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(54) Titre : ACIDES NUCLEIQUES, PROTEINES ET ANTICORPS  
 (54) Title: NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES

(57) **Abrégé/Abstract:**

The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

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2000/11/17 (60/249,244) US; 2000/11/17 (60/249,245) US; 2000/11/17 (60/249,207) US; 2000/11/17 (60/249,212) US;  
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60/225,268	14 August 2000 (14.08.2000)	US	60/236,327	29 September 2000 (29.09.2000)
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60/225,213	14 August 2000 (14.08.2000)	US	60/237,039	2 October 2000 (02.10.2000)
60/225,266	14 August 2000 (14.08.2000)	US	60/237,038	2 October 2000 (02.10.2000)
60/225,214	14 August 2000 (14.08.2000)	US	60/237,040	2 October 2000 (02.10.2000)
60/226,279	18 August 2000 (18.08.2000)	US	60/237,037	2 October 2000 (02.10.2000)
60/226,868	22 August 2000 (22.08.2000)	US	60/236,802	2 October 2000 (02.10.2000)
60/227,182	22 August 2000 (22.08.2000)	US	60/239,937	13 October 2000 (13.10.2000)

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(54) Title: NUCLEIC ACIDS, PROTEINS, AND ANTIBODIES

(57) Abstract: The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

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60/241,785	20 October 2000 (20.10.2000)	US	60/251,989	8 December 2000 (08.12.2000)	US
60/241,809	20 October 2000 (20.10.2000)	US	60/251,869	8 December 2000 (08.12.2000)	US
60/240,960	20 October 2000 (20.10.2000)	US	60/251,856	8 December 2000 (08.12.2000)	US
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60/241,808	20 October 2000 (20.10.2000)	US	60/251,990	8 December 2000 (08.12.2000)	US
60/241,221	20 October 2000 (20.10.2000)	US	60/254,097	11 December 2000 (11.12.2000)	US
60/241,786	20 October 2000 (20.10.2000)	US	60/259,678	5 January 2001 (05.01.2001)	US
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60/244,617	1 November 2000 (01.11.2000)	US			
60/246,474	8 November 2000 (08.11.2000)	US	<b>(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC.</b> [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).		
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60/246,476	8 November 2000 (08.11.2000)	US	<b>(72) Inventors; and</b>		
60/246,526	8 November 2000 (08.11.2000)	US	<b>(75) Inventors/Applicants (for US only): ROSEN, Craig, A.</b> [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). <b>BARASH, Steven, C.</b> [US/US]; 111 Watkins Pond Blvd. #301, Rockville, MD 20850 (US). <b>RUBEN, Steven, M.</b> [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US).		
60/246,475	8 November 2000 (08.11.2000)	US			
60/246,525	8 November 2000 (08.11.2000)	US	<b>(74) Agents: HOOVER, Kenley, K. et al.;</b> Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).		
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.



## DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3  
CONTENANT LES PAGES 1 À 340

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

## JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 3  
CONTAINING PAGES 1 TO 340

NOTE: For additional volumes, please contact the Canadian Patent Office

NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

## **Nucleic Acids, Proteins, and Antibodies**

[1] This application refers to a "Sequence Listing" that is provided only on electronic media in computer readable form pursuant to Administrative Instructions Section 801(a)(i). The Sequence Listing forms a part of this description pursuant to Rule 5.2 and Administrative Instructions Sections 801 to 806, and is hereby incorporated in its entirety.

[2] The Sequence Listing is provided as an electronic file (PJZ05\_seqList.txt, 825,391 bytes in size, created on January 13, 2001) on four identical compact discs (CD-R), labeled "COPY 1," "COPY 2," "COPY 3," and "CRF." The Sequence Listing complies with Annex C of the Administrative Instructions, and may be viewed, for example, on an IBM-PC machine running the MS-Windows operating system by using the V viewer software, version 2000 (see World Wide Web URL: <http://www.fileviewer.com>).

### ***Field of the Invention***

[3] The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic

methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

### *Background of the Invention*

[4] The immune system is an intricate network of cells, tissues and soluble molecules that function to protect the body from invasion by foreign substances and pathogens. The major cells of the immune system are lymphocytes, including B cells and T cells, and myeloid cells, including basophils, eosinophils, neutrophils, mast cells, monocytes, macrophages and dendritic cells. In addition to these cellular components of the immune system, soluble molecules- such as antibodies, complement proteins, and cytokines- circulate in lymph and blood plasma, and play important roles in immunity.

[5] The immune system can be subdivided into the acquired and innate immune systems. The cells of the innate immune system (e.g., neutrophils, eosinophils, basophils, mast cells) are not antigen specific and their action is not enhanced by repeated exposure to the same antigen. The cells of the acquired immune system (B and T cells) are antigen specific. Repeated exposure of B and T cells to an antigen results in improved immune responses (memory responses) produced by these cell types. The cells and products of the acquired immune system can recruit components of the innate system to mount a focused immune response. For a more extensive review of the immune system, see Fundamental Immunology, 4th edition, Ed. William Paul, Lippincott-Raven Pub. (1998).

[6] An immune response is seldom carried out by a single cell type, but rather requires the coordinated efforts of several cell types. In order to coordinate an immune response, it is necessary that cells of the immune system communicate with each other and with other cells of the body. Communication between cells may be made by cell-cell contact, between membrane bound molecules on each cell, or by the interaction of soluble components of the immune system with cellular receptors. Signaling between cell types may have one or more of a variety of consequences, including activation, proliferation, differentiation, and apoptosis. Activation and differentiation of immune cells may result in the expression or



secretion of polypeptides, or other molecules, which in turn affect the function of other cells and/or molecules of the immune system.

[7] Molecules which stimulate or suppress immune system function are known as immunomodulators. These molecules, which include endogenous proteins (e.g., cytokines, cytokine receptors, and intracellular signal transduction molecules), molecules derived from microorganisms, and synthetic agents, may exert their modulatory effects at one or more stages of the immune response, such as antigen recognition, stimulation of cytokine production and release, and/or activation/differentiation of lymphocytes and myeloid cells. Immunomodulators may enhance (immunoprophylaxis, immunostimulation), restore (immunosubstitution, immunorestitution) or suppress (immunosuppression, immunodeviation) immunological functions or activities.

[8] Immunomodulatory compounds have many important applications in clinical practice. For example, immunosuppressing agents (which attenuate or prevent unwanted immune responses) can be used to prevent tissue rejection during organ transplantation, to prevent Rh hemolytic disease of the newborn, or to treat autoimmune disorders. A mechanism of action common to many immunosuppressants is the inhibition of T cell activation and/or differentiation. Antilymphocyte antibodies have also been used to attenuate immune system functions. Currently-used immunosuppressive agents can produce a number of side effects which limit their use. Among the most serious secondary effects include kidney and liver toxicity, increased risk of infection, hyperglycemia, neoplasia, and osteoporosis (see, e.g., Freeman, Clin. Biochem. 24(1):9-14 (1991); Mitchison, Dig. Dis. 11(2):78-101 (1993)).

[9] Immunostimulants, which enhance the activity of immune cells and molecules, comprise another class of immunomodulatory agents with important clinical applications. Such applications include, for example, the treatment of immunodeficiency disorders (e.g. AIDS and severe combined immunodeficiency), chronic infectious diseases (e.g. viral hepatitis, papillomavirus, and herpesvirus), and cancer. An important class of endogenous immunostimulants is the cytokines. These soluble signaling molecules are produced by a number of cell types, and are critical to the regulation of the immune response. Immunostimulatory mechanisms can include proliferation, differentiation and/or activation of immune cells or progenitors of immune cells. For example, interleukin-2 (IL-2) binds to IL-2 receptors on T lymphocytes and induces proliferation and differentiation. Another cytokine, interferon alpha, stimulates the immune system through a variety of mechanisms, including

activation of macrophages, T lymphocytes, and natural killer cells. Interferon alpha also induces the expression of antiviral proteins (see Chapter 50, The Pharmacological Basis of Therapeutics, 9<sup>th</sup> Edition, Eds. Hardman, Limbird, Molinoff, Ruddon, and Gilman, McGraw Hill (1996)). Limitations of current immunostimulant therapies include anaphylaxis, pulmonary edema, and renal toxicity, to name a few.

[10] The discovery of new human immunomodulatory polynucleotides, the polypeptides encoded by them, and antibodies that immunospecifically bind these polypeptides, satisfies a need in the art by providing new compositions which are useful in the diagnosis, treatment, prevention and/or prognosis of disorders of the immune system, including, but not limited to, autoimmune disorders (e.g., systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura and multiple sclerosis), immunodeficiencies (e.g., X-linked agammaglobulinemia, severe combined immunodeficiency, Wiskott-Aldrich syndrome, and ataxia telangiectasia), chronic infections (e.g., HIV, viral hepatitis, and herpesvirus), and neoplastic disorders. Additionally, immunomodulatory molecules would be useful as agents to boost immune responsiveness to pathogens or to suppress immune reactions, for example as is necessary in conjunction with organ transplantation.

### *Summary of the Invention*

[11] The present invention relates to novel proteins. More specifically, isolated nucleic acid molecules are provided encoding novel polypeptides. Novel polypeptides and antibodies that bind to these polypeptides are provided. Also provided are vectors, host cells, and recombinant and synthetic methods for producing human polynucleotides and/or polypeptides, and antibodies. The invention further relates to diagnostic and therapeutic methods useful for diagnosing, treating, preventing and/or prognosing disorders related to these novel polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of polynucleotides and polypeptides of the invention. The present invention further relates to methods and/or compositions for inhibiting or enhancing the production and function of the polypeptides of the present invention.

### *Detailed Description*

#### Tables



[12] Table 1A summarizes some of the polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:)) and contig nucleotide sequence identifier (SEQ ID NO:X)) and further summarizes certain characteristics of these polynucleotides and the polypeptides encoded thereby. The first column provides the gene number in the application for each clone identifier. The second column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence disclosed in Table 1A. The third column provides a unique contig identifier, "Contig ID:" for each of the contig sequences disclosed in Table 1A. The fourth column provides the sequence identifier, "SEQ ID NO:X", for each of the contig sequences disclosed in Table 1A. The fifth column, "ORF (From-To)", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:X that delineate the preferred open reading frame (ORF) that encodes the amino acid sequence shown in the sequence listing and referenced in Table 1A as SEQ ID NO:Y (column 6). Column 7 lists residues comprising predicted epitopes contained in the polypeptides encoded by each of the preferred ORFs (SEQ ID NO:Y). Identification of potential immunogenic regions was performed according to the method of Jameson and Wolf (CABIOS, 4; 181-186 (1988)); specifically, the Genetics Computer Group (GCG) implementation of this algorithm, embodied in the program PEPTIDESTRUCTURE (Wisconsin Package v10.0, Genetics Computer Group (GCG), Madison, Wisc.). This method returns a measure of the probability that a given residue is found on the surface of the protein. Regions where the antigenic index score is greater than 0.9 over at least 6 amino acids are indicated in Table 1A as "Predicted Epitopes". In particular embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the predicted epitopes described in Table 1A. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly. Column 8, "Tissue Distribution" shows the expression profile of tissue, cells, and/or cell line libraries which express the polynucleotides of the invention. The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the key provided in Table 4. Expression of these polynucleotides was not observed in the other tissues and/or cell libraries tested. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon), represents the number of times a sequence corresponding to the reference polynucleotide sequence (e.g., SEQ ID NO:X) was identified in the tissue/cell source. Those tissue/cell



source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of  $^{33}\text{P}$  dCTP, using oligo(dT) to prime reverse transcription. After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a Phosphorimager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill in the art could routinely use this information to identify normal and/or diseased tissue(s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression. Column 9 provides the chromosomal location of polynucleotides corresponding to SEQ ID NO:X. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Given a presumptive chromosomal location, disease locus association was determined by comparison with the Morbid Map, derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM<sup>TM</sup>. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) 2000. World Wide Web URL: <http://www.ncbi.nlm.nih.gov/omim/>). If the putative chromosomal location of the Query overlaps with the chromosomal location of a Morbid Map entry, an OMIM identification number is disclosed in column 10 labeled "OMIM Disease Reference(s)". A key to the OMIM reference identification numbers is provided in Table 5.

[13] Table 1B summarizes additional polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:) contig nucleotide sequence identifiers (SEQ ID NO:X)), and genomic



sequences (SEQ ID NO:B). The first column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence. The second column provides the sequence identifier, "SEQ ID NO:X", for each contig sequence. The third column provides a unique contig identifier, "Contig ID:" for each contig sequence. The fourth column, provides a BAC identifier "BAC ID NO:A" for the BAC clone referenced in the corresponding row of the table. The fifth column provides the nucleotide sequence identifier, "SEQ ID NO:B" for a fragment of the BAC clone identified in column four of the corresponding row of the table. The sixth column, "Exon From-To", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e.g., polypeptides containing amino acid sequences encoded by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

[14] Table 2 summarizes homology and features of some of the polypeptides of the invention. The first column provides a unique clone identifier, "Clone ID NO:Z", corresponding to a cDNA clone disclosed in Table 1A. The second column provides the unique contig identifier, "Contig ID:" corresponding to contigs in Table 1A and allowing for correlation with the information in Table 1A. The third column provides the sequence identifier, "SEQ ID NO:X", for the contig polynucleotide sequence. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. Comparisons were made between polypeptides encoded by the polynucleotides of the invention and either a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM") as further described below. The fifth column provides a description of the PFAM/NR hit having a significant match to a polypeptide of the invention. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, "Score/Percent Identity", provides a quality score or the percent identity, of the hit disclosed in columns five and six. Columns 8 and 9, "NT From" and "NT To" respectively, delineate the polynucleotides in "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth and sixth columns. In specific embodiments polypeptides of the invention comprise, or alternatively consist of, an amino acid sequence encoded by a polynucleotide in SEQ ID NO:X as delineated in columns 8 and 9, or fragments or variants thereof.

[15] Table 3 provides polynucleotide sequences that may be disclaimed according to



certain embodiments of the invention. The first column provides a unique clone identifier, "Clone ID", for a cDNA clone related to contig sequences disclosed in Table 1A. The second column provides the sequence identifier, "SEQ ID NO:X", for contig sequences disclosed in Table 1A. The third column provides the unique contig identifier, "Contig ID:", for contigs disclosed in Table 1A. The fourth column provides a unique integer 'a' where 'a' is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, and the fifth column provides a unique integer 'b' where 'b' is any integer between 15 and the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. For each of the polynucleotides shown as SEQ ID NO:X, the uniquely defined integers can be substituted into the general formula of a-b, and used to describe polynucleotides which may be preferably excluded from the invention. In certain embodiments, preferably excluded from the invention are at least one, two, three, four, five, ten, or more of the polynucleotide sequence(s) having the accession number(s) disclosed in the sixth column of this Table (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone).

[16] Table 4 provides a key to the tissue/cell source identifier code disclosed in Table 1A, column 8. Column 1 provides the tissue/cell source identifier code disclosed in Table 1A, Column 8. Columns 2-5 provide a description of the tissue or cell source. Codes corresponding to diseased tissues are indicated in column 6 with the word "disease". The use of the word "disease" in column 6 is non-limiting. The tissue or cell source may be specific (e.g. a neoplasm), or may be disease-associated (e.g., a tissue sample from a normal portion of a diseased organ). Furthermore, tissues and/or cells lacking the "disease" designation may still be derived from sources directly or indirectly involved in a disease state or disorder, and therefore may have a further utility in that disease state or disorder. In numerous cases where the tissue/cell source is a library, column 7 identifies the vector used to generate the library.

[17] Table 5 provides a key to the OMIM reference identification numbers disclosed in Table 1A, column 10. OMIM reference identification numbers (Column 1) were derived from Online Mendelian Inheritance in Man (Online Mendelian Inheritance in Man, OMIM.



McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine, (Bethesda, MD) 2000. World Wide Web URL: <http://www.ncbi.nlm.nih.gov/omim/>). Column 2 provides diseases associated with the cytologic band disclosed in Table 1A, column 9, as determined using the Morbid Map database.

[18] Table 6 summarizes ATCC Deposits, Deposit dates, and ATCC designation numbers of deposits made with the ATCC in connection with the present application.

[19] Table 7 shows the cDNA libraries sequenced, and ATCC designation numbers and vector information relating to these cDNA libraries.

[20] Table 8 provides a physical characterization of clones encompassed by the invention. The first column provides the unique clone identifier, "Clone ID NO:Z", for certain cDNA clones of the invention, as described in Table 1A. The second column provides the size of the cDNA insert contained in the corresponding cDNA clone.

### **Definitions**

[21] The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

[22] In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

[23] As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence encoding SEQ ID NO:Y or a fragment or variant thereof; a nucleic acid sequence contained in SEQ ID NO:X (as described in column 3 of Table 1A) or the complement thereof; a cDNA sequence contained in Clone ID NO:Z (as described in column 2 of Table 1A and contained within a library deposited with the ATCC); a nucleotide sequence encoding



the polypeptide encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B or a fragment or variant thereof; or a nucleotide coding sequence in SEQ ID NO:B as defined in column 6 of Table 1B or the complement thereof. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having an amino acid sequence encoded by a polynucleotide of the invention as broadly defined (obviously excluding poly-Phenylalanine or poly-Lysine peptide sequences which result from translation of a polyA tail of a sequence corresponding to a cDNA).

[24] In the present invention, "SEQ ID NO:X" was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID NO:X is deposited at Human Genome Sciences, Inc. (HGS) in a catalogued and archived library. As shown, for example, in column 2 of Table 1A, each clone is identified by a cDNA Clone ID (identifier generally referred to herein as Clone ID NO:Z). Each Clone ID is unique to an individual clone and the Clone ID is all the information needed to retrieve a given clone from the HGS library. Furthermore, certain clones disclosed in this application have been deposited with the ATCC on October 5, 2000, having the ATCC designation numbers PTA 2574 and PTA 2575; and on January 5, 2001, having the depositor reference numbers TS-1, TS-2, AC-1, and AC-2. In addition to the individual cDNA clone deposits, most of the cDNA libraries from which the clones were derived were deposited at the American Type Culture Collection (hereinafter "ATCC"). Table 7 provides a list of the deposited cDNA libraries. One can use the Clone ID NO:Z to determine the library source by reference to Tables 6 and 7. Table 7 lists the deposited cDNA libraries by name and links each library to an ATCC Deposit. Library names contain four characters, for example, "HTWE." The name of a cDNA clone (Clone ID) isolated from that library begins with the same four characters, for example "HTWEP07". As mentioned below, Table 1A correlates the Clone ID names with SEQ ID NO:X. Thus, starting with an SEQ ID NO:X, one can use Tables 1, 6 and 7 to determine the corresponding Clone ID, which library it came from and which ATCC deposit the library is contained in. Furthermore, it is possible to retrieve a given cDNA clone from the source library by techniques known in the art and described elsewhere herein. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposits were made pursuant to the terms



of the Budapest Treaty on the international recognition of the deposit of microorganisms for the purposes of patent procedure.

[25] In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

[26] A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, or the complement thereof (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments described herein), the polynucleotide sequence delineated in columns 8 and 9 of Table 2 or the complement thereof, and/or cDNA sequences contained in Clone ID NO:Z (e.g., the complement of any one, two, three, four, or more of the polynucleotide fragments, or the cDNA clone within the pool of cDNA clones deposited with the ATCC, described herein), and/or the polynucleotide sequence delineated in column 6 of Table 1B or the complement thereof. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

[27] Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH<sub>2</sub>PO<sub>4</sub>; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS.



In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

[28] Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

[29] Of course, a polynucleotide which hybridizes only to polyA<sup>+</sup> sequences (such as any 3' terminal polyA<sup>+</sup> tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

[30] The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

[31] The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous



research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth. Enzymol. 182:626-646 (1990); Rattan et al., Ann. N.Y. Acad. Sci. 663:48-62 (1992)).

[32] "SEQ ID NO:X" refers to a polynucleotide sequence described, for example, in Tables 1A or 2, while "SEQ ID NO:Y" refers to a polypeptide sequence described in column 6 of Table 1A. SEQ ID NO:X is identified by an integer specified in column 4 of Table 1A. The polypeptide sequence SEQ ID NO:Y is a translated open reading frame (ORF) encoded by polynucleotide SEQ ID NO:X. "Clone ID NO:Z" refers to a cDNA clone described in column 2 of Table 1A.

[33] "A polypeptide having functional activity" refers to a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide for binding) to an anti-polypeptide antibody], immunogenicity (ability to generate antibody which binds to a



specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide.

[34] The polypeptides of the invention can be assayed for functional activity (e.g. biological activity) using or routinely modifying assays known in the art, as well as assays described herein. Specifically, one of skill in the art may routinely assay immunomodulatory polypeptides (including fragments and variants) of the invention for activity using assays as described in Examples 21, 22, 23, 29, 32, 33, 35, 40, and 45.

[35] "A polypeptide having biological activity" refers to a polypeptide exhibiting activity similar to, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention).

[36] Table 1A summarizes some of the polynucleotides encompassed by the invention (including contig sequences (SEQ ID NO:X) and clones (Clone ID NO:Z) and further summarizes certain characteristics of these polynucleotides and the polypeptides encoded thereby.

Polynucleotides and Polypeptides of the InventionTABLE 1A

Gene No:	Clone ID NO: Z	Contig ID:	SEQ ID NO: X	ORF (From-To)	AA SEQ ID NO: Y	Predicted Epitopes	Tissue Distribution Library code: count (see Table IV for Library Codes)	Cytologic Band	OMIM Disease Reference(s):
1	HTTEK47	573649	11	2 - 349	175	Leu-13 to Val-18, Thr-37 to Lys-46.	AR061: 8, AR089: 6 L0439: 5, H0622: 3, H0040: 2, L0794: 2, L0805: 2, L0758: 2, L0803: 1, L0375: 1, L0659: 1, L0789: 1, L0665: 1, H0579: 1, L0750: 1, L0779: 1, L0777: 1, L0752: 1 and L0755: 1.		
2	HMSKF13	708207	12	2 - 400	176	Arg-1 to Leu-7.	S0002: 1, H0134: 1 and L0596: 1.		
3	HLHCT68	764745	13	44 - 217	177		AR061: 7, AR089: 6 L0748: 2 and H0024: 1.		
4	HKAFF33	974200	14	2 - 187	178	His-1 to Pro-7.	H0521: 174, H0556: 138, H0581: 90, S0278: 66, L0665: 66, H0542:		





























5	HTLAQ18	1193114	15	267 - 758	179	Thr-40 to Gly-66, Gly-78 to Pro-84, Gln-93 to Ser-107, Ala-138 to Gln-145.	S0194: 1, S0452: 1, S0462: 1 and S0384: 1. AR061: 11, AR089: 6 L0779: 3, L0758: 3, H0618: 2, H0253: 1, H0009: 1 and H0012: 1.			
6	HLYAW15	811792	118	2 - 493	282	Ala-1 to Glu-11.	H0039: 1, H0521: 1 and H0445: 1.			
		976531	16	3 - 395	180	Arg-42 to Glu-47, Asp-65 to Arg-76, Gln-82 to Trp-88, Pro-90 to Thr-99.				
7	HMCIFY36	974192	119	3 - 533	283	Arg-42 to Glu-47, Asp-65 to Arg-76, Gln-82 to Arg-111.	S0344: 1 and L0601: 1. 6p21.3			106300, 108800, 120290, 120290, 120810, 120820, 142857, 142858, 150270, 167250, 170261, 177900,
		943638	17	1 - 291	181	Gln-1 to Glu-12, Tyr-20 to Glu-25.				





