

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 September 2010 (30.09.2010)

PCT

(10) International Publication Number
WO 2010/110914 A2

(51) International Patent Classification:

C12N 15/31 (2006.01) *A61K 48/00* (2006.01)
C12N 1/21 (2006.01) *A61P 31/00* (2006.01)
C12Q 1/68 (2006.01)

(21) International Application Number:

PCT/US2010/000916

(22) International Filing Date:

26 March 2010 (26.03.2010)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/211,178 27 March 2009 (27.03.2009) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report (Rule 48.2(g))

(54) Title: MAMMALIAN GENES INVOLVED IN INFECTION

(57) Abstract: The present invention relates to cellular proteins that are involved in infection or are otherwise associated with the life cycle of one or more pathogens.



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MAMMALIAN GENES INVOLVED IN INFECTION

This application claims the benefit of U.S. Application No. 61/211,178, filed on March 27, 2009, which is hereby incorporated in its entirety by this reference.

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FIELD OF THE INVENTION

The present invention relates to nucleic acid sequences and cellular proteins encoded by these sequences that are involved in infection or are otherwise associated with the life cycle of one or more pathogens, such as a virus, a bacteria, a fungus or a parasite. The invention also relates to modulators of nucleic acid sequences and cellular proteins encoded by these sequences that are involved in infection or are otherwise associated with the life cycle of a pathogen.

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BACKGROUND

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Infectious diseases affect the health of people and animals around the world, causing serious illness and death. Black Plague devastated the human population in Europe during the middle ages. Pandemic flu killed millions of people in the 20th century and is a threat to reemerge.

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Some of the most feared, widespread, and devastating human diseases, are caused by viruses that interfere with normal cellular processes. These include influenza, poliomyelitis, smallpox, Ebola, yellow fever, measles and AIDS, to name a few. Viruses are also responsible for many cases of human disease including encephalitis, meningitis, pneumonia, hepatitis and cervical cancer, warts and the common cold. Furthermore, viruses causing respiratory infections, and diarrhea in young children lead to millions of deaths each year in less-developed countries. Also, a number of newly emerging human diseases such as SARS are caused by viruses. In addition, the threat of a bioterrorist-designed pathogen is ever present.

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While vaccines have been effective to prevent certain viral infections, relatively few vaccines are available or wholly effective, have inherent risks and tend to be specific for particular conditions. Vaccines are of limited value against rapidly mutating viruses and cannot anticipate emerging viruses or new bioterrorist-designed viruses. Currently there is no good answer to these threats. Traditional treatments for viral infection include pharmaceuticals aimed at specific virus derived proteins, such as HIV protease or reverse transcriptase, or the administration of recombinant (cloned) immune modulators (host derived), such as the interferons. However, the vast majority of viruses lack an effective drug. Those drugs that exist have several limitations and drawbacks that including limited effectiveness, toxicity, and high rates of viral mutations which render antiviral pharmaceuticals ineffective. Thus, an urgent need exists for alternative treatments for viruses and other infectious diseases, and methods of identifying new drugs to combat these threats.

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SUMMARY OF THE INVENTION

The present invention provides genes and gene products set forth in Tables 1, 2, 3 and 4 that are involved in infection by one or more pathogens such as a virus, a parasite, a bacteria or a fungus, or are otherwise associated with the life cycle of a pathogen. Also provided are methods of decreasing infection in a cell by a pathogen comprising decreasing expression or activity of one or more of these genes or gene products set forth in Tables 1, 2, 3 and 4. Also provided are methods of decreasing infection by a pathogen in a subject by administering an agent that decreases the expression and/or activity of of the genes or gene products set forth in Tables 1, 2, 3 and 4. Further provided are methods of identifying an agent that decreases infection by a pathogen.

DETAILED DESCRIPTION OF THE INVENTION

The present invention may be understood more readily by reference to the following detailed description of preferred embodiments of the invention and the Examples included therein.

Before the present compounds, compositions and/or methods are disclosed and described, it is to be understood that this invention is not limited to specific nucleic acids, specific polypeptides, or to particular methods, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only and is not intended to be limiting.

As used in the specification and the appended claims, the singular forms “a,” “an” and “the” include plural referents unless the context clearly dictates otherwise. The term “or” refers to a single element of stated alternative elements or a combination of two or more elements, unless the context clearly indicates otherwise. As used herein, “comprises” means “includes.” Thus, “comprising A or B,” means “including A, B, or A and B,” without excluding additional elements.

Ranges may be expressed herein as from “about” one particular value, and/or to “about” another particular value. When such a range is expressed, another embodiment includes from the one particular value and/or to the other particular value. Similarly, when values are expressed as approximations, by use of the antecedent “about,” it will be understood that the particular value forms another embodiment. It will be further understood that the endpoints of each of the ranges are significant both in relation to the other endpoint, and independently of the other endpoint.

“Optional” or “optionally” means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances where it does not. For example, the phrase “optionally obtained prior to treatment” means obtained before treatment, after treatment, or not at all.

As used throughout, by “subject” is meant an individual. Preferably, the subject is a mammal such as a primate, and, more preferably, a human. Non-human primates include marmosets, monkeys, chimpanzees, gorillas, orangutans, and gibbons, to name a few. The term “subject” includes domesticated animals, such as cats, dogs, etc., livestock (for example, cattle, horses, pigs, sheep, goats, etc.), laboratory animals (for example, ferret, chinchilla, mouse, rabbit, rat, gerbil, guinea pig, etc.) and avian species (for example, chickens, turkeys, ducks, pheasants, pigeons, doves, parrots, cockatoos, geese, etc.). The subjects of the present invention can also include, but are not limited to fish (for example, zebrafish, koi, goldfish, tilapia, salmon and trout), amphibians and reptiles.

In the present application, the genes listed in Table 1, 2, 3 or 4 are host genes involved in viral infection. As utilized throughout, “gene product” is the RNA or protein resulting from the expression of a gene listed in Table 1, 2, 3 or 4.

The nucleic acids of these genes and their encoded proteins can be involved in all phases of the viral life cycle including, but not limited to, viral attachment to cellular receptors, viral infection, viral entry, internalization, disassembly of the virus, viral replication, genomic integration of viral sequences, transcription of viral RNA, translation of viral mRNA, transcription of cellular proteins, translation of cellular proteins, trafficking, proteolytic cleavage of viral proteins or cellular proteins, assembly of viral particles, budding, cell lysis and egress of virus from the cells.

Although the genes set forth herein were identified as cellular genes involved in viral infection, as discussed throughout, the present invention is not limited to viral infection. Therefore, any of these nucleic acid sequences and the proteins encoded by these sequences can be involved in infection by any infectious pathogen such as a bacteria, a fungus or a parasite which includes involvement in any phase of the infectious pathogen’s life cycle.

As utilized herein, when referring to any of the genes in Table 1, 2, 3 or 4, for example, and not to be limiting, ABTB1, this includes any ABTB1 gene, ABTB1 gene product, for example, an ABTB1 nucleic acid (DNA or RNA) or ABTB1 protein, from any organism that retains at least one activity of ABTB1 and can function as an ABTB1 nucleic acid or protein utilized by a pathogen. For example, the nucleic acid or protein sequence can be from or in a cell in a human, a non-human primate, a mouse, a rat, a cat, a dog, a chimpanzee, a horse, a cow, a pig, a sheep, a guinea pig, a rabbit, a zebrafish, a chicken, to name a few.

As used herein, a gene is a nucleic acid sequence that encodes a polypeptide under the control of a regulatory sequence, such as a promoter or operator. The coding sequence of the gene is the portion transcribed and translated into a polypeptide (*in vivo*, *in vitro* or *in situ*) when placed under the control of an appropriate regulatory sequence. The boundaries of the coding sequence can be determined by a start codon at the 5' (amino) terminus and a stop codon at the 3' (carboxyl) terminus. If the coding sequence is intended to be expressed in a eukaryotic cell, a polyadenylation signal and transcription termination sequence can be included 3' to the coding sequence.

Transcriptional and translational control sequences include, but are not limited to, DNA regulatory sequences such as promoters, enhancers, and terminators that provide for the expression of the coding sequence, such as expression in a host cell. A polyadenylation signal is an exemplary eukaryotic control sequence. A promoter is a regulatory region capable of binding RNA polymerase and initiating transcription of a downstream (3' direction) coding sequence. Additionally, a gene can include a signal sequence at the beginning of the coding sequence of a protein to be secreted or expressed on the surface of a cell. This sequence can encode a signal peptide, N-terminal to the mature polypeptide, which directs the host cell to translocate the polypeptide.

Tables 1, 2, 3 and 4, provide the Entrez Gene numbers for the human genes set forth herein. The information provided under the Entrez Gene numbers listed in Tables 1, 2, 3 and 4 is hereby incorporated entirely by this reference. One of skill in the art can readily obtain this information from the National Center for Biotechnology Information at the National Library of Medicine (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene>). By accessing Entrez Gene, one of skill in the art can readily obtain information about every gene listed in Table 1, 2, 3 or 4, such as the genomic location of the gene, a summary of the properties of the protein encoded by the gene, expression patterns, function, information on homologs of the gene as well as numerous reference sequences, such as the genomic, mRNA and protein sequences for each gene. Therefore, one of skill in the art can readily obtain sequences, such as genomic, mRNA and protein sequences by accessing information available under the Entrez Gene number provided for each gene. Thus, all of the information readily obtained from the Entrez Gene Nos. set forth herein is also hereby incorporated by reference in its entirety. These examples are not meant to be limiting as one of skill in the art would know that sequences for the genes and gene products listed in Table 1, 2, 3 or 4 from human or from other species are available at GenBank (Benson et al. *Nucleic Acids Res.* 2004 January 1; 32(Database issue); D23-D26), the EMBL Database (Stoesser et al., (2000) *Nucleic Acids Res.*, 28, 19-23) or other sequence databases. Table 5 (column 2) provides one or more aliases for genes set forth herein. Therefore, it is clear

that when referring to a gene, this also includes known alias(es) and any aliases attributed to the genes listed herein, in the future. The proteins encoded by the genes, if available, are also listed in column 3 of Table 5. In addition to the function of being involved in pathogenic infection as provided herein, a function of the proteins is also provided, if available, in column 4 of Table 5.

The chromosomal location of the gene in the human genome (column 5) is also set forth. Thus, the present invention identifies a genomic loci of genes associated with viral infection. By identifying the gene and its location in the genome, the invention provides both the gene and its product(s) as targets for therapies such as antiviral, antibacterial, antifungal and antiparasitic therapies, to name a few.

Also provided in Table 5 are the GenBank Accession Nos. for the coding sequences (human mRNA sequences) (column 6) and the GenBank Accession Nos. for the human protein sequences (column 7), for genes and gene products set forth in Tables 1, 2, 3 or 4. It is understood that in any coding sequence, a T can be replaced with a U to obtain an RNA sequence for each gene. The nucleic acid sequences and protein sequences provided under the GenBank Accession numbers mentioned herein are hereby incorporated in their entireties by this reference. One of skill in the art would know that the nucleotide sequences provided under the GenBank Accession numbers set forth herein can be readily obtained from the National Center for Biotechnology Information at the National Library of Medicine (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=nucleotide>). Similarly, the protein sequences set forth herein can be readily obtained from the National Center for Biotechnology Information at the National Library of Medicine (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=protein>). The nucleic acid sequences and protein sequences provided under the GenBank Accession numbers mentioned herein are hereby incorporated in their entireties by this reference. Compounds that can be utilized to inhibit genes or gene products set forth herein are also set forth in Table 5.

TABLE 1

Entrez Gene ID	Gene		Entrez Gene ID	Gene
339010	A26B1		9443	MED7
53947	A4GALT		112950	MED8
404744	AAA1		79036	MGC2749
22848	AAK1		126626	MGC29891
10157	AASS		375791	MGC59937 (C9orf169)
28	ABO		57553	MICAL3
80325	ABTB1		4277	MICB
32	ACACB		58526	MID1IP1
36	ACADSB		406956	MIRN181B2

53	ACP2		406992	MIRN210
11096	ADAMTS5		442917	MIRN372
156	ADRBK1		407050	MIRN93
121536	AEBP2		407054	MIRN98
166	AES		83881	MIXL1
172	AFG3L1		23609	MKRN2
10939	AFG3L2		2315	MLANA
173	AFM		4322	MMP13
	AK127507		4318	MMP9
11214	AKAP13		mmu-miR-294 (transcript)	mmu_miR_294
199857	ALG14		84057	MND1
91801	ALKBH8		116255	MOGAT1
8092	ALX1		4342	MOS
29882	ANAPC2		8777	MPDZ
51479	ANKFY1		10200	MPHOSPH6
27063	ANKRD1		4353	MPO
22881	ANKRD6		4355	MPP2
308	ANXA5		3140	MRI
8906	APIG2		4361	MRE11A
63941	APBA2BP		124995	MRPL10
338	APOB		6150	MRPL23
9716	AQR		79590	MRPL24
8289	ARID1A		65080	MRPL44
10865	ARID5A		6183	MRPS12
132946	ARL9		57380	MRS2
91947	ARRDC4		219995	MS4A15
51593	ARS2		4501	MT1X
142689	ASB12		4502	MT2A
80816	ASXL3		727897	MUC5B
9140	ATG12		80198	MUS81
89849	ATG16L2		50804	MYEF2
10533	ATG7		85366	MYLK2
475	ATOX1		4542	MYO1F
506	ATP5B		7994	MYST3
545	ATR		342538	NACA2 (NACAL)
6311	ATXN2		23218	NBEAL2
338707	B4GALNT4		10787	NCKAP1
25825	BACE2		23054	NCOA6
8815	BANF1		9612	NCOR2
7917	BAT3		80762	NDFIP1
29994	BAZ2B		4705	NDUFA10
8537	BCAS1		4700	NDUFA6
53335	BCL11A		4722	NDUFS3
83596	BCL2L12		4726	NDUFS6
607	BCL9		374291	NDUFS7
9774	BCLAF1		4734	NEDD4
613	BCR		55247	NEIL3
23299	BICD2		91754	NEK9
331	BIRC4		50674	NEUROG3
640	BLK		4790	NFKB1
649	BMP1		25791	NGEF

55589	BMP2K		4820	NKTR
672	BRCA1		54413	NLGN3
676	BRDT		197358	NOD3
138151	BTBD14A		8996	NOL3
7832	BTG2		388677	NOTCH2NL
143379	c10orf82		27031	NPHP3
745	C11orf9		8431	NR0B2
145200	C14orf72		4929	NR4A2
23742	c15orf2		29959	NRBP1
283987	C17orf28		22978	NT5C2
64762	C18orf11		9423	NTN1
163882	C1orf71		55190	NUDT11
140701	c20orf135		11165	NUDT3
90288	C3orf25		11163	NUDT4
255330	C3orf46		9253	NUMBL
132321	C4orf33 (LOC132321)		23279	NUP160
7905	C5orf18		8021	NUP214
78996	C7orf49		10762	NUP50
83655	C8orf14		23636	NUP62
158046	C9orf121		4928	NUP98
157983	C9orf66		10482	NXF1
80010	C9orf76		113746	ODF3
760	CA2		25903	OLFML2B
51150	Cab45		3175	ONECUT1
790	CAD		94233	OPN4
57118	CAMK1D		23538	OR52A1
10645	CAMKK2		341799	OR6S1
124583	CANT1		26031	OSBPL3
10753	CAPN9		114880	OSBPL6
55749	CCAR1		114881	OSBPL7
10576	CCT2		220213	OTUD1
9332	CD163		5026	P2RX5
8763	CD164		64425	PAF53
920	CD4		79646	PANK3
976	CD97		83666	PARP9
51362	CDC40		55742	PARVA
10602	CDC42EP3		29780	PARVB
64405	CDH22		10923	PC4 (SUB1)
1036	CDO1		56146	PCDHA2
116986	CENTG1		84759	PCGF1
23177	CEP68		5105	PCK1
81494	CFHR5		51586	PCQAP
8837	CFLAR		5046	PCSK6
51005	CGI-14		58488	PCTP
25813	CGI-51		5833	PCYT2
10669	CGREF1		84306	PDCD2L
150356	CHADL (LOC150356)		5151	PDE8A
10036	CHAF1A		2923	PDIA3

26973	CHORDC1		23590	PDSS1
1139	CHRNA7		57162	PELI1
8534	CHST1		8863	PER3
166012	CHST13		64065	PERP
113189	CHST14		5211	PFKL
10518	CIB2		5213	PFKM
51192	CKLF		5232	PGK2
9074	CLDN6		5236	PGM1
387836	CLEC2A		10424	PGRMC2
25999	CLIPR-59		5252	PHF1
1201	CLN3		5253	PHF2
1207	CLNS1A		5297	PI4KA
9575	CLOCK		5283	PIGH
1211	CLTA		5313	PKLR
1240	CMKLR1		5586	PKN2
80347	COASY		51365	PLA1A
22796	COG2		65977	PLEKHA3 (FAPPI)
83548	COG3		5347	PLK1
25839	COG4		5352	PLOD2
1289	COL5A1		5372	PMM1
114769	COP1		5379	PMS2L1
125965	COX6B2		10957	PNRC1
1370	CPN2		5426	POLE
1380	CR2		5430	POLR2A
51232	CRIM1		5432	POLR2C
285464	CRIPAK		5437	POLR2H
200186	CRTC2		5438	POLR2I
64784	CRTC3		5439	POLR2J
1410	CRYAB		5440	POLR2K
79848	CSPP1		5441	POLR2L
128821	CST9L		11128	POLR3A
9150	CTDP1		5463	POU6F1
1522	CTSZ		152926	PPM1K
7852	CXCR4		54776	PPP1R12C
203429	CXorf50		54866	PPP1R14D
1536	CYBB		5529	PPP2R5E
54205	CYCS		5546	PRCC
1576	CYP3A4		56980	PRDM10
10858	CYP46A1		5562	PRKAA1
57834	CYP4F11		5583	PRKCH
7818	DAP3		79033	PRNPIP
23604	DAPK2		84950	PRPF38A
9802	DAZAP2		24148	PRPF6
285761	DCBLD1		10594	PRPF8
167227	DCP2		51538	PS1D
8528	DDO		5664	PSEN2
1650	DDOST		11168	PSIP1 (LEDGF)
9416	DDX23		5682	PSMA1
1654	DDX3X		5683	PSMA2
54555	DDX49		5686	PSMA5
79009	DDX50		5690	PSMB2
168400	DDX53		5694	PSMB6

57696	DDX55		5702	PSMC3
91351	DDX60L		5704	PSMC4
644414	DEFB131		5705	PSMC5
221120	DEPC1		5718	PSMD12
9681	DEPDC5		5710	PSMD4
1665	DHX15		9861	PSMD6
56919	DHX33		9791	PTDSS1
79132	DHX58		10728	PTGES3
27292	DIMT1L		5745	PTHR1
257160	DKFZp547C195		5795	PTPRJ
83989	DKFZP564D172		5799	PTPRN2
25915	DKFZP564J0123		10076	PTPRU
	DKFZp686N0244		65263	PYCRL
374383	DKFZp686O24166		23518	R3HDM
22839	DLGAP4		441400	RAB1C
1743	DLST		9364	RAB28
1657	DMXL1		5862	RAB2A
10294	DNAJA2		11021	RAB35
3337	DNAJB1		5870	RAB6A
10049	DNAJB6		84084	RAB6C (WTH3)
83544	DNAL1		4218	RAB8A
1778	DNCH1		56852	RAD18
1785	DNM2		5885	RAD21
55619	DOCK10		5886	RAD23A
220164	DOK6		5899	RALB
8813	DPM1		10928	RALBP1
1803	DPP4		5902	RANBP1
56896	DPYSL5		64901	RANBP17
23220	DTX4		5903	RANBP2
11266	DUSP12		5908	RAP1B
80824	DUSP16		5915	RARB
1855	DVL1		9821	RB1CC1
	DW462575		8241	RBM10
8291	DYSF		84991	RBM17
1909	EDNRA		9904	RBM19
80258	EFHC2		58517	RBM25
1950	EGF		10181	RBM5
1956	EGFR		10179	RBM7
8893	EIF2B5		5970	RELA
192669	EIF2C3		29803	REPIN1
8667	EIF3H (EIF3S3)		340526	RGAG4
1974	EIF4A2		9827	RGP1
25909	ELYS		727851	RGPD8
2010	EMD		29984	RHOD
8507	ENC1		6041	RNASEL
2033	EP300		27289	RND1
2034	EPAS1		9921	RNF10

2059	EPS8		81790	RNF170
2067	ERCC1		6048	RNF5
2073	ERCC5		6050	RNH
10595	ERN2		10921	RNPS1
121506	ERP27 (C12orf46)		164714	RP3-355C18.2
23474	ETHE1		255313	RP6-166C19.11
2114	ETS2		4736	RPL10A
2117	ETV3		6136	RPL12
2122	EVII		6141	RPL18
2123	EVI2A		6197	RPS6KA3
112479	EXOD1		10325	RRAGB
5394	EXOSC10		6239	RREB1
51010	EXOSC3		26156	RSL1D1
2147	F2		222967	RSPH10B
2168	FABP1		6253	RTN2
283991	FAM100B		10313	RTN3
57795	FAM5B		9853	RUSC2
143684	FAM76B		6271	S100A1
57697	FANCM		81846	SBF2
89885	FATE1		58506	SCAF1 (SR-A1)
54751	FBLP-1		23256	SCFD1
23014	FBXO21		6382	SDC1
23291	FBXW11		23480	SEC61G
55079	FEZF2		54437	SEMA5B
2314	FLII		205564	SENP5
55258	FLJ10916		5269	SERPINB6
79714	FLJ12436		91404	SESTD1
55654	FLJ20507		10291	SF3A1
79671	FLJ21478		23451	SF3B1
80131	FLJ23420		10992	SF3B2
220081	FLJ32682		6422	SFRP1
147699	FLJ40125		6427	SFRS2
ENST0000038 0709 (Transcript)	FLJ43399		6431	SFRS6
389690	FLJ43860		113402	SFT2D1
ENST0000034 2892 (Transcript)	FLJ44380		81855	SFXN3
ENST0000038 0022 (Transcript)	FLJ44675		79801	SHCBP1
HSG00238652	FLJ45600		8487	SIP1
ENST0000038 2724 (Transcript)	FLJ45796		6554	SLC10A1
400627	FLJ46026		6512	SLC1A7
401103	FLJ46066		9187	SLC24A1
AK128830 (Transcript)	FLJ46317		9481	SLC25A27
400926	FLJ90680		28965	SLC27A6
55810	FOXJ2		114134	SLC2A13

2356	FPGS		6515	SLC2A3
8087	FXR1		7355	SLC35A2
8322	FZD4		145389	SLC38A6
11337	GABARAP		113235	SLC46A1 (HCP1)
11345	GABARAPL2 (ATG8)		9497	SLC4A7
2553	GABPB2		10479	SLC9A6
374378	GALNTL4		6578	SLCO2A1
23193	GANAB		84296	SLD5
54815	GATAD2A		10569	SLU7
2645	GCK		57154	SMURF1
2689	GH2		150094	SNF1LK
2760	GM2A		6626	SNRPA
283796	GOLGA9P		6627	SNRPA1
26003	GORASP2		6631	SNRPC
2820	GPD2		6634	SNRPD3
11318	GPR182		22938	SNW1
9524	GPSN2		3431	SP110
84706	GPT2		6683	SPAST
2891	GRIA2		132851	SPATA4
2904	GRIN2B		60559	SPCS3
2907	GRINA		6687	SPG7
79774	GRTPI		6709	SPTAN1
2957	GTF2A1		6716	SRD5A2
2962	GTF2F1		6725	SRMS
2965	GTF2H1		26576	SRPK3
2966	GTF2H2		6741	SSB
9330	GTF3C3		6745	SSR1
3020	H3F3A		6747	SSR3
10542	HBXIP		29101	SSU72
29115	HCNGP		8869	ST3GAL5
3065	HDAC1		23166	STAB1
55127	HEATR1		342667	STAC2
3280	HES1		10963	STIP1
138050	HGSNAT		3703	STT3A
9026	HIP1R		6812	STXBP1
3111	HLA-DOA		8801	SUCLG2
256158	HMCN2		6613	SUMO2
3146	HMGB1		51111	SUV420H1
3157	HMGCS1		8407	TAGLN2
3166	HMX1		83940	TATDN1
3185	HNRNPF (HNRPF)		83874	TBC1D10A
9987	HNRPDL		6907	TBL1X
3187	HNRPH1		387332	TBPL2
hsa-mir-137 (transcript)	hsa_miR_137		6921	TCEB1
has-miR-181c (transcript)	hsa_miR_181c		6924	TCEB3
has-miR-302a (transcript)	hsa_miR_302a		6942	TCF20
has-miR-302b (transcript)	hsa_miR_302b		10732	TCFL5

has-miR-302c (transcript)	hsa_miR_30 2c		284672	TEBP
has-miR-302d (transcript)	hsa_miR_30 2d		7014	TERF2
has-miR-92 (transcript)	hsa_miR_92		7023	TFAP4
54972	HSPA5BP1		7030	TFE3
29075	HSPC072		23483	TGDS
10075	HUWE1		7043	TGFB3
7866	IFRD2		57215	THAP11
3514	IGKC		90326	THAP3
3550	IK		79228	THOC6
8809	IL18R1		10245	TIMM17B
3552	IL1A		1678	TIMM8A
56300	IL1F9		11011	TLK2
58985	IL22RA1		9375	TM9SF2
286676	ILDR1		117531	TMC1
26512	INTS6		11018	TMED1
25896	INTS7 (C1orf73)		286102	TMED10P
10527	IPO7		92293	TMEM132C
79781	IQCA		57583	TMEM181 (GPR178)
81875	ISG20L2		387914	TMEM46
3735	KARS		9725	TMEM63A
3767	KCNJ11		51669	TMEM66
3762	KCNJ5		7112	TMPO
10657	KHDRBS1		7293	TNFRSF4
10656	KHDRBS3		8600	TNFSF11
23300	KIAA0431		8711	TNK1
23240	KIAA0922		10043	TOM1
23067	KIAA1076		9868	TOMM70A
57658	KIAA1536		8940	TOP3B
57576	KIF17		27433	TOR2A
84643	KIF2B		11076	TPPP
11127	KIF3A		7178	TPT1
10365	KLF2		7179	TPTE
57626	KLHL1		54476	TRIAD3
43849	KLK12		23650	TRIM29
3822	KLRC2		287015	TRIM42
23633	KPNA6		54765	TRIM44
3837	KPNB1		81844	TRIM56
124751	KRBA2		9866	TRIM66
200634	KRTCAP3		81786	TRIM7
7805	LAPTM5		81603	TRIM8
51520	LARS		51605	TRMT6
353144	LCE3C		7223	TRPC4
3937	LCP2		83707	TRPT1
10637	LEFTY1		55503	TRPV6
3981	LIG4		7267	TTC3
3985	LIMK2		51807	TUBA8
55327	LIN7C		5756	TWF1
10960	LMAN2		6675	UAPI

150763	LOC150763		53347	UBASH3A
153657	LOC153657		7320	UBE2B
255275	LOC255275		11065	UBE2C
26010	LOC26010		7324	UBE2E1
284214	LOC284214		7328	UBE2H
286187	LOC286187		7332	UBE2L3
375190	LOC375190		65264	UBE2Z
390350	LOC390530		29978	UBQLN2
390876	LOC390876		51366	UBR5
391352	LOC391352		89766	UMODL1
391429	LOC391429		7372	UMPS
391800	LOC391800		65109	UPF3B
392447	LOC392447		7384	UQCRC1
400723	LOC400723		7386	UQCRFS1
402117	LOC402117		10868	USP20
22861	LOC440398		10713	USP39
440585	LOC440585		7404	UTY
441032	LOC441032		7421	VDR
256158	LOC441470		27183	VPS4A
51149	LOC51149		7450	VWF
51252	LOC51252		11193	WBP4
554207	LOC554207		23038	WDTC1
651106	LOC651106		259240	WFDC9
91942	LOC91942		8839	WISP2
9170	LPAR2		65125	WNK1
4023	LPL		56949	XAB2
84918	LRP11		114786	XKR4
9684	LRRC14		7518	XRCC4
55144	LRRC8D		7520	XRCC5
84125	LRRIQ1		8565	YARS
149986	LSM14B		4904	YBX1
27258	LSM3		58486	ZBED5
8581	LY6D		23264	ZC3H7B
147719	LYPD4		253832	ZDHHC20
10434	LYPLA1		84619	ZGPAT
4102	MAGEA3		10269	ZMPSTE24
4105	MAGEA6		7559	ZNF12
4121	MAN1A1		7707	ZNF148
4126	MANBA		7569	ZNF182 (ZNF21)
9020	MAP3K14		9534	ZNF254
6885	MAP3K7		23036	ZNF292
4293	MAP3K9		6940	ZNF354A
4134	MAP4		80818	ZNF436
28956	MAPBPIP		147657	ZNF480
4139	MARK1		57473	ZNF512B (GM632)
4144	MAT2A		9658	ZNF516
8888	MCM3AP		9745	ZNF536
23195	MDN1		79818	ZNF552
55850	MDS032		84914	ZNF587
400569	MED11		84622	ZNF594
9282	MED14		146542	ZNF688
9440	MED17		124411	ZNF720

219541	MED19		65988	ZNF747
9477	MED20		146540	ZNF785
9441	MED26		163049	ZNF791
9442	MED27		30834	ZNRD1
80306	MED28		80345	ZSCAN16
51003	MED31		65249	ZSWIM4
29079	MED4		7791	ZYX
10001	MED6			

TABLE 2

ENR/	GENE		ENR/	GENE
GENE ID	GENE		GENE ID	GENE
23456	ABCB10		1469	CST1
6059	ABCE1			
10006	ABI1		1473	CST5
3983	ABLIM1		84951	CTEN
84448	ABLIM2		1510	CTSE
22885	ABLIM3		11325	DDX28
			55794	DDX42
6296	ACSM3		63946	DMRTC2
203054	ADCK5		64641	EBF2
10555	AGPAT2		1954	EGFL4
273	AMPH		55531	ELMOD1
200539	ANKRD23		83715	ESPN
84079	ANKRD27		85302	FBF1
256006	ANKRD31		84467	FBN3
9114	ATP6V0D1		84929	FIBCD1
528	ATP6V1C1		84140	FLJ13305
529	ATP6V1E1			
145173	B3GTL		139716	GAB3
2683	B4GALT1		64090	GAL3ST2
9031	BAZ1B		64395	GCL
593	BCKDHA		113263	GLCC11
146227	BEAN		2912	GRM2
60467	BPESC1		8925	HERC1
60680	BRUNOL5		128872	HMG4L
79892	C10orf119		3228	HOXC12
79863	C18orf22		3222	HOXC5
773	CACNA1A		3268	HRBL
797	CALCB		84447	HRD1
4680	CEACAM6		259307	IL4I1
81494	CFHL5		83986	ITFG3
64581	CLEC7A		23416	KCNH3
1192	CLIC1		9424	KCNK6
1267	CNP		202243	KENAE
64784	CRTC3 (TORC3)		80256	KIAA1539
547	KIF1A		140738	PR1
57626	KLHL1		54886	PRG-3
90070	LACRT		8000	PSCA
81887	LAS1L		9491	PSMF1
8861	LDB1		170680	PSORS1C2
55891	LENEP		2185	PTK2B
55854	LEREPO4			
83752	LONP		83452	RAB33B

