagccccuua uuguuauacg a 21

<210> 1258

<211> 19

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1258

uuaucgaggc ucauucuca 19

<210> 1259

<211> 19

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1259

gccccuuauu guuauacga 19

<210> 1260

<211> 22

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1260

acagccccuu auuguuauac ga 22

<210> 1261

<211> 22

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<400> 1261

aaagccccuu auuguuauac ga 22

<210> 1262

<211> 21

<212> DNA

<213> artificial sequence

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<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,4,6,8,10,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,9,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1262

ugagaaugag ccucgauaau u 21

<210> 1263

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,4,6,8,9,10,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 1263

tcguauaaca auaaggggcu u 21

<210> 1264

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,4,6,8,10,12,14,16,18

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 3,5,7,9,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "2'-MOE nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end cyclopropyl phosphonate modification"

<400> 1264

tcguauaaca auaaggggcu u 21

<210> 1265

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,9,12,14,18,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,6,7,8,10,11,13,15,16,17,19,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1265

ucguauaaca auaaggggcu gccuau 26

<210> 1266

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,6,9,12,14,18,22

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,4,5,7,8,10,11,13,15,16,17,19,20,21,23,24,26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 25

<223> /mod_base = "2'-hydroxy nucleoside"

<220>

<221> modified_base

<222> 2,3,23,24

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1266

ucguauaaca auaaggggcu gccuau 26

<210> 1267

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

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<223> 2,4,6,12,14,16,18,20

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,3,5,7,8,9,10,11,13,15,17,19,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,20,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1267

ucguauaaca auaaggggcu u 21

<210> 1268

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<220>

<221> modified_base

<223> 2,4,6,8,9,10,12,14,16,18

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<220>

<221> modified_base

<222> 1,3,5,7,11,13,15,17,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 2,3,4,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1268

ucguauaaca auaaggggcu u 21

<210> 1269

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 14,15,16

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<220>

<221> modified_base

<222> 1-13,17-26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1269

uauauaguua ucgaggcuca uucuca 26

<210> 1270

<211> 19

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 7,8,9

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19

<223> /mod_base = "2'-O-methyl nucleoside"

<400> 1270

uuaucgaggc ucauucuca 19

<210> 1271

<211> 19

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 1,2,5,7,8,9,11,13,15,17

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 2,4,6,10,12,14,16,18,19

<223> /mod_base = "2'-O-methyl nucleoside"

<400> 1271

gccccuuauu guuauacga 19

<210> 1272

<211> 21

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 7,8,9

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 21

<223> /mod_base = "phosphorothioate linked nucleoside"

<400> 1272

gccccuuauu guuauacgau u 21

<210> 1273

<211> 26

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 14,15,16

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<220>

<221> modified_base

<222> 1-13,17-26

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 6,7

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25) modification"

<400> 1273

uauaucagcc ccuuauuguu auacga 26

<210> 1274

<211> 19

<212> DNA

<213> artificial sequence

<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 7,8,9

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19

<223> /mod_base = "2'-O-methyl nucleoside"

<400> 1274

gccccuuauu guuauacga 19

<210> 1275

<211> 21

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 9,10,11

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2,21

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1275

aagccccuua uuguuauacg a 21

<210> 1276

<211> 21

<212> DNA

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<220>

<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 9,10,11

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1276

cagccccuua uuguuauacg a 21

<210> 1277

<211> 19

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<220>

<223> LPA RNAi agent sense strand

<220>

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<223> 7,8,9

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<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18,19

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1277

gccccuuauu guuauacga 19

<210> 1278

<211> 19

<212> DNA

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<223> LPA RNAi agent sense strand

<220>

<221> modified_base

<223> 7,8,9

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,10,11,12,13,14,15,16,17,18

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2,19

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1278

gccccuuauu guuauacga 19

<210> 1279

<211> 21

<212> DNA

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<223> LPA RNAi agent sense strand

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<221> modified_base

<223> 9,10,11

<223> /mod_base = "2'-deoxy-2'-fluoro nucleoside"

<220>

<221> modified_base

<222> 1,2,3,4,5,6,7,8,12,13,14,15,16,17,18,19,20,21

<223> /mod_base = "2'-O-methyl nucleoside"

<220>

<221> modified_base

<222> 1,2

<223> /mod_base = "phosphorothioate linked nucleoside"

<220>

<221> modified_base

<222> 1

<223> /mod_base = "5' end (NAG25)s modification"

<400> 1279

aagccccuua uuguuauacg a 21

<210> 1280

<211> 18

<212> RNA

<213> artificial sequence

<220>

<223> LPA RNAi agent antisense strand

<400> 1280

cguauaacaa uaaggggc 18

<210> 1281

<211> 18

<212> RNA

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<220>

<223> LPA RNAi agent antisense strand

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