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(54) **GENES MAMMALIENS INTERVENANT DANS L'INFECTION
VIRALE ET LA NEUTRALISATION TUMORALE**
(54) **MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND
TUMOR SUPPRESSION**

(57) L'invention concerne des procédés permettant d'identifier des gènes cellulaires nécessaires à la multiplication des virus et des gènes cellulaires nécessaires à la neutralisation tumorale. L'invention concerne donc des acides nucléiques et des procédés liés à la réduction ou à la prévention de l'infection virale ou du cancer. L'invention concerne également des procédés permettant de fournir des cultures cellulaires sensiblement dépourvues de virus et des procédés relatifs au criblage de gènes additionnels de ce type.

(57) The present invention provides methods of identifying cellular genes necessary for viral growth and cellular genes that function as tumor suppressors. Thus, the present invention provides nucleic acids related to and methods of reducing or preventing viral infection or cancer. The invention also provides methods of producing substantially virus-free cell cultures and methods for screening for additional such genes.

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(21) International Application Number: PCT/US98/21276 (22) International Filing Date: 8 October 1998 (08.10.98) (30) Priority Data: 60/062,021 10 October 1997 (10.10.97) US (71) Applicant (for all designated States except US): VAN- DERBILT UNIVERSITY [US/US]; 305 Kirkland Hall, Nashville, TN 37240 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): RUBIN, Donald, H. [US/US]; 1937 Edenbridge Way, Nashville, TN 37215 (US). ORGAN, Edward, L. [US/US]; 2505 Essex Place, Nashville, TN 37202 (US). DUBOIS, Raymond, N. [US/US]; 281 St. Andrew Drive, Franklin, TN 37064 (US). (74) Agents: KIMPEL, Janice, A. et al.; Needle & Rosenberg, P.C., 127 Peachtree Street, N.E., Atlanta, GA 30303 (US).		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>Without international search report and to be republished upon receipt of that report.</i>
(54) Title: MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION (57) Abstract The present invention provides methods of identifying cellular genes necessary for viral growth and cellular genes that function as tumor suppressors. Thus, the present invention provides nucleic acids related to and methods of reducing or preventing viral infection or cancer. The invention also provides methods of producing substantially virus-free cell cultures and methods for screening for additional such genes.		

MAMMALIAN GENES INVOLVED IN VIRAL INFECTION AND TUMOR SUPPRESSION

BACKGROUND

Field of the Invention

The present invention provides methods of identifying cellular genes used for
5 viral growth or for tumor progression. Thus, the present invention relates to nucleic
acids related to and methods of reducing or preventing viral infection and for suppressing
tumor progression. The invention also relates to methods for screening for additional
such genes.

Background art

10 Various projects have been directed toward isolating and sequencing the genome
of various animals, notably the human. However, most methodologies provide
nucleotide sequences for which no function is linked or even suggested, thus limiting the
immediate usefulness of such data.

The present invention, in contrast, provides methods of screening only for nucleic
15 acids that are involved in a specific process, *i.e.*, viral infection or tumor progression.
For viral infection, the nucleic acids isolated are useful in treatments for these processes
because by this method only nucleic acids which are also nonessential to the cell are
isolated. Such methods are highly useful, since they ascribe a function to each isolated
gene, and thus the isolated nucleic acids can immediately be utilized in various specific
20 methods and procedures.

For, example, the present invention provides methods of isolating nucleic acids
encoding gene products used for viral infection, but nonessential to the cell. Viral
infections are significant causes of human morbidity and mortality. Understanding the
molecular mechanisms of such infections will lead to new approaches in their treatment
25 and control.

Viruses can establish a variety of types of infection. These infections can be
generally classified as lytic or persistent, though some lytic infections are considered
persistent. Generally, persistent infections fall into two categories: (1) chronic
(productive) infection, *i.e.*, infection wherein infectious virus is present and can be
30 recovered by traditional biological methods and (2) latent infection, *i.e.*, infection

wherein viral genome is present in the cell but infectious virus is generally not produced except during intermittent episodes of reactivation. Persistence generally involves stages of both productive and latent infection.

Lytic infections can also persist under conditions where only a small fraction of the total cells are infected (smoldering (cycling) infection). The few infected cells release virus and are killed, but the progeny virus again only infect a small number of the total cells. Examples of such smoldering infections include the persistence of lactic dehydrogenase virus in mice (Mahy, B.W.J., *Br. Med. Bull.* 41: 50-55 (1985)) and adenovirus infection in humans (Porter, D.D. pp. 784-790 in Baron, S., ed. *Medical Microbiology* 2d ed. (Addison-Wesley, Menlo Park, CA 1985)).

Furthermore, a virus may be lytic for some cell types but not for others. For example, evidence suggests that human immunodeficiency virus (HIV) is more lytic for T cells than for monocytes/macrophages, and therefore can result in a productive infection of T cells that can result in cell death, whereas HIV-infected mononuclear phagocytes may produce virus for considerable periods of time without cell lysis. (Klatzmann, et al. *Science* 225:59-62 (1984); Koyanagi, et al. *Science* 241:1673-1675 (1988); Sattentau, et al. *Cell* 52:631-633 (1988)).

Traditional treatments for viral infection include pharmaceuticals aimed at specific virus derived proteins, such as HIV protease or reverse transcriptase, or recombinant (cloned) immune modulators (host derived), such as the interferons. However, the current methods have several limitations and drawbacks which include high rates of viral mutations which render anti-viral pharmaceuticals ineffective. For immune modulators, limited effectiveness, limiting side effects, a lack of specificity all limit the general applicability of these agents. Also the rate of success with current antivirals and immune-modulators has been disappointing.

One aspect of the current invention focuses on isolating genes that are not essential for cellular survival when disrupted in one or both alleles, but which are required for virus replication. This may occur with a dose effect, in which one allele knock-out may confer the phenotype of virus resistance for the cell. As targets for therapeutic intervention, inhibition of these cellular gene products, including: proteins, parts of proteins (modification enzymes that include, but are not restricted to glycosylation, lipid modifiers [myriolate, etc.]), lipids, transcription elements and RNA

regulatory molecules, may be less likely to have profound toxic side effects and virus mutation is less likely to overcome the 'block' to replicate successfully.

The present invention provides a significant improvement over previous methods of attempted therapeutic intervention against viral infection by addressing the cellular
5 genes required by the virus for growth. Therefore, the present invention also provides an innovative therapeutic approach to intervention in viral infection by providing methods to treat viruses by inhibiting the cellular genes necessary for viral infection. Because these genes, by virtue of the means by which they are originally detected, are nonessential to the cell's survival at a level of expression necessary to inhibit virus
10 replication, these treatment methods can be used in a subject without serious detrimental effects to the subject, as has been found with previous methods. The present invention also provides the surprising discovery that virally infected cells are dependent upon a factor in serum to survive. Therefore, the present invention also provides a method for treating viral infection by inhibiting this serum survival factor. Finally, these discoveries
15 also provide a novel method for removing virally infected cells from a cell culture by removing, inhibiting or disrupting this serum survival factor in the culture so that non-infected cells selectively survive.

The selection of tumor suppressor gene(s) has become an important area in the discovery of new target for therapeutic intervention of cancer. Since the discovery that
20 cells are restricted from promiscuous entry into the cell cycle by specific genes that are capable of suppressing a 'transformed' phenotype, considerable time has been invested in the discovery of such genes. Some of these genes include the gene associated by rhabdomyosarcoma (Rb) and the p53 (apoptosis related) encoding gene. The present invention provides a method, using gene-trapping, to select cell lines that have a
25 transformed phenotype from cells that are not transformed and to isolate from these cells a gene that can suppress a malignant, or transformed, phenotype. Thus, by the nature of the isolation process, a function is associated with the isolated genes. The capacity to select quickly tumor suppressor genes can provide unique targets in the process of treating or preventing, and even for diagnostic testing of, cancer.

DETAILED DESCRIPTION OF THE INVENTION

The present invention utilizes a "gene trap" method along with a selection process to identify and isolate nucleic acids from genes associated with a particular
5 function. Specifically, it provides a means of isolating cellular genes necessary for viral infection but not essential for the cell's survival, and it provides a means of isolating cellular genes that suppress tumor progression.

The present invention also provides a core discovery that virally infected cells become dependent upon at least one factor present in serum for survival, whereas non-
10 infected cells do not exhibit this dependence. This core discovery has been utilized in the present invention in several ways. First, inhibition of the "serum survival factor" can be utilized to eradicate persistently virally infected cells from populations of non-infected cells. Inhibition of this factor can also be used to treat virus infection in a subject, as further described herein. Additionally, inhibition of or withdrawal of the
15 serum survival factor in tissue culture allows for the detection of cellular genes required for viral replication yet nonessential for an uninfected cell to survive. The present invention further provides several such cellular genes, as well as methods of treating viral infections by inhibiting the functioning of such genes.

The invention also provides cellular genes whose overexpression is associated
20 with inhibition of viral growth and/or reproduction.

The present method provides several cellular genes that are necessary for viral growth in the cell but are not essential for the cell to survive. These genes are important for lytic and persistent infection by viruses. These genes were isolated by generating gene trap libraries by infecting cells with a retrovirus gene trap vector, selecting for cells
25 in which a gene trap event occurred (*i.e.*, in which the vector had inserted such that the promoterless marker gene was inserted such that a cellular promoter promotes transcription of the marker gene, *i.e.*, inserted into a functioning gene), starving the cells of serum, infecting the selected cells with the virus of choice while continuing serum starvation, and adding back serum to allow visible colonies to develop, which colonies
30 were cloned by limiting dilution. Genes into which the retrovirus gene trap vector inserted were then isolated from the colonies using probes specific for the retrovirus gene trap vector. Thus nucleic acids isolated by this method are isolated portions of genes. Additionally, utilizing this method, several cellular genes were isolated whose

overexpression prevents viral infection or tumor growth, and they provide methods of treating viral infection or tumor growth/suppression by overexpression of these genes.

Thus the present invention provides a method of identifying a cellular gene necessary for viral growth in a cell and nonessential for cellular survival, comprising (a) transferring into a cell culture, *e.g.* growing in serum-containing medium, a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, (c) removing serum from the culture medium, (d) infecting the cell culture with the virus, and (e) isolating from the surviving cells a cellular gene within which the marker gene is inserted, thereby identifying a gene necessary for viral growth in a cell and nonessential for cellular survival. The present invention also provides a method of identifying a cellular gene used for viral growth in a cell and nonessential for cellular survival, comprising (a) transferring into a cell culture growing in serum-containing medium a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, (c) removing serum from the culture medium, (d) infecting the cell culture with the virus, and (e) isolating from the surviving cells a cellular gene within which the marker gene is inserted, thereby identifying a gene necessary for viral growth in a cell and nonessential for cellular survival or a gene whose overexpression prevents viral reproduction but is not fatal to the survival to the cell. In any selected cell type, such as Chinese hamster ovary cells, one can readily determine if serum starvation is required for selection. If it is not, serum starvation may be eliminated from the steps.

Alternatively, instead of removing serum from the culture medium, a serum factor required by the virus for growth can be inhibited, such as by the administration of an antibody that specifically binds that factor. Furthermore, if it is believed that there are no persistently infected cells in the culture, the serum starvation step can be eliminated and the cells grown in usual medium for the cell type. If serum starvation is used, it can be continued for a time after the culture is infected with the virus. Serum can then be added back to the culture. If some other method is used to inactivate the factor, it can be discontinued, inactivated or removed (such as removing the anti-factor antibody, *e.g.*, with a bound antibody directed against that antibody) prior to adding fresh serum back to the culture. Cells that survive are mutants having an inactivating insertion in a gene necessary for growth of the virus. The genes having the insertions can then be isolated by isolating sequences having the marker gene sequences. This mutational process

disturbs a wild type function. A mutant gene may produce at a lower level a normal product, it may produce a normal product not normally found in these cells, it may cause the overproduction of a normal product, it may produce an altered product that has some functions but not others, or it may completely disrupt a gene function. Additionally, the
5 mutation may disrupt an RNA that has a function but is never translated into a protein. For example, the alpha-tropomyosin gene has a 3' RNA that is very important in cell regulation but never is translated into protein. (*Cell* 75 pg 1107-1117, 12/17/93).

As used herein, a cellular gene "nonessential for cellular survival" means a gene for which disruption of one or both alleles results in a cell viable for at least a period of
10 time which allows viral replication to be inhibited for preventative or therapeutic uses or use in research. A gene "necessary for viral growth" means the gene product, either protein or RNA, secreted or not, is necessary or beneficial, either directly or indirectly in some way for the virus to grow, and therefore, in the absence of that gene product (*i.e.*, a functionally available gene product), the virus does not spread. For example, such genes
15 can encode cell cycle regulatory proteins, proteins affecting the vacuolar hydrogen pump, or proteins involved in protein folding and protein modification, including but not limited to: phosphorylation, methylation, glycosylation, myristylation or other lipid moiety, or protein processing via enzymatic processing. Some examples of such genes include vacuolar H⁺ATPase, alpha tropomyosin, gas5 gene, ras complex, N-acetyl-
20 glucosaminy-l-transferase I mRNA, annexin II, c-golgi CM130 and calcyclin.

Any virus capable of infecting the cell can be used for this method. Virus can be selected based upon the particular infection desired to study. However, it is contemplated by the present invention that many viruses will be dependent upon the same cellular genes for survival; thus a cellular gene isolated using one virus can be used
25 as a target for therapy for other viruses as well. Any cellular gene can be tested for relevancy to any desired virus using the methods set forth herein, *i.e.*, in general, by inhibiting the gene or its gene product in a cell and determining if the desired virus can grow in that cell. Some examples of viruses include HIV (including HIV-1 and HIV-2); parvovirus; papillomaviruses; hantaviruses; influenza viruses (*e.g.*, influenza A, B and C
30 viruses); hepatitis viruses A to G; caliciviruses; astroviruses; rotaviruses; coronaviruses, such as human respiratory coronavirus; picornaviruses, such as human rhinovirus and enterovirus; ebola virus; human herpesvirus (*e.g.*, HSV-1-9); human adenovirus; for animal, the animal counterpart to any above listed human virus, animal retroviruses, such

as simian immunodeficiency virus, avian immunodeficiency virus, bovine immunodeficiency virus, feline immunodeficiency virus, equine infectious anemia virus, caprine arthritis encephalitis virus, arenaviruses, arvoviruses, tickborne viruses or visna virus.

5 The nucleic acids comprising cellular genes of this invention were isolated by the above method and as set forth in the examples. The invention includes a nucleic acid comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, 10 SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, 15 SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, 20 SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ 25 ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127 (this list is sometimes referred to herein as "SEQ LIST 1" for brevity). Thus these nucleic acids can contain, in addition to the nucleotides set forth in each SEQ ID NO in the sequence listing, additional nucleotides at either end of the molecule. Such additional nucleotides can be added by 30 any standard method, as known in the art, such as recombinant methods and synthesis methods. Examples of such nucleic acids comprising the nucleotide sequence set forth in any entry of the sequence listing contemplated by this invention include, but are not limited to, for example, the nucleic acid placed into a vector; a nucleic acid having one or

more regulatory region (*e.g.*, promoter, enhancer, polyadenylation site) linked to it, particularly in functional manner, *i.e.* such that an mRNA or a protein can be produced; a nucleic acid including additional nucleic acids of the gene, such as a larger or even full length genomic fragment of the gene, a partial or full length cDNA, a partial or full length RNA. Making and/or isolating such larger nucleic acids is further described below and is well known and standard in the art.

Also provided in this invention are the double-stranded nucleic acids corresponding to the nucleic acid sequences set forth in SEQ ID 1 through SEQ ID 136, inclusive. It is recognized that "nucleic acid" as used herein, can refer to either or both strands of such double-stranded nucleic acids, such strands often referred to as the "positive" and "negative" strands. Either strand of such double-stranded nucleic acids may encode the polypeptides of this invention, and the coding sequences for such polypeptides may be translated in either direction along the strand. Examples of polypeptides encoded by either strand are disclosed herein.

The invention also provides a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1, as well as allelic variants and homologs of each such gene. The gene is readily obtained using standard methods, as described below and as is known and standard in the art. The present invention also contemplates any unique fragment of these genes or of the nucleic acids set forth in any of the sequences listed in SEQ LIST 1. Examples of inventive fragments of the inventive genes can include the nucleic acids whose sequence is set forth in any of the sequences listed in SEQ LIST 1. To be unique, the fragment must be of sufficient size to distinguish it from other known sequences, most readily determined by comparing any nucleic acid fragment to the nucleotide sequences of nucleic acids in computer databases, such as GenBank. Such comparative searches are standard in the art. Typically, a unique fragment useful as a primer or probe will be at least about 20 to about 25 nucleotides in length, depending upon the specific nucleotide content of the sequence. Additionally, fragments can be, for example, at least about 30, 40, 50, 75, 100, 200 or 500 nucleotides in length. The nucleic acids can be single or double stranded, depending upon the purpose for which it is intended.

The present invention further provides a nucleic acid comprising the regulatory region of a gene comprising any one of the nucleotide sequences set forth in SEQ LIST 1, as well as homologs of each such gene. Additionally provided is a construct

comprising such a regulatory region functionally linked to a reporter gene. Such reporter gene constructs can be used to screen for compounds and compositions that affect expression of the gene comprising the nucleic acids whose sequence is set forth in SEQ LIST 1, or any homologs thereof.

- 5 The nucleic acids set forth in the sequence listing are gene fragments; the entire coding sequence and the entire gene that comprises each fragment are both contemplated herein and are readily obtained by standard methods, given the nucleotide sequences presented in the sequence listing (*see. e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989; *DNA cloning: A Practical Approach*, Volumes I and II, Glover, D.M. ed., IRL Press Limited, Oxford, 1985). To obtain the entire genomic gene, briefly, a nucleic acid whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127, or preferably in any of the sequences listed in SEQ LIST 1, or a smaller fragment thereof, is utilized as a probe to screen a genomic library under high stringency conditions, and
- 10 isolated clones are sequenced. Once the sequence of the new clone is determined, a probe can be devised from a portion of the new clone not present in the previous fragment and hybridized to the library to isolate more clones containing fragments of the gene. In this manner, by repeating this process in organized fashion, one can "walk" along the chromosome and eventually obtain nucleotide sequence for the entire gene.
- 15 Similarly, one can use portions of the present fragments, or additional fragments obtained from the genomic library, that contain open reading frames to screen a cDNA library to obtain a cDNA having the entire coding sequence of the gene. Repeated screens can be utilized as described above to obtain the complete sequence from several clones if necessary. The isolates can then be sequenced to determine the nucleotide
- 20 sequence by standard means such as dideoxynucleotide sequencing methods (*see, e.g., Sambrook et al., Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989).
- 25 The present genes were isolated from rat; however, homologs in any desired species, preferably mammalian, such as human, can readily be obtained by screening a

- 30 human library, genomic or cDNA, with a probe comprising sequences of the nucleic acids set forth in the sequence listing herein, or fragments thereof, and isolating genes specifically hybridizing with the probe under preferably relatively high stringency hybridization conditions. For example, high salt conditions (*e.g., in 6X SSC or 6X*

SSPE) and/or high temperatures of hybridization can be used. For example, the stringency of hybridization is typically about 5°C to 20°C below the T_m (the melting temperature at which half of the molecules dissociate from its partner) for the given chain length. As is known in the art, the nucleotide composition of the hybridizing region factors in determining the melting temperature of the hybrid. For 20mer probes, for example, the recommended hybridization temperature is typically about 55-58°C. Additionally, the rat sequence can be utilized to devise a probe for a homolog in any specific animal by determining the amino acid sequence for a portion of the rat protein, and selecting a probe with optimized codon usage to encode the amino acid sequence of the homolog in that particular animal. Any isolated gene can be confirmed as the targeted gene by sequencing the gene to determine it contains the nucleotide sequence listed herein as comprising the gene. Any homolog can be confirmed as a homolog by its functionality.

Additionally contemplated by the present invention are nucleic acids, from any desired species, preferably mammalian and more preferably human, having 98%, 95%, 90%, 85%, 80%, 70%, 60%, or 50% homology, or greater, in the region of homology, to a region in an exon of a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1 or to homologs thereof. Also contemplated by the present invention are nucleic acids, from any desired species, preferably mammalian and more preferably human, having 98%, 95%, 90%, 85%, 80%, 70%, 60%, or 50% homology, or greater, in the region of homology, to a region in an exon of a nucleic acid comprising the nucleotide sequence set forth in any of the sequences listed in SEQ LIST 1 or to homologs thereof. These genes can be synthesized or obtained by the same methods used to isolate homologs, with stringency of hybridization and washing, if desired, reduced accordingly as homology desired is decreased, and further, depending upon the G-C or A-T richness of any area wherein variability is searched for. Allelic variants of any of the present genes or of their homologs can readily be isolated and sequenced by screening additional libraries following the protocol above. Methods of making synthetic genes are described in U.S. Patent No. 5,503,995 and the references cited therein.

The nucleic acid encoding any selected protein of the present invention can be any nucleic acid that functionally encodes that protein. For example, to functionally encode, *i.e.*, allow the nucleic acid to be expressed, the nucleic acid can include, for

example, exogenous or endogenous 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 can be promoters derived
5 from metallothionine genes, actin genes, immunoglobulin genes, CMV, SV40, adenovirus, bovine papilloma virus, etc. Expression control sequences can be selected for functionality in the cells in which the nucleic acid will be placed. A nucleic acid encoding a selected protein can readily be determined based upon the amino acid sequence of the selected protein, and, clearly, many nucleic acids will encode any selected
10 protein.