10	HSSJM44	1175100	20	62 - 1867	184	Arg-94 to Arg-99, Val-144 to Tyr-151, Arg-180 to Asn-185, Leu-231 to Pro-236, Pro-393 to Tyr-399, Asn-422 to Gly-435, Leu-457 to Trp-464, Tyr-469 to Val-474, Lys-488 to Lys-497,	AR089: 1, AR061: 1 L0439: 5, H0620: 3, L0769: 3, H0556: 2, H0012: 2, H0024: 2, S0051: 2, H0100: 2, L0770: 2, L0774: 2, L0438: 2, L0751: 2, L0779: 2, S0444: 1, H0550: 1, H0013: 1,			167250, 170261, 177900, 179450, 201910, 217000, 222100, 233100, 235200, 248611, 256550, 256550, 600202, 600261, 601868, 602280, 602475
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											15, L0651: 15, H0619: 14, H0150: 14, L0657: 14, H0593: 14, L0754: 14, H0638: 13, H0063: 13, H0646: 13, L0599: 13, H0663: 12, S0376: 12, H0597: 12, H0644: 12, H0087: 12, L0648: 12, S0052: 12, H0576: 12, L0751: 12, S0026: 12, L0600: 12, T0002: 11, T0049: 11, S0212: 11, H0402: 11, S0356: 11, H0427: 11, H0040: 11, H0264: 11, H0561: 11, S0426: 11, L0653: 11, S0322: 11, S0134: 10, S0218: 10, H0650: 10, H0545: 10, H0510: 10, H0416: 10, S0022: 10, S0146: 10, S0027: 10, H0014: 9, H0188: 9, H0124: 9, L0646: 9, L0374: 9, H0660: 9, S0330: 9, S0044: 9, L0740: 9, H0656: 8,											
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			H0341: 8, H0587: 8, H0599: 8, H0036: 8, H0024: 8, S0003: 8, H0560: 8, H0647: 8, L0438: 8, H0670: 8, L0757: 8, S0040: 7, H0559: 7, H0004: 7, H0085: 7, L0483: 7, H0628: 7, L0762: 7, L0647: 7, S0380: 7, S3014: 7, S0011: 7, H0550: 6, H0574: 6, H0618: 6, H0421: 6, H0544: 6, H0050: 6, H0375: 6, T0006: 6, H0553: 6, H0488: 6, S0053: 6, H0682: 6, S0378: 6, H0187: 6, L0750: 6, L0581: 6, H0141: 5, L0785: 5, H0254: 5, H0661: 5, S0140: 5, S0222: 5, H0497: 5, H0632: 5, T0060: 5, H0251: 5, H0596: 5, H0213: 5, H0181: 5, H0598: 5,												
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			T0010: 1, H0083: 1, H0109: 1, H0247: 1, H0266: 1, S0316: 1, H0290: 1, H0292: 1, S0314: 1, S0250: 1, H0252: 1, H0615: 1, H0428: 1, L0194: 1, H0180: 1, L0055: 1, H0165: 1, S0364: 1, H0361: 1, S0366: 1, H0163: 1, H0372: 1, H0433: 1, T0069: 1, L0370: 1, T0041: 1, S0370: 1, S0382: 1, S0306: 1, S0466: 1, S0440: 1, H0538: 1, L0598: 1, L0520: 1, L0640: 1, L0371: 1, L0535: 1, L0631: 1, L0638: 1, L0761: 1, L0630: 1, L0772: 1, L0373: 1, L0641: 1, L0765: 1, L0771: 1, L0521: 1, L0768: 1, L0766: 1, L0386: 1, L0774: 1, L0806: 1,											
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										L0652: 1, L0776: 1, L0661: 1, L0628: 1, L0658: 1, L0547: 1, L0546: 1, L0383: 1, L0519: 1, L0545: 1, L0528: 1, T0068: 1, S0148: 1, H0519: 1, S0122: 1, H0579: 1, S0332: 1, S0350: 1, S0190: 1, S0188: 1, H0214: 1, H0626: 1, H0631: 1, L0611: 1, S0118: 1, S3012: 1, S0028: 1, S0206: 1, L0742: 1, L0743: 1, L0749: 1, L0756: 1, L0753: 1, L0731: 1, S0260: 1, H0595: 1, L0604: 1, L0366: 1, S0106: 1, S0192: 1, S0194: 1, S0452: 1, S0462: 1 and S0384: 1.							
12	HRKPA05	974201	22	3 - 149	186	Arg-15 to Arg-28.	AR089: 0, AR061: 0 H0521: 174, H0556: 138, H0581: 90, S0278: 66, L0665: 66, H0542:										

























13	HTGFY58	974198	23	2 - 277	187	Arg-1 to Asn-13, Tyr-20 to Gly-27.	S0194: 1, S0452: 1, S0462: 1 and S0384: 1. H0521: 174, H0556: 138, H0581: 90, S0278: 66, L0665: 66, H0542: 66, S0360: 64, H0543: 61, H0046: 57, S0344: 57, L0659: 55, S0358: 54, H0271: 50, S0142: 49, H0522: 49, S0144: 48, L0664: 46, H0265: 45, H0585: 45, H0657: 42, L0655: 41, H0445: 41, H0555: 37, L0666: 36, H0518: 35, H0486: 34, L0662: 34, S0132: 33, H0318: 33, H0622: 32, S0354: 31, H0090: 31, S0372: 31, H0575: 30, H0435: 29, H0641: 27, H0635: 26, S0126: 26, H0457: 25, H0634: 25, H0436: 25, H0423: 25, H0255: 24, H0250: 24, H0069: 22, H0591: 22, S0328: 22, H0509:			
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		<p>11, S0426: 11, L0653:                  11, S0322: 11, S0134:                  10, S0218: 10, H0650:                  10, H0545: 10, H0510:                  10, H0416: 10, S0022:                  10, S0146: 10, S0027:                  10, H0014: 9, H0188: 9,                  H0124: 9, L0646: 9,                  L0374: 9, H0660: 9,                  S0330: 9, S0044: 9,                  L0740: 9, H0656: 8,                  H0341: 8, H0587: 8,                  H0599: 8, H0036: 8,                  H0024: 8, S0003: 8,                  H0560: 8, H0647: 8,                  L0438: 8, H0670: 8,                  L0757: 8, S0040: 7,                  H0559: 7, H0004: 7,                  H0085: 7, L0483: 7,                  H0628: 7, L0762: 7,                  L0647: 7, S0380: 7,                  S3014: 7, S0011: 7,                  H0550: 6, H0574: 6,                  H0618: 6, H0421: 6,                  H0544: 6, H0050: 6,                  H0375: 6, T0006: 6,</p>							
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H0553: 6, H0488: 6, S0053: 6, H0682: 6, S0378: 6, H0187: 6, L0750: 6, L0581: 6, H0141: 5, L0785: 5, H0254: 5, H0661: 5, S0140: 5, S0222: 5, H0497: 5, H0632: 5, T0060: 5, H0251: 5, H0596: 5, H0213: 5, H0181: 5, H0598: 5, H0135: 5, H0551: 5, L0369: 5, L0372: 5, L0364: 5, L0375: 5, L0382: 5, S0216: 5, H0689: 5, L0602: 5, L0744: 5, L0439: 5, S0436: 5, H0653: 5, H0665: 5, H0394: 4, H0584: 4, S0046: 4, H0640: 4, H0431: 4, H0592: 4, H0204: 4, H0086: 4, S0051: 4, H0354: 4, H0038: 4, H0059: 4, H0652: 4, L0606: 4, L0783: 4,







		<p>L0627: 2, L0642: 2,                  L0654: 2, L0527: 2,                  L0636: 2, L0540: 2,                  S0174: 2, H0134: 2,                  S0404: 2, S0406: 2,                  L0777: 2, L0755: 2,                  L0758: 2, L0759: 2,                  S0031: 2, S0308: 2,                  H0343: 2, L0588: 2,                  L0605: 2, L0595: 2,                  L0361: 2, H0668: 2,                  H0667: 2, S0456: 2,                  H0395: 1, H0224: 1,                  H0139: 1, H0159: 1,                  S0470: 1, S0342: 1,                  S0402: 1, H0662: 1,                  H0300: 1, S0442: 1,                  S0444: 1, H0675: 1,                  S0408: 1, H0208: 1,                  H0645: 1, H0393: 1,                  H0411: 1, H0437: 1,                  H0369: 1, H0608: 1,                  H0442: 1, H0409: 1,                  H0600: 1, H0333: 1,                  H0331: 1, H0257: 1,                  L0622: 1, L0623: 1,</p>							
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		H0485: 1, N0009: 1, H0101: 1, S0280: 1, H0156: 1, L0021: 1, H0053: 1, H0349: 1, H0025: 1, H0253: 1, H0196: 1, H0194: 1, H0184: 1, L0040: 1, H0327: 1, H0439: 1, H0045: 1, H0041: 1, N0006: 1, H0081: 1, H0620: 1, L0163: 1, T0010: 1, H0083: 1, H0109: 1, H0247: 1, H0266: 1, S0316: 1, H0290: 1, H0292: 1, S0314: 1, S0250: 1, H0252: 1, H0615: 1, H0428: 1, L0194: 1, H0180: 1, L0055: 1, H0165: 1, S0364: 1, H0361: 1, S0366: 1, H0163: 1, H0372: 1, H0433: 1, T0069: 1, L0370: 1, T0041: 1, S0370: 1, S0382: 1, S0306: 1, S0466: 1,									
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		S0440: 1, H0538: 1, L0598: 1, L0520: 1, L0640: 1, L0371: 1, L0535: 1, L0631: 1, L0638: 1, L0761: 1, L0630: 1, L0772: 1, L0373: 1, L0641: 1, L0765: 1, L0771: 1, L0521: 1, L0768: 1, L0766: 1, L0386: 1, L0774: 1, L0806: 1, L0652: 1, L0776: 1, L0661: 1, L0628: 1, L0658: 1, L0547: 1, L0546: 1, L0383: 1, L0519: 1, L0545: 1, L0528: 1, T0068: 1, S0148: 1, H0519: 1, S0122: 1, H0579: 1, S0332: 1, S0350: 1, S0190: 1, S0188: 1, H0214: 1, H0626: 1, H0631: 1, L0611: 1, S0118: 1, S3012: 1, S0028: 1, S0206: 1, L0742: 1, L0743: 1,								
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									L0749: 1, L0756: 1, L0753: 1, L0731: 1, S0260: 1, H0595: 1, L0604: 1, L0366: 1, S0106: 1, S0192: 1, S0194: 1, S0452: 1, S0462: 1 and S0384: 1.		
14	HTXJB01	1124596	24	55 - 999	188	Arg-35 to Trp-49.			H0556: 2, H0266: 2, H0265: 1, T0002: 1, H0561: 1 and H0521: 1.		
		542372	122	54 - 446	286	Arg-35 to Trp-49, Lys-57 to Thr-76, Glu-100 to Arg-108.					
15	HUFAK35	636241	25	1 - 222	189				H0586: 1 and H0506: 1.		
16	HWHKC91	974191	26	3 - 410	190	Arg-38 to Glu-43.			H0521: 174, H0556: 138, H0581: 90, S0278: 66, L0665: 66, H0542: 66, S0360: 64, H0543: 61, H0046: 57, S0344: 57, L0659: 55, S0358: 54, H0271: 50, S0142: 49, H0522: 49, S0144: 48, L0664: 46, H0265: 45, H0585: 45, H0657: 42, L0655: 41, H0445:		





















			H0266: 1, S0316: 1, H0290: 1, H0292: 1, S0314: 1, S0250: 1, H0252: 1, H0615: 1, H0428: 1, L0194: 1, H0180: 1, L0055: 1, H0165: 1, S0364: 1, H0361: 1, S0366: 1, H0163: 1, H0372: 1, H0433: 1, T0069: 1, L0370: 1, T0041: 1, S0370: 1, S0382: 1, S0306: 1, S0466: 1, S0440: 1, H0538: 1, L0598: 1, L0520: 1, L0640: 1, L0371: 1, L0535: 1, L0631: 1, L0638: 1, L0761: 1, L0630: 1, L0772: 1, L0373: 1, L0641: 1, L0765: 1, L0771: 1, L0521: 1, L0768: 1, L0766: 1, L0386: 1, L0774: 1, L0806: 1, L0652: 1, L0776: 1, L0661: 1, L0628: 1,						
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							<p>L0658: 1, L0547: 1, L0546: 1, L0383: 1, L0519: 1, L0545: 1, L0528: 1, T0068: 1, S0148: 1, H0519: 1, S0122: 1, H0579: 1, S0332: 1, S0350: 1, S0190: 1, S0188: 1, H0214: 1, H0626: 1, H0631: 1, L0611: 1, S0118: 1, S3012: 1, S0028: 1, S0206: 1, L0742: 1, L0743: 1, L0749: 1, L0756: 1, L0753: 1, L0731: 1, S0260: 1, H0595: 1, L0604: 1, L0366: 1, S0106: 1, S0192: 1, S0194: 1, S0452: 1, S0462: 1 and S0384: 1.</p>		
17	HTSFJ40	1172826	27	3 - 515	191	<p>Gly-17 to Gly-33, Val-109 to Val-114, His-132 to Leu-137, Leu-158 to Thr-167. Leu-7 to Ala-13.</p>	<p>AR089: 30, AR061: 6 H0081: 1, H0087: 1, S0144: 1 and H0538: 1.</p>		
18	HEONO59	722406 741361	123 28	3 - 392 325 - 756	287 192		<p>AR089: 5, AR061: 3</p>		

19	HEMBZ62	1078797	29	1 - 849	193	Arg-29 to Ser-39, Glu-108 to Arg-114.	H0457: 1 and L0752: 1. AR089: 6, AR061: 2 H0663: 2, S0328: 2, S0420: 1, S0046: 1, H0559: 1, T0082: 1, H0050: 1, H0100: 1, H0494: 1, L0640: 1, L0789: 1, H0436: 1 and L0439: 1.		
		742551	124	2 - 454	288				
20	HWBAO18	751125	30	1 - 396	194	Arg-1 to Ser-7, Pro-22 to Ala-28, Lys-84 to Ala-89, Pro-92 to Ala-99.	AR089: 3, AR061: 2 L0777: 7, L0439: 6, L0809: 3, S0126: 3, S0342: 2, H0580: 2, H0581: 2, S0002: 2, L0776: 2, L0438: 2, L0748: 2, L0745: 2, L0749: 2, L0779: 2, L0757: 2, L0759: 2, H0556: 1, H0294: 1, L0415: 1, S0418: 1, H0333: 1, H0559: 1, H0486: 1, H0250: 1, H0505: 1, H0052: 1, H0546: 1, L0471: 1,		





22	HTADZ74	1172825	32	1 - 897	196	5. Val-26 to Arg-33, Arg-93 to Asp-107, Leu-142 to Tyr-148, Val-261 to Thr-268, Gly-283 to Trp-299.	AR050: 18, AR089: 2, AR061: 2, AR051: 2, AR054: 1 S0114: 1, H0069: 1, H0014: 1, L0667: 1, L0804: 1, L0659: 1, S0052: 1 and H0422: 1.		
		811489	126	23 - 586	290	Ile-5 to Lys-10, Arg-78 to Asp-92.			
23	HELHB88	1226704	33	256 - 3360	197	Gln-1 to Thr-7, Glu-28 to Gln-35, Lys-188 to Lys-207, Ser-238 to Gly-245, Asp-278 to Gly-283, Pro-317 to Ser-324, Ser-335 to Glu-342, Pro-344 to Lys-355, Glu-362 to Asn-373, Glu-385 to Arg-393, Arg-399 to Gln-417, Lys-422 to Gln-457, Glu-461 to Glu-477, Leu-514 to Glu-529, Leu-538 to Met-548, Gln-562 to Gln-567,	AR061: 2, AR089: 2 L0777: 3, L0794: 2, S0027: 2, L0748: 2, L0747: 2, L0601: 2, S0342: 1, S0212: 1, S0282: 1, L0004: 1, S0045: 1, H0581: 1, T0110: 1, L0471: 1, S6028: 1, H0551: 1, H0494: 1, H0509: 1, L0646: 1, L0665: 1, H0520: 1, H0547: 1, S0390: 1, L0591: 1, L0366: 1 and H0653: 1.		





							H0265: 1, H0686: 1, H0656: 1, H0341: 1, S0212: 1, H0638: 1, H0125: 1, S0360: 1, H0411: 1, S0222: 1, H0409: 1, H0587: 1, H0014: 1, S0003: 1, H0163: 1, H0591: 1, H0488: 1, H0494: 1, H0641: 1, L0598: 1, H0529: 1, L0772: 1, L0764: 1, L0768: 1, L0774: 1, L0655: 1, L0783: 1, L0809: 1, L0792: 1, L0663: 1, L0665: 1, H0702: 1, H0519: 1, S0126: 1, H0682: 1, H0435: 1, H0672: 1, H0704: 1, S3012: 1, L0751: 1, L0750: 1, L0777: 1, L0752: 1, L0757: 1, L0758: 1, L0759: 1, L0362: 1, H0423: 1 and H0506: 1.		
31	HKACD80	1206594	41	98 - 1834	205	Pro-34 to Val-40,	AR089: 12, AR061: 6		



					<p>Thr-65 to Trp-72,                  Val-362 to Gly-367,                  Asp-416 to Met-426,                  Arg-491 to Gln-496,                  Lys-510 to Thr-520,                  Gly-524 to Pro-532,                  Pro-538 to Gln-552.</p>	<p>L0766: 4, H0052: 3,                  L0662: 3, L0776: 3,                  L0666: 3, L0665: 3,                  H0521: 3, H0438: 2,                  H0581: 2, H0263: 2,                  H0494: 2, L0763: 2,                  L0770: 2, L0769: 2,                  L0649: 2, L0664: 2,                  L0748: 2, L0439: 2,                  L0747: 2, S0436: 2,                  H0265: 1, H0556: 1,                  S0040: 1, H0656: 1,                  S0444: 1, S0278: 1,                  H0415: 1, H0403: 1,                  H0643: 1, S0280: 1,                  H0575: 1, H0194: 1,                  H0309: 1, H0545: 1,                  H0046: 1, L0157: 1,                  H0375: 1, L0483: 1,                  H0553: 1, H0412: 1,                  H0646: 1, S0002: 1,                  L0796: 1, L0644: 1,                  L0764: 1, L0774: 1,                  L0376: 1, L0806: 1,                  L0654: 1, L0659: 1,                  L0383: 1, H0547: 1,</p>		
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										L0771: 1, L0773: 1, L0767: 1, L0387: 1, L0803: 1, L0804: 1, L0607: 1, L0657: 1, L0517: 1, L0809: 1, H0648: 1, H0672: 1, L0748: 1, L0740: 1, L0749: 1, L0756: 1, L0758: 1, L0591: 1, L0592: 1 and H0543: 1.		
33	HE8TI39	1222770	43	3 - 1178	207		Ser-8 to Thr-15, Arg-73 to Thr-79, Phe-86 to Leu-92, Thr-124 to Arg-132, Thr-163 to Trp-168, Thr-214 to Val-230, Arg-257 to Tyr-269, Val-346 to Pro-354, Asp-356 to Gln-367.			AR061: 2, AR089: 2 L0438: 4, L0746: 4, H0581: 2, H0656: 1, H0013: 1, L0471: 1, H0266: 1, H0328: 1, H0553: 1, S0438: 1, H0529: 1, L0766: 1, L0805: 1, H0520: 1, H0521: 1, L0752: 1 and S0192: 1.		
		849161	130	3 - 470	294		Ser-8 to Thr-15, Arg-73 to Thr-79, Phe-86 to Leu-92.					
34	HSDJH12	1163916	44	3 - 554	208		Thr-1 to Asp-19, Cys-23 to Cys-34, Gln-36 to Gln-58,			AR089: 24, AR061: 6 S0134: 1, L0749: 1, L0759: 1, S0260: 1 and		

							Leu-78 to Gly-87, Asp-164 to His-169.							
	876344	131	3 - 623	295			Thr-1 to Asp-19, Cys-23 to Cys-34, Gln-36 to Gln-58, Leu-78 to Gly-87, Asp-164 to His-169.							
35	HE8PY29	45	2 - 277	209			Asp-28 to Ser-36, Glu-47 to Gln-60, Phe-68 to Gly-77, Pro-81 to Val-86.			AR061: 2, AR089: 1 H0013: 1 and S0126: 1.				
36	HNTMB90	46	3 - 533	210			Pro-18 to Pro-27, Leu-34 to Lys-39, Lys-90 to Pro-95.			AR051: 2, AR050: 1, AR054: 1, AR061: 1, AR089: 1 H0519: 2, H0046: 1, L0803: 1, H0520: 1 and L0758: 1.				
37	HMKCH92	47	78 - 704	211			Pro-32 to Glu-37, Gly-56 to Ser-61, Gly-144 to Arg-149, Glu-161 to Gly-168, Thr-182 to Lys-187.			AR089: 1, AR061: 1 L0439: 4, H0392: 1 and L0749: 1.	3p26-p25		154705, 193300, 193300, 227646, 253260, 278720, 601154, 601253, 602011	



38	HTELV86	1126499	48	1545 - 178	212			AR089: 7, AR061: 6 H0616: 4, H0038: 1, L0745: 1 and L0779: 1.	
		910946	132	1 - 927	296	Thr-5 to Ser-11, Asp-78 to His-85, Ser-153 to Ser-162, Glu-221 to Ala-234, Gly-247 to Glu-252.			
39	HNTAF23	910947	49	24 - 251	213	His-1 to Gly-12, Trp-69 to Glu-75.		AR089: 2, AR061: 1 L0439: 4, S0192: 3, L0776: 2, L0438: 2, L0777: 2, H0254: 1, L0534: 1, H0333: 1, L0763: 1, H0519: 1, H0593: 1, L0750: 1, L0779: 1 and L0758: 1.	
40	HNBTUT01	1025375	50	126 - 746	214	Pro-12 to Leu-19, Pro-43 to Ser-55, His-72 to Ser-80, Pro-98 to Pro-104, Asn-117 to Ile-124, Gly-129 to Ile-137, Ser-177 to Leu-201.		AR089: 15, AR061: 5 S0360: 2, L0766: 2, L0747: 2, T0002: 1, H0686: 1, H0662: 1, S0046: 1, H0023: 1, H0560: 1, H0647: 1, L0662: 1, L0666: 1, H0576: 1, L0779: 1, L0596: 1, L0590: 1, L0601: 1 and H0667: 1.	

41	HEMFI21	913838	133	3 - 827	297	Arg-1 to Gly-10.			
		1128266	51	1 - 1503	215	Thr-27 to Arg-32, Gly-63 to Gly-71, Ile-95 to Gly-101, Asn-108 to Ser-115, Pro-174 to Pro-179, Asp-185 to Ser-197, Phe-209 to Glu-216, Ile-220 to Lys-227, Asp-243 to Glu-248, Arg-282 to Gly-287, Glu-298 to Cys-303, Lys-332 to Pro-356, Lys-363 to Tyr-372, Glu-378 to Thr-398, Ser-402 to Asp-409, Ile-413 to Ile-420, Glu-437 to Arg-501.	AR061: 4, AR089: 3 L0794: 4, S0376: 3, L0596: 3, H0266: 2, S0003: 2, H0553: 2, H0616: 2, H0551: 2, L0665: 2, S0028: 2, L0747: 2, L0779: 2, L0759: 2, S0046: 1, H0574: 1, H0013: 1, H0427: 1, H0156: 1, H0046: 1, H0050: 1, H0031: 1, H0212: 1, L0455: 1, H0598: 1, H0625: 1, H0509: 1, S0422: 1, L0521: 1, L0766: 1, L0803: 1, L0653: 1, L0659: 1, L0809: 1, L0789: 1, L0666: 1, H0659: 1, H0539: 1, S0174: 1, L0777: 1, L0758: 1, L0599: 1 and L0462: 1.		
		917436	134	1 - 1503	298	Thr-27 to Arg-32, Gly-63 to Gly-71, Ile-95 to Gly-101,			

42	HMSOL52	921126	52	90 - 473	216	Asn-108 to Ser-115. Glu-29 to Gly-35, Arg-53 to Pro-59, Thr-88 to Met-99, Pro-109 to Asp-118.	AR061: 5, AR089: 2 L0770: 4, L0803: 4, H0638: 1, H0123: 1, S0426: 1, L0662: 1, H0648: 1, L0747: 1, L0756: 1, L0779: 1, L0752: 1 and L0759: 1.		
43	HHGAE47	922194	53	3 - 503	217	Gly-25 to Arg-45, Asp-53 to Glu-60, Asp-66 to Lys-72, Arg-89 to Trp-106, Asn-121 to Gly-147, Val-152 to Gly-159, Ala-161 to Ser-166.	AR061: 3, AR089: 2 L0769: 5, L0774: 5, L0756: 4, H0624: 2, S0358: 2, S0444: 2, S0408: 2, H0587: 2, L0764: 2, L0766: 2, L0775: 2, L0601: 2, H0170: 1, S0442: 1, S0410: 1, H0497: 1, H0333: 1, H0632: 1, H0156: 1, L0022: 1, L0738: 1, H0271: 1, H0039: 1, S0344: 1, L0637: 1, L0772: 1, L0646: 1, L0773: 1, L0662: 1, L0518: 1, L0783: 1, L0791: 1, L0663: 1, S0374: 1,		











H0657: 1, H0306: 1, S0420: 1, S0354: 1, S0360: 1, S0046: 1, L0717: 1, H0550: 1, H0592: 1, H0333: 1, H0331: 1, H0559: 1, H0486: 1, H0013: 1, H0244: 1, H0635: 1, H0575: 1, H0596: 1, T0110: 1, H0123: 1, H0615: 1, H0033: 1, H0553: 1, H0212: 1, H0124: 1, H0040: 1, H0616: 1, H0264: 1, H0488: 1, H0100: 1, H0494: 1, H0131: 1, H0529: 1, L0637: 1, L0772: 1, L0766: 1, L0775: 1, L0375: 1, L0776: 1, L0628: 1, L0657: 1, L0664: 1, S0374: 1, H0547: 1, H0593: 1, S3014: 1, S0027: 1, L0748: 1, L0750: 1, L0731: 1, L0758: 1, H0595: 1,
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			H0575: 2, H0545: 2, H0041: 2, H0413: 2, L0775: 2, H0696: 2, S0037: 2, L0748: 2, L0751: 2, L0754: 2, L0749: 2, L0758: 2, H0445: 2, S0276: 2, H0624: 1, L0778: 1, L0005: 1, H0645: 1, H0441: 1, H0391: 1, S0005: 1, T0040: 1, H0069: 1, H0427: 1, S0280: 1, H0042: 1, T0048: 1, H0505: 1, H0309: 1, H0544: 1, H0009: 1, H0266: 1, H0617: 1, H0412: 1, H0623: 1, T0004: 1, L0564: 1, T0041: 1, H0494: 1, H0633: 1, H0646: 1, H0652: 1, L0769: 1, L0646: 1, L0655: 1, L0659: 1, L0546: 1, L0783: 1, L0809: 1, H0144: 1, L0565: 1, S0126: 1,								
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									H0689: 1, H0435: 1, H0659: 1, H0672: 1, S0378: 1, H0555: 1, S0206: 1, L0777: 1, L0780: 1, S0434: 1, S0011: 1, S0194: 1 and H0506: 1.			
51	HMTBB17	1125265	61	549 - 121	225	Arg-9 to Arg-18.			AR089: 3, AR061: 3 L0438: 3, L0439: 3, L0749: 3, L0758: 3, L0766: 2, L0375: 2, L0731: 2, L0759: 2, L0803: 1, L0655: 1, L0517: 1, L0666: 1, L0664: 1, H0518: 1, L0748: 1, L0779: 1, L0599: 1 and H0008: 1.			
		950884	138	513 - 100	302	Arg-34 to Pro-39, Pro-41 to Gly-53, Ile-64 to Ile-77, Asp-85 to Gly-90, Ser-121 to Asn-128.						
52	HKGDE58	1125264	62	3 - 491	226	Asp-1 to Cys-10, Glu-31 to Pro-38, Met-43 to Val-48, Asp-97 to Phe-110,			AR089: 2, AR061: 2 H0538: 1, L0803: 1 and L0731: 1.			