51691	LSM8		83871	RAB34
56925	LXN		9545	RAB3D
4061	LY6E		27342	RABGEF1
8785	MATN4		5888	RAD51
79084	MEP50		10181	RBM5
79140	MGC1203		64326	RFWD2
84326	MGC13114		140730	RIMS4
58526	MID1IP1 (MIG12)		6017	RLBP1
58529	MYOZ1		63891	RNF123
3340	NDST1		84676	RNF28
4796	NFKBIL2		22838	RNF44
85407	NKD1		57140	RNPEPL1
79159	NOL12		83694	RPS6KL1
22906	OIP106		83546	RTBDN
23548	OSRF		9853	RUSC2
78990	OTUB2		147199	RYD5
55593	OTUD5		79595	SAP130
5058	PAK1		10284	SAP18
126006	PCP2		23256	SCFD1
5121	PCP4		85477	SCIN
5140	PDE3B		90507	SCRN2
79955	PDZK7		83482	SCRT1
114771	PGLYRP3		118980	SFXN2
5255	PHKA1		25970	SH2B
64600	PLA2G2F		79628	SH3TC2
283748	PLA2G4D		6464	SHC1
57664	PLEKHA4		25759	SHC2
10733	PLK4		56961	SHD
201266	SLC39A11		10600	USP16
9351	SLC9A3R2		9098	USP6
81796	SLCO5A1		55823	VPS11
9580	SOX13			
6672	SP100		260294	WBSCR20C
80320	SP6		57418	WDR18
65244	SPATS2		91833	WDR20
245711	SPY1		80232	WDR26
6489	ST8SIA1		25886	WDR51A
			9942	XYLB
6788	STK3		10413	YAPI
56164	STK31		7761	ZNF214
65975	STK33		79692	ZNF322A
8189	SYMPK		57507	ZNF608
55333	SYNJ2BP		80036	TRPM3
90019	SYT8		51393	TRPV2
10460	TACC3		23508	TTC9
56165	TDRD1		7846	TUBA3
7003	TEAD1		10381	TUBB4
7005	TEAD3		282809	TUWD12
7046	TGFBR1		80761	UPK3B
80764	THAP7		8237	USP11
84870	THSD2			
200728	TMEM17			
10673	TNFSF13B			
30000	TNPO2			
58485	TRAPPC1			

TABLE 3

ENTREZ GENE ID	GENE		ENTREZ GENE ID	GENE
146	ADRA1D		56106	PCDHGA10
54812	AFTPH		56107	PCDHGA9
3268	AGFG2		9063	PIAS2
65061	ALS2CR7		57605	PITPNM2
8907	AP1M1		83483	PLVAP
10239	AP3S2		5413	PNUTL1
64333	ARHGAP9		5414	PNUTL2
91947	ARRDC4		55696	RBM22
537	ATP6AP1		23480	SEC61G
523	ATP6V1A		56904	SH3GLB2
526	ATP6V1B2		64694	SPANXB2
56970	ATXN7L3		27347	STK39
10134	BCAP31		8848	TGFB114
80114	BICC1		29953	TRHDE
5067	CNTN3		7329	UBE2I
1471	CST3		7337	UBE3A
117285	DEFB118		89891	WDR34
51009	DERL2		56949	XAB2
1665	DHX15		7535	ZAP70
79665	DHX40		167465	ZNF366
5393	EXOSC9			
83786	FKSG44			
116113	FOXP4			
2549	GAB1			
2671	GFER			
145258	GSC			
60484	HAPLN2			
255488	IBRDC2			
57571	KIAA1394			
57576	KIF17			
65996	MGC2752			
80762	NDFIP1			
10528	NOL5A			
26167	PCDHB5			

TABLE 4

ENTREZ GENE ID	GENE		ENTREZ GENE ID	GENE
5479	CYPB		5725	PTBP1
1654	DDX3X		51495	PTPLAD1
1655	DDX5		5970	RELA
23405	DICER1		6193	RPS5
5610	EIF2AK2		949	SCARB1
1968	EIF2S3		23157	SEPT6
8661	EIF3A		5265	SERPINA1
1973	EIF4A		6560	SLC12A4
1994	ELAVL1		57468	SLC12A5
2203, 8789	FBP		81788	SNARK
25827	FBXL2		8651	SOCS1
2549	GAB1		9021	SOCS3
2597	GAPDH		10847	SRCAP

3178	HNRPA1		6646	STAT (SOAT1)
23640	HSPBP1		6774	STAT3
3614, 3615	IMPDH		8417	STX7
3843	IPO5		128637	TBC1D20
3725	JUN		6915	TBXA2R
6741	LA(SSB)		7098	TLR3 agonist
4050	LTB		51284	TLR7 agonist
5594	MAPK1		54106	TLR9 agonist
406906	MIRN122		7186	TRAF2
5609	MKK7		11274	USP18
4691	NCL		6843, 6844	VAMP
4791	NFKB2		9218	VAPA
10492	NSAP1		9217	VAPB
5094	PCBP2		9217	VAPC
7157	PI3K		57558	USP35
5586	PKN2			
5499	PP1A			
58155	PTB			
9276	COPB2		2067	ERCC1
1314	COPA		220441	RNF152
27243	CHMP2A		390157	OR8K1
22818	COPZ1		10194	TSHZ1
372	ARCN1		8089	YEATS4
5297	PIK4CA		29110	TBK1
9793	CKAP5		9277	WDR46
998	CDC42		254240	BPIL2
7051	TGM1		3297	HSF1
10568	SLC34A2		64434	NOM1
1315	COPB1		400	ARL1
0	DLX6		3881	KRT31
2178	FANCE		81788	NUAK2
8775	NAPA		3036	HAS1
55223	TRIM62		786	CACNG1
22820	COPG		1052	CEBPD
594	BCKDHB		5055	SERPINB2
221178	SPATA13		54979	HRASLS2
55501	CHST12		50834	TAS2R1
57817	HAMP		9682	JMJD2A
391114	OR6K3		8722	CTSF
259307	IL4I1		7176	TPS1
4664	NAB1		162972	ZNF550
84790	TUBA1C		5709	PSMD3
486	FXYD2		83540	NUF2
26135	SERBP1		10244	RABEPK
27035	NOX1		5901	RAN
8723	SNX4		246100	CTAG1A
5454	POU3F2		151903	CCDC12
10572	SIVA1		51602	NOP5/NOP58
3423	IDS		7879	RAB7A
4108	MAGEA9		570	BAAT
164237	WFDC13		348801	LNP1
7380	UPK3A		10951	CBX1
94115	CGB8		0	LOC390205
0	LOC54103		8971	H1FX
10607	TBL3		23054	NCOA6

256329	C11orf35		151636	DTX3L
23145	SSPO		10639	HHCM
56413	LTB4R2		50801	KCNK4
57215	THAP11		9020	MAP3K14
3182	HNRPAB		8519	IFITM1
89781	HPS4		586	BCAT1
2862	MLNR		9355	LHX2
23553	HYAL4		10005	ACOT8
5707	PSMD1		3679	ITGA7
80347	COASY		54908	CCDC99
8788	DLK1		26254	OPTC

Table 5

Gene	Alias	Definition	Function/ Association	Human Chrom. Location	Human GenBank Accession No. for coding sequence/ mRNA	Human GenBank Accession No. for protein	Entrez Gene No.	Compounds
BCR	ALL; CML; PHL; BCR1; D22S11; D22S662; FLJ16453	breakpoint cluster region	The protein has serine/threonine kinase activity and is a GTPase-activating protein for p21rac.	22q11.23	NM_004327.3 NM_021574.2	NP_004318.3 NP_067585.2	613	imatinib
	CAII; Car2; CA-II	carbonic anhydrase II	Catalyzes reversible hydration of carbon dioxide.	8q22	NM_000067.2	NP_000058.1	760	acetazolamide; benzthiazide; brinzolamide; chlorothiazide; chlorthalidone; dorzolamide; dorzolamide/timolol; hydrochlorothiazide; methazolamide; sulfacetamide; topiramate; trichloromethiazide
CA2	NACHRA7; CHRNA7-2	cholinergic receptor, nicotinic, alpha 7	Nicotinic acetylcholine receptors (nAChRs) are members of a superfamily of ligand- gated ion channels that mediate fast signal transmission at synapses.	15q14	NM_000746.3	NP_000737.1	1139	amobarbital; atracurium; cisatracurium; D- tubocurarine; doxacurium; mecamylamine; metocurine; mivacurium; pancuronium; pipecuronium; rapacuronium; rocuronium; succinylcholine; vecuronium; enflurane; isoflurane
CHRNA7 CXCR4	FB22; HM89;	chemokine (C-X-C)	Gene encodes a CXC	2q21	NM_001008540.1	NP_001008540.1	7852	plerixafor

	LAP3; LCR1; NPYR; WHIM; CD184; LESTR; NPY3R; NPYRL; HSY3RR; NPYY3R; D2S201E	motif) receptor 4	chemokine receptor specific for stromal cell-derived factor-1. The protein has 7 transmembrane regions and is located on the cell surface.		NM_003467.2	NP_003458.1		
EDNRA	ETA; ETAR; ETRA	endothelin receptor type A	Encodes the receptor for endothelin-1, a peptide that plays a role in potent and long- lasting vasoconstriction.	4q31.22	NM_001166055.1 NM_001957.3	NP_001159527.1 NP_001948.1	1909	ambrisentan; avosentan; bosentan; BSF 302146; clazosentan; PD 180988; SB 234551 sitaxsentan; TBC 3214; ZD4054; atrasentan
EGFR	ERBB; HER1; mENA; ERBB1; PIG61	epidermal growth factor receptor	Protein encoded by this gene is a transmembrane glycoprotein that binds to epidermal growth factor.	7p12	NM_005228.3 NM_201282.1 NM_201283.1 NM_201284.1	NP_005219.2 NP_958439.1 NP_958440.1 NP_958441.1	1956	AEE 788; ARRY- 334543; BMS- 599626; canertinib; cetuximab; erlotinib; gefitinib; HKI-272; lapatinib; PD 153035; vandetanib; XL647
F2	PT	coagulation factor II (thrombin)	Proteolytically cleaved to form thrombin in the first step of the coagulation cascade.	11p11	NM_000506.3	NP_000497.1	2147	antithrombin alfa; argatroban; bivalirudin; dabigatran etexilate; desirudin; enoxaparin; lepirudin
GRIA2	GLUR2; GLURB; HBGR2; GluR-K2	glutamate receptor, ionotropic, AMPA 2	Belongs to a family of glutamate receptors that are sensitive to AMPA, and function as ligand- activated cation channels.	4q32-q33	NM_000826.3 NM_001083619.1 NM_001083620.1	NP_000817.2 NP_001077088.1 NP_001077089.1	2891	talampanel; tezampanel
HDAC1	HD1; RPD3; GON- 10; RPD3L1; DKFZp686H12203	histone deacetylase 1	Protein encoded by this gene belongs to the histone deacetylase/acuc/apha family and is a component of the histone deacetylase	1p34	NM_004964.2	NP_004955.2	3065	MGC00103; PXD101; pyroxamide; romidepsin; tributyrin; vorinostat

			potassium inwardly-rectifying channel, subfamily J, member 11	complex. Protein encoded by this gene is an integral membrane protein and inward-rectifier type potassium channel.	11p15.1	NM_000525.3 NM_001166290.1	NP_000516.3 NP_001159762.1	3767	Acetohexamide; chlorpropamide; glimepiride; glipizide glyburide; minoxidil nateglinide; phenitamine; repaglinide; tolazamide; tolbutamide
KCNJ11	FLJ16150; HsT19550	phospho-diesterase 8A		PDEs regulate the intracellular levels of cAMP and cGMP.	15q25.3	NM_002605.2 NM_173454.1	NP_002596.1 NP_775656.1	5151	aminophylline; anagrelide; dipyridamole; dyphylline; milrinone; nitroglycerin; pentoxifylline; theophylline; tolbutamide
PDE8A	PLK; STPK13	polo-like kinase 1 (Drosophila)		Serine/threonine-protein kinase that performs several important functions throughout M phase of the cell cycle.	16p12.2	NM_005030.3	NP_005021.2	5347	BI 2536
PLK1	POLE1; FLJ21434; DKFZp434F222	polymerase (DNA directed), epsilon		Participates in DNA repair and in chromosomal DNA replication.	12q24.3	NM_006231.2	NP_006222.2	5426	clofarabine; gemcitabine; nelarabine; trifluridine
POLE	MGC138457	steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)		Gene encodes a microsomal protein expressed at high levels in androgen-sensitive tissues such as the prostate.	2p23	NM_000348.3	NP_000339.2	6716	dutasteride; finasteride
SRD5A2	TUBAL2	tubulin, alpha 8		Tubulin is the major constituent of microtubules. It binds two moles of GTP, one	22q11.1	NM_018943.1	NP_061816.1	51807	docetaxel; ixabepilone; milataxel; NPI-2358; podophyllotoxin; TPI
TUBA8									

			at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha-chain.	2q24.3	NM_001935.3	NP_001926.2	1803	287; AL 108; paclitaxel; TTI-237; XRP9881; EC145; E7389; vinblastine; vincristine; vinflunine; vinorelbine
DPP4	CD26; ADABP; ADCP2; DPPIV; TP103	dipeptidyl-peptidase 4	Protein encoded by this gene is an intrinsic membrane glycoprotein and a serine exopeptidase that cleaves X-proline dipeptides from the N-terminus of polypeptides.	7q31.3-q32	NM_000883.3 NM_001102605.1 NM_001142573.1 NM_001142574.1 NM_001142575.1 NM_001142576.1 NM_183243.2	NP_000874.2 NP_001096075.1 NP_001136045.1 NP_001136046.1 NP_001136047.1 NP_001136048.1 NP_899066.1	3614	mycophenolic acid; ribavirin; thioguanine; VX-944
IMPDH1	IMPD; RP10; IMPD1; LCA11; sWSS2608; DKFZp781N0678	IMP (inosine monophosphate) dehydrogenase 1	Protein encoded by this gene is an enzyme that catalyzes the synthesis of xanthine monophosphate (XMP) from inosine-5'-monophosphate (IMP).	3p21.2	NM_000884.2	NP_000875.2	3615	mycophenolic acid; ribavirin; thioguanine; VX-944
IMPDH2	IMPD2; IMPDH-II	IMP (inosine monophosphate) dehydrogenase 2	Encoded protein catalyzes the NAD-dependent oxidation of inosine-5'-monophosphate into xanthine-5'-monophosphate, which is then converted into guanosine-5'-monophosphate.	1q25	NM_003101.4	NP_003092.4	6646	pactimibe
STAT (SOAT1)	ACAT; SOAT; ACAC1; ACAT1; RP11-215123.2; SOAT1	sterol O-acyltransferase 1	Catalyzes the formation of fatty acid-cholesterol esters. Plays a role in lipoprotein assembly and dietary cholesterol absorption.	19p13.3	NM_001060.5 NM_201636.2	NP_001051.1 NP_963998.2	6915	S-18886; torsemide
TBXA2R	TXA2-R	thromboxane A2 receptor	Gene encodes a member of the G					

				protein-coupled receptor family that interacts with thromboxane A2 to induce platelet aggregation and regulate hemostasis.		20p13	NM_000678.3	NP_000669.1	146	carvedilol; dapiprazole; ergotamine; guanadrel; labetalol; phenoxybenzamine; prazosin; terazosine; alfuzosin; aripiprazole; asenapine; dihydroergotamine; DL 017; epinastine; guanethidine; iloperidone; nefazodone; olanzapine; paliperidone; phenotolamine; quetiapine; quinidine; risperidone; tolazoline; UK-294315; ziprasidone; dobutamine; apraclonidine; arbutamine; clonidine; tamsulosin; venlafaxine
ADRA1D	DAR; ADRA1; ADRA1A; ADRA1R; ALPHA1; dJ779E11.2	adrenergic, alpha-1D-, receptor		Gene encodes alpha-1D-adrenergic receptor activates mitogenic responses and regulate growth and proliferation of many cells.		19p13.2-p13.1	NM_001127221.1 NM_001127222.1	NP_001120693.1 NP_001120694.1	773	clevipidine butyrate
CACNA1A	EA2; FHM; MHP; APCA; HPCA; MHP1; SCA6; CAV2.1; CACNL1A4	calcium channel, voltage-dependent, P/Q type, alpha 1A subunit		Gene encodes the alpha-1A subunit of the voltage-dependent calcium channels.		11p15.1	NM_000922.3	NP_000913.2	5140	aminophylline; amrinone; cilostazol;
PDE3B	HcGIP1; cGIPDE1	phosphodiesterase 3B, cGMP-		PDEs regulate the intracellular levels of						

									dipyridamole; dyphylline; medorinone; nitroglycerin; pentoxifylline; theophylline; tolbutamide
	TUBB5; beta-5	tubulin, beta 4	Tubulin is the major constituent of microtubules. It binds two moles of GTP, one at an exchangeable site on the beta chain and one at a non-exchangeable site on the alpha-chain.	19p13.3	NM_006087.2	NP_006078.2	10382		ABT-751; BMS-275183; docetaxel; E7389; milataxel; MST-997; NPI-2358; podophyllotoxin; TPI 287; AL 108; ixabepilone; paclitaxel; TTL-237; XRP9881; epothilone B; EC145; vinblastine; vincristine; vinflunine; vinorelbine
TUBB4									
	GELB; CLG4B; MMP-9; MANDP2	matrix metalloproteinase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	The enzyme encoded by this gene degrades type IV and V collagens.	20q11.2-q13.1	NM_004994.2	NP_004985.2	4318		minocycline
MMP9									

As used herein, the term “nucleic acid” refers to single or multiple stranded molecules which may be DNA or RNA, or any combination thereof, including modifications to those nucleic acids. The nucleic acid may represent a coding strand or its complement, or any combination thereof. Nucleic acids may be identical in sequence to the sequences which are naturally occurring for any of the moieties discussed herein or may include alternative codons which encode the same amino acid as that which is found in the naturally occurring sequence. These nucleic acids can also be modified from their typical structure. Such modifications include, but are not limited to, methylated nucleic acids, the substitution of a non-bridging oxygen on the phosphate residue with either a sulfur (yielding phosphorothioate deoxynucleotides), selenium (yielding phosphorselenoate deoxynucleotides), or methyl groups (yielding methylphosphonate deoxynucleotides), a reduction in the AT content of AT rich regions, or replacement of non-preferred codon usage of the expression system to preferred codon usage of the expression system. The nucleic acid can be directly cloned into an appropriate vector, or if desired, can be modified to facilitate the subsequent cloning steps. Such modification steps are routine, an example of which is the addition of oligonucleotide linkers which contain restriction sites to the termini of the nucleic acid. General methods are set forth in in Sambrook *et al.* (2001) *Molecular Cloning - A Laboratory Manual* (3rd ed.) Vol. 1-3, Cold Spring Harbor Laboratory, Cold Spring Harbor Press, NY, (Sambrook).

Once the nucleic acid sequence is obtained, the sequence encoding the specific amino acids can be modified or changed at any particular amino acid position by techniques well known in the art. For example, PCR primers can be designed which span the amino acid position or positions and which can substitute any amino acid for another amino acid. Alternatively, one skilled in the art can introduce specific mutations at any point in a particular nucleic acid sequence through techniques for point mutagenesis. General methods are set forth in Smith, M. “In vitro mutagenesis” *Ann. Rev. Gen.*, 19:423-462 (1985) and Zoller, M.J. “New molecular biology methods for protein engineering” *Curr. Opin. Struct. Biol.*, 1:605-610 (1991), which are incorporated herein in their entirety for the methods. These techniques can be used to alter the coding sequence without altering the amino acid sequence that is encoded.

The sequences contemplated herein include full-length wild-type (or native) sequences, as well as allelic variants, variants, fragments, homologs or fusion sequences that retain the ability to function as the cellular nucleic acid or protein involved in viral infection. In certain examples, a protein or nucleic acid sequence has at least 50% sequence identity, for example at least 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 98% sequence identity to a native sequences of the genes set forth in any of tables 1-4. In other examples, a nucleic acid sequence involved in viral infection has a sequence that hybridizes to a sequence of a gene set

forth in Table 1, 2 3 or 4 and retains the activity of the sequence of the gene set forth in Table 1, 2 3, or 4. For example, and not to be limiting, a nucleic acid that hybridizes to an ABTB1 nucleic acid sequence and encodes a protein that retains ABTB1 activity is contemplated by the present invention. Such sequences include the genomic sequence for the genes set forth in Table 1, 2, 3 or 4. The examples set forth above for ABTB1 are merely illustrative and should not be limited to ABTB1 as the analysis set forth in this example applies to every nucleic acid and protein for the genes listed in Table 1, 2, 3 or 4.

Unless otherwise specified, any reference to a nucleic acid molecule throughout this application includes the reverse complement of the nucleic acid. For example, any siRNA sequence set forth herein also includes the reverse complement of that sequence. Except where single-strandedness is required by the text herein (for example, a ssRNA molecule), any nucleic acid written to depict only a single strand encompasses both strands of a corresponding double-stranded nucleic acid. For example, depiction of a plus-strand of a dsDNA also encompasses the complementary minus-strand of that dsDNA. Additionally, any reference to the nucleic acid molecule that encodes a specific protein, or a fragment thereof, encompasses both the sense strand and its reverse complement. Fragments of the nucleic acids set forth in Table 1, 2, 3 or 4 are also contemplated. These fragments can be utilized as primers and probes to amplify, inhibit or detect any of the nucleic acids or genes set forth in Table 1, 2, 3 or 4.

Hybridization conditions resulting in particular degrees of stringency will vary depending upon the nature of the hybridization method and the composition and length of the hybridizing nucleic acid sequences. Generally, the temperature of hybridization and the ionic strength (such as the Na⁺ concentration) of the hybridization buffer will determine the stringency of hybridization. Calculations regarding hybridization conditions for attaining particular degrees of stringency are discussed in Sambrook *et al.*, (1989) Molecular Cloning, second edition, Cold Spring Harbor Laboratory, Plainview, NY (chapters 9 and 11). The following is an exemplary set of hybridization conditions and is not limiting:

Very High Stringency (detects sequences that share 90% identity)

Hybridization:	5x SSC at 65°C for 16 hours
Wash twice:	2x SSC at room temperature (RT) for 15 minutes each
Wash twice:	0.5x SSC at 65°C for 20 minutes each

High Stringency (detects sequences that share 80% identity or greater)

Hybridization:	5x-6x SSC at 65°C-70°C for 16-20 hours
Wash twice:	2x SSC at RT for 5-20 minutes each

Wash twice: 1x SSC at 55°C-70°C for 30 minutes each

Low Stringency (detects sequences that share greater than 50% identity)

Hybridization: 6x SSC at RT to 55°C for 16-20 hours

5 Wash at least twice: 2x-3x SSC at RT to 55°C for 20-30 minutes each.

Also provided is a vector, comprising a nucleic acid set forth herein. The vector can direct the *in vivo* or *in vitro* synthesis of any of the proteins or polypeptides described herein. The vector is contemplated to have the necessary functional elements that direct and regulate transcription of the inserted nucleic acid. These functional elements include, but are not limited to, a promoter, regions upstream or downstream of the promoter, such as enhancers that may regulate the transcriptional activity of the promoter, an origin of replication, appropriate restriction sites to facilitate cloning of inserts adjacent to the promoter, antibiotic resistance genes or other markers which can serve to select for cells containing the vector or the vector containing the insert, RNA splice junctions, a transcription termination region, or any other region which may serve to facilitate the expression of the inserted gene or hybrid gene (See generally, *Sambrook et al.*). The vector, for example, can be a plasmid. The vectors can contain genes conferring hygromycin resistance, ampicillin resistance, gentamicin resistance, neomycin resistance or other genes or phenotypes suitable for use as selectable markers, or methotrexate resistance for gene amplification.

There are numerous other *E. coli* (*Escherichia coli*) expression vectors, known to one of ordinary skill in the art, which are useful for the expression of the nucleic acid insert. Other microbial hosts suitable for use include bacilli, such as *Bacillus subtilis*, and other enterobacteriaceae, such as *Salmonella*, *Serratia*, and various *Pseudomonas* species. In these prokaryotic hosts one can also make expression vectors, which will typically contain expression control sequences compatible with the host cell (e.g., an origin of replication). In addition, any number of a variety of well-known promoters will be present, such as the lactose promoter system, a tryptophan (Trp) promoter system, a beta-lactamase promoter system, or a promoter system from phage lambda. Additionally, yeast expression can be used. The invention provides a nucleic acid encoding a polypeptide of the present invention, wherein the nucleic acid can be expressed by a yeast cell. More specifically, the nucleic acid can be expressed by *Pichia pastoris* or *S. cerevisiae*.

Mammalian cells also permit the expression of proteins in an environment that favors important post-translational modifications such as folding and cysteine pairing, addition of complex carbohydrate structures, and secretion of active protein. Vectors useful for the

expression of active proteins are known in the art and can contain genes conferring hygromycin resistance, gentamicin or G418 resistance, or other genes or phenotypes suitable for use as selectable markers, or methotrexate resistance for gene amplification. A number of suitable host cell lines capable of secreting intact human proteins have been developed in the art, and include

the CHO cell lines, HeLa cells, COS-7 cells, myeloma cell lines, Jurkat cells, etc. Expression vectors for these cells can include expression control sequences, such as an origin of replication, a promoter, an enhancer, and necessary information processing sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences.

Preferred expression control sequences are promoters derived from immunoglobulin genes, SV40, Adenovirus, Bovine Papilloma Virus, etc.

The expression vectors described herein can also include nucleic acids of the present invention under the control of an inducible promoter such as the tetracycline inducible promoter or a glucocorticoid inducible promoter. The nucleic acids of the present invention can also be under the control of a tissue-specific promoter to promote expression of the nucleic acid in specific cells, tissues or organs. Any regulatable promoter, such as a metallothionein promoter, a heat-shock promoter, and other regulatable promoters, of which many examples are well known in the art are also contemplated. Furthermore, a Cre-loxP inducible system can also be used, as well as a F1p recombinase inducible promoter system, both of which are known in the art.

Insect cells also permit the expression of mammalian proteins. Recombinant proteins produced in insect cells with baculovirus vectors undergo post-translational modifications similar to that of wild-type proteins. The invention also provides for the vectors containing the contemplated nucleic acids in a host suitable for expressing the nucleic acids. The host cell can be a prokaryotic cell, including, for example, a bacterial cell. More particularly, the bacterial cell can be an *E. coli* cell. Alternatively, the cell can be a eukaryotic cell, including, for example, a Chinese hamster ovary (CHO) cell, a COS-7 cell, a HELA cell, an avian cell, a myeloma cell, a *Pichia* cell, or an insect cell. A number of other suitable host cell lines have been developed and include myeloma cell lines, fibroblast cell lines, a cell line suitable for infection by a pathogen, and a variety of tumor cell lines such as melanoma cell lines. The vectors containing the nucleic acid segments of interest can be transferred into the host cell by well-known methods, which vary depending on the type of cellular host. For example, calcium chloride transformation is commonly utilized for prokaryotic cells, whereas calcium phosphate, DEAE dextran, Lipofectamine, or lipofectin mediated transfection, electroporation or any method now known or identified in the future can be used for other eukaryotic cellular hosts.

Polypeptides

The present invention provides isolated polypeptides comprising the polypeptide or protein sequences for the genes set forth in Table 1, 2, 3 or 4. The present invention also provides fragments of these polypeptides. These fragments can be of sufficient length to serve
5 as antigenic peptides for the generation of antibodies. The present invention also contemplates functional fragments that possess at least one activity of a gene or gene product listed in Table 1, 2, 3 or 4, for example, involved in viral infection.

By “isolated polypeptide” or “purified polypeptide” is meant a polypeptide that is substantially free from the materials with which the polypeptide is normally associated in nature
10 or in culture. The polypeptides of the invention can be obtained, for example, by extraction from a natural source if available (for example, a mammalian cell), by expression of a recombinant nucleic acid encoding the polypeptide (for example, in a cell or in a cell-free translation system), or by chemically synthesizing the polypeptide. In addition, a polypeptide can be obtained by cleaving full length polypeptides. When the polypeptide is a fragment of a
15 larger naturally occurring polypeptide, the isolated polypeptide is shorter than and excludes the full-length, naturally-occurring polypeptide of which it is a fragment.

Also provided by the present invention is a polypeptide comprising an amino acid sequence at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%,
20 98% or 99% identical to the native polypeptide sequence for any gene set forth in Table 1, 2, 3 or 4.

It is understood that as discussed herein the use of the terms “homology” and “identity” mean the same thing as similarity. Thus, for example, if the use of the word homology is used to refer to two non-natural sequences, it is understood that this is not necessarily indicating an evolutionary relationship between these two sequences, but rather is looking at the similarity or
25 relatedness between their nucleic acid sequences. Many of the methods for determining homology between two evolutionarily related molecules are routinely applied to any two or more nucleic acids or proteins for the purpose of measuring sequence similarity regardless of whether they are evolutionarily related.

In general, it is understood that one way to define any known variants and derivatives or
30 those that might arise, of the disclosed nucleic acids and polypeptides herein, is through defining the variants and derivatives in terms of homology to specific known sequences. In general, variants of nucleic acids and polypeptides herein disclosed typically have at least, about 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99 percent homology to the stated sequence or the native sequence. Those of skill in the
35 art readily understand how to determine the homology of two polypeptides or nucleic acids.

Methods of Decreasing Infection

The present invention provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of a gene or gene product set forth in Table 1, wherein the pathogen is not HIV. For example, and not to be limiting, the present invention provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of, BCR, CA2, CHRNA7, CXCR4, EDNRA, EGFR, F2, GRIA2, HDAC1, KCNJ11, MMP9, PDE8A, PLK1, POLE, SRD5A2, TUBA8 or DPP4, wherein the pathogen is not HIV. For example, imatinib can be used to inhibit BCR. Acetazolamide, benzothiazide, brinzolamide, chlorothiazide, chlorthalidone, dorzolamide, dorzolamide/timolol, hydrochlorothiazide, methazolamide, sulfacetamide, topiramate or trichloromethiazide can be used to inhibit CA2. Amobarbital, atracurium, cisatracurium, D-tubocurarine, doxacurium, mecamylamine, metocurine, mivacurium, pancuronium, pipecuronium, rapacuronium, rocuronium, succinylcholine, vecuronium, enflurane or isoflurane can be used to inhibit CHRNA7. Plerixafor can be used to inhibit CXCR4. Ambrisentan, avosentan, bosentan, BSF 302146, clazosentan, PD 180988, SB 234551, sitaxsentan, TBC 3214, ZD4054 or atrasentan can be utilized to inhibit EDNRA. AEE 788, ARRY-334543, BMS-599626, canertinib, cetuximab, erlotinib, gefitinib, HKI-272, lapatinib, PD 153035, vandetanib or XL647 can be used to inhibit EGFR. Antithrombin, alfa, argatroban, bivalirudin, dabigatran etexilate, desirudin, enoxaparin, or lepirudin can be utilized to inhibit F2. Talampanel or tezampanel can be utilized to inhibit GRIA2. MGCD0103, PXD101, pyroxamide, romidepsin, tributyrin or vorinostat can be utilized to inhibit HDAC1. Acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, minoxidil, nateglinide, phentolamine, repaglinide, tolazamide or tolbutamide can be utilized to inhibit KCNJ11. Aminophylline, anagrelide, dipyridamole, dyphylline, milrinone, nitroglycerin, pentoxifylline, theophylline or tolbutamide can be utilized to inhibit PDE8A. BI2536 can be utilized to inhibit PLK1. Clofarabine, gemcitabine, nelarabine or trifluridine can be utilized to inhibit POLE. Dutasteride or finasteride can be utilized to inhibit SRD5A2. Docetaxel, ixabepilone, milataxel, NPI-2358, podophyllotoxin, TPI 287, AL 108, paclitaxel, TTI-237, XRP9881 (larotaxel), EC145, E7389, vinblastine, vincristine, vinflunine or vinorelbine can be utilized to inhibit TUBA8. Saxagliptin, sitagliptin, SYR-322 or talabostat can be utilized to inhibit DPP4. Minocycline can be utilized to inhibit MMP9. Combinations of two or more of the compounds set forth can be utilized to inhibit infection. These combinations can be utilized to inhibit one or more of the gene products selected from the group consisting of BCR, CA2, CHRNA7, CXCR4, EDNRA, EGFR, F2, GRIA2, HDAC1, KCNJ11, PDE8A, PLK1, POLE, SRD5A2, TUBA8 and DPP4. Therefore, two or more compounds that inhibit expression or

activity of the same gene product can be used, or two or more compounds that inhibit expression or activity of two or more different gene products can be used to inhibit infection.