The present invention additionally provides a nucleic acid that selectively hybridizes under stringent conditions with a nucleic acid set forth in SEQ LIST 1 or with a nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in any sequence listed in SEQ LIST 1. This hybridization can be
15 specific. The degree of complementarity between the hybridizing nucleic acid and the sequence to which it hybridizes should be at least enough to exclude hybridization with a nucleic acid encoding an unrelated protein. Thus, a nucleic acid that selectively hybridizes with a nucleic acid of the present protein coding sequence will not selectively hybridize under stringent conditions with a nucleic acid for a different, unrelated protein,
20 and vice versa. Typically, the stringency of hybridization to achieve selective hybridization involves hybridization in high ionic strength solution (6X SSC or 6X SSPE) at a temperature that is about 12-25°C below the T_m (the melting temperature at which half of the molecules dissociate from its partner) followed by washing at a combination of temperature and salt concentration chosen so that the washing temperature is about 5°C
25 to 20°C below the T_m of the hybrid molecule. The temperature and salt conditions are readily determined empirically in preliminary experiments in which samples of reference DNA immobilized on filters are hybridized to a labeled nucleic acid of interest and then washed under conditions of different stringencies. Hybridization temperatures are typically higher for DNA-RNA and RNA-RNA hybridizations. The washing
30 temperatures can be used as described above to achieve selective stringency, as is known in the art. (Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989; Kunkel et al. *Methods Enzymol.* 1987:154:367, 1987). Nucleic acid fragments that selectively hybridize to any

given nucleic acid can be used, *e.g.*, as primers and or probes for further hybridization or for amplification methods (*e.g.*, polymerase chain reaction (PCR), ligase chain reaction (LCR)) . A preferable stringent hybridization condition for a DNA:DNA hybridization can be at about 68°C (in aqueous solution) in 6X SSC or 6X SSPE followed by washing
 5 at 68°C.

The present invention additionally provides a polypeptide comprising the amino acid sequence encoded by the gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ
 10 ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID
 15 NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID
 20 NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108,
 25 SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127 (*i.e.*, SEQ LIST 1). Additionally, polypeptides comprising the amino acid sequence encoded by a nucleic acid that selectively hybridizes under stringent conditions with a nucleic acid in SEQ LIST 1 are provided. Further, polypeptides comprising the amino acid sequence
 30 encoded by a nucleic acid having a region within an exon wherein the region has at least 50, 60, 70, 80, 90, or 95% homology with a nucleic acid in SEQ LIST 1. These polypeptides can be readily obtained by any of several means. For example, the nucleotide sequence of coding regions of the gene can be translated and then the

corresponding polypeptide can be synthesized mechanically by standard methods. Additionally, the coding regions of the genes can be expressed or synthesized, an antibody specific for the resulting polypeptide can be raised by standard methods (see, *e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1988), and the protein can be isolated from other cellular proteins by selective hybridization with the antibody. This protein can be purified to the extent desired by standard methods of protein purification (see, *e.g.*, Sambrook et al., *Molecular Cloning: A Laboratory Manual*, 2nd Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, New York, 1989). The amino acid sequence of any protein, polypeptide or peptide of this invention can be deduced from the nucleic acid sequence, or it can be determined by sequencing an isolated or recombinantly produced protein.

The terms "peptide," "polypeptide" and "protein" can be used interchangeably herein and refer to a polymer of amino acids and includes full-length proteins and fragments thereof. As used in the specification and in the claims, "a" can mean one or more, depending upon the context in which it is used. An amino acid residue is an amino acid formed upon chemical digestion (hydrolysis) of a polypeptide at its peptide linkages. The amino acid residues described herein are preferably in the L isomeric form. However, residues in the D isomeric form can be substituted for any L-amino acid residue, as long as the desired functional property is retained by the polypeptide. Standard polypeptide nomenclature (described in *J. Biol. Chem.*, 243:3552-59 (1969) and adopted at 37 CFR § 1.822(b)) is used herein.

As will be appreciated by those skilled in the art, the invention also includes those polypeptides having slight variations in amino acid sequences or other properties. Amino acid substitutions can be selected by known parameters to be neutral (*see, e.g.*, Robinson WE Jr, and Mitchell WM., *AIDS* 4:S151-S162(1990)). Such variations may arise naturally as allelic variations (*e.g.*, due to genetic polymorphism) or may be produced by human intervention (*e.g.*, by mutagenesis of cloned DNA sequences), such as induced point, deletion, insertion and substitution mutants. Minor changes in amino acid sequence are generally preferred, such as conservative amino acid replacements, small internal deletions or insertions, and additions or deletions at the ends of the molecules. Substitutions may be designed based on, for example, the model of Dayhoff, *et al.* (in *Atlas of Protein Sequence and Structure* 1978, Nat'l Biomed. Res. Found., Washington,

D.C.). These modifications can result in changes in the amino acid sequence, provide silent mutations, modify a restriction site, or provide other specific mutations. Likewise, such amino acid changes result in a different nucleic acid encoding the polypeptides and proteins. Thus, alternative nucleic acids are also contemplated by such modifications.

5 The present invention also provides cells containing a nucleic acid of the invention. A cell containing a nucleic acid encoding a protein typically can replicate the DNA and, further, typically can express the encoded protein. The cell can be a prokaryotic cell, particularly for the purpose of producing quantities of the nucleic acid, or a eukaryotic cell, particularly a mammalian cell. The cell is preferably a mammalian
10 cell for the purpose of expressing the encoded protein so that the resultant produced protein has mammalian protein processing modifications.

Nucleic acids of the present invention can be delivered into cells by any selected means, in particular depending upon the purpose of the delivery of the compound and the target cells. Many delivery means are well-known in the art. For example,
15 electroporation, calcium phosphate precipitation, microinjection, cationic or anionic liposomes, and liposomes in combination with a nuclear localization signal peptide for delivery to the nucleus can be utilized, as is known in the art.

The present invention also contemplates that the mutated cellular genes necessary for viral growth, produced by the present method, as well as cells containing these
20 mutants can also be useful. These mutated genes and cells containing them can be isolated and/or produced according to the methods herein described and using standard methods.

It should be recognized that the sequences set forth herein may contain minor sequencing errors. Such errors can be corrected, for example, by using the hybridization
25 procedure described above with various probes derived from the described sequences such that the coding sequence can be reisolated and resequenced.

As described in the examples, the present invention provides the discovery of a "serum survival factor" present in serum that is necessary for the survival of persistently virally infected cells. Isolation and characterization of this factor have shown it to be a
30 protein, to have a molecular weight of between about 50 kD and 100 kD, to resist inactivation in low pH (*e.g.*, pH2) and chloroform extraction, to be inactivated by boiling for about 5 minutes and in low ionic strength solution (*e.g.*, about 10 mM to about 50 mM). The present invention thus provides a purified mammalian serum protein having a

molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus selectively substantially prevents survival of cells persistently infected with reovirus. The factor, fitting the physical characteristics described above, can readily be verified by adding it to non-serum-containing medium (which previously could not support survival of persistently virally infected cells) and determining whether this medium with the added putative factor can now support persistently virally infected cells, particularly cells persistently infected with reovirus. As used herein, a "purified" protein means the protein is at least of sufficient purity such that an approximate molecular weight can be determined.

The amino acid sequence of the protein can be elucidated by standard methods. For example, an antibody to the protein can be raised and used to screen an expression library to obtain nucleic acid sequence coding the protein. This nucleic acid sequence is then simply translated into the corresponding amino acid sequence. Alternatively, a portion of the protein can be directly sequenced by standard amino acid sequencing methods (amino-terminus sequencing). This amino acid sequence can then be used to generate an array of nucleic acid probes that encompasses all possible coding sequences for a portion of the amino acid sequence. The array of probes is used to screen a cDNA library to obtain the remainder of the coding sequence and thus ultimately the corresponding amino acid sequence.

The present invention also provides methods of detecting and isolating additional serum survival factors. For example, to determine if any known serum components are necessary for viral growth, the known components can be inhibited in, or eliminated from, the culture medium, and it can be observed whether viral growth is inhibited by determining if persistently infected cells do not survive. One can add the factor back (or remove the inhibition) and determine whether the factor allows for viral growth.

Additionally, other, unknown serum components can also be found to be essential for growth. Serum can be fractionated by various standard means, and fractions added to serum free medium to determine if a factor is present in a reaction that allows growth previously inhibited by the lack of serum. Fractions having this activity can then be further fractionated until the factor is relatively free of other components. The factor can then be characterized by standard methods, such as size fractionation, denaturation and/or

inactivation by various means, etc. Preferably, once the factor has been purified to a desired level of purity, it is added to cells in serum free medium to confirm that it bestows the function of allowing virus to grow when serum-free medium alone did not. This method can be repeated to confirm the requirement for the specific factor for any desired virus, since each serum factor found to be required by any one virus can also be required by many other viruses. In general, the closer the viruses are related and the more similar the infection modes of the viruses, the more likely that a factor required by one virus will be required by the other.

The present invention also provides methods of treating virus infections utilizing applicants' discoveries. The subject of any of the herein described methods can be any animal, preferably a mammal, such as a human, a veterinary animal, such as a cat, dog, horse, pig, goat, sheep, or cow, or a laboratory animal, such as a mouse, rat, rabbit, or guinea pig, depending upon the virus.

The present invention provides a method of reducing or inhibiting, and thereby treating, a viral infection in a subject, comprising administering to the subject an inhibiting amount of a composition that inhibits functioning of the serum protein described herein, *i.e.* the serum protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with the virus prevents survival of at least some cells persistently infected with the virus, thereby treating the viral infection. The composition can comprise, for example, an antibody that specifically binds the serum protein, or an antisense RNA that binds an RNA encoded by a gene functionally encoding the serum protein.

Any virus capable of infecting the selected subject to be treated can be treated by the present methods. As described above, any serum protein or survival factor found by the present methods to be necessary for growth of cells infected with any one virus can be found to be necessary for growth of the cells infected with many other viruses. For any given cell-virus combination, the serum protein or factor can be confirmed to be required for growth by the methods described herein. The cellular genes identified by the examples using reovirus, a mammalian pathogen, and a rat cell system have general applicability to other virus infections that include all of the known as well as yet to be discovered human pathogens, including, but not limited to: human immunodeficiency

viruses (*e.g.*, HIV-1, HIV-2); parvovirus; papillomaviruses; hantaviruses; influenza viruses (*e.g.*, influenza A, B and C viruses); hepatitis viruses A to G; caliciviruses; astroviruses; rotaviruses; coronaviruses, such as human respiratory coronavirus; picornaviruses, such as human rhinovirus and enterovirus; ebola virus; human
5 herpesvirus (*e.g.*, HSV-1-9); human adenovirus; hantaviruses; for animal, the animal counterpart to any above listed human virus, animal retroviruses, such as simian immunodeficiency virus, avian immunodeficiency virus, bovine immunodeficiency virus, feline immunodeficiency virus, equine infectious anemia virus, caprine arthritis encephalitis virus, arenaviruses, arvoviruses, tickborne virus or visna virus.

10 A protein inhibiting amount of the composition can be readily determined, such as by administering varying amounts to cells or to a subject and then adjusting the effective amount for inhibiting the protein according to the volume of blood or weight of the subject. Compositions that bind to the protein can be readily determined by running the
15 putatively bound protein on a protein gel and observing an alteration in the protein's migration through the gel. Inhibition of the protein can be determined by any desired means such as adding the inhibitor to complete media used to maintain persistently infected cells and observing the cells' viability. The composition can comprise, for example, an antibody that specifically binds the serum protein. Specific binding by an
20 antibody means that the antibody can be used to selectively remove the factor from serum or inhibit the factor's biological activity and can readily be determined by radio immune assay (RIA), bioassay, or enzyme-linked immunosorbant (ELISA) technology. The composition can comprise, for example, an antisense RNA that specifically binds an RNA encoded by the gene encoding the serum protein. Antisense RNAs can be synthesized and used by standard methods (*e.g.*, *Antisense RNA and DNA*, D. A. Melton, Ed., Cold
25 Spring Harbor Laboratory, Cold Spring Harbor, NY (1988)).

The present methods provide a method of screening a compound for effectiveness in treating or preventing a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product necessary for reproduction of the virus in the cell but not necessary for survival of the cell and detecting the level
30 and/or activity (*i.e.* function) of the gene product produced, a decrease or elimination of the gene product and/or the gene product activity indicating a compound for treating or preventing the viral infection. The cellular gene can be, for example, a nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ

ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82; SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 (herein sometimes referred to as SEQ LIST 2, for brevity), any homolog thereof, or any other gene obtained using the methods provided herein for obtaining such genes. It is understood that the cellular gene can be present naturally in the cell being screened, or it can be introduced into the cell in a suitable expression vector, as are well known in the art. 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 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 protein to a nucleic acid, for example. Examples of gene products disclosed herein whose activity/function can be measured include tristetraproline (human ZFP-36), 6-pyruvoyl-tetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucos-aminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b). The activity can be compared to the activity in a control cell not contacted with the compound or in the same cell prior to addition of the compound. Relatedly, the regulatory region of the gene can be functionally linked to a reporter gene and compounds can be screened for inhibition of the reporter gene. Such reporter constructs are described herein.

The present invention also provides a method of screening a compound for effectiveness in treating or preventing a viral infection comprising contacting the compound with the gene product of a cellular gene comprising a nucleic acid of SEQ LIST 2, or any homolog thereof, and detecting the function of the gene product, a decrease or elimination of the function indicating a compound effective for treating or preventing viral infection. Examples of gene products disclosed herein that can be utilized in this method include tristetraproline (human ZFP-36), 6-pyruvoyl-tetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucos-aminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

The present invention provides a method of selectively eliminating cells persistently infected with a virus from an animal cell culture capable of surviving for a first period of time in the absence of serum, comprising propagating the cell culture in the absence of serum for a second time period during which a persistently infected cell cannot survive without serum, thereby selectively eliminating from the cell culture cells persistently infected with the virus. The second time period should be shorter than the first time period. Thus one can simply eliminate serum from a standard culture medium composition for a period of time (e.g. by removing serum containing medium from the culture container, rinsing the cells, and adding serum-free medium back to the container), then, after a time of serum starvation, return serum to the culture medium. Alternatively, one can inhibit a serum survival factor from the culture in place of the step of serum starvation. Furthermore, one can instead interfere with the virus-factor interaction. Such a

viral elimination method can periodically be performed for cultured cells to ensure that they remain virus-free. The time period of serum removal can greatly vary, with a typical range being about 1 to about 30 days; a preferable period can be about 3 to about 10 days, and a more preferable period can be about 5 days to about 7 days. This time period can be
5 selected based upon ability of a specific cell to survive without serum as well as the life cycle of the target virus, *e.g.*, for reovirus, which has a life cycle of about 24 hours, 3 days' starvation of cells provides dramatic results.

Furthermore, the time period can be shortened by also passaging the cells during the starvation; in general, increasing the number of passages can decrease the time of
10 serum starvation (or serum factor inhibition) needed to get full clearance of the virus from the culture. While passaging, the cells typically are exposed briefly to serum (typically for about 3 to about 24 hours). This exposure both stops the action of the trypsin used to dislodge the cells and stimulates the cells into another cycle of growth, thus aiding in this selection process. Thus a starvation/serum cycle can be repeated to optimize the selective
15 effect. Other standard culture parameters, such as confluency of the cultures, pH, temperature, etc. can be varied to alter the needed time period of serum starvation (or serum survival factor inhibition). This time period can readily be determined for any given viral infection by simply removing the serum for various periods of time, then testing the cultures for the presence of the infected cells (*e.g.*, by ability to survive in the
20 absence of serum and confirmed by quantitating virus in cells by standard virus titration and immunohistochemical techniques) at each tested time period, and then detecting at which time periods of serum deprivation the virally infected cells were eliminated. It is preferable that shorter time periods of serum deprivation that still provide elimination of the persistently infected cells be used. Furthermore, the cycle of starvation, then adding
25 back serum and determining amount of virus remaining in the culture can be repeated until no virtually infected cells remain in the culture.

Thus, the present method can further comprise passaging the cells, *i.e.*, transferring the cell culture from a first container to a second container. Such transfer can facilitate the selective lack of survival of virally infected cells. Transfer can be repeated several times.
30 Transfer is achieved by standard methods of tissue culture (*see, e.g.*, Freshney, *Culture of Animal Cells, A Manual of Basic Technique*, 2nd Ed. Alan R. Liss, Inc., New York, 1987).

The present method further provides a method of selectively eliminating from a cell culture cells persistently infected with a virus, comprising propagating the cell culture

in the absence of a functional form of the serum protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus substantially prevents survival of cells persistently infected with reovirus. The absence of the functional form can be achieved by any of several standard means, such as by binding the protein to an antibody selective for it (binding the antibody in serum either before or after the serum is added to the cells; if before, the serum protein can be removed from the serum by, *e.g.*, binding the antibody to a column and passing the serum over the column and then administering the survival protein-free serum to the cells), by administering a compound that inactivates the protein, or by administering a compound that interferes with the interaction between the virus and the protein.

Thus, the present invention provides a method of selectively eliminating from a cell culture propagated in serum-containing medium cells persistently infected with a virus, comprising inhibiting in the serum the protein having a molecular weight of between about 50 kD and 100 kD which resists inactivation in low pH and resists inactivation by chloroform extraction, which inactivates when boiled and inactivates in low ionic strength solution, and which when removed from a cell culture comprising cells persistently infected with reovirus substantially prevents survival of cells persistently infected with reovirus. Alternatively, the interaction between the virus and the serum protein can be disrupted to selectively eliminate cells persistently infected with the virus.

Any virus capable of some form of persistent infection may be eliminated from a cell culture utilizing the present elimination methods, including removing, inhibiting or otherwise interfering with a serum protein, such as the one exemplified herein, and also including removing, inhibiting or otherwise interfering with a gene product from any cellular gene found by the present method to be necessary for viral growth yet nonessential to the cell. For example, DNA viruses or RNA viruses can be targeted. One can readily determine whether cells infected with a selected virus can be selectively removed from a culture through removal of serum by starving cells permissive to the virus of serum (or inhibiting the serum survival factor), adding the selected virus to the cells, adding serum to the culture, and observing whether infected cells die (*i.e.*, by titering levels of virus in the surviving cells with an antibody specific for the virus).

A culture of any animal cell (*i.e.*, any cell that is typically grown and maintained in culture in serum) that can be maintained for a period of time in the absence of serum, can be purified from viral infection utilizing the present method. For example, primary cultures as well as established cultures and cell lines can be used. Furthermore, cultures of
5 cells from any animal and any tissue or cell type within that animal that can be cultured and that can be maintained for a period of time in the absence of serum can be used. For example, cultures of cells from tissues typically infected, and particularly persistently infected, by an infectious virus could be used.

As used in the claims "in the absence of serum" means at a level at which
10 persistently virally infected cells do not survive. Typically, the threshold level is about 1% serum in the media. Therefore, about 1% serum or less can be used, such as about 1%, 0.75%, 0.50%, 0.25%, 0.1% or no serum can be used.

As used herein, "selectively eliminating" cells persistently infected with a virus means that substantially all of the cells persistently infected with the virus are killed such
15 that the presence of virally infected cells cannot be detected in the culture immediately after the elimination procedure has been performed. Furthermore, "selectively eliminating" includes that cells not infected with the virus are generally not killed by the method. Some surviving cells may still produce virus but at a lower level, and some may be defective in pathways that lead to death by the virus. Typically, for cells persistently
20 infected with virus to be substantially all killed, more than about 90% of the cells, and more preferably more than about 95%, 98%, 99%, or 99.99% of virus-containing cells in the culture are killed.

The present method also provides a nucleic acid comprising the regulatory region of any of the genes. Such regulatory regions can be isolated from the genomic sequences
25 isolated and sequenced as described above 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. The present invention also provides a construct comprising the regulatory region functionally linked to a reporter gene. Such constructs are made by routine subcloning methods, and many vectors are available into which
30 regulatory regions can be subcloned upstream of a marker gene. Marker genes can be chosen for ease of detection of marker gene product.

The present method therefore also provides a method of screening a compound for treating a viral infection, comprising administering the compound to a cell containing any

of the above-described constructs, comprising a regulatory region of one of the genes comprising any of the nucleotide sequences set forth in SEQ LIST 2, or any homologs thereof, whose inhibition or reduction in expression causes inhibition of viral replication wherein the region is functionally linked to a reporter gene, and detecting the level of the reporter gene product produced, a decrease or elimination of the reporter gene product indicating a compound for treating the viral infection. Compounds detected by this method would inhibit transcription of the gene from which the regulatory region was isolated, and thus, in treating a subject, would inhibit the production of the gene product produced by the gene, and thus treat the viral infection.

Some genes when disrupted by the present method of retrovirus insertion, resulted in over expression of the gene product, and this overexpression inhibited viral replication. Thus the present invention provides a method of screening a compound for effectiveness in treating a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection. Typically, an increase will be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher increase over gene product produced when the compound is not present.