							Asp-119 to Gly-137, Ser-154 to Ile-160.				
			139	11 - 937	303	945039	Asp-17 to Cys-26, Glu-47 to Pro-54, Met-59 to Val-64, Asp-113 to Phe-126, Asp-135 to Gly-153.				
			140	469 - 119	304	950885	Ser-20 to Gly-32, Ile-43 to Ile-56, Asp-64 to Gly-69, Ser-100 to Asn-107.				
53	HCHMW40	1129560	63	540 - 1	227		Phe-1 to Trp-6, Ser-41 to Arg-56.			AR089: 9, AR061: 4 H0586: 14, H0587: 8, L0763: 6, H0592: 4, H0484: 3, H0081: 3, H0063: 3, H0483: 2, H0664: 2, H0601: 1, H0600: 1, H0494: 1, L0648: 1, H0658: 1, S0328: 1 and L0747: 1.	
			141	84 - 572	305	951518	Ser-7 to Gly-14, Leu-22 to Ala-28, Thr-57 to Ser-62.				
54	HE8QZ34	1086807	64	3 - 1025	228		Ser-85 to Arg-90, His-99 to Met-105, Met-119 to Val-125,			AR089: 4, AR061: 1 H0046: 4, H0591: 2, T0067: 2, L0766: 2,	













57	HWLEY40	1172021	67	3 - 1100	231	Glu-12 to Gly-17, Gly-70 to Ser-76, Val-146 to Val-151, His-169 to Leu-174, Leu-195 to Lys-204, Asn-277 to Phe-282.	AR089: 2, AR061: 2 L0438: 12, L0439: 11, H0617: 5, H0556: 4, H0618: 3, H0253: 3, L0769: 3, L0761: 3, L0759: 3, H0544: 2, H0031: 2, H0135: 2, H0038: 2, H0641: 2, L0764: 2, L0783: 2, L0809: 2, L0790: 2, L0666: 2, L0663: 2, L0665: 2, H0144: 2, S0330: 2, L0751: 2, L0779: 2, H0543: 2, H0265: 1, H0685: 1, H0657: 1, H0306: 1, S0420: 1, S0354: 1, S0360: 1, S0046: 1, L0717: 1, H0550: 1, H0592: 1, H0333: 1, H0331: 1, H0559: 1, H0486: 1, H0013: 1, H0244: 1, H0635: 1, H0575: 1, H0596: 1,	H0667: 1, S0192: 1 and H0542: 1.		
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							<p>T0110: 1, H0123: 1,                  H0615: 1, H0033: 1,                  H0553: 1, H0212: 1,                  H0124: 1, H0040: 1,                  H0616: 1, H0264: 1,                  H0488: 1, H0100: 1,                  H0494: 1, H0131: 1,                  H0529: 1, L0637: 1,                  L0772: 1, L0766: 1,                  L0775: 1, L0375: 1,                  L0776: 1, L0628: 1,                  L0657: 1, L0664: 1,                  S0374: 1, H0547: 1,                  H0593: 1, S3014: 1,                  S0027: 1, L0748: 1,                  L0750: 1, L0731: 1,                  L0758: 1, H0595: 1,                  S0276: 1 and H0423: 1.</p>		
	957875	144	3 - 881	308	<p>Glu-6 to Gly-11,                  Gly-64 to Ser-70,                  Val-140 to Val-145,                  His-163 to Leu-168,                  Leu-189 to Lys-198,                  Ser-221 to Thr-227,                  His-261 to Pro-270.</p>				
58	HHA WC08 1088146	68	338 - 3	232	Ser-41 to Gly-48,	AR061: 0, AR089: 0			



60	HMSGF27	1206683	70	61 - 1455	234	Pro-28 to His-39, Thr-69 to Trp-76, Leu-166 to Asn-171, Val-248 to Gly-253, Asp-302 to Met-312, Arg-377 to Gln-382, Lys-396 to Thr-406, Gly-410 to Pro-418, Pro-424 to Gln-438.	AR089: 12, AR061: 8 L0766: 4, H0052: 3, L0662: 3, L0776: 3, L0666: 3, L0665: 3, H0521: 3, H0438: 2, H0581: 2, H0263: 2, H0494: 2, L0763: 2, L0770: 2, L0769: 2, L0649: 2, L0664: 2, L0748: 2, L0439: 2, L0747: 2, S0436: 2, H0265: 1, H0556: 1, S0040: 1, S0444: 1, S0278: 1, H0415: 1, H0403: 1, H0643: 1, S0280: 1, H0575: 1,	H0617: 1, H0413: 1, L0762: 1, L0638: 1, L0639: 1, L0761: 1, L0764: 1, L0662: 1, L0774: 1, L0807: 1, L0657: 1, S0053: 1, S0126: 1, H0626: 1, L0747: 1, L0757: 1, L0759: 1, L0597: 1 and L0608: 1.		
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		<p>S0132: 1, S0222: 1,                  H0441: 1, H0586: 1,                  H0587: 1, H0497: 1,                  H0069: 1, H0427: 1,                  S0280: 1, H0046: 1,                  H0457: 1, H0081: 1,                  H0024: 1, T0010: 1,                  H0594: 1, H0188: 1,                  H0687: 1, H0553: 1,                  H0124: 1, H0494: 1,                  H0641: 1, S0422: 1,                  S0002: 1, S0426: 1,                  L0372: 1, L0646: 1,                  L0374: 1, L0648: 1,                  L0649: 1, L0803: 1,                  L0651: 1, L0653: 1,                  L0656: 1, L0635: 1,                  L0542: 1, L0526: 1,                  L0783: 1, L0809: 1,                  L0647: 1, L0791: 1,                  L0792: 1, H0698: 1,                  H0699: 1, H0693: 1,                  H0547: 1, H0689: 1,                  H0690: 1, H0683: 1,                  H0670: 1, S0378: 1,                  S0152: 1, H0555: 1,</p>						
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												H0436: 1, S0392: 1, L0742: 1, L0751: 1, L0780: 1, H0668: 1, H0653: 1, S0242: 1, H0542: 1, H0543: 1 and S0460: 1.		
62	HTTCT34	1097598	72	3 - 635	236	Phe-86 to Tyr-94, Val-149 to Lys-155.						AR061: 5, AR089: 2 H0040: 3		
		973210	147	3 - 1049	311	Phe-86 to Tyr-94, Val-149 to Lys-155, Trp-169 to Asn-179, Thr-189 to Glu-197.								
63	HAWAM69	943104	73	1010 - 1441	237	Cys-38 to Gly-43, Gly-70 to Pro-82, Arg-129 to Glu-134, Gly-139 to Gly-144.						AR054: 334, AR050: 251, AR051: 249, AR061: 6, AR089: 6 L0758: 12, L0662: 11, H0251: 9, L0731: 9, S0360: 5, H0013: 5, L0659: 5, L0747: 5, H0252: 4, H0328: 4, L0666: 4, L0439: 4, H0135: 3, L0764: 3, L0783: 3, L0749: 3, S0358: 2, L0776: 2, L0663: 2, H0651: 2, L0744: 2, L0754: 2,		





64	HMTAV95	614936	74	3 - 281	238	312	Leu-23 to Gly-32, Lys-34 to Lys-40. Asp-1 to Ile-6, Trp-13 to Glu-21, Met-27 to Lys-34, Ala-50 to Thr-56.	AR089: 0, AR061: 0 H0518: 2		
65	HSXCB49	1172424	75	459 - 85	239			AR051: 6, AR061: 1, AR089: 0 S0036: 2		
		800501	149	459 - 85	313					
		909820	150	40 - 273	314		Lys-7 to His-19.			
66	HTEON29	1126522	76	1204 - 653	240		Pro-39 to Ala-47, Ser-150 to Asn-156.	AR061: 6, AR089: 3 H0038: 4, L0758: 3, H0616: 2, L0794: 2, L0747: 2, L0803: 1, L0789: 1 and L0590: 1.		
		815852	151	2 - 520	315		Pro-27 to Ala-35.			
67	HHFGP83	1174826	77	199 - 1692	241		Gly-10 to Gly-17.	AR089: 12, AR061: 9 L0731: 9, L0665: 6, H0024: 4, L0745: 4, L0747: 4, L0662: 3, L0794: 3, H0550: 2, H0081: 2, H0012: 2, S0022: 2, H0100: 2, L0769: 2, L0764: 2, L0659: 2, H0520: 2,		



69	HCHAT01	1202214	79	2 - 2443	243	<p>Phe-34 to Ile-39,  Arg-41 to Lys-47,  Leu-49 to Gly-55,  Lys-104 to Lys-110,  Asp-119 to Gly-124.</p> <p>Ser-6 to Ser-14,  Ser-20 to Ala-37,  Gln-52 to Glu-61,  Glu-133 to Glu-144,  Leu-234 to Gln-239,  Ser-334 to Ala-340,  Leu-378 to Lys-383,  Met-424 to Ser-431,  Leu-472 to Asp-477,  Thr-529 to His-564,  Lys-571 to Ile-580,  Pro-584 to Gln-590,  Asp-605 to Asp-610,  Ala-634 to Cys-643,  Glu-646 to His-656.</p>	<p>AR089: 1, AR061: 0  L0439: 12, L0748: 11,  L0751: 11, L0769: 7,  H0046: 6, L0756: 6,  L0775: 5, L0666: 5,  L0747: 5, L0770: 4,  L0438: 4, L0740: 4,  L0777: 4, H0617: 3,  L0662: 3, L0774: 3,  L0776: 3, H0521: 3,  S0037: 3, L0749: 3,  L0731: 3, L0757: 3,  L0758: 3, S0212: 2,  S0222: 2, H0586: 2,  H0587: 2, H0333: 2,  H0156: 2, H0052: 2,  S0388: 2, H0290: 2,  L0640: 2, L0521: 2,  L0766: 2, L0375: 2,  L0659: 2, L0783: 2,  H0144: 2, H0539: 2,</p>		
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		L0755: 2, H0445: 2, L0596: 2, L0599: 2, H0149: 1, S0342: 1, H0294: 1, S0114: 1, H0484: 1, H0483: 1, H0664: 1, H0638: 1, S0418: 1, S0420: 1, L0005: 1, S0046: 1, S0300: 1, H0549: 1, H0550: 1, H0370: 1, H0497: 1, H0331: 1, H0486: 1, H0575: 1, S0010: 1, H0434: 1, H0327: 1, H0457: 1, H0041: 1, H0081: 1, H0620: 1, H0024: 1, H0057: 1, H0051: 1, H0083: 1, H0266: 1, H0188: 1, S0250: 1, H0688: 1, H0644: 1, H0674: 1, S0366: 1, H0087: 1, H0116: 1, H0488: 1, H0494: 1, H0131: 1, S0150: 1, H0633: 1, H0649: 1, H0652: 1, L0369: 1,
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74	HEMCL65	910900	84	3 - 368	248	Val-7 to Arg-13.	AR054: 8, AR051: 3, AR061: 2, AR089: 1, AR050: 0 S0046: 5, L0747: 4, H0575: 3, H0266: 3, L0741: 3, L0748: 3, L0750: 3, S0045: 2, H0150: 2, H0012: 2, H0039: 2, H0622: 2, L0751: 2, L0749: 2, L0780: 2, H0445: 2, L0605: 2, L0599: 2, H0171: 1, T0049: 1, H0261: 1, H0587: 1, L0021: 1, H0599: 1, H0253: 1, T0048: 1, H0024: 1, S0051: 1, L0483: 1, H0644: 1, H0268: 1, T0004: 1, H0647: 1, L0771: 1, L0662: 1, L0775: 1, L0512: 1, L0659: 1, L0790: 1, S3012: 1, S0028: 1, L0743: 1, H0444: 1, L0588: 1,		
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75	HMAMB94	1225343	85	3 - 2132	249	<p>Trp-1 to Gly-6, Gln-20 to Asn-26, Pro-30 to Glu-35, Asn-43 to Tyr-50, Ser-57 to Pro-65, Ser-74 to Thr-82, Lys-98 to Gly-107, Asp-119 to Asn-125, Gly-159 to Glu-166, Thr-217 to Val-222, Asn-253 to Asp-262, Glu-294 to Ser-299, Gly-311 to Ser-316.</p>	<p>L0603: 1 and H0506: 1. AR061: 1, AR089: 1 H0266: 2, H0644: 2, H0341: 1, S0278: 1, H0051: 1, L0602: 1 and L0601: 1.</p>		
		910909	158	3 - 587	322	<p>Trp-1 to Gly-6, Gln-20 to Asn-26, Pro-30 to Glu-35, Asn-43 to Tyr-50, Ser-57 to Pro-65, Ser-74 to Thr-82, Lys-98 to Gly-107, Asp-119 to Asn-125, Gly-159 to Glu-166.</p>			
76	HCQCI06	915000	86	3 - 764	250	<p>Arg-16 to Ile-28, Glu-39 to Ser-46, Lys-52 to Leu-57,</p>	<p>AR061: 4, AR089: 2 L0747: 6, L0777: 5, L0794: 4, S0126: 4,</p>		





79	HCYBK19	1225324	.89	2776 - 1331	253	Glu-49 to Val-56, Leu-77 to Tyr-83, Ala-125 to Glu-138, Tyr-144 to Gly-154, Gly-227 to Thr-233, His-286 to Arg-292, Pro-366 to Lys-373.	S0364: 10, H0373: 7, L0604: 7, H0196: 4, L0485: 3, L0002: 1, H0411: 1, H0599: 1, H0327: 1, L0471: 1, L0163: 1, S0366: 1, L0747: 1 and L0750: 1. AR089: 1, AR061: 0 L0794: 18, L0770: 10, L0779: 9, L0438: 8, L0754: 7, H0052: 6, H0553: 6, L0803: 6, L0747: 6, S0222: 4, H0013: 4, S0010: 4, L0769: 4, L0659: 4, L0809: 4, L0439: 4, L0752: 4, L0758: 4, S6016: 3, H0244: 3, H0144: 3, S0126: 3, L0599: 3, S0046: 2, L0157: 2, H0032: 2, H0169: 2, S0036: 2, H0038: 2, H0616: 2, L0763: 2, L0761: 2, L0766: 2, L0804: 2, L0650: 2, L0775: 2,		
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		L0805: 2, L0792: 2, L0665: 2, H0520: 2, H0436: 2, L0731: 2, L0596: 2, L0592: 2, L0581: 2, L0366: 2, H0423: 2, L0393: 1, H0656: 1, L0808: 1, S0282: 1, H0662: 1, S0376: 1, S0132: 1, H0393: 1, H0411: 1, H0369: 1, H0550: 1, H0441: 1, H0333: 1, T0114: 1, H0156: 1, L0021: 1, H0085: 1, H0050: 1, H0014: 1, H0020: 1, H0051: 1, S6028: 1, H0644: 1, S0364: 1, H0124: 1, H0068: 1, H0135: 1, H0591: 1, L0564: 1, H0342: 1, H0633: 1, L0640: 1, L0638: 1, L0764: 1, L0648: 1, L0662: 1, L0768: 1, L0649: 1, L0774: 1, L0636: 1, L0789: 1,
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82	HWFW06	933671	92	3 - 533	256	5.	AR089: 13, AR061: 6 H0556: 2, L0770: 2, H0395: 1, S0040: 1, H0657: 1, H0194: 1, H0024: 1, L0667: 1, L0766: 1, H0521: 1, L0740: 1, L0779: 1 and L0588: 1.		
83	HOSDR06	1229558	93	1622 - 174	257		AR061: 7, AR089: 5 H0345: 10, L0766: 4, H0032: 3, L0803: 3, H0556: 2, T0002: 2, H0014: 2, H0031: 2, L0666: 2, H0521: 2, L0731: 2, H0624: 1, H0171: 1, H0642: 1, H0331: 1, T0114: 1, S0314: 1, S0003: 1, H0615: 1, H0688: 1, T0006: 1, H0090: 1, H0038: 1, H0040: 1, H0529: 1, L0638: 1, L0805: 1, L0655: 1, H0144: 1, S0374: 1, S0330: 1, S0044: 1,		



									L0750: 1, L0756: 1, L0779: 1, L0755: 1, L0759: 1 and L0480: 1.	
937599	163	1 - 1260	327							
84	HNFHW14	939763	94	2 - 448	258					
85	HSDHB12	941973	95	3 - 638	259					



87	HELDR74	1218982	97	2 - 1231	261	His-17 to Gln-22, Gly-42 to Ala-50, Pro-61 to Thr-68, Tyr-171 to Lys-179, Gln-188 to Tyr-195, Glu-262 to Pro-268, Arg-314 to Asp-329, Glu-347 to Gly-354, Ser-367 to Thr-372, Gly-391 to Thr-399.	AR089: 1, AR061: 0 H0305: 4, L0731: 3, L0581: 3, H0622: 2, H0059: 2, L0764: 2, L0766: 2, L0741: 2, L0740: 2, L0749: 2, H0423: 2, H0149: 1, H0159: 1, S0114: 1, H0656: 1, H0255: 1, H0306: 1, H0402: 1, S0045: 1, H0351: 1, H0550: 1, H0441: 1, H0036: 1, T0048: 1, H0318: 1, H0581: 1, H0024: 1, H0051: 1, H0083: 1, H0510: 1, H0617: 1, H0412: 1, H0280: 1, H0647: 1, L0646: 1, L0374: 1, L0385: 1, L0662: 1, L0767: 1, L0794: 1,	H0519: 1, H0658: 1, H0539: 1, S0152: 1, H0522: 1, L0740: 1, L0777: 1, L0603: 1, S0276: 1 and H0542: 1.		
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H0144: 2, L0749: 2, L0592: 2, H0422: 2, L0002: 1, H0583: 1, H0656: 1, S0045: 1, S0046: 1, L0717: 1, H0261: 1, H0455: 1, H0013: 1, H0575: 1, T0082: 1, S0665: 1, S0346: 1, H0581: 1, H0251: 1, H0046: 1, H0009: 1, H0050: 1, H0014: 1, T0010: 1, S0003: 1, S0214: 1, S0366: 1, H0316: 1, H0598: 1, L0351: 1, S0150: 1, L0643: 1, L0764: 1, L0662: 1, L0794: 1, L0805: 1, L0653: 1, L0659: 1, L0666: 1, L0665: 1, H0539: 1, H0521: 1, S0146: 1, H0436: 1, H0478: 1, H0345: 1, L0745: 1, L0758: 1, L0588: 1, L0366: 1, S0026: 1, H0667: 1,	
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91	HFXJJ27	971046	101	173 - 367	265	Pro-48 to Leu-53.	<p>H0673: 1, S0036: 1,                      L0769: 1, L0800: 1,                      L0794: 1, L0803: 1,                      L0661: 1, L0636: 1,                      L0529: 1, L0543: 1,                      L0665: 1, H0521: 1,                      H0696: 1, H0694: 1,                      L0747: 1, L0779: 1,                      L0777: 1, L0752: 1 and                      H0352: 1.</p> <p>AR089: 10, AR061: 7                      L0754: 21, H0553: 10,                      H0574: 6, L0771: 5,                      L0598: 4, L0659: 4,                      L0663: 4, L0745: 4,                      L0731: 4, L0599: 4,                      S0414: 3, H0328: 3,                      L0776: 3, L0439: 3,                      L0756: 3, H0624: 2,                      S0358: 2, S0376: 2,                      S0444: 2, L0717: 2,                      H0596: 2, H0687: 2,                      H0615: 2, L0646: 2,                      L0662: 2, L0803: 2,                      L0774: 2, L0438: 2,                      H0670: 2, S0330: 2,</p>		
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H0478: 2, L0779: 2,  
L0777: 2, L0755: 2,  
S0260: 2, S0452: 2,  
H0171: 1, S0402: 1,  
H0583: 1, H0650: 1,  
H0341: 1, S0282: 1,  
H0638: 1, S0360: 1,  
S0132: 1, H0497: 1,  
H0632: 1, H0156: 1,  
H0575: 1, L0105: 1,  
H0052: 1, H0251: 1,  
H0545: 1, L0471: 1,  
H0012: 1, H0051: 1,  
H0510: 1, S0003: 1,  
S0214: 1, H0622: 1,  
H0124: 1, H0090: 1,  
H0591: 1, H0038: 1,  
H0616: 1, H0551: 1,  
T0067: 1, H0413: 1,  
L0065: 1, S0422: 1,  
UNKWN: 1, L0649: 1,  
L0378: 1, L0655: 1,  
L0517: 1, L0783: 1,  
L0666: 1, L0664: 1,  
L0665: 1, H0144: 1,  
S0374: 1, H0520: 1,





97	HHFGZ38	1117192	107	1 - 1335	271		AR089: 8, AR061: 2 H0556: 1, S0040: 1, H0657: 1, H0306: 1, H0393: 1, H0050: 1, H0266: 1, H0112: 1, H0063: 1, S0142: 1, S0002: 1, L0794: 1, L0378: 1, L0655: 1, L0791: 1, L0665: 1, H0539: 1, H0521: 1, L0596: 1, L0593: 1, L0595: 1 and H0653: 1.		
		785591	170	302 - 1165	334				
98	HAHEF22	910996	108	3 - 839	272	Lys-51 to Gly-58, Asp-67 to Glu-73.	AR089: 16, AR061: 8 L0803: 4, L0794: 3, L0747: 3, H0599: 2, L0659: 2, L0789: 2, S0364: 1, L0804: 1, H0539: 1, L0720: 1 and S0031: 1.		
99	HCUEV29	816065	109	2 - 298	273		AR089: 1, AR061: 1 H0457: 15, H0271: 11, H0494: 7, H0521: 7, H0141: 6, H0255: 6, S0434: 6, L0758: 5, S0354: 4, S0358: 4,		









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120820, 142857, 142858, 150270, 167250, 170261, 177900, 179450, 201910, 217000, 222100, 233100, 235200, 248611, 256550, 256550, 600202, 600261, 601868, 602280, 602475										
102	HEQAY32	1207206	112	2611 - 2147	276	Tyr-23 to Ser-30, Pro-47 to Gly-52, Ala-86 to Ser-91, Pro-114 to Arg-124, Thr-129 to Pro-135.	AR089: 2, AR061: 0 L0438: 6, L0439: 5, H0052: 3, L0743: 3, L0731: 3, H0265: 2, H0617: 2, H0634: 2,			



L0769: 2, L0766: 2,  
L0381: 2, L0751: 2,  
L0749: 2, L0758: 2,  
S0282: 1, S0356: 1,  
H0675: 1, S0132: 1,  
H0645: 1, S0222: 1,  
H0438: 1, T0082: 1,  
H0194: 1, H0544: 1,  
H0178: 1, H0355: 1,  
H0428: 1, H0181: 1,  
H0361: 1, H0038: 1,  
H0040: 1, H0616: 1,  
H0063: 1, H0087: 1,  
T0067: 1, H0059: 1,  
H0649: 1, S0002: 1,  
H0529: 1, L0535: 1,  
L0761: 1, L0646: 1,  
L0771: 1, L0767: 1,  
L0806: 1, L0653: 1,  
L0776: 1, L0659: 1,  
L0789: 1, L0663: 1,  
H0144: 1, L0565: 1,  
H0690: 1, H0682: 1,  
H0696: 1, H0436: 1,  
S0028: 1, L0741: 1,  
L0759: 1, H0667: 1,



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107	HRODF07	1222093	117	830 - 1138	281	AR061: 5, AR089: 4 S0328: 7, S0330: 7, L0648: 6, L0549: 5, H0329: 1, H0039: 1, H0598: 1, S0352: 1, L0551: 1, S0432: 1 and L0755: 1.		
		952426	174	31 - 195	338			

[37] The first column in Table 1A provides the gene number in the application corresponding to the clone identifier. The second column in Table 1A provides a unique "Clone ID NO:Z" for a cDNA clone related to each contig sequence disclosed in Table 1A. This clone ID references the cDNA clone which contains at least the 5' most sequence of the assembled contig and at least a portion of SEQ ID NO:X was determined by directly sequencing the referenced clone. The reference clone may have more sequence than described in the sequence listing or the clone may have less. In the vast majority of cases, however, the clone is believed to encode a full-length polypeptide. In the case where a clone is not full-length, a full-length cDNA can be obtained by methods described elsewhere herein.

[38] The third column in Table 1A provides a unique "Contig ID" identification for each contig sequence. The fourth column provides the "SEQ ID NO:" identifier for each of the contig polynucleotide sequences disclosed in Table 1A. The fifth column, "ORF (From-To)", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence "SEQ ID NO:X" that delineate the preferred open reading frame (ORF) shown in the sequence listing and referenced in Table 1A, column 6, as SEQ ID NO:Y. Where the nucleotide position number "To" is lower than the nucleotide position number "From", the preferred ORF is the reverse complement of the referenced polynucleotide sequence.

[39] The sixth column in Table 1A provides the corresponding SEQ ID NO:Y for the polypeptide sequence encoded by the preferred ORF delineated in column 5. In one embodiment, the invention provides an amino acid sequence comprising, or alternatively consisting of, a polypeptide encoded by the portion of SEQ ID NO:X delineated by "ORF (From-To)". Also provided are polynucleotides encoding such amino acid sequences and the complementary strand thereto.

[40] Column 7 in Table 1A lists residues comprising epitopes contained in the polypeptides encoded by the preferred ORF (SEQ ID NO:Y), as predicted using the algorithm of Jameson and Wolf, (1988) *Comp. Appl. Biosci.* 4:181-186. The Jameson-Wolf antigenic analysis was performed using the computer program PROTEAN (Version 3.11 for the Power MacIntosh, DNASTAR, Inc., 1228 South Park Street Madison, WI). In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, at least one, two, three, four, five or more of the predicted epitopes as described in Table 1A. It will be appreciated that depending on the analytical criteria used to predict antigenic determinants, the exact address of the determinant may vary slightly.



[41] Column 8 in Table 1A provides an expression profile and library code: count for each of the contig sequences (SEQ ID NO:X) disclosed in Table 1A, which can routinely be combined with the information provided in Table 4 and used to determine the tissues, cells, and/or cell line libraries which predominantly express the polynucleotides of the invention. The first number in column 8 (preceding the colon), represents the tissue/cell source identifier code corresponding to the code and description provided in Table 4. For those identifier codes in which the first two letters are not "AR", the second number in column 8 (following the colon) represents the number of times a sequence corresponding to the reference polynucleotide sequence was identified in the tissue/cell source. Those tissue/cell source identifier codes in which the first two letters are "AR" designate information generated using DNA array technology. Utilizing this technology, cDNAs were amplified by PCR and then transferred, in duplicate, onto the array. Gene expression was assayed through hybridization of first strand cDNA probes to the DNA array. cDNA probes were generated from total RNA extracted from a variety of different tissues and cell lines. Probe synthesis was performed in the presence of <sup>33</sup>P dCTP, using oligo(dT) to prime reverse transcription. After hybridization, high stringency washing conditions were employed to remove non-specific hybrids from the array. The remaining signal, emanating from each gene target, was measured using a Phosphorimager. Gene expression was reported as Phosphor Stimulating Luminescence (PSL) which reflects the level of phosphor signal generated from the probe hybridized to each of the gene targets represented on the array. A local background signal subtraction was performed before the total signal generated from each array was used to normalize gene expression between the different hybridizations. The value presented after "[array code]:" represents the mean of the duplicate values, following background subtraction and probe normalization. One of skill in the art could routinely use this information to identify normal and/or diseased tissue(s) which show a predominant expression pattern of the corresponding polynucleotide of the invention or to identify polynucleotides which show predominant and/or specific tissue and/or cell expression.

[42] Column 9 in Table 1A provides a chromosomal map location for certain polynucleotides of the invention. Chromosomal location was determined by finding exact matches to EST and cDNA sequences contained in the NCBI (National Center for Biotechnology Information) UniGene database. Each sequence in the UniGene database is assigned to a "cluster"; all of the ESTs, cDNAs, and STSs in a cluster are believed to be derived from a single gene. Chromosomal mapping data is often available for one or more

sequence(s) in a UniGene cluster; this data (if consistent) is then applied to the cluster as a whole. Thus, it is possible to infer the chromosomal location of a new polynucleotide sequence by determining its identity with a mapped UniGene cluster.

[43] A modified version of the computer program BLASTN (Altschul et al., J. Mol. Biol. 215:403-410 (1990); and Gish and States, Nat. Genet. 3:266-272 (1993)) was used to search the UniGene database for EST or cDNA sequences that contain exact or near-exact matches to a polynucleotide sequence of the invention (the 'Query'). A sequence from the UniGene database (the 'Subject') was said to be an exact match if it contained a segment of 50 nucleotides in length such that 48 of those nucleotides were in the same order as found in the Query sequence. If all of the matches that met this criteria were in the same UniGene cluster, and mapping data was available for this cluster, it is indicated in Table 1A under the heading "Cytologic Band". Where a cluster had been further localized to a distinct cytologic band, that band is disclosed; where no banding information was available, but the gene had been localized to a single chromosome, the chromosome is disclosed.

[44] Once a presumptive chromosomal location was determined for a polynucleotide of the invention, an associated disease locus was identified by comparison with a database of diseases which have been experimentally associated with genetic loci. The database used was the Morbid Map, derived from OMIM™ (*supra*). If the putative chromosomal location of a polynucleotide of the invention (Query sequence) was associated with a disease in the Morbid Map database, an OMIM reference identification number was noted in column 10, Table 1A, labelled "OMIM Disease Reference(s)". Table 5 is a key to the OMIM reference identification numbers (column 1), and provides a description of the associated disease in Column 2.