Also provided is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of a gene or gene product set forth in Table 2, wherein the pathogen is not West Nile Virus. Further provided is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of CACNA1A, PDE3B or TUBB4, wherein the pathogen is not West Nile Virus. Clevidipine butyrate can be utilized to inhibit CACNA1A. Aminophylline, amrinone, cilostazol, dipyridamole, dyphylline, medorinone, nitroglycerin, pentoxifylline, theophylline or tolbutamide can be utilized to inhibit PDE3B. ABT-751, BMS-275183, docetaxel, E7389, milataxel, MST-997, NPI-2358, podophyllotoxin, TPI 287, AL 108, ixabepilone, paclitaxel, TTI-237, XRP9881, epothilone B, EC145, vinblastine, vincristine, vinflunine, minocycline or vinorelbine can be utilized to inhibit TUBB4.

Further provided is a method of inhibiting infection in a cell by a pathogen, comprising decreasing expression or activity of a gene or gene product set forth in Table 3, wherein the pathogen is not West Nile Virus or Dengue Fever Virus. Further provided is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of ADRA1D, wherein the pathogen is not West Nile Virus or Dengue Fever Virus. Carvedilol, dapiprazole, ergotamine, guanadrel, Labetalol, phenoxybenzamine, prazosin, terazosine, alfuzosin, aripiprazole, asenapine, dihydroergotamine, DL 017, epinastine, guanethidine, iloperidone, nefazodone, olanzapine, paliperidone, phentolamine, quetiapine, quinidine, risperidone, tolazoline, UK-294315, ziprasidone, dobutamine, apraclonidine, arbutamine, clonidine, tamsulosin or venlafaxine can be utilized to inhibit ADRA1D.

The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of a gene or gene product set forth in Table 4, wherein the pathogen is not hepatitis C virus. The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or STAT (SOAT1) or TBXA2R, wherein the pathogen is not hepatitis C virus. Pactimibe can be utilized to inhibit STAT (SOAT1). S-18886 or torsemide can be utilized to inhibit TBXA2R.

Also provided by the present invention is a method of decreasing infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, wherein the pathogen is not HIV. Further provided is a method of decreasing infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, wherein the pathogen is not West Nile Virus. Also provided by the present invention is a method of decreasing infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s)

set forth in Table 3, wherein the pathogen is not West Nile Virus or Dengue Fever Virus. Also provided by the present invention is a method of decreasing infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, wherein the pathogen is not HCV. As utilized herein, one or more includes, two or
5 more, three or more, four or more, five or more, six or more, seven or more, etc.

As stated above, an infection can be a viral infection, bacterial infection, fungal infection or a parasitic infection, to name a few. A decrease or inhibition of infection can occur in a cell, *in vitro*, *ex vivo* or *in vivo*. As utilized throughout, the term "infection" encompasses all phases of pathogenic life cycles including, but not limited to, attachment to cellular receptors, entry,
10 internalization, disassembly, replication, genomic integration of pathogenic sequences, transcription of viral RNA, translation of viral RNA, transcription of host cell mRNA, translation of host cell mRNA, proteolytic cleavage of pathogenic proteins or cellular proteins, assembly of particles, endocytosis, cell lysis, budding, and egress of the pathogen from the cells. Therefore, a decrease in infection can be a decrease in attachment to cellular receptors, a
15 decrease in entry, a decrease in internalization, a decrease in disassembly, a decrease in replication, a decrease in genomic integration of pathogenic sequences, a decrease in translation of mRNA, a decrease in proteolytic cleavage of pathogenic proteins or cellular proteins, a decrease in assembly of particles, a decrease in endocytosis, a decrease in cell lysis, a decrease in budding, or a decrease in egress of the pathogen from the cells. This decrease does not have
20 to be complete as this can range from a slight decrease to complete ablation of the infection. A decrease in infection can be at least about 10%, 20%, 30%, 40%, 50%, 60, 70%, 80%, 90%, 95%, 100% or any other percentage decrease in between these percentages as compared to the level of infection in a cell wherein expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4 has not been decreased.

25 In the methods set forth herein, expression can be inhibited, for example by inhibiting transcription of the gene, or inhibiting translation of its gene product. Similarly, the activity of a gene product (for example, an mRNA, a polypeptide or a protein) can be inhibited, either directly or indirectly. Inhibition or a decrease in expression does not have to be complete as this can range from a slight decrease in expression to complete ablation of expression. For example,
30 expression can be inhibited by about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or any percentage in between as compared to a control cell wherein the expression of a gene or gene product set forth in Table 1, 2, 3 or 4 has not been decreased or inhibited. Similarly, inhibition or decrease in the activity of a gene product does not have to be complete as this can range from a slight decrease to complete ablation of the activity of the gene product.
35 For example, the activity of a gene product can be inhibited by about 10%, 20%, 30%, 40%,

50%, 60%, 70%, 80%, 90%, 95%, 99%, 100% or any percentage in between as compared to a control cell wherein activity of a gene or gene product set forth in Table 1, 2, 3 or 4 has not been decreased or inhibited. As utilized herein, "activity of a gene product" can be an activity that is involved in pathogenicity, for example, interacting directly or indirectly, with pathogen, e.g.

5 viral protein or viral nucleic acids, or an activity that the gene product performs in a normal cell, i.e. in a non-infected cell. Depending on the gene product, one of skill in the art would know how to assay for an activity that is involved in pathogenicity, an activity that is involved in normal cellular function, or both. As set forth above, an activity of the proteins and nucleic acids listed herein can be the ability to bind or interact with other proteins. Therefore, the present
10 invention also provides a method of decreasing infection by inhibiting or decreasing the interaction between any of the proteins of the present invention and other cellular proteins, such as, for example, transcription factors, receptors, nuclear proteins, transporters, microtubules, membrane proteins, enzymes (for example, ATPases, phosphorylases, oxidoreductases, kinases, phosphatases, synthases, lyases, aromatases, helicases, hydrolases, proteases, transferases,
15 nucleases, ligases, reductases and polymerases) and hormones, provided that such inhibition correlates with decreasing infection by the pathogen. Also provided is a method of decreasing infection by inhibiting or decreasing the interaction between any of the proteins of the present invention and a viral, bacterial, parasitic or fungal protein (i.e. a non-host protein).

The cells of the present invention can be prokaryotic or eukaryotic, such as a cell from
20 an insect, fish, crustacean, mammal, bird, reptile, yeast or a bacterium, such as *E. coli*. The cell can be part of an organism, or part of a cell culture, such as a culture of mammalian cells or a bacterial culture. Therefore, the cell can also be part of a population of cells. The cell(s) can also be in a subject.

Examples of viral infections include but are not limited to, infections caused by RNA
25 viruses (including negative stranded RNA viruses, positive stranded RNA viruses, double stranded RNA viruses and retroviruses), DNA viruses. All strains and types of RNA viruses and DNA viruses are contemplated herein.

Examples of RNA viruses include, but are not limited to picornaviruses, which include
aphthoviruses (for example, foot and mouth disease virus O, A, C, Asia 1, SAT1, SAT2 and
30 SAT3), cardioviruses (for example, encephalomyocarditis virus and Theiler's murine encephalomyelitis virus), enteroviruses (for example polioviruses 1, 2 and 3, human enteroviruses A-D, bovine enteroviruses 1 and 2, human coxsackieviruses A1-A22 and A24, human coxsackieviruses B1-B5, human echoviruses 1-7, 9, 11-12, 24, 27, 29-33, human enteroviruses 68-71, porcine enteroviruses 8-10 and simian enteroviruses 1-18), erboviruses (for
35 example, equine rhinitis virus), hepatovirus (for example human hepatitis A virus and simian

hepatitis A virus), kobuviruses (for example, bovine kobuvirus and Aichi virus), parechoviruses (for example, human parechovirus 1 and human parechovirus 2), rhinovirus (for example, rhinovirus A, rhinovirus B, HRV₁₆ (VR-11757), HRV₁₄ (VR-284), or HRV_{1A} (VR-1559), human rhinovirus 1-100 and bovine rhinoviruses 1-3) and teschoviruses (for example, porcine teschovirus).

Additional examples of RNA viruses include caliciviruses, which include noroviruses (for example, Norwalk virus), sapoviruses (for example, Sapporo virus), lagoviruses (for example, rabbit hemorrhagic disease virus and European brown hare syndrome) and vesiviruses (for example vesicular exanthema of swine virus and feline calicivirus).

Other RNA viruses include astroviruses, which include mamastorviruses and avastroviruses. Togaviruses are also RNA viruses. Togaviruses include alphaviruses (for example, Sindbis virus, Chikungunya virus, Semliki Forest virus, Western equine encephalitis, Getah virus, Everglades virus, Venezuelan equine encephalitis virus and Aura virus) and rubella viruses. Additional examples of RNA viruses include the the flaviviruses (for example, tick-borne encephalitis virus, Tyulenyi virus, Aroa virus, Dengue virus (types 1 to 4), Kedougou virus, Japanese encephalitis virus (JEV), West Nile virus (WNV), Kokobera virus, Ntaya virus, Spondweni virus, Yellow fever virus, Entebbe bat virus, Modoc virus, Rio Bravo virus, Cell fusing agent virus, pestivirus, GB virus A, GBV-A like viruses, GB virus C, Hepatitis G virus, hepacivirus (hepatitis C virus (HCV)) all six genotypes), bovine viral diarrhea virus, and GB virus B).

Other examples of RNA viruses are the coronaviruses which include, human respiratory coronaviruses such as SARS-CoV, HCoV-229E, HCoV-NL63 and HCoV-OC43.

Coronaviruses also include bat SARS-like CoV, turkey coronavirus, chicken coronavirus, feline coronavirus and canine coronavirus. Additional RNA viruses include arteriviruses (for example, equine arterivirus, porcine reproductive and respiratory syndrome virus, lactate dehydrogenase elevating virus of mice and simian hemorrhagic fever virus). Other RNA viruses include the rhabdoviruses, which include lyssaviruses (for example, rabies, Lagos bat virus, Mokola virus, Duvenhage virus and European bat lyssavirus), vesiculoviruses (for example, VSV-Indiana, VSV-New Jersey, VSV-Alagoas, Piry virus, Cocal virus, Maraba virus, Isfahan virus and Chandipura virus), and ephemeroviruses (for example, bovine ephemeral fever virus, Adelaide River virus and Berrimah virus). Additional example of RNA viruses include the filoviruses. These include the Marburg and Ebola viruses (for example, EBOV-Z, EBOV-S, EBOV-IC and EBOV-R).

The paramyxoviruses are also RNA viruses. Examples of these viruses are the rubula viruses (for example, mumps, parainfluenza virus 5, human parainfluenza virus type 2, Mapuera

virus and porcine rubulavirus), avulaviruses (for example, Newcastle disease virus),
respopviruses (for example, Sendai virus, human parainfluenza virus type 1 and type 3, bovine
parainfluenza virus type 3), henipaviruses (for example, Hendra virus and Nipah virus),
morbilloviruses (for example, measles, Cetacean morvilliirus, Canine distemper virus, Peste-
des-petits-ruminants virus, Phocine distemper virus and Rinderpest virus), pneumoviruses (for
example, human respiratory syncytial virus A2, B1 and S2, bovine respiratory syncytial virus
and pneumonia virus of mice), metapneumoviruses (for example, human metapneumovirus and
avian metapneumovirus). Additional paramyxoviruses include Fer-de-Lance virus, Tupaia
paramyxovirus, Menangle virus, Tioman virus, Beilong virus, J virus, Mossman virus, Salem
virus and Nariva virus.

Additional RNA viruses include the orthomyxoviruses. These viruses include influenza
viruses and strains (*e.g.*, influenza A (H1N1 (including but not limited to A/WS/33 or
A/California/04/2009 strains) H2N2, H3N2, H5N1, H7N7, H1N2, H9N2, H7N2, H7N3 and
H10N7), influenza A strain A/Victoria/3/75, influenza A strain A/Puerto Rico/8/34, influenza B
strain Lee, influenza B (for example B strain Lee) and C viruses, as well as avian influenza (for
example, strains H5N1, H5N2, H7N1, H7N7 and H9N2) thogotoviruses and isaviruses.
Orthobunyaviruses (for example, Akabane virus, California encephalitis, Cache Valley virus,
Snowshoe hare virus,) nairoviruses (for example, Nairobi sheep virus, Crimean-Congo
hemorrhagic fever virus Group and Hughes virus), phleboviruses (for example, Candiru, Punta
Toro, Rift Valley Fever, Sandfly Fever, Naples, Toscana, Sicilian and Chagres), and hantaviruses
(for example, Hantaan, Dobrava, Seoul, Puumala, Sin Nombre, Bayou, Black Creek Canal, Andes
and Thottapalayam) are also RNA viruses. Arenaviruses such as lymphocytic choriomeningitis
virus, Lassa fever virus, Argentine hemorrhagic fever virus, Bolivian hemorrhagic fever virus,
Venezuelan hemorrhagic fever virus, SABV and WWAV are also RNA viruses. Borna disease
virus is also an RNA virus. Hepatitis D (Delta) virus and hepatitis E are also RNA viruses.

Additional RNA viruses include reoviruses, rotaviruses, birnaviruses, chrysoviruses,
cystoviruses, hypoviruses, partitiviruses and totoviruses. Orbiviruses such as African horse
sickness virus, Blue tongue virus, Changuinola virus, Chenuda virus, Chobar Gorge Corripata
virus, epizootic hemorrhagic disease virus, equine encephalosis virus, Eubenangee virus, Ieri
virus, Great Island virus, Lebombo virus, Orungo virus, Palyam virus, Peruvian Horse Sickness
virus, St. Croix River virus, Umatilla virus, Wad Medani virus, Wallal virus, Warrego virus and
Wongorr virus are also RNA viruses.

Retroviruses include alpharetroviruses (for example, Rous sarcoma virus and avian leukemia virus), betaretroviruses (for example, mouse mammary tumor virus, Mason-Pfizer monkey virus and Jaagsiekte sheep retrovirus), gammaretroviruses (for example, murine leukemia virus and feline leukemia virus, deltaretroviruses (for example, human T cell leukemia viruses (HTLV-1, HTLV-2), bovine leukemia virus, STLV-1 and STLV-2), epsilonretroviruses (for example, Walleye dermal sarcoma virus and Walleye epidermal hyperplasia virus 1), reticuloendotheliosis virus (for example, chicken syncytial virus, lentiviruses (for example, human immunodeficiency virus (HIV) type 1, human immunodeficiency virus (HIV) type 2, simian immunodeficiency virus, equine infectious anemia virus, feline immunodeficiency virus, caprine arthritis encephalitis virus and Visna maedi virus) and spumaviruses (for example, human foamy virus and feline syncytia-forming virus).

Examples of DNA viruses include polyomaviruses (for example, simian virus 40, simian agent 12, BK virus, JC virus, Merkel Cell polyoma virus, bovine polyoma virus and lymphotropic papovavirus), papillomaviruses (for example, human papillomavirus, bovine papillomavirus, adenoviruses (for example, adenoviruses A-F, canine adenovirus type I, canined adenovirus type 2), circoviruses (for example, porcine circovirus and beak and feather disease virus (BFDV)), parvoviruses (for example, canine parvovirus), erythroviruses (for example, adeno-associated virus types 1-8), betaparvoviruses, amoviruses, densovirus, iteraviruses, brevidensoviruses, pefudensoviruses, herpes viruses (for example, herpes simplex virus 1, herpes simplex virus 2, varicella-zoster virus, Epstein-Barr virus, cytomegalovirus, Kaposi's sarcoma associated herpes virus, human herpes virus-6 variant A, human herpes virus-6 variant B and cercophithecine herpes virus 1 (B virus)), poxviruses (for example, smallpox (variola), cowpox, monkeypox, vaccinia, Uasin Gishu, camelpox, psuedocowpox, pigeonpox, horsepox, fowlpox, turkeypox and swinepox), and hepadnaviruses (for example, hepatitis B and hepatitis B-like viruses). Chimeric viruses comprising portions of more than one viral genome are also contemplated herein.

For animals, in addition to the animal viruses listed above, viruses include, but are not limited to, the animal counterpart to any above listed human virus. The provided genes can also decrease infection by newly discovered or emerging viruses. Such viruses are continuously updated on <http://en.wikipedia.org/wiki/Virus> and www.virology.net.

Examples of bacterial infections include, but are not limited to infections caused by the following bacteria: *Listeria* (sp.), *Fransicella tularensis*, *Mycobacterium tuberculosis*, *Rickettsia* (all types), *Ehrlichia*, *Chlamydia*. Further examples of bacteria that can be targeted

by the present methods include *M. tuberculosis*, *M. bovis*, *M. bovis* strain BCG, BCG substrains, *M. avium*, *M. intracellulare*, *M. africanum*, *M. kansasii*, *M. marinum*, *M. ulcerans*, *M. avium* subspecies *paratuberculosis*, *Nocardia asteroides*, other *Nocardia* species, *Legionella pneumophila*, other *Legionella* species, *Salmonella typhi*, other *Salmonella* species, *Shigella* species, *Yersinia pestis*, *Pasteurella haemolytica*, *Pasteurella multocida*, other *Pasteurella* species, *Actinobacillus pleuropneumoniae*, *Listeria monocytogenes*, *Listeria ivanovii*, *Brucella abortus*, other *Brucella* species, *Cowdria ruminantium*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Chlamydia psittaci*, *Coxiella burnetii*, other *Rickettsial* species, *Ehrlichia* species, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Bacillus anthracis*, *Escherichia coli*, *Vibrio cholerae*, *Kingella kingae*, *Campylobacter* species, *Neisseria meningitidis*, *Neisseria gonorrhea*, *Pseudomonas aeruginosa*, other *Pseudomonas* species, *Haemophilus influenzae*, *Haemophilus ducreyi*, other *Hemophilus* species, *Clostridium tetani*, other *Clostridium* species, *Yersinia enterocolitica*, and other *Yersinia* species.

Examples of parasitic infections include, but are not limited to infections caused by the following parasites: *Cryptosporidium*, *Plasmodium* (all species), American trypanosomes (*T. cruzi*), African trypanosomes, *Acanthamoeba*, *Entamoeba histolytica*, *Angiostrongylus*, *Anisakis*, *Ascaris*, *Babesia*, *Balantidium*, *Baylisascaris*, lice, ticks, mites, fleas, *Capillaria*, *Clonorchis*, *Chilomastix mesnili*, *Cyclospora*, *Diphyllobothrium*, *Dipylidium caninum*, *Fasciola*, *Giardia*, *Gnathostoma*, *Heterophyes*, *Hymenolepsis*, *Isospora*, *Loa loa*, *Microsporidia*, *Naegleria*, *Toxocara*, *Onchocerca*, *Opisthorchis*, *Paragonimus*, *Baylisascaris*, *Strongyloides*, *Taenia*, *Trichomonas* and *Trichuris*.

Furthermore, examples of protozoan and fungal species contemplated within the present methods include, but are not limited to, *Plasmodium falciparum*, other *Plasmodium* species, *Toxoplasma gondii*, *Pneumocystis carinii*, *Trypanosoma cruzi*, other trypanosomal species, *Leishmania donovani*, other *Leishmania* species, *Theileria annulata*, other *Theileria* species, *Eimeria tenella*, other *Eimeria* species, *Histoplasma capsulatum*, *Cryptococcus neoformans*, *Blastomyces dermatitidis*, *Coccidioides immitis*, *Paracoccidioides brasiliensis*, *Penicillium marneffei*, and *Candida* species. The provided genes can also decrease infection by newly discovered or emerging bacteria, parasites or fungi, including multidrug resistant strains of same.

Further provided by the present invention is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the pathogen is a respiratory virus. Respiratory viruses include, but are not limited to, picornaviruses, orthomyxoviruses, paramyxoviruses,

coronaviruses and adenoviruses. More specifically, and not to be limiting, the respiratory virus can be an influenza virus, a parainfluenza virus, an adenovirus, a rhinovirus or a respiratory syncytial virus (RSV).

Also provided by the present invention is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, wherein the pathogen is a gastrointestinal virus. Gastrointestinal viruses include, but are not limited to, picornaviruses, filoviruses, flaviviruses, caliciviruses, adenoviruses and reoviruses. More specifically, and not to be limiting, the gastrointestinal virus can be a reovirus, a Norwalk virus, an Ebola virus, a Marburg virus, a rotavirus, an enterovirus, an adenovirus, a Dengue fever virus, a yellow fever virus, or a West Nile virus.

Also provided by the present invention is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, wherein the pathogen is a gastrointestinal virus that is not West Nile virus. Gastrointestinal viruses include, but are not limited to, picornaviruses, filoviruses, flaviviruses, caliciviruses, adenoviruses and reoviruses. More specifically, and not to be limiting, with respect to the genes listed in Table 2, the gastrointestinal virus can be a reovirus, a Norwalk virus, an adenovirus, an Ebola virus, a Marburg virus, a rotavirus, an enterovirus, or a Dengue fever virus.

Further provided by the present invention is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, wherein the pathogen is a gastrointestinal virus that is not West Nile virus or Dengue fever virus. Gastrointestinal viruses include, but are not limited to, picornaviruses, filoviruses, flaviviruses, caliciviruses, adenoviruses and reoviruses. More specifically, and not to be limiting, with respect to the genes listed in Table 3, the gastrointestinal virus can be a reovirus, an adenovirus, a Norwalk virus, an Ebola virus, a Marburg virus, a rotavirus, or an enterovirus.

Also provided by the present invention is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, wherein the pathogen is a gastrointestinal virus. With respect to the genes listed in Table 4, gastrointestinal viruses include, but are not limited to, picornaviruses, filoviruses, flaviviruses, caliciviruses and reoviruses. More specifically, and not to be limiting, the gastrointestinal virus can be a reovirus, an adenovirus, a Norwalk virus, an Ebola virus, a Marburg virus, a rotavirus, an enterovirus, a West Nile virus or a Dengue fever virus.

The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s)

set forth in Table 1, wherein the pathogen is a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Hepatitis E virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, a hepatitis E virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies or Chikungunya virus.

The present invention also provides a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, a Dengue Fever virus, West Nile virus or Chikungunya virus.

Also provided is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2 or 4, wherein the pathogen is a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, hantavirus, Rift Valley Fever virus Ebola virus, Marburg virus or Dengue
5 Fever virus.

Further provided is a method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, wherein the pathogen is a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa
Fever virus, hantavirus, Rift Valley Fever virus, Ebola virus or Marburg virus.

10 Further provided is a method of decreasing the toxicity of a toxin in a cell comprising administering to the cell an effective amount of a composition that decreases expression or activity of one or more gene(s) or a gene product(s) set forth in Table 1, 2, 3 or 4.

Toxins can include, but are not limited to, a bacterial toxin, a neurotoxin, such as a botulinum neurotoxin, a mycotoxin, ricin, a *Clostridium perfringens* toxin, a *Clostridium*
15 *difficile* toxin, a saxitoxin, a tetrodotoxin, abrin, a conotoxin, a *Staphylococcal* toxin, such as *staphylococcal aureus*, an *E. coli* toxin, a streptococcal toxin, a shigatoxin, a T-2 toxin, an anthrax toxin, chimeric forms of the toxins listed herein, and the like. The decrease in toxicity can be at least about 10%, 20%, 30%, 40%, 50%, 60, 70%, 80%, 90%, 95%, 100% or any other percentage decrease in between these percentages as compared to the level of toxicity in a cell
20 wherein expression or activity of the same gene or gene product from Table 1, 2, 3 or 4 that has not been decreased, or compared to the level of toxicity in a cell not contacted with a compound that decreases expression or activity of the gene or gene product.

Toxicity can be measured, for example, via a cell viability, apoptosis assay, LDH release assay or cytotoxicity assay (See, for example, Kehl-Fie and St. Geme "Identification and
25 characterization of an RTX toxin in the emerging pathogen *Kingella kingae*," *J. Bacteriol.* 189(2):430-6 (2006) and Kirby "Anthrax Lethal Toxin Induces Human Endothelial cell Apoptosis," *Infection and Immunity* 72: 430-439 (2004), both of which are incorporated herein in their entireties by this reference.)

In the methods of the present invention, expression and/or activity of a gene or gene
30 product set forth in Table 1, 2, 3 or 4, can be decreased by contacting the cell with any composition that can decrease expression or activity. For example, the composition can be a chemical, a small or large molecule (organic or inorganic), a drug, a protein, a peptide, a cDNA, an antibody, an aptamer, a morpholino, a triple helix molecule, an siRNA, an LNA, a shRNA, an miRNA, an antisense RNA, a ribozyme or any other compound now known or identified in
35 the future that decreases the expression and/or activity of a gene or gene product set forth in

Table 1, 2, 3 or 4. A decrease in expression or activity can occur by decreasing transcription of mRNA or decreasing translation of RNA. A composition can also be a mixture or “cocktail” of two or more of the compositions described herein. A decrease in expression and/or activity can also occur by inhibiting the interaction between any of the proteins set forth in Table 1, 2, 3 or 4 and other cellular proteins, such as, for example, transcription factors, receptors, nuclear proteins, transporters, microtubules, membrane proteins, enzymes (for example, ATPases, phosphorylases, oxidoreductases, kinases, phosphatases, synthases, lyases, aromatases, helicases, hydrolases, proteases, transferases, nucleases, ligases, reductases and polymerases) and hormones. A decrease in expression and/or activity can also occur by inhibiting or decreasing the interaction between any of the proteins of the present invention and a cellular nucleic acid or a viral nucleic acid. A decrease can also occur by inhibiting or decreasing the interaction, either direct or indirect, between any of the proteins of the present invention and a viral, bacterial, parasitic or fungal protein (i.e. a non-host protein).

A composition can also be single composition or a mixture, cocktail or combination of two or more compositions, for example, two or more compositions selected from the group consisting of chemical, a compound, a small molecule, an inorganic molecule, an organic molecule, an aptamer, a drug, a protein, a cDNA, an antibody, a morpholino, a triple helix molecule, an siRNA, an shRNAs, an LNA, an antisense nucleic acid or a ribozyme. The two or more compositions can be the same or different types of compositions. The two or more compositions can decrease expression or activity of the same target or different targets, as one or more genes or gene products set forth in Table 1,2, 3 or 4 can be modulated to effect a decrease in infection. It is understood that two or more compositions comprises three or more, four or more, five or more etc. For example, and not to be limiting two or more compositions can be any two or more compositions comprising an antisense and a small molecule; or two or more antisense molecules; or two or more small molecules; or two or more compositions comprising an siRNA and a small molecule, etc. It is understood that any combination of the types of compositions set forth herein can be utilized in the methods set forth herein.

These compositions can be used alone or in combination with other therapeutic agents such as antiviral compounds, antibacterial agents, antifungal agents, antiparasitic agents, anti-inflammatory agents, anti-cancer agents, etc. All of the compounds described herein can be contacted with a cell *in vitro*, *ex vivo* or *in vivo*.

Examples of antiviral compounds include, but are not limited to, amantadine, rimantadine, zanamavir and oseltamavir (Tamiflu) for the treatment of flu and its associated symptoms. Antiviral compounds useful in the treatment of HIV include Combivir® (lamivudine-zidovudine), maraviroc, Crixivan® (indinavir), Emtriva® (emtricitabine), Efavir®

(lamivudine), Fortovase® (saquinavir-sg), Hivid® (zalcitabine), Invirase® (saquinavir-hg), Kaletra® (lopinavir-ritonavir), Lexiva™ (fosamprenavir), Norvir® (ritonavir), Retrovir® (zidovudine) Sustiva® (efavirenz), Videx EC® (didanosine), Videx® (didanosine), Viracept® (nelfinavir) Viramune® (nevirapine), Zerit® (stavudine), Ziagen® (abacavir), Fuzeon® (enfuvirtide) Rescriptor® (delavirdine), Reyataz® (atazanavir), Trizivir® (abacavir-lamivudine-zidovudine) Viread® (tenofovir disoproxil fumarate) and Agenerase® (amprenavir). Other antiviral compounds useful in the treatment of Ebola and other filoviruses include ribavirin and cyanovirin-N (CV-N). For the treatment of herpes virus, Zovirax® (acyclovir) is available. Antibacterial agents include, but are not limited to, antibiotics (for example, penicillin and ampicillin), sulfa Drugs and folic acid Analogs, Beta-Lactams, aminoglycosides, tetracyclines, macrolides, lincosamides, streptogramins, fluoroquinolones, rifampin, mupirocin, cycloserine, aminocyclitol and oxazolidinones.

Antifungal agents include, but are not limited to, amphotericin, nystatin, terbinafine, itraconazole, fluconazole, ketoconazole, and griseofulvin.

Antiparasitic agents include, but are not limited to, antihelmintics, antinematodal agents, antiplatyhelminthic agents, antiprotozoal agents, amebicides, antimalarials, antitrichomonal agents, aoccidiostats and trypanocidal agents.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression and/or activity of a gene product set forth in Table 1, 2, 3, or 4 and a composition that decreases expression and/or activity of a different gene product(s) set forth in Table 1, 2, 3 or 4. For example, and not to be limiting, the present invention provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression and/or activity of EDNRA and a composition that decreases expression and/or activity of KCNJ11. This is merely exemplary, as any two or more different gene product(s) set forth in Table 1, 2, 3 or 4 can be inhibited to decrease infection. It is understood that these methods are not limited to administration of two compositions as the combination can be a combination of two, three, four, five or six compositions, wherein each composition comprises a chemical, a compound, a small molecule, an inorganic molecule, an organic molecule, a drug (for example, an FDA approved drug, a European Medicines Agency approved drug, a drug approved by the Japanese Pharmaceutical and Medical Device Agency) a protein, a cDNA, an aptamer, a peptide, an antibody, a morpholino, a triple helix molecule, an siRNA, an shRNAs, an LNA, an miRNA, an antisense nucleic acid or a ribozyme. As set forth herein, these combinations can comprise two or more compounds selected from the group consisting of imatinib, acetazolamide, benzthiazide, brinzolamide, chlorothiazide,

chlorthalidone, dorzolamide, dorzolamide/timolol, hydrochlorothiazide, methazolamide, sulfacetamide, topiramate, trichloromethiazide, amobarbital, atracurium, cisatracurium, D-tubocurarine, doxacurium, mecamlamine, metocurine, mivacurium, pancuronium, pipecuronium, rapacuronium, rocuronium, succinylcholine, vecuronium, enflurane, isoflurane, plerixafor, ambrisentan, avosentan, bosentan, BSF 302146, clazosentan, PD 180988, SB 234551, sitaxsentan, TBC 3214, ZD4054, atrasentan, AEE 788, ARRY-334543, BMS-599626, canertinib, cetuximab, erlotinib, gefitinib, HKI-272, lapatinib, PD 153035, vandetanib, XL647, antithrombin alfa, argatroban, bivalirudin, dabigatran etexilate, desirudin, enoxaparin, lepirudin, lonafarnib, talampanel, tezampanel, MGCD0103, PXD101, pyroxamide, romidepsin, tributyrin, vorinostat, acetohexamide, chlorpropamide, glimepiride, glipizide, glyburide, minoxidil, nateglinide, phentolamine, repaglinide, tolazamide, tolbutamide, aminophylline, anagrelide, dipyrindamole, dyphylline, milrinone, nitroglycerin, pentoxifylline, theophylline, tolbutamide, BI 2536, clofarabine, gemcitabine, nelarabine, trifluridine, dutasteride, finasteride, docetaxel, ixabepilone, milataxel, NPI-2358, podophyllotoxin, TPI 287, AL 108, paclitaxel, TTI-237, XRP9881 (larotaxel), EC145, E7389, vinblastine, vincristine, vinflunine, vinorelbine, enzastaurin, saxagliptin, sitagliptin, SYR-322, talabostat, mycophenolic acid, thioguanine, VX-944, mycophenolic acid, ribavirin, thioguanine, VX-944, pactimibe, S-18886, torsemide, carvedilol, dapiprazole, ergotamine, guanadrel, Labetalol, phenoxybenzamine, prazosin, terazosine, alfuzosin, aripiprazole, asenapine, dihydroergotamine, DL 017, epinastine, guanethidine, iloperidone, nefazodone, olanzapine, paliperidone, phentolamine, quetiapine, quinidine, risperidone, tolazoline, UK-294315, ziprasidone, dobutamine, apraclonidine, arbutamine, clonidine, tamsulosin, venlafaxine, clevidipine butyrate, aminophylline, amrinone, cilostazol, dipyrindamole, dyphylline, medorinone, nitroglycerin, pentoxifylline, theophylline, tolbutamide, ABT-751, BMS-275183, docetaxel, E7389, milataxel, MST-997, NPI-2358, podophyllotoxin, TPI 287, AL 108, ixabepilone, paclitaxel, TTI-237, XRP9881, epothilone B, EC145, vinblastine, vincristine, vinflunine, minocycline and vinorelbine, or a pharmaceutically acceptable salt thereof. These combinations can further comprise an antiviral compound, an antiparasitic compound or an antifungal compound as described herein.

Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of a one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more pathogens. The two or more pathogens can be two or more, three or more, four or more, five or more, six or more; or seven or more viruses, bacteria, parasites, fungi or a combination thereof.

In particular, the present invention provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of a gene or a gene product set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more, three or more, four or more, five or more, six or
5 more; or seven or more viruses. Table 6 shows gene products set forth in Table 1, 2, 3 or 4 for which at least 50% inhibition of viral replication was observed via siRNA experiments as indicated by an X. It is understood that one of skill in the art can select a gene product from Table 6 and decrease its expression or activity to reduce infection by one or more viruses marked with an X, for that gene product. One of skill in the art can readily select the gene
10 product(s) in Table 6 that can be inhibited in order to effect inhibition of infection by two or more, three or more, four or more, five or more, six or more, seven or more viruses etc.

The viruses are not restricted to the viruses set forth in Table 6 as this data can be combined with data for a composition that decreases expression and/or activity of any gene product from Table 1, 2, 3 or 4 and inhibits any other virus, bacteria, fungi or parasite not listed
15 in Table 6. For example, data for EDNRA can be combined with data showing that decreased expression and/or activity of EDNRA leads to inhibition of HCV infection, thus showing that activity or expression of EDNRA can be decreased to inhibit infection by RSV, pox, rhinovirus, Dengue fever virus, HIV and HCV. This example is merely exemplary as data for any gene product set forth in Table 6 can be combined with data for any other virus, bacteria, fungi or
20 parasite.

Therefore, the present invention provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of a gene or a gene product set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more, three or more, four or more, five or more, six or
25 more; or seven or more viruses, wherein at least two or more of the viruses are selected from the group consisting of influenza, RSV, HSV, cowpox, rhinovirus, HIV and Dengue. Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of a gene or a gene product set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more,
30 three or more, four or more, five or more, six or more; or seven or more viruses, wherein at least two or more of the viruses are selected from the group consisting of influenza, RSV, HSV, cowpox, rhinovirus, Dengue, HIV and HCV.

TABLE 6

Gene ID	Gene	Flu	RSV	HSV2	Cowpox	R-16	Dengue	HIV	HCV	WNV	Spectrum
53947	A4GALT	X			X	X		X			4
6059	ABCE1	X			X	X	X	X		X	6
91801	ALKBH8				X			X			2
22881	ANKRD6	X						X			2
306	ANXA3			X		X	X	X			4
8906	APIG2	X			X	X		X			4
9140	ATG12	X				X		X			3
89849	ATG16L2				X			X			2
10533	ATG7	X		X		X		X			4
535	ATP6V0A1			X		X	X	X		X	5
607	BCL9			X	X	X	X	X			5
132321	C4orf33 (LOC132321)				X			X			2
920	CD4				X			X			2
116986	CENTG1	X	X	X	X			X			5
56650	CLDND1		X	X		X	X	X			5
9074	CLDN6	X					X	X	X		4
1201	CLN3							X			1
1207	CLNS1A	X	X	X			X	X			5
22796	COG2							X			1
83548	COG3			X				X			2
25839	COG4				X	X	X	X			4
114769	COP1							X			1
285464	CRIPAK	X				X		X			3
200186	CRTC2					X	X	X			3
79848	CSPP1			X		X	X	X			4
9150	CTDP1			X		X	X	X			4
7852	CXCR4	X		X		X		X			4
203429	CXorf50		X	X		X	X	X			5
1650	DDOST	X	X	X	X	X	X	X			7

[illegible]

[illegible]

[illegible]

[illegible]

[illegible]

Antibodies

The present invention also provides antibodies that specifically bind to the gene products, proteins and fragments thereof set forth in Table 1, 2, 3 or 4. The antibody of the present invention can be a polyclonal antibody or a monoclonal antibody. The antibody of the invention selectively binds a polypeptide. By “selectively binds” or “specifically binds” is meant an antibody binding reaction which is determinative of the presence of the antigen (in the present case, a polypeptide set forth in Table 1, 2, 3 or 4, or antigenic fragment thereof among a heterogeneous population of proteins and other biologics). Thus, under designated immunoassay conditions, the specified antibodies bind preferentially to a particular peptide and do not bind in a significant amount to other proteins in the sample. Preferably, selective binding includes binding at about or above 1.5 times assay background and the absence of significant binding is less than 1.5 times assay background.

This invention also contemplates antibodies that compete for binding to natural interactors or ligands to the proteins set forth in Table 1, 2, 3 or 4. In other words, the present invention provides antibodies that disrupt interactions between the proteins set forth in Table 1, 2, 3 or 4 and their binding partners. For example, an antibody of the present invention can compete with a protein for a binding site (e.g. a receptor) on a cell or the antibody can compete with a protein for binding to another protein or biological molecule, such as a nucleic acid that is under the transcriptional control of a transcription factor set forth in Table 1, 2, 3 or 4. An antibody can also disrupt the interaction between a protein set forth in Table 1, 2, 3 or 4 and a pathogen, or the product of a pathogen. For example, an antibody can disrupt the interaction between a protein set forth in Table 1, 2, 3 or 4 and a viral protein, a bacterial protein, a parasitic protein, a fungal protein or a toxin. The antibody optionally can have either an antagonistic or agonistic function as compared to the antigen. Antibodies that antagonize pathogenic infection are utilized to decrease infection. Similarly antibodies that antagonize toxicity can be utilized to decrease toxicity in a cell or subject.

Preferably, the antibody binds a polypeptide *in vitro*, *ex vivo* or *in vivo*. Optionally, the antibody of the invention is labeled with a detectable moiety. For example, the detectable moiety can be selected from the group consisting of a fluorescent moiety, an enzyme-linked moiety, a biotin moiety and a radiolabeled moiety. The antibody can be used in techniques or procedures such as diagnostics, screening, or imaging. Anti-idiotypic antibodies and affinity matured antibodies are also considered to be part of the invention.

As used herein, the term “antibody” encompasses chimeric antibodies and hybrid antibodies, with dual or multiple antigen or epitope specificities, and fragments, such as F(ab')₂,

Fab', Fab and the like, including hybrid fragments. Thus, fragments of the antibodies that retain the ability to bind their specific antigens are provided. Such antibodies and fragments can be made by techniques known in the art and can be screened for specificity and activity according to the methods set forth in the Examples and in general methods for producing antibodies and screening antibodies for specificity and activity (See Harlow and Lane. Antibodies, A Laboratory Manual. Cold Spring Harbor Publications, New York, (1988)).

Also included within the meaning of "antibody" are conjugates of antibody fragments and antigen binding proteins (single chain antibodies) as described, for example, in U.S. Pat. No. 4,704,692, the contents of which are hereby incorporated by reference.

Optionally, the antibodies are generated in other species and "humanized" for administration in humans. In one embodiment of the invention, the "humanized" antibody is a human version of the antibody produced by a germ line mutant animal. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂, or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a CDR of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In one embodiment, the present invention provides a humanized version of an antibody, comprising at least one, two, three, four, or up to all CDRs of a monoclonal antibody that specifically binds to a protein or fragment thereof set forth in Table 1, 2, 3 or 4. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues that are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of or at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); and Presta, Curr. Op. Struct. Biol., 2:593-596 (1992)).

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source that is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially

performed following the method of Winter and co-workers (Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-327 (1988); Verhoeyen et al., *Science*, 239:1534-1536 (1988)), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Pat. No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

10 Peptides

Peptides that inhibit expression or activity of a gene or a gene product set forth in Table 1, 2, 3 or 4 are also provided herein. Peptide libraries can be screened utilizing the screening methods set forth herein to identify peptides that inhibit activity of any of the genes or gene products set forth in Table 1, 2, 3 or 4. These peptides can be derived from a protein that binds to any of the genes or gene products set forth in Table 1, 2, 3 or 4. These peptides can be any peptide in a purified or non-purified form, such as peptides made of D-and/or L-configuration amino acids (in, for example, the form of random peptide libraries; see Lam *et al.*, *Nature* 354:82-4, 1991), phosphopeptides (such as in the form of random or partially degenerate, directed phosphopeptide libraries; see, for example, Songyang *et al.*, *Cell* 72:767-78, 1993).

20 RNA interference

Numerous RNA interference technologies are known to those of skill in the art, for example, but not limited to, siRNA, antisense, locked nucleic acids (LNA), morpholinos, and shRNA. One of skill in the art can utilize any RNA interference technology, known or identified in the future to decrease expression of any gene product set forth in Table 1, 2, 3 or 4.

siRNAs

Short interfering RNAs (siRNAs), also known as small interfering RNAs, are double-stranded RNAs that can induce sequence-specific post-transcriptional gene silencing, thereby decreasing gene expression (See, for example, U.S. Patent Nos. 6,506,559, 7,056,704, 7,078,196, 6,107,094, 5,898,221, 6,573,099, and European Patent No. 1.144,623, all of which are hereby incorporated in their entireties by this reference). siRNAs can be of various lengths as long as they maintain their function. In some examples, siRNA molecules are about 19-23 nucleotides in length, such as at least 21 nucleotides, for example at least 23 nucleotides. In one example, siRNA triggers the specific degradation of homologous RNA molecules, such as mRNAs, within the region of sequence identity between both the siRNA and the target RNA.

For example, WO 02/44321 discloses siRNAs capable of sequence-specific degradation of target mRNAs when base-paired with 3' overhanging ends. The direction of dsRNA processing determines whether a sense or an antisense target RNA can be cleaved by the produced siRNA endonuclease complex. Thus, siRNAs can be used to modulate transcription or translation, for example, by decreasing expression of a gene set forth in Table 1, 2, 3 or 4. The effects of siRNAs have been demonstrated in cells from a variety of organisms, including *Drosophila*, *C. elegans*, insects, frogs, plants, fungi, mice and humans (for example, WO 02/44321; Gitlin *et al.*, *Nature* 418:430-4, 2002; Caplen *et al.*, *Proc. Natl. Acad. Sci.* 98:9742-9747, 2001; and Elbashir *et al.*, *Nature* 411:494-8, 2001).

Utilizing sequence analysis tools, one of skill in the art can design siRNAs to specifically target one or more of the genes set forth in Table 1, 2, 3 or 4 for decreased gene expression. siRNAs that inhibit or silence gene expression can be obtained from numerous commercial entities that synthesize siRNAs, for example, Ambion Inc. (2130 Woodward Austin, TX 78744-1832, USA), Qiagen Inc. (27220 Turnberry Lane, Valencia, CA USA) and Dharmacon Inc. (650 Crescent Drive, #100 Lafayette, CO 80026, USA). The siRNAs synthesized by Ambion Inc., Qiagen Inc. or Dharmacon Inc. can be readily obtained from these and other entities by providing a GenBank Accession No. for the mRNA of any gene set forth in Table 1, 2, 3 or 4. In addition, siRNAs can be generated by utilizing Invitrogen's BLOCK-IT™ RNAi Designer <https://rnaidesigner.invitrogen.com/rnaiexpress>. siRNA sequences can comprise a 3' TT overhang and/or additional sequences that allow efficient cloning and expression of the siRNA sequences. siRNA sequences can be cloned into vectors and utilized *in vitro*, *ex vivo* or *in vivo* to decrease gene expression. One of skill in the art would know that it is routine to utilize publicly available algorithms for the design of siRNA to target mRNA sequences. These sequences can then be assayed for inhibition of gene expression *in vitro*, *ex vivo* or *in vivo*.

shRNA

shRNA (short hairpin RNA) is a DNA molecule that can be cloned into expression vectors to express siRNA (typically 19-29 nt RNA duplex) for RNAi interference studies. shRNA has the following structural features: a short nucleotide sequence ranging from about 19-29 nucleotides derived from the target gene, followed by a short spacer of about 4-15 nucleotides (*i.e.* loop) and about a 19-29 nucleotide sequence that is the reverse complement of the initial target sequence.

Antisense Nucleic Acids

Generally, the term "antisense" refers to a nucleic acid molecule capable of hybridizing to a portion of an RNA sequence (such as mRNA) by virtue of some sequence complementarity.

The antisense nucleic acids disclosed herein can be oligonucleotides that are double-stranded or

single-stranded, RNA or DNA or a modification or derivative thereof, which can be directly administered to a cell (for example by administering the antisense molecule to the subject), or which can be produced intracellularly by transcription of exogenous, introduced sequences (for example by administering to the subject a vector that includes the antisense molecule under control of a promoter).

Antisense nucleic acids are polynucleotides, for example nucleic acid molecules that are at least 6 nucleotides in length, at least 10 nucleotides, at least 15 nucleotides, at least 20 nucleotides, at least 100 nucleotides, at least 200 nucleotides, such as 6 to 100 nucleotides. However, antisense molecules can be much longer. In particular examples, the nucleotide is modified at one or more base moiety, sugar moiety, or phosphate backbone (or combinations thereof), and can include other appending groups such as peptides, or agents facilitating transport across the cell membrane (Letsinger *et al.*, *Proc. Natl. Acad. Sci. USA* 1989, 86:6553-6; Lemaitre *et al.*, *Proc. Natl. Acad. Sci. USA* 1987, 84:648-52; WO 88/09810) or blood-brain barrier (WO 89/10134), hybridization triggered cleavage agents (Krol *et al.*, *BioTechniques* 1988, 6:958-76) or intercalating agents (Zon, *Pharm. Res.* 5:539-49, 1988). Additional modifications include those set forth in U.S. Patent Nos. 7,176,296; 7,329,648; 7,262,489, 7,115,579; and 7,105,495.

Examples of modified base moieties include, but are not limited to: 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5-carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine, inosine, N⁶-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N⁶-adenine, 7-methylguanine, 5-methylaminomethyluracil, methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'-methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N⁶-isopentenyladenine, uracil-5-oxyacetic acid, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2-thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, uracil-S-oxyacetic acid, 5-methyl-2-thiouracil, 3-(3-amino-3-N-2-carboxypropyl) uracil, and 2,6-diaminopurine.

Examples of modified sugar moieties include, but are not limited to: arabinose, 2-fluoroarabinose, xylose, and hexose, or a modified component of the phosphate backbone, such as phosphorothioate, a phosphorodithioate, a phosphoramidothioate, a phosphoramidate, a phosphordiamidate, a methylphosphonate, an alkyl phosphotriester, or a formacetal or analog thereof.

In a particular example, an antisense molecule is an α -anomeric oligonucleotide. An α -anomeric oligonucleotide forms specific double-stranded hybrids with complementary RNA in

which, contrary to the usual β -units, the strands run parallel to each other (Gautier *et al.*, *Nucl. Acids Res.* 15:6625-41, 1987). The oligonucleotide can be conjugated to another molecule, such as a peptide, hybridization triggered cross-linking agent, transport agent, or hybridization-triggered cleavage agent. Oligonucleotides can include a targeting moiety that enhances uptake of the molecule by host cells. The targeting moiety can be a specific binding molecule, such as an antibody or fragment thereof that recognizes a molecule present on the surface of the host cell.

In a specific example, antisense molecules that recognize a nucleic acid set forth herein, include a catalytic RNA or a ribozyme (for example see WO 90/11364; WO 95/06764; and Sarver *et al.*, *Science* 247:1222-5, 1990). Conjugates of antisense with a metal complex, such as terpyridylCu (II), capable of mediating mRNA hydrolysis, are described in Bashkin *et al.* (*Appl. Biochem Biotechnol.* 54:43-56, 1995). In one example, the antisense nucleotide is a 2'-O-methylribonucleotide (Inoue *et al.*, *Nucl. Acids Res.* 15:6131-48, 1987), or a chimeric RNA-DNA analogue (Inoue *et al.*, *FEBS Lett.* 215:327-30, 1987).

Antisense molecules can be generated by utilizing the Antisense Design algorithm of Integrated DNA Technologies, Inc. (1710 Commercial Park, Coralville, IA 52241 USA; <http://www.idtdna.com/Scitools/Applications/AntiSense/Antisense.aspx>).

Any antisense sequence that is not the full length mRNA for any of the genes listed in Table 1, 2, 3 or 4 can be used as antisense sequences. It is known to those of skill in the art that once a mRNA sequence is routinely obtained for any of the genes set forth in Table 1, 2, 3 or 4, it is routine to walk along the mRNA sequence to generate antisense sequences that decrease expression of the gene. Therefore all antisense sequences for the genes set forth herein are disclosed. The methods of the present invention can utilize any antisense sequence that decreases the expression of a gene set forth in Table 1, 2, 3 or 4.

Morpholinos

Morpholinos are synthetic antisense oligos that can block access of other molecules to small (about 25 base) regions of ribonucleic acid (RNA). Morpholinos are often used to determine gene function using reverse genetics methods by blocking access to mRNA.

Morpholinos, usually about 25 bases in length, bind to complementary sequences of RNA by standard nucleic acid base-pairing. Morpholinos do not degrade their target RNA molecules. Instead, Morpholinos act by "steric hindrance", binding to a target sequence within an RNA and simply interfering with molecules which might otherwise interact with the RNA. Morpholinos have been used in mammals, ranging from mice to humans.

Bound to the 5'-untranslated region of messenger RNA (mRNA), Morpholinos can interfere with progression of the ribosomal initiation complex from the 5' cap to the start codon. This prevents translation of the coding region of the targeted transcript (called "knocking down" gene expression). Morpholinos can also interfere with pre-mRNA processing steps, usually by preventing the splice-directing snRNP complexes from binding to their targets at the borders of introns on a strand of pre-RNA. Preventing U1 (at the donor site) or U2/U5 (at the polypyrimidine moiety & acceptor site) from binding can cause modified splicing, commonly leading to exclusions of exons from the mature mRNA. Targeting some splice targets results in intron inclusions, while activation of cryptic splice sites can lead to partial inclusions or exclusions. Targets of U11/U12 snRNPs can also be blocked. Splice modification can be conveniently assayed by reverse-transcriptase polymerase chain reaction (RT-PCR) and is seen as a band shift after gel electrophoresis of RT-PCR products. Methods of designing, making and utilizing morpholinos are disclosed in U.S. Patent No. 6,867,349 which is incorporated herein by reference in its entirety.

Small Molecules

Any small molecule that inhibits activity of a gene or a gene product set forth in Table 1, 2, 3 or 4 can be utilized in the methods of the present invention to decrease infection. These molecules are available in the scientific literature, in the StarLite/CHEMBL database available from the European Bioinformatics Institute, in DrugBank (Wishart et al. *Nucleic Acids Res.* 2006 Jan 1;34 (Database issue):D668-72), package inserts, brochures, chemical suppliers (for example, Sigma, Tocris, Aurora Fine Chemicals, to name a few), or by any other means, such that one of skill in the art makes the association between a gene product of Table 1, 2 3, or 4 and inhibition of this gene product by a molecule. Preferred small molecules are those small molecules that have IC₅₀ values of less than about 1mM, less than about 500 micromolar, less than about 100 micromolar, less than about 75 micromolar, less than about 50 micromolar, less than about 25 micromolar, less than about 10 micromolar, less than about 5 micromolar, less than about 1 micromolar, less than about 0.5 micromolar, less than about 0.25 micromolar, or less than about .10 micromolar. The half maximal inhibitory concentration (IC₅₀) is a measure of the effectiveness of a compound in inhibiting biological or biochemical function. This quantitative measure indicates how much of a particular compound or other substance (inhibitor) is needed to inhibit a given biological process (or component of a process, i.e. an enzyme, cell, cell receptor or microorganism) by half. In other words, it is the half maximal (50%) inhibitory concentration (IC) of a substance (50% IC, or IC₅₀). It is commonly used as a measure of antagonist drug potency in pharmacological research. Sometimes, it is also converted to the

pIC₅₀ scale (-log IC₅₀), in which higher values indicate exponentially greater potency. According to the FDA, IC₅₀ represents the concentration of a drug that is required for 50% inhibition *in vitro*. It is comparable to an EC₅₀ for agonist drugs. EC₅₀ also represents the plasma concentration required for obtaining 50% of a maximum effect *in vivo*.

5 The present invention also provides the synthesis of small molecules that inhibit activity of a gene product set forth in Table 1, 2, 3 or 4. The present invention describes gene products for which three-dimensional structures are well known and can be obtained from the RCSB Protein Databank <http://www.rcsb.org/pdb/home/home.do> or <http://www.rcsb.org>.

10 Crystal structures can also be generated. Alternatively, one of skill in the art can obtain crystal structures for proteins, or domains of proteins, that are homologous to the proteins set forth in Table 1, 2,3 or 4 from the RCSB Protein Databank or elsewhere in the scientific literature for use in homology modeling studies.

15 Routine high throughput *in silico* or *in vitro* screening of compound libraries for the identification of small molecules is also provided by the present invention. Compound libraries are commercially available. With an available crystal structure, it is routine for one of skill in the art to screen a library *in silico* and identify compounds with desirable properties, for example, binding affinity.

20 Numerous computer programs are available and suitable for rational drug design and the processes of computer modeling, model building, and computationally identifying, selecting and evaluating potential compounds. These include, for example, SYBYL (available from TRIPOS, St. Louis Mo.), DOCK (available from University of California, San Francisco), GRID (available from Oxford University, UK), MCSS (available from Molecular Simulations Inc., Burlington, Mass.), AUTODOCK (available from Oxford Molecular Group), FLEX X (available from TRIPOS, St. Louis Mo.), CAVEAT (available from University of California, 25 Berkeley), HOOK (available from Molecular Simulations Inc., Burlington, Mass.), and 3-D database systems such as MACCS-3D (available from MDL Information Systems, San Leandro, Calif.), UNITY (available from TRIPOS, St. Louis Mo.), and CATALYST (available from Molecular Simulations Inc., Burlington, Mass.). Compounds can also be computationally modified using such software packages as LUDI (available from Biosym TechMA), and 30 LEAPFROG (TRIPOS Associates, St. Louis, Mo.). These computer-modeling techniques can be performed on any suitable hardware including for example, workstations available from Silicon Graphics, Sun Microsystems, and the like. These techniques, methods, hardware and software packages are representative and are not intended to be comprehensive listing. Other modeling techniques known in the art can also be employed in accordance with this invention.

A filter can be applied to the results to yield one or more compounds with a binding affinity in a particular range, for example, and not to be limiting, from about 100 micromolar to about 100 nanomolar, from about 10 micromolar to about 10 nanomolar, from about 1 micromolar to about 1 nanomolar, or from about 0.5 micromolar to about 0.5 nanomolar.

Another filter can provide compounds with a certain binding affinity and size, for example, less than 1000 daltons, less than 500 daltons, less than 400 daltons, less than 300 daltons, less than 200 daltons, less than 100 daltons or less than 50 daltons or any size in between. The ranges and properties can be modified depending on the protein being studied. The compounds identified via this screening method can be further studied *in silico*, *in vitro* or *in vivo*. For example, the compounds can be modified *in silico* and rescreened *in silico* to determine the effects of chemical modifications on binding affinity or other properties being assessed *in silico*. The compounds identified *in silico* can be synthesized for *in vitro* or *in vivo* analysis.

All of the screening leading up to *in vivo* testing can be done *in silico* or in combination with *in vitro* assays. The initial compounds identified *in silico* and the resulting modified compounds can be screened *in vitro*, for example, in cellular assays to determine the effect of the compound on the cellular host protein as well as in viral assays, to determine antiviral activity. IC₅₀ values can be obtained from the cellular assays, which may or may not be similar to the concentration necessary to effect 50% inhibition of viral infection in a viral assay. However, although not required, it is desirable to have a compound that has an IC₅₀ value of less than about 1mM, less than about 100 micromolar, less than about 75 micromolar, less than about 50 micromolar, less than about 25 micromolar, less than about 10 micromolar, less than about 5 micromolar, less than about 1 micromolar, less than about 0.5 micromolar or less than about 0.1 micromolar. Similarly, although not required, it is desirable to have a compound that effects 50% inhibition of viral infection at a concentration of less than about 1mM, less than about 100 micromolar, less than about 75 micromolar, less than about 50 micromolar, less than about 25 micromolar, less than about 10 micromolar, less than about 5 micromolar, less than about 1 micromolar, less than about 0.5 micromolar, less than about 0.1 micromolar or any concentration in between.

Further modifications of the compounds can be done after *in vitro* screening, either *in silico* or via chemical synthesis, for further evaluation, prior to additional *in vitro* screening or *in vivo* studies. It is understood that this process can be iterative, involving a combination of *in silico* and wet chemistry techniques, but routine in drug development.

Other filters can be applied to the *in silico* screening process, for example, a filter that takes ADMET (adsorption, distribution, metabolism, excretion, toxicity) properties into consideration can be applied. ADMET modeling can be used during compound optimization to

define an acceptable property space that contains compounds likely to have the desired properties. These filters can be applied sequentially or simultaneously depending.

Libraries for virtual or *in vitro* screening are available for the skilled artisan, for example from ChemBridge Corporation (San Diego, CA), such as a GPCR library, a kinase targeted library (KINACore), or an ion channel library (Ion Channel Set), to name a few. Compound libraries can also be obtained from the National Institutes of Health. For example, the NIH Clinical Collection of compounds that have been used in clinical trials can also be screened. Biofocus DPI (Essex, United Kingdom) also maintains and designs compound libraries that can be purchased for screening. One of skill in the art can select a library based on the protein of interest. For example, a kinase library can be screened to identify a compound that binds to and/or modulates a kinase. Other libraries that target enzyme families, for example, ATPases, hydrolases, isomerases, polymerases, transferases, phosphatases, etc., can also be screened, depending on the type of enzyme.

Compound libraries can also be screened in order to identify a compound that disrupts or inhibits specific interactions between two proteins. Compounds can be administered to cells comprising two or more proteins that interact with each other in order to identify compounds that disrupt this interaction and result in decreased interaction between of the two or more proteins. Co-immunoprecipitation experiments can be utilized. Similarly, FRET analysis or surface plasmon resonance can be utilized, to identify compounds that disrupt the interaction between a two proteins.

Transcription factors set forth herein are available to identify inhibitors in screening assays that are known to the skilled person. Gel shift assays can be employed to assess the activity of a transcription factor (see, for example, Wang et al. 2000 *The Journal of Biological Chemistry*, 275, 27013-27020). One of skill in the art can also utilize the techniques set forth in Wang et al., as they apply to the transcription factors set forth herein to assess transcription factor activity via binding of the transcription factor to a regulatory region that drives expression of a reporter protein. These cellular assays and other transcription factor assays standard in the art are applicable to any transcription factor described herein. Compounds can be introduced into these assays to assess the effect of the compound on transcriptional activity. For example, a cellular assay can be utilized to measure reporter activity in the presence of a transcription factor, in the presence or absence of a compound, to determine the effect of the compound on transcription. If reporter activity is reduced, the compound is an inhibitor of transcription by that particular transcription factor. Utilizing these assays can also identify compounds that inhibit the activity of for example, any zinc finger protein set forth in this application.

Interactions between membrane proteins and their ligands, can also be measured, for example, via plasmon-waveguide resonance (PWR) spectroscopy (see, for example, Hruby and Tollin, *Curr. Opin. Pharmacol.* 2007 October: 7(5): 507-514; and Salamon et al. *Methods Enzymol.* 2009; 461:123-46) or plasmon surface resonance (Alves et al. *Curr Protein Pept Sci.* 2005 August; 6(4): 293-312.) These techniques can be utilized to identify compounds that alter the interaction between a membrane protein and a ligand by quantitating changes in binding affinity, protein aggregation and other parameters detectable by these methods.

Additional inhibitors include compositions comprising carbon and hydrogen, and optionally comprising one or more of -S, -N, -O, -Cl, -Br, or -F, appropriately bonded as a structure, with a size of less than about 1000 daltons, less than about 500 daltons, less than about 300 daltons, less than about 200 daltons, or less than about 100 daltons, that fits into a binding pocket or an active site of a gene product set forth herein. In particular, inhibitors that have the properties described in Lipinsky's Rule of Five are included herein. Lipinski's rule of five states that a drug/inhibitor has a weight under 500 Daltons, a limited lipophilicity or octanol-water partition coefficient (expressed by $\text{Log } P < 5$, with $P = [\text{drug}]_{\text{org.}}/[\text{drug}]_{\text{aq.}}$), a maximum of 5 H-bond donors (expressed as the sum of OHs and NHs), and a maximum of 10 H-bond acceptors (expressed as the sum of oxygen and nitrogen atoms). Inhibitors that violate no more than one of the above-listed five rules are also included herein.

The following compounds are provided as inhibitors of pathogenic infection and/or toxicity. More specifically, the present invention provides a method of decreasing infection by a pathogen, in a cell or a subject, said method comprising administering to the cell or subject an effective amount of one or more compounds selecting from the group of compounds having the structure of imatinib, acetazolamide, benzthiazide, brinzolamide, chlorothiazide, chlorthalidone, dorzolamide, dorzolamide/timolol, hydrochlorothiazide, methazolamide, sulfacetamide, topiramate, trichloromethiazide, amobarbital, atracurium, cisatracurium, D-tubocurarine, doxacurium, mecamlamine, metocurine, mivacurium, pancuronium, pipecuronium, rapacuronium, rocuronium, succinylcholine, vecuronium, enflurane, isoflurane, plerixafor, ambrisentan, avosentan, bosentan, BSF 302146, clazosentan, PD 180988, SB 234551, sitaxsentan, TBC 3214, ZD4054, atrasentan, AEE 788, ARRY-334543, BMS-599626, canertinib, cetuximab, erlotinib, gefitinib, HKI-272, lapatinib, PD 153035, vandetanib, XL647, antithrombin alfa, argatroban, bivalirudin, dabigatran etexilate, desirudil, enoxaparin, lepirudin, lonafarnib, talampanel, tezampanel, MGCD0103, PXD101, pyroxamide, romidepsin, tributyrin, vorinostat, acetoexamide, chlorpropamide, glimepiride, glipizide, glyburide, minoxidil, nateglinide, phentolamine, repaglinide, tolazamide, tolbutamide, aminophylline, anagrelide, dipyridamole, dyphylline, milrinone, nitroglycerin, 2-chloro-N-(3,5-dichlorophenyl)-4-

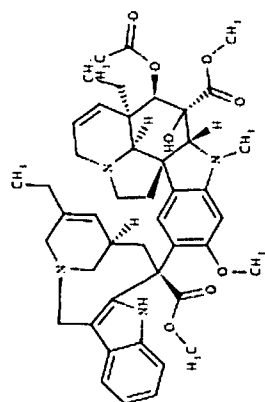
(trifluoromethyl)pyrimidine-5-carboxamide, pentoxifylline, theophylline, tolbutamide, BI 2536, clofarabine, gemcitabine, nelarabine, trifluridine, dutasteride, finasteride, docetaxel, ixabepilone, milataxel, NPI-2358, podophyllotoxin, TPI 287, AL 108, paclitaxel, TTI-237, XRP9881 (larotaxel), EC145, E7389, vinblastine, vincristine, vinflunine, vinorelbine, enzastaurin, saxagliptin, sitagliptin, SYR-322, talabostat, mycophenolic acid, thioguanine, VX-944, mycophenolic acid, ribavirin, thioguanine, VX-944, pactimibe, S-18886, torsemide, carvedilol, dapiprazole, ergotamine, guanadrel, Labetalol, phenoxybenzamine, prazosin, terazosine, alfuzosin, aripiprazole, asenapine, dihydroergotamine, DL 017, epinastine, guanethidine, iloperidone, nefazodone, olanzapine, paliperidone, phentolamine, quetiapine, quinidine, risperidone, tolazoline, UK-294315, ziprasidone, dobutamine, apraclonidine, arbutamine, clonidine, tamsulosin, venlafaxine, clevidipine butyrate, aminophylline, amrinone, cilostazol, dipyridamole, dyphylline, medorinone, nitroglycerin, pentoxifylline, theophylline, tolbutamide, ABT-751, BMS-275183, docetaxel, E7389, milataxel, MST-997, NPI-2358, podophyllotoxin, TPI 287, AL 108, ixabepilone, paclitaxel, TTI-237, XRP9881, epothilone B, EC145, vinblastine, vincristine, vinflunine, minocycline, vinorelbine and (5-(6-amino-9H-purin-9-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methyl dihydrogen phosphate, or a pharmaceutically acceptable salt thereof.