The present invention additionally provides a method of reducing or inhibiting a viral infection in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in any of SEQ LIST 2, or a homolog thereof, thereby treating the viral infection. Reducing or inhibiting viral infection naturally can include both the initial infection of the subject and the infection of uninfected cells within an already infected subject, e.g. inhibiting viral replication in cells of the subject. The composition can comprise, for example, an antibody that binds a protein encoded by the gene. The composition can also comprise an antibody that binds a receptor for a protein encoded by the gene. Such an antibody can be raised against the selected protein by standard methods as set forth above, and can be either polyclonal or monoclonal, though monoclonal is preferred. Alternatively, the composition can comprise an antisense RNA that binds an RNA encoded by the gene, as described above. Examples of antisense RNA useful therapeutically include the fragments of the nucleic acids described above.

Furthermore, the composition can comprise a nucleic acid functionally encoding an antisense RNA that binds an RNA encoded by the gene. Other useful compositions will be readily apparent to the skilled artisan.

The present invention also provides a method of treating a viral infection in a subject comprising administering to the subject a treatment effective amount of a composition that increases expression of a gene whose over expression reduces or inhibits viral replication. Typically, an increase will be a 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher increase over gene product produced when the composition is not present.

10 The present invention further provides a method of reducing or inhibiting a viral infection in a subject comprising mutating *ex vivo* in a selected cell, for example from the subject or from an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2 whose inhibition or reduction in expression causes inhibition of viral replication, or a homolog thereof, to a gene form incapable of producing a functional gene product of the gene or a gene form producing a reduced amount of a functional gene product of the gene, and placing (or replacing, in the case of the subject's own cells) the cell in the subject, thereby reducing viral infection of cells in the subject. The cell can be selected according to the typical target cell of the specific virus whose infection is to be reduced, prevented or inhibited. A preferred cell for several viruses is a hematopoietic cell. When the selected cell is a hematopoietic cell, viruses which can be reduced or inhibited from infection can include, for example, HIV, including HIV-1 and HIV-2. However, many other virus-cell combinations will be apparent to the skilled artisan.

The invention also includes a method of reducing or inhibiting viral infection in a subject comprising mutating *ex vivo* in a selected cell, for example from a subject or an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2 whose overexpression causes inhibition of viral replication, or a homolog thereof, to a gene form that expresses the gene at a higher level than the endogenous gene, and placing or replacing the cell in the subject. Typically, a higher level can be 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, 125%, 150%, 175%, 200%, 300%, 400%, 500% or higher than the non-mutated, endogenous gene. The cell can be selected according to the typical target cell of the specific virus whose infection is to be reduced, prevented or inhibited. A preferred cell for several viruses is a hematopoietic cell. When the selected cell is a hematopoietic cell, viruses which can be reduced or inhibited from infection can

include, for example, HIV, including HIV-1 and HIV-2. However, many other virus-cell combinations will be apparent to the skilled artisan.

The present invention additionally provides a method of increasing viral infection resistance in a subject comprising mutating *ex vivo* in a selected cell, for example from the
5 subject or from an allogenic source, an endogenous gene comprising a nucleic acid set forth in SEQ LIST 2, whose inhibition or reduction in expression increases viral infection resistance, said endogenous gene being mutated to a mutated gene form incapable of producing a functional gene product of the gene or a gene form producing a reduced amount of a functional gene product of the gene, and placing the cell in the subject,
10 thereby increasing viral infection resistance of cells in the subject. The virus can be HIV, particularly when the cell is a hematopoietic cell. However, many other virus-cell combinations will be apparent to the skilled artisan.

Furthermore, the present invention provides a method for isolation of cellular genes utilized in tumor progression. The present invention provides a method of identifying a
15 cellular gene that can suppress a malignant phenotype in a cell, comprising (a) transferring into a cell culture incapable of growing well in soft agar or Matrigel a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, and (c) isolating from selected cells which are capable of growing in soft agar or Matrigel a cellular gene within which the marker gene is inserted, thereby
20 identifying a gene that can suppress a malignant phenotype in a cell. This method can be performed using any selected non-transformed cell line, of which many are known in the art.

The present invention additionally provides a method of identifying a cellular gene that can suppress a malignant phenotype in a cell, comprising (a) transferring into a cell
25 culture of non-transformed cells a vector encoding a selective marker gene lacking a functional promoter, (b) selecting cells expressing the marker gene, and (c) isolating from selected and transformed cells a cellular gene within which the marker gene is inserted, thereby identifying a gene that can suppress a malignant phenotype in a cell. A non-transformed phenotype can be determined by any of several standard methods in the
30 art, such as the exemplified inability to grow in soft agar, or inability to grow in Matrigel.

The present invention further provides a method of screening for a compound for suppressing a malignant phenotype in a cell comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product involved in

establishment of a malignant phenotype in the cell and detecting the level of the gene product produced, a decrease, inhibition or elimination of the gene product indicating a compound effective for suppressing the malignant phenotype. Detection of the level, or amount, of gene product produced can be measured, directly or indirectly, by any of
5 several methods standard in the art (*e.g.*, protein gel, antibody-based assay, detecting labeled RNA) for assaying protein levels or amounts, and selected based upon the specific gene product.

The present invention also provides a method of screening for a compound for suppressing a malignant phenotype in a cell comprising administering the compound to a
10 cell containing a cellular gene functionally encoding a gene product whose overexpression is involved in suppressing a malignant phenotype in the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for suppressing the malignant phenotype.

The present invention further provides a method of suppressing a malignant
15 phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, or any gene whose overexpression is found by the present method to be
20 involved in suppressing a malignant phenotype in the cell (*e.g.*, any clone designated herein with an "x") thereby suppressing a malignant phenotype. The composition can, for example, comprise an antibody that binds a protein encoded by the gene. The composition can, as another example, comprise an antibody that binds a receptor for a protein encoded by the gene. The composition can comprise an antisense RNA that binds an RNA
25 encoded by the gene. Further, the composition can comprise a nucleic acid functionally encoding an antisense RNA that binds an RNA encoded by the gene.

The present invention further provides a method of suppressing a malignant phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that increases expression of a gene product whose overexpression is involved
30 in suppressing a malignant phenotype in the cell. The gene product can be the product of a gene wherein disruption of an upstream gene by the present vector resulted in overexpression of the downstream gene, and the overexpression of the downstream gene

demonstrated a transformed phenotype. The composition can be, for example, an inhibitor, such as a small molecule inhibitor, of the COX 2 enzyme.

Diagnostic or therapeutic agents of the present invention can be administered to a subject or an animal model by any of many standard means for administering therapeutics or diagnostics to that selected site or standard for administering that type of functional entity. For example, an agent can be administered orally, parenterally (e.g., intravenously), by intramuscular injection, by intraperitoneal injection, topically, transdermally, or the like. Agents can be administered, e.g., as a complex with cationic liposomes, or encapsulated in anionic liposomes. Compositions can include various amounts of the selected agent in combination with a pharmaceutically acceptable carrier and, in addition, if desired, may include other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, etc. Parental administration, if used, is generally characterized by injection. Injectables can be prepared in conventional forms, either as liquid solutions or suspensions, solid forms suitable for solution or suspension in liquid prior to injection, or as emulsions. Depending upon the mode of administration, the agent can be optimized to avoid degradation in the subject, such as by encapsulation, etc.

Dosages will depend upon the mode of administration, the disease or condition to be treated, and the individual subject's condition, but will be that dosage typical for and used in administration of antiviral or anticancer agents. Dosages will also depend upon the composition being administered, e.g., a protein or a nucleic acid. Such dosages are known in the art. Furthermore, the dosage can be adjusted according to the typical dosage for the specific disease or condition to be treated. Furthermore, viral titers in culture cells of the target cell type can be used to optimize the dosage for the target cells *in vivo*, and transformation from varying dosages achieved in culture cells of the same type as the target cell type can be monitored. Often a single dose can be sufficient; however, the dose can be repeated if desirable. The dosage should not be so large as to cause adverse side effects. Generally, the dosage will vary with the age, condition, sex and extent of the disease in the patient and can be determined by one of skill in the art. The dosage can also be adjusted by the individual physician in the event of any complication.

For administration to a cell in a subject, the composition, once in the subject, will of course adjust to the subject's body temperature. For *ex vivo* administration, the composition can be administered by any standard methods that would maintain viability of the cells, such as by adding it to culture medium (appropriate for the target cells) and

adding this medium directly to the cells. As is known in the art, any medium used in this method can be aqueous and non-toxic so as not to render the cells non-viable. In addition, it can contain standard nutrients for maintaining viability of cells, if desired. For *in vivo* administration, the complex can be added to, for example, a blood sample or a tissue sample from the patient, or to a pharmaceutically acceptable carrier, e.g., saline and buffered saline, and administered by any of several means known in the art. Examples of administration include parenteral administration, e.g., by intravenous injection including regional perfusion through a blood vessel supplying the tissues(s) or organ(s) having the target cell(s), or by inhalation of an aerosol, subcutaneous or intramuscular injection, topical administration such as to skin wounds and lesions, direct transfection into, e.g., bone marrow cells prepared for transplantation and subsequent transplantation into the subject, and direct transfection into an organ that is subsequently transplanted into the subject. Further administration methods include oral administration, particularly when the composition is encapsulated, or rectal administration, particularly when the composition is in suppository form. A pharmaceutically acceptable carrier includes any material that is not biologically or otherwise undesirable, i.e., the material may be administered to an individual along with the selected complex without causing any undesirable biological effects or interacting in a deleterious manner with any of the other components of the pharmaceutical composition in which it is contained.

Specifically, if a particular cell type *in vivo* is to be targeted, for example, by regional perfusion of an organ or tumor, cells from the target tissue can be biopsied and optimal dosages for import of the complex into that tissue can be determined *in vitro*, as described herein and as known in the art, to optimize the *in vivo* dosage, including concentration and time length. Alternatively, cultured cells of the same cell type can also be used to optimize the dosage for the target cells *in vivo*.

For either *ex vivo* or *in vivo* use, the complex can be administered at any effective concentration. An effective concentration is that amount that results in reduction, inhibition or prevention of the viral infection or in reduction or inhibition of the transformed phenotype of the cells.

A nucleic acid can be administered in any of several means, which can be selected according to the vector utilized, the organ or tissue, if any, to be targeted, and the characteristics of the subject. The nucleic acids, if desired in a pharmaceutically acceptable carrier such as physiological saline, can be administered systemically, such as

intravenously, intraarterially, orally, parenterally, subcutaneously. The nucleic acids can also be administered by direct injection into an organ or by injection into the blood vessel supplying a target tissue. For an infection of cells of the lungs or trachea, it can be administered intratracheally. The nucleic acids can additionally be administered topically,
5 transdermally, etc.

The nucleic acid or protein can be administered in a composition. For example, the composition can comprise other medicinal agents, pharmaceutical agents, carriers, adjuvants, diluents, etc. Furthermore, the composition can comprise, in addition to the vector, lipids such as liposomes, such as cationic liposomes (e.g., DOTMA, DOPE,
10 DC-cholesterol) or anionic liposomes. Liposomes can further comprise proteins to facilitate targeting a particular cell, if desired. Administration of a composition comprising a vector and a cationic liposome can be administered to the blood afferent to a target organ or inhaled into the respiratory tract to target cells of the respiratory tract. Regarding liposomes, see, e.g., Brigham et al. *Am. J. Resp. Cell. Mol. Biol.* 1:95-100
15 (1989); Felgner et al. *Proc. Natl. Acad. Sci USA* 84:7413-7417 (1987); U.S. Pat. No.4,897,355.

For a viral vector comprising a nucleic acid, the composition can comprise a pharmaceutically acceptable carrier such as phosphate buffered saline or saline. The viral vector can be selected according to the target cell, as known in the art. For example,
20 adenoviral vectors, in particular replication-deficient adenoviral vectors, can be utilized to target any of a number of cells, because of its broad host range. Many other viral vectors are available, and their target cells are known.

Throughout this application, various publications are referenced. The disclosures
25 of these publications in their entireties are hereby incorporated by reference into this application in order to more fully describe the state of the art to which this invention pertains.

EXAMPLES

30

Selective elimination of virally infected cells from a cell culture

Rat intestinal cell line-1 cells (RIE-1 cells) were standardly grown in Dulbecco's modified Eagle's medium, high glucose, supplemented with 10% fetal bovine serum. To

begin the experiment, cells persistently infected with reovirus were grown to near confluence, then serum was removed from the growth medium by removing the medium, washing the cells in PBS, and returning to the flask medium not supplemented with serum. Typically, the serum content was reduced to 1% or less. The cells are starved for serum
5 for several days, or as long as about a month, to bring them to quiescence or growth arrest. Media containing 10% serum is then added to the quiescent cells to stimulate growth of the cells. Surviving cells are found to not be persistently infected cells by immunohistochemical techniques used to establish whether cells contain any infectious virus (sensitivity to 1 infectious virus per ml of homogenized cells).

10

Cellular Genomic DNA Isolation

Gene Trap Libraries: The libraries are generated by infecting the RIE-1 cells with a retrovirus vector (U3 gene-trap) at a ratio of less than one retrovirus for every ten cells. When a U3 gene trap retrovirus integrates within an actively transcribed gene, the
15 neomycin resistance gene that the U3 gene trap retrovirus encodes is also transcribed, thus conferring resistance to the cell to the antibiotic neomycin. Cells with gene trap events are able to survive exposure to neomycin while cells without a gene trap event die. The various cells that survive neomycin selection are then propagated as a library of gene trap events. Such libraries can be generated with any retrovirus vector that has the properties
20 of expressing a reporter gene from a transcriptionally active cellular promoter that tags the gene for later identification.

Reovirus selection: Reovirus infection is typically lethal to RIE-1 cells but can result in the development of persistently infected cells. These cells continue to grow while producing infective reovirus particles. For the identification of gene trap events that
25 confer reovirus resistance to cells, the persistently infected cells must be eliminated or they will be scored as false positives. We have found that RIE-1 cells persistently infected with reovirus are very poorly tolerant to serum starvation, passaging and plating at low density. Thus, we have developed protocols for the screening of the RIE-1 gene trap libraries that select against both reovirus sensitive cells and cells that are persistently infected with
30 reovirus.

1. RIE-1 library cells are grown to near confluence and then the serum is removed from the media. The cells are starved for serum for several days to bring them to quiescent or growth arrest.

2. The library cells are infected with reovirus at a titer of greater than ten reovirus per cell and the serum starvation is continued for several more days.
3. The infected cells are passaged, (a process in which they are exposed to serum for three to six hours) and then starved for serum for several more days.
- 5 4. The surviving cells are then allowed to grow in the presence of serum until visible colonies develop at which point they are cloned by limiting dilution.

MEDIA: DULBECCO'S MODIFIED EAGLE'S MEDIUM, HIGH GLUCOSE (DME/HIGH) Hyclone Laboratories cat. no. SH30003.02.

NEOMYCIN: The antibiotic used to select against the cells that did not have a U3 gene trap retrovirus, e.g. GENETICIN, from Sigma. [cat. no. G9516].

RAT INTESTINAL CELL LINE-1 CELLS (RIE-1 CELLS): These cells are from the laboratory of Dr. Ray Dubois (VAMC). They are typically cultured in Dulbecco's Modified Eagle's Medium supplemented with 10% fetal calf serum.

REOVIRUS: Laboratory strains of either serotype 1 or serotype 3 are used. They were originally obtained from the laboratories of Bernard N. Fields (deceased). These viruses have been described in detail.

RETROVIRUS: The U3 gene trap retrovirus used here were developed by Dr. Earl Ruley (VAMC) and the libraries were produced using a general protocol suggested by him.

SERUM: FETAL BOVINE SERUM Hyclone Laboratories cat. no. A-1115-L.

20

Identification Tags for Isolated Nucleic Acids

Genomic sequences, tagged with a vector, such as the U3 gene trap vector, are given a number corresponding to the genomic library of mutant cells from which the sequence was isolated., and a letter indicating a unique member of the library. More than one sequence with the same number and letter indicates multiple, unique sequences obtained from the genome surrounding the vector insert that "tagged" the gene. Such genomic sequences are obtained using vector-based primers, from which sequencing occurs 3' to 5' or 5' to 3'. In the former case, to recover the orientation of the gene into which the vector inserted, the sequence derived from the vector primer must be reversed and complemented. Such reverse complement sequences are designated "rE". In the case of genome sequencing from a primer that occurs 5' to 3' (i.e. the primer is at the 3' end of the vector), no changes are needed, since the derived sequence is the sequence as it appears

in the gene disrupted. Such sequences are designated "B4". Homologies indicated below each genomic sequence are in the positive direction, unless explicitly noted to be on the negative strand. As an example, SEQ ID NO. 27 comprises a nucleic acid sequence encoding a novel polypeptide on the positive strand, while the negative strand encodes
5 ferritin.

	SEQ ID NO:	Lab Designation
	1	32-3-2#1E/-rE
	2	L191B2E#1-RE
10	3	L191B2E#3+-rE
	4	21-5-9E-RE
	homology to: emb/AL021154/HS15005 human DNA sequence	
	5	14A14E-rE
15	6	4cx-b4
	7	5a-b4
	8	6BSA12-B4
	9	X7B/B4
	10	x27b4f_1
20	11	12C#A-rE
	12	10-3b(5/2/96)/-rE
	13	10_4B_4-rE
	14	6BE60-rE
	homology to: alpha-trophomyosin	
25	15	19D3E-rE
	16	L19D16E-rE
	17	2b_rE
	18	14_24_#6-rE
30	19	7A7'-rE
	homology to: annexin II/dynein I	
	20	L12cx#6-rE
	homology to: gb:X51760 human zinc finger protein ZFP-36	
35	21	L12cx#11-rE

- 22 19D5E-rE
homology to: 6-pyruvoyl-tetrahydropterin synthase (gb/M77850/RAT6PTHS)
- 23 12_3b#7-rE
- 5 24 12_3B#8-RE
homology to: gb/AA871174/vq32a08.r1 Barskad bowel MPLRBg Mus musculus cDNA clone 10959265'
- 25 9B27-2-E
homology to: RAT LOCUS RNU53922 04-MAY-1996; Rattus norvegicus DnaJ-like protein (RDJ1) mRNA, complete Cds, ACCESSION U53922 (on negative strand)
- 10 26 x15-rE
- 27 X11-rE
homology to: ferritin H (on the negative strand)
- 15 28 X20-rE
homology to: LOCUS RATGL5A Rat NICER element (GL5-14)5' long terminal repeat, Acc.No. M59028 M33535N1D
- 20 29 X4-rE
- 30 14A7E-rE
homology to: MMSMAD7 3681 bp mRNA ROD 31-JUL-1998 DEFINITION Mus musculus mRNA for Mad-related protein Smad7 ,149 bases
- 25 31 14A13E-rE
- 32 14_7#2E-rE
homology to: N-acetylglucosaminyltransferase I
- 33 12CX#6-rE
- 30 homology to: gb|AA522204|AA522204 vf98g09_r1 Soares mouse mammary gland NbMMG Mus musculus cDNA clone 851872; also 5' similar to gb X51760 zinc finger protein ZFP-36 (HUMAN), gb L20450 Mus musculus DNA-binding protein mRNA, complete cds (MOUSE); Length = 442, 925 bases (shares homology with SEQ ID NO:20)
- 35 34 12C_2B#9E-rE
- 35 12CX#11E-rE
- 36 x5-rE
- 37 8C5_11-rE
- 38 191E2E-rE
- 40 39 19_7AE-rE

- 40 19_9BE-rE
homology to: LOCUS HS347M6 56583 bp DNA PRI 14-JAN-1998 Human DNA
sequence from PAC 347M6 on chromosome Xq22, CSTF2 (Cleavage Stimulation Factor,
CF-1, Polyadenylation Factor) 64 kD subunit gene
- 5 41 191E9E-rE
42 191E8E-rE
43 14C_2E/-rE
homology to: gb/H31084/EST104778 Rattus sp. cDNA - 5' end similar to signal
10 recognition particle subunit(19kDa) (on negative strand)
- 44 14H1E-rE
45 14G3E-rE
46 14G_2E-rE
15 47 6_3_6_2E/-rE
homology to: Rattus norvegicus cis-golgi gp130 (on negative strand); and
a HUMAN EST (on positive strand) AI127398; qb70g11.x1 Soares fetal heart NbHH19W
Homo sapiens cDNA clone (1705508 3' mRNA sequence)
- 20 48 14H4E/-rE
49 18A_8_4E-rE
50 18A_8_1E-rE
51 SCB2_19E-rE
52 L197B3E-rE
25 53 L195C5E-rE
homology to: H. pylori and C.jejuni
- 54 21_5_7E-rE
homology to: id3 gene; emb|AL021154|HS150O5 Human DNA sequence from clone
30 150O5; HTGS phase 1 [Homo sapiens]; containing the E2F2 gene for transcription factor
E2F-2 and the ID3 gene for Inhibitor of DNA binding 3 (dominant negative
helix-loop-helix protein), 1R2, Length = 133667, 971 bases
- 55 L195B1E-rE
35 homology to: vK72b07.s1 Knowles Solter mouse 2 cell Mus musculus cDNA clone
960181 5'
- 56 L194c4E-rE
57 L193A1E#A-rE
40 58 L192A3E-rE
59 L1739E-rE

- 60 L192B3E#13-rE
contains sequence identical to: insulin growth factorII/mannose-6-phosphate receptor
- 61 3 2 4 rE
5 located in the same region of the genome as calcyclin, but the gene is "read" in the
opposite direction
- 62 36 7 1 a-rE
63 36 5 1 4 a-rE
64 34 25 5a-rE
10 rat satellite DNA (RATRSSID 93 bp, ROD 12-MAR-1984)
- 65 34 24-126/rE
homology to:
15 HSU49928 (3096 bp mRNA) PRI 06-APR-1998, Homo sapiens TAK1 binding protein
(TAB1) mRNA, complete cds, ACCESSION U49928 NID g1401125, and
HS333H23 (142274 bp DNA) HTG 17-JUL-1998 Human DNA sequence
- 66 34 23-1/rE
67 36 5 2-6/rE
20 68 36 5 2-196/rE
69 34 23-3/rE
homology to: gb|L16546|RATAP1X Rat P-glycoprotein (mdr1b) gene
70 34 25 23-rE
71 36 5 2-196/rE
25 72 31 3 9/rE
homology to: AA798638 568 bp mRNA EST 10-FEB-1998, vw34b06.r1 Soares mouse
mammary gland NbMMG Mus musculus cDNA clone1245683 5, mRNA sequence, 824
bases.
73 31 3 6-2-rE
30 74 31 3 17-rE
75 31 3 5-rE
homology to: AF046001 2347 bp mRNA PRI 19-FEB-1998, Homo sapiens zinc finger
transcription factor (ZNF207) mRNA, complete Cds, 833 bases.
- 35 76 31 3 15#1/rE
77 24 3 5#1/rE
78 31 4 4#1/rE
79 31 3 19#2/rE
80 31 4 5#1/rE
40 81 24 9 3#2/rE
82 L24_26_1-BL

homology to: AI045472 396 bp mRNA EST 06-JUL-1998, UI-R-C1-jz-h-09-0-UI.s2
UI-R-C1 Rattus norvegicus cDNA clone UI-R-C1-jz-h-09-0-UI 3', mRNA sequence.