**TABLE 1B**

Clone ID NO:Z	SEQ ID NO:X	CONTIG ID:	BAC ID: A	SEQ ID NO:B	EXON From-To
HMSKF13	12	708207	AC023891	339	1-32 159-474 659-1496 2796-2957 3160-3603 5493-5676 8391-8506 8716-8880 8891-9116 9977-10703 11326-12477
HMSKF13	12	708207	AC023891	340	1-169
HLHCT68	13	764745	AC010344	341	1-121 2985-3815 4282-4423
HLHCT68	13	764745	AC008496	342	1-96 2321-2645 5406-5532 5545-5688 6055-6205 9065-9895 10362-10503
HLHCT68	13	764745	AC010344	343	1-144
HLHCT68	13	764745	AC010344	344	1-2396
HLHCT68	13	764745	AC008496	345	1-1684
HMWDR50	19	667595	AB014080	346	1-748 763-1070 1455-2783 2926-4756
HMWDR50	19	667595	AC006139	347	1-748 763-1070 1455-2783 2926-4756
HMWDR50	19	667595	AB014080	348	1-276 1137-2218 3982-4096
HMWDR50	19	667595	AC006139	349	1-115
HUFAK35	25	636241	AC004172	350	1-92

					195-494 721-1360 1581-1892
HUFAK35	25	636241	AC004204	351	1-1285 1392-3372
HUFAK35	25	636241	AC004182	352	1-2744 2917-3357
HUFAK35	25	636241	AC018433	353	1-2744 2917-3357
HUFAK35	25	636241	AC004204	354	1-351
HWBAO18	30	751125	AL136222	355	1-35 90-146 603-976 1504-1816 1908-2118 2389-2496 3139-4163 5195-5455 5670-5784 5971-6356 6876-7025 7363-7661
HWBAO18	30	751125	AL109947	356	1-35 90-146 603-976 1504-1816 1908-2118 2389-2496 3139-4163 5195-5455 5670-5784 5971-6356 6875-7024 7362-8082 8097-9620 9776-9985 10108-10621 10759-10899 10954-11030 11405-11696
HWBAO18	30	751125	AL359711	357	1-35

					90-146 603-976 1504-1816 1908-2118 2389-2496 3139-4163 5195-5455 5670-5784 5971-6356 6875-7024 7362-8082 8097-9620 9776-9985 10108-10621 10759-10899 10954-11030 11405-11696
HWBAO18	30	751125	AL136222	358	1-532
HWBAO18	30	751125	AL109947	359	1-479 502-655 841-948 1038-1393 1624-1713 1856-1951 2057-2373 2467-2567 2696-3160
HWBAO18	30	751125	AL359711	360	1-479 502-655 841-948 1038-1393 1624-1713 1856-1951 2057-2373 2467-2567 2696-3160
HWBAO18	30	751125	AL109947	361	1-532
HWBAO18	30	751125	AL359711	362	1-532
HGBDG55	35	815858	AL360268	363	1-201 2570-2699 2786-2870

					3478-4132
HE8PY29	45	887862	AC009948	364	1-385 1363-1519 3205-3305 5439-5548 7982-8455 8792-8926 10682-10771 12645-14919
HE8PY29	45	887862	AC009948	365	1-439
HE8PY29	45	887862	AC009948	366	1-569
HMKCH92	47	910936	AC026206	367	1-52 416-535 1184-1340 1502-1651 4581-4649 10517-10753 10870-10987 13190-13220
HMKCH92	47	910936	AC034192	368	1-52 416-535 1184-1338 1500-1651 4583-4659 10526-10754 10871-10957
HMKCH92	47	910936	AC022381	369	1-52 416-535 1184-1340 1502-1651 4583-4651 10520-10756 10873-10990 13187-13217
HMKCH92	47	910936	AC026206	370	1-107
HMKCH92	47	910936	AC022381	371	1-107
HSOBC04	56	927280	AC012192	372	1-892 1064-1588 1828-2485 2619-2673 2847-3001



					3025-3053 3060-3223 3526-3729 3873-5129 6990-7582
HHFOC79	60	935406	AC008745	373	1-707
HBGMG39	71	971414	AL390719	374	1-1344 1786-2894
HMTAV95	74	614936	AL137000	375	1-47 321-642 2386-2508 3316-3493 4104-4572 6015-6340 6520-6573
HMTAV95	74	614936	AL137000	376	1-539
HMTAV95	74	614936	AL137000	377	1-510
HCQCI06	86	915000	AC068763	378	1-590 819-1083
HCQCI06	86	915000	AC069223	379	1-362
HCQCI06	86	915000	AC068763	380	1-593
HE8UT58	100	973153	AC032004	381	1-120
HBGQN46	110	945370	AF038458	382	1-630 1311-1416 2481-4022 4952-5252 6370-6479 7623-8269
HLTEH39	116	943641	AC004204	383	1-1285 1392-3372
HLTEH39	116	943641	AC004204	384	1-351

[45] Table 1B summarizes additional polynucleotides encompassed by the invention (including cDNA clones related to the sequences (Clone ID NO:Z), contig sequences (contig identifier (Contig ID:) contig nucleotide sequence identifiers (SEQ ID NO:X)), and genomic sequences (SEQ ID NO:B). The first column provides a unique clone identifier, "Clone ID NO:Z", for a cDNA clone related to each contig sequence. The second column provides the sequence identifier, "SEQ ID NO:X", for each contig sequence. The third column provides a unique contig identifier, "Contig ID:" for each contig sequence. The fourth column, provides a BAC identifier "BAC ID NO:A" for the BAC clone referenced in the corresponding row of the table. The fifth column provides the nucleotide sequence identifier, "SEQ ID NO:B" for a fragment of the BAC clone identified in column four of the corresponding row of the table. The sixth column, "Exon From-To", provides the location (i.e., nucleotide position numbers) within the polynucleotide sequence of SEQ ID NO:B which delineate certain polynucleotides of the invention that are also exemplary members of polynucleotide sequences that encode polypeptides of the invention (e.g., polypeptides containing amino acid sequences encoded by the polynucleotide sequences delineated in column six, and fragments and variants thereof).

TABLE 2

Clone ID NO:Z	Contig ID:	SEQ ID NO:X	Analysis Method	PFam/NR Description	PFam/NR Accession Number	Score/ Percent Identity	NT From	NT To
HTTEK47	573649	11	HMMER 1.8 blastx.2	PFAM: EF hand  DJ534K7.2 (novel protein).	PF00036  sp CAB92087 CAB9 2087	10.82  100% 65% 52%	224	289 301 378 410
HMSKF13	708207	12	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	10.64	98	193
HLHCT68	764745	13	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	16.02	65	136
HKAFF33	974200	14	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	58.44	56	127
HTLAQ18	811792	118	HMMER 1.8 blastx.2	PFAM: Fibronectin type III domain hypothetical protein DKFZp434H2215.1 - human	PF00041  pir T42656 T42656	31.34  96%	56	331 457
HLYAW15	974192	119	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	330.87	87	488
HMCIFY36	943638	17	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	164.66	1	216



HMSPF61	861249	120	HMMER 2.1.1	PFAM: Phytoene dehydrogenase related enzyme	PF02032	53.7	424	573
HMWDR50	667595	19	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	69.78	347	535
HSSJM44	871067	121	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	8.5	694	936
HPTXN38	974195	21	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	161.95	15	350
HRKPA05	974201	22	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	32.12	36	77
HTGFY58	974198	23	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	151.01	23	217
HTXJB01	542372	122	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	54.86	54	398
HUFAK35	636241	25	HMMER 2.1.1	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	69.9	28	120
HWHKC91	974191	26	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1	PF00129	116.47	75	218



HTSFJ40	1172826	27	blastx.14	and 2 similar to hypothetical proteins [Bacillus subtilis]	gi 2633977 emb CAB 13478.1	39% 37% 31%	105 426 321	311 545 377
HTSFJ40	722406	123	HMMER 2.1.1	PFAM: GTPase of unknown function	PF01926	37.5	96	356
HEONO59	741361	28	HMMER 2.1.1 blastx.2	PFAM: Fibronectin type III domain HOST CELL FACTOR 2.	PF00041 sp Q9Y5Z7 Q9Y5Z7	39.4 99% 74% 97%	508 331 29 707	582 702 253 847
HEMBZ62	1078797	29	blastx.14	(AJ235273) POSSIBLE THIOPHENE AND FURAN OXIDATION PROTEIN THDF (thdF) [Rickettsia prowazekii]	gi 3861288 emb CAA: 15187.1	39% 30% 37%	4 643 298	297 849 402
HEMBZ62	742551	124	HMMER 2.1.1	PFAM: GTPase of unknown function	PF01926	42.4	23	175
HWBAO18	751125	30	HMMER 2.1.1 blastx.2	PFAM: FAD binding domain CG11685 PROTEIN.	PF01494 sp Q9VH40 Q9VH40	25.1 53%	313 196	396 396
HTLEN77	1147024	31	blastx.14	(AF081671) VU91D calmodulin [synthetic construct]	gi 3800851 gb AAC6 8892.1	43%	233	385
HTLEN77	772363	125	HMMER 1.8 blastx.2	PFAM: EF hand CALTRACTIN (CENTRIN).	PF00036 sp P53441 CATR_N AEGR	26.93 30%	294 111	380 374
HTADZ74	1172825	32	blastx.14	(AF077346) interleukin- 18 receptor accessory protein-like [Homo]	gi 3851060 gb AAC7 2196.1	90%	19	897

HTADZ74	811489	126	HMMER 2.1.1	sapiens] PFAM: TIR domain	PF01582	53.1	305	538
HELHB88	811935	127	HMMER 1.8	PFAM: EF hand	PF00036	12.8	247	330
HE9TD31	815845	34	blastx.2 HMMER 1.8	INTERSECTIN LONG ISOFORM.	sp Q9UNK2 Q9UNK 2	84% 46% 100% 30%	139 145 78 361	567 375 146 495
HGBDG55	815858	35	HMMER 1.8	PFAM: EF hand	PF00036	17.53	519	605
HOUHL51	815891	128	blastx.2 HMMER 2.1.1	Intersectin 2 short isoform.	sp AAF59904 AAF59 904	81% 40%	3 378	626 626
HEOPP67	827630	37	HMMER 2.1.1	PFAM: EF hand	PF00036	17.24	302	385
HKAOV71	827679	38	blastx.2 HMMER 2.1.1	Calcium-binding transporter (Fragment).	sp AAF28888 AAF28 888	61% 64% 37%	209 381 284	388 530 388
HFUJC31	828148	39	HMMER 1.8	PFAM: EF hand	PF00036	29.3	429	506
			blastx.2 HMMER 2.1.1	CENTRIN, PUTATIVE.	sp Q9U5I9 Q9U5I9	26%	48	506
			blastx.2 HMMER 2.1.1	PFAM: EF hand	PF00036	35	233	316
			blastx.2	NADPH thyroid oxidase 2.	sp AAF73922 AAF73 922	98%	56	433
			HMMER 2.1.1	PFAM: EF hand	PF00036	50.7	220	300
			blastx.2	Calcium-binding transporter (Fragment).	sp AAF28888 AAF28 888	88% 93%	61 711	753 755
			HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	22.67	138	404



HDQID90	831976	40	HMMER 1.8 blastx.2	PFAM: EF hand  Intersectin 2.	PF00036  sp AAF63600 AAF63 600	10.08	413	496
HKACD80	837698	129	HMMER 2.1.1 blastx.2	PFAM: Glycosyl hydrolase family 47  CDNA FLJ10783 FIS, CLONE NT2RP4000417, WEAKLY SIMILAR TO 1	PF01532  sp BAA91806 BAA9 1806	125.1  90% 49% 71% 65% 63%	198  165 511 508 624 605	521  521 687 570 683 637
HTEED80	849075	42	HMMER 1.8 blastx.2	PFAM: Fibronectin type III domain  CDNA FLJ10688 FIS, CLONE NT2RP3000320, HIGHLY SIMILAR TO 1 1	PF00041  sp BAA91751 BAA9 1751	12.84  99% 80%	521  254 1	808  850 267
HE8TI39	849161	130	HMMER 1.8 blastx.2	PFAM: EF hand  CDNA FLJ11040 FIS, CLONE PLACE1004388.	PF00036  sp BAA91969 BAA9 1969	12.66  98% 64% 63%	9  3 299 627	86  371 685 719
HSDJH12	1163916	44	blastx.14	(AK002163) unnamed protein product [Homo sapiens]	gi 7023874 dbj BAA9 2116.1	99%	60	530
HSDJH12	876344	131	HMMER 2.1.1	PFAM: GTPase of unknown function	PF01926	115.7	207	572
HE8PY29	887862	45	HMMER 1.8 blastx.2	PFAM: EF hand  FK506-BINDING PROTEIN.	PF00036  sp Q9Y6B0 Q9Y6B0	13.65  100%	191  2	250  277







HMSOL52	921126	52	HMMER	PFAM: EF hand	PF00036	32%	1282	1374
			1.8				1309	1407
			blastx.2				1430	1540
HHGAE47	922194	53	HMMER	CG11041 PROTEIN. PFAM: EF hand	sp Q9V8Z6 Q9V8Z6 PF00036	45%	102	464
			1.8				171	257
			blastx.2					
HMCGL45	922195	54	HMMER	calmodulin [validated] - human PFAM: EF hand	pir S48728 MCHU PF00036	48%	310	576
			2.1.1				138	260
			blastx.2				460	546
HEOQN14	923752	55	HMMER	CALMODULIN. PFAM: GTPase of unknown function	sp Q9U6D3 Q9U6D3 PF01926	45%	460	867
			2.1.1				927	562
			blastx.14					
HSOBC04	927280	56	HMMER	(AC002510) unknown protein [Arabidopsis thaliana] PFAM: EF hand	gi 2618702 gb AAB8 4349.1  PF00036	54%	951	787
			2.1.1				278	346
			blastx.2					
HTXKL86	1212283	57	HMMER	hypothetical protein DKFZp586I0821.1 - human (fragment) CG17141 PROTEIN.	pir T42709 T42709 sp Q9VCU5 Q9VCU 5	88%	41	388
			2.1.1				448	885
			blastx.14				208	324
HTXKL86	928194	135	HMMER	PFAM: GTPase of unknown function similar to hypothetical	PF01926 gi 2633977 emb CAB	49%	10	636
			2.1.1				325	405
			blastx.14				985	1065
						42%	418	459
						133.3		
						37%	4	219



				proteins [Bacillus subtilis]	13478.1]			33%	493	690
HUJCT05	1125408	58	blastx.14	(AF155116) NY-REN-60 antigen [Homo sapiens]	gi 5360127 gb AAD42882.1 AF155116.1			100%	380	117
HUJCT05	929264	136	HMMER 1.8	PFAM: EF hand	PF00036			11.52	359	433
			blastx.2	CG8334 PROTEIN (FRAGMENT).	sp Q9VW49 Q9VW49			59%	56	499
HBGMR22	1171965	59	blastx.14	MhpA [Escherichia coli]	gi 1665746 dbj BAA13052.1			99%	326	811
HBGMR22	933922	137	HMMER 2.1.1	PFAM: FAD binding domain	PF01494			60.3	360	545
			blastx.2	probable monooxygenase (EC 1.14.13.-) mphA - Escherichia coli	pir C64762 C64762			98%	309	542
HHFOC79	935406	60	HMMER 1.8	PFAM: EF hand	PF00036			92%	545	583
			blastx.2	EH domain containing 2.	sp AAF40470 AAF40470			13.96	186	263
HMTBB17	950884	138	HMMER 1.8	PFAM: EF hand	PF00036			98%	54	248
			blastx.2	CDNA FLJ10466 FIS, CLONE NT2RP1001665.	sp BAA91628 BAA91628			15.74	285	202
HKGDE58	945039	139	blastx.2	CDNA FLJ10466 FIS, CLONE NT2RP1001665.	sp BAA91628 BAA91628			100%	513	100
								86%	17	835
								30%	281	691
								55%	697	825
								36%	690	914
								35%	32	208
HKGDE58	950885	140	HMMER	PFAM: EF hand	PF00036			15.98	304	221





HHEFL55	957539	66	HMMER 2.1.1	this gene PFAM: Divalent cation transporter	PF01769	41.7	419	610
HWLEY40	1172021	67	blastx.14	similar to hypothetical proteins [Bacillus subtilis]	gj 2633977 emb CAB 13478.1	43% 30% 54%	183 696 537	422 929 608
HWLEY40	957875	144	HMMER 2.1.1	PFAM: GTPase of unknown function	PF01926	103.9	192	632
			blastx.14	(AC002510) unknown protein [Arabidopsis thaliana]	gj 2618702 gb AAB8 4349.1	54% 50% 70%	1209 168 516	1373 347 575
HHAWC08	957942	145	HMMER 1.8	PFAM: IMP dehydrogenase / GMP reductase	PF00478	231.99	361	978
			blastx.2	Guanosine monophosphate reductase isolog.	sp BAA93080 BAA9 3080	100% 100%	334 975	975 1376
HCEHD66	959160	69	HMMER 2.1.1	PFAM: EF hand	PF00036	64.2	311	397
			blastx.2	Neuronal calcium sensor- 1.	sp AAD01642 AAD0 1642	100%	14	583
HMSGF27	962420	146	HMMER 2.1.1	PFAM: Glycosyl hydrolase family 47	PF01532	38.1	198	323
			blastx.2	CDNA FLJ10783 FIS, CLONE NT2RP4000417, WEAKLY SIMILAR TO	sp BAA91806 BAA9 1806	90% 34%	204 76	332 204

HBGMG39	971414	71	HMMER 1.8	1	PFAM: EF hand	PF00036	10.69	61	141
									blastx.2
HTTCT34	973210	147	HMMER 2.1.1	PFAM: Divalent cation transporter	PF01769	46.7	93	251	
			blastx.2						(AK000480) unnamed protein product [Homo sapiens]
HAWAM69	943104	73	blastx.2	SPARC-RELATED PROTEIN.	sp Q9WVN9 Q9WVN9	51%	31	261	
			HMMER 1.8						PFAM: EF hand
HAWAM69	973465	148	blastx.14	(AF070470) SPARC-related protein [Mus musculus]	gi 5305327 gb AAD41590.1 AF070470_1	62%	133	5	
			HMMER 1.8						PFAM: Fibronectin type III domain
HMTAV95	614936	74	blastx.2	CG4668 PROTEIN.	sp Q9VJJ8 Q9VJJ8	37%	6	281	
			HMMER 1.8						protein with the immunological activity of human 1
HSXCB49	1172424	75	blastx.14	PFAM: Interferon alpha/beta domain	PF00143	24.1	447	373	
			HMMER 2.1.1						IFN-omega1/alpha2(Bg1II) [synthetic construct]
HSXCB49	800501	149	blastx.14	IFN-omega1/alpha2(Bg1II) [synthetic construct]	gi 490347 emb CAA00297.1	55%	65	145	
			HMMER 2.1.1						IFN-omega1/alpha2(Bg1II) [synthetic construct]
HSXCB49	909820	150	blastx.14	IFN-omega1/alpha2(Bg1II) [synthetic construct]	gi 490347 emb CAA00297.1	34%	153	230	
			HMMER 2.1.1						IFN-omega1/alpha2(Bg1II) [synthetic construct]



HTEON29	1126522	76	blastx.14	(AB021866) CIB [Homo sapiens]	gi 4092850 dbj BAA36281.1	76% 41%	360 193	398 243
HTEON29	815852	151	HMMER 1.8 blastx.2	PFAM: EF hand CALCIUM-AND INTEGRIN-BINDING PROTEIN CIB.	PF00036 sp Q9R010 Q9R010	22.29 41%	266 2	349 496
HHFGP83	828162	152	HMMER 1.8 blastx.2	PFAM: Fibronectin type III domain CDO protein - human	PF00041 pir T03097 T03097	34.53 68% 55%	68 68 258	271 265 317
HTEKS20	1123458	78	blastx.14	calcineurin [Bos taurus]	gj 312969 emb CAA50659.1	77%	1018	509
HTEKS20	846714	153	HMMER 2.1.1 blastx.2	PFAM: EF hand calcineurin regulatory chain - human	PF00036 pir A33391 A33391	84.7 77%	453 60	539 569
HCHAT01	867209	154	HMMER 1.8 blastx.2	PFAM: EF hand AD 3 (FRAGMENT).	PF00036 sp Q9UQ32 Q9UQ32	24.01 47% 72% 57% 79%	1227 795 14 472 375	1304 1409 367 783 476
HAPNZ77	1171962	80	blastx.14	(AF051152) Toll/interleukin-1 receptor-like protein 4 [Homo sapiens]	gj 3132528 gb AAC34377.1	46% 33% 29%	393 576 279	599 701 380

HAPNZ77	887072	155	HMMER 2.1.1	PFAM: TIR domain	PF01582	31.9	292	483					
HSIAO78	889498	156	HMMER 1.8	PFAM: EF hand	PF00036	19.91	389	463					
			blastx.2	HYPOTHETICAL 22.5 KDA PROTEIN.					97%	38	622		
HWBEG18	909798	82	HMMER 2.1.1	PFAM: EF hand	PF00036	33.3	505	591					
			blastx.2	RAS ACTIVATOR RASGRP.					55%	103	684		
HFCBB56	1204322	83	blastx.14	inositol 1,4,5- trisphosphate-binding protein, 130K - rat	pir S62358 S62358	44%	269	376					
									428	601			
									587	733			
HFCBB56	910073	157	HMMER 1.8	PFAM: EF hand	PF00036	23.95	431	514					
			blastx.2	1-phosphatidylinositol- 4,5-bisphosphate phosphodiesterase 1					36%	275	565		
HEMCL65	910900	84	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	22.41	93	278					
			blastx.2	ROUNDABOUT 1.					41%	9	311		
HMAMB94	910909	158	HMMER 2.1.1	PFAM: Fibronectin type III domain	PF00041	73.7	234	497					
									blastx.2	CG4668 PROTEIN.	36%	45	551
									3	638			
HCQCI06	915000	86	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	24.42	6	191					
									54	557			
						29%	96	575					



				blastx.2	hypothetical protein DKFZp586L2024.1 - human (fragment)	pir T17344 T17344	99% 100%	3 593	596 646
HWLFG75	1227642	87		blastx.14	DJ63M2.4 (novel protein).	sp CAC08483 CAC08483	83% 92% 100%	457 847 1125	846 1059 1148
HWLFG75	916563	159		HMMER 2.1.1	PFAM: EF hand	PF00036	24.1	187	273
HBODA38	923456	88		blastx.2	DJ63M2.4 (novel protein).	sp CAC08483 CAC08483	89% 75% 100%	720 457 1123	1058 717 1146
HCYBK19	1225324	89		HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	31.21	418	648
HCYBK19	925494	160		blastx.2	Stretch response protein 553 (Fragment).	sp CAC08495 CAC08495	90%	853	1470
HCYBK19	925494	160		blastx.14	hypothetical protein T10H4.4 - Caenorhabditis elegans	pir T24812 T24812	32% 37% 26%	1744 1951 1477	1526 1766 1343
HWNCY05	1223031	90		HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	26.97	368	658
HWNCY05	928789	161		blastx.2	hypothetical protein M01B2.10 - Caenorhabditis elegans	pir T23642 T23642	32%	596	1336
HTXNN68	1143300	91		blastx.14	Containing ATP/GTP-binding site motif A(P-loop): 1 alpha-mannosidase(P1:B54407)	sp Q13586 Q13586	66%	1190	237
				HMMER 1.8	PFAM: EF hand	PF00036	12.55	18	101
				blastx.2	GOK.	sp Q13586 Q13586	60%	6	1292
				blastx.14	GOK.	sp Q13586 Q13586	100% 96% 29%	516 1 304	1169 522 396

HTXNN68	933670	162	HMMER 2.1.1 blastx.2	[Homo sapiens] PFAM: Glycosyl- hydrolase family 47	PF01532	540.8	1	906	
								hypothetical protein C47E12.3 - Caenorhabditis elegans	pir T20009 T20009
HWWFW06	933671	92	HMMER 2.1.1 blastx.2	PFAM: Glycosyl hydrolase family 47	PF01532	159.3	78	320	
								hypothetical protein C47E12.3 - Caenorhabditis elegans	pir T20009 T20009
HOSDR06	1229558	93	blastx.14	hypothetical protein F14L2.150 - Arabidopsis thaliana	pir T48940 T48940	74%	638	228	
							40%	1808	1359
							56%	1112	921
							44%	1325	1095
							61%	2026	1901
							51%	752	666
							48%	809	717
							62%	224	177
21%	929	738							
40%	764	699							
HOSDR06	937599	163	HMMER 1.8 blastx.14	PFAM: Peptidyl-prolyl cis-trans isomerases	PF00160	216.99	808	1260	
								The ha1539 protein is related to cyclophilin. [Homo sapiens]	gi 559713 dbj BAA07 555.1
HNFHW14	939763	94	HMMER 2.1.1 blastx.2	PFAM: Latrophilin/CL-1- like GPS domain (AF166382) serpentine receptor [Mus musculus]	PF01825	35.1	44	196	
								PFAM: Fibronectin type III domain	gb AAF00617.1 AF1 66382.1
HSDHB12	941973	95	HMMER 2.1.1	PFAM: Fibronectin type III domain	PF00041	110.6	156	416	



HSDHB12	969094	164	blastx.2	165K protein, skeletal muscle - human	pir S43529 S43529	49%	15	635
			HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	14.26	15	536
			blastx.14	165kD protein [Homo sapiens]	gi 407097 emb CAA48832.1	48%	15	443
HSDHB12	969097	165	HMMER 2.1.1	PFAM: Fibronectin type III domain	PF00041	110.6	691	446
			blastx.14	165kD protein [Homo sapiens]	gi 407097 emb CAA48832.1	49%	754	446
						34%	691	536
						32%	691	419
						30%	592	404
						50%	508	401
						50%	691	596
						78%	206	165
						45%	691	620
						47%	136	68
						40%	92	27
						32%	221	147
HTTJW49	948107	96	HMMER 1.8	PFAM: EF hand	PF00036	11.98	283	348
			blastx.2	CITRIN.	sp Q9UNI7 Q9UNI7	84%	94	627
HELD74	1218982	97	blastx.14	Toll/interleukin-1 receptor 8.	sp AAF26200 AAF26200	73%	263	733
			HMMER 2.1.1	PFAM: TIR domain	PF01582	77%	830	1231
HELD74	963001	166	blastx.2	(AF113795) toll/interleukin-1 receptor 8 [Mus musculus]	gb AAF26200.1 AF113795_1	46.5	492	779
						74%	201	1223

HOEET48	963290	98	HMMER 2.1.1	PFAM: EF hand	PF00036	26	656	727
HBODE51	1188998	99	blastx.2	Reticulocabin precursor.	sp AAG09692 AAG09692	96%	47	1030
			blastx.14	aralar1 [Homo sapiens]	gi 3559910 emb CAA74834.1	93%	19	1152
						86%	1328	2050
						100%	1113	1325
						26%	1673	1831
						30%	1122	1238
						27%	1427	1663
						41%	1152	1244
HBODE51	964235	167	HMMER 1.8	PFAM: Mitochondrial carrier proteins	PF00153	235.26	995	1834
			blastx.14	aralar1 [Homo sapiens]	gi 3559910 emb CAA74834.1	93%	20	2053
HE8UT58	973153	100	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	15.44	72	191
			blastx.2	ASTROTACTIN2.	sp Q9QY74 Q9QY74	96%	3	662
HFXJ127	975381	168	HMMER 2.1.1	PFAM: Fibronectin type III domain	PF00041	22	21	110
HETHO38	552107	169	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	45.8	133	507
HTEIL07	953803	103	HMMER 1.8	PFAM: EF hand	PF00036	11.27	192	263
			blastx.2	Hypothetical 41.3 kDa protein.	sp CAB91065 CAB91065	79%	57	392
HDPTC44	553453	104	HMMER	PFAM: Class I	PF00129	138.61	130	438



HHPDE40	552112	105	1.8	HMMER 1.8	Histocompatibility antigen, domains alpha 1 and 2	PF00129	42.2	147	347
HCEP56	827671	106	HMMER 1.8	HMMER 1.8	Pfam: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00036	11.86	240	317
HHFGZ38	1117192	107	blastx.14	blastx.2	HYPOTHETICAL 27.4 KDA PROTEIN (FRAGMENT).	sp Q9UJF6 Q9UJF6	100%	186	452
HHFGZ38	785591	170	HMMER 2.1.1	blastx.14	(AK001475) unnamed protein product [Homo sapiens]	gi 7022755 dbj BAA91712.1	93%	4	1335
HAHEF22	910996	108	HMMER 2.1.1	HMMER 2.1.1	Pfam: GTPase of unknown function	PF01926	97.2	338	799
HCUEV29	816065	109	HMMER 1.8	HMMER 2.1.1	Pfam: Fibronectin type III domain	PF00041	146.8	396	656
HBGQN46	945370	110	HMMER 1.8	blastx.2	M-PROTEIN.	sp O55124 O55124	43%	3	803
							28%	3	779
							25%	90	683
							40%	396	686
							29%	306	686
							31%	3	365
							31.87	143	229
							59%	89	286
							49%	312	500
							11	171	314

HMQCE42	806815	111	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	18.32	112	153
HEQAY32	869178	171	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	12.25	736	867
HOEFI09	974194	113	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	43.51	203	439
HSDGJ23	1182294	114	blastx.14	DNA-damage- inducible protein [Escherichia coli]	gi 146611 gb AAA2406 9.1	89%	68	745

HSDGJ23	714160	172	HMMER 2.1.1	PFAM: Uncharacterized membrane protein family	PF01554	45.1	229	405
			blastx.2	DNA-damage- inducible protein f- Escherichia coli (strain K-12)	pir C65212 C65212	81% 97%	68 280	232 405
HCEOR02	921110	173	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	14.8	149	373
HLTEH39	943641	116	HMMER 1.8	PFAM: Class I Histocompatibility antigen, domains alpha 1 and 2	PF00129	132.16	2	178

HRODF07	952426	174	HMMER 1.8	PFAM: Fibronectin type III domain	PF00041	16.63	82	192
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[46] Table 2 further characterizes certain encoded polypeptides of the invention, by providing the results of comparisons to protein and protein family databases. The first column provides a unique clone identifier, "Clone ID NO:", corresponding to a cDNA clone disclosed in Table 1A. The second column provides the unique contig identifier, "Contig ID:" which allows correlation with the information in Table 1A. The third column provides the sequence identifier, "SEQ ID NO:", for the contig polynucleotide sequences. The fourth column provides the analysis method by which the homology/identity disclosed in the Table was determined. The fifth column provides a description of the PFAM/NR hit identified by each analysis. Column six provides the accession number of the PFAM/NR hit disclosed in the fifth column. Column seven, score/percent identity, provides a quality score or the percent identity, of the hit disclosed in column five. Comparisons were made between polypeptides encoded by polynucleotides of the invention and a non-redundant protein database (herein referred to as "NR"), or a database of protein families (herein referred to as "PFAM"), as described below.