As utilized herein, "pharmaceutically acceptable salts" are those salts derived from pharmaceutically acceptable inorganic and organic acids and bases. Examples of suitable acids include hydrochloric, hydrobromic, sulfuric, nitric, perchloric, fumaric, maleic, phosphoric, glycolic, lactic, salicylic, succinic, toluene-p-sulfonic, tartaric, acetic, citric, methanesulfonic, formic, benzoic, malonic, naphthalene-2-sulfonic and benzenesulfonic acids. Salts derived from appropriate bases include alkali metal (e.g. sodium), alkaline earth metal (e.g. magnesium) and ammonium salts. Preferred salts include hydrochlorides, hydrobromides, sulfates, mesylates, maleates, and fumarates. Throughout this application, references to a compound, according to the invention, includes the compounds as well as its pharmaceutically acceptable salts.

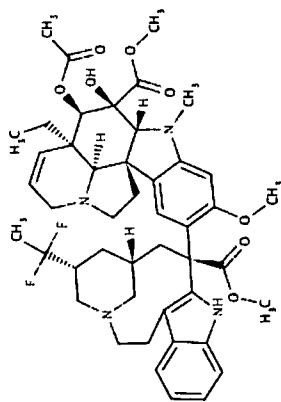
As utilized herein, one or more includes, two or more, three or more, four or more, five or more, six or more, etc. Therefore, combinations of the compounds set forth herein are provided by the present invention. The available structures for these compounds are set forth below. As set forth throughout the application, the infection can be a viral, bacterial, fungal or parasitic infection. The pathogen can be a respiratory virus. Respiratory viruses include, but are not limited to, picornaviruses, orthomyxoviruses, paramyxoviruses, coronaviruses and adenoviruses. More specifically, and not to be limiting, the respiratory virus can be an influenza virus, a parainfluenza virus, an adenovirus, a rhinovirus or a respiratory syncytial virus (RSV) or any strain thereof. The pathogen can also be a gastrointestinal virus. Gastrointestinal viruses

include, but are not limited to, picornaviruses, adenoviruses, filoviruses, flaviviruses, caliciviruses and reoviruses. More specifically, and not to be limiting, the gastrointestinal virus can be a reovirus, an adenovirus, a Norwalk virus, an Ebola virus, a Marburg virus, an adenovirus, a rotavirus, an enterovirus, a Dengue fever virus, a yellow fever virus, or a West Nile virus. The pathogen can also be a hemorrhagic fever virus. These include, but are not limited to, flaviviruses, bunyaviruses, arenaviruses, filoviruses and hantaviruses. More specifically and not to be limiting, the hemorrhagic fever virus can be an Ebola virus, a Marburg virus, a Dengue fever virus (types 1-4), a yellow fever virus, a Sin Nombre virus, a Junin virus, Crimean Congo hemorrhagic fever virus, a Machupo virus, a Lassa virus, a Rift Valley fever virus, or a Kyasanur forest disease virus. The pathogen can also be a pathogen selected from the group consisting of: a pox virus, a herpes virus, an RSV virus, HIV, an influenza virus, a hepatitis C virus, a hepatitis B virus, a hepatitis E virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus. As mentioned above, the compounds can also be utilized to decrease toxicity of a toxin set forth herein.

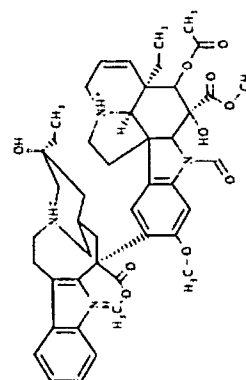
TUBB4 and TUBA8A
vinorelbine



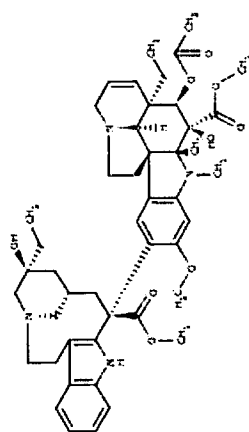
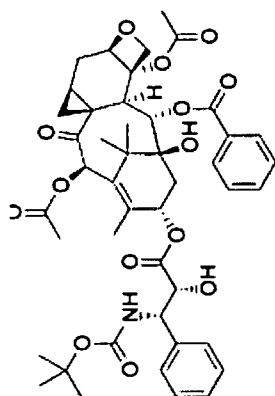
vinflunine



vincristine

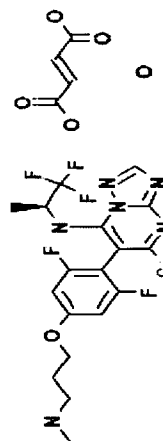


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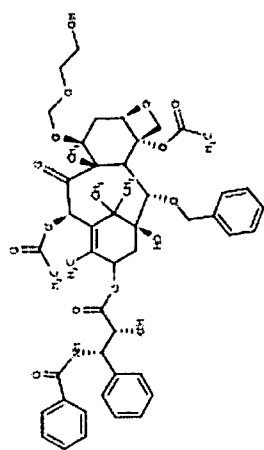


vinblastine

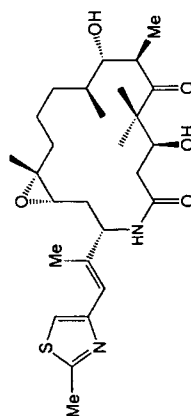
TTI-237



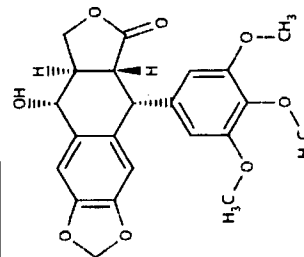
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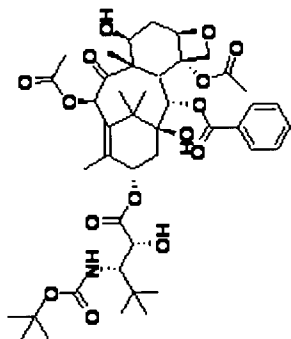
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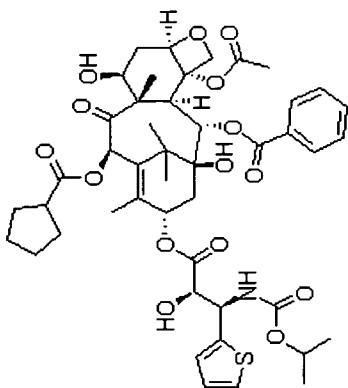
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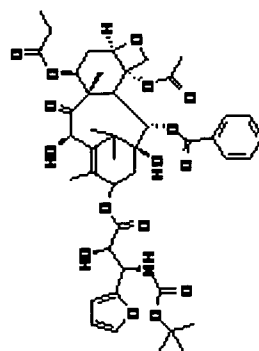
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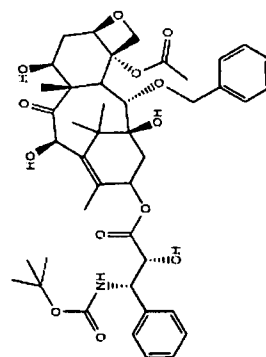
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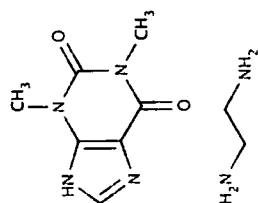
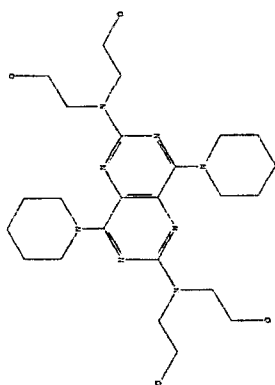
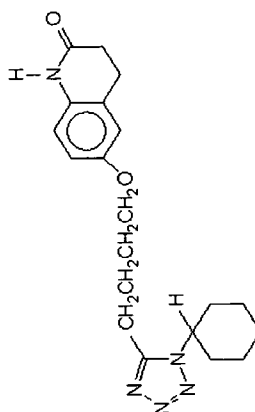
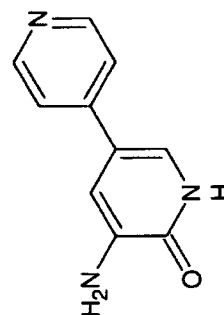
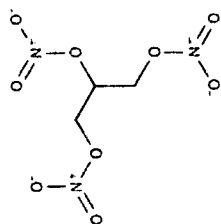
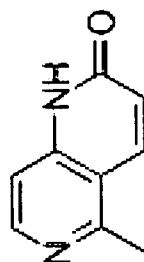
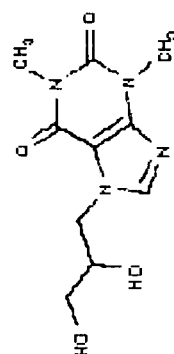
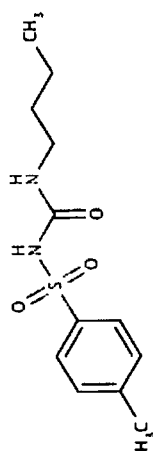
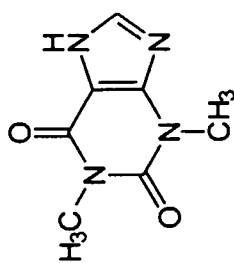
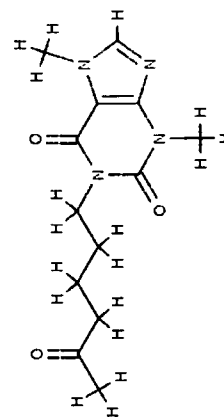


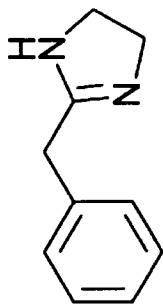
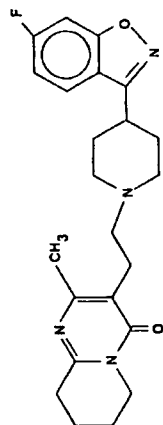
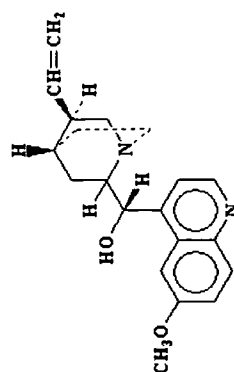
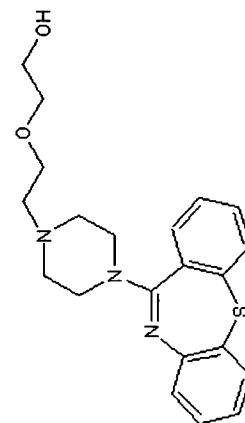
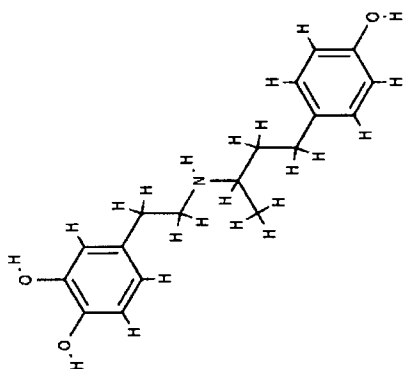
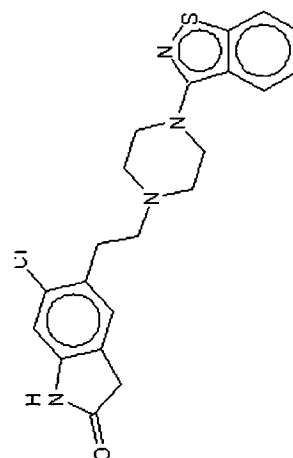
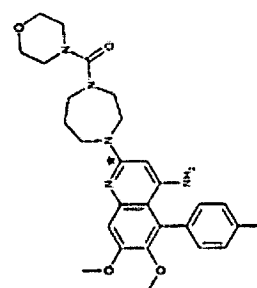
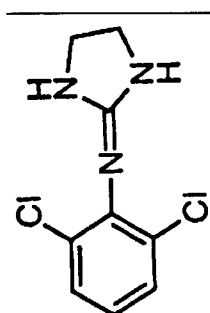
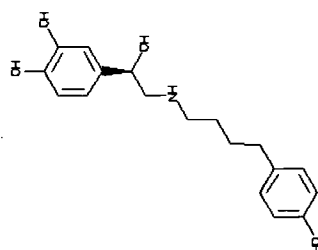
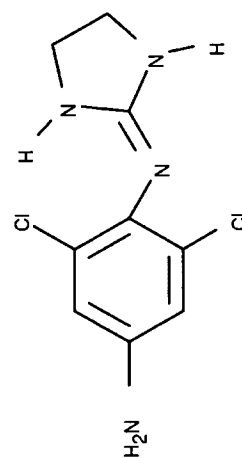
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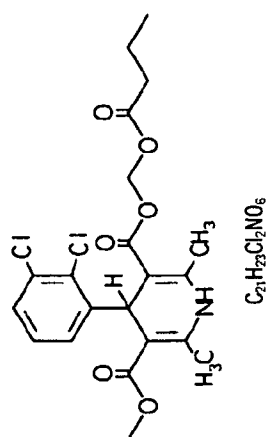
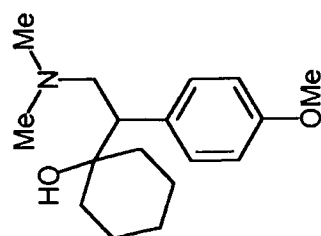
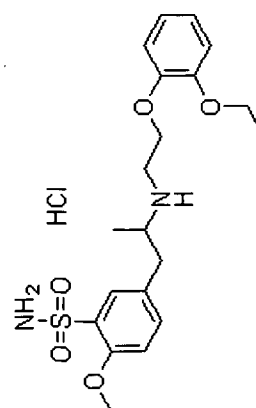
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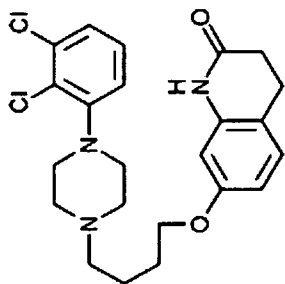


AminophyllineDypyridamoleCilostazolAmrinonenitroglycerinmedorinonedyphylline**PDE3B**tolbutamidetheophyllinepentoxifylline

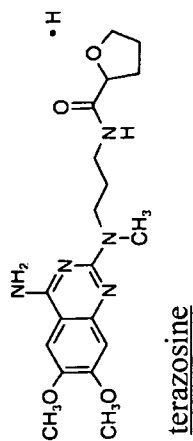
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clevidine butyrate

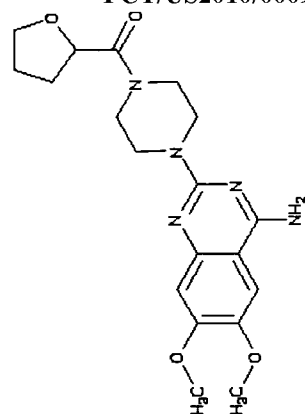
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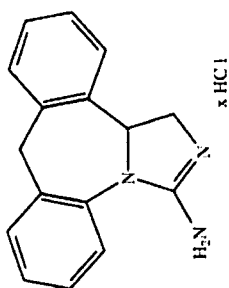
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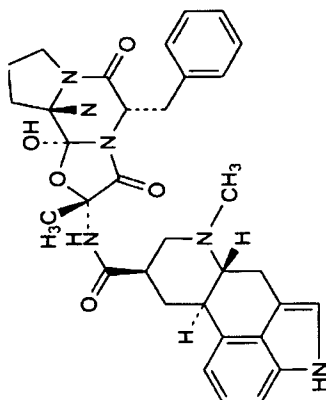
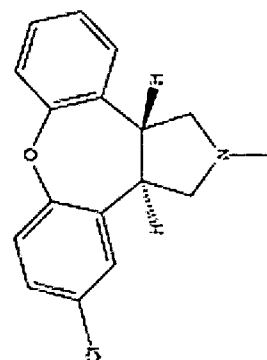
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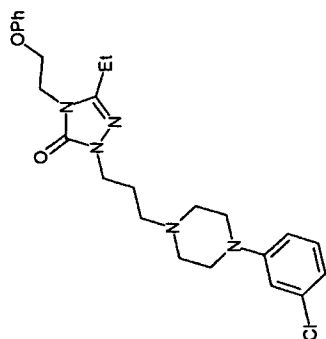
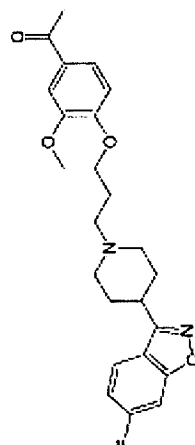
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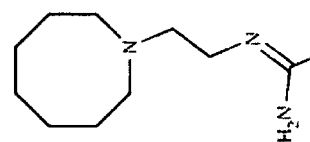
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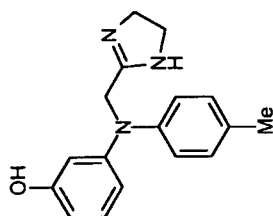
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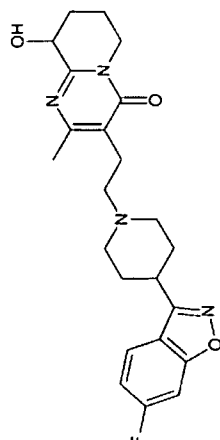
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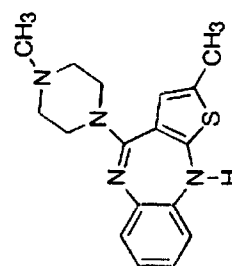
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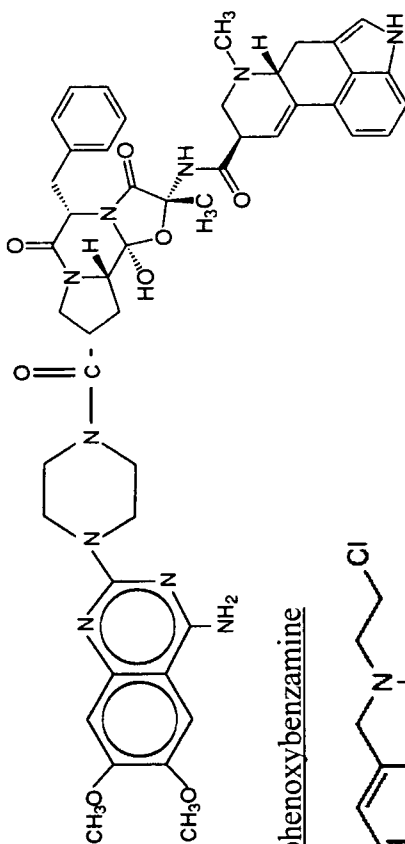
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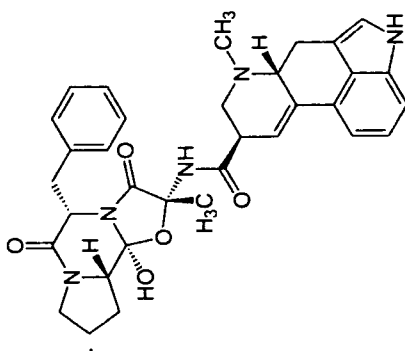
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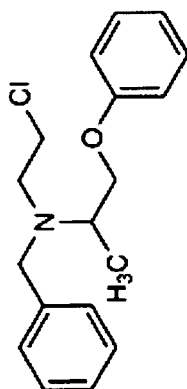
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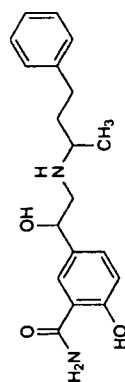
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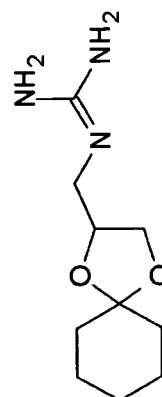
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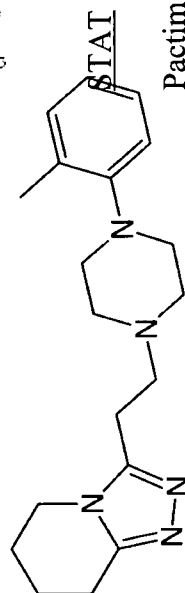
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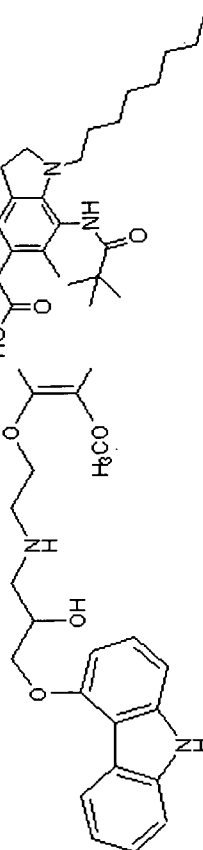
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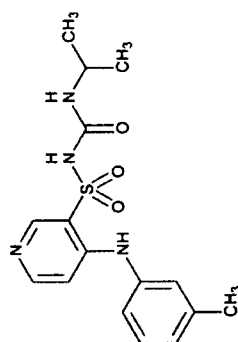
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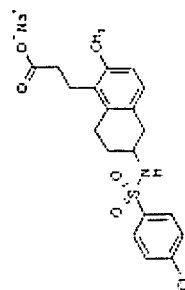
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TBXA2R
Torsemide



S-18886

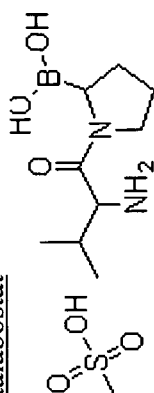


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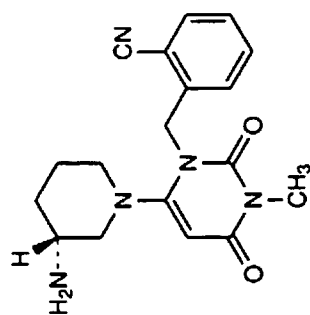
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DPP4

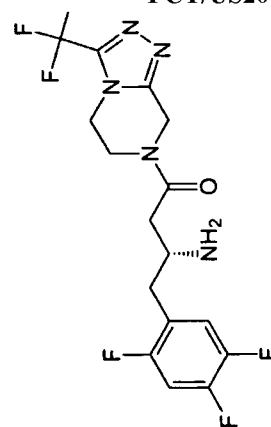
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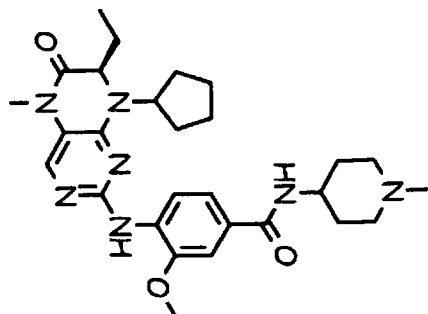
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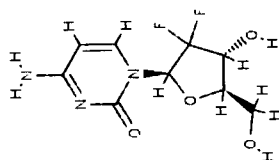
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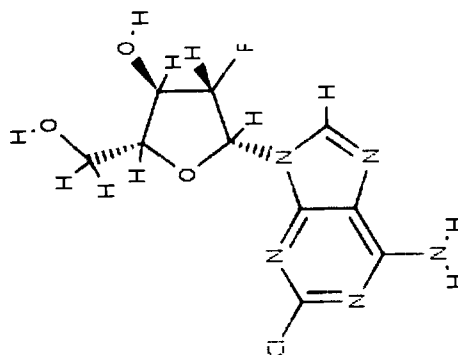
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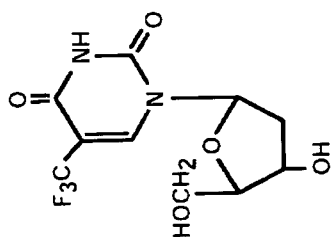
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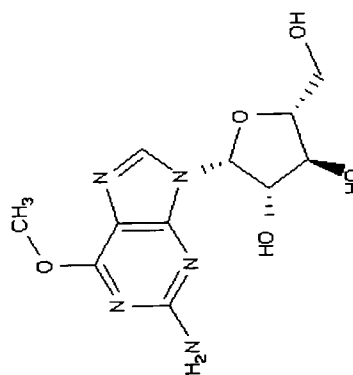
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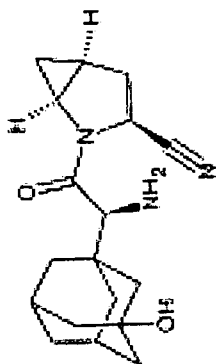
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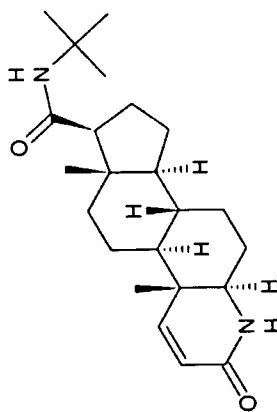


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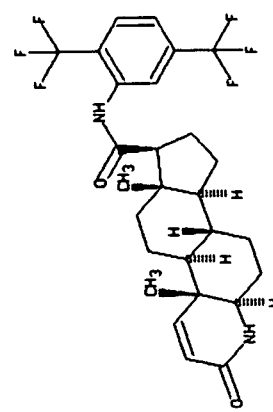


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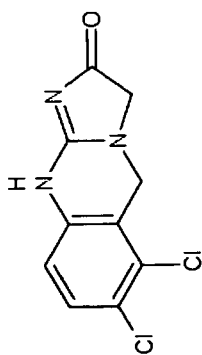
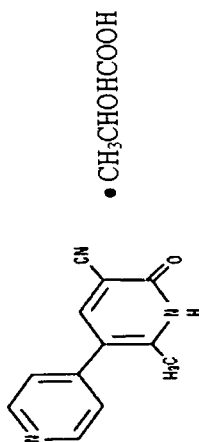
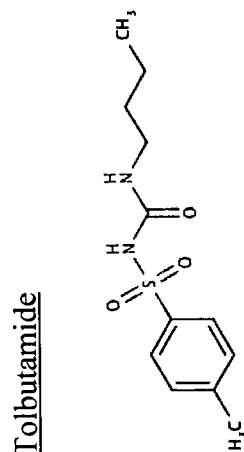
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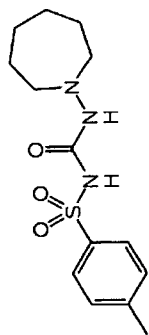
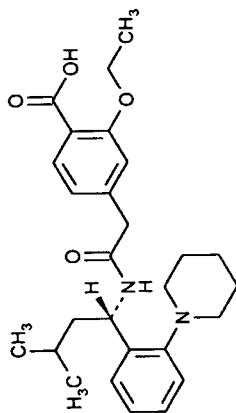
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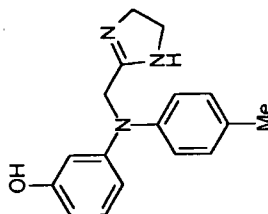
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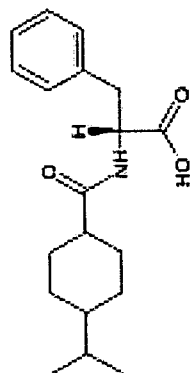
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repaglinide