	83	L24_26_1-B4
5	84	L22_5A1/rE
	85	L24_3_2B/rE
	86	L24 4-2/rE
	87	L24 5-2/rE
	88	L24 5-3/rE
10	89	(15-)L28AP/rE
	90	L24 26-10/rE
	homology to: LOCUS R06687 403 bp mRNA EST 03-APR-1995; yf10a10.r1 Soares fetal liver spleen 1NFLS Homo sapiens cDNA clone 126426 5'	
15	91	L24 26-2A/rE
	92	L24 26-2B/rE
	homology to: gb AA590026 AA590026 vm22g03.r1 Knowles Solter mouse blastocyst B1 Mus musculus cDNA clone 990964 , 459 bases, 139A; and Rattus norvegicus Eker rat-associated intracisternal-A particle element	
20	93	14 7#2E-rE
	homology to: N-acetylglucosaminyltransferase I; this sequence shares homology with SEQ ID NO:32.	
25	94	x18
	95	31_3_9-rE
	96	31_3_6_2-rE
	97	31_3_17-rE
	98	31_3_15#1-rE
30	99	24_3_5#1-rE
	100	31_4_4#1-rE
	101	31_3_19#2-rE
	102	31_4_5#1-rE
	103	24_9_3#2-rE
35	104	14XD#12E-rE
	105	70A-rE
	106	31-3-4-rE
	107	3_6_9-NeoG-rE

- 108 31_4_2-rE
- 109 3_2_13-rE
homology to: calcyclin
- 5 110 3_2_4-E
homology to: pistlre-alpha 1 (with homology to calcyclin on negative strand)
- 111 L25-10/-rE
homology to: calcyclin
- 10 112 L24-4-3/-rE
- 113 L24-9-1-rE
rat id sequence
- 15 114 17-L25-27#7-rE
homology to: calcyclin
- 115 L21C1E-rE
homology to: calcyclin
- 20 116 L24-5-3BE-rE.
homology to:
LOCUS H32572 310 bp mRNA EST 08-SEP-1995 EST107805 Rat PC-12 cells, untreated
Rattus sp cDNA 5' end, ACCESSION H32572, and
- 25 LOCUS AA858747 470 bp mRNA EST 10-MAR-1998 UI-R-A0-bb-e-01-0-UI.s1 UI-R-A0
Rattus norvegicus cDNA clone UI-R-A0-bb-e-01-0-UI, 3' similar to gb|AA473081|AA473081
vd44b07-r1 Barstead MPLRB1 Mus musculus cDNA clone 803413 5' mRNA sequence
- 117 L24-4-2BE-rE
- 30 homology to: LOCUS MMU51002 6495 bp DNA ROD 16-JAN-1997 Mus musculus Dlx-2
gene, complete cds, ACCESSION U51002 NID g1477589
- 118 17-3-3B-B4
- 119 L24-26-3/-rE
- 35 homology to: RNU23776, DNA ROD 10-AUG-1995, Rattus norvegicus Eker rat-associated
intracisternal-A particle element
- 120 12_2B#2-rE
- 121 05-17-3-3He-1-T7
- 40 122 21_5_8E-rE
homology to: emb|AL021154|HS150O5 Human DNA sequence from clone 150O5;
1p36_13-36_22, contains the E2F2 gene for transcription factor E2F-2 and the ID3 gene for
Inhibitor of DNA binding 3(dominant negative helix-loop-helix protein, 1R2, Length =
133667, 971 bases
- 45 123 X18H-t7

124	18A_8_4E-rE
125	L24-5-2BE-rE
126	L24-4-2AE-rE
127	L24-10-1BE-rE

5

Genes Necessary for Viral Infection

Some of the isolated sequences disclosed here comprise sequence encoding the following proteins: tristetraprolin (human ZFP-36), 6-pyruvoyltetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucos-
 10 aminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

Isolation of cellular genes that suppress a malignant phenotype

15 We have utilized a gene-trap method of selecting cell lines that have a transformed phenotype (are potentially tumor cells) from a population of cells (RIE-1 parentals) that are not transformed. The parental cell line, RIE-1 cells, does not have the capacity to grow in soft agar or to produce tumors in mice. Following gene-trapping, cells were screened for their capacity to grow in soft agar. These cells were cloned and genomic sequences were obtained
 20 5' or 3' of the retrovirus vector, i.e. SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94; sequences designated with an "x" in the clone name). All of the cell lines behave as if they are tumor cell lines, as they also induce tumors in mice.

Of the cell lines, two are associated with the enhanced expression of the prostaglandin
 25 synthetase gene II or COX 2. It has been shown that disruption of gene function by retroviral targeting of an upstream gene has lead to increased expression of a downstream gene product, COX 2. When a small molecule inhibitor of COX 2 enzyme was added, reversion of the transformed phenotype occurred. The COX 2 gene has been found to be increased in pre-malignant adenomas in humans and overexpressed in human colon cancer. Inhibitors of COX
 30 2 expression also arrests the growth of the tumor. One of the cell lines, x18 (SEQ ID NO:94), has disrupted a gene that is now represented in the EST (dbest) database, but the gene is not known (not present in GenBank).

Each of the genes from which the provided nucleotide sequences is isolated (and all clones designated with an "x") represents a tumor suppressor gene. The mechanism by which the disrupted genes may suppress a transformed phenotype is at present unknown. However, each one represents a tumor suppressor gene that is potentially unique, as none of the genomic sequences correspond to a known gene. The capacity to select quickly tumor suppressor genes may provide unique targets in the process of treating or preventing (potential for diagnostic testing) cancer.

Isolation of entire genomic genes

10 An isolated nucleic acid of this invention (whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127), or a smaller fragment thereof, is labeled by a detectable label and utilized as a probe to screen a rat genomic library (lambda phage or yeast artificial chromosome vector library) under high stringency conditions, *i.e.*, high salt and high temperatures to create hybridization and wash temperature 5-20°C. Clones are isolated and
15 sequenced by standard Sanger dideoxynucleotide sequencing methods. Once the entire sequence of the new clone is determined, it is aligned with the probe sequence and its orientation relative to the probe sequence determined. A second and third probe is designed using sequences from either end of the combined genomic sequence, respectively. These probes are used to screen the library, isolate new clones, which are sequenced. These
20 sequences are aligned with the previously obtained sequences and new probes designed corresponding to sequences at either end and the entire process repeated until the entire gene is isolated and mapped. When one end of the sequence cannot isolate any new clone, a new library can be screened. The complete sequence includes regulatory regions at the 5' end and a polyadenylation signal at the 3' end.

25

Isolation of cDNAs

An isolated nucleic acid (whose sequence is set forth in any of SEQ ID NO:1 through SEQ ID NO:127), or a smaller fragment thereof, or additional fragments obtained from the genomic library, that contain open reading frames, is labeled by a detectable label and utilized
30 as a probe to screen a portions of the present fragments, to screen a cDNA library. A rat cDNA library obtains rat cDNA; a human cDNA library obtains a human cDNA. Repeated screens can be utilized as described above to obtain the complete coding sequence of the gene

from several clones if necessary. The isolates can then be sequenced to determine the nucleotide sequence by standard means such as dideoxynucleotide sequencing methods.

Serum survival factor isolation and characterization

5 The lack of tolerance to serum starvation is due to the acquired dependence of the persistently infected cells for a serum factor (survival factor) that is present in serum. The serum survival factor for persistently infected cells has a molecular weight between 50 and 100 kD and resists inactivation in low pH (pH2) and chloroform extraction. It is inactivated by boiling for 5 minutes [once fractionated from whole serum (50 to 100 kD fraction)], and
10 in low ionic strength solution [10 to 50 mM].

 The factor was isolated from serum by size fraction using centriprep molecular cut-off filters with excluding sizes of 30 and 100 kd (Millipore and Amnicon), and dialysis tubing with a molecular exclusion of 50 kd. Polyacrylamide gel electrophoresis and silver staining was used to determine that all of the resulting material was between 50 and 100 kd,
15 confirming the validity of the initial isolation. Further purification was performed on using ion exchange chromatography, and heparin sulfate adsorption columns, followed by HPLC. Activity was determined following adjusting the pH of the serum fraction (30 to 100 kd fraction) to different pH conditions using HCl and readjusting the pH to pH 7.4 prior to assessment of biologic activity. Low ionic strength sensitivity was determined by dialyzing
20 the fraction containing activity into low ionic strength solution for various lengths of time and readjusting ionic strength to physiologic conditions prior to determining biologic activity by dialyzing the fraction against the media. The biologic activity was maintained in the aqueous solution following chloroform extraction, indicating the factor is not a lipid. The biologic activity was lost after the 30 to 100 kd fraction was placed in a 100°C water bath for 5
25 minutes.

Isolated nucleic acids

 Tagged genomic DNAs isolated were sequenced by standard methods using Sanger dideoxynucleotide sequencing. The sequences were run through computer databanks in a
30 homology search. These genes can be therapy targets particularly because disruption of one or both alleles results in a viable cell.

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SEQUENCE LISTING

<110> Rubin, Donald H.
Organ, Edward L.
DuBois, Raymond N.

<120> Mammalian Genes Involved in Viral
Infection and Tumor Suppression

<130> 22000.0086/P

<150> 60/062,021

<151> 1997-10-10

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<213> Rattus norvegicus

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<211> 891

<212> DNA

<213> Rattus norvegicus

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cngtaacaat	gccctntttt	cctaagccta	accagtcctt	tangaggant	gctcttgggn	360
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catctctgtg	acttccagac	cggcntcgcc	agagcaagtt	ccaggccacc	cagatgagat	840
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<211> 974

<212> DNA

<213> Rattus norvegicus

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<210> 5

<211> 850

<212> DNA

<213> Rattus norvegicus

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cacaaatntg	ggaggtgncg	gggaatgntg	ncnttttctt	gngatgaggg	ntgccgtnc	300
ggantaacag	ngnttgcntt	gtntngcnaa	acgaagagtn	tcctgnttgg	aataggngtt	360
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 <212> DNA
 <213> Rattus norvegicus

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<210> 8
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 <212> DNA
 <213> Rattus norvegicus

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 agagcccccc agaaancccc tntctcaaan aaagagaaag agaaganca gnagnagaga 180
 ganaganaga gagagagtgt ggancntnt cctcnganc ccannnanan ngtgnggcnc 240
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 ncccgg 906

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 <211> 914
 <212> DNA
 <213> Rattus norvegicus

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<210> 10
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 <213> Rattus norvegicus

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<210> 12
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 <212> DNA
 <213> Rattus norvegicus

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 <213> Rattus norvegicus

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gtgaaaccac	ctcggcatcc	ttttatntca	tagaggcaaa	tntagcttgt	ttctgccgag	660
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aagtaaagtt	aggaagccat	gaggcagtgg	tgcaggaagt	taggaagaaa	naccgggttg	780
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<210> 15
 <211> 896
 <212> DNA
 <213> Rattus norvegicus

<400> 15						
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nggnggnaaa	gagnnanttn	tttcaagggt	ccgnaacaaa	aagttgagng	angattccna	180
acaagggntn	nccacccaan	ctgntaaagg	gangatttgg	ncaaacanaa	accngtattg	240

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gggagttaaa	aagagtcacc	aaatagggaa	aaaaagttng	ggggaggggn	aacnacnggg	300
taaaggttcc	aggaccagag	ngttcagnac	caagtttcag	tattcaggag	gacagagttc	360
aggatcnntt	tggaacattg	gggtttgggt	agcntggnaa	cacgaaccct	tttgttcata	420
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gttctgtggt	tgccggtgga	tgntctgcag	ctgtntaccc	caccgaaaac	gaatggatgg	660
gatgtcactc	ccaggcagta	gggggcgcac	gcgcattgtg	ttntagagag	anttccccag	720
cctccccngg	aannacaaca	cgttntcttc	ttcttaaggt	gggtgggtggg	ggggggggga	780
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<210> 16

<211> 858

<212> DNA

<213> Rattus norvegicus

<400> 16

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tatatthttat	taaatatata	cttagattca	ntctttgcct	aagcctggat	gttgttggtt	360
tttgthttttg	ttttgttggt	nggagagttt	tcattttccc	aagctggctt	tgaacattca	420
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<210> 17

<211> 551

<212> DNA

<213> Rattus norvegicus

<400> 17

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gngatctntc	tctctgtgca	cgaganattt	tagaggggga	tatccccggg	gtgtngccng	180
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gagngganaa	catttttntg	tgngggcccc	ccacaananc	acnaacaana	tattttcgag	300
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nanagacacn	nnatatntct	ggngtgtgna	aanataanac	aagancanac	atngggagan	420
natgtgagan	tgtgcacacc	ctggtgtgac	atgtgaggtg	gggggctgat	gatnccctnc	480
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<210> 18

<211> 888

<212> DNA

<213> Rattus norvegicus

<400> 18

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gaggggccaa	aaggataagg	aggatgattg	attgggtttg	gagcagtact	tggaaagagt	180
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aaaagatttc	aggagatctt	gatttttttc	gggtcgagct	atgttggggg	atgtgagggg	300
acaattcaca	agatttggtc	acagggaggt	ctaggaggtg	gtcccatag	ccggtagggg	360
ggttttctca	ataaatgggt	tcagtcaggt	gtttgcctag	atctttcatt	agttcctccc	420

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ttcaaaggga	ttttgaagga	gtgctttgtc	ctgtggagca	attgactcaa	tcaataaact	480
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gaatcacaat	ttcctaacca	tatgattttt	gttaatctca	ccacataaac	ccacaattct	600
cgcgtccttt	gtgatgggtt	caaagtctgg	aatatttttt	cctccatccc	tcctttcctt	660
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aaaccatgtc	cagttacttc	ctcctaattc	catcttcaga	tatcctttta	gaccaaatta	840
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<210> 19

<211> 867

<212> DNA

<213> Rattus norvegicus

<400> 19

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tggggaacaa	aaaaaaaaa	ttaaaaattt	ccaggggggt	tttgaaggca	ggtgatttaa	180
aaaccgcccc	tcagttaagg	gggttttatt	tttttttaat	aaaaaataaa	attaggattc	240
tggaatagaa	tttttaattc	agggatcctt	atTTTTaatg	tttccagggt	aaaagggaga	300
tattcttata	aggtttctgg	aaaaagtgtg	cttggtttcc	tttggcagga	gagaggttta	360
aaaaagactt	catttgaact	ttttgatcat	tgtgtaaaac	tttttttttt	gaacaaaaca	420
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<210> 20

<211> 897

<212> DNA

<213> Rattus norvegicus

<400> 20

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aatttgggca	cttcnattgg	gaaggttaaa	accagggcaa	gtgntaccgg	gntatgcaag	180
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gaggacttgt	gagnacaggt	catgcccacc	aaagggagga	gcaaggggtg	gcagtggtag	300
gtggtgtgtg	gttcctttct	gggggntggg	cggggagaca	gatgagaacg	ntattggagg	360
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cttgatgctt	gggccggcaa	ctgtgnacct	tccctgnacg	ttcagccccc	ccacccttac	480
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<210> 21

<211> 435

<212> DNA

<213> Rattus norvegicus

<400> 21

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gcagagtata	cactggttgg	gtaaataaag	aggagagaca	gagtgggaag	tcggcttagt	180
ggatatggac	ttcaaatttg	atgaacaagc	aattcaaatg	agtatcgtgg	gcttgantgg	240
tatgaagacc	cgtttgcaaa	gcagtgggtca	taagagagaa	aagagagaga	gagagagaga	300

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gagagagaga	gagagagnaa	gagagagagn	gtgtgttgtt	gttggttgttg	ttgttgttta	360
ttggtnata	acaanatnta	cctttgggcn	ctttngaaag	actntncaca	aaggagcttg	420
ncaagctaga	aaggt					435

<210> 22
 <211> 894
 <212> DNA
 <213> Rattus norvegicus

<400> 22

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ctagaggana	accggccnat	aggnggggn	agnatggaag	gattttccag	agaggaatca	180
gtttggngag	agaatttgat	aaggagtcc	ttggaaccaa	ccnggagggg	gttttggttt	240
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<210> 23
 <211> 594
 <212> DNA
 <213> Rattus norvegicus

<400> 23

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nagagtaatt	tcaaaagccc	cagntttgtg	gaatcanttt	ttgaanatat	gaaaaggccc	180
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gtttntggca	gaaacagaac	agccccgttg	gcacggacag	tgtccactgt	ttatctataa	300
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gggagtcaga	gaggtcggaa	caatgaggcg	gaaaccaaaa	ntntgaaaca	cgcccacctg	420
aacaggacga	aagggtgggg	cttgggtccac	ccagaaggaa	acctcgaact	ccacntttca	480
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<210> 24
 <211> 586
 <212> DNA
 <213> Rattus norvegicus

<400> 24

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aacacgcccc	cctgaacagg	angaaagggt	ggggcttggg	ccaccagaa	ggaaacctcg	480
aactccacnt	tcaaggtatc	cgctccgggt	tagcagcccg	ccaaacgccc	tgctggnttc	540
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<210> 25
 <211> 909
 <212> DNA
 <213> Rattus norvegicus

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<400> 25

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gacngaggga	gacccaagga	cntagantca	ccggtgagcg	ggccggcgcc	ggagagcgga	480
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<210> 26

<211> 576

<212> DNA

<213> Rattus norvegicus

<400> 26

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<210> 27

<211> 853

<212> DNA

<213> Rattus norvegicus

<400> 27

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<210> 28

<211> 825

<212> DNA

<213> Rattus norvegicus

<400> 28

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<210> 29

<211> 861

<212> DNA

<213> Rattus norvegicus

<400> 29

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cccngagnan	naaaattgag	tcagtngggg	gnaaccgacg	nananaggaa	caggtttccc	180
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caaccggta	agacagattt	ntcgccantg	ccagcagcca	ntggtaacag	gattagcaga	420
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tagntttnga	tcccggcaga	caaaccaccg	ttggnagcgg	tggntccttt	gnntgnaagc	600
agcagantan	gcgcagaaaa	aaaggatctc	gagaagatcc	tangatatnt	tgttcggggg	660
cagacgctna	annggtnctg	natnntganc	ggntgaccat	agagcacagt	antgnngatt	720
gcagtcggcc	ccnaggacga	naggagacca	ggggcccang	ctgnagtaac	naatcaacta	780
ccctnacnag	atgnancaga	gagagagagn	accgtatant	nantgnaaga	gaggtcccgg	840
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<210> 30

<211> 149

<212> DNA

<213> Rattus norvegicus

<400> 30

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gaggcttttc	ctcccttcag	taggtcagc				149

<210> 31

<211> 857

<212> DNA

<213> Rattus norvegicus

<400> 31

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ttccaggngn	acangaacgg	gtgcggnggg	antaggggga	aangtttgga	gtgngccaaa	180
acggaaaagn	agacgnttgt	angggttggg	aaccagnacc	ntggaaagan	tnagttctn	240
atcngcaaca	accaccggag	gtaggggggt	ttttgtngca	gcacagatan	gcgcagaaaa	300
aaggatttca	ggagatcctt	tgatttttat	tcgggtanga	cgttcangtn	gnggggattg	360
ggagcggana	accatttnna	cacaggattn	tatgaactat	ggtcanttgc	tttgttgtec	420
angtcgttgt	gggattgctg	tttttagtag	ctgcaaaccg	ttcgttttnt	gctatctttg	480
ttnggataaa	tcagccccgg	gcagangana	ttcgaaagtt	cccttttagga	gcttatttan	540
acgggctcaa	ngccaccggt	ttcgtttttn	taggcacgtt	ctgcgcattt	tttttttttn	600
gnatntttgg	atcgcgtttc	gtgggatctt	aaaaaccgtt	ttctgtgatt	ggcacgcaag	660
aaanactcat	gagctggtcc	ctgttggtgc	tctcaggacc	aatcaaanac	ccatttccaa	720