[47] The NR database, which comprises the NBRF PIR database, the NCBI GenPept database, and the SIB SwissProt and TrEMBL databases, was made non-redundant using the computer program nrdb2 (Warren Gish, Washington University in Saint Louis). Each of the polynucleotides shown in Table 1A, column 3 (e.g., SEQ ID NO:X or the 'Query' sequence) was used to search against the NR database. The computer program BLASTX was used to compare a 6-frame translation of the Query sequence to the NR database (for information about the BLASTX algorithm please see Altshul et al., J. Mol. Biol. 215:403-410 (1990); and Gish and States, Nat. Genet. 3:266-272 (1993). A description of the sequence that is most similar to the Query sequence (the highest scoring 'Subject') is shown in column five of Table 2 and the database accession number for that sequence is provided in column six. The highest scoring 'Subject' is reported in Table 2 if (a) the estimated probability that the match occurred by chance alone is less than  $1.0e-07$ , and (b) the match was not to a known repetitive element. BLASTX returns alignments of short polypeptide segments of the Query and Subject sequences which share a high degree of similarity; these segments are known as High-Scoring Segment Pairs or HSPs. Table 2 reports the degree of similarity between the Query and the Subject for each HSP as a percent identity in Column 7. The percent identity is determined by dividing the number of exact matches between the two aligned sequences in the HSP, dividing by the number of Query amino acids in the HSP



and multiplying by 100. The polynucleotides of SEQ ID NO:X which encode the polypeptide sequence that generates an HSP are delineated by columns 8 and 9 of Table 2.

[48] The PFAM database, PFAM version 2.1, (Sonnhammer et al., Nucl. Acids Res., 26:320-322, 1998)) consists of a series of multiple sequence alignments; one alignment for each protein family. Each multiple sequence alignment is converted into a probability model called a Hidden Markov Model, or HMM, that represents the position-specific variation among the sequences that make up the multiple sequence alignment (see, e.g., Durbin et al., *Biological sequence analysis: probabilistic models of proteins and nucleic acids*, Cambridge University Press, 1998 for the theory of HMMs). The program HMMER version 1.8 (Sean Eddy, Washington University in Saint Louis) was used to compare the predicted protein sequence for each Query sequence (SEQ ID NO:Y in Table 1A) to each of the HMMs derived from PFAM version 2.1. A HMM derived from PFAM version 2.1 was said to be a significant match to a polypeptide of the invention if the score returned by HMMER 1.8 was greater than 0.8 times the HMMER 1.8 score obtained with the most distantly related known member of that protein family. The description of the PFAM family which shares a significant match with a polypeptide of the invention is listed in column 5 of Table 2, and the database accession number of the PFAM hit is provided in column 6. Column 7 provides the score returned by HMMER version 1.8 for the alignment. Columns 8 and 9 delineate the polynucleotides of SEQ ID NO:X which encode the polypeptide sequence which show a significant match to a PFAM protein family.

[49] As mentioned, columns 8 and 9 in Table 2, "NT From" and "NT To", delineate the polynucleotides of "SEQ ID NO:X" that encode a polypeptide having a significant match to the PFAM/NR database as disclosed in the fifth column. In one embodiment, the invention provides a protein comprising, or alternatively consisting of, a polypeptide encoded by the polynucleotides of SEQ ID NO:X delineated in columns 8 and 9 of Table 2. Also provided are polynucleotides encoding such proteins, and the complementary strand thereto.

[50] The nucleotide sequence SEQ ID NO:X and the translated SEQ ID NO:Y are sufficiently accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, the nucleotide sequences of SEQ ID NO:X are useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in Clone ID NO:Z. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling



immediate applications in chromosome mapping, linkage analysis, tissue identification and/or typing, and a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used to generate antibodies which bind specifically to these polypeptides, or fragments thereof, and/or to the polypeptides encoded by the cDNA clones identified in, for example, Table 1A.

[51] Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

[52] Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X, and a predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing cDNA Clone ID NO:Z (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575; deposited with the ATCC on January 5, 2001, and having depositor reference numbers TS-1, TS-2, AC-1, and AC-2; and/or as set forth, for example, in Table 1A, 6 and 7). The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. Further, techniques known in the art can be used to verify the nucleotide sequences of SEQ ID NO:X.

[53] The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

#### ***RACE Protocol For Recovery of Full-Length Genes***

[54] Partial cDNA clones can be made full-length by utilizing the rapid amplification of cDNA ends (RACE) procedure described in Frohman, M.A., et al., Proc. Nat'l. Acad.



Sci. USA, 85:8998-9002 (1988). A cDNA clone missing either the 5' or 3' end can be reconstructed to include the absent base pairs extending to the translational start or stop codon, respectively. In some cases, cDNAs are missing the start codon of translation, therefore. The following briefly describes a modification of this original 5' RACE procedure. Poly A<sup>+</sup> or total RNA is reverse transcribed with Superscript II (Gibco/BRL) and an antisense or complementary primer specific to the cDNA sequence. The primer is removed from the reaction with a Microcon Concentrator (Amicon). The first-strand cDNA is then tailed with dATP and terminal deoxynucleotide transferase (Gibco/BRL). Thus, an anchor sequence is produced which is needed for PCR amplification. The second strand is synthesized from the dA-tail in PCR buffer, Taq DNA polymerase (Perkin-Elmer Cetus), an oligo-dT primer containing three adjacent restriction sites (XhoI, Sall and ClaI) at the 5' end and a primer containing just these restriction sites. This double-stranded cDNA is PCR amplified for 40 cycles with the same primers as well as a nested cDNA-specific antisense primer. The PCR products are size-separated on an ethidium bromide-agarose gel and the region of gel containing cDNA products the predicted size of missing protein-coding DNA is removed. cDNA is purified from the agarose with the Magic PCR Prep kit (Promega), restriction digested with XhoI or Sall, and ligated to a plasmid such as pBluescript SKII (Stratagene) at XhoI and EcoRV sites. This DNA is transformed into bacteria and the plasmid clones sequenced to identify the correct protein-coding inserts. Correct 5' ends are confirmed by comparing this sequence with the putatively identified homologue and overlap with the partial cDNA clone. Similar methods known in the art and/or commercial kits are used to amplify and recover 3' ends.

[55] Several quality-controlled kits are commercially available for purchase. Similar reagents and methods to those above are supplied in kit form from Gibco/BRL for both 5' and 3' RACE for recovery of full length genes. A second kit is available from Clontech which is a modification of a related technique, SLIC (single-stranded ligation to single-stranded cDNA), developed by Dumas et al., *Nucleic Acids Res.*, 19:5227-32 (1991). The major differences in procedure are that the RNA is alkaline hydrolyzed after reverse transcription and RNA ligase is used to join a restriction site-containing anchor primer to the first-strand cDNA. This obviates the necessity for the dA-tailing reaction which results in a polyT stretch that is difficult to sequence past.

[56] An alternative to generating 5' or 3' cDNA from RNA is to use cDNA library double-stranded DNA. An asymmetric PCR-amplified antisense cDNA strand is



synthesized with an antisense cDNA-specific primer and a plasmid-anchored primer. These primers are removed and a symmetric PCR reaction is performed with a nested cDNA-specific antisense primer and the plasmid-anchored primer.

*RNA Ligase Protocol For Generating The 5' or 3' End Sequences To Obtain Full Length Genes*

[57] Once a gene of interest is identified, several methods are available for the identification of the 5' or 3' portions of the gene which may not be present in the original cDNA plasmid. These methods include, but are not limited to, filter probing, clone enrichment using specific probes and protocols similar and identical to 5' and 3' RACE. While the full length gene may be present in the library and can be identified by probing, a useful method for generating the 5' or 3' end is to use the existing sequence information from the original cDNA to generate the missing information. A method similar to 5' RACE is available for generating the missing 5' end of a desired full-length gene. (This method was published by Fromont-Racine et al., *Nucleic Acids Res.*, 21(7):1683-1684 (1993)). Briefly, a specific RNA oligonucleotide is ligated to the 5' ends of a population of RNA presumably containing full-length gene RNA transcript and a primer set containing a primer specific to the ligated RNA oligonucleotide and a primer specific to a known sequence of the gene of interest, is used to PCR amplify the 5' portion of the desired full length gene which may then be sequenced and used to generate the full length gene. This method starts with total RNA isolated from the desired source, poly A RNA may be used but is not a prerequisite for this procedure. The RNA preparation may then be treated with phosphatase if necessary to eliminate 5' phosphate groups on degraded or damaged RNA which may interfere with the later RNA ligase step. The phosphatase if used is then inactivated and the RNA is treated with tobacco acid pyrophosphatase in order to remove the cap structure present at the 5' ends of messenger RNAs. This reaction leaves a 5' phosphate group at the 5' end of the cap cleaved RNA which can then be ligated to an RNA oligonucleotide using T4 RNA ligase. This modified RNA preparation can then be used as a template for first strand cDNA synthesis using a gene specific oligonucleotide. The first strand synthesis reaction can then be used as a template for PCR amplification of the desired 5' end using a primer specific to the ligated RNA oligonucleotide and a primer specific to the known sequence of the gene of interest. The resultant product is then sequenced and analyzed to confirm that the 5' end sequence belongs to the relevant gene.



[58] The present invention also relates to vectors or plasmids which include such DNA sequences, as well as the use of the DNA sequences. The material deposited with the ATCC (deposited with the ATCC on October 5, 2000, and receiving ATCC designation numbers PTA 2574 and PTA 2575; deposited with the ATCC on January 5, 2001, and receiving ATCC designation numbers TS-1, TS-2, AC-1, and AC-2; and/or as set forth, for example, in Table 1A, Table 6, or Table 7) is a mixture of cDNA clones derived from a variety of human tissue and cloned in either a plasmid vector or a phage vector, as described, for example, in Table 7. These deposits are referred to as "the deposits" herein. The tissues from which some of the clones were derived are listed in Table 7, and the vector in which the corresponding cDNA is contained is also indicated in Table 7. The deposited material includes cDNA clones corresponding to SEQ ID NO:X described, for example, in Table 1A (Clone ID NO:Z). A clone which is isolatable from the ATCC Deposits by use of a sequence listed as SEQ ID NO:X, may include the entire coding region of a human gene or in other cases such clone may include a substantial portion of the coding region of a human gene. Furthermore, although the sequence listing may in some instances list only a portion of the DNA sequence in a clone included in the ATCC Deposits, it is well within the ability of one skilled in the art to sequence the DNA included in a clone contained in the ATCC Deposits by use of a sequence (or portion thereof) described in, for example Tables 1A or 2 by procedures hereinafter further described, and others apparent to those skilled in the art.

[59] Also provided in Table 7 is the name of the vector which contains the cDNA clone. Each vector is routinely used in the art. The following additional information is provided for convenience.

[60] Vectors Lambda Zap (U.S. Patent Nos. 5,128,256 and 5,286,636), Uni-Zap XR (U.S. Patent Nos. 5,128,256 and 5,286,636), Zap Express (U.S. Patent Nos. 5,128,256 and 5,286,636), pBluescript (pBS) (Short, J. M. et al., *Nucleic Acids Res.* 16:7583-7600 (1988); Alting-Mees, M. A. and Short, J. M., *Nucleic Acids Res.* 17:9494 (1989)) and pBK (Alting-Mees, M. A. et al., *Strategies* 5:58-61 (1992)) are commercially available from Stratagene Cloning Systems, Inc., 11011 N. Torrey Pines Road, La Jolla, CA, 92037. pBS contains an ampicillin resistance gene and pBK contains a neomycin resistance gene. Phagemid pBS may be excised from the Lambda Zap and Uni-Zap XR vectors, and phagemid pBK may be excised from the Zap Express vector. Both phagemids may be transformed into *E. coli* strain XL-1 Blue, also available from Stratagene.



[61] Vectors pSport1, pCMVSPORT 1.0, pCMVSPORT 2.0 and pCMVSPORT 3.0, were obtained from Life Technologies, Inc., P. O. Box 6009, Gaithersburg, MD 20897. All Sport vectors contain an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, also available from Life Technologies. See, for instance, Gruber, C. E., et al., *Focus* 15:59- (1993). Vector lafmid BA (Bento Soares, Columbia University, New York, NY) contains an ampicillin resistance gene and can be transformed into *E. coli* strain XL-1 Blue. Vector pCR<sup>®</sup>2.1, which is available from Invitrogen, 1600 Faraday Avenue, Carlsbad, CA 92008, contains an ampicillin resistance gene and may be transformed into *E. coli* strain DH10B, available from Life Technologies. See, for instance, Clark, J. M., *Nuc. Acids Res.* 16:9677-9686 (1988) and Mead, D. et al., *Bio/Technology* 9: (1991).

[62] The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, and/or the deposited clone (Clone ID NO:Z). The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

[63] Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X or the complement thereof, polypeptides encoded by genes corresponding to SEQ ID NO:X or the complement thereof, and/or the cDNA contained in Clone ID NO:Z, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

[64] The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

[65] The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often



advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification, such as multiple histidine residues, or an additional sequence for stability during recombinant production.

[66] The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, *Gene* 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the polypeptides of the present invention in methods which are well known in the art.

[67] The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA sequence contained in Clone ID NO:Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X or a complement thereof, a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or the polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y, a polypeptide encoded by SEQ ID NO:X, a polypeptide encoded by the cDNA contained in Clone ID NO:Z, and/or a polypeptide sequence encoded by a nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B are also encompassed by the invention. The present invention further encompasses a polynucleotide comprising, or alternatively consisting of, the complement of the nucleic acid sequence of SEQ ID NO:X, a nucleic acid sequence encoding a polypeptide encoded by the complement of the nucleic acid sequence of SEQ ID NO:X, and/or the cDNA contained in Clone ID NO:Z.

[68] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in Table 1B column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in Table 1B column 6, or any



combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[69] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated



in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[70] Further, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2), or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2), or any combination thereof. In further embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in column 6 of Table 1B which correspond to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2) and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (See Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.



[71] Moreover, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of Table 1B column 6, or any combination thereof. Additional, representative examples of polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1B column 6, or any combination thereof. In preferred embodiments, the polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the complementary strand(s) of the sequences delineated in the same row of Table 1B column 6, wherein sequentially delineated sequences in the table (i.e. corresponding to those exons located closest to each other) are directly contiguous in a 5' to 3' orientation. In further embodiments, above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated in the same row of Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[72] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1B, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.



[73] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same Clone ID NO:Z. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[74] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more of the sequences delineated in the same row of column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. In preferred embodiments, the delineated sequence(s) and polynucleotide sequence of SEQ ID NO:X correspond to the same row of column 6 of Table 1B. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[75] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[76] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent



hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[77] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[78] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides, are also encompassed by the invention.

[79] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization



conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[80] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same Clone ID NO:Z (see Table 1B, column 1) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[81] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, a polynucleotide sequence in which the 3' 10 polynucleotides of one sequence in column 6 corresponding to the same contig sequence identifier SEQ ID NO:X (see Table 1B, column 2) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[82] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 corresponding to the same row are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B is directly contiguous with the 5' 10 polynucleotides of the next



sequential exon delineated in Table 1B, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[83] Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. Accordingly, for each contig sequence (SEQ ID NO:X) listed in the fourth column of Table 1A, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 and the final nucleotide minus 15 of SEQ ID NO:X, b is an integer of 15 to the final nucleotide of SEQ ID NO:X, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:X, and where b is greater than or equal to a + 14. More specifically, preferably excluded are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a and b are integers as defined in columns 4 and 5, respectively, of Table 3. In specific embodiments, the polynucleotides of the invention do not consist of at least one, two, three, four, five, ten, or more of the specific polynucleotide sequences referenced by the Genbank Accession No. as disclosed in column 6 of Table 3 (including for example, published sequence in connection with a particular BAC clone). In further embodiments, preferably excluded from the invention are the specific polynucleotide sequence(s) contained in the clones corresponding to at least one, two, three, four, five, ten, or more of the available material having the accession numbers identified in the sixth column of this Table (including for example, the actual sequence contained in an identified BAC clone). In no way is this listing meant to encompass all of the sequences which may be excluded by the general formula, it is just a representative example. All references available through these accessions are hereby incorporated by reference in their entirety.

**TABLE 3**

Clone ID NO: Z	SEQ ID NO: X	Contig ID:	EST Disclaimer		Accession #'s
			Range of a	Range of b	
HTTEK47	11	573649	1 - 396	15 - 410	AA400005, AW205244, AW134723, and AI689951.
HMSKF13	12	708207	1 - 387	15 - 401	AA148393, AC023891, and AC023891.
HLHCT68	13	764745	1 - 425	15 - 439	R91150, H67895, AI205078, Z25012, C05212, Z30134, AA194359, AC010344, AC010344, AC010344, AC008496, and AC008496.
HKAFF33	14	974200	1 - 175	15 - 189	AA335761, T58784, AA053162, AA220207, F07425, N34268, AA535485, C16914, F11628, F00945, AA380834, AA321294, AA437332, AA132565, T27675, AA527306, H11697, H63653, W24084, AW374230, AA158146, AL035930, AA369234, AW407037, AA361916, W24054, AA977833, AI910189, AA358563, AA385962, T28025, N42582, AA336109, AA321393, AI910249, AI696864, AA305941, AW179215, H98493, AW385684, AA522541, AW062331, W44848, AA188398, AA535767, AA159383, C18543, AA053691, AA371996, AW384708, AA133506, AW404398, AI910244, AI565209, AI114563, AI910095, N24326, AA382286, H95866, H68295, AW361810, M24045, Z33459, AJ001977, L38251, M24046, D83957, X99704, D50852, D64145, X76189, U41420, Z47377, U07230, AF220291, D49820, D83030, D64146, D64151, D64152, D64147, M24097, L20091, M84386, AF115462, D83031, Z83247, X73518, X96582, Y09156, X82122, X78343, D31817, M28172, M84174, X87841, U06487, U06695, Y11843, L54059, M99388, U41386, X67818, X70856, X70857, Y18552, M21963, U60218, M24096, AJ005590, D83956, M28206, M26432, X58536, D64148, Z15144, AJ010748, M84173, D50854, AJ001975, AJ001976, AJ001973, AJ001974, AJ272049, M26429, D83029, AF118891, AJ133100, E02883, M24030, AJ238694, AJ133267, AJ251755, AP000508, AF017331, AF015557, AF038574, AF201475, AF144665, AF102689, U61274, M12679, U06835, M26712, M28160, D64149, U56246, Y10520, D84394, M11799, U50088, AF198649, Y18649, AJ131853, U56260, AF028596, U60324, M63454, M16272, M26430, U11267, M32320, D49552, AJ010749, U09853, X83394, M16273, M54883, AP000507, E01341, M12967, S39758, X03945, AR008238, AJ245869, U60423, X55711, U38976, U41833, AF215919, D89334, U81012, Y18658, AF042290, AF115461, AF117767, AJ132660, Y11229, AJ133472, AJ249725, AF061862, AF205535, AF205539, AF213682, X83003,



					AC004204, U74386, U17572, AF115460, M24036, M24035, M24034, X61710, U04244, U64801, X81363, U88407, M24048, X83005, U74387, A93993, U76397, AF017317, AF065641, AF054010, AF061868, U70581, U90241, U91331, AF102568, AF110264, AF110261, AF098266, AF176080, AF220289, I14657, Y15745, AJ010323, AJ133476, AJ249164, Y14767, Y17065, AF061858, U96787, AF019568, AF015555, AF036553, AF145761, AF145763, AF104219, AF179632, AF189726, AF108425, U05581, AF017321, X75953, L42280, U05580, M24044, L20088, D85761, Y09058, D50300, M77774, M77778, M77777, D25275, M94052, M94053, M94051, L22028, M24040, M24039, M24032, U04243, L22649, L36318, L36591, U29083, U29480, L17005, U63653, D38526, X97321, X13116, M30679, AC004182, M24038, Y08994, U36492, M28207, L42024, U38975, AJ242661, L42345, X60253, X13115, M28204, M15470, Z46810, Z49112, Z79751, U11261, U11263, U60322, U05582, M24037, X61706, AF168611, U05579, I14637, I14638, and I14642.
HTLAQ18	15	1193114	1 - 820	15 - 834	AA442624, AI382107, AW269016, AI286158, AA719238, AI001168, AI280133, AW339870, AA009701, AA932363, AI783808, AA587120, AI241143, AI266558, AI584159, AI370392, AW161202, AI499325, AI702343, AI494201, AI818728, W19236, AI491904, AI537516, AI916720, AI621341, AW059828, H89138, AA938181, AI357283, AI499581, AI817253, AI174819, AA749425, AI859644, AW020419, AI680369, AW080531, AI539260, AI273856, AI434760, AW083168, AA493923, AI801325, AL047344, AI690620, AI366959, AW058275, AW022494, AW020288, AI630474, AA769285, AW081110, AA768550, AW022542, AW020144, AA587590, AI634919, AI289791, AI360816, AA837290, AI345396, AI344935, AI656270, AW193299, AW189563, AA420722, AI312210, AI334893, AI611728, AA928539, AI208112, AI343091, AI401697, AI289436, AI865116, AI335476, AI311892, AI582871, AI336503, AI500706, AI345370, AL047152, AA888196, AI828806, AI687568, AL121270, AI538850, AL041772, AI582434, AI336565, AI440511, AI421662, N29277, AI340552, AI345471, AI954721, AI347569, AW191003, AL048499, AI961590, AA555145, AA504514, AL079910, AI050881, AI349279, AI440457, AW020381, AI538885, AI590755, AA651924, AL133054, S79832, AF022363, AL110218, AF132676, AF061836, D00174, AF205861, U87620, AF114168, Y10823, S77771, AL137292, X00861, A08456, A31057, AF111849, AF026124, I77092, A18777, AF028823, AF177401,

					AF085809, AF120268, AR038854, AR050959, D44497, AL122111, AL117583, M79462, A08910, A08911, A08909, X52128, A08907, A08908, U95739, AC004686, AC007392, AC009233, A70386, AL137523, U49908, Y18680, I18355, AL133099, I34392, AB022159, AC009501, E08516, AF200416, AF013249, AF036941, A27171, AF146568, AF022857, AF022858, AJ131955, A07588, AR012379, AL137284, AB007812, AL080162, AL080057, AL133010, AC002540, AC007172, AC002287, AC007458, S61953, AF090934, S36676, U76419, AF054988, AR059958, AL117457, AL133014, M64936, AF098162, AC004837, AC018767, AF035161, X72387, AF074604, A65336, E04233, U96683, AL080150, AF100931, A20553, AF082526, AL049300, AF113699, AR029490, D83989, AF111851, AL050277, AL133016, AL110228, Y08616, U95114, U75604, AF201468, I08319, AF169154, AF113690, AF110329, AL109672, AL133640, AF126488, AL110158, AL133062, AL133047, AL137662, AL117432, AL133565, E02221, AF108357, E06743, AC005968, AF161699, AF113689, X00474, AL137495, I32738, AL050092, AF124435, E01963, AC004399, AC003032, AC005353, AL096776, AF179633, AC005057, AP000161, AP000020, AL034374, AC005091, AL022147, AC005048, AC002416, Z94277, AC004690, AC008067, AC006222, AC008014, AL022170, AC007056, AC005291, AC007298, U66059, AF115410, AR016469, X73361, and AB026995.
HLYAW15	16	976531	1 - 383	15 - 397	AI124815, AW402317, AW402511, AW405194, F13067, AI826037, AA160317, AW408434, AW403392, AA381090, AA224068, AA381088, AL039796, AA381030, D82221, AA102697, AA263135, AW402322, AA663896, D82177, AW327936, AA336651, D82189, AA295685, AA401643, H23327, W40489, AA227277, AA151951, AL138056, AW402698, AW402264, U46382, AW401505, AW401719, C18310, T29764, AA344828, AA310808, T52219, AW408440, AW403793, AW402754, D56208, AA159230, T52124, AA295712, AA380938, AA351420, AI359260, AW403872, AA449607, AA121088, R19052, AW402402, AA075796, AA100848, AW239462, R20954, F07582, AW402383, AA348993, AA157351, AA350486, AA173111, AA313847, AW401548, AW405127, AI750810, AA381116, F05537, AA152039, AA299668, AW403070, AW402855, F06315, AW405549, AA352960, AA348075, AW403114, AW408321, AW401393, AW404182, AI365653, AW273557, AA381988, AW385684, AA378689, AW402401;