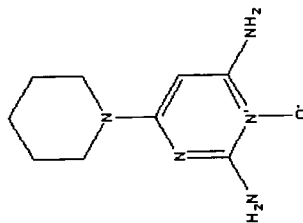
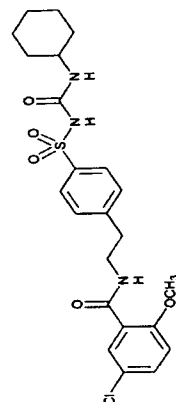
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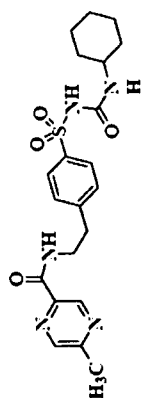
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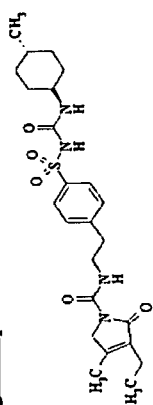
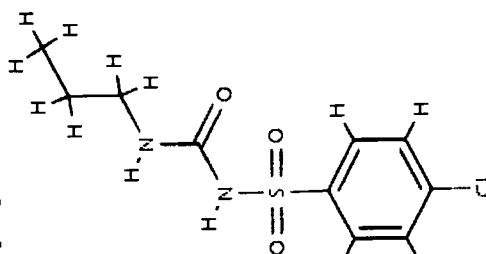
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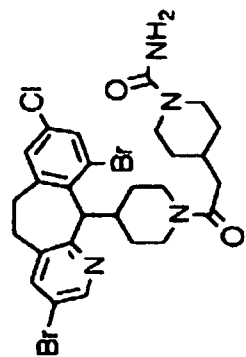
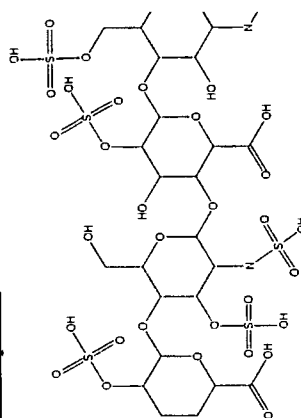
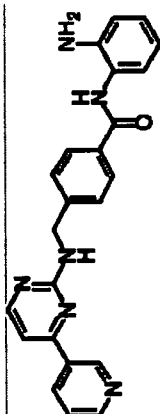
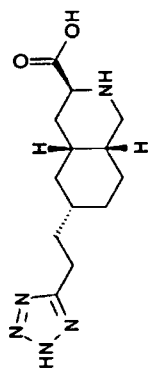
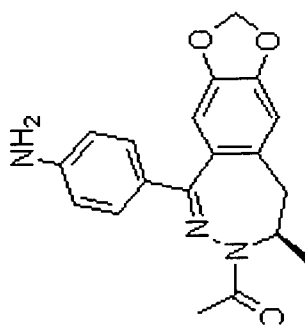
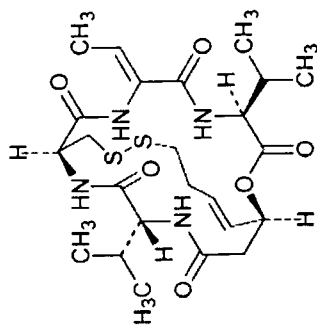
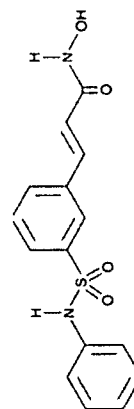
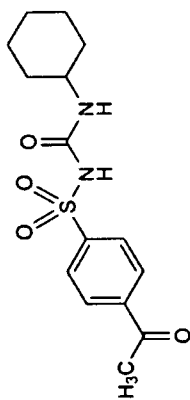
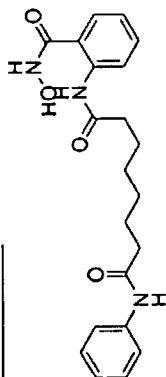
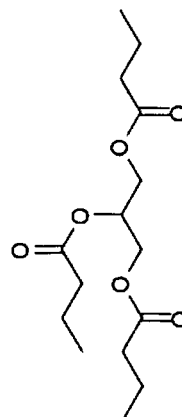
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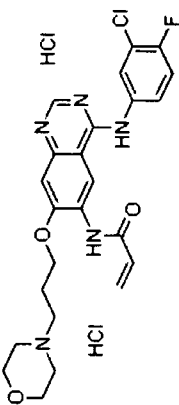
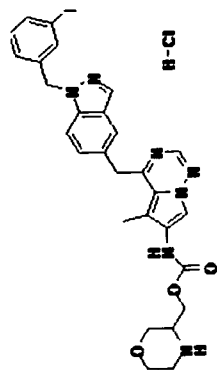
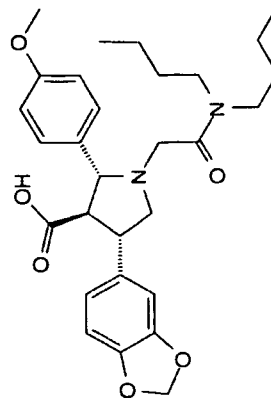
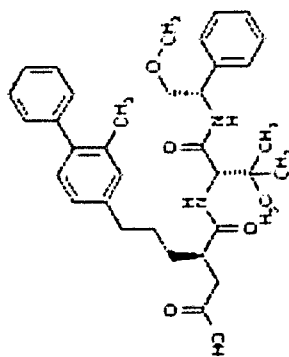
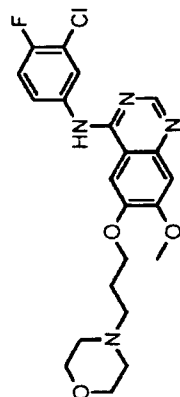
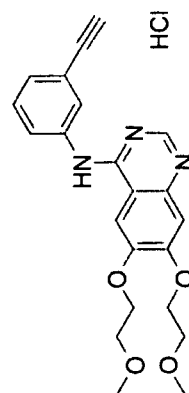
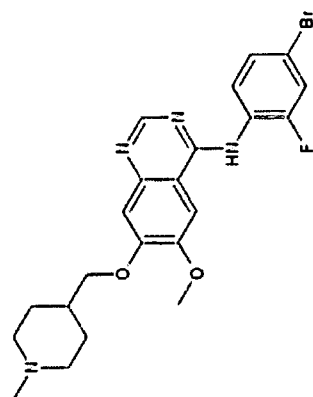
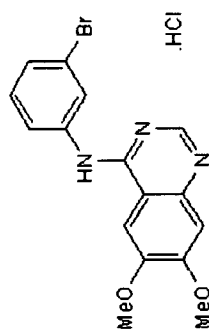
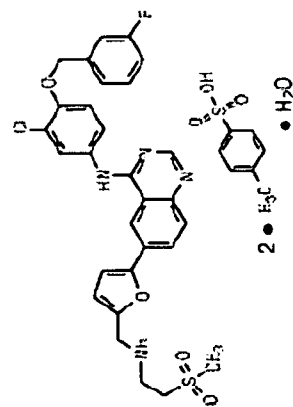
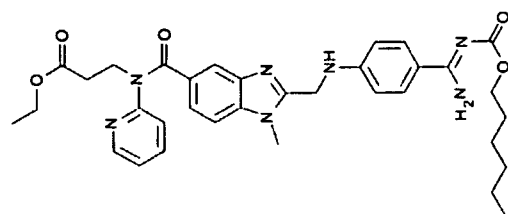
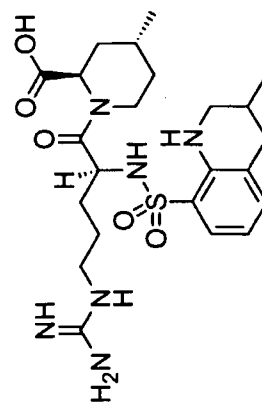
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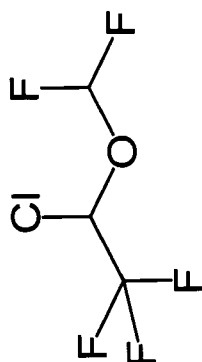
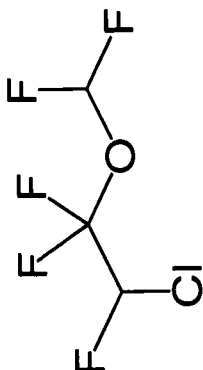
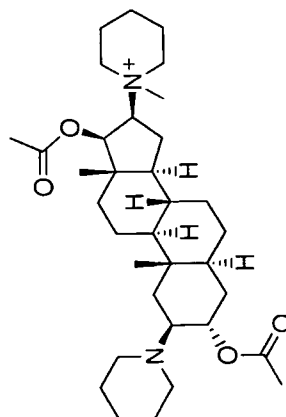
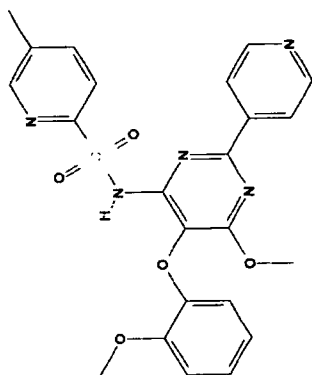
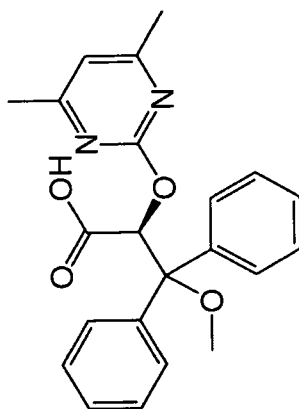
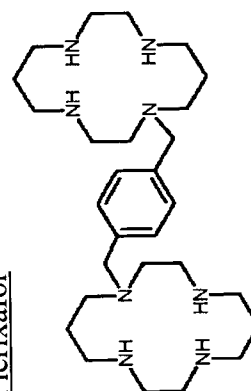
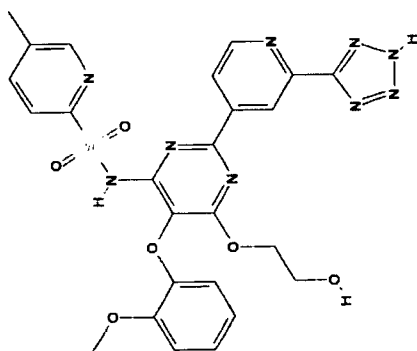
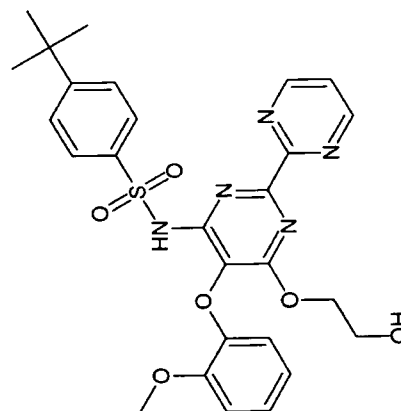
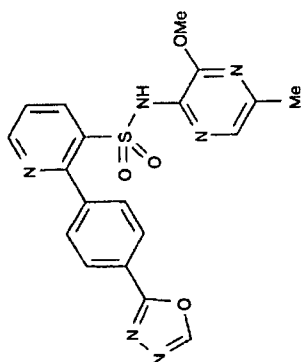
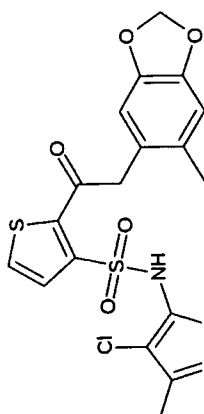
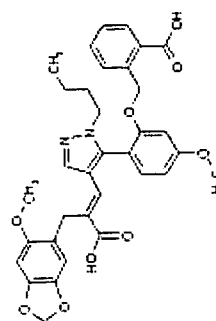


glimepiride

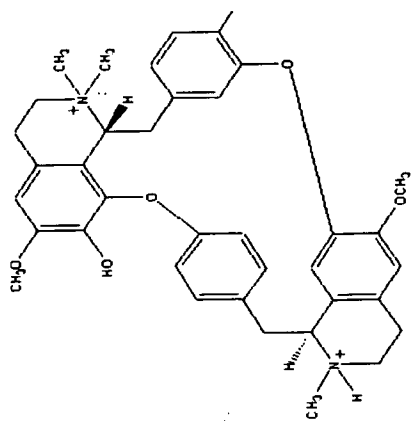
chlorpropamide

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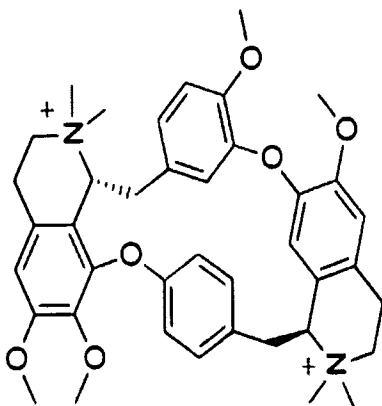
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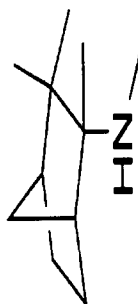
d-tubocurarine



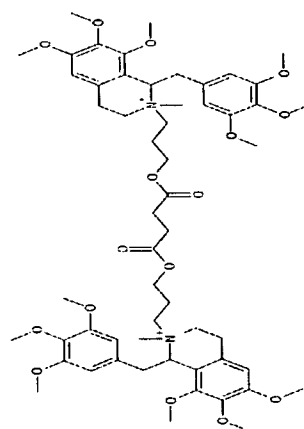
metocurine



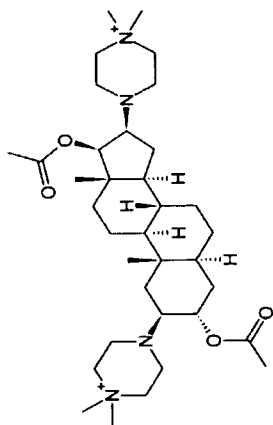
mecamylamine



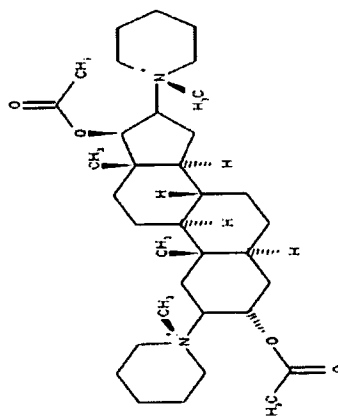
doxacurium



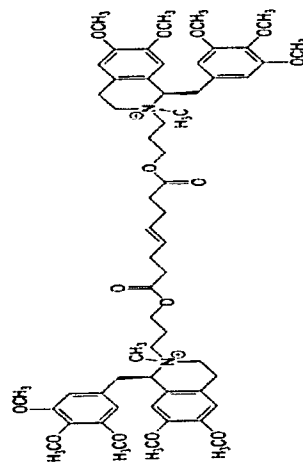
pipecuronium



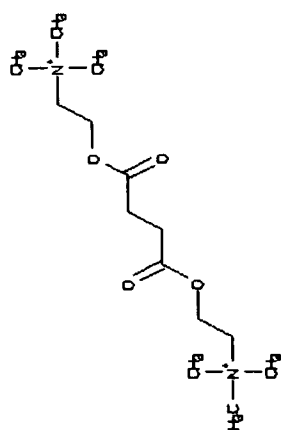
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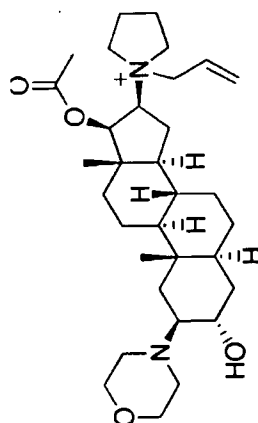
mivacurium



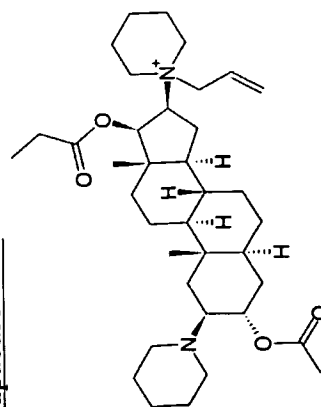
succinylcholine



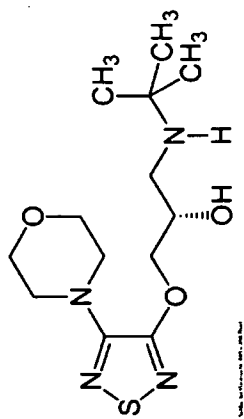
rocuronium



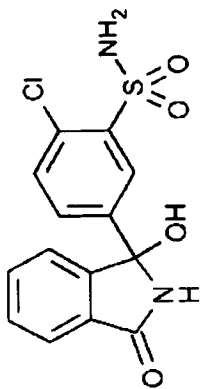
rapacuronium



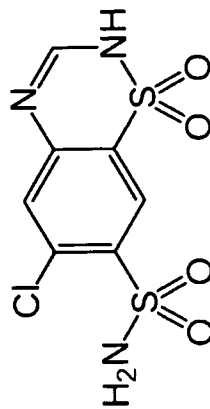
timolol



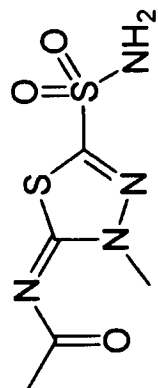
chlorthalidone



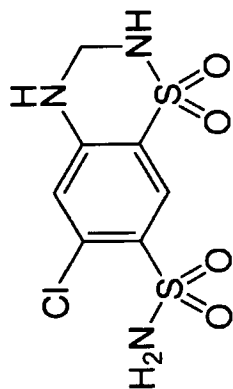
chlorothiazide



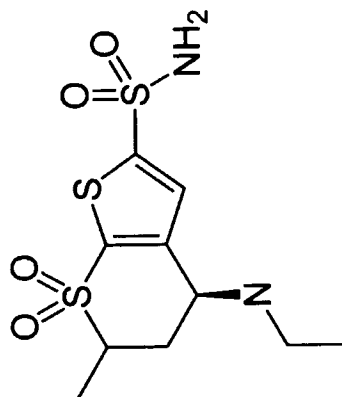
methazolamide



hydrochlorothiazide

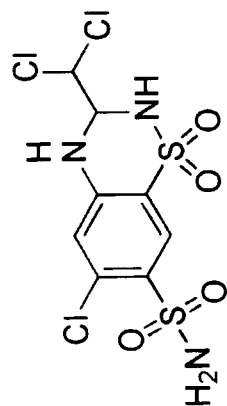


dorzolamide

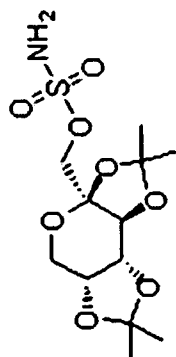


CA2

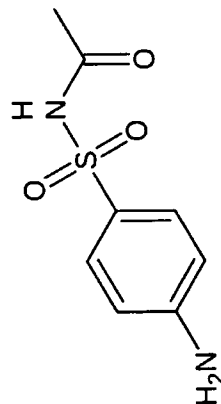
Trichlormethiazide



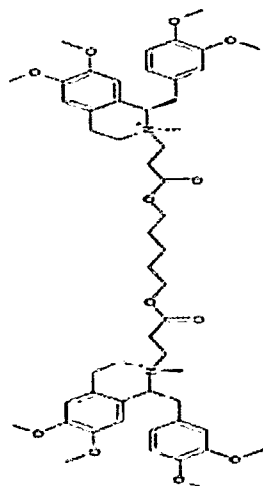
topiramate



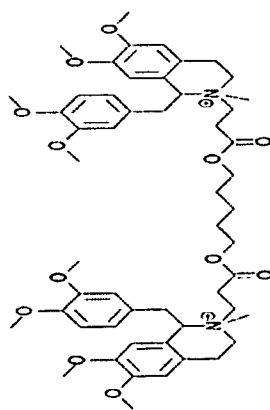
sulfacetamide



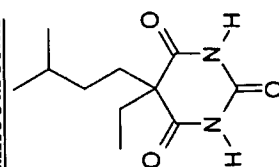
Cisatracurium



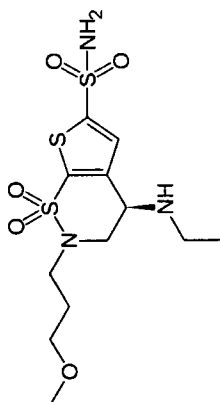
atracurium



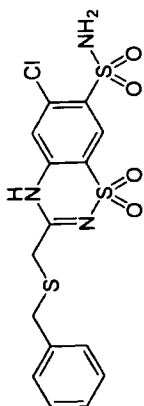
amobarbital



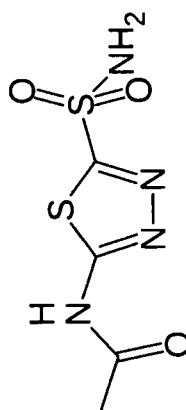
Brinzolamide



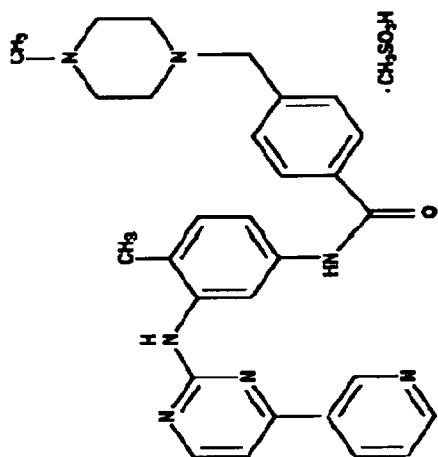
benzthiazide



acetazolamide



BCR
Imatinib



Other methods of decreasing expression and/or activity include methods of interrupting or altering transcription of mRNA molecules by site-directed mutagenesis (including mutations caused by a transposon or an insertional vector). Chemical mutagenesis can also be performed in which a cell is contacted with a chemical (for example ENU) that mutagenizes nucleic acids by introducing mutations into a gene set forth in Table 1, 2, 3 or 4. Transcription of mRNA molecules can also be decreased by modulating a transcription factor that regulates expression of any of the genes set forth in Table 1, 2, 3 or 4. Radiation can also be utilized to effect mutagenesis.

10 **Pharmaceutical Compositions and Modes of Administration**

The present invention provides a method of decreasing infection by a pathogen in a subject by decreasing the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, said method comprising administering to the subject an effective amount of a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, in the subject, wherein the pathogen is not HIV.

Also provided is a method of decreasing infection by a pathogen in a subject by decreasing the expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, said method comprising administering to the subject an effective amount of a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, in the subject, wherein the pathogen is not West Nile Virus.

Further provided is a method of decreasing infection by a pathogen in a subject by decreasing the expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, said method comprising administering to the subject an effective amount of a that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, in the subject, wherein the pathogen is not West Nile Virus or Dengue Fever Virus.

The present invention also provides a method of decreasing infection by a pathogen in a subject by decreasing the expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, said method comprising administering to the subject an effective amount of a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, in the subject, wherein the pathogen is not hepatitis C.

Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more respiratory viruses. Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that

decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by three or more respiratory viruses. Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by four or more respiratory viruses. Also provided is a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by five or more respiratory viruses. These can be selected from the group consisting of: a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus and an adenovirus. Since picornaviruses, orthomyxoviruses, paramyxoviruses, coronaviruses and adenoviruses are families of viruses, two or more, three or more, four or more, or five or more respiratory viruses can be from the same or from different families. For example, and not to be limiting, the composition can inhibit infection by two or more orthomyxoviruses; two or more picornaviruses; an orthomyxovirus, an adenovirus, and a picornavirus; an orthomyxovirus, a paramyxovirus and an adenovirus; an orthomyxovirus, two picornaviruses and a paramyxovirus; three orthomyxoviruses, a picornavirus and an adenovirus, etc. More particularly, the composition can inhibit infection by two or more, three or more or four or more respiratory viruses selected from the group consisting of an influenza virus, a parainfluenza virus, an adenovirus, a rhinovirus and an RSV virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more gastrointestinal viruses. The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by three or more gastrointestinal viruses. The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by four or more gastrointestinal viruses. The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by five or more

gastrointestinal viruses. These viruses can be selected from the group consisting of: a filovirus, an adenovirus, a picornavirus, a calcivirus, a flavivirus or a reovirus. Since filoviruses, picornaviruses, calciviruses, flaviviruses and reoviruses are families of viruses, the composition can inhibit infection by two or more, three or more, four or more, or five or more gastrointestinal viruses from the same or from different families. More particularly, the composition can inhibit infection by two or more, three or more, four or more, or five or more gastrointestinal viruses selected from the group consisting of a reovirus, a Norwalk virus, an adenovirus, an Ebola virus, a Marburg virus, a Dengue fever virus, a West Nile virus, a yellow fever virus, a rotavirus and an enterovirus. It is noted that in the methods of the present invention, if the composition decreases expression or activity of a gene or gene product set forth in Table 3, the combination of viruses inhibited by the composition is not West Nile Virus and Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by one or more pathogens selected from the group consisting of: a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus, an adenovirus, and inhibits infection by one or more pathogens selected from the group consisting of: a flavivirus, a filovirus, an adenovirus, a calcivirus or a reovirus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more pathogens selected from the group consisting of HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more pathogens selected from the group consisting of: influenza, a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa

Fever virus, hantavirus, Rift Valley Fever virus Ebola virus, Marburg virus or Dengue Fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by three or more pathogens. The three or more pathogens can be selected from the viruses, bacteria, parasites and fungi set forth herein. More particularly, the three or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by four or more pathogens. The three or more pathogens can be selected from the viruses, bacteria, parasites and fungi set forth herein. More particularly, the four or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by five or more pathogens. The five or more pathogens can be selected from the viruses, bacteria, parasites and fungi set forth herein. More particularly, the five or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a

hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by six or more pathogens. The six or more pathogens can be selected from the viruses, bacteria, parasites and fungi set forth herein. More particularly, the five or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The present invention also provides a method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits co-infection by HIV and one or more viruses, bacteria, parasites or fungi. For example, decreasing co-infection of HIV and any of the viruses, including for example any families, genus, species, or group of viruses. As a further example, co-infection of HIV and a respiratory virus is provided herein. Respiratory viruses include picornaviruses, orthomyxoviruses, paramyxoviruses, coronaviruses, and adenoviruses. More specifically, the respiratory virus can be any strain of influenza, rhinovirus, adenovirus, parainfluenza virus or RSV. Also provided is decreasing co-infection of HIV and a gastrointestinal virus. Gastrointestinal viruses include picornaviruses, filoviruses, flaviviruses, calciviruses and reoviruses. More specifically, and not to be limiting, the gastrointestinal virus can be any strain of reovirus, a Norwalk virus, an Ebola virus, a Marburg virus, an adenovirus, a rotavirus, an enterovirus, a Dengue fever virus, a yellow fever virus, or a West Nile virus. Further provided is a method of decreasing co-infection of HIV with a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, hantavirus, Rift Valley Fever virus

Ebola virus, Marburg virus or Dengue Fever virus. More particularly, decreasing co-infection of HIV and a hepatitis virus, such as Hepatitis A, Hepatitis B or Hepatitis C is provided. It is noted that in a method of decreasing co-infection of HIV and Hepatitis C, the gene or gene product is not ERCC1, THAP11, COASY, NCOA6 or MAP3K14. Also provided is decreasing co-infection of HIV and a herpes virus, for example, HSV-1 or HSV-2. In addition decreasing co-infection of HIV and tuberculosis is also provided. Further provided is decreasing co-infection of HIV and CMV, as well as decreasing co-infection of HIV and HPV.

As described herein, the genes set forth in Tables 1, 2, 3 or 4 can be involved in the pathogenesis of two or more respiratory viruses. Therefore, the present invention provides methods of treating or preventing an unspecified respiratory infection in a subject by administering a composition that decreases activity or expression of a gene involved in the pathogenesis of two or more respiratory viruses. More particularly, the present invention provides a method of decreasing an unspecified respiratory infection in a subject comprising: a) diagnosing a subject with an unspecified respiratory infection; and b) administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more respiratory viruses selected from the group consisting of picornaviruses, orthomyxoviruses, paramyxoviruses, coronaviruses, or adenoviruses. As set forth above, in the methods of the present invention, the two or more respiratory viruses can be from the same family or from a different family of respiratory viruses. More specifically, the respiratory virus can be any strain of influenza, rhinovirus, adenovirus, parainfluenza virus or RSV. In this method, the composition can be a composition that inhibits infection by three or more, four or more, five or more; or six or more respiratory viruses selected from the group consisting of a picornaviruses, an orthomyxoviruses, paramyxoviruses, coronaviruses, or adenoviruses.

As described herein, the genes set forth in Tables 1, 2, 3 or 4 can be involved in the pathogenesis of two or more gastrointestinal viruses. Therefore, the present invention provides methods of treating or preventing an unspecified gastrointestinal infection in a subject by administering a composition that decreases activity or expression of a gene involved in the pathogenesis of two or more gastrointestinal viruses. More particularly, the present invention provides a method of decreasing an unspecified gastrointestinal infection in a subject comprising: a) diagnosing a subject with an unspecified gastrointestinal infection; and b) administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits infection by two or more gastrointestinal viruses selected

from the group consisting of a flavivirus, an adenovirus, a filovirus, a calcivirus or a reovirus. It is noted that if the gene or gene product is from Table 3, the two gastrointestinal viruses are not West Nile virus and Dengue fever virus. As set forth above, in the methods of the present invention, the two or more gastrointestinal viruses can be from the same family or from a different family of gastrointestinal viruses. More particularly, and not to be limiting, the gastrointestinal virus can be any strain of reovirus, adenovirus, a Norwalk virus, an Ebola virus, a Marburg virus, a rotavirus, an enterovirus, a Dengue fever virus, a yellow fever virus, or a West Nile virus. In this method, the composition can be a composition that inhibits infection by three or more, four or more, five or more; or six or more gastrointestinal viruses selected from the group consisting of a flavivirus, an adenovirus, a filovirus, a calcivirus or a reovirus.

The present invention also provides a method of preventing or decreasing an unspecified pandemic or bioterror threat in a subject comprising: a) diagnosing a subject with an unspecified pandemic or bioterrorist inflicted infection; and b) administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits infection by two or more, three or more, four or more; or five or more viruses selected from the group consisting of a pox virus, an influenza virus, West Nile virus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus and a Dengue fever virus. It is noted that the present invention also provides a method wherein the composition administered is not a composition that decreases expression or activity of a gene set forth in Table 3 for West Nile virus and Dengue Fever virus.

Also provided by the present invention is a method of managing secondary infections in a patient comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition can inhibit infection by HIV and one or more, two or more, three or more, four or more; or five or more secondary infections.

As set forth above, the genes set forth in Tables 1, 2, 3 or 4 can be involved in the pathogenesis of three or more pathogens. Therefore, the present invention provides methods of treating or preventing an unspecified infection by administering a composition that decreases the activity or expression of a gene that is involved in the pathogenesis of three or more pathogens. Therefore, the present invention provides a method of decreasing infection in a subject comprising: a) diagnosing a subject with an unspecified infection and; b) administering a

composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition decreases infection by three or more pathogens. More specifically, the three or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

The infection can be a viral infection, a parasitic infection, a bacterial infection or a fungal infection, to name a few. As utilized herein, "an unspecified infection" is an infection that presents symptoms associated with an infection, but is not identified as specific infection. One of skill in the art, for example, a physician, a nurse, a physician's assistant, a medic or any other health practitioner would know how to diagnose the symptoms of infection even though the actual pathogen may not be known. For example, the patient can present with one or more symptoms, including, but not limited to, a fever, fatigue, lesions, weight loss, inflammation, a rash, pain (for example, muscle ache, headache, ear ache, joint pain, etc.), urinary difficulties, respiratory symptoms (for example, coughing, bronchitis, lung failure, breathing difficulties, bronchiolitis, airway obstruction, wheezing, runny nose, sinusitis, congestion, etc.), gastrointestinal symptoms (for example, nausea, diarrhea, vomiting, dehydration, abdominal pain, intestinal cramps, rectal bleeding, etc.). This can occur in the event of a bioterrorist attack or a pandemic. In this event, one of skill in the art would know to administer a composition that inhibits infection by decreasing the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4 that is involved in the pathogenesis of several pathogens. Similarly, if there is a threat of an unspecified infection, for example, a threat of a bioterrorist attack, a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4 can be administered prophylactically to a subject to prevent an unspecified infection in a subject.

By "treat," "treating," or "treatment" is meant a method of reducing the effects of an existing infection. Treatment can also refer to a method of reducing the disease or condition itself rather than just the symptoms. The treatment can be any reduction from native levels and can be, but is not limited to, the complete ablation of the disease or the symptoms of the disease. Treatment can range from a positive change in a symptom or symptoms of viral infection to complete amelioration of the viral infection as detected by art-known techniques. For example, a

disclosed method is considered to be a treatment if there is about a 10% reduction in one or more symptoms of the disease in a subject with the disease when compared to native levels in the same subject or control subjects. Thus, the reduction can be about a 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%, or any amount of reduction in between as compared to native or control levels.

The methods of the present invention can also result in a decrease in the amount of time that it normally takes to see improvement in a subject. For example, a decrease in infection can be a decrease of hours, a day, two days, three days, four days, five days, six days, seven days, eight days, nine days, ten days, eleven days, twelve days, thirteen days, fourteen days, fifteen days or any time in between that it takes to see improvement in the symptoms, viral load or any other parameter utilized to measure improvement in a subject. For example, if it normally takes 7 days to see improvement in a subject not taking the composition, and after administration of the composition, improvement is seen at 6 days, the composition is effective in decreasing infection. This example is not meant to be limiting as one of skill in the art would know that the time for improvement will vary depending on the infection.

As utilized herein, by "prevent," "preventing," or "prevention" is meant a method of precluding, delaying, averting, obviating, forestalling, stopping, or hindering the onset, incidence, severity, or recurrence of infection. For example, the disclosed method is considered to be a prevention if there is about a 10% reduction in onset, incidence, severity, or recurrence of infection, or symptoms of infection (e.g., inflammation, fever, lesions, weight loss, etc.) in a subject exposed to an infection when compared to control subjects exposed to an infection that did not receive a composition for decreasing infection. Thus, the reduction in onset, incidence, severity, or recurrence of infection can be about a 10, 20, 30, 40, 50, 60, 70, 80, 90, 100%, or any amount of reduction in between as compared to control subjects. For example, and not to be limiting, if about 10% of the subjects in a population do not become infected as compared to subjects that did not receive preventive treatment, this is considered prevention.

Also provided is a method of decreasing infection in a subject comprising: a) administering a composition that decreases the expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4, in a subject with an unspecified infection; b) diagnosing the type of infection in the subject and; c) administering a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4 for the diagnosed infection. Also provided is a method wherein the diagnosed infection is HIV and the composition is not a composition that decreases the expression or activity of a gene or gene product set forth in Table 1. Further provided is a method wherein the diagnosed infection is West Nile Virus and the composition is not a composition that decreases the expression or

activity of a gene or gene product set forth in Table 2. Further provided is a method wherein the diagnosed infection is West Nile Virus or Dengue fever virus and the composition is not a composition that decreases the expression or activity of a gene or gene product set forth in Table 3. Further provided is a method wherein the diagnosed infection is Hepatitis C and the composition is not a composition that decreases the expression or activity of a gene or gene product set forth in Table 4.