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cggctttata	atgtctgggt	ctgtttgcac	aggaagcgaa	gtcacggctt	gcacccgtga	780
agtctgggga	ggttcagagc	tgggaactgc	ccagaggaag	gggttcgggg	ctacagccat	840
caatcttcca	gttggttt					857

<210> 32
 <211> 1630
 <212> DNA
 <213> Rattus norvegicus

<400> 32

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gnnttaannc	ttttngngaa	tgtnnacccc	aatnttcccc	tnaattttga	gtngngataat	180
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aaatcccgtt	gttttagatct	tgaccgtaat	caggagtcag	cgtagaggag	gccccggaag	360
gagggcccag	cgcggttcg	cccgcggcag	ggcggggacc	aacagagggc	cntcggggat	420
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cagacccgga	ggaggccgct	ccagcgttgg	tggtgccggt	ccggggctag	cctgatccgg	540
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ccagaggagg	aactgaagca	gtggttcttt	aagtaactga	ctcagggctt	tcctgcctgg	1560
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gaagagcctg						1630

<210> 33
 <211> 883
 <212> DNA
 <213> Rattus norvegicus

<400> 33

aaaaattgta	aggagtggg	ggnatcccc	ataattnaaa	nagggaaaca	nccntaaagg	60
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ggaatttggt	anaattttnn	taatggaaat	ngggcacttc	aattgggang	ataaaaacccc	180
aggaagtgat	accngggtta	tcaagtnaaa	cntgattcct	ggngnngagg	gaaaggatat	240
tgaatttgag	tgagtgcagg	tgaagtgaga	cttgggagna	caggtcatgc	ccacccaagg	300
gaggagcaag	ggntgggcag	tgtaggtggt	gnggtgggtc	ttcctggggg	gggcggggag	360
acagatgaga	acgttattgg	aggacaggca	caagtgttac	tgaaatgcaa	atccctgtag	420
atntggaaaa	gttctggntt	caggcttgat	gcttggggccg	gcaactgtgn	actttccctg	480
tacgttcagc	ccccccaccc	ttacggaagt	tntcgtcact	gagantagtg	gctaatacaga	540
gtcttcaatg	gacctgcaa	tcagaaagga	aggcgggcct	ttccgggtgc	ntaggtgtag	600
gattcgctca	gtagttaagc	agtcttaact	ggttntggct	gctgtgctct	ctgtcctgcc	660
gttggaattnt	ntgaggcatg	ttcaggcaag	ctccaaagtt	gcgacatggg	gagcacaggg	720
gcaggggggg	cgggcgagcg	ggcaggggac	tgagcagtg	gagctgggtg	gggtgggtctt	780
tcccggggct	gagttggaat	ccgcggctac	ccgtgaggtc	ttagccactc	actagacca	840
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<210> 34
 <211> 913
 <212> DNA

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<213> Rattus norvegicus

<400> 34

ttccccccna	gaaaaatatt	tttnggggacc	canaaaaaan	ggccccnggn	cctgttttct	60
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ggttttntcc	naggggggga	gaccccnttn	nccgcggggc	tttcgnaatt	ttttggtcca	180
ccngtnaaag	attttcccat	ggcgcacccat	gtacggggtg	cgaggngtat	taggcggnaa	240
cggtttttna	gtgggcctaa	tacggnanat	aggaggacga	tttgtnttgg	tttgtngagc	300
cagtaccttn	gnaaagagtt	gtagttttga	tccggcaacc	aaccacngtt	gtagcgnggt	360
tttttggtga	agcagcanta	acgcgcagaa	aaaaggatnt	caggagatcc	tttgattttt	420
cttcgggttc	ngacgttatg	ttgtgtggat	tgtgagcgga	taacaatttc	acacagattc	480
cgatngtagt	ccaatttggt	aaagacagga	tatntttccc	ttcaaagaaa	acagaaaaat	540
acagaaacgt	taattttcaa	atctcnaatc	tttcntttct	tcttcntca	ttcattcntt	600
cnttctttct	tctttcttct	tntctttctn	nagaggaggc	atgctagggt	aacagtagct	660
catttttaaaa	tctggcacct	ggaattaatt	tagggacaaa	acacctttat	gcaaaaaaaaa	720
gtttatgttt	ttccatggaa	cacagtaaaa	tcaaaattaa	aagaatataa	caaaggcttt	780
ggtgatttgg	taggattttt	tttttcctgg	aggggaaaac	agatgacttg	gaaagtgtta	840
ggaacatatc	aagccccagg	gaaagaaaaa	cgtttgattg	gtattaatta	aaacactgct	900
aatatattct	aat					913

<210> 35

<211> 320

<212> DNA

<213> Rattus norvegicus

<400> 35

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aatttgatga	acaagcaatt	caaattgagta	tcgtgggctt	gactggtatg	aagacccggt	180
tgcaaagcag	tgntcataag	agagaaaaga	gagagagaga	gagagagaga	gagagagaga	240
gagaaagaga	gagagtgtgt	gttggtgttg	ttgttggtgt	tgtttattgg	tttataacaa	300
gatntacntt	tggttaacttt					320

<210> 36

<211> 389

<212> DNA

<213> Rattus norvegicus

<400> 36

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ctnttanann	tnttcnggg	gtncctcncc	gntgtgggga	atganatntc	gntctcgaca	120
tcaggggatt	ggagattntc	tgngctcncc	nctcacnacc	cagaagaagc	gcacagagan	180
cagagtanca	catcatacac	acctnttcag	ctacagagcg	antnctctan	aaggggactc	240
ggggganaac	acaacctctc	tcctcttctg	actgngagng	ccgcntgtag	gntctgtcta	300
cccancaagn	cttgtgcagn	ntgngaacct	ctctntgggg	tagagtgtgt	tgngggagca	360
gggcgtantg	ttccaggngt	agnctttca				389

<210> 37

<211> 882

<212> DNA

<213> Rattus norvegicus

<400> 37

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gnagcgctcg	gngannnccc	acnggnagac	nnnggctgcc	ccncgngncc	anggenttnn	120
nccnncccc	cgnatccggn	ncnccccccc	ctccctnggg	gngcgggggt	ccngngcccg	180
ngnggatacc	nggcganncn	ttgtgcccc	gcnggggggg	naggaccccc	ggcacccggc	240
cngacccana	ncagnngctt	ngtggggggc	ccccccgcca	nagaacgaat	tnccgcnccg	300
gccgcggcca	tcggaacncc	cctagcagng	cgtcntgcta	ggcnggnnna	cgggnatccg	360
caancccncc	cttngtaccg	ggacagccgn	gggnccgtat	gggctgngcg	ntnggccgta	420
gccanntncc	tttngaaang	acncggnagc	tnttcatccg	cctcacaac	cnccnggncc	480
gngggggctn	tntcntgngc	cgcccggcgc	gtgngcgcan	aaaaaaaaaa	aannccggcn	540
tcnccccctc	ttttggccng	ggtnccccgc	ncaccccggt	ccgagtnccn	nccccccac	600
aacctcacac	cgatcccngt	gggttcccn	ngggagtcgc	ncngncnnag	cnggnttctc	660

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cccatnnccg	gnngcttnag	cgngccnnnn	cacngtttgt	nnngnnntgc	ctcccccttcn	720
tccttgaggc	aaaagcccgn	acngtntctg	tggaccacnn	tgctgaggng	ctgggcgcen	780
cgntctctct	ctctctcnct	ctctctctct	ctctatctct	ctttctctct	ctggggcccc	840
tccttgntg	nngccanaag	nnngcnnacc	cgtaaagtaa	gt		882

<210> 38

<211> 975

<212> DNA

<213> Rattus norvegicus

<400> 38

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tngatcctna	naatttcaac	aaccgcagga	ccatttttga	acttggcggn	ngtttaccct	180
tnatgnnctt	tcennaaaat	ggcttccttt	gncatcnaat	agtgtgtccc	ctaacccttn	240
ggttccggag	gatgcatnng	tggntgtgng	tttgnccttg	agcatgcngt	tcctgnacgg	300
gancaagntt	ntcaatgttc	cntcacncca	tacttnggct	tgggggtacaa	nttgatatatc	360
ttcgggatta	tatnagttta	tgtctgnttt	tcataaaaatc	acttgtggat	ttggcttttaa	420
ngttaggaca	acttnccaca	gtttcttgga	tctccntcaa	catgttaacg	ccattttgtt	480
cttgatatact	aaagtgcacat	gtcnttntng	acactaacia	tcacaaatta	ggagtaccaa	540
tcaactttga	gaaaatttta	aagatgcccc	atctcttgta	tcagcaagta	ttcagccagg	600
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tatttcttta	tgaattatta	tccatgaatg	tttgatctgt	atagctatnt	tatataagta	780
tatgcaagga	ttgctaaaac	aatttttgag	tgaaaaaaga	tcctaggtag	aaaatgttta	840
agactaccta	taccgtcatt	aaaaactcct	caccagcatt	tactatgggt	ggactttcag	900
agatctcaat	caactctttc	ccacccagtc	tactgaaagn	ttccacctgt	agcggcccaa	960
gcaaactgag	atntt					975

<210> 39

<211> 850

<212> DNA

<213> Rattus norvegicus

<400> 39

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ngaangcctt	ccngagggcc	ngaaaancat	tncttcngga	gccgttcaag	ccagnagggtg	120
ggtttcaaac	aatgcttaag	ttgtggggag	aacnagnacg	tcctgtccng	accngtttta	180
tcntaaagga	gacggnggtt	aaagggttagg	gggttngaca	gtcctgctgg	tgttcaagga	240
ggaggagaca	agttgncatc	caggngngca	ggaanacctg	ttaaattcct	gaccnaccgg	300
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ggtatcacgg	ccccctnng	gtttccattt	gcagtgtgta	ttggaccatg	gatcactgct	480
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tgccgntggg	actttttnta	atatcntggt	acccgcttcc	catttcccca	ccccntgnt	600
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<210> 40

<211> 889

<212> DNA

<213> Rattus norvegicus

<400> 40

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attaaggggg	gccgggggaa	aaaggagatt	nattaaancn	ccacccgaat	tnaaacnccc	120
nccgggaccg	naaccgtttt	tggccnaaan	ncgagaagtg	ccttccnggc	aaagtagggg	180
accaaaggtn	gggggagaga	attgggggtt	gtncagngtt	ccggttcnac	ggaaggagcc	240
ggttggtggg	attgtttcca	aggagngngt	ttgngaccgg	agcacctcng	ggnggaccat	300
ggggnttgcc	tgtagagac	cngcgngatg	ttttgggttc	gnattcgggg	agggatttcg	360
ggggcctcag	acnggggagg	agtcccntgc	gttcccnatg	ggaccgggtg	tcgggcgggg	420

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gcagtttcgc	tgctgtcctt	tggcaatgng	cntgggnatt	ngtgggcaga	ngagattccc	480
cngccccgc	natttcccn	gttccagttc	ntaggnacca	gaggttttcc	gcagtgtgat	540
tcagggagnt	agantntagc	gtctgtnttn	tntgctgttt	ccccttcacg	attctcagtt	600
atTTTTtagg	agaaaagggtg	cgtggaaaca	gagcgtccct	gttccgtgct	gtttctcnta	660
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ataaacgtgt	aatatggctt	gctttttcct	tgtaacgttt	catccaacca	tagtggtagc	780
ggccacctgg	catcttgagg	tgggttgcca	atgagtgaat	gaatgagtga	gtgaatgaat	840
gaatgaatga	atgaatgaag	caagcttcag	ggagattttc	agagaagtg		889

<210> 41
 <211> 929
 <212> DNA
 <213> Rattus norvegicus

<400> 41						
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nttggggccc	ttgtttaagg	gttttnagcc	ttaaattgnt	tgntnagnnt	ctcctaatt	240
agttcattcc	tttgaccatc	ttttgnccct	ccatcttgta	aacanttaag	tctattgcat	300
tccactttnc	tntcagttnc	cgtttnaccc	tcctnagcag	aacccgnttc	tcagctntgg	360
atggttccaa	anggtttccc	aacctatgct	caataccaca	ggcagcttgc	aggagggaga	420
antggtatgt	atttaacagc	atTTtgacc	aaacttttag	gagcagagag	gactttaccc	480
aggacaggaa	ggcaaaagac	ttgaatctta	aacaaaggat	taagaacagg	atgtcatctg	540
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gaagcttggg	gcttatgttt	tgcagatcca	ttgtaattaa	aaaagaattg	taaggagatg	900
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<210> 42
 <211> 943
 <212> DNA
 <213> Rattus norvegicus

<400> 42						
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natcccaatt	aaggntnaac	nggtttaatt	tgtnntccnc	ntaccnaccn	ggtttncctg	180
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ggaacccagc	nagtgccttg	aggtaaaaga	tcacttccnt	ntcccttagt	caggancntt	420
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cgtccactaa	agctgcctcc	aattcaaact	ggattgagtg	acaagtggct	tgggtgtctc	540
tcaaagattt	ataggtggca	atggccactc	ctctgtgtaa	ttaccctnta	tgcacgtctt	600
ttntttctct	cccactccat	ccccacccc	tctttgtttc	ttentccntt	cctntccctc	660
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gctntagaaa	gctttgcttc	ccctctgctc	cctggctggc	tggaactcag	cctccggtgt	780
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tctctgaagt	caaggagccg	caccagcact	tcagttgtgg	gccataatca	agnccangact	900
gaaagttgcc	acctgtagn	gccgcaagca	aactgagatn	ttg		943

<210> 43
 <211> 867
 <212> DNA
 <213> Rattus norvegicus

<400> 43						
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gttttgngng	nattttcccc	ntgggtcgttt	tntgnacgat	ccacgggtga	ccgacgacgn	180

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acggaccgac	aaccaanacg	taaaggggaa	ttgtggaggg	gttggaagtt	tagatgcccc	240
gacccaggac	gtgcggccan	cttccggaga	cccacctttc	ttgtnggccg	ggnccggcgg	300
cagcgnagcc	atttccaccg	gatccctata	gcnggccagc	ctagcaggcn	gaacaccagc	360
gggaagttga	ntnggacctc	ggagagcgcc	cgcccttccg	gcggaagtnc	taattccaaa	420
gcggcccgcg	gcngagtttc	ccatacaggt	tggttccgtc	tcggagtga	gtggcttgaa	480
ggacggtctt	cgcgcgagaa	gagtaccctg	cctttcaggt	gcgggagtta	cntcagcctg	540
ctgcacaccc	ggctgtgcgc	antcttcttg	tgtggccggg	acggttcacc	cagaggagtc	600
tctgtagttc	ggagcaagat	gtcggttaaa	tctggcagga	aatgccttc	tatgctcatn	660
tatatattcc	tgcttccctc	agcttgcttt	cgacttagta	aggtaacatt	tcagagcggt	720
gcacttagta	ctttttggca	ctgtgctgta	taaatataaa	tgttccacac	ttaacatctt	780
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tatttttgca	tacattggtc	agctgtg				867

<210> 44
 <211> 303
 <212> DNA
 <213> Rattus norvegicus

<400> 44						
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ggtgggcatt	aacctgatct	tccacttgag	ggtaagggaa	atgattagtc	caagaaatat	180
ttgagcagaa	gggagttagg	gttttcaa	taggaaagtg	gaatccacag	agttcccttg	240
acagagaata	taaaaaggac	tctgggggtgt	cagaatgggtg	ggcattaacc	tgatcttcca	300
ctt						303

<210> 45
 <211> 840
 <212> DNA
 <213> Rattus norvegicus

<400> 45						
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tnngaaaaaa	gganggggan	aaggcaggng	nccnactnaa	aanggncttt	tcnaagnng	120
anagagntgg	naatnagna	naggacattc	ttinnaacctc	cnangngngn	nggaannaat	180
ngggattgag	cngccaccat	tagggangaa	gttngaattn	nggggcccgn	gngagttaaa	240
angattcccn	ggttttttaa	aacagagaat	acctncagg	acagatnaac	ccgagattgg	300
ttccctngaa	aattnnngan	aaagataaan	gtaggagcat	tcaaagtag	anggtaaaa	360
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cgcacntaga	tccaggcgnt	ggggggcggg	cgggggcggc	ntngncagng	aagntnnngc	540
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tcccaacccc	ggcccccna	cccnaccccc	nttgctccctg	tggcattcgc	gttctttccg	720
ccgtctccct	cgcgggccgn	ttntctgcgc	ctggtgatcc	tttcgccatg	gtcctntgga	780
gaaagaaaaa	atctttaatt	tnctagggac	gtccttttcc	tgtagtcgta	attgtagaaa	840

<210> 46
 <211> 893
 <212> DNA
 <213> Rattus norvegicus

<400> 46						
gagaaggann	aggnggggng	agngaagana	gaggagggaa	gaaangaagg	tggaganaag	60
tggannaaaa	agagggagan	ggagggagaa	ntaaaganag	ganaagagng	gggaggaggg	120
gnagnatagg	agaggaaaga	aagganggan	agaagagaaa	agaanganga	gagaaaggaa	180
agaggaaaga	aagaggggag	aagaggaaga	aanagaggag	gggangagag	ggaggataag	240
agaggaaaga	gggaganagg	nttgaaaagg	gaaagagaag	gagaaaggna	gnaggngngg	300
aagagaggna	agggagagg	gganaanggt	aagggggnaa	agaangagaa	gtatnggggg	360
aaaggaggag	angaaagaag	aaagaganga	ggaggagagg	gagagtgagg	aataaagggg	420
agggaaggag	angagaaaga	gagagaggga	gagggaagaa	nagagaagga	tagnggggtg	480
gagaaggaga	aaggagagaa	ggagaaggng	agaggagaan	tgaagaagga	gggagtaaga	540
aaggantgag	naggaaagga	ganagagagg	tagagagaaa	anaaagagg	aaanggagg	600
gaggagggng	nanaaggaa	agaggngnga	aanangagag	aggggaaang	gggaaggaaa	660

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ggaggaaaaa	aagnagagaa	gaagagnaat	gggaaggang	nagtagnaaa	agaaaagnag	720
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nacccccccc	ccccacacac	acacacagcc	ttttcgccgg	cggaagtgca	ggttggtcca	840
ggagcctgtg	gtcaatccag	tcagtagtg	gcgaggtgta	acatctgtgt	ccg	893

<210> 47
 <211> 789
 <212> DNA
 <213> Rattus norvegicus

<400> 47						
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cgtttccana	gncaaccatt	ctgggngncc	caaggttnga	ngagntccgn	tcaaggngaa	180
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agcgtttact	ttttnttgnc	cgcagccaat	ttgttntgct	tggtttcttc	ngaattccgg	420
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ttccggcagn	tacgantctt	caacaagagc	cagagaaggc	gggtgcagag	nttcattagg	540
acgntcgga	acccggcggt	acttactttt	tccaagccca	ttggttgatg	agaatgatga	600
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aagctgcgcg	cgcagccatg	accctcaca	gccacntatc	ggagggagg	gcgggacagc	720
tttagcttgg	tgcgtgcgca	gccggacgtg	aggcagttgg	tggctctcca	tcgtcgattt	780
ctggttacc						789

<210> 48
 <211> 872
 <212> DNA
 <213> Rattus norvegicus

<400> 48						
gggggnggct	tttttnggag	gcatanatng	gggnngtcc	ggnaaacccc	attggtcggc	60
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catnggccag	gaangcagat	tcaaaaatgt	tccaagtggg	aaaccanggt	tggnanaggc	180
cctccnggnc	gtnaaggagg	agaggagaga	tggagtttca	ggtgtgtttc	ccaccagtg	240
ttcccaggga	acacaaaacg	gataggtcac	cntcaatgna	caaggaatta	aaagcttggg	300
tgtatnggga	ggcctgcttc	caaagccacc	agaaaatccg	gagagccggn	ggatcntacn	360
caccagagg	ttcataggga	gggcantatt	aggggtgtgc	ccttgtgaga	ggaagtgtgg	420
cacngtgggg	ctgggtttga	gatntcagat	gntcaagcca	ggcccatnt	ntctctctca	480
gtntctctcg	gtctctttct	cngtctctnt	tcagtctntt	cagtctctct	cagactctct	540
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caccangacg	ataataggct	aaacttntga	actctaagcc	agcctcaatt	aaattntan	720
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ctcagaagcc	caagagggaa	aagaccttga	at			872

<210> 49
 <211> 785
 <212> DNA
 <213> Rattus norvegicus

<400> 49						
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tatagcgtgn	acngtttttg	agtnggctaa	aaggaaatgg	agacntattg	tnnttggtttt	120
gtgaccata	acttcggaaa	ggttggtgtt	tatccggcaa	caaccacngt	gtagcggtgt	180
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ttnttcgggt	tctgacgntc	atgttggtgt	gaattgtgag	cggataacaa	tttcacacag	300
aattcaaagg	agaggagcca	atatagagg	ggaaaaaaa	agaaggggaa	agcattagtt	360
taaaaagttg	agagaacaaa	gtatgttttg	cttggtatgg	caaccaaa	agcntgccag	420
gaatggctcg	taaaaggtgt	aagagtcagt	aaacgtcttc	tgtccaaccg	ttaccggaaa	480
catgcaagga	atttcttaga	ctggccagga	ttggattgtg	ggaaaggtct	cttcaagcnt	540
ccccttggt	tttatggcaa	gaaaatagtg	cggactatag	agagcgtcgt	tctcaaagct	600