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HMCFY36	17	943638	1 - 302	15 - 316	AW408434, AW402317, C03945, AW327936, AW405194, AI696864, AW402511, AA263135, T68508, AW402322, AA663896, AA294911, AW405525, AW401505, AA352603, AW401548, AW239462, AA366365, AW402264, AW401719, AA361489, AA158146, AA147151, C18310, AA488534, AA361477, D82189, AA159413, AA158109, AI124815, AA112349, AA151951, AA160714, AA477506, AW403872, AL039796, AA372227, C19056, AA263158, AA121088, AA581164, AA385962, AW402402, AA100848, AA335761, AA151891, W24084, F11628, H11697, R34651, W24054, AA220207, N42582, AA361916, D82221, AW403392, AI359260, T75330, AA160037, D82177, T28025, X94481, L76091, AB030573, X96473, Z46808, L20090, E03438, U06697, AJ005590, E02248, M80670, E03437, Y08994, M68964, L41925, M32319, AF004370, L76931, U58110, U31334, Y13029, D50300, D50291, U75533, M19757, U14943, M28205, U03698, M95530, AJ002151, U28759, L41086, U32660, U11263, Z15143, M24037, L41214, U16309, D31816, M84380, U15639, M33573, U05581, U16298, Y15840, L31798, X84725, M24035, U70528, L36591, M84382, AF035648, AF035649, D50295, U09864, U29083, U96942, AB030574, U37325, X13116, AJ271160, L22028, L42024, U34810, U83580, M29864, AF118891, U15638, AF035647, E02885, X90391, D50290, M58636, L42282, M24075, L42345, L42146, AB032598, AF118894, AJ223282, U15640, U14756, U11261, U11267, X75953, X64366, Y08995, L11571, M24038, AJ131118, X61710, X61706, U04244, U64801, L42283, M32320, U90560, U05577, X90390, U50091, Y15841, AB032097, AB036049, AB036050, X86704, X95410, L76094, U18659, L42280, U74387, U18660, D44499, U11262, U17572, AB032094, AB032095, AB032096, AB032599, AB036051, AJ002676, X94480, L76088, L76089, L76090, L42506, AF033351, M83193, M83191, AJ238702, L07950, U05575, U03027, U03859, L11570, D25275, M94053, L09735, L22027, M24039, L11603, L19937, X61709, U04243, L36318,

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HMSPF61	18	1226544	1 - 644	15 - 658	D80195, D80193, D59927, D51423, D59619, D80210, D81030, D80391, D80240, D80253, T03269, D80227, D80196, D80219, D80043, D58283, D80188, D80022, D59889, D80366, D51799, D80038, F13647, D59275, C75259, D80045, C15076, D80378, C14014, D50995, D80134, D81026, D59467, D59787, D80949, D80168, D80212, AA285331, C14227, C14429, D50979, T11417, D80164, D58253, T11051, D80166, D59695, D59859, D80269, D80268, D80064, D59502, D80024, D57483, D59610, AW178893, D80241, D81111, D52291, C14331, AW177440, D51060, AW178775, C14389, AW369651, AA305409, AW179328, AW378532, D51079, AI905856, AW352158, D51097, AW178762, AW360834, AW177501, D80522, AW177511, D80014, D51022, AI557751, AW360811, AW378540, AA305578, AW366296, AW375405, AW378534, AW377671, D80251, AW360817, D80248, AW375406, AW179220, AW179332, AW377672, AW179023, AW178905, AA514188, AW177505, AW360841, AW352171, AW377676, AW352170, AW177731, AW178907, AW179019, AW179024, AA514186, C05695, D80133, AW178906, AW179020, AW177456, D80258, AW367967, AW179329, AW178980, AW177733, AW378528, AW178908, AW179018, AW178774, AW178914, AW378543, AW378525, D80132, D80302, AW178781, AW352174, D80439, AW178911, AW352163, D80247, AA809122, T48593, AL048680, D51103, AA033512, D80157, AW367950, AW378533, C06015, D45260, D58246, D59503, AI557774, AI525923,



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HMWDR50	19	667595	1 - 565	15 - 579	AA005245, AA021087, AA313847, W44826, AI750810, AA243092, AW408321, AW405127, AW401393, AA176192, AW405549, C17443, AA052922, AW403070, W56226, AW402424, AA129140, R27263, AA013055, W60367, AA299668, AA348993, N35264, T52117, AA381239, AA381052, AA296474, AA378689, F05537, AA853431, AW404182, AW401666, AA381988, AI214149, AI214126, AA152039, AW404586, AA058454, AA130130, N25137, AA100680, AA092258, AA158109, AA160037, R54504, M21533, AB014080, AC006139, AP000514, M16714, AJ251960, AF117228, L76290, AJ245567, Y18651, AB012686, AJ271225, AB005048, X64880, AJ223972, AB012685, AF055066, K02883, AB023056, AP000519, M20022, M30681, X00492, M31183, AF101046, Z93949, Z93776, X55710, AF148862, AJ002533, M32505, X87678, M32506, X87680, L78455, L78934, L79943, AF111103, Z55558, Z58713, AF111102, Z58696, U02976, U02977, U41837, AF004918, X03210, M18964, X03443, X01652, AB014080, AB014080, AC006139, and AC006139.
HSSJM44	20	1175100	1 - 2355	15 - 2369	AA633868, AI953254, AA858030, AI377035, AA600028, AI948432, AI347033, AI819852,



					AI953812, AI274863, AA913660, AI221391, AA402834, AI682227, AA313382, AI393729, R43673, T07940, T75200, AA402685, Z46198, H10173, T34442, AA594521, AW050919, T07941, AI150326, AA921803, AA775669, AI301221, AI394223, AI869224, Z41820, AW074819, R13072, AI424149, AA357096, AA383450, AI335517, AW302961, AI611494, AI348865, AI224202, AA368045, AW302995, and AI252073.
HPTXN38	21	974195	1 - 350	15 - 364	AW327936, AI696864, AW408434, AA263135, AW402317, AW385684, AA970332, AA294911, AW402511, AW239462, C03945, AA527306, AA190717, AA158146, AW405194, T68508, AA366365, AA663896, AW402322, AA112349, AA321294, AA361489, AA385962, AW401505, AA335761, AA352603, F00945, AW351546, AW402698, AA147151, AA305941, AW405525, AA988615, AW401548, H11697, AA243206, AW293543, AW402264, AW401719, AA159413, AA158109, C18310, AI365653, AA527504, AA581164, AA220207, W24084, AA377064, AA372227, D82189, AA304603, AA477506, N42582, R34651, AA337991, AA160714, T10924, H98493, AI124815, AA151951, F11628, W24054, AA367387, AW403872, AA263158, C04018, AA100848, AA121088, AA361916, T28025, AW407037, AW392650, AA321393, AL035930, AA126083, AI359260, D82221, AW403392, AA160037, L76091, AB030573, D50291, M19757, U14943, AJ223282, U16309, X94481, AB032598, L31798, AB032097, U11263, L20090, M24037, U75533, X96473, U16298, U32660, L76090, D50290, M24075, D50300, AF035647, L76935, AB032599, L76089, U18660, Z46808, E03438, U18659, AB036049, AB036050, X95410, X86704, L76931, AB030575, AF004370, AB032095, U06697, AJ005590, U58110, L76934, U31334, Y15841, AB032094, X99734, U11261, M80670, M68964, L41925, M32319, X94482, Y08995, X61706, U28759, AB032096, L76088, X84725, L76095, AF035649, AJ002151, X90391, L42282, Y08994, Y14205, X87268, L76094, X61710, E02248, E03437, X86703, U18790, X64366, AJ131118, L42283, L22028, L36591, AB030574, AB032093, L76933, L36979, D50693, U70528, M84382, U29083, X75953, AJ002676, X94480, AF033351, L76930, U11267, L42280, M94053, U04243, AF035648, M29864, M28205, M32320, L42024, AF056981, U34618, L76932, U29880, U32678, U18789, L42146, L41214, M24035, U90562, U64801, Z15143, M58636, U15639, M83191, U90561, U96942, AB036051, L42506, L75942,

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HRKPA05	22	974201	1 - 136	15 - 150	AA158146, H63653, AA437332, N42582, AA053162, H11697, N34268, AA977833, AA190717, AA053691, AA535767, T58784, AA133506, AA188398, W24054, W24084, F07425, AA321294, W44848, and N24326.
HTGFY58	23	974198	1 - 289	15 - 303	AW327936, AW408434, AI696864, T68508, AA294911, AW402317, AW402511, AW385684, C03945, AW239462, AW402322, AW405194, AA663896, AW385181, AA243206, AA147151, F00945, AA190717, AA321294, AW402698, AA385962, AA581164, AA159413, AW402264, AW401719, AA335761, AA361477, D82189, AI124815, AA263158, AA367387, H11697, AA361916, R34651, W24084, W24054, N42582, AA151891, F11628, T28025, D82221, AW403392, AI359260, T75330, AB032093, L76933, L36979, X87268, U16309, L31798, U28759, AF035648, AF035649, U34618, U29880, U31334, X96473, AB032598, E02885, M58636, U15640, U90566, L76930, U14756, U83580, U15638, AF035647, L75942, L76932, L76094, U18660, U11265, E02884, L04696, L04695, U30904, D50295, Z15143, U32678, X94481, L76091, X94574, X86703, Z22651, U32660, L20089, U06862, L40599, D50299, L42345, AJ002676, X94480, X99734, AF033351, AB030573, L76090, L42506, U15639, M86403, U09864, D50290, L36591, X90391,



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HTXJB01	24	1124596	1 - 987	15 - 1001	<p>AA988703, AA675914, AA303646, AA675909, AW367626, AW058625, N40329, T54177, AA352261, AA595003, AA565043, AA079556, U95729, AF021222, U95731, AF021221, AF021223, AF021224, X91625, U69978, U95730, U95732, U95733, U95734, AF021225, AF021226, AF055384, L14848, AB000878, AB000882, AP000506, U65416, AC006046, AP000507, AJ249394, AC004180, D84394, AF055385, AF055387, X92841, Y16807, Y18113, AF045598, U56944, Y16811, U56947, U56948, AF055388, Y16804, AB015600, U56942, U56943, U56945, Y16803, Y16809, AF097406, U56949, U56955, Y16801, Y16805, Y18111, Y18114, Y18116, U56941, Y16808, Y18112, Y18115, U56946, U56952, U56954, Y16810, AF097403, Y16806, Y18117, Y18118, U56940, U56950, AF097404, U56951, U56953, Y18110, AF045600, AF045597, AF045599, AF055386, AF045601, AF045596, AF045604, AJ242442, AJ242439, Y16802, AJ242438, AF045603, AF055389, AF045602, AJ242441, AJ242440, AJ242443, AF055390,</p>



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HUFAK35	25	636241	1 - 209	15 - 223	<p>AA449607, AA351420, AA295712, AW402698, AA401643, AL138056, N44225, H23327, AW385684, D56208, AW402402, AW403793, AW402754, AA151951, D82221, AW403114, AW403392, AW393618, AA380938, AW403872, AW405525, AA336651, AA160317, AW401548, AW402264, AW401719, AW401505, D82177, C18310, AW408440, AA310808, AI365653, AW402322, D82189, AW239462, AW405194, AW402511, AW402317, AW408434, AA962801, AL039796, T29764, AA263135, AW327936, AI359260, AA350486, F07582, AA381116, AA075796, AA100680, AA132653, AA083156, AA348075, AA129140, AW402855, AW402401, AA227277, AA159230, R19052, AA081491, AA143626, U46382, F06589, AA055685, W52004, R54504, AA005245, AA352534, AA358919, AA970332, F06198, AA295230, AA160070, AF039198, AJ272049, U44064, AJ001977, AJ001975, AJ001976, AJ001973, AJ001974, D83957, Z22752, AP000508, D84394, AC004204, Y14624, AF223221, AF221124, M17567, M17566, Y16411, AJ133474, AF036554, AF147701, AJ245869, AJ133100, AF105226, M16273, M16272, AF223219, AJ238694, D50710, U90558, Y15746, Y17064, Y18538, U56246, Y18552, D83956, AJ238702, AF056981, U90561, E01341, M12967, S39758, X03945, AR008238, U90563, U90564, U90565, U90566, D50693, AF017330, AF015556, Y18533, AF145466, AJ249163, U56259,</p>

					<p>Y18660, AF036552, AF062587, AF015558, U90562, AJ251755, D50709, M54883, M11799, M59865, AF019567, AF145760, AF220290, AF015554, AF104218, AF016304, AF173007, L24491, U90560, U89946, U90179, AP000507, M63454, X00495, D77998, AB005048, AJ223972, L41086, X55711, AJ005199, AF065646, I14616, U31373, AF101046, AC004182, AJ245567, AJ271225, AJ133267, AJ133475, AF105240, L76290, D64150, U89947, U90178, X03664, X03665, M16007, D50853, M84172, M99389, U60321, AF017323, U90559, J03027, Z72423, AF042289, A93992, AF181857, AF072765, AF105029, AJ251960, K02883, AF117228, AJ250917, X99704, AJ251541, AJ271626, Y14684, AF002271, AF036556, U38975, AJ242661, D83741, D64149, AC004172, AC004193, U06835, U58643, AF115462, Y10520, Z46810, D89333, U93915, AF017328, AF081275, AF017334, AF205536, AF226838, Z93949, Z93776, Z72422, Z97370, L20091, D83031, X73518, X78343, X87841, M99388, U06695, X67818, X55710, M15497, AL022723, AJ238151, AF148863, U38976, L47206, L47231, L76288, L76291, L76289, Z96924, Z72007, AF076476, Z80228, Z75172, Z49112, Z79751, D64146, D64152, D83029, AF115464, L54059, U70580, AF096631, Y18648, AJ131852, AJ007603, M22794, U67748, U67330, U55022, AF002273, AF061863, AF072767, AF056483, U52175, U88254, AF108428, AF184216, AF208430, D38526, X97321, Z83247, X76189, X82122, M28172, M24030, Y11843, U41420, L38251, X70856, AF072763, U90244, AF189013, AF102563, AF170578, U59701, AF055066, I14588, AF002275, AF034409, AF135540, M26712, M24097, AB008136, Z80227, Y15842, U80670, D49820, AB032095, AP000519, Z33459, D64147, D64151, D64148, AJ007605, U76396, AF054011, U58315, U90240, AF188886, U76394, AC018433, AC004172, AC004182, AC004204, and AC004204.</p>
HWHKC91	26	974191	1 - 419	15 - 433	<p>AA663896, AA263135, AL039796, AW401505, C18310, AW401719, AW402264, AW402317, AW402322, AW405194, AI124815, AW402511, AW403872, AW408440, AW402402, AW239462, AW408434, AA401643, AA160317, D82221, AA151951, AA310808, AW403793, D82189, AW402698, AW401548, AW402754, H23327, AA227277, AA100680, AW402383, AA548636, AA121088, AW327936, AI826037, AA224068, AA449607, AW405525, AW403392, AA102697, AA075796, AA158109, AA173111, AW385684, AA132653, AI365653,</p>



					<p> AW401393, AW408321, AW405127,  AI750810, AW403114, R20954, D82177,  AA160714, AA313847, AI359260, F13067,  W52004, T29764, T52124, AA488534,  AA381090, AA100848, AW405549, W40489,  R19052, AW402424, D56208, AW403070,  AA381088, AA058454, AA380938, T72958,  AL138056, AA083156, AA005245,  AA159413, AA381030, AA127128,  AA336651, AA352960, AI214126, AI214149,  AA152039, AA295712, N44225, AA351420,  T52219, AA350486, AA344828, AA299668,  F07582, AA378689, AA295685, AA381116,  AA381239, AA159230, AA853431,  AW404182, AW393618, F05537, AA348993,  AA157351, AA381988, W44826, AA160037,  AA296474, AA348075, AA381052,  AA352502, AA962801, AW402855, F06315,  U46382, AA160101, AW402401, AA776025,  F06589, AA358919, AW273557, AA143652,  AA055685, AW404586, AA081491, T10924,  AW403253, C19056, F06198, AA143468,  AA352603, AA361477, R54504, AA129140,  AA085102, AA160070, AA294911,  AA295230, AA916617, AA143626,  AA431065, AA102181, AA319533, R30668,  T75330, T71226, AA527306, AW009172,  AA372227, C16914, D44499, U03027,  U03859, L11603, L19937, Y13029, L22027,  D49824, D50294, L11666, U50710, AJ250917,  D44500, U06862, D50293, U70528, M84382,  L32862, X61709, M28203, D44501, U80945,  U11262, U11266, L07950, M24033, L11571,  L11570, D50296, AF016641, U36392,  AF170577, D50295, L42281, M95530,  M84385, U17572, D31816, U03698, M84380,  X81363, U11265, E02884, D50299, L04696,  U17107, U30904, U30936, L40599, U04243,  M84381, Z22651, Y09118, L41214, L04695,  M94053, Z46808, U01848, U35431, U09864,  L22649, M24039, X64454, AJ245869,  D85762, M33573, M24036, U21053, Y09058,  M24035, L36318, U64801, E03438, M94052,  M94051, L09736, M84694, M84383, U96942,  U11261, D50290, Z15143, M24075, D85761,  M77775, M24032, AF115461, Y08995,  X61710, X61706, D25275, L42345, U11267,  E02885, M58636, X13116, M30679, M24040,  U29480, U31971, M32320, L41925, Y13567,  X91749, M24034, U04245, U21052, U29057,  L41353, M32317, M19756, M84384, X75953,  M80670, E03437, Y08994, M68964, D50291,  U75533, X64366, X90391, M24038, L42283,  M32319, M19757, L17005, U88407, U14943,  L42024, L36591, AJ131118, L42282,  AF022783, M28205, AF189017, X90390,  X84725, M63454, X60253, U04244, L09735,  L22028, U29083, U11263, M24037, U90563,  U90564, U90565, X60255, X60693, M77778, </p>
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HTSFJ40	27	1172826	1 - 1080	15 - 1094	W28953, AA313257, AI401170, H19139, R54508, H10122, H08285, R59784, F08505, AA490183, AI270117, AL046409, AI284640, Z43765, AI963720, R52605, AW088846, AI431303, AI334443, AW193265, AA682912, AW303196, AI305766, AI613280, AW301350, AW419262, AA720702, AA470969, AL042853, AW327868, AA610491, AA857486, AL045053, AL044940, AL041690, AW265385, AL138455, AI350211, AL138265, AI623720, AI345654, AI110770, AW072923, AI890348, AL037683, AA468022, AW276827, AI754658, AA581903, AA483223, AW407578, AL046205, AI307608, AW238278, AI281881, AI133164, AL119691, AA101689, AI754336, AL038474, AA877817, AA577906, AL134972, AW270270, AI801482, AA551503, AI355206, AI821271, AI538852, AW274349, AI457397, AA623002, AW410400, AW408717, AA515909, AI345681, AI345675, AA680243, AA503473, AI732120, AL042420, AA908687, AW438643, AL038705, AI679782, AL048626, AI537506, AW028429, AA522942, AA523837, AI289067, AI559705, AI619997, AA584167, AW302903, AI754253, AW021207, AW304584, AI375710, AI064864, AA587256, AW406755, AW268300, AA533333, F08180, AA531372, AL120687, AW083402, F36273, AW004911, AW274346, AA631507, AW088202, AA846876, AI345518, AI688846, AA507824, AA719292, AL038785, AL119984, AA521399, AI341664, AI254615, AA446657, AI469968, AA601355, AI568678, AW193432,

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HEONO59	28	741361	1 - 848	15 - 862	W37916, AW369323, AL138197, AA292636, AA789205, AA278688, AI077497, AI670821, AW117287, AA608906, AA382777, AA724269, AA278680, AA827227, AI160796, AA600253, AI990171, AA625768, W37874, AA421286, AA292637, AA844108, AA917528, AW316905, AA768446, and AF117210.
HEMBZ62	29	1078797	1 - 1196	15 - 1210	AW138235, AW070706, R13025, AA346549, and AA317149.
HWBAO18	30	751125	1 - 383	15 - 397	AL359711, AL359711, AL359711, AL109947, AL109947, AL109947, AL136222, and AL136222.
HTLEN77	31	1147024	1 - 1190	15 - 1204	T89857, T89583, AL121270, AI349772, AI064830, AL121365, AL047042, AL045500, AL036396, AW117882, AW238730, AL119791, AI687376, AW268253, AI636456, AI349004, AI433976, AI868831, AL036274, AL047763, AI285735, AL038778, AW301409, AL135661, AI436456, AL036802, AI475371, AW103371, AI275175, AI909666, AL040243, AW071349, AI433157, AI815383, AI521012, AL036146, AI697137, AI687728, AI349645, AI635461, AI250293, AI702406, AI538716, AW195957, AI439087, AW162071, AI678302, AI568870, AI564719, AL036759, AI620284, AI340582, AL119049, AW169653, AI349933, AI866608, AI445432, AW089572, AI625079, AW274192, AI699857, AW071417, AI440426, AI590128, AL046849,



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HTADZ74	32	1172825	1 - 1283	15 - 1297	AI735624, AW192167, AI307682, AF077346, and AC007278.
HELHB88	33	1226704	1 - 3452	15 - 3466	AI671143, AI580905, AI632369, AA773823, AW370310, AA773263, AA313515, AA985166, AL121153, AI382884, AA181724, AI750406, AI469456, AA024936, AA155593, AA024853, AL120063, T78993, T78788, T82245, AA155607, AI750407, AL134372, AA670080, L25219, AA247838, AI525585, AF114487, AF114488, AF064243, AF064244, U61166, AF127798, AF132672, AF132478, AF132481, AP000311, AP000117, AP000193, AP000049, AP000116, AP000050, AP000048, AP000308, AP000115, and AW594325.
HE9TD31	34	815845	1 - 941	15 - 955	AI475682, AI439613, AA815076, AB033082, AF132480, and AF132479.
HGBDG55	35	815858	1 - 522	15 - 536	AA368408, and AL360268.



HOUHL51	36	1126480	1 - 760	15 - 774	AA431822, AI341790, AW295199, AI656610, AA037543, AW292290, AA431419, AA974280, AA815270, AA037457, AI651702, AA583011, AI208605, AI419858, AA620408, AA417333, AA417321, W28051, AA251183, AI917695, W28536, AI557751, D80258, T11417, D80064, D59627, C06015, D81026, C15076, D59467, C14331, D80164, D80014, D59787, C14227, AI535686, D81030, D59503, F13647, D80166, AI557774, C14389, D51799, AA809122, D59859, D80212, D58283, D59619, D80210, D80240, D51423, D80022, D50995, D80195, D80253, D58246, D50979, D80391, D59275, D80038, D80043, D80227, D80188, D59502, D80219, D57483, D59889, D80196, D80269, D80168, D80522, AA305578, AA514184, D80439, C14014, D80268, D80133, D80045, AA305409, D80247, D80366, D51022, D80157, D80251, D51250, H67854, Z21582, C03092, H67866, AI024754, AI525920, C14973, C05763, T02974, D59551, AI525227, AI525235, D45273, AI535961, C16955, Z33452, A84916, A62298, A62300, A82595, AR018138, AR008278, AJ132110, AR060385, AB028859, AF058696, AB002449, AR008277, AR008281, I14842, AR054175, and I79511.
HEOPP67	37	827630	1 - 436	15 - 450	AA641653, Z99396, AF181972, and AF181973.
HKAOV71	38	827679	1 - 743	15 - 757	AF123303, and AF004161.
HFIJC31	39	828148	1 - 519	15 - 533	AA885328, N79858, and AI184184.
HDQID90	40	831976	1 - 953	15 - 967	AA767219, AI809238, AI219470, AA767092, AA114887, T71487, AA464762, AA504439, Z25261, N87679, D57415, AA278335, AW300598, W46278, AA669095, D56990, D54675, AI797687, AI948608, AA909071, AW236181, AI718165, AB033082, AF132480, AF132479, and AC002350.
HKACD80	41	1206594	1 - 1937	15 - 1951	AI191318, AI978812, AA586860, AA805184; AI628509, AI582366, W73797, W73745, AI620297, AW083832, AW239293, AW386876, AI056600, AI056739, AI362766, AI494212, AI077551, AA935678, AI348675, AI358232, AA251769, AA968828, AA659758, AI891139, C06060, AA746268, AA251926, AA506524, H58621, D81244, AA291462, H58622, AW193598, R38144, R67182, AI919497, AI250032, AA604444, AI567397, AA905208, AA836253, AA551675, AW087829, AI364618, AI421662, R57498, AW080157, AW166086, AI813914, R59996, AL043152, AI680498, AI469754, AL079794, AI540179, AI554821, AI874261, AL119511, AL045413, AL119399, AL042382, AI560545, AI366900, AW262491, AW262042, AI954504, AI089970, AI677646, AI679164, AL119457, AI868204, AI431909, AI453328, AI538085, AI680221, AI056328, AI536923, AW162194, AI553926, AI567302, AI538908,



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HTEED80	42	849075	1 - 1299	15 - 1313	W87655, AA465429, AA203572, AI479983, AI540082, AA192438, AA836236, AA465358, AA829419, AA507269, AW290970, AI796504, AA904433, AA368409, AA688079, AW189971, AA601527, AA393948, F36549, W87656, AA320120, AI862710, F30605, AA196706, and AJ242978.
HE8TI39	43	1222770	1 - 2807	15 - 2821	AI681280, AA251688, W60548, Z45463, H86769, F07768, H86760, Z42543, AW339546, R15292, Z44339, H86765, H86774, H86962, AA091738, R58217, F06562, AW377760, and R21166.
HSDJH12	44	1163916	1 - 788	15 - 802	AA428452, AA134294, T83462, AI219740, AA010048, AI478566, and AI990289.
HE8PY29	45	887862	1 - 741	15 - 755	AI271550, AI753504, AA809220, AW081079, W78099, AW386283, AI264068, AI219556, AW082138, AA455733, AI382746, AA548778, AA431230, AF092137, AF100751, AF040252, AC009948, AC009948, and AC009948.