Further provided is a method of treating viral infection comprising: a) diagnosing a subject with a viral infection; and b) removing a drug from the subject that decreases the expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4, if the viral infection is not a viral infection that is inhibited by a composition that decreases the expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4. As mentioned above, upon recognizing that a subject has an infection or the symptoms of an infection, for example, in the case of a bioterrorist attack or a pandemic, given that a gene or gene product set forth in Table 1, 2, 3 or 4 can be involved in the pathogenesis of several pathogens, a practitioner can prescribe or administer a composition that decreases the expression or activity of the gene or gene product. After administration, the practitioner, who can be the same practitioner or a different practitioner, can diagnose the type of infection in a subject. This diagnosis can be a differential diagnosis where the practitioner distinguishes between infections by comparing signs or symptoms and eliminates certain types of infection before arriving at the diagnosis for a specific infection, or a diagnosis based on a test that is specific for a particular infection. Once a specific infection is diagnosed, if the gene or gene product is involved in the pathogenesis of this infection, the practitioner can prescribe or administer a composition that decreases the expression or activity of that gene or gene product. This can be the same composition administered prior to diagnosis of the specific infection or a different composition that decreases expression or activity.

Also provided is a method of preventing infection in a subject comprising administering to a subject susceptible to an unspecified infection a composition that decreases the expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4. The composition can be administered in response to a lethal outbreak of an infection. For example, the infection can be a pandemic or a bioterrorist created infection. If there is a threat of an unspecified infection, such as a viral infection, a bacterial infection, a parasitic infection or an infection by a chimeric pathogenic agent, to name a few, a composition can be administered prophylactically to a subject to prevent an unspecified infection in a subject. The threat can also come in the form of a toxin. One of skill in the art would know to administer a composition that inhibits infection by decreasing the expression or activity of any one or more gene(s) or gene product(s) set forth in

Table 1, 2, 3 or 4 that is involved in the pathogenesis of two or more, three or more, four or more; or five or more pathogens.

Such prophylactic use can decrease the number of people in a population that are infected, thus preventing further spread of a pandemic or decreasing the effects of a bioterrorist attack.

In the methods of the present invention, the composition can comprise one or more of, a chemical, a compound, a small molecule, an inorganic molecule, an aptamer, an organic molecule, a drug, a protein, a cDNA, a peptide, an antibody, a morpholino, a triple helix molecule, an siRNA, an shRNAs, an miRNA, an LNA, an antisense nucleic acid or a ribozyme that decreases the expression or activity of a gene or gene product set forth in Table 1, 2, 3 or 4. The composition can be administered before or after infection. The decrease in infection in a subject need not be complete as this decrease can be a 10% , 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or any other percentage decrease in between as long as a decrease occurs. This decrease can be correlated with amelioration of symptoms associated with infection. These compositions can be administered to a subject alone or in combination with other therapeutic agents described herein, such as anti-viral compounds, antibacterial agents, antifungal agents, antiparasitic agents, anti-inflammatory agents, anti-cancer agents, etc. Examples of viral infections, bacterial infections, fungal infections parasitic infections are set forth above. The compounds set forth herein or identified by the screening methods set forth herein can be administered to a subject to decrease infection by any pathogen or infectious agent set forth herein. Any of the compounds set forth herein or identified by the screening methods of the present invention can also be administered to a subject to decrease infection by any pathogen, now known or later discovered in which a gene or gene product set forth in Table 1, 2, 3 or 4 is involved.

Various delivery systems for administering the therapies disclosed herein are known, and include encapsulation in liposomes, microparticles, microcapsules, expression by recombinant cells, receptor-mediated endocytosis (Wu and Wu, *J. Biol. Chem.* 1987, 262:4429-32), and construction of therapeutic nucleic acids as part of a retroviral or other vector. Methods of introduction include, but are not limited to, mucosal, topical, intradermal, intrathecal, intratracheal, via nebulizer, via inhalation, intramuscular, otic delivery (ear), eye delivery (for example, eye drops), intraperitoneal, vaginal, rectal, intravenous, subcutaneous, intranasal, and oral routes. The compounds can be administered by any convenient route, for example by infusion or bolus injection, by absorption through epithelial or mucocutaneous linings (for example, oral mucosa, rectal, vaginal and intestinal mucosa, etc.) and can be administered together with other biologically active agents. Administration can be systemic or local.

Pharmaceutical compositions can be delivered locally to the area in need of treatment, for example by topical application or local injection.

Pharmaceutical compositions are disclosed that include a therapeutically effective amount of a RNA, DNA, antisense molecule, ribozyme, an LNA, siRNA, shRNA molecule, miRNA molecule, aptamer, drug, protein, small molecule, peptide inorganic molecule, organic molecule, antibody or other therapeutic agent, alone or with a pharmaceutically acceptable carrier. Furthermore, the pharmaceutical compositions or methods of treatment can be administered in combination with (such as before, during, or following) other therapeutic treatments, such as other antiviral agents, antibacterial agents, antifungal agents and antiparasitic agents.

For all of the administration methods disclosed herein, each method can optionally comprise the step of diagnosing a subject with an infection or diagnosing a subject in need of prophylaxis or prevention of infection.

Delivery systems

The pharmaceutically acceptable carriers useful herein are conventional. *Remington's Pharmaceutical Sciences*, by Martin, Mack Publishing Co., Easton, PA, 15th Edition (1975), describes compositions and formulations suitable for pharmaceutical delivery of the therapeutic agents herein disclosed. In general, the nature of the carrier will depend on the mode of administration being employed. For instance, parenteral formulations usually include injectable fluids that include pharmaceutically and physiologically acceptable fluids such as water, physiological saline, balanced salt solutions, aqueous dextrose, sesame oil, glycerol, ethanol, combinations thereof, or the like, as a vehicle. The carrier and composition can be sterile, and the formulation suits the mode of administration. In addition to biologically-neutral carriers, pharmaceutical compositions to be administered can contain minor amounts of non-toxic auxiliary substances, such as wetting or emulsifying agents, preservatives, and pH buffering agents and the like, for example sodium acetate or sorbitan monolaurate.

The composition can be a liquid solution, suspension, emulsion, tablet, pill, capsule, sustained release formulation, or powder. For solid compositions (for example powder, pill, tablet, or capsule forms), conventional non-toxic solid carriers can include, for example, pharmaceutical grades of mannitol, lactose, starch, sodium saccharine, cellulose, magnesium carbonate, or magnesium stearate. The composition can be formulated as a suppository, with traditional binders and carriers such as triglycerides.

Embodiments of the disclosure including medicaments can be prepared with conventional pharmaceutically acceptable carriers, adjuvants and counterions as would be known to those of skill in the art.

The amount of therapeutic agent effective in decreasing or inhibiting infection can depend on the nature of the pathogen and its associated disorder or condition, and can be determined by standard clinical techniques. Therefore, these amounts will vary depending on the type of virus, bacteria, fungus, parasite or other pathogen. For example, the dosage can be anywhere from 0.01 mg/kg to 100 mg/kg. Multiple dosages can also be administered depending on the type of pathogen, and the subject's condition. In addition, *in vitro* assays can be employed to identify optimal dosage ranges. The precise dose to be employed in the formulation will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each subject's circumstances. Effective doses can be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

The disclosure also provides a pharmaceutical pack or kit comprising one or more containers filled with one or more of the ingredients of the pharmaceutical compositions. Optionally associated with such container(s) can be a notice in the form prescribed by a governmental agency regulating the manufacture, use or sale of pharmaceuticals or biological products, which notice reflects approval by the agency of manufacture, use or sale for human administration. Instructions for use of the composition can also be included. Instructions for the use of a composition to decrease infection or toxicity can also be included. For example instructions for decreasing infection by an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis B virus, a Hepatitis C virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, a Dengue Fever virus, West Nile virus or Chikungunya virus can be provided.

In an example in which a nucleic acid is employed to reduce infection, such as an antisense or siRNA molecule, the nucleic acid can be delivered intracellularly (for example by expression from a nucleic acid vector or by receptor-mediated mechanisms), or by an appropriate nucleic acid expression vector which is administered so that it becomes intracellular, for example by use of a retroviral vector (see U.S. Patent No. 4,980,286), or by direct injection, or by use of microparticle bombardment (such as a gene gun; Biolistic, Dupont), or coating with lipids or cell-surface receptors or transfecting agents, or by administering it in linkage to a

homeobox-like peptide which is known to enter the nucleus (for example Joliot *et al.*, *Proc. Natl. Acad. Sci. USA* 1991, 88:1864-8). siRNA carriers also include, polyethylene glycol (PEG), PEG-liposomes, branched carriers composed of histidine and lysine (HK polymers), chitosan-thiamine pyrophosphate carriers, surfactants (for example, Survanta and Infasurf), nanochitosan carriers, and D5W solution. The present disclosure includes all forms of nucleic acid delivery, including synthetic oligos, naked DNA, plasmid and viral delivery, integrated into the genome or not.

As mentioned above, vector delivery can be via a viral system, such as a retroviral vector system which can package a recombinant retroviral genome (see e.g., Pastan *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* 85:4486, 1988; Miller *et al.*, *Mol. Cell. Biol.* 6:2895, 1986). The recombinant retrovirus can then be used to infect and thereby deliver to the infected cells a nucleic acid, for example an antisense molecule or siRNA. The exact method of introducing the altered nucleic acid into mammalian cells is, of course, not limited to the use of retroviral vectors. Other techniques are widely available for this procedure including the use of adenoviral vectors (Mitani *et al.*, *Hum. Gene Ther.* 5:941-948, 1994), adeno-associated viral (AAV) vectors (Goodman *et al.*, *Blood* 84:1492-1500, 1994), lentiviral vectors (Naidini *et al.*, *Science* 272:263-267, 1996), and pseudotyped retroviral vectors (Agrawal *et al.*, *Exper. Hematol.* 24:738-747, 1996). Other nonpathogenic vector systems such as the foamy virus vector can also be utilized (Park *et al.* "Inhibition of simian immunodeficiency virus by foamy virus vectors expressing siRNAs." *Virology*. 2005 Sep 20). It is also possible to deliver short hairpin RNAs (shRNAs) via vector delivery systems in order to inhibit gene expression (See Pichler *et al.* "In vivo RNA interference-mediated ablation of MDR1 P-glycoprotein." *Clin Cancer Res.* 2005 Jun 15;11(12):4487-94; Lee *et al.* "Specific inhibition of HIV-1 replication by short hairpin RNAs targeting human cyclin T1 without inducing apoptosis." *FEBS Lett.* 2005 Jun 6;579(14):3100-6.).

Physical transduction techniques can also be used, such as liposome delivery and receptor-mediated and other endocytosis mechanisms (see, for example, Schwartzberger *et al.*, *Blood* 87:472-478, 1996) to name a few examples. This invention can be used in conjunction with any of these or other commonly used gene transfer methods.

Transgenic Cells and Non-Human Mammals

The present invention also provides a non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 1, 2, 3 or 4, wherein the mammal has decreased susceptibility to infection by a pathogen, such as a virus, a bacterium, a fungus or a parasite. Exemplary transgenic non-human mammals include, but are not limited to, ferrets, fish, guinea

piags, chinchilla, mice, monkeys, rabbits, rats, chickens, cows, and pigs. Such knock-out animals are useful for reducing the transmission of viruses from animals to humans and for further validating a target. In the transgenic animals of the present invention one or both alleles of a gene set forth in Table 1, 2, 3 or 4 can be functionally deleted.

5 By "decreased susceptibility" is meant that the animal is less susceptible to infection or experiences decreased infection by a pathogen as compared to an animal that does not have one or both alleles of a gene set forth in Table 1, 2, 3 or 4 functionally deleted. The animal does not have to be completely resistant to the pathogen. For example, the animal can be 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or any percentage in between less susceptible to
10 infection by a pathogen as compared to an animal that does not have a functional deletion of a gene set forth in Table 1, 2, 3 or 4. Furthermore, decreasing infection or decreasing susceptibility to infection includes decreasing entry, replication, pathogenesis, insertion, lysis, or other steps in the replication strategy of a virus or other pathogen into a cell or subject, or combinations thereof.

15 Therefore, the present invention provides a non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 1, 2, 3 or 4, wherein the mammal has decreased susceptibility to infection by a pathogen, such as a virus, a bacterium, a parasite or a fungus. A functional deletion is a mutation, partial or complete deletion, insertion, or other variation made to a gene sequence that inhibits production of the gene product or renders a gene product that is
20 not completely functional or non-functional. Functional deletions can be made by insertional mutagenesis (for example via insertion of a transposon or insertional vector), by site directed mutagenesis, via chemical mutagenesis, via radiation or any other method now known or developed in the future that results in a transgenic animal with a functional deletion of a gene set forth in Table 1, 2, 3 or 4.

25 More particularly, the present invention provides a non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 1, wherein the mammal has decreased susceptibility to infection by a pathogen, wherein the pathogen is not HIV. Also provided is a non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 2, wherein the mammal has decreased susceptibility to infection by a pathogen, wherein
30 the pathogen is not West Nile Virus. Further provided is non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 3, wherein the mammal has decreased susceptibility to infection by a pathogen, wherein the pathogen is not West Nile Virus or Dengue Fever Virus. The present invention also provides a non-human transgenic mammal comprising a functional deletion of a gene set forth in Table 4, wherein the mammal has
35 decreased susceptibility to infection by a pathogen, wherein the pathogen is not hepatitis C.

Alternatively, a nucleic acid sequence such as siRNA, antisense, LNA, a morpholino or another agent that interferes with a gene set forth in Table 1, 2, 3 or 4 mRNA expression can be delivered. The expression of the sequence used to knock-out or functionally delete the desired gene can be regulated by an appropriate promoter sequence. For example, constitutive
5 promoters can be used to ensure that the functionally deleted gene is not expressed by the animal. In contrast, an inducible promoter can be used to control when the transgenic animal does or does not express the gene of interest. Exemplary inducible promoters include tissue-specific promoters and promoters responsive or unresponsive to a particular stimulus (such as light, oxygen, chemical concentration, such as a tetracycline inducible promoter).

10 The transgenic animals of the present invention that comprise a functionally deleted a gene set forth in Table 1, 2, 3 or 4 can be examined during exposure to various pathogens. Comparison data can provide insight into the life cycles of pathogens. Moreover, knock-out animals or functionally deleted (such as birds or pigs) that are otherwise susceptible to an infection (for example influenza) can be made to resist infection, conferred by disruption of the
15 gene. If disruption of the gene in the transgenic animal results in an increased resistance to infection, these transgenic animals can be bred to establish flocks or herds that are less susceptible to infection.

Transgenic animals, including methods of making and using transgenic animals, are described in various patents and publications, such as WO 01/43540; WO 02/19811; U.S. Pub.
20 Nos: 2001-0044937 and 2002-0066117; and U.S. Pat. Nos: 5,859,308; 6,281,408; and 6,376,743; and the references cited therein.

The transgenic animals of this invention also include conditional gene knockdown animals produced, for example, by utilizing the SIRIUS-Cre system that combines siRNA for specific gene-knockdown, Cre-loxP for tissue-specific expression and tetracycline-on for
25 inducible expression. These animals can be generated by mating two parental lines that contain a specific siRNA of interest gene and tissue-specific recombinase under tetracycline control. See Chang et al. "Using siRNA Technique to Generate Transgenic Animals with Spatiotemporal and Conditional Gene Knockdown." American Journal of Pathology 165: 1535-1541 (2004) which is hereby incorporated in its entirety by this reference regarding production of conditional
30 gene knockdown animals.

The present invention also provides cells including an altered or disrupted gene set forth in Table 1, 2, 3 or 4 that are resistant to infection by a pathogen. These cells can be *in vitro*, *ex vivo* or *in vivo* cells and can have one or both alleles altered. These cells can also be obtained from the transgenic animals of the present invention. Such cells therefore include cells having

decreased susceptibility to a virus or any of the other pathogens described herein, including bacteria, parasites and fungi.

Since the genes set forth herein are involved in viral infection, also provided herein are methods of overexpressing any of the genes set forth in Table 1 in host cells. Overexpression of these genes can provide cells that increase the amount of virus produced by the cell, thus allowing more efficient production of viruses. Also provided is the overexpression of the genes set forth herein in avian eggs, for example, in chicken eggs.

Methods of screening agents, such as a chemical, a compound, a small or large molecule, an organic molecule, an inorganic molecule, a peptide, a drug, a protein, a cDNA, an antibody, a morpholino, a triple helix molecule, an siRNA, an shRNAs, an miRNA, an antisense nucleic acid or a ribozyme set forth using the transgenic animals described herein are also provided.

Screening for Resistance to Infection

Also provided herein are methods of screening host subjects for resistance to infection by characterizing a nucleotide sequence or amino acid sequence of a host gene set forth in Table 1, 2, 3 or 4. The nucleic acid or amino acid sequence of a subject can be isolated, sequenced, and compared to the wildtype sequence of a gene set forth in Table 1, 2, 3 or 4. The greater the similarity between that subject's nucleic acid sequence or amino acid sequence and the wildtype sequence, the more susceptible that person is to infection, while a decrease in similarity between that subject's nucleic acid sequence or amino acid sequence and the wildtype sequence, the more resistant that subject can be to infection. Such screens can be performed for any gene set forth in Table 1, 2, 3 or 4 for any species.

Assessing the genetic characteristics of a population can provide information about the susceptibility or resistance of that population to viral infection. For example, polymorphic analysis of alleles in a particular human population, such as the population of a particular city or geographic area, can indicate how susceptible that population is to infection. A higher percentage of alleles substantially similar to a wild-type gene set forth in Table 1, 2, 3 or 4 can indicate that the population is more susceptible to infection, while a large number of polymorphic alleles that are substantially different than a wild-type gene sequence can indicate that a population is more resistant to infection. Such information can be used, for example, in making public health decisions about vaccinating susceptible populations.

The present invention also provides a method of screening a cell for a variant form of a gene set forth in Table 1, 2, 3 or 4. A variant can be a gene with a functional deletion, mutation or alteration in the gene such that the amount or activity of the gene product is altered. These cells containing a variant form of a gene can be contacted with a pathogen to determine if cells

comprising a naturally occurring variant of a gene set forth in Table 1, 2, 3 or 4 differs in their resistance to infection. For example, cells from an animal, for example, a chicken, can be screened for a variant form of a gene set forth in Table 1, 2, 3 or 4. If a naturally occurring variant is found and chickens possessing a variant form of the gene in their genome are less susceptible to infection, these chickens can be selectively bred to establish flocks that are resistant to infection. By utilizing these methods, flocks of chickens that are resistant to avian flu or other pathogens can be established. Similarly, other animals can be screened for a variant form of a gene set forth in Table 1, 2, 3 or 4. If a naturally occurring variant is found and animals possessing a variant form of the gene in their genome are less susceptible to infection, these animals can be selectively bred to establish populations that are resistant to infection. These animals include, but are not limited to, cats, dogs, fish, livestock (for example, cattle, horses, pigs, sheep, goats, etc.), laboratory animals (for example, mouse, monkey, rabbit, rat, gerbil, guinea pig, etc.) and avian species (for example, flocks of chickens, geese, turkeys, ducks, pheasants, pigeons, doves etc.). Therefore, the present application provides populations of animals that comprise a naturally occurring variant of a gene set forth in Table 1, 2, 3 or 4 that results in decreased susceptibility to viral infection, thus providing populations of animals that are less susceptible to viral infection. Similarly, if a naturally occurring variant is found and animals possessing a variant form of the gene in their genome are less susceptible to bacterial, parasitic or fungal infection, these animals can be selectively bred to establish populations that are resistant to bacterial, parasitic or fungal infection.

Screening Methods

The present invention provides a method of identifying a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and can decrease infection of a cell by a pathogen comprising: a) contacting a compound with a gene product set forth in Table 1, 2, 3 or 4; b) detecting binding of the compound to the gene product; and c) associating the binding with a decrease in infection by the pathogen.

The present invention provides a method of identifying an agent that decreases infection of a cell by a pathogen comprising: a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 1, 2, 3 or 4; and b) detecting the level and/or activity of the gene product produced by the cellular gene, a decrease or elimination of the gene product and/or gene product activity indicating an agent with antipathogenic activity. Also provided is a method of identifying an agent that decreases infection in a cell by a pathogen comprising: a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 1; b) contacting the cell with a pathogen, wherein the pathogen is not HIV; and c)

determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.

Further provided is a method of identifying an agent that decreases infection in a cell by a pathogen comprising: a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 2; b) contacting the cell with a pathogen, wherein the pathogen is not West Nile Virus; and c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.

Further provided is a method of identifying an agent that decreases infection in a cell by a pathogen comprising: a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 3; b) contacting the cell with a pathogen, wherein the pathogen is not West Nile Virus or Dengue Fever Virus; and c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.

The present invention also provides a method of identifying an agent that decreases infection in a cell by a pathogen comprising: a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 4; b) contacting the cell with a pathogen, wherein the pathogen is not hepatitis C virus; and c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection. This method can further comprise measuring the level of expression and/or activity of the gene product. The level of infection can be determined by determining the level of replication of the pathogen.

The present invention also provides a method of identifying a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and can decrease infection by three or more pathogens comprising: a) contacting a compound with a gene product set forth in Table 1, 2, 3 or 4; b) detecting binding of the compound to the gene product; and c) associating binding with a decrease in infection by three or more pathogens. This method can further comprise optimizing a compound that binds the gene product in an assay that determines the functional ability to decrease infection by three or more pathogens. This method can be cell based or an *in vivo* assay. The three or more pathogens can be any three or more pathogens set forth herein. For example, the three or more pathogens can be respiratory pathogens selected from the group consisting of picornaviruses, orthomyxoviruses, paramyxoviruses, coronaviruses or adenoviruses. In another example, the three or more pathogens can be gastrointestinal pathogens selected from filoviruses, flaviviruses, calciviruses and reoviruses. The three or more pathogens can also be a combination of respiratory and gastrointestinal viruses. In another example, the three or more pathogens can be selected from the group consisting of : an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a

hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus. The cell population used in the method can be the same cell population for each pathogen or can be different cell populations. Typically, the agent would be administered to a different cell population for each pathogen assayed. For example, and not to be limiting, if the pathogens are viruses, a cell population is contacted with the agent and a first virus, another cell population is contacted with the agent and second virus, a third cell population is contacted with the agent and a third virus etc. in order to determine whether the agent inhibits infection by three or more viruses. Since the cell type will vary depending on whether or not a given virus can infect the cell, one of skill in the art would know how to pair the cell type with the virus in order to perform the assay.

This method can further comprise measuring the level of expression and/or activity of the gene product set forth in Table 1, 2, 3 or 4. This method can further comprise associating the level of infection with the level of expression and/or activity a gene product set forth in Table 1, 2, 3 or 4. In the screening methods disclosed herein, the level of infection can be measured, for example, by measuring viral replication.

In the methods of the present invention, if the agent has previously been identified as an agent that decreases or inhibits the level and/or activity of a gene product set forth in Table 1, 2, 3 or 4, this can indicate a decrease in infection. Previous identification of the agent can occur via experimentation, literature, chemical databases, catalogues, or any other means that allow one of skill in the art to associate the agent as an inhibitor of the gene or gene product. A decrease in infection as compared to infection in a cell that was not contacted with the agent known to decrease or inhibit the level and/or activity of the gene product can be sufficient to identify the agent as an agent that decreases or inhibits infection.

The methods described above can be utilized to identify any agent with an activity that decreases infection, prevents infection or promotes cellular survival after infection with a pathogen(s). Therefore, the cell can be contacted with a pathogen before, or after being contacted with the agent. The cell can also be contacted concurrently with the pathogen and the agent. The agents identified utilizing these methods can be used to inhibit infection in cells either *in vitro*, *ex vivo* or *in vivo*.

In the methods of the present invention any cell that can be infected with a pathogen can be utilized. The cell can be prokaryotic or eukaryotic, such as a cell from an insect, fish,

crustacean, mammal, bird, reptile, yeast or a bacterium, such as *E. coli*. The cell can be part of an organism, or part of a cell culture, such as a culture of mammalian cells or a bacterial culture. The cell can also be in a nonhuman subject thus providing *in vivo* screening of agents that decrease infection by a pathogen. Cells susceptible to infection are well known and can be selected based on the pathogen of interest.

The test agents or compounds used in the methods described herein can be, but are not limited to, chemicals, small molecules, inorganic molecules, organic molecules, drugs, proteins, cDNAs, aptamers, large molecules, antibodies, morpholinos, triple helix molecule, peptides, siRNAs, shRNAs, miRNAs, LNAs, antisense RNAs, ribozymes or any other compound. The compound can be random or from a library optimized to bind to a gene or gene product set forth in Table 1, 2, 3 or 4. Drug libraries optimized for the proteins in the class of proteins provided herein can also be screened or tested for binding or activity. Compositions identified with the disclosed approaches can be used as lead compositions to identify other compositions having even greater antipathogenic activity. For example, chemical analogs of identified chemical entities, or variants, fragments or fusions of peptide agents, can be tested for their ability to decrease infection using the disclosed assays. Such analogs can be purchased or synthesized via routine methods known to those of skill in the art. Candidate agents can also be tested for safety in animals and then used for clinical trials in animals or humans.

In the methods described herein, once the cell containing a cellular gene encoding a gene product set forth in Table 1, 2, 3 or 4 has been contacted with an agent, the level of infection can be assessed by measuring an antigen or other product associated with a particular infection. For example, the level of viral infection can be measured by real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR) assay (See for example, Payungporn et al. "Single step multiplex real-time RT-PCR for H5N1 influenza A virus detection." *J Virol Methods*. Sep 22, 2005; Landolt et la. "Use of real-time reverse transcriptase polymerase chain reaction assay and cell culture methods for detection of swine influenza A viruses" *Am J Vet Res*. 2005 Jan;66(1):119-24). If there is a decrease in infection then the composition is an effective agent that decreases infection. This decrease does not have to be complete as the decrease can be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% decrease or any percentage decrease in between.

In the methods set forth herein, the level of the gene product can be measured by any standard means, such as by detection with an antibody specific for the protein. The nucleic acids set forth herein and fragments thereof can be utilized as primers to amplify nucleic acid sequences, such as a gene transcript of a gene set forth in Table 1, 2, 3 or 4 by standard amplification techniques. For example, expression of a gene transcript can be quantified by real

time PCR using RNA isolated from cells. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see White (1997) and the publication entitled "PCR Methods and Applications" (1991, Cold Spring Harbor Laboratory Press), which is incorporated herein by reference in its entirety for amplification methods. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites. PCR has further been described in several patents including U.S. Pat. Nos. 4,683,195, 4,683,202 and 4,965,188. Each of these publications is incorporated herein by reference in its entirety for PCR methods. One of skill in the art would know how to design and synthesize primers that amplify any of the nucleic acid sequences set forth herein or a fragment thereof.

A detectable label may be included in an amplification reaction. Suitable labels include fluorochromes, e.g. fluorescein isothiocyanate (FITC), rhodamine, Texas Red, phycoerythrin, allophycocyanin, 6-carboxyfluorescein (6-FAM), 2',7'-dimethoxy-4',5'-dichloro-6-carboxyfluorescein (JOE), 6-carboxy-X-rhodamine (ROX), 6-carboxy-2',4',7',4,7-hexachlorofluorescein (HEX), 5-carboxyfluorescein (5-FAM) or N,N,N',N'-tetramethyl-6-carboxyrhodamine (TAMRA), radioactive labels, e.g., ³²P, ³⁵S, ³H; etc. The label may be a two stage system, where the amplified DNA is conjugated to biotin, haptens, etc. having a high affinity binding partner, e.g. avidin, specific antibodies, etc., where the binding partner is conjugated to a detectable label. The label may be conjugated to one or both of the primers. Alternatively, the pool of nucleotides used in the amplification is labeled, so as to incorporate the label into the amplification product.

The sample nucleic acid, e.g. amplified fragment, can be analyzed by one of a number of methods known in the art. The nucleic acid can be sequenced by dideoxy or other methods. Hybridization with the sequence can also be used to determine its presence, by Southern blots, dot blots, etc.

In the methods of the present invention, the level of gene product can be compared to the level of the gene product in a control cell not contacted with the compound. The level of gene product can be compared to the level of the gene product in the same cell prior to addition of the compound. Activity or function, can be measured by any standard means, such as by enzymatic

assays that measure the conversion of a substrate to a product or binding assays that measure the binding of a gene product set forth in Table 1, 2, 3 or 4 to another protein, for example.

Moreover, the regulatory region of a gene set forth in Table 1, 2, 3 or 4 can be functionally linked to a reporter gene and compounds can be screened for inhibition of reporter gene expression. Such regulatory regions can be isolated from genomic sequences and identified by any characteristics observed that are characteristic for regulatory regions of the species and by their relation to the start codon for the coding region of the gene. As used herein, a reporter gene encodes a reporter protein. A reporter protein is any protein that can be specifically detected when expressed. Reporter proteins are useful for detecting or quantitating expression from expression sequences. Many reporter proteins are known to one of skill in the art. These include, but are not limited to, β -galactosidase, luciferase, and alkaline phosphatase that produce specific detectable products. Fluorescent reporter proteins can also be used, such as green fluorescent protein (GFP), cyan fluorescent protein (CFP), red fluorescent protein (RFP) and yellow fluorescent protein (YFP).

Viral infection can also be measured via cell-based assays. Briefly, cells (20,000 to 2,500,000) are infected with the desired pathogen, and the incubation continued for 2-7 days. The incubation time is routinely determined by one of skill in the art who would know the incubation times for a particular pathogen. The antiviral agent can be applied to the cells before, during, or after infection with the pathogen. The amount of virus and agent administered can be determined by skilled practitioners. In some examples, several different doses of the potential therapeutic agent can be administered, to identify optimal dose ranges. Following transfection, assays are conducted to determine the resistance of the cells to infection by various agents.

For example, if analyzing viral infection, the presence of a viral antigen can be determined by using antibody specific for the viral protein then detecting the antibody. In one example, the antibody that specifically binds to the viral protein is labeled, for example with a detectable marker such as a fluorophore. In another example, the antibody is detected by using a secondary antibody containing a label. The presence of bound antibody is then detected, for example using microscopy, flow cytometry and ELISA. Similar methods can be used to monitor bacterial, protozoal, or fungal infection (except that the antibody would recognize a bacterial, protozoal, or fungal protein, respectively).

Alternatively, or in addition, the ability of the cells to survive viral infection is determined, for example, by performing a cell viability assay, such as trypan blue exclusion. Plaque assays can be utilized as well.

The amount of protein in a cell, can be determined by methods standard in the art for quantitating proteins in a cell, such as Western blotting, ELISA, ELISPOT,

immunoprecipitation, immunofluorescence (e.g., FACS), immunohistochemistry, immunocytochemistry, etc., as well as any other method now known or later developed for quantitating protein in or produced by a cell.

The amount of a nucleic acid in a cell can be determined by methods standard in the art for quantitating nucleic acid in a cell, such as *in situ* hybridization, quantitative PCR, RT-PCR, Taqman assay, Northern blotting, ELISPOT, dot blotting, etc., as well as any other method now known or later developed for quantitating the amount of a nucleic acid in a cell.