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tgtccccaat	agcagaaaag	cattgtccta	aattccttaa	aaggcaccgt	gaaataaata	660
ttacgaggac	acgatggcac	aagaaggagc	tttcaactct	gccaccagaa	cagttatact	720
tcatagtaac	catgttgccc	tgttcaatga	caaggcacgc	tctccagcag	aaagggaaaa	780
ggagc						785

<210> 50
 <211> 889
 <212> DNA
 <213> Rattus norvegicus

<400> 50						
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natgggcgca	gggatagngn	gttcnggntt	cccacangaa	tttgatttnt	ggaatcacia	180
gtnaccagtn	gccgnaatca	cgagtttgcc	gctttntttc	ctaccttana	ttcataatan	240
gaatgagtan	ttttttttta	ttgagnaang	ttttnacagg	tttagtaaac	atgaggacag	300
aggttttaag	ttgangatta	ggaaggagag	ttccggggga	cagaatgtgt	gtattntcag	360
tcagtgcact	acccggaaga	gttgagtcac	gggtgaggaa	gggagcggat	ttcctggagg	420
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gagaaggggtg	tttaccttta	tataaaatgt	ctcctaactg	cgtgactgtg	tgactttgtt	540
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taaattttat	ttattattta	tgtcacgtgn	acacttggtg	cttttgtttt	tgttctaatt	660
ttatctgcat	atatgtctgc	ataccacgtg	catttctgat	gcntacagat	gccagaaaag	720
gacaccgagt	ttcccctggg	antggagtta	tagatggtta	taagtctctg	agtaggtact	780
gggaagtga	cttcagtttc	ctctggaagg	gcagaaagcg	cttttcaaat	gctgggccat	840
gtatttcagc	ccctacttaa	tttataattt	tatttttagag	gatgtgctc		889

<210> 51
 <211> 947
 <212> DNA
 <213> Rattus norvegicus

<400> 51						
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aaggagaaga	nggaaggnta	acataggagn	caagaatana	aaganaaaaa	gaggtagaga	180
anncagagaa	cgagaaaaga	tgaaanaaa	antanaangg	aagaaagang	nccagnanaa	240
anaaggcaga	aanaagatgn	cgtaaaaana	gagagaagat	aggnaaaata	gaggagaagg	300
ccnaacagga	ngggaagagc	agcgaattnn	agataaaaacc	ggagganagn	nagagaaggn	360
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gncnagangg	tgagggngng	cacngncnt	tccccttagg	aggncgccc	cccagagatc	480
aggtttcnag	gncaccgagt	tggatacnag	attatncacc	naggcaggaa	angantatng	540
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aggagggngg	gaaactctng	acagaaatng	caagcangaa	gccagccnca	cccaagcccc	660
nacngaagca	gcngagangt	tgcanngcgg	naggtccaaa	tcancgnagt	catggagnga	720
gcttcggngg	ggcccnganc	cantgaggaa	gggcaggaaa	ccatatcnag	ccgagccnng	780
nganggntgc	cctganacac	ccggagaggt	aatttttatt	tnacgggaag	cgtccagnca	840
agttcgtggg	ccggaagaga	cggtaactta	gtatacaneg	ctnntgctnc	gagttgttng	900
nccttntnat	gnnagatctc	acaaangaag	ctnanaagta	gatatgt		947

<210> 52
 <211> 860
 <212> DNA
 <213> Rattus norvegicus

<400> 52						
aagggaattt	ttaccccgggt	tnccttttgn	cnggggggna	aaaaaannaa	aaaataattt	60
tttaaaatta	aagggngngg	angtttttcc	ggttctattn	ngccnatctg	gggttacact	120
tttatccanc	ntttgntttt	ttancgggcc	gggttaaaaa	tgggggggga	ttagttcggg	180
taggngttnc	cnacagcaca	gccctgtttn	tcttcgttcc	ngaaaaaaa	aaattttgct	240
ggtntcacia	ttttnttaaa	caggatttnc	ttcaaccatg	gattaataca	tttccgggtg	300
agnttgcccc	gtttgttttt	tggnrtggata	gggatgccag	caggattcag	ggatgcccat	360
tgtgnttagt	ntctggccct	ttaggagagc	tttgggctaa	ttatgtgacc	gattttaaga	420
agtgggtgtg	ttgtgggtcc	agggactcac	ggatcagcct	ttattttata	aggacactgt	480

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ggaggagaga	cagaggctga	gctgcattct	gatgtcattt	gtgctgctgt	ggaagttaaa	540
gaaaagctgc	agaagtcagc	aaaacagatg	aataccaaga	agggcagtgt	gagtacagga	600
atggagagaa	aagtcagagt	ccagcttttg	ttaactccct	aggatcagac	anttctgcgt	660
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ggcaggcagg	aaatggaaca	tttaactgga	aacactgaac	ccacccatgg	caaacttagc	780
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gagtttgagg	ctagactggt					860

<210> 53
 <211> 191
 <212> DNA
 <213> Rattus norvegicus

<400> 53						
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aattcctcag	gatggggaac	agccattggg	cttttagtag	aggagggaca	ggcccttttg	120
cagcaacagt	tctcccctga	atggtggatc	tccacctata	cacatggggg	acttagcctt	180
atggatgccc	c					191

<210> 54
 <211> 988
 <212> DNA
 <213> Rattus norvegicus

<400> 54						
ttnttggnna	cgggtntccg	nantatgaan	ccnttcccgg	ggttttttaa	aancccngga	60
tattcgggga	tttgggtttt	nnacggcctt	tttttnagag	gccaaatncc	cntntnaang	120
ccttttatcc	ttcentttnt	gccccncttc	naattaggaa	gcntggtttg	nccgantntt	180
aaggttttta	gtcntccttc	gttnntnttt	cccttntttt	ttccctnaag	ttataaagcn	240
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ntggattcct	gngancaggg	cctntgtttc	atggaagcaa	actcccttaa	ntatttacca	480
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tgcccatgga	gggaggggac	cttctcaaaa	gggttcacgc	agcangcatt	gaaagtnccc	960
cacntgtagg	gncgcaagca	actgagat				988

<210> 55
 <211> 665
 <212> DNA
 <213> Rattus norvegicus

<400> 55						
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catttcacac	ggatttgtaa	anacngtnac	ngaaacttgg	nggttcgtag	atccactttt	120
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ccttgcttaa	agcaattaca	agttaaatta	aaagtaagag	atggctnata	gctctcatta	300
ctgggatgca	ggtgtgaaac	aagtgatttg	tgtagaagct	ggcaggatgg	gtataaacia	360
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gttactccat	gccaaggag	ggtaggagaa	aggtttgggc	ttagctttga	ggacggaggg	600
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cttct						665

<210> 56
 <211> 857

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<212> DNA

<213> Rattus norvegicus

<400> 56

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aaaggaacaa	aaganaagn	anggaagana	aagggagaaa	aaanaagagg	gagaaangga	180
ggaggggaan	agagaanaga	gggggagaga	anncagagaa	nagaannag	aaaaggngga	240
gacnaanana	gagggaagaa	aagngaggag	aagagagggg	agaanaaant	tgaagaagaa	300
gaagangaga	agangagnag	aggaaganga	ggggaagaag	aagaggngga	ggagaagaag	360
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ggagggaggat	actanggagg	ttgtttcaat	aaaagagnng	gatntaagat	taananaagn	480
aataatgccg	gtttntatct	gttcgggggg	ggtccttggt	ctccaaacac	aganntgggc	540
cagttnttca	aaattnaant	gngaagattt	cttggnntga	gagcagntca	gattnantng	600
nattnttttc	tagtttttnaa	cacaancttt	gtgntaacia	agagnnganga	ttcnaggana	660
actcgntttt	ntttgggagg	agactttgtt	cctttcnatg	aagatgcagg	acngngaaga	720
cgcaggggtg	gaacaggaca	cagnnacgct	tnngtntntg	tcngcntcag	cngcgtggga	780
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tgcaaggcngc	ggcccag					857

<210> 57

<211> 902

<212> DNA

<213> Rattus norvegicus

<400> 57

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ccgaacttcc	ngcaaggaaa	aaaaatttgg	ngggngtaaa	gggcaccncn	tcccacaaaa	180
ttttgntaan	tttgggcgca	aattcangca	ggntttngtt	ggaaaggngn	ananaccaa	240
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ataagtcaga	acactgagca	aagcaatagn	ttctcctcca	cntactgant	cacacgtgca	780
caacagccac	acccgcaatg	cttntaggag	caggtccagn	gnacttttgt	tttaactatt	840
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<210> 58

<211> 852

<212> DNA

<213> Rattus norvegicus

<400> 58

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atttttnnnn	tattnaggat	caggataaat	angaaaangg	gnanatttttn	nnnangnggg	180
tttttttttt	tttttttttt	ttttttnngng	gnnnnnannan	annnnnaaat	ggcgncgggc	240
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atgaattcag	ntaccaacca	ggttggtacc	agcatttttaa	cattcgagtt	agacatcaat	360
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cttntgggtt	ntacaaggag	cttgaggtag	tcgcccacca	gtagctgtca	ggcaggtggc	480
ttaagttcag	aaccgnttcg	tggaaaccga	gaagcagaaa	aagacataag	ttntgcngct	540
tcanaatcca	ctcntgaata	cananatctc	ggccaaagaa	gcacagccag	tctttccggt	600
nacangaggc	cgggagcaac	aantccacag	ccagcccaag	ganatacaaa	ggacttgggt	660
cagttctgna	ccagttggag	tcagagatgg	ggccctcaaa	gtcccagcag	tgaagggcag	720
ggtctccagc	nnacagtggg	acctttaaga	ggtggggact	tgtaggagga	gttagataat	780
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<210> 59
 <211> 884
 <212> DNA
 <213> Rattus norvegicus

<400> 59
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 ttaaaanaca aaaatttgan ggggnngng ngttacaaaa agacaggatg ttttccgagt 180
 cggattcaat cccaccacaa catgggggttc acaccatngt aaggaatcgn tgcctttttg 240
 ggggtatcct aggggggtana nttccaaata nngataanaa tttttttaaa aatttaattg 300
 tanatatatta ttanataatt taataaataa tatttggana nantnatgtt ctngcgcctt 360
 gnggactggt agttttttnt ccnnattnna actttcccag nactnggtag cctatgtgnt 420
 tatgcaaccc nttagaagct gccttcanta ttnaactcat actgtttctc gataatcngg 480
 ggagtagctc cagttngcta tgaagctgcg gaaaggtagg cggacatccc aggcttagac 540
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 tntgggtccc gtagttccgg tcgccaggag tagtgtattg cttaggacca ttctgggtgg 660
 aatgcatctg gtgggtctta aannatgtca ggcagggcct ggcaccaggg tctggcggga 720
 agcctcacat accgttntaa tgacttcata tgcttagaat ttgtggggaa acgatgcaga 780
 aaaatctaac cagggatgtt tctgggccag tcatgttggg gatgcctcag tcatgtaaaa 840
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<210> 60
 <211> 955
 <212> DNA
 <213> Rattus norvegicus

<400> 60
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 ggnngttgct tctcttggan cgcnttttgt tcgaccgggg tgactaaggn catgtngggg 180
 acgantaatt gtttccgggg gcngntcggc acctccnan gngngngngg tttggttctg 240
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 gattatcctg taggatgtga gcccagacnt gtctgtggtt tctttccatg acacaagaga 480
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 nttatatgcc acggcagagt ggtacgtgat gccccacat gttatgtgga agttntcatg 660
 cagggttca gaacacagta gatggagatt gtgaaaatct gttgttnact taagagactg 720
 gcccgaagga tccatgtgat gntacttctg ttgcttgtgc tttaaaatct tatgtgatgt 780
 tttgcagact centtcggga cccagacaca cagctgagag tctgccctgc tggcactgct 840
 gctgtgtgc tgaaggggaa cccaggcatt tgatgttggc cggcccaagg aggggctgaa 900
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<210> 61
 <211> 1107
 <212> DNA
 <213> Rattus norvegicus

<400> 61
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 ccttcttgac cccnagaaan gcngtttagn tttccnccca tggngntccct taccctgggn 240
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 ngaccaggag tgacaaattt ngngggacnc cccagtngna gctcacaaca ngtnagacatt 420
 gaggcnccaa aggattgttg aggggatgga ttgtgtcgca gtctgggtgc ctttatagt 480
 ccagcatcgt tgagccccgc ccaggagtg ttggcacgcc caaaccena cccagcgctt 540
 gaggcaaggc aaacacactt cccagcccct taanttnna cgcctttgtt gcttggacgt 600
 cccggantgg gagcaggatg aaggatttta gtgcaggaga agaccagtgc aagccggaga 660
 catngagttc cctntaatc ggtgttcagt ttgcenttnt ggcacgtgac tcgtaactct 720
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tactgcggat	taatacattc	ttcatgttgt	ggtgacgctc	caaccataaa	gtgattttcg	960
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<210> 62
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 <212> DNA
 <213> Rattus norvegicus

<400> 62		
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		92

<210> 63
 <211> 209
 <212> DNA
 <213> Rattus norvegicus

<400> 63		
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tccggaaaca	gaggcagngg	gatctctgtg
agttcccagg	cgaganttct	ttgtacaggg
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		120
		180
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<210> 64
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 <212> DNA
 <213> Rattus norvegicus

<400> 64		
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acatgcgaat	cgtattggga	acctactgaa
ttccgat		
		60
		97

<210> 65
 <211> 1047
 <212> DNA
 <213> Rattus norvegicus

<400> 65		
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aattccaant	tacccaaaat	ttcatgttcc
atccanaatt	naattccgga	aattttacaat
aatttgaatt	ntagttttcc	caattntaat
ntcagtagtt	tgnntttgtg	tgcccnatt
ntaanatcag	accggtccaa	tcacccaatt
gnttttttnaa	attgaatngt	tttcccntgt
accttccttg	caangttgct	ttaaattnga
attttcagaat	ccccattgaa	aagaatccgg
gnnaaagcaa	caccnttaag	gacccagga
aaccagaaat	tnagnagaaan	ttggacgnag
gganttnaca	ttnttnccgc	canaggatgn
ttgggntaaa	aaccgcgttt	gcgcaaggct
cntgtgttgg	cctcttttcc	gccgggggcg
ctgtggataa	tctctgggtc	agtcgaaccg
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ctggcgcnen	gcgggttcct	ccaagatggc
ggcgagagg	aggagcttgc	tccagagtgt
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cagaagctgt	tgtctttaga	tggcagagtg
cggacccctc	gccccagagg	ccntaggggtg
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cgccggggtc	ctgcggaatg	ggagcgctcct
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cgggccatcc	ggagggcgga	cacgactaat
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aaggcgcgct	gtatctcttg	cattgtgtgg
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gcagtagaga	atggcttgaa	agacnttnac
ctgtaggttt	ggcnagcttt	aaaagat
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		780
		840
		900
		960
		1020
		1047

<210> 66
 <211> 1063
 <212> DNA

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<213> Rattus norvegicus

<400> 66

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ccngaacagt	ccantnttaa	aattgggcct	nttgggatta	acggattcca	aggttgcaac	180
anattggcaa	gttttnggac	aggaggtttc	aantggntaa	agtggataaa	tngtgaattt	240
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tgtcactttt	ccaggtttct	gtcttacagc	atggtggctt	ggttctgaag	ggccatcact	960
ctaattggtg	ctgggttccc	agcgagaacc	agtgganccc	aaggatagct	tttgggtgact	1020
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<210> 67

<211> 815

<212> DNA

<213> Rattus norvegicus

<400> 67

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cgggggnccn	tntgtncccc	ccnttcccn	aaatnnentt	nngaaaagg	ttnaanantg	300
ttnaaaance	cnaangttaa	angggnnnat	nnaaanggtt	tccctnnenn	ggggngggna	360
aaaaggtttc	gcgcgganac	cnntgatgcc	caggttcagt	ttccccggag	cttggggcca	420
gacccgcggc	gcgccttggg	tgtggcgagg	gcgcgcgggc	ttgcgcggcg	acggcttctc	480
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tctcaaactg	ccttcttccc	ttttgagact	tgaaaatacc	cgaagcctgc	cttgtactga	780
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<210> 68

<211> 1034

<212> DNA

<213> Rattus norvegicus

<400> 68

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gggttaagtn	tttncccaaa	agttggtttt	tnnaaaaanc	ccctttnncc	cggacgtttt	180
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cccttgnaaa	cgggttnccg	ggggngtnt	tnaggggttg	aacnggggtt	taaangtgcc	300
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gcgcggnta	agccncggaa	aaaaaggatn	ccnggagacc	ttgnattttt	nnnggggttt	480
nacgcnatnt	tttttggaat	tttgggggga	taanaatttt	nnaccnga	tttngngggc	540
cncncnnngg	gnnaaaaatc	tnannannat	tnggntattg	aacatttctt	ccntgcata	600
ttatngangt	atgacccttt	aaacaattaa	gtacttggct	tcagtgggag	agaaagtgt	660
tagcctcaaa	aagacttgaa	gtgcccagg	tgtgtgtgtg	tgtgtgtgtg	tgtgtgtgtg	720
tatgtgtgtg	tgtgtgtgtt	tgtgtgtgtg	taaccagag	gggtgcccac	ttgctcaaaa	780
gagaaggggc	agaggaatat	gaggggaagga	ttgtgggagg	gagtgaccag	taggggaaaca	840
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gtctacaaag tcaattactc ctttcccttc ctccaccctt tcttctaata ttaggcaaaa	960
acaaacncaa aaacanaaac aancaaactg aaagactnta acctgtaggt tggncagctt	1020
gaaagagatn ttcc	1034

<210> 69
 <211> 186
 <212> DNA
 <213> Rattus norvegicus

<400> 69	
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aagaagtagc caccgttggt ttacttaact catggtccac ggggtgagct gaggtctcct	120
tcctgagcaa gatggaaatt ttacttggtc tgtaactag cgtgcattga atggangaca	180
tatgat	186

<210> 70
 <211> 1028
 <212> DNA
 <213> Rattus norvegicus

<400> 70	
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cttaaattta ggnatttttg aatnatttca acccnttgca ggcagtttgt nccatgttnt	120
gggaaagtgt taacaggatg gttatttnga caaaacaggt ttttccagac catttgtna	180
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tgacttcaat ttgtatanac aggttcttaa caaacagtgt gtaactgagt accttgcccc	300
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taaataaggc tgctgctcag atgtcagcac attttacgct ttactggaag acttctgctt	960
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aaaagatc	1028

<210> 71
 <211> 1034
 <212> DNA
 <213> Rattus norvegicus

<400> 71	
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gggttaagtn ttncccaaa agttggttt tnnaaaaanc ccctttnncc cggacgtttn	180
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aaaacgggta aattggaggc attttngnaa tggttttgt tnaaccntc ccttgggaaa	360
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gtctacaaag tcaattactc ctttcccttc ctccaccctt tcttctaata ttaggcaaaa	960
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gaaagagatn ttcc	1034

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<210> 72
 <211> 824
 <212> DNA
 <213> Rattus norvegicus

<400> 72

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aattcgtgga	ggcgactcta	accaggaagc	ctaattccnt	agattcccgg	gacactgggg	420
caggcgctct	aaaaacagct	ttgtggggct	tcagtcctcc	gtgcgggttc	agtccgggtc	480
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<210> 73
 <211> 774
 <212> DNA
 <213> Rattus norvegicus

<400> 73

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antaggttnt	catntggatt	gccngngttc	cngttggcat	ccgggaaaan	tgagactgtg	180
tcggtaccag	agntaggatg	gcentccttc	ccngccccgg	ccttnttggc	gccttgcgat	240
ccttcccga	ccggcccntg	gcgtctccgc	cttnggcact	tgcacatntg	gcggcccagg	300
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tactaatcca	gggttacaca	gtgaaaccct	gtctcgaaaa	ataaacacag	ggctggagag	600
atggctcact	gattaagaac	actgactgct	cttccagaag	tcttgagttc	aattccgagc	660
aagcacatgg	tggctcacia	ccatctgtaa	cagattctgg	tttatgtnga	gacaactaca	720
gtgtactcgt	attgaaagnt	nccacactgt	aggttnggca	agctaaanga	gatc	774

<210> 74
 <211> 248
 <212> DNA
 <213> Rattus norvegicus

<400> 74

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tagctcaggc	tggttttgaa	atcaggatcc	tgaccctcag	gaatgttaaa	gtgcctaaaa	180
gtgnggacaa	attattttac	gtgcctttga	aagacttcac	ctgtaggttn	ggcnagctag	240
aagagatc						248

<210> 75
 <211> 833
 <212> DNA
 <213> Rattus norvegicus

<400> 75

aanggggtta	tnntggagan	atnctaagnt	cccaaagcaa	nttaggattg	ctnccnnnng	60
aattnttaag	cntttgcatt	aagtantaat	gccaaaatga	ccccaanata	tngntccttg	120
antgtnttaa	aaangaggat	cttcnttgnc	catanacgcc	ntatatgaaa	gcaactgaac	180
aagatttaaa	attggacagg	tcacaancgg	gcgtgtgcct	ttaatcccag	cactcgntgg	240
ctgatagaag	cagatgcatn	tatgtgggtt	tgaggacagn	tngnttnacg	tagagagttc	300

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ntatatcagt	agggccttgt	agagaccnta	tctcaaaaaa	caaaagcaaa	acaacagaga	360
aaaaatcaat	tgaccatgtc	ccaattacct	ttatttatct	gtaacctatc	cttagttata	420
ctcgtaatct	ttttctctct	tcagtttgcg	tacgggacag	cagacctact	cacaacccaa	480
gctntaaatg	atgagcgtac	tcagccaggg	agcttcaccc	cacttaaccc	cataagatgg	540
cggcagcgcc	tcttcaccca	ctcagggctg	aagcacgcat	cacgtgatgc	gctccagctc	600
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<210> 76
 <211> 880
 <212> DNA
 <213> Rattus norvegicus

<400> 76						
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taaggcgggt	tcaaacaaac	ttggatttcc	ngccctttgg	ggcgggggaa	atgggcacgg	180
gngcattcca	agcngntcaa	ggttccggct	tgcggacggg	taacacaant	aggttttctca	240
tctagattgg	ccngcgttgc	ggttgagcat	ccgggaaaat	tgagattgtg	tcggtaccag	300
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ccggcccttg	ggtctccggc	cttggggcact	tgcacatctg	gcggccagga	tgcgcttccg	420
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cttaggagcc	tgcgcgtact	cccagcaagg	aagatgtagg	acaaaaatgt	agaagcactt	540
aacatgaacg	tcaaaacgat	gaccaatcac	agggcgatat	atgcgcgatgc	gcaatgttcc	600
aatcatggct	cataagcaat	ccggaagtgg	ccaattaaat	atactattta	ctaattccagg	660
gttacacagt	gaaaccctgt	ctcgaaaaat	aaacacaggg	ctggagagat	ggctcactga	720
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gctcacaacc	atctgtaaca	gattctggtt	tatctggntt	cnactacagt	gtannggcat	840
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<210> 77
 <211> 864
 <212> DNA
 <213> Rattus norvegicus

<400> 77						
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caggaantga	tccntntggg	ttacagtcac	tttagcatag	gntgacagtt	ggngaccaan	180
tnatcttgcc	gtgttggaag	gagaggggan	taaggntgaa	gctcttgagt	ccnttgangc	240
ccttggaate	gggaantccc	ttaaaccaac	cccttttgcc	gttgaattgc	accaaccaga	300
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gggagttgac	ntnacagggc	tcagggattc	ttttagaagg	gtccagggtt	atggcttccc	420
ccccccccag	ccaggtcaga	cactaaagtg	tcttaagccc	ctccataact	gccgctcccc	480
cacnttggat	gaagccggcc	attaggcagg	gaccgtctct	gggagaggcc	aagccctctg	540
gctcacttgt	ggatttcctt	taagcaagac	ttcctctctg	cttccaggac	tcctgtcaaa	600
caagagggtc	cctggcttag	agtttgagg	ctgcaggcag	aacagacatt	ccccgatgac	660
tcacaagcct	ggaactctgt	gggccagcag	gaatggggat	ggctttcttg	tcagtcaggg	720
tcaactggga	cactcactct	gagacaggga	ggcaagggag	aaacaggtca	gaggtagaga	780
gagctcagtc	ccagggactc	acgttgaggt	ccctaagggtg	cgctagggag	aggnttttac	840
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<210> 78
 <211> 874
 <212> DNA
 <213> Rattus norvegicus

<400> 78						
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tagtttgaa	cagaggcttg	ggcagaaata	tgggcaagta	ttaggaaagt	acaaggggaa	120
atgttgtcaa	cgcgnttggt	ttcccagttg	ttgnactgat	ccnccagga	tgttttccca	180
cntatgntat	ggaaccttct	ctttcaggaa	gccattntna	ncntatggnt	tgcaaccctt	240

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ttgggggtcgc	aacagcaggt	attaacatta	ggattcataa	cgntagcaaa	atnacagtta	300
tggagtagca	atgaaataac	tctatgnttg	ggaggggtcac	cacaacanga	gggacgggtat	360
cacaggnttt	tagcattagg	aagggttgagg	accttatttc	agagtgtcnt	gacaatcntt	420
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cgccatacat	tctgtatttg	ccctccttcc	tcattttaa	aggaatttgt	tgctgtttaa	720
tttttccatta	tttgtgtgtg	tgtgtgtgtg	tgtgtgtgtg	tgtgtgtgtg	tgtgtgtgtg	780
tgcgcgcgca	cgtaatatg	ccgctcagaa	tagtctaaaa	ctgctgggct	tgaagacnt	840
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<210> 79

<211> 886

<212> DNA

<213> Rattus norvegicus

<400> 79

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atagtatgtg	cataacactt	gagcagtaac	tgttttcttc	aatctcattt	atctcagaag	180
ttccccctgn	tgattcagac	gttattaatt	aggcaaacca	atgttgattg	tcattaccca	240
tgagttgctt	ggcttgtgag	atgcatactg	tgtgttcgtg	aggcacntac	tgtgaggcat	300
gtgcccgtga	ggttcatggc	tgtgaggtgt	gtgcccgtga	ggttcatggc	tttctngacc	360
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tcccgctctca	aaacaaaatg	aagaagtaga	gagattagtg	ttaataagca	actgaggcct	480
tgaagggctg	aggtcaggcg	gtgccctggg	gcacacacag	aagcgtgcc	gtgacgtcag	540
acagactcag	ccctgtgtca	gacaggccgg	agggtgactg	gccatgtggc	gtgattggac	600
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tatgtgactt	gtgcgagatt	agtctcatac	cctattgcta	gcctgtgcct	ggtaccacgg	720
acatggtaca	atccagggag	gagccgtaag	cactacaggg	gagccatcct	gaatcccagc	780
aagtccaact	tctgtttttt	cttccttccc	cgcaacatta	ggaatgactt	ctaagagngc	840
tgttgaaaga	ctttcacctg	taggttgggc	aagcttaaaa	gaggat		886

<210> 80

<211> 865

<212> DNA

<213> Rattus norvegicus

<400> 80

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ggcccantgc	tcagagctcc	gggcgccagc	gaagggcaaa	cggccactga	ttggaaagnt	180
gcagttttaa	gacatgtccc	aggaactggg	anccttgtgt	gactggactt	agccttgcaa	240
ntctgtctga	agcataacnt	gntgctgtct	ntgggcgagc	atttatgtgc	cccacttgag	300
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agggnccatc	agtgagcttc	caaggacagg	ggaccagaac	ggtgaaaaca	aaccagggct	420
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tccaaatagg	agctgtgatc	aggctgtgtg	tgtgtgcctg	gtgaaagact	ttnacctgta	840
ggtttgggcn	agcttgaaaa	gtatc				865

<210> 81

<211> 859

<212> DNA

<213> Rattus norvegicus

<400> 81

cangagcant	ntgaancagg	catttntgga	agggtccng	agaaaacacg	tggaattnct	60
tgtctctggg	acttttagtnc	cagcnaggan	gatncagtga	gggaacacac	cgggcttttg	120

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agtgatccag	gggacatgta	cacatgggga	actgnccagg	cagagaaaga	caagagaaaa	240
tctcaaanga	tgaagacaga	gangagtaat	atggccagaa	ngatacagtg	cctcntgcat	300
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aagtaataaa	tttataggat	gttagtatca	cactgttcag	aatagctcaa	aaaatcctgc	420
cntgtcctct	taagtatgtg	aatcatcttt	tactgcaacg	tgtccacaat	gtatatacta	480
catacccaaa	agtcctcact	gttatcccaa	ttagtaggct	ggctgccaat	agttgtccat	540
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gaaagggaca	caggcccaag	gtgggaggcc	ttagataaag	gcccacatg	ctcaggaaag	720
gatttntaca	gatctcttag	ggaagttaca	atcaaattca	tacctcacag	cagagctcag	780
gagaagaatc	cataaagnnt	gaagacatgc	ttgtngtgnc	tgaaggacnn	tacntgtagn	840
tngggccngc	tgaaatttt					859

<210> 82
 <211> 1021
 <212> DNA
 <213> Rattus norvegicus

<400> 82

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<210> 83
 <211> 1013
 <212> DNA
 <213> Rattus norvegicus

<400> 83

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acactcgtgt	gggntctttc	aaaacantgt	ncnntggata	cncagacact	cnncnagngn	180
ggtntatctn	cacnngtgtc	tcngngnttt	nngcnngnnn	tcnaantca	aaagcgncat	240
nnggcacata	tntntgacac	ngnggtatat	nngnctctcn	ggnganacat	ttgntncgca	300
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aatnacggg	ngggtttaaca	tnnggccnnc	gttgnnacgt	natanccnga	aacacactcn	660
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cncnttgga	aggggnntnt	tnaaccgggg	ttcnaantta	tagggggggt	tanatcnccc	900
catttttttna	aaaagngttt	accntggggc	ccntnttttn	cnaaaaaatt	tgnccccngt	960
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<210> 84

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<211> 1002
 <212> DNA
 <213> Rattus norvegicus

<400> 84

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ctctgcttta	cctttttatac	tcattttattn	tgttatttgt	gtatgaaagc	cttccgtatg	960
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<210> 85
 <211> 1031
 <212> DNA
 <213> Rattus norvegicus

<400> 85

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<210> 86
 <211> 1039
 <212> DNA
 <213> Rattus norvegicus

<400> 86

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ccntgggata	anaagtggaa	tcattgacag	ttttgtggtc	cttttnncat	ccccatgngg	180
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tgtgtatttg	ctcatcntgt	gagggagaga	ctttgtactc	tgctctgaga	aggcagaact	540
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agtaacaaag	cactaaacag	aaaggggttg	aagagactgg	tcagtggctg	agagctttta	660
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<210> 87
 <211> 1058
 <212> DNA
 <213> Rattus norvegicus

<400> 87

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<210> 88
 <211> 1043
 <212> DNA
 <213> Rattus norvegicus

<400> 88

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<210> 89
 <211> 454
 <212> DNA
 <213> Rattus norvegicus

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<400> 89

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<210> 90

<211> 873

<212> DNA

<213> Rattus norvegicus

<400> 90

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<210> 91

<211> 876

<212> DNA

<213> Rattus norvegicus

<400> 91

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<210> 92

<211> 459

<212> DNA

<213> Rattus norvegicus

<400> 92

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<210> 93

<211> 3133

<212> DNA

<213> Rattus norvegicus

<400> 93

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<210> 94
 <211> 2161
 <212> DNA
 <213> Rattus norvegicus

<400> 94

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 <212> DNA
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<400> 95

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ggcccttctc	ggtgcccacg	cacccccga	tcgaacccga	ggatgagcat	agggtgtatt	660
ttaggcgtgc	tgggcttccc	cgcctccctc	tgcccactta	gctggcaaga	agaaagccag	720
cactataaag	gaggccaggg	ccaaggactg	gcctcctctt	gctcacgagg	tcagacgcga	780
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<210> 96
 <211> 774
 <212> DNA
 <213> Rattus norvegicus

<400> 96

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antaggttnt	catntggatt	gccngngttc	cngttggcat	ccgggaaaan	tgagactgtg	180
tcggtaccag	agntaggatg	gcentccttc	ccngccccgg	ccttnttggc	gccttgcgat	240
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atggcgcttc	cgggatggcg	ccagcgcgcg	tacgtcatca	cggagcgccc	atgtgttctt	360
tctgtccaag	cgcntaggag	cctgcgcgta	ctcccagcaa	ggaagatgta	ggaccaaata	420
gtagaagcac	ttaacatgaa	cgtcaaaaacg	atgaccaatc	acagggcgat	atatgcgcat	480
gcgcaatgtt	ccaatcatgg	ctcataagca	atccggaagt	ggccaattaa	atatactatt	540
tactaatcca	gggttacaca	gtgaaaccct	gtctcgaaaa	ataaacacag	ggctggagag	600
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aagcacatgg	tggctcacia	ccatctgtaa	cagattctgg	tttatgtnga	gacaactaca	720
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<210> 97
 <211> 248
 <212> DNA
 <213> Rattus norvegicus

<400> 97

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tagctcaggc	tggttttgaa	atcaggatcc	tgaccctcag	gaatgttaaa	gtgcctaaaa	180
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aagagatc						248

<210> 98
 <211> 880
 <212> DNA
 <213> Rattus norvegicus

<400> 98

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taaggcggt	tcaaacaaac	ttggatttcc	ngcccttttg	ggcgggggaa	atgggcacgg	180
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ccggcccttg	ggtctccggc	cttggggcact	tgcacatctg	gcggccagga	tgcgcttccg	420
ggatggcgcc	agcgcgcgta	cgtcatcacg	gagcgtccat	gtgttcnttc	tgtccaagcg	480
cttaggagcc	tgcgcgtact	cccagcaagg	aagatgtagg	acaaaaatgt	agaagcactt	540
aacatgaacg	tcaaaacgat	gaccaatcac	agggcgatat	atgcgcatgc	gcaatgttcc	600
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gctcacaacc	atctgtaaca	gattctgggt	tatctgggnt	cnactacagt	gtannggcat	840
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<210> 99
 <211> 864
 <212> DNA
 <213> Rattus norvegicus

<400> 99

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cagccaattg	ggggagaant	ttntgtcag	tatcatattt	ttcgttaggg	aacggaggcn	120
caggaantga	tcntntggg	ttacagtcac	tttagcatag	gntgacagtt	ggngaccaan	180
tnatcttgcc	gtgttggaag	gagaggggan	taaggntgaa	gctcttgagt	ccnttgange	240

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ccttggaatc	gggaantccc	ttaaaccaac	cccttttgcc	gttgaattgc	accaaccaga	300
ttcttccagt	ctgcttgagg	angacaggac	ttcattgctn	tgagagagg	caggagggtt	360
gggagttgac	ntnacagggc	tcagggattc	ttttagaagg	gtccagggtc	atggcttccc	420
cccccccccag	ccaggtcaga	cactaaagt	tcttaagccc	ctccatactt	gccgctcccc	480
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gctcacttgt	ggatttcctt	taagcaagac	tctctctctg	cttccaggac	tcctgtcaaa	600
caagagggtc	cctggcttag	agtttgggag	ctgcaggcag	aacagacatt	ccccgatgac	660
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tcaactggga	cactcactct	gagacaggga	ggcaagggag	aaacagggtca	gaggtagaga	780
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<210> 100

<211> 874

<212> DNA

<213> Rattus norvegicus

<400> 100

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cacaggnttt	tagcattagg	aagggtgagg	accttatttc	agagtgtcnt	gacaatcntt	420
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ctgcacagct	ctntgaggct	tagagcggtc	tttcttcata	gctttccntt	ttccttcagg	540
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tgcgcgcgca	cgtaatatg	ccgctcagaa	tagtctaaaa	ctgctgggct	tgaaagacnt	840
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<210> 101

<211> 886

<212> DNA

<213> Rattus norvegicus

<400> 101

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atagtatgtg	cataacactt	gagcagtaac	tgTTTTcttc	aatctcattt	atctcagaag	180
ttccccttgn	tgattcagac	gttattaatt	aggcaaacca	atgttgattg	tcattaccca	240
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gtgcccgtga	ggttcatggc	tgtgaggtgt	gtgcccgtga	ggttcatggc	tttctngacc	360
acngggagta	tgaaggagag	gaatcctacg	tttgatgcc	gccaggggta	tacagcaaga	420
tcccgtctca	aaacaaaatg	aagaagtaga	gagattagtg	ttaataagca	actgaggcct	480
tgaagggctg	aggtcaggcg	gtgccctgg	gcacacacag	aagcgtgcc	gtgacgtcag	540
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acatgggtaca	atccaggggag	gagccgtaag	cactacaggg	gagccatcct	gaatcccagc	780
aagtccaact	tctgtttttt	cttccttccc	cgcaacatta	ggaatgactt	ctaagagngc	840
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<210> 102

<211> 865

<212> DNA

<213> Rattus norvegicus

<400> 102

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ggcccantgc	tcagagctcc	gggcgccagc	gaagggcaaa	cggccactga	ttggaaagnt	180
gcagtttaaa	gacatgtccc	aggaactggt	anccttgtgt	gactggactt	agccttgcaa	240
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<210> 103

<211> 859

<212> DNA

<213> Rattus norvegicus

<400> 103

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aacccttgag	tttaattttcc	agggtcaact	gtattttgaa	agtataaatg	aaagttcctg	360
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<210> 104

<211> 883

<212> DNA

<213> Rattus norvegicus

<400> 104

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tttgggcgga	gggggaaatt	tttttggttt	ttttnttttn	gggatttttg	aaaaaaaaan	180
gaanttttta	ggtttcccn	angtaattta	tttcaatgga	ccattttttg	ggttctccct	240
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tcngtagcag	accagttttt	catttttgagn	tggtnccnaa	aaggnttccc	aactatgttc	360
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<210> 105

<211> 987

<212> DNA

<213> Rattus norvegicus

<400> 105

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canntttccc	ntanccgaaa	ntttnttttt	ggcccaaccn	gtaagacgga	tttttttncaa	60
ttgcggancc	aatggaaccg	gtttgcccgg	nngtnttttg	gggtgaacgg	ttntnttaant	120
ggngccaaan	aaggttnatt	ggaggnctta	tttgaattgg	tntgtaaanc	ntttntcttgg	180
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<210> 106

<211> 1031

<212> DNA

<213> Rattus norvegicus

<400> 106

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<210> 107

<211> 1138

<212> DNA

<213> Rattus norvegicus

<400> 107

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nanganannaa	nccgngnnga	ncanncagnn	gggaaacagc	ccagagagat	aggacancaa	180
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<210> 108

<211> 1072

<212> DNA

<213> Rattus norvegicus

<400> 108

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tgccaggaca	caagtttcc	aaagcttatt	tcagtgtcag	ccgctgggga	gacacattca	840
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cacacaggct	gctcagaagg	agctagagct	cccaaatagg	agctgtgatc	aggctgtgtg	1020
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<210> 109

<211> 1094

<212> DNA

<213> Rattus norvegicus

<400> 109

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ccaatttttg	nanttttagga	aaagtctctt	gggtnaattc	cagcmttgat	tggaggagca	180
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<210> 110

<211> 1107

<212> DNA

<213> Rattus norvegicus

<400> 110

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agcaaaaata	tagttatgaa	gcagcaacga	aatcacttt	atggttggag	cgtcaccaca	180
acatgaagaa	tgtattaatc	cgcagtatta	gagaggtcga	gaaccactat	cttagaggat	240
gcggtagact	gactgcttcc	cctctcgctt	ggagttgacc	ttgccactag	agggcaacag	300
catcagtatt	gttcccagtc	cccctcacac	tgattcgaac	tttaaggaca	ctgatctctg	360
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ttccttgaan	ccngggggaa	nntttaaaac	ccnaancccc	tccattntta	acccccccca	1080
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<210> 111

<211> 1069

<212> DNA

<213> Rattus norvegicus

<400> 111

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ttctgggntt	ggcccathtt	tgcacattag	gganagtnt	ttggggtaaa	nttccagcng	120
ttgattggag	gagcaagtga	tnttggtana	atztatggtt	gtgggggatg	ntgttaaaat	180
cttttaggat	tggttccctt	tntgtctccc	tttttgga	tggntcttan	ataggtggnt	240
caaaattcta	cntnttgga	tcagcntatn	tcatcaggat	ttagcccagt	gtgntnaacc	300
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<210> 112

<211> 1058

<212> DNA

<213> Rattus norvegicus

<400> 112

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cgaccttcgg	ttaccggtag	ctgcccncct	tttcccttgg	gagggtgggn	tttttcatag	180
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ngattattgc	cattggcagc	agcaatgtaa	caggttngca	gagcgaggta	tgtaggcggt	360
gtacnggggt	cttgaagtgg	tgccttaant	tacggntaca	ntngagggac	agtatttggt	420
atattgcgctn	ttgttgaagc	cagttacttt	nggaaaggag	ttgntagtte	ttnatccggc	480
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aaactatttt	aacatgcctc	tcccacccaa	ctactcaaga	ttccccgtgc	acagttgaaa	1020
gnnttnccac	ctgnaggtgg	ggccaagcta	aaagagat			1058

<210> 113
 <211> 1046
 <212> DNA
 <213> Rattus norvegicus

<400> 113

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aaantcncca	nntggngccc	caaatnnncn	aattgancca	aancnntaga	ggnncccaag	180
acnaatgggc	actntganna	gancnggcca	gaagncaagn	gggggannnt	catagnnaca	240
tggnanaaat	aaagntntgt	aaacccggan	tggcaatnga	aaccagcaaa	gacccatgaa	300
cgtgagngan	accagttgga	aacaatgaan	nnantgggtg	antnacagga	atgnggtnan	360
gacgcnnagt	gancccaaan	aggcaacncc	attgaaagcc	ttcnccncca	tggaaatact	420
gtanntaaaa	caaacaaca	aatnacaaaa	anaaaaaacc	caaagcttaa	gtggagtgcc	480
cnttccagnt	agccaccnnn	taagaactgt	aaatcgcacc	ntcccangcc	agatgcaggt	540
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ggcncnggtg	anttncgcta	cntcgnaaaa	aangagaagt	catgtgggac	gnatgtgtgt	660
aagcacagct	cntgtgangt	caagtcagca	acantatgcc	atactctgaa	gacagaggnc	720
cataatagna	ttgttacang	atncnngact	tttanaaaan	caaaatccta	aatcctattc	780
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<210> 114
 <211> 1083
 <212> DNA
 <213> Rattus norvegicus

<400> 114

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ttgnntgggg	tgaattcccg	ccntngnttg	gaggaggnaa	ttatnttgta	gaaatthtatg	180
gttgtggggg	atnttggtta	atcttttgaa	tgtgttcccc	ttntgtttcc	cttttgggac	240
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cgacgtgtgg	tgagctctca	ctggggcgtc	cctctaagat	ctgtccactc	ctggtttagg	1020
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ntt						1083

<210> 115
 <211> 913
 <212> DNA
 <213> Rattus norvegicus

<400> 115

ggggaaaaaa	atntgggncc	ctttnaaaga	aattctggaa	anccgcccgt	ggggnattht	60
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cnaanttccc	tttgacgcgc	ntttacaaga	ttagccngtg	tgtaaccttt	gggcccttta	180

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acaggattnc	ttggccntnt	gaaacacgta	tttatgtcag	gnttntaccg	tngcaaantt	240
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taatccgcag	tattagagag	tcgagaacca	ntatcttaga	ggatcggtag	actgatgttt	360
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<210> 116

<211> 1123

<212> DNA

<213> Rattus norvegicus

<400> 116

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aaatgaggnt	aattggnttn	gaaangenta	tcaggcattc	caaattntta	aatttccctt	180
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ccgtccatac	ctgggtgtag	tcagggacct	ttatgggtggc	tgtcacgcag	gcgatttgnc	1080
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<210> 117

<211> 1116

<212> DNA

<213> Rattus norvegicus

<400> 117

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aaaaaacnnt	gttcttnaat	gcaagggtant	tgggggttat	tattntgaaa	ggcaactaat	180
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ggaatggtac	actttgcacc	tcacactctt	ccagaggggac	agtcataca	acactcagct	1020
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1116

<210> 118
 <211> 900
 <212> DNA
 <213> Rattus norvegicus

<400> 118

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ccaggggnntg	ttttgggnaa	aatatanenn	anagnggtgt	ntntnanatc	tcgggggggtg	240
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<210> 119
 <211> 498
 <212> DNA
 <213> Rattus norvegicus

<400> 119

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<210> 120
 <211> 380
 <212> DNA
 <213> Rattus norvegicus

<400> 120

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caacccccaa	ggggaaggga	anggaangga	aaatnaattn	ccttttnaaa	aaggagnaaa	180
tncgggtang	gaaaattccg	gtgngggggt	ttcaaagggt	cccccccggn	ggnttaaaaa	240
attgaagttt	antcnnnggg	gggaacccaa	nagaatataa	anaaacgggg	gtttcccccn	300
gggagttcct	tgggggtttt	ccgggttcgac	ccgncgntta	ccggaaacct	ntcncctttt	360
tcccttgggg	nagggggggg					380

<210> 121
 <211> 998
 <212> DNA
 <213> Rattus norvegicus

<400> 121

acatgtacac	aactgggtcc	cagccaagtc	aggttccagc	tgccagcaga	ggcctggagc	60
tagcttcgcg	tgcactacca	ccctgcccac	cctggcactg	tgcccattga	cttcgggggg	120
ccgggggcag	gaggtaccca	cctccccacc	ctcctcttcc	ctcctctcag	gagcttatct	180
atcgggtgag	agcaagtagg	aaaaggtaag	ctgagaaaga	gcacttggtc	ggctacagga	240

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cctcagcctg	aggtgtgaaa	caggagactg	ggcactgggg	aaacagcagc	actggctggg	300
ccaaagggga	gggaggaagg	caatgaatgg	gcaagcctgt	gccttacaga	aacagactcc	360
cttgggctgg	gtgctggaat	cctaaccctt	cagtgatggg	ggaactctgc	tccagtgagc	420
tgaagtatac	atgtggggaa	ttgggggggtg	gggtaggggg	aaggcaatcc	aaaggctcact	480
cccctgacct	agttggacca	cagttaatta	aggctcccaa	gccctgctga	ctcttnacgt	540
ctggtttctg	gaaagaaggg	agttaatcag	caaacaattt	aagaaaggta	taactgtcta	600
cccctgcaga	ggatcatggg	ttncctctct	anncttctga	gccgtggatc	tcagccaaaa	660
acaaaaacca	aaacaaagaa	acaaacgcct	atttaaaagg	gggttggagt	tgggcagggg	720
tgaggtngtt	agatcatctg	agagctccag	gacacgcana	tagttgaaga	ggaaaccaag	780
atccaaatgt	cttctgacat	cacacgggat	gcagcagcac	accaacatat	actttancct	840
cnccagagag	gaaaacaacc	gcctagttaa	taagcagagt	tgggctgttg	gcaaaccgtc	900
attccagatc	tgaggnaagt	tggatggttc	gggtgtctat	gttnacntaa	gacctgtttt	960
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<210> 122

<211> 970

<212> DNA

<213> Rattus norvegicus

<400> 122

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tccgttttnt	tccccccctt	caatttgga	gtttggtttg	ccgaanttta	agttnttgtc	180
ntcctncgtt	ntttttttcc	ntnttttttt	cccaaaagta	acaanccggg	attggtttcc	240
aaggntnttn	ttgaaccctg	aatngcggnt	ttccgggtta	ccnagggttt	gttcctnngc	300
cgnttcctcc	aattttttgga	ntttcccagn	tnggggtccn	ttntcttggt	nacngttcca	360
aacntaattg	acanttaatt	tttcctgtgt	aanttgtccc	cgganattnt	gggntcttgg	420
ngcagggcct	tttttcattg	gaagcaaccc	cntaaatttt	taccaggctt	gattgtttag	480
gaagtaatcc	ttgcttngaa	nccccacttn	ttntttccaa	ggntggaaac	caggattttg	540
gaactgcaga	ggcttcaggg	tctgggaagc	ggagcangca	aagantggag	tgcactgtcc	600
ttttgcaata	tggggtttgc	ttgcttgctg	gctcntntcn	tgctntntca	gatggtgact	660
gaggctactt	cagcaggact	aggaataatc	atgtccagggt	ggntgccctt	ccgagcagaa	720
agggacagac	gtggggcgat	gaagttgcta	tcgttttttt	ttttttctgc	acagactgca	780
aagtgtgcag	agggagggag	gctgtgcaaa	aaaaaaaaaa	aaaaaaaaaa	aaaaaaaaaac	840
cgaggacgca	gaagttagac	tgctgaccca	tttggtgcat	gtgtgcccac	ggagggaggg	900
gaccttctca	aaagggttca	cgcagcaagc	attgaaagnt	tccacntgta	gngtcgcaag	960
caactgagat						970

<210> 123

<211> 884

<212> DNA

<213> Rattus norvegicus

<400> 123

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agaagcaatt	tagtgtcctn	tgctcctctga	cctccacaag	tgctgtggca	tggggacaca	120
ggactgtaca	cacacacaca	cacacacaca	cacacacaca	cacacacgca	cgcacacaca	180
cccctcaagt	aaccgtggaa	taaagggtccg	accagaaacc	acgctgggac	gggagatgct	240
ggagcacatc	aggggtgggc	taagcagcag	atcggcctgt	aactggcagc	agaggggtgt	300
ggctctttca	gaaccaggag	ggcatcgccc	ctccagccag	actctccagc	tttcttcccc	360
tccttgccct	ctgtttttcct	tctgcctacc	ttcctttggc	ctcaaaccat	aatgtgcaac	420
acattcaaac	tgtagtaagt	gttttaattt	tctactaaac	aataaaacct	ttagattttc	480
actgggccag	tgctggtaac	agcagactgg	gtggagtatc	acagaggggtg	tggagcaagc	540
tggctaccca	gggctgggca	cactcaacac	tctggcattc	ngtggaagtt	ctgggcagta	600
aaaacagaag	canacgtcac	gcacagggttc	catagtgtna	ggcatcttaa	tctancnaga	660
anacctgggtg	ttnagtntgt	nnacaaaann	gantgntgna	cttggacagn	ggtgtttttn	720
tcccagggct	tccaggantt	aggggtatac	caggcccann	acattgggna	aacgtgtgtg	780
tnaannnttt	cntntnaaac	cnccnnggtt	gacnactngn	nntccntttt	aanggnccca	840
gttccccctg	gggggttngn	tntggaaaaa	ggctttccgg	tttc		884

<210> 124

<211> 855

<212> DNA

<213> Rattus norvegicus

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<400> 124

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tnacgagggg	attnggggtt	anagtttttg	agtggggccaa	nangaacatg	gaggaatatt	180
tgtttttggt	tgngaaccat	accttgga	gattgtattt	ttatccgcca	acaaccacng	240
tggtaggggt	tttttttggt	tgcagcagca	gataagggca	gaaaaaagat	ntcagagatc	300
ctttgatntt	tnttcggggt	ngacgttcat	gttgngngga	ttgggagcgg	anaacaattt	360
cacacagcaa	ggagaggagc	caatatagag	gggaaaaaaa	aagaagggga	aagcagttag	420
tttaaaaagt	tgagagaaca	aagtatgttt	tgnttggtatg	ggcaaccaa	gaagcntgcc	480
aggaatgggt	ggtaaaagg	gtaagagtca	tgaaggtntt	ctgtccaacc	gttaccggaa	540
acatgcaagg	aatttcttag	actggccagg	attggattgt	gggaaaggtn	tnttcaagcn	600
tccccttggc	ttttatggca	agaaaatagt	gcggactata	gagagcgtcg	ttctcaaagc	660
tttccccaat	agcagaaaag	cattgtccta	aattccctaa	aaggcaccgt	gaaataaata	720
ttacgggaca	cgatggcaca	agaaggagct	ttcaactctg	ccaccagaac	agttatactt	780
catagtaacc	atgttgccct	gttcaatgac	aaggcacgct	ctccagcaga	aagggaaaag	840
gagctgagtt	cgcac					855

<210> 125

<211> 1059

<212> DNA

<213> Rattus norvegicus

<400> 125

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ntttnaaccc	caaaaccatg	nnttgncctt	tcccctnacc	ngtnatagt	nttgnantgt	120
aacccaacaa	tcaacggnta	tttggttcagg	ganttnttgg	taccaggcnn	ttggttttga	180
naanacggta	ggtccgggaa	gcnttgacgg	taagcccnng	gganaagggc	caacggngat	240
cccaaattag	gagcttgacg	cattgttttc	ntttgcntgg	aatgncattc	ttctcttctc	300
cntttatcta	gaaaacgntt	actcatgctt	caaancacn	gttgacttcc	ccagcattgn	360
ttcnentagc	tccttctttg	aaacaactga	ttgggaaatc	aggaggatan	gaaaagcttt	420
aacaagagct	ttcaggggct	ttcggagaga	actcattctt	gtaggacgca	ggccatgcaa	480
gcatcaggct	ctgccttctg	gacccagta	tacagacata	tgcaacaactg	cagtgggttca	540
tacttgtaat	cccagtgtta	ggaagactta	gacttgagc	ttgctgggtca	gactggtaag	600
cccagttcag	tgagaccctg	acttaaaaaat	gaagttggaa	agaaatttgg	aaagataatc	660
tggtattcat	ctctgggctc	tatttgacaca	ggcacacaca	caaataatacc	aatataacat	720
acacagaaag	agaaggggag	ggaggaagag	agggagggcg	gtagagaact	tgtgaatgtc	780
ttttgatagg	ttttttttta	agttattgga	ttaaaccatc	agcagtgtca	cattgggttaa	840
gttaaaaata	ataaaatgaa	gcaacttatc	tttgctgaaa	ttcattactc	attatgagag	900
tttgataaaa	aaaaagagga	gtctcccaca	gttttcctgt	ctcatctttt	actccagggg	960
acggtcacac	tattcagtaa	gatacctagg	ctatctggct	cactggactn	ggcgtgaaag	1020
actnnacctg	taggtttgng	cgctgaaaag	atcttnaac			1059

<210> 126

<211> 1042

<212> DNA

<213> Rattus norvegicus

<400> 126

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ccctttttnt	naatcnncat	ngagggttct	aantgaacct	naaggnnatt	taacttttna	180
tggaacaaac	ccgttggtgt	gtcccctcct	tggaganttg	agttggaact	taaaaaaaac	240
ctttccnaaa	aattgtgtaa	tctgantcca	aacccaaatg	aggacaaatc	cagtgtagga	300
ggnatttagg	caaattaaac	tgacttggtc	aactttctga	aaatgatgtc	ttgatttcag	360
gaaggatccc	cagtgcntcg	gggacntgaa	agggagatgt	aacccttgag	ctcatggnta	420
ggaagggaaa	tcttagagac	agcttggtaa	aatctgagtg	aggttgagag	gttggaggac	480
cacattgtgt	atntgctcat	ccctgtgagg	gagagacttg	tactctgctc	ttgagaaggc	540
agaactgtta	ggcagacact	tagagaatat	atgtcatggc	aaangacatc	cacccaacaa	600
gtcttcagta	acaaagcact	aaacagaaaag	gggttgaaga	gacttggtca	gtggcatgag	660
agntttttatt	gctcttacag	aggactcggc	atgcntagca	gctcacaaca	gcctgtgact	720
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ttaaaaataa	aagaaatctt	ttaaacattg	agcaaagtga	atcagggtact	aacattgaat	840
atatctgggg	ccaggaatta	ttctgggtta	ttgccttttt	cggaagccta	atatcacaca	900
tagagaaata	ggcagcacag	gcctaacagc	ccatantgtg	tgctattcta	tcaatagtgc	960

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caagtattga catggactat tnttaaggcc aaangagagg tcnccagaaa gttatacatg	1020
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<210> 127
 <211> 960
 <212> DNA
 <213> Rattus norvegicus

<400> 127						
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ntgcncccaa	agtaaagncc	aantttaggg	ngganntttn	ttgaaacgta	attaanattt	180
ttccgataag	gaaacggagg	cccgggaant	gatccntttg	gagttaccag	gtcagtttag	240
cattaggntg	acagttgnga	ccaattnatc	cttgcccgtt	ggttggaagg	agaggggant	300
aagggttaag	ctcntgagtc	ccttgaaggc	cttggaatcg	ggaattccct	taaagccaac	360
ccctttgccg	ttgaactgca	ccaaccagat	gtctnccagt	ttgcttgaag	agacgggatt	420
cantgntgtg	gagaggggca	ggagggntgg	gaggtgacnt	nacagggttc	agggattctt	480
ttagaagggt	ccaggctcat	ggcttcccc	ccccccagcc	aggtcagaca	ctaaagtgtc	540
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gcaggcagaa	cagacattcc	ccgatgactc	acaagcctgg	aactctgtgg	gccagcagga	780
atggggatgg	ctttctggtc	agtcagggtc	aactgggaca	ctcactctga	gacagggagg	840
caagggagaa	acaggtcaga	ggtagagaga	gctcagtcca	gggactcacg	gtgaggtccc	900
taaggtgcgt	agggagagga	tntaacattc	ggtttggnna	gctagaaaag	atctntaaaa	960

What is claimed:

1. An isolated nucleic acid comprising a nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127.
2. A nucleic acid comprising at least 20 consecutive nucleotides of a nucleotide sequence of claim 1.
3. A nucleic acid comprising at least 30 consecutive nucleotides of a nucleotide sequence of claim 1.
4. A nucleic acid comprising at least 40 consecutive nucleotides of a nucleotide sequence of claim 1.
5. An isolated nucleic acid encoding the protein encoded by the gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5,

SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127, or a homolog thereof.

6. A host cell containing the nucleic acid of claim 1 or 5.
7. A nucleic acid comprising a nucleic acid that selectively hybridizes under stringent conditions with the nucleic acid of claim 1 or 5.
8. A nucleic acid having a region within an exon wherein the region has at least 50 % homology with a nucleic acid of claim 1 or 5.
9. A nucleic acid having a region within an exon wherein the region has at least 60 % homology with a nucleic acid of claim 1 or 5.
10. A nucleic acid having a region within an exon wherein the region has at least 70 % homology with a nucleic acid of claim 1 or 5.

11. A nucleic acid having a region within an exon wherein the region has at least 80 % homology with a nucleic acid of claim 1 or 5.
12. A nucleic acid having a region within an exon wherein the region has at least 90 % homology with a nucleic acid of claim 1 or 5.
13. A nucleic acid having a region within an exon wherein the region has at least 95 % homology with a nucleic acid of claim 1 or 5.
14. A polypeptide comprising the amino acid sequence encoded by the nucleic acid of claims 1 or 5.
15. A nucleic acid comprising a regulatory region of a gene comprising the nucleotide sequence set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:91, SEQ ID NO:94, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:112, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, and SEQ ID NO:127, or a homolog thereof.

16. A construct comprising a regulatory region of claim 15, wherein the regulatory region is functionally linked to a reporter gene.

17. A method of reducing or inhibiting a viral infection in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 or a homolog thereof, thereby treating the viral infection.

18. The method of claim 17, wherein the gene is selected from a nucleic acid encoding a gene product from the group consisting or, or the gene product is selected from the group

consisting of: tristetraprolin (human ZFP-36), 6-pyruvoyltetrahydropterin synthase, a eukaryotic DnaJ-like protein, ID3 (inhibitor of DNA binding 3), N-acetylglucosaminyltransferase I (mGAT-1), cleavage stimulation factor (CSTF2), TAK1 binding protein, human zinc transcription factor ZPF207, Dlx2, Smad7 (Mad-related protein), and P-glycoprotein (mdr1b).

19. The method of claim 17, wherein the subject is a human.

20. A method of reducing or inhibiting a viral infection in a subject comprising mutating *ex vivo* in a selected cell an endogenous gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127 or a homolog thereof, to a mutated gene

incapable of producing a functional gene product of the gene or to a mutated gene producing a reduced amount of a functional gene product of the gene, and placing the cell in the subject, thereby reducing viral infection of cells in the subject.

21. The method of claim 20, wherein the cell is a hematopoietic cell.

22. The method of claim 20, wherein the subject is a human.

23. The method of claim 20, wherein the cell is from the subject.

24. A method of screening a compound for effectiveness in treating or preventing a viral infection, comprising administering the compound to a cell containing a cellular gene comprising the nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117,

SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127, or a homolog thereof, and functionally encoding a gene product necessary for reproduction of the virus in the cell but not necessary for survival of the cell and detecting the level and/or activity of the gene product produced, a decrease or elimination of the gene product and/or gene product activity indicating a compound effective for treating or preventing the viral infection.

25. A method of screening a compound for reducing or inhibiting a viral infection, comprising administering the compound to a cell containing the construct of claim 16 and detecting the level of the reporter gene product produced, a decrease or elimination of the reporter gene product indicating a compound for reducing or inhibiting the viral infection.

26. A method of screening a compound for effectiveness in treating or preventing a viral infection comprising contacting the compound with the gene product of a cellular gene comprising nucleic acid set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:30, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:40, SEQ ID NO:41, SEQ ID NO:42, SEQ ID NO:43, SEQ ID NO:44, SEQ ID NO:45, SEQ ID NO:46, SEQ ID NO:47, SEQ ID NO:48, SEQ ID NO:49, SEQ ID NO:50, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:54, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:62, SEQ ID NO:63, SEQ ID NO:64, SEQ ID NO:65, SEQ ID NO:66, SEQ ID NO:67, SEQ ID NO:68, SEQ ID NO:69, SEQ ID NO:70, SEQ ID NO:71, SEQ ID NO:72, SEQ ID NO:73, SEQ ID NO:74, SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85, SEQ ID NO:86, SEQ ID NO:87, SEQ ID NO:88, SEQ ID NO:89, SEQ ID NO:90, SEQ ID NO:91, SEQ ID NO:92, SEQ ID NO:93, SEQ ID NO:95, SEQ ID NO:96, SEQ ID NO:97, SEQ ID NO:98, SEQ ID NO:99, SEQ ID NO:100, SEQ ID NO:101, SEQ ID NO:102, SEQ ID

NO:103, SEQ ID NO:104, SEQ ID NO:105, SEQ ID NO:106, SEQ ID NO:107, SEQ ID NO:108, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:111, SEQ ID NO:112, SEQ ID NO:113, SEQ ID NO:114, SEQ ID NO:115, SEQ ID NO:116, SEQ ID NO:117, SEQ ID NO:118, SEQ ID NO:119, SEQ ID NO:120, SEQ ID NO:121, SEQ ID NO:122, SEQ ID NO:123, SEQ ID NO:124, SEQ ID NO:125, SEQ ID NO:126, or SEQ ID NO:127, or a homolog thereof, and detecting the function of the gene product, a decrease or elimination of the function indicating a compound for reducing or inhibiting viral function.

27. A method of suppressing a malignant phenotype in a cell in a subject, comprising administering to the subject an amount of a composition that inhibits expression or functioning of a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, thereby suppressing a malignant phenotype.

28. A method of screening a compound for effectiveness in treating a viral infection, comprising administering the compound to a cell containing a cellular gene functionally encoding a gene product whose overexpression inhibits reproduction of the virus but does not prevent survival of the cell and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for treating the viral infection.

29. A method of screening for a compound that can suppress a malignant phenotype in a cell comprising administering the compound to a cell containing a nucleic acid functionally encoding a gene product encoded by a gene comprising the nucleic acid set forth in SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:26, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:36 or SEQ ID NO:94, or a homolog thereof, and detecting the level of the gene product produced, an increase in the gene product indicating a compound effective for suppressing the malignant phenotype.