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HNTMB90	46	910934	1 - 718	15 - 732	Z99396, AL038837, AL037051, AL036725, AA631969, AL039074, AW392670, AL036418, AL039085, AL039564, AL036858, AL039156, AL039108, AL038509, AL039109, AL039128, AL036924, AL037094, AL039659, AL038531, AL036196, AL039625, AL039648, AL045337, AL036767, AL119497, AL037082, AL037526, AL036190, AL038447, AL119483, AL037639, AW372827, AL039678, AW363220, AL039629, AW384394, AL119457, AL039423, AL036238, AL039150, AL119319, AL040992, AL119324, AL042909, U46350, AL038520, AL119484, AL119391, AL037077, AL119443, AL119522, U46351, AL119355, AL119363, AL037726, U46341, U46347, U46349, AL134533, AL039410, AL038851, AL119341, AL134531, AL119335, AL119418, AL119396, AL039386, AL036998, AL036733, AL119496, AL037615, AL119439, AL036268, AL037085, AL119401, AL119444, AL037205, AL037027, AL037178, AL045353, U46346, AL036679, AL042614, AL036765, AL042965, AL042975, AL134528, AL134538, AL042984, AL036191, AL119399, AL134920, AL042544, U46345, AL036719, AL043003, AL043019, AL042542, AL042551, AL042450, AL043029, AL134542, AL134532, AL037021, AL037054, AL036836, AL036158, AL119464, AL036774, AL036886, AL036999, AL036964, AR066494, AR060234, AR023813, AR064707, A81671, AR069079, AB026436, AR054110, and AR064706.
HMKCH92	47	910936	1 - 789	15 - 803	T78768, R13299, R14933, AB003592, D87248, AC018833, AC034192, AC026206, AC026206, AC022381, and AC022381.
HTELV86	48	1126499	1 - 1572	15 - 1586	AW241703, AA923237, AA382531, AA918449, AA738033, AA019310, C14331, AA305409, D80164, D51060, D51799, D80166, D59619, D80210, D80240, C14014, D81030, D59859, D80212, D59502, C14389, D80219, C15076, D51423, D59275, D80253, D50979, AA514186, D80188, D80439, D80022, D80366, D80195, D58283, D80133, D80391, D80248, D59787, D59467, D80043, D80227, D81026, D59610, D57483, D80024, AI557751, D80196, D80269, AA809122, D59889, D51022, D80522, D80268, D50995, D59927, AA305578, D80038, AA514188, D80193, D80045, D80247, D80241, D80251, AW360811, D80378, AI535686, AW177440, N71180, D51103, D80302, AW178893, C14407, D80157, AW377671, AW375405, T03269, AW178906, AW366296, D51759, AW360817, C14344, AW179328, AW375406, AA853033, AW378534, AW179332, AW377672, AW179023, AW178905, AW020592, AW378532, N71199, AW378528, AW178762, H67854, N81164, C06015, AI345688, AI696583, AW377676,



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HNTAF23	49	910947	1 - 239	15 - 253	AW392670, AL119355, AW372827, U46341, AL119483, AL119319, U46349, AL119457, AL119324, AW384394, AL119497, AW363220, Z99396, AL134920, AL134524, AL119484, AL119363, AL119391, U46350, U46347, U46351, AL119443, AL119444, AI142137, AL119341, AL134538, AL119439, AL119522, AL119396, U46346, AL043029, AL037205, AL134531, AL119335, AL042614, AL119399, AI142139, AL119496, AL134533, AL119418, U46345, AL043011, AL042984, AL043019, AL042544, AL042896, AL043033, AL042965, AL042975, AL042450, AL042542, AL043003, AL119464, AL042551, AB026436, A81671, AR060234, AR054110, AR066494, AR069079, and AR043113.
HNBUT01	50	1025375	1 - 1009	15 - 1023	AA279757, AI632246, AI478566, AA977612, AI219740, AA716656, AA687260, AI801069, AA071046, AI985849, AW370598, AA630617, AW370599, AW370625, AA134295, AW390691, AI143764, D30955, AI990289, T79236, AW370620, AA352142, AA074442, AW071043, and AI744728.
HEMFI21	51	1128266	1 - 2215	15 - 2229	AI670810, AI720056, AW195755, AW268679, AI400941, AI867849, AA053882, AI672024, AI880208, AW196438, AI655564, AI682042, AA034417, W27229, AW376127, AA425562, AI972198, AA883340, AA132258, AI584045, AA770253, AW137059, AA132362, AA132257, AA425357, T62545, AW243732, AA491390, AI915665, AA721474, AA483037, AI269187, AA724043, AA346646, AW390324, N22655, AW377734, AC006042, and AL078581.
HMSOL52	52	921126	1 - 1290	15 - 1304	AI911515, AI360955, AW028045, AI796049, AI609712, AW195544, AI184337, AI470056, AI361065, N34939, AI017177, AI038779, AI440241, AI651451, AA789292, AA854683, AI765258, AI702748, and AA384884.
HHGAE47	53	922194	1 - 705	15 - 719	AW025529, AW026010, AA657904, AA662803, AA886335, AA158820, AI475932, AW050607, AI885090, AI056120, AI244837, AA485566, AI375435, AA922036, AA878578, AA643750, AI056614, AW449834, AW197722, AI393408, AA485405, AI560410,



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HMCGL45	54	922195	1 - 1141	15 - 1155	AW025529, AI475932, AW026010, AA886335, AA662803, AI056120, AW050607, AI885090, AI375435, AW449834, AA161103, AI244837, AA878578, AA922036, AW197722, AI056614, AI393408, AW058170, AA643750, AI560410, AI749095, AI720931, AI446208, N52768, AI913781, AI277003, AI268967, AA910277, AI914599, AI192693, N52783, AW050712, AA485405, AI673692, AA631339, AA657904, AA485566, AA158820, AI619710, AI560351, AI919380, N57590, AI832600, N57604, T25136, AW198090, AI499963, AW023338, AI638644, AI890214, AI538850, N75779, AI633125, AI686817, AI499570, AI500061, AI860027, AI473536, AI925164, AW163834, AI690813, AW162194, AA641818, AI684244, AI469505, AI376425, AI802542, AI673363, AI670009, AI498067, AW082532, AI433157, AI886055, AW080700, AI702073, AI884318, AW128834, AI633198, AI289310, AI620056, AI590043, AW103928, AI890907, AW152182, AI589428, AI961589, AI679550, AI961414, AI698391, AI479292, AI701097, AI570861, AI147292, AW169604, AL045413, AW081383, AI345688, AI245008, AI539800, AI950729, AI927233, AL079799, AI491775, AI872423, AI538980, AI288050, AI635634, AI440239, AA805434, AW161579, AW151893, AW148363, AI866465, AI538564, AI571439, AW083374, AL041150, AI973152, AI445611, AL047100, AI538116, AI687362, AI281757, AI241923, AA580663, AI440399, AI095003, AW022808, AI540674, AI954475, AI499890, AI471282, AI648494, AI927755, AI621341, AI445829, AI432030, AI915291, AI932503, AI341690, AI613038, AI866040, AW073865, AI699823, AW190194, AI559619, AL037582, AL037602, AI627988, AI685005, AL039086, AI348901, R41605, AI932794, AI345415, AI636588, AW163554, AI572096, AI612852, AW050998, AI580436, AI627893, AI568138, AA587590, AI869377, AL046466, AL118781, AI819545, AI270183, AI912434, AI567513, AI524179, AA830709, AW051088, I48978, I48979, AL137550, AF061573, A15345, I89947, I68732, A65340, AL117460, A77033, A77035, X63162, AF153205, AR029490, AL023657, D16301, AL117587, U78525, AL050366, E12747, AF067728, AF115392, AF090900, AR038854, A76335, E02349,



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HEOQN14	55	923752	1 - 1031	15 - 1045	AI014538, AW006457, AI479414, AI805243, AI290929, AI129301, AI872459, AI601146, AI708870, AI973043, AI540074, AI186894, AI682389, AI654747, AA460832, AI392777, AA405714, AA649837, AI356090, AI358510, AW294364, AA954900, AA991687, AI540589, AI953865, AA977875, AW190678, R61326, R54477, AW009738, AA724308, AW297100, R54409, AA627570, AA504833, AA489470, H08185, R08582, AA778454, AI810108, Z41744, R43473, AA765208,

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HSOBC04	56	927280	1 - 1206	15 - 1220	AA115298, AI741325, AI688227, AI819333, AA452504, AI925664, AI742595, AI174530, AA115338, AI567500, AA563582, AA461615, AI142563, AA807844, N94422, AI095261, AA569395, W58424, AA687480, AA479551, AA582573, AI081428, AA779677, AI280806, N24393, AA988617, AI863187, AA834079, AW302361, AI362861, AW273442, AA150123, AA553678, AI752480, AI312661, W52661, AI298150, AA463418, W72509, AA024450, W72139, AI037968, W79868, AI028169, AA477651, H39596, W02690, AI198327, AI952450, AA926794, AI087245, W74236, AW004736, AI334346, AI870989, H98040, AI689546, AI332748, W76066, AA150031, R40403, AI349417, AA595996, W80872, H99144, AW166280, W52767, AA496878, H25985, AI357863, R55375, AA363023, AW104147, AA378409, AI979074, AI376184, AI687489, T32290, N26307, H97338, N95244, W77880, AI917258, W25604, AI536791, AA024802, AA577352, AA328156, AA359865, AA367475, AA461442, AA358275, W80763, T09474, AA987427, AI611160, AA888165, AA595303, AI918172, W30769, AI201782, AA187662, W21074, AA411955, AA935961, AA090719, AA411956, AA451977, AI371307, AW074526, N79974, AI635472, N39751, AI612934, AA478489, AA102215, AI802295, AI750502, AA496836, AL133116, L07063, and AC012192.
HTXKL86	57	1212283	1 - 1486	15 - 1500	AI014538, AW006457, AI401170, AI479414, AI805243, AI290929, AI129301, AI872459, AI601146, AI708870, W28953, AI973043, AI540074, AI186894, AI682389, AI810108, AI654747, AA460832, AI392777, AA405714, AA649837, H10122, AI356090, AA313257, AW294364, AI358510, AI540589, AA954900, AA991687, H19139, H08285, AW408231, AI953865, AA371650, R54508, AA977875, AW009738, AW297100, R59784, R54477, AW407594, F07194, AA724308, F08180, F08505, Z43765, AA627570, H08185, R52605, AA489470, F07185, AW190678, AW407965, R08582, F05493, AA504833, AA778454, R43473, AI698394, AA765208, R13670, H19140, Z45409, Z39824, AA461135, R13641, Z41120, F03843, AW131981, AA701889, AA159318, AA404221, H84256, AI475002, AA405779, AW189730, F01761, AA502309, R61326,



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HUJCT05	58	1125408	1 - 1625	15 - 1639	AW268357, AI889091, C15588, AI949350, AI056961, AI124874, R39133, AA887911, AW023386, AC003962, and AF155116.
HBGMR22	59	1171965	1 - 808	15 - 822	
HHFOC79	60	935406	1 - 1024	15 - 1038	AI569931, AA450162, AA405198, H26214, H14443, N28528, R73380, AW015358, R48456, AI750978, AA358230, Z19130, AA359395, AA744173, H26831, and AC008745.
HMTBB17	61	1125265	1 - 576	15 - 590	AA582539, AI963340, AI097093, AA286856, AI761614, AI149781, AI460219, AI032670, AI636161, AI819154, AI089302, H12042, AI811219, H05308, T95010, AA836993, AW271462, R37000, AI001803, AA904906, AA743196, AI015200, AA453607, F05000, AA578803, AI241466, AI033193, AA330970, F03322, F01968, AA037601, T75492, N47542, AW183219, AI288171, AA054759, F01965, AA651907, AL119324, AL119457, AL042544, AL119399, AW392670, AL119484, AL119439, U46347, AL119443, U46351, AL134530, AL134519, AL119391, AL119319, AL119418, AW372827, U46350, AW363220, AW384394, AL119522, Z99396, AL119497, AL119363, AL119355, U46349, AL119444, U46341, AL037205, AL119483, AL119396, AL119401, AL119341, AL119464, AL134525, AL043003, U46346, AL119335, AL134528, AL119496, AL134538, U46345, AL043019, AI142132, AL042542, AL042614, AL042450, AL042984, AL042965, AL042975, AL043029, AL042551, AL122084, AL049611, AB026436, AR060234, AR066494, AR054110, A81671, AR043113, AR069079, and AW612030.
HKGDE58	62	1125264	1 - 1332	15 - 1346	AW271462, AA582539, AI963340, AI097093, AI460219, AA286856, AI761614, AI149781, AI032670, AI819154, AI089302, AI636161, AA448686, H12042, AI811219, AA287162, AA836993, T95010, AI001803, AA904906, AA743196, AI015200, R37000, H05308, AA453607, F05000, AA578803, AI241466, AI033193, F03322, AA037601, AA330970, F01968, R13858, H12041, T75492, Z46111, F07044, T94956, H05358, N47542, AA053290, AW183219, T75535, AA454139, F05720, AI288171, AA651907, AA054759, F01965, F05717, AL122084, and AL049611.
HCHMW40	63	1129560	1 - 906	15 - 920	AI732539, AI791495, AI791325, AA709067, AW082062, AI791964, AI732667, AA505923, AW057561, AI909857, AI909862, AA601601, AI909853, AW151270, AI597748, AA938181, AA079317, AI017427, AI285826, AI473547, AA689584, AL036241, AI251221, AI571699, AA836392, AI624279, AI343091, AW403717,



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HE8QZ34	64	1086807	1 - 1070	15 - 1084	R35313, AA210809, W28575, AA112126, R86156, AA286753, AW405566, AA385668, AA384297, H25863, H50786, R25032, Z46079, AA334931, AA490204, and AW367213.
HE8TM80	65	1185770	1 - 1438	15 - 1452	AW368592, AL040968, AW390796, AW361341, AA125853, AW361336, R56714, AW368596, AA127005, AA436573, AI610191, AL040878, H53723, AW386767, R72151, AA662674, H06566, AI620201, AW272525, AA428869, AA876119, AA643689, AI810630, T70821, AA126031, AI242268, AI525912, AI624158, AA715437, AI139291, AA506178, AA366775, AW295598, AA071351, AI635219, AI628041, AA126626, AI223312, AI831145, AW272772, AA223723, AI393334, AA101504, AA125839, AA609710, AA166669, AA969727, AA813942, AA627552, AA588589, AA569083, T70552, AI520735, AI654578, AW173734, AW245101, AI128760, AI589990, AA436546, AW377757, AA653217, AA909871, N25030, H98122, AA706136, AA182573, AI612136, AI612151, AW301938, AW074868, AI308036, AA281089, H84055, H29320, T90829, H06511, AW338571, AW292509, R56868, AI474847, AI682762, AW028456, AA307834, AA969587, R10267, and AF191018.
HHEFL55	66	957539	1 - 1273	15 - 1287	AW411262, AW239479, AA306419, C75208, AA311414, H06122, W38676, AA297279, T50005, AA302953, AW192348, AA334000, AA151050, AW383613, AW383609, AW383535, AA226372, and AA938031.
HWLEY40	67	1172021	1 - 1422	15 - 1436	AI014538, AW006457, AI479414, AI805243, AI129301, AI401170, AI290929, AI872459, AI601146, AI708870, W28953, AI973043, AI540074, AI682389, AI810108, AI392777, AI186894, AA460832, AA405714, AA649837, H10122, AW294364, AA313257, AI654747, AI358510, AI540589, AA954900, H19139, AA991687, H08285, AW408231, AI953865, AA371650, AI356090, AW009738, R54508, AA977875, R59784, AW407594, F07194, F08180, F08505, Z43765, AA489470, R54477, AA627570, R52605, AW297100, F07185, AA724308, AW407965, AA778454, R08582,

					F05493, AA504833, R43473, AI698394, AA765208, R13670, H08185, Z45409, AW190678, Z39824, AA461135, H19140, AW131981, R13641, AA701889, AA159318, AA404221, H84256, AI475002, AW189730, AA405779, F01761, H84262, AA404687, Z41120, F03843, F04422, R61326, H29188, AA749407, AA581151, AA477301, AA502309, R54409, AA477302, AI144326, and Z41744.
HHAWC08	68	1088146	1 - 461	15 - 475	H06763, F13201, T75396, N41533, AA310599, N26380, AW403968, AW247011, W07220, N43834, N44897, AA322203, N25010, and AR009648.
HCEHD66	69	959160	1 - 1311	15 - 1325	AI968437, AI824971, AW104052, AI762197, AI598138, AI088543, AI492390, AI827280, AA058923, AW007187, AW135225, AI391466, AI808139, AA534403, AW028554, AI369729, AA460467, AA135928, AW006062, AW138526, AA507443, AI479413, AI400940, AW137272, AW381735, AA135929, AA085774, W81153, AA918755, C03738, R85039, AI472852, AI937792, AI867512, AA599118, N62215, AI864402, H41491, N62216, D44882, H14329, W30972, H40979, AA463408, AI744140, H40980, N62166, AA319197, AI766568, N62223, AF186409, AF020184, L27421, L27420, and AC006241.
HMSGF27	70	1206683	1 - 1566	15 - 1580	AI191318, AI978812, AA586860, AI628509, AA805184, W73797, AI582366, W73745, AW239293, AI620297, AW083832, AW386876, AI056600, AI056739, AI362766, AI494212, AI077551, AA935678, AI348675, AI358232, AA251769, AA968828, AA659758, AI891139, C06060, R67182, AA746268, AA251926, AA506524, H58621, D81244, AA291462, H58622, AW193598, AI919497, AI250032, AA604444, AI567397, AA905208, AA836253, R57498, AI525934, AA551675, AI364618, AI421662, AW080157, AW087829, AI813914, R38144, AW166086, AI680498, AI523628, R59996, AI554821, AI874261, AL045413, AI469754, AI366900, AW262491, AI540179, AI560545, AW262042, AI954504, AI089970, AI677646, AL043152, AI679164, AI431909, AI868204, AI453328, AI538085, AI680221, AW089006, AI056328, AI470293, AI567302, AW162194, AI799199, AI690748, AI921746, AA741027, AI553926, AI582871, AI805671, AI280747, AI536563, AI687134, AA514684, AI184903, AI610667, AI609409, AW089932, AI812107, AW020381, AI355277, AW148876, AI564426, AI628015, AL037454, AI648458, AW079572, AI891084, AI375702, AI865906, AI818353, AI950688, AI439745, AI783569, AI801152, AW080346, AI673278, AL042191, AI538908, AI863382, AA848053, AI633125,



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HBGMG39	71	971414	1 - 471	15 - 485	<p>AA024454, AA024670, AI458409, AI740930, AI742565, AI743686, AI066465, AI168481, AI379125, AI569972, AW069135, AI497641, AW192429, AW084071, AW339039, AW102701, AI061450, AI693756, AI991329, AW003414, AI342244, AI870883, AW007899, AI609020, AI453165, AI248142, AI129686, AI992036, AI761292, AI623708, AI864435, AW151858, AI362058, AW044270, AI378430, AW008808, AI479128, AL036585, AI923881, AI963067, AI740972, AL045227, AI351617, AI334039, AI452903, AI700412, AI475537, AI469546, AI187911, AI066744, AI190677, AI812069, AI081231, AI050026, AI890929, AA551905, AI080156, AI554840, AW073739, AI926062, AA577674, AW190499, AW250073, AI524714, AI884727, AW168902, AI096904, AI369151, AI858574, AI422058, AA304774, AI890721, AI052823, AI683215, AI087154,</p>

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HTTCT34	72	1097598	1 - 623	15 - 637	C75208, AA311414, AW411262, H06122, W38676, AA334000, AA297279, T50005, AA302953, AW383613, AW383609, AW192348, AW239479, AW383535, and AA151050.
HAWAM69	73	943104	1 - 1901	15 - 1915	AA430300, AA541688, AA776700, AW385785, AA679037, AA573270, AA126614, AL045796, AA682186, AI268236, AI963606, AW192904, AI926591, AI924827, AI922590, AI032288, AI375804, AA705172, AW081541, AA694514, AI130883, N25288, AA931725, AI800450, AI270687, AI366906, AW058362, AI683319, AA436891, W69578, AI597744, AI446542, R59176, AW453004, AI911821, AA687634, AI095665, AI130013, W69579, AA722782, AI191864, AI587015, AA398533, AA676733, AI476374, AA115447, AA554327, AA759328, AW242281, AA042956, AI139766, AA135916, AA886732, AA664356, AA358590, H71919, AI565897, AW304844, AA916086, AA618576, AA363371, Z44808, AA430199, AI370031, AA320329, AA393105, AW452852, AA135927, AI004140, AA135926, AA042816, H44791, T35731, AI865731, AA813424, R42647, R27785, T32691, AI934183, AA115446, AI857286, AW008428, AI631988, AA678468, AW075384, H44790, AI569918, AI918635, AA603858, AA601518, AI745618, H42641, AI445766, R27874, AI939990, AA677131, AW364938, AI569374, AW029062, C01947, and AA732827.



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HMTAV95	74	614936	1 - 395	15 - 409	AB023187, AL137000, AL137000, and AL137000.
HSXCB49	75	1172424	1 - 684	15 - 698	
HTEON29	76	1126522	1 - 1190	15 - 1204	AW004028, AI968030, AW237673, AA432290, AI143780, AW138422, AA428635, AA112090, AI143791, and AA861634.
HHFGP83	77	1174826	1 - 2635	15 - 2649	AW027467, AW021001, AI679358, AA628405, AW002474, AA142868, AI720221, AI559580, AI952940, AI971163, AA126704, AW189486, AI086066, AI338366, AI632310, AW089385, W92463, AI372019, AI335800, N67118, AW130513, AI339087, W72626, AI962685, AI811098, AA043282, AI268440, AA054560, AI564240, AI623726, AA748136, AA012896, AA716090, AA047297, AA652890, AI869611, AI199091, AA938386, AA708870, AA760924, AA043925, AA582637, AA056075, AA017551, AI202160, AI916439, AA618223, AA632478, AA975496, AA249580, AI422146, AA932810, AA628573, AA628559, AW195978, D81448, AW188932, AI857354, AI914554, AW193055, AA046731, R75666, AI873760, AI127156, AW023470, AA043406, AW023472, AI690518, AA043200, AA054620, AA468866, AW382445, AA047158, C01055, W76609, AA043281, AI918561, AI570316, AA338995, AI653300, AI917733, W27493, AL133599, AF004840, and AF090866.
HTEKS20	78	1123458	1 - 1063	15 - 1077	AI936596, AA868353, AI797296, AA725553, AI221970, AA428462, AA429551, AA431190, AA629305, AA629047, AI073397, AW235895, AI123443, AI808267, AA609412, AI914363, AA953895, AI214385, AA431516, AA911681, AA781953, AI825106, AA298758, AI215028, AA909534, AA723768, D10393, and S63991.
HCHAT01	79	1202214	1 - 3835	15 - 3849	AI357645, AW372245, AW372243, AI870876, AL079756, W80383, AA143521, AI934507, AI497785, AA131786, AA143522, AA775429, N73794, AI190675, AA570709, AL041943, AW026848, AA746031, AI950978, AI422318, AA131772, AI885729, AW026326, AA635171, AA934699, AA316540, AI246491, AI160357, AA487855, AI041954, H11648, AI660052, AW152198, AI285004, AW028295, AI561088, AW166539, AI635148, AI094048, AW072627, AA464017, N24219, AA458881, AI094041, AI092047, AA464078, AA588471, AI804530, AI348338, AA487856, H99677, AI186100, H99573, AI025641, AA909894, N32879, AI081468, AW273806, AA872312, W78982, AA740804, M78765, AW337818, AI160858, AA977238, AA627981, AA985314, AA653069, AI610235, AI288191, AA492020, AI937558, AI357858, AW273022, H23489,



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HAPNZ77	80	1171962	1 - 1522	15 - 1536	AI829331, AI307338, AA831880, AI379982, AA768459, AW270258, AW271904, AI345157, AI431303, AL042756, AI755214, AA584489, AW265385, AI354423, AI963720, AL038936, AL040054, AI754105, AW021917, AI754567, AI733856, AW419389, AA402129, AW419262, AA680243, AA410788, AA634837, AI613459, AI926728, AW023672, AL041894, AI625604, AI282253, AA455483, AW327868, AW193265, AW069227, AA574442, AI064864, AA521323, AI244127, AA629992, AL046409, AI284640, AW327624, T05834, AI192631, AL048626, AI054333, AI305766, AI613280, AA013168, AI962030, AI732120, AW075979, AA630854, AI753488, AA521399, AL079734, AA659832, AA019973, AI061313, AI336054, AI885572, AW270256, AA644090, H05940, AI799607, AA613627, AL118991, AI345654, AI587583, AA526625, AI291823, AI587565, AI003611, AI754767, AW166611, AA533176, AW020088, AA833875, AA833896, AA176605, AI332615, AI675615, AI039809, AW157456, AA526326, AW275432, AW162697, AW007759, AA857486, AW023111, AI279417, AL046746, AL037683, AA634786, AI306232, AI017251, AW303196, AA864603, AI307201, AI457397, T49633, AI251104, AI290405, AA502991, AA904275, AI753113, AA491814, AW062724, AW439558, AA226584, AW301350, AI696793, AW274191, AW190505, AI133102, AL041706, AI867058, AW274349, AA904137, AI888468, AA513851, AW302903, AI270117, AA613227, AI016704, AI570943, AI377413, AW022934, AI110770,

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HSIAO78	81	1222343	1 - 1988	15 - 2002	AA527435, AW195324, AI653000, AW051613, AA514619, AI675204, AI652532, AA435717, AI659333, AI796596, AI273289, AI880669, AI826786, AA889355, AI174916, AW004627, AA377072, AA255838, AA397980, AA430523, AI565825, AI435476, AW001866, N52904, AA430608, AI760594, AA298640, W69756, AA594479, AI149418, AI911011, AI871818, N71537, AI089421, AA400874, AI038591, AA854839, AI565867, AI131012, AI144119, H65663, AW044396, N47230, AI732273, AW079534, AA847967, AW027678, AL044698, AA224892, T36269, AA009702, AI668849, AW182206, AA011130, N78511, AI676028, AA968449, AI984040, AA207018, AA658246, N73670, AI937659, R53598, AA453038, AA904224, AW293549, R48261, AA775033, H52314, R38289, H48428, AW083969, AA588654, F10880, AA578060, AW298073, W25831, AA889378, AA483944, AC002302, X62260, AC002288, AL035588, AC007425, AF181896, AC004216, AP000280, AP000038, AF003528, AL033525, AC009498, AC007676, AP000107, AC006080, AC005704, AC005332, AC005011, AL022328, AL118497, AC007221, AC005213, AL132987, U69570, Z48484, AB020858, AC004382, AL049753, AC004874, AC006023, AC003976, AL035668, AL035671, AL139165, K03021, AC005771, AC004894, D83402, AC005004, AC005183, AC004129, AC004671, AC006354, AC005046, AC005161, AL117338, AC005184, AC006599, AF042484, AC004100, AJ006345, AC005235, AC004875, AC003693, AC004982, AL021877, AL009183, AC002546, Z83822, Z75741, AC002541, AC004098, U61375, AC007637, AC004061, AC005922, AL049821, Z95114, AC006952, AC007529, AF095703, AL021395, AL080286, AL035696, AL117436, AC006973, Z82246, AP000466, AL078638, AC007680,



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HWBEG18	82	909798	1 - 940	15 - 954	AA906863, AW408789, AW452373, AA352977, AA732349, AI269653, AI492098, and AB020653.
HFCBB56	83	1204322	1 - 2090	15 - 2104	AA491955, AA053463, AI620992, AW005974, F13749, AW408767, AA864271, AW162288, AA565232, AA501867, AW265688, AI493583, AA744094, AA904211, AW316599, AI224619, AA019542, AA339423, AI696793, AA878492, AW081610, AI492579, AI623364, AI445373, AA630535, AA513983, AI243793, AI889426, AW054936, AI678867, AI049955, AA828834, AI190648, AA721645, AI278372, AW236219, AI633386, AI797998, AA744048, AA669155, AA572983, AA862312, AI889995, AI636734, AI368862, AA283081, AI279417, AW407889, AI312090, AI049630, AI689019, AL042667, AL042670, AW337805, AI887755, AA832016, AA833896, AL049869, Z84469, AL122020, AC004821, Z95114, Z83822, AL022315, AC002477, AC004815, AC007298, AL034429, AC005800, AC005736, AL031311, AL009172, AC012384, AL034400, AF053356, AC007435, AC002312, AC009516, AC004185,

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HEMCL65	84	910900	1 - 453	15 - 467	AI902552, and AI902562.
HMAMB94	85	1225343	1 - 2440	15 - 2454	AW369653, AW024321, AA766018, AA905970, AI652025, AA158332, AI627492, AW068035, AA158041, Z25180, W40230, AI493579, AI536877, AA191353, W45464, AW175724, AA670064, AA190444, AA248856, AA247921, AL121448, AI926451, AI983662, W60091, AW068830, R90961, R90977, R90972, and AA309409.
HCQCI06	86	915000	1 - 1190	15 - 1204	AI123952, AI751915, AA343597, W79144, AA345718, AA304549, AA256582, W81545, D45547, AL117664, AC068763, AC068763, and AC069223.
HWLFG75	87	1227642	1 - 2026	15 - 2040	AI356559, AW163067, AI937030, AI652337, AW028706, AW157098, AW028808, AA443325, AA004795, AW005140, AW173645, R60229, AA442531, AI274924, AI810652, AI924004, AI572794, AI336556, AI672253, AI147260, AI872258, AI347103, AA467751, AA724594, AI280850, R52646, AA536110, H16834, AW450707, AW444512, AI376913, AA468349, AI807962, AA927875, R42625, AA609873, W28566, AI918962, AA578362, AA578062, R17389, C18386, R15375, AI016851, R60462, H16941, AI423739, AA467933, AA740299, AA025666, R42116, AA978110, AI423740, AW117517, AI886594, AA443338, AL040243, AI275175, AL119748, AL121270, AI857296, AI433157, AL045500, AI433976, AW071349, AL047763, AI702406, AI250293, AI436456, AL048871, AW117882, AI620284, AW195957, AL119791, AI064830, AI568870, AI863014, AI702433, AI499463, AI538716, AI439087, AI349933, AI678302, AI633419, AI868831, AI440239, AW074993, AW162071, AW235035, AW071417, AW274192, AI349256, AI866608, AI349645, AI690835, AI498579, AI613017, AI349004, AI349772, AW301409, AL135661, AI699857, AI540832, AI440426, AW103371, AI628205, AI281779, AI500659, AL036146, AL036396, AI340582, AI521012, AI500077, AW169653, AI249257, AI567351, AI500553, AW238730, AW268253, AI224992, AI312152, AI345735, AI349937, AW089572, AL120736, AI366549, AI564719, AL047042, AI568854, AI597918, AI866002, AI673256, AI281773, AI590128, AI539771, AL038605, AI497733, AI969601, AI636456, AL036802, AW087445, AL119049, AW068845, AI282655, AI690751, AI612913, AW148320, AI800453, AI800433, AI343112, AI909666, AI567632, AI635461, AI687728, AI686926, AI800411, AI682841, AW303152, AI348897, AI610645, AI349614, AI207510,



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HBODA38	88	923456	1 - 1882	15 - 1896	AA196401, W79841, AA112831, AA197134, C05212, W19681, AA195812, Z25012, AI004215, Z30134, AA194641, AI809925, AA258550, Z28480, F29133, AA699576, F20387, AI129717, AA194359, AI079487, AA195355, AA195094, AA931319, F34387, Z19343, F36761, H67895, AA258604, AI378821, F19321, AI089231, R91150, AI702453, AI288969, AI313118, AI351843, F31038, N56278, AI381419, AA195356, AA131264, AA195051, AA192095, AI264911, and AA086284.
HCYBK19	89	1225324	1 - 2764	15 - 2778	AI829726, AI809562, AI927757, AI927758, AI927768, AW297770, AA165336, AI638072, AI149852, AW298053, AI365991, AA904547, H15885, AA985065, AI359235, AW207262, AI470080, AI421572, AA305419, AA985170, AW341104, AI423550, AI362528, AI453702, AI654827, AA927292, AI365149, AI365324, H91991, D81295, AI797740, R62753, AI357382, AI953516, AA909430, H01576, AA969956, AA379840, H52748, R37302, AA905264, Z43289, R18887, R68272, H04859, AA746048, T31617, H04764, Z44077, T78758, T32807, D60323, AA634475, H01477, AI193962, H00918, D81446, M86147, AA983881, AA318875, N64328, AA165369, D62629, Z39361, T16370, F03272, H00919, N34301, H46107, AW590162, AW593404, AW593449, AW593464, and AW593480.
HWNCY05	90	1223031	1 - 1181	15 - 1195	W40569, AW025860, D63226, AA334307, AL038838, AL037436, AL037323, AL038983, AI142134, AL134524, AL038822, AL037727, AL038532, AL037343, AL040617, AL044186, AL041238, AL047012, AL037335, AL037435, AL044125, AL044037, AL047170, AL040463, AL045684, AL040625, AL047219, AL044162, AL043677, AL040193, AL043467, AL040510, AL040621, AL043538, AL041752, AL047183, AL043496, AL040464, AL043923, AL043814, AL037443, AL040576, AL043845, AL040839, AL045753, AL041635, AL041133, AL041347, AL040294, AL041324, AL046442, AL044064, AL041459, AL041577, AL040322, AL043492, AL041602, AL041098, AL044074, AL046850,



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HTXNN68	91	1143300	1 - 1516	15 - 1530	AA287304, AI418151, AA885205, N32677, AA147402, AI630898, AI362039, AW075796, AA905465, and D86967.
HWWFW0 6	92	933671	1 - 880	15 - 894	AA287304, AI418151, AA885205, N32677, AI630898, AA147402, AI362039, AW075796, AA905465, AL134533, AW392670, AL134531, AI142139, AL119418, AL119483, AL119319, AL119443, AL119324, AL119522, U46350, AL119457, AL134920, AW372827, AW363220, AL119484, AL119391, AL134538, AL134902, AL119341, Z99396, AW384394, AL119497, AL119363, AL119355, AL119396, AL119496, D86967, AR069079, AB026436, AR066494, AR060234, and A81671.
HOSDR06	93	1229558	1 - 2170	15 - 2184	AI942417, AI800288, AI830283, AW384845, AA442721, AI637544, AA252612, AA305619, AA224269, N63098, AI670786, AA811590, N80213, AA431396, AI498460, AA371384, N30797, AI280008, AA298474, Z24818, AA432386, AI770070, AA364533, AA280152, AA297828, F13799, AA875925, N93459, AI110673, AA090893, AA029327, AA825662, F30025, AA029328, N41572, AA298473,

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HNFW14	94	939763	1 - 522	15 - 536	
HSDHB12	95	941973	1 - 624	15 - 638	AA447298.
HTTJW49	96	948107	1 - 648	15 - 662	AA199865, AI769428, AI061340, AW268880, AA707168, AI970984, AI884812, AW444872, AI479954, AI356088, AI701720, AI765045, AA722812, AW236544, AA410516, AI267987, AA005114, AI298592, AI865503, AI633370, AA878382, AW389168, AF118838, Y17571, AF164632, AF164526, AF164527, AC004458, AF164528, and AF164525.
HELDR74	97	1218982	1 - 1428	15 - 1442	AI741422, AW249482, AA573909, AA085764, AW272801, AI052311, AA490620, AI683396, AA151131, AI700257, AA310938, AI284596, AA961817, AA862960, AW073675, R87485, AI828443, AI925221, AI969547, AW001375, AI521481, N24896, AI925228, AI695515, AA609182, AA151130, AI245859, AA490809, AA040451, AW139250, AI970384, AI961068, T67610, AA923298, AA513675, AW027490, T96070, AI624751, T67494, AI936161, AW196036, AI917354, AA679554, N36317, AA302588, AI932690, AW250249, R88163, T72363, AI796143, W32439, AA582049, AI539047, W45013, and AF113795.
HOEET48	98	963290	1 - 1466	15 - 1480	AI797684, AW239200, AA456267, AI478733, AI751749, AI990902, AA427646, AI379565, AI970534, W95460, AA788855, AA405402, AW068453, AW294114, AI751750, AA594137, AA947297, AW177719, AI057073, AA427487, AI341112, AA232452, AA041304, AW068711, H73236, AA041328, W95567, AW167569, AA853047, AI652166, W02069, H74164, R34003, AI341381, AW176526, AA580289, D30965, D31176, AA367502, and AR035969.
HBODE51	99	1188998	1 - 2580	15 - 2594	AW083201, AA056328, AA404251, AA404701, AA610014, AA535370, AA479540, W26963, AI803179, AA693610, AA167788, AA477641, T30626, AW118235, AA148356, R20037, T10239, W40184, AA677785, AA780412, T33085, T15444, Z36286, F37344, AA166644, Z43182, AW367537, AI699497, AA258857, AA480033, W28626, AI625089, F27424, R61287, AI569618, AW376308, AA324131, AW337372, T10238, Z41030, AA319764, R19966, AW058317, AW268504, AA091588, F04174, AI807608, AA249876, AI758553, AI887457, AA665925, R54586, AW009070, AA641818, AW166832, AI627360, T80262, AI619820, AI698391, AA767924, AI918435, AI553645, AI636507, AI244343, AI872423, AW238688, AI524179, AI913330, AI824458,



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HE8UT58	100	973153	1 - 1090	15 - 1104	AL079991, AW409774, AA404732, AA782257, AI808909, AA099036, AA677654, AA405418, AW341107, AW409667, AA659407, AA503263, AI433410, AI885266, AI341147, AA905366, AI692534, AI027623, AA468344, AA923181, AA778251, AI681129, AA533117, AI986154, AA099037, AI955317, AI276678, H29006, AA404602, AI347168, AA371047, AI420387, AW135263, AA868124, T12623, H09118, AA430277, AA365338, T08839, AA813337, H29109, H11272, AW137535, AB014534, AF116574, AF116573, and AC032004.
HFXJI27	101	971046	1 - 427	15 - 441	AI335925, AI890750, AA187638, N39062, AI268071, D79411, N75622, N22381, H13284, R43578, F10497, R26373, AI625385, AI220697, R21997, AA932204, AI493179, AI373111, AA909963, AI476063, AA909961, AI888010, AI619918, AA976881, AW339040, AI432041, AA015789, AI049514, AI355877, AI888471, N59174, AI679618, AI373318, AA670204, AI358468, AI336216, AI266210, AA947133, R33792, AW081307, AA610540, AA928678, AA922947, AA922946, AI817788, AI245931, AA948492, AA044223, T63607, AI433872, AW269052, AI587384, AA827770, AW182646, AI127888, H89128, AI268557, D62713, T63317, R35227, AA018661, AW023089, N67948, T62565, H01498, R21841, AW151373, D29213, AW022288, AA678512, and AB023187.
HETHO38	102	1124598	1 - 1393	15 - 1407	AA675914, AW058625, AA595003, AA565043, AW192302, T54086, AI287312, AA988703, AW438698, AA675910, AI990695, N40329, AA079650, T54177, AI824376, AI675850, AA079556, AA303646, N71782, AW367626, AA675909, T29568, H69835, C01666, AA352261, AI969951, AA077925, AA441887, L14848, AF055384, AB015600, U56947, U56949, U56955, Y16801, Y16809, Y16811, Y16807, Y18114, Y16804, U56944, U56948, Y18113, Y18116, U56943, U56945, Y16803, AF097406, U56942, Y18111, Y18115, X91625, Y18117, U56952, Y16808, Y16805, U69978, Y18112, U56941, U56946, Y16806, Y18118, U56953,



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HTEIL07	103	953803	1 - 445	15 - 459	H55431, and AL031843.
HDPTC44	104	553453	1 - 561	15 - 575	AF010446, U22963, AF031469, AF010447, AF073485, AF073486, AJ132011, U94989, AF010448, AF035672, and AF068692.
HHPDE40	105	552112	1 - 582	15 - 596	AW449998, U60319, AF079407, Z92910, AR036572, U91328, Y09800, AF079409, AF079408, and Y09801.
HCESP56	106	827671	1 - 500	15 - 514	AW247740, AW247029, AW204207, W39269, AA325536, R14422, W52568, Y16752, AL022170, and Z65186.
HHFGZ38	107	1117192	1 - 1546	15 - 1560	AA372117, AI864976, AI468754, AA133546, AA160339, AW449104, AI206956, AW374444, AA595656, AA278441, AI767157, AI263438, AI859910, AA216640, AA070240, T59738, and AA311762.
HAHEF22	108	910996	1 - 872	15 - 886	AA447298.
HCUEV29	109	816065	1 - 491	15 - 505	AW410192, AI570209, AA583494, AW087991, AW337550, T30350, T24722, AW246233, and AL031283.

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HBGQN46	110	945370	1 - 888	15 - 902	AA479990, AW293680, AI473367, AI184880, AI086741, AI081183, AI214276, AA742259, AA836754, R55060, AA251267, AI285889, AI813391, AW297831, AI819671, AF038458, and AF038458.
HMQCE42	111	806815	1 - 194	15 - 208	D56208, N44225, AA348075, AA351420, R19052, AA449607, H23327, AA227277, AA081491, AA102697, R54504, AA083156, Z46810, D38526, D49552, AJ010749, X96582, X97321, Y09156, X83394, Z33459, D64147, U09853, X70857, M28160, D11383, AJ001977, D83957, and AP000508.
HEQAY32	112	1207206	1 - 2599	15 - 2613	AA459604, AA703415, AA703508, AI337830, AA993540, AI924185, AA398958, AA047107, AI581879, R88084, H08326, AA399541, AA047244, AI479681, AI570681, AW007699, AA826082, R50486, AA742413, AI278602, AA810070, AW129039, AI346375, AI636166, AI468327, Z44337, AW248520, AI817167, AI188457, AI923575, AI480234, AI184221, AI289600, AW005514, AI696876, AA864258, AW248475, AI804579, AW000853, AI091327, AI192782, AW104750, AI299237, AA766769, AI124027, AI309629, AA450027, AI378094, AA829783, AA505829, AA421949, AI721136, AI923569, T79992, AA317334, AI269575, AA878088, R50042, H08229, AA852854, N27053, T36249, Z45648, AA454095, AA878089, M78847, AI523984, AA740396, H08868, AI366112, AA322162, AW138078, F04540, AI824732, AA373622, AI864722, AI383526, F04098, AW009838, AA825440, Z43430, F02816, F07842, R50380, AI983715, AA383971, T24108, AI979211, AA402090, AW271173, AA335352, R14266, AL110339, AW080157, W45039, AI359744, AA713657, H03560, AA582025, AI553645, AL036673, AI640375, AI824576, AI287449, AA102339, AI871660, AI582900, AI743505, AI401697, AW007284, AB033004, AF104222, AC006529, AF124728, AL137294, AW514348, and AW778993.
HOEFI09	113	974194	1 - 426	15 - 440	C18310, AW402322, AW405194, AW402317, AW408434, AW401505, AL039796, AW239462, D82221, AW402511, AA158109, AA160317, AA263135, AI124815, AA310808, AW327936, D82189, AW401719, AW402264, AW402698, AA160714, AA151951, AW403872, AA663896, AW402402, D82177, AA100848, AA100680, AW405525, R19052, AA102697, AW401548, AW403793, AA224068, AW402754, AW408440, AA401643, W40489, F13067, AI826037, AW403392, AA381090, H23327, AA121088, AW402383, AA449607, T52124, AA380938, AA381088, AA160037, AA159230, AA336651, R12066, AI359260, AL138056, AA157351, AW403114, AA295712, AA381030, AA351420, T29764, AA548636,



				AA058454, AW402855, AI365653, N44225, AA295685, AA227277, AA350486, F07582, T72958, AA127128, AA159413, AW402401, AA160101, D56208, AA112349, W52004, AA152039, AA344828, AA348075, AW273557, F06315, AA143652, AA102181, AA488534, AI696864, T52219, H23377, AA159125, F06589, AA358919, AW403253, AA085102, U46382, AA263158, AA143468, AA143626, R59764, AA916617, R30668, AA295230, T75330, Y13029, U96942, Z46808, L36591, L22028, L36318, M94052, M94051, M24040, Y09058, M24032, L22649, U29083, M94053, D44501, U04243, U11262, U11266, U09864, L42024, L07950, U21053, L11571, L11570, D50296, AF016641, U36392, M84380, M24036, U04244, X64454, L20088, AB032096, X61709, U29480, L42280, D50300, U56246, U16298, AJ223282, X94574, AB032097, U58110, L76931, D44500, X99735, U17572, U11267, L76093, D31816, M95530, D50294, L22027, L11666, D44499, D50295, Y18552, L17005, U03698, M32320, X81363, AF170577, U80945, U05578, L32862, L41353, D83956, D50293, U03027, U03859, L11603, L19937, L42281, M24039, U05575, X13116, M30679, L41925, Z15143, AJ245869, M24035, U90558, AJ002676, D49824, M80670, E03437, Y08994, M68964, M32319, U31334, Y09118, L09736, M84694, U50710, L41214, X94480, AF033351, L42506, AJ250917, E03438, X91749, M24034, U21052, Y13567, L76088, M84383, AJ006020, M28203, U70528, L76094, M84382, U04245, U29057, M32317, U88407, M28205, X90391, X84725, M84384, M33573, L42345, U32678, AB036051, M19756, AF161881, X94481, X75953, AF189017, X64366, M24038, L42282, L42283, D83030, AF118894, AJ131118, D50290, M24075, X60255, X60693, U64801, X90390, D50291, M19757, AF022783, AF115460, M77775, X77658, L24373, M15470, M28204, D25275, U01848, U35431, X60253, M84386, D85761, U11263, U14943, AF118895, U75533, X96582, Y09156, L38504, L54059, U90566, D85762, M24037, X13115, U18789, X60254, L20089, U90559, U31971, U90563, U90564, U90565, U11261, L09735, L20090, M84381, M77778, M77777, M77776, AJ133267, E02885, M58636, U05580, D50068, U11265, Y08995, X61710, X61706, X58536, D50299, U17107, U30936, M24045, M84385, X03664, U63653, D83043, E02884, L04696, U30904, L40599, U05576, U05577, D14343, M29864, AJ223602, U34810, AF115461, Y09157, X61707, L41086, D50710, M26432, M59840, U06862, L04695, AJ237703, X99704, AB032094,
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					AJ002675, AJ003063, AJ002677, L76935, Z22651, U41832, M32318, U05582, AF130734, AF118893, M77774, AP000507, M29865, D64149, and X60251.
HSDGJ23	114	1182294	1 - 731	15 - 745	
HCEOR02	115	1227680	1 - 2094	15 - 2108	AW292158, AI933139, AA325666, AA317428, and AI887071.
HLTEH39	116	943641	1 - 170	15 - 184	AA970332, AA361489, AA158146, AW402698, AW405525, AW402322, AW385684, AW401505, C18310, AW401548, AW239462, AW402264, AW401719, AA294911, AA151951, AA663896, AA263135, AA352603, AA243206, C03945, AA527306, AW351546, AW405194, AW402317, AW408434, AI696864, AW327936, AA160714, AA477506, AA190717, AA305941, AA367387, AI365653, AA366365, AA527504, AA158109, T68508, AA337991, AA372227, AA321294, AA159413, AL039796, AA100848, AW403872, AA112349, AA385962, AA581164, F00945, H98493, AA335761, AW402402, AA121088, AA127128, AA310808, AA100680, T10924, T71226, AA401643, R34651, AA352534, AA058454, AA126083, AA227277, N42582, W24084, W24054, AA304603, H11697, AW402383, H23327, AA361916, AA220207, AW403793, AA449607, F11628, AW402754, AA492406, AA503610, T55088, U15638, D83030, M84386, X96582, Y09156, L54059, M26432, X58536, U43337, M77775, U36492, U15640, U14756, AF035647, D64148, L76088, L20091, D83031, AJ010748, M99388, AF168611, X67818, X60251, U18789, AB032096, AB032097, AJ223282, X94482, U29480, U74387, U18661, U06835, D64149, Z33459, D64147, L42280, Y09058, M94052, M94053, M94051, U04243, L22649, L36318, L17005, X78343, X87841, X70857, Y10520, X60249, X60248, M24096, M28160, X94574, AB032091, AB032094, AB032095, U38976, AF033351, AF115464, Z46810, AF076476, Z80227, X99704, U83580, D64151, D83029, L20088, M77774, M77778, M77777, M77776, M24040, M24032, M24033, Z15144, M84381, U63653, D49552, D50854, AJ010749, Z83247, X76189, X97321, U09853, M84173, M84174, Y11843, X83394, X95410, M28207, M26712, M28206, M26430, AB036049, AB036050, AB036051, X94480, X87268, L76090, L42506, AJ242661, L76931, U58110, D38526, D64145, M11886, Y13029, U32660, M29865, D44499, D44501, U11262, U11266, M83193, M83191, M83194, L07950, M86403, AF118894, D85762, U03027, U03698, U03859, L11571, L11570, D50294, D50296, D50299, D31816, L22027, M24039, M95530, L11666, L11603, L19937, X61709, U80945,

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HRODF07	117	1222093	1 - 1299	15 - 1313	AW238558, AI278521, AW238227, AW084017, AW265370, AW440242, AW238497, AW238306, AW238292, AW082445, AI355144, AW082458, AW238597, AW079466, AW366290, AW381175, AW366622, AW276887, AW270776, AW438489, AW270547, AW270610, AW438542, AI821931, AW270648, AW265248, AA610773, AW276814, AW277207, AA729444, AW276866, AW270597, AI732543, AW276913, AW265112, AW265170, AW438551, AW270550, AA501809, AW276884, AJ243667, AF077374, and AI355145.



**TABLE 4**

<u>Code</u>	<u>Description</u>	<u>Tissue</u>	<u>Organ</u>	<u>Cell Line</u>	<u>Disease</u>	<u>Vector</u>
AR022	a_Heart	a_Heart				
AR023	a_Liver	a_Liver				
AR024	a_mammary gland	a_mammary gland				
AR025	a_Prostate	a_Prostate				
AR026	a_small intestine	a_small intestine				
AR027	a_Stomach	a_Stomach				
AR028	Blood B cells	Blood B cells				
AR029	Blood B cells activated	Blood B cells activated				
AR030	Blood B cells resting	Blood B cells resting				
AR031	Blood T cells activated	Blood T cells activated				
AR032	Blood T cells resting	Blood T cells resting				
AR033	brain	brain				
AR034	breast	breast				
AR035	breast cancer	breast cancer				
AR036	Cell Line CAO3	Cell Line CAO3				
AR037	cell line PA-1	cell line PA-1				
AR038	cell line transformed	cell line transformed				
AR039	colon	colon				
AR040	colon (9808co65R)	colon (9808co65R)				
AR041	colon (9809co15)	colon (9809co15)				
AR042	colon cancer	colon cancer				
AR043	colon cancer (9808co64R)	colon cancer (9808co64R)				
AR044	colon cancer 9809co14	colon cancer 9809co14				
AR045	corn clone 5	corn clone 5				
AR046	corn clone 6	corn clone 6				
AR047	corn clone2	corn clone2				
AR048	corn clone3	corn clone3				
AR049	Corn Clone4	Corn Clone4				
AR050	Donor II B Cells 24hrs	Donor II B Cells 24hrs				
AR051	Donor II B Cells 72hrs	Donor II B Cells 72hrs				
AR052	Donor II B-Cells 24 hrs.	Donor II B-Cells 24 hrs.				
AR053	Donor II B-Cells 72hrs	Donor II B-Cells 72hrs				
AR054	Donor II Resting B Cells	Donor II Resting B Cells				
AR055	Heart	Heart				
AR056	Human Lung (clonotech)	Human Lung (clonotech)				
AR057	Human Mammary (clontech)	Human Mammary (clontech)				



AR058	Human Thymus (clontech)	Human Thymus (clontech)				
AR059	Jurkat (unstimulated)	Jurkat (unstimulated)				
AR060	Kidney	Kidney				
AR061	Liver	Liver				
AR062	Liver (Clontech)	Liver (Clontech)				
AR063	Lymphocytes chronic lymphocytic leukaemia	Lymphocytes chronic lymphocytic leukaemia				
AR064	Lymphocytes diffuse large B cell lymphoma	Lymphocytes diffuse large B cell lymphoma				
AR065	Lymphocytes follicular lymphoma	Lymphocytes follicular lymphoma				
AR066	normal breast	normal breast				
AR067	Normal Ovarian (4004901)	Normal Ovarian (4004901)				
AR068	Normal Ovary 9508G045	Normal Ovary 9508G045				
AR069	Normal Ovary 9701G208	Normal Ovary 9701G208				
AR070	Normal Ovary 9806G005	Normal Ovary .. 9806G005				
AR071	Ovarian Cancer	Ovarian Cancer				
AR072	Ovarian Cancer (9702G001)	Ovarian Cancer (9702G001)				
AR073	Ovarian Cancer (9707G029)	Ovarian Cancer (9707G029)				
AR074	Ovarian Cancer (9804G011)	Ovarian Cancer (9804G011)				
AR075	Ovarian Cancer (9806G019)	Ovarian Cancer (9806G019)				
AR076	Ovarian Cancer (9807G017)	Ovarian Cancer (9807G017)				
AR077	Ovarian Cancer (9809G001)	Ovarian Cancer (9809G001)				
AR078	ovarian cancer 15799	ovarian cancer 15799				
AR079	Ovarian Cancer 17717AID	Ovarian Cancer 17717AID				
AR080	Ovarian Cancer 4004664B1	Ovarian Cancer 4004664B1				
AR081	Ovarian Cancer 4005315A1	Ovarian Cancer 4005315A1				
AR082	ovarian cancer 94127303	ovarian cancer 94127303				
AR083	Ovarian Cancer 96069304	Ovarian Cancer 96069304				
AR084	Ovarian Cancer 9707G029	Ovarian Cancer 9707G029				
AR085	Ovarian Cancer 9807G045	Ovarian Cancer 9807G045				

AR086	ovarian cancer 9809G001	ovarian cancer 9809G001				
AR087	Ovarian Cancer 9905C032RC	Ovarian Cancer 9905C032RC				
AR088	Ovarian cancer 9907 C00 3rd	Ovarian cancer 9907 C00 3rd				
AR089	Prostate	Prostate				
AR090	Prostate (clonotech)	Prostate (clonotech)				
AR091	prostate cancer	prostate cancer				
AR092	prostate cancer #15176	prostate cancer #15176				
AR093	prostate cancer #15509	prostate cancer #15509				
AR094	prostate cancer #15673	prostate cancer #15673				
AR095	Small Intestine (Clontech)	Small Intestine (Clontech)				
AR096	Spleen	Spleen				
AR097	Thymus T cells activated	Thymus T cells activated				
AR098	Thymus T cells resting	Thymus T cells resting				
AR099	Tonsil	Tonsil				
AR100	Tonsil geminal center centroblast	Tonsil geminal center centroblast				
AR101	Tonsil germinal center B cell	Tonsil germinal center B cell				
AR102	Tonsil lymph node	Tonsil lymph node				
AR103	Tonsil memory B cell	Tonsil memory B cell				
AR104	Whole Brain	Whole Brain				
AR105	Xenograft ES-2	Xenograft ES-2				
AR106	Xenograft SW626	Xenograft SW626				
H0004	Human Adult Spleen	Human Adult Spleen	Spleen			Uni-ZAP XR
H0008	Whole 6 Week Old Embryo					Uni-ZAP XR
H0009	Human Fetal Brain					Uni-ZAP XR
H0011	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0012	Human Fetal Kidney	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0013	Human 8 Week Whole Embryo	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0014	Human Gall Bladder	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0015	Human Gall Bladder, fraction II	Human Gall Bladder	Gall Bladder			Uni-ZAP XR
H0020	Human Hippocampus	Human Hippocampus	Brain			Uni-ZAP XR
H0024	Human Fetal Lung III	Human Fetal Lung	Lung			Uni-ZAP XR
H0025	Human Adult Lymph Node	Human Adult Lymph Node	Lymph Node			Lambda ZAP II
H0028	Human Old Ovary	Human Old Ovary	Ovary			pBluescript
H0030	Human Placenta					Uni-ZAP XR

H0031	Human Placenta	Human Placenta	Placenta			Uni-ZAP XR
H0032	Human Prostate	Human Prostate	Prostate			Uni-ZAP XR
H0033	Human Pituitary	Human Pituitary				Uni-ZAP XR
H0036	Human Adult Small Intestine	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0038	Human Testes	Human Testes