The ability of an antiviral agent to prevent or decrease infection by a virus, for example, any of the viruses listed above, can be assessed in an animal model. Several animal models for viral infection are known in the art. For example, mouse HIV models are disclosed in Sutton et al. (*Res. Initiating Treat. Action*, 8:22-4, 2003) and Pincus et al. (*AIDS Res. Hum. Retroviruses* 19:901-8, 2003); guinea pig models for Ebola infection are disclosed in Parren et al. (*J. Virol.* 76:6408-12, 2002) and Xu et al. (*Nat. Med.* 4:37-42, 1998); chimpanzee models for HCV are disclosed (Lanford et al., *ILAR J.* 2001;42(2):117-26); cynomolgus monkey (*Macaca fascicularis*) models for influenza infection are disclosed in Kuiken et al. (*Vet. Pathol.* 40:304-10, 2003); mouse models for RSV are also disclosed (Sudo et al. *Antivir Chem Chemother.* 1999 May;10(3):135-9) mouse models for herpes are disclosed in Wu et al. (*Cell Host Microbe* 22:5(1):84-94, 2009); mouse models for rhinovirus are disclosed (Bartlett et al. *Nat Med.* 2008 Feb;14(2):199-204); pox models are disclosed in Smee et al. (*Nucleosides Nucleotides Nucleic Acids* 23(1-2):375-83, 2004) and in Bray et al. (*J. Infect. Dis.* 181(1):10-19); animal models for Dengue are available (Shresta et al. *J Virol.* 2006 October; 80(20): 10208–1021; Bente and Rico-Hesse, *Drug Discovery Today: Disease Models* 3(1) 2006: 97-103; Martin et al. *Microbiol Immunol.* 2009 Apr;53(4):216-23); and *Francisella tularensis* models are disclosed in Klimpel et al. (*Vaccine* 26(52): 6874-82, 2008). Other animal models for influenza infection are also available. These include, but are not limited to, a cotton rat model disclosed by Ottolini et al. (*J. Gen. Virol.*, 86(Pt 10): 2823-30, 2005), as well as ferret and mouse models disclosed by Maines et al. (*J. Virol.* 79(18):11788-11800, 2005). One of skill in the art would know how to select an animal model for assessing the *in vivo* activity of an agent for its ability to decrease infection by viruses, bacteria, fungi and parasites.

One of skill in the art would know how to select an animal model for assessing the *in vivo* activity of an agent for its ability to decrease infection by viruses, bacteria, fungi and parasites. Such animal models can also be used to test agents for the ability to ameliorate symptoms associated with viral infection. In addition, such animal models can be used to determine the LD₅₀ and the ED₅₀ in animal subjects, and such data can be used to determine the *in vivo* efficacy of potential agents. LD₅₀ is an index of toxicity (lethal dose 50%), the amount of

the substance that kills 50% of the test population of experimental animals when administered as a single dose. ED₅₀ is the dose of a drug that is pharmacologically effective for 50% of the population exposed to the drug or a 50% response in a biological system that is exposed to the drug. Animal models can also be used to assess antibacterial, antifungal and antiparasitic agents.

Animals of any species, including, but not limited to, birds, ferrets, cats, mice, rats, rabbits, fish (for example, zebrafish or koi) guinea pigs, pigs, micro-pigs, goats, and non-human primates, e.g., baboons, monkeys, and chimpanzees, can be used to generate an animal model of viral infection, bacterial infection, fungal infection or parasitic infection if needed.

For example, for a model of viral infection, the appropriate animal is inoculated with the desired virus, in the presence or absence of the antiviral agent. The amount of virus and agent administered can be determined by skilled practitioners. In some examples, several different doses of the potential therapeutic agent (for example, an antiviral agent) can be administered to different test subjects, to identify optimal dose ranges. The therapeutic agent can be administered before, during, or after infection with the virus. Subsequent to the treatment, animals are observed for the development of the appropriate viral infection and symptoms associated therewith. A decrease in the development of the appropriate viral infection, or symptoms associated therewith, in the presence of the agent provides evidence that the agent is a therapeutic agent that can be used to decrease or even inhibit viral infection in a subject. For example, a virus can be tested which is lethal to the animal and survival is assessed. In other examples, the weight of the animal or viral titer in the animal can be measured. Similar models and approaches can be used for bacterial, fungal and parasitic infections.

In the methods of the present invention, the level of infection can be associated with the level of gene expression and/or activity, such that a decrease or elimination of infection associated with a decrease or elimination of gene expression and/or activity indicates that the agent is effective against the pathogen. For example, the level of infection can be measured in a cell after administration of siRNA that is known to inhibit a gene product set forth in Table 1, 2, 3 or 4. If there is a decrease in infection then the siRNA is an effective agent that decreases infection. This decrease does not have to be complete as the decrease can be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% decrease or any percentage decrease in between. In the event that the compound is not known to decrease expression and/or activity of a gene product set forth in Table 1, 2, 3 or 4, the level of expression and/or activity of can be measured utilizing the methods set forth above and associated with the level of infection. By correlating a decrease in expression and/or activity with a decrease in infection, one of skill in the art can confirm that a decrease in infection is effected by a decrease in expression and/or activity of a gene or gene

product set forth in Table 1, 2, 3 or 4. Similarly, the level of infection can be measured in a cell, utilizing the methods set forth above and known in the art, after administration of a chemical, small molecule, drug, protein, cDNA, antibody, aptamer, shRNA, miRNA, morpholino, antisense RNA, LNA, ribozyme or any other compound. If there is a decrease in infection, then the chemical, small molecule, drug, protein, cDNA, antibody, shRNA, miRNA, morpholino, antisense RNA, ribozyme or any other compound is an effective antipathogenic agent.

The genes and nucleic acids of the invention can also be used in polynucleotide arrays. Polynucleotide arrays provide a high throughput technique that can assay a large number of polynucleotide sequences in a single sample. This technology can be used, for example, to identify samples with reduced expression of as compared to a control sample. This technology can also be utilized to determine the effects of reduced expression of a gene set forth in Table 1, 2, 3 or 4 on other genes. In this way, one of skill in the art can identify genes that are upregulated or downregulated upon reducing expression of a gene set forth in Table 1, 2, 3 or 4. Similarly, one of skill in the art can identify genes that are upregulated or downregulated upon increased expression of a gene set forth in Table 1, 2, 3, or 4. This allows identification of other genes that are upregulated or downregulated upon modulation of expression that can be targets for therapy, such as antiviral therapy, antibacterial therapy, antiparasitic therapy or antifungal therapy.

To create arrays, single-stranded polynucleotide probes can be spotted onto a substrate in a two-dimensional matrix or array. Each single-stranded polynucleotide probe can comprise at least 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, or 30 or more contiguous nucleotides selected from nucleotide sequences set forth under GenBank Accession Nos. herein and other nucleic acid sequences that would be selected by one of skill in the art depending on what genes, in addition to one or more of the genes set forth in Table 1, 2, 3 or 4 are being analyzed.

The array can also be a microarray that includes probes to different polymorphic alleles of these genes. A polymorphism exists when two or more versions of a nucleic acid sequence exist within a population of subjects. For example, a polymorphic nucleic acid can be one where the most common allele has a frequency of 99% or less. Different alleles can be identified according to differences in nucleic acid sequences, and genetic variations occurring in more than 1% of a population (which is the commonly accepted frequency for defining polymorphism) are useful polymorphisms for certain applications. The allelic frequency (the proportion of all allele nucleic acids within a population that are of a specified type) can be determined by directly counting or estimating the number and type of alleles within a

population. Polymorphisms and methods of determining allelic frequencies are discussed in Hartl, D.L. and Clark, A.G., Principles of Population Genetics, Third Edition (Sinauer Associates, Inc., Sunderland Massachusetts, 1997), particularly in chapters 1 and 2.

These microarrays can be utilized to detect polymorphic alleles in samples from subjects.

5 Such alleles may indicate that a subject is more susceptible to infection or less susceptible to infection. For example, microarrays can be utilized to detect polymorphic versions of genes set forth in Table 1, 2, 3 or 4 that result in decreased gene expression and/or decreased activity of the gene product to identify subjects that are less susceptible to viral infection. In addition, the existence of an allele associated with decreased expression in a healthy individual can be used to
10 determine which genes are likely to have the least side effects if the gene product is inhibited or bound or may be selected for in commercial animals and bred into the population.

The substrate can be any substrate to which polynucleotide probes can be attached, including but not limited to glass, nitrocellulose, silicon, and nylon. Polynucleotide probes can be bound to the substrate by either covalent bonds or by non-specific interactions, such as
15 hydrophobic interactions. Techniques for constructing arrays and methods of using these arrays are described in EP No. 0 799 897; PCT No. WO 97/29212; PCT No. WO 97/27317; EP No. 0 785 280; PCT No. WO 97/02357; U.S. Pat. Nos. 5,593,839; 5,578,832; EP No. 0 728 520; U.S. Pat. No. 5,599,695; EP No. 0 721 016; U.S. Pat. No. 5,556,752; PCT No. WO 95/22058; and U.S. Pat. No. 5,631,734. Commercially available polynucleotide arrays, such as Affymetrix
20 GeneChip.TM., can also be used. Use of the GeneChip.TM. to detect gene expression is described, for example, in Lockhart et al., Nature Biotechnology 14:1675 (1996); Chee et al., Science 274:610 (1996); Hacia et al., Nature Genetics 14:441, 1996; and Kozal et al., Nature Medicine 2:753, 1996.

The present invention also provides a method of identifying an agent that can decrease
25 infection by three or more pathogens comprising: a) administering the agent to three or more cell populations containing a cellular gene encoding a gene product set forth in Table 1, 2, 3 or 4; b) contacting the three or more cell populations with a pathogen selected wherein each population is contacted with a different pathogen; and c) determining the level of infection, a decrease or elimination of infection by three or more pathogens indicating that the agent is an
30 agent that decreases infection by three or more pathogens. In the screening methods set forth herein, the three or more pathogens can be three or more respiratory viruses selected from the one or more families from group consisting of: picornaviruses, an orthomyxoviruses, a paramyxoviruses, a coronaviruses, or an adenoviruses. The three or more pathogens can be three or more gastrointestinal viruses selected from one or more families from the group

consisting of: flaviviruses, filoviruses, calciviruses or reoviruses. In another example, the three or more pathogens can be three or more viruses selected from gastrointestinal viruses and respiratory viruses. In another example, the three or more pathogens can be selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, West Nile virus, Chikungunya virus or a Dengue fever virus. The three or more pathogens can also be selected from the group consisting of: HIV, a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, hantavirus, Rift Valley Fever virus Ebola virus, Marburg virus or Dengue Fever virus. In another example, the three or more pathogens can be selected from the group consisting of: influenza, a pox virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, hantavirus, Rift Valley Fever virus Ebola virus, Marburg virus or Dengue Fever virus

Also provided is a method of identifying a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and can decrease infection by three or more pathogens comprising: a) contacting a compound with a gene product set forth in Table 1, 2, 3 or 4; b) detecting binding of the compound to the gene product; and c) associating binding with a decrease in infection by three or more pathogens. This method can further comprise optimizing a compound that binds the gene product in an assay that determines the functional ability to decrease infection by three or more pathogens. A set forth above, as utilized herein "three or more" includes four or more, five or more, six or more, seven or more, etc. This assay can be cell based or *in vivo* based.

Methods of making compounds

The present invention provides a method of making a compound that decreases infection of a cell by a pathogen, comprising: a) synthesizing a compound; b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 1; c) contacting the cell with an infectious pathogen, wherein the pathogen is not HIV; d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection; and e) associating the agent with decreasing expression or activity of the gene product.

Also provided is a method of making a compound that decreases infection of a cell by a pathogen, comprising: a) synthesizing a compound; b) administering the compound to a cell

containing a cellular gene encoding a gene product set forth in Table 2; c) contacting the cell with an infectious pathogen, wherein the pathogen is not West Nile Virus; d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection; and e) associating the agent with decreasing expression or activity of the gene product.

Further provided is a method of making a compound that decreases infection of a cell by a pathogen, comprising: a) synthesizing a compound; b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 3; c) contacting the cell with an infectious pathogen, wherein the pathogen is not West Nile virus or Dengue fever virus; d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection; and e) associating the agent with decreasing expression or activity of the gene product.

The present invention also provides a method of making a compound that decreases infection of a cell by a pathogen, comprising: a) synthesizing a compound; b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 4; c) contacting the cell with an infectious pathogen, wherein the pathogen is not hepatitis C; d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection; and e) associating the agent with decreasing expression or activity of the gene product. The association can be made by measuring the level of expression and/or activity of the gene product. As set forth above, the association can also be made by one of skill in the art if there is *a priori* knowledge, for example, via experimentation, literature, chemical databases or catalogues that the agent decreases expression and or activity of a gene or gene product. The level of infection can be determined by determining the level of replication of the pathogen.

Further provided is a method of making a compound that decreases infection in a cell by a pathogen, comprising: a) optimizing a compound to bind a gene product set forth in Table 1, 2, 3 or 4; b) administering the compound to a cell containing a cellular gene encoding the gene product; c) contacting the cell with an infectious pathogen; d) determining the level of infection, a decrease or elimination of infection indicating the making of a compound that decreases infection in a cell by a pathogen. This method can further synthesizing therapeutic quantities of the compound. The method can further comprise packaging of the therapeutic quantities.

The present invention also provides a method of synthesizing a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and decreases infection by a pathogen comprising: a) contacting a library of compounds with a gene product set forth in Table 1, 2, 3 or 4; b)

associating binding with a decrease in infection; and c) synthesizing derivatives of the compounds from the library that bind to the gene product.

The present invention also provides a business method to reduce the cost of drug discovery of drugs that can reduce infection by a pathogen comprising: screening, outside of the United States, for drugs that reduce infection by binding to or reducing the function of a gene product set forth in Table 1, 2, 3 or 4; and b) importing drugs that reduce infection into the United States. Also provided is a method of making drugs comprising directing the synthesis of drugs that reduce infection by binding to or reducing the function of a gene or gene product set forth in Table 1, 2, 3 or 4.

EXAMPLES

siRNA studies

Any of the genes set forth in Table 1, 2, 3 or 4 is further analyzed by contacting cells comprising a gene set forth in Table 1, 2, 3 or 4 with siRNA that specifically targets the gene product of the gene, and any pathogen set forth herein to identify the gene as a gene involved in pathogenic infection (for example, and not to be limiting, an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, West Nile virus, Chikungunya virus or a Dengue fever virus). A decrease in viral infection indicates that the gene is a gene that is involved in pathogenic infection. This process can be performed for all of the genes set forth herein with any of the viruses, bacteria, parasites or fungi set forth herein.

siRNA Transfections can be performed as follows: Pools of 4 duplexed siRNA molecules targeting a gene of interest are reconstituted to a final working concentration of 50uM as directed by the manufacturer (Qiagen). Twenty-four hours prior to transfection, cells are plated in 6-well dishes at 3×10^5 cells per well, such that at the time of transfection, the cells are approximately 30% confluent. Prior to transfection, the cells are washed once with 1X phosphate buffered saline, and the medium replaced with approximately 1.8ml antibiotic-free medium. siRNA aliquots are diluted with Opti-MEM and RNaseOUT (Invitrogen), 100ul and 1ul per transfection, respectively. In a separate tube, transfection reagent Lipofectamine2000 (Invitrogen) or Oligofectamine (Invitrogen) are diluted in Opti-MEM as directed by the manufacturer. Following a 5 minute incubation at room temperature, the diluted siRNA is

added to the transfection reagent mixture, and incubated for an additional 20 minutes prior to adding to independent wells of the 6-well dishes. Transfections are incubated at 37°C for 48 hours without changing the medium.

Virus Infections: Following 48-hour transfection, medium is aspirated from 6-well plates. Viruses are diluted in the appropriate medium and 500ul of either virus-free medium or virus dilution is added to each well, and adsorption is allowed to occur at the appropriate temperature for 1 hour. Following adsorption, inoculum is aspirated off the cells, cells are washed once with 1X phosphate buffered saline, and 2ml growth medium is added to the cells. The infected cells are incubated for 72 hours at the appropriate temperature prior to harvesting samples for viral titration.

Viral Genomic Extractions: Seventy-hours after inoculating cells, medium is harvested from 6-well dishes and centrifuged for 2 minutes at 10,000 rpm to remove any cellular debris. 200ul of clarified medium is added to 25ul Proteinase K, to which 200ul PureLink96 Viral RNA/DNA lysis buffer (Invitrogen) is added according to the manufacturer. Samples were processed and viral genomic RNA or DNA is extracted using an epMotion 5075 robotics station (Eppendorf) and the PureLink96 Viral RNA/DNA kit (Invitrogen).

cDNA and Quantitative Real-Time PCR Reactions: 3ul of extracted viral RNA is converted to cDNA using M-MLV reverse transcriptase (Invitrogen) and AmpliTaq Gold PCR buffer (Applied Biosystems). MgCl₂, dNTPs and RNaseOUT (Invitrogen) are added to achieve a final concentration of 5mM, 1mM and 2U/ul, respectively. Random hexamers (Applied Biosystems) are added to obtain 2.5mM final concentration. Reactions are incubated at 42°C for 1 hour, followed by heat inactivation of the reverse transcriptase at 92°C for 10 minutes. Quantitative real-time PCR reactions are set up in 10ul volumes using 1ul of template cDNA or extracted viral DNA using virus-specific TaqMan probes (Applied Biosystems) and RealMasterMix (Eppendorf). 2-step reactions are allowed to proceed through 40 to 50 cycles on an ep RealPlex thermocycler (Eppendorf). Quantitative standards for real-time PCR are constructed by cloning purified amplicons into pCR2-TOPO (Invitrogen) and sequenced as necessary. The amount of viral replication in the cells contacted with siRNA to the gene of interest is calculated and compared to the amount of viral replication in control cells that did not receive siRNA targeting the gene of interest.

Compounds are assessed as follows. Duplicate experiments are performed as follows. Prior to compound exposure cells are seeded into 12-well tissue culture plates and allowed to adhere to the vessel surface. The compounds are serially diluted and 100μl is added to the growth medium in triplicate wells to obtain the indicated final concentration of compound or

solvent. Cells are incubated in the presence of the test compound for about 24 hours at 37°C under 5% CO₂.

Following the pre-treatment period, cells are examined under a phase-contrast microscope to determine any cytotoxic effects at the treatment dosages. The pre-treatment medium is then aspirated off the cells, and the specified virus, diluted in serum- and compound-free growth medium, is added to the cells. Virus is allowed to adsorb to the cells at 37°C under 5% CO₂. Following adsorption, the viral inoculum is aspirated off the cells and replaced with growth medium supplemented with 2% FBS, 1% L-glutamine, 1% penicillin/streptomycin and the respective concentration of test compound. Cells are incubated under the same conditions for an additional 72 hours. As stated above, incubation period can vary depending on the pathogen. 200µl samples are harvested from each well and viral RNA or DNA is extracted using the PureLink 96 Viral RNA/DNA extraction kit (Invitrogen) as directed by the manufacturer. Viral nucleic acid is subjected to reverse transcription to generate cDNA, which is subsequently used as the template for quantitative real-time TaqMan PCR to titrate viral replication using a Mastercycler ep realplex² (Eppendorf). The experiment described above can be performed to determine the effect of any of the compounds set forth herein on any pathogenic infection, for example, and not to be limiting, a pox virus, BVDV, HIV, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.

Any of the experiments set forth herein can optionally comprise the step of assessing toxicity of any of the compounds set forth herein via any of the toxicity measurement methods described herein, or via any of the toxicity measurement methods known to one of skill in the art, such as, for example, the CytoTox-Glo assay (see Niles, A. et al. (2007) *Anal. Biochem.* 366, 197–206) or the Cell-Titer-Glo assay from Promega.

What is claimed is:

1. A method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) selected from the group consisting of EDNRA, BCR, CA2, CHRNA7, CXCR4, EGFR, F2, GRIA2, HDAC1, KCNJ11, MMP9, PDE8A, PLK1, POLE, SRD5A2, TUBA8 and DPP4, wherein the pathogen is not HIV.
2. A method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, wherein the pathogen is not HIV.
3. A method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 2, wherein the pathogen is not West Nile Virus.
4. The method of claim 3, wherein the gene(s) or gene product(s) are selected from the group consisting of CACNA1A, PDE3B and TUBB4.
5. A method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 3, wherein the pathogen is not West Nile Virus or Dengue Fever Virus.
6. The method of claim 5, wherein the gene(s) or gene product(s) is ADRA1D.
7. A method of inhibiting infection in a cell by a pathogen comprising decreasing expression or activity of one or more gene(s) or gene product(s) set forth in Table 4, wherein the pathogen is not hepatitis C virus.
8. The method of claim 7, wherein the gene(s) or gene product(s) are selected from the group consisting of STAT and TBXA2R.
9. The method of any of claims 1-8, wherein infection is decreased by decreasing the replication of the pathogen.
10. The method of any of claims 1-9, wherein the pathogen is a respiratory virus.
11. The method of claim 10, wherein the respiratory virus is a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus, or an adenovirus.
12. The method of claim 11, wherein the respiratory virus is selected from the group consisting of influenza virus, parainfluenza virus, adenovirus, rhinovirus and RSV.
13. The method of any of claims 1-9, wherein the pathogen is a gastrointestinal virus.

14. The method of claim 13, wherein the gastrointestinal virus is a picornavirus, a filovirus, an adenovirus, a calicivirus or a reovirus.
15. The method of claim 14, wherein the gastrointestinal virus is selected from the group consisting of: a reovirus, a Norwalk virus, an Ebola virus, a Marburg virus, an adenovirus, a rotavirus and an enterovirus.
16. The method of claim 1 or 2, wherein the pathogen is a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Hepatitis E virus, Epstein Barr Virus, Human Papilloma Virus, CMV, West Nile virus, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.
17. The method of claim 3 or 4, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, a hepatitis E virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, Chikungunya virus or a Dengue fever virus.
18. The method of claim 5 or 6, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis C virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies or Chikungunya virus.
19. The method of claim 7 or 8, wherein the pathogen is an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis B virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE,

Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, a Dengue Fever virus, West Nile virus or Chikungunya virus.

20. The method of any of claims 1-19, wherein expression or activity of the gene or gene product is decreased by contacting the cell with a composition comprising a chemical, a compound, an LNA, an aptamer, a small molecule, a drug, a protein, a cDNA, an antibody, a morpholino, a triple helix molecule, an miRNA, an siRNA, an shRNA, an antisense nucleic acid or a ribozyme.
21. The method of claim 20, wherein decreasing expression comprises decreasing translation of an mRNA encoding a gene product set forth in Table 1, 2, 3 or 4.
22. The method claim 20, wherein the composition comprises an antisense nucleic acid that specifically hybridizes and decreases expression or activity of the gene product.
23. The method of claim 20, wherein the composition comprises an siRNA that decreases expression or activity of the gene product.
24. The method of claim 20, wherein the composition comprises an antibody that specifically binds to a protein.
25. The method of claims 1-24, wherein the cell is an *in vitro*, an *ex vivo* or an *in vivo* cell.
26. The method of any of claims 1-25, wherein the cell is in a subject.
27. The method of claim 26, wherein an effective amount of a composition that decreases the expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4 is administered to the subject.
28. A method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by two or more respiratory viruses selected from the group consisting of: a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus and an adenovirus.
29. The method of claim 28, wherein the two or more respiratory viruses are selected from the group consisting of an influenza virus, a parainfluenza virus, an adenovirus, a rhinovirus and an RSV virus.
30. A method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits infection by two or more

- gastrointestinal viruses selected from the group consisting of: a flavivirus, an adenovirus, a filovirus, a calcivirus or a reovirus.
31. The method of claim 30, wherein the two or more gastrointestinal viruses are selected from the group consisting of: a reovirus, an adenovirus, a Norwalk virus, an Ebola virus, a Marburg virus, an adenovirus, a rotavirus, a Dengue fever virus and an enterovirus.
 32. A method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by one or more pathogens selected from the group consisting of: a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus, an adenovirus, and inhibits infection by one or more pathogens selected from the group consisting of: a flavivirus, a filovirus, a calcivirus or a reovirus.
 33. A method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4 wherein the composition inhibits infection by three or more pathogens.
 34. The method of claim 33, wherein the pathogen is a virus.
 35. The method of claim 34, wherein the three or more viruses are selected from the group consisting of: an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis B virus, a Hepatitis C virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, a Dengue Fever virus, West Nile virus or Chikungunya virus.
 36. A method of decreasing infection in a subject comprising administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, 2, 3 or 4, wherein the composition inhibits infection by an HIV virus and a hepatitis virus.
 37. The method of claim 36, wherein the hepatitis virus is hepatitis B or hepatitis C.
 38. A method of decreasing an unspecified respiratory infection in a subject comprising:

- a) diagnosing a subject with an unspecified respiratory infection; and
 - b) administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits infection by two or more respiratory viruses selected from the group consisting of a picornavirus, an orthomyxovirus, a paramyxovirus, a coronavirus, or an adenovirus.
39. A method of decreasing an unspecified gastrointestinal infection in a subject comprising:
- a) diagnosing a subject with an unspecified gastrointestinal infection; and
 - b) administering to the subject an effective amount of a composition that decreases expression or activity of one or more gene(s) or gene product(s) set forth in Table 1, Table 2, Table 3 or Table 4, wherein the composition inhibits infection by two or more gastrointestinal viruses selected from the group consisting of a flavivirus, an adenovirus, a filovirus, a calcivirus or a reovirus.
40. A method of identifying a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and can decrease infection of a cell by a pathogen comprising:
- a) contacting a compound with a gene product set forth in Table 1, 2, 3 or 4;
 - b) detecting binding of the compound to the gene product; and
 - c) associating binding with a decrease in infection by the pathogen.
41. The method of claim 40, further comprising optimizing a compound that binds the gene product in an assay that determines the functional ability to decrease infection.
42. The method of claim 40-41, wherein the assay is a cell based assay.
43. The method of claim 40-41, wherein the assay is an *in vivo* assay.
44. A method of identifying an agent that decreases infection of a cell by a pathogen comprising:
- a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 1, 2, 3 or 4; and
 - b) detecting the level and/or activity of the gene product produced by the cellular gene, a decrease or elimination of the gene product and/or gene product activity indicating an agent with antipathogenic activity.

45. The method of claim 44, wherein the activity is binding between a gene product set forth in Table 1, 2, 3 or 4 and another cellular protein or binding between a gene product set forth in Table 1, 2, 3 or 4 and a pathogenic (i.e. non-host) protein .
46. A method of identifying an agent that decreases infection in a cell by a pathogen comprising:
- a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 1;
 - b) contacting the cell with a pathogen, wherein the pathogen is not HIV; and
 - c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
47. A method of identifying an agent that decreases infection in a cell by a pathogen comprising:
- a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 2;
 - b) contacting the cell with a pathogen, wherein the pathogen is not West Nile Virus; and
 - c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
48. A method of identifying an agent that decreases infection in a cell by a pathogen comprising:
- a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 3;
 - b) contacting the cell with a pathogen, wherein the pathogen is not West Nile Virus or Dengue Fever Virus; and
 - c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
49. A method of identifying an agent that decreases infection in a cell by a pathogen comprising:
- a) administering the agent to a cell containing a cellular gene encoding a gene product set forth in Table 4;
 - b) contacting the cell with a pathogen, wherein the pathogen is not Hepatitis C; and
 - c) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.

50. The method of claims 46-49, further comprising measuring the level of expression and/or activity of the gene product.
51. The method of claim 50, wherein the level of infection is determined by determining the level of replication of the pathogen.
52. A method of making a compound that decreases infection of a cell by a pathogen, comprising:
- a) synthesizing a compound;
 - b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 1;
 - c) contacting the cell with an infectious pathogen, wherein the pathogen is not HIV;
 - d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
 - e) associating the agent with decreasing expression or activity of the gene product.
53. A method of making a compound that decreases infection of a cell by a pathogen, comprising:
- a) synthesizing a compound;
 - b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 2;
 - c) contacting the cell with an infectious pathogen, wherein the pathogen is not West Nile Virus;
 - d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
 - e) associating the agent with decreasing expression or activity of the gene product.
54. A method of making a compound that decreases infection of a cell by a pathogen, comprising:
- a) synthesizing a compound;
 - b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 3;
 - c) contacting the cell with an infectious pathogen, wherein the pathogen is not West Nile Virus or Dengue Fever Virus;

- d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
 - e) associating the agent with decreasing expression or activity of the gene product.
55. A method of making a compound that decreases infection of a cell by a pathogen, comprising:
- a) synthesizing a compound;
 - b) administering the compound to a cell containing a cellular gene encoding a gene product set forth in Table 4;
 - c) contacting the cell with an infectious pathogen, wherein the pathogen is not hepatitis C;
 - d) determining the level of infection, a decrease or elimination of infection indicating that the agent is an agent that decreases infection.
 - e) associating the agent with decreasing expression or activity of the gene product.
56. The method of claims 52-55, comprising making the association by measuring the level of expression and/or activity of the gene product.
57. The method of claims 52-55, wherein the level of infection is determined by determining the level of replication of the pathogen.
58. A method of making a compound that decreases infection in a cell by a pathogen, comprising:
- a) optimizing a compound to bind a gene product set forth in Table 1, 2, 3 or 4;
 - b) administering the compound to a cell containing a cellular gene encoding the gene product;
 - c) contacting the cell with an infectious pathogen;
 - d) determining the level of infection, a decrease or elimination of infection indicating the making of a compound that decreases infection in a cell by a pathogen.
59. The method of claim 58, wherein the level of infection is determined by determining the level of replication of the pathogen.

60. A method of making a compound that decreases infection in a cell by a pathogen comprising further synthesizing therapeutic quantities of the compound made in claim 58.
61. A method of synthesizing a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and decreases infection by a pathogen comprising:
- a) contacting a library of compounds with a gene product set forth in Table 1, 2, 3 or 4;
 - b) associating binding with a decrease in infection and;
 - c) synthesizing derivatives of the compounds from the library that bind to the gene product.
62. A business method to reduce the cost of drug discovery of drugs that can reduce infection by a pathogen comprising:
- a) screening, outside of the United States, for drugs that reduce infection by binding to or reducing the function of a gene product set forth in Table 1, 2, 3 or 4; and
 - b) importing drugs that reduce infection into the United States.
63. A method of making drugs comprising directing the synthesis of drugs that reduce infection by binding to or reducing the function of a gene or gene product set forth in Table 1, 2, 3 or 4.
64. A method of identifying an agent that can decrease infection by three or more pathogens comprising:
- a) administering the agent to three or more cell populations containing a cellular gene encoding a gene product set forth in Table 1, 2, 3 or 4;
 - b) contacting the three or more cell populations with a pathogen selected wherein each population is contacted with a different pathogen; and
 - c) determining the level of infection, a decrease or elimination of infection by three or more pathogens indicating that the agent is an agent that decreases infection by three or more pathogens.
65. A method of identifying a compound that binds to a gene product set forth in Table 1, 2, 3 or 4 and can decrease infection by three or more pathogens comprising
- a) contacting a compound with a gene product set forth in Table 1, 2, 3 or 4;
 - b) detecting binding of the compound to the gene product; and

- c) associating binding with a decrease in infection by three or more pathogens.
66. The method of claim 65, further comprising optimizing a compound that binds the gene product in an assay that determines the functional ability to decrease infection by three or more pathogens.
67. The method of claim 66, wherein the assay is a cell based assay.
68. The method of claim 67, wherein the assay is an *in vivo* assay.
69. The method of claim 67 or 68, wherein the three or more pathogens are selected from the group consisting of an HIV virus, a pox virus, a herpes virus, an RSV virus, an influenza virus, a hepatitis B virus, a Hepatitis C virus, Epstein Barr Virus, Human Papilloma Virus, CMV, a rhinovirus, an adenovirus, measles virus, Marburg virus, Ebola virus, Rift Valley Fever Virus, LCM, Junin virus, Machupo virus, Guanarito virus, Lassa Fever virus, Hantavirus, SARS virus, Nipah virus, Caliciviruses, Hepatitis A, LaCrosse, California encephalitis, VEE, EEE, WEE, Japanese Encephalitis Virus, Kyasanur Forest Virus, Yellow Fever, Rabies, a Dengue Fever virus, West Nile virus or Chikungunya virus.
70. A method of decreasing the toxicity of a toxin in a cell comprising administering to the cell an effective amount of a composition that decreases expression or activity of one or more gene(s) or a gene product (s) set forth in Table 1, 2, 3 or 4.
71. The method of claim 70, wherein the toxin is a ricin toxin, a *C. perfringens* toxin, *Clostridium botulinum* toxin, a *C. difficile* toxin or a *staphylococcal* toxin.
72. The method of claim 71, wherein the cell is *in vitro*, *ex vivo*, or *in vivo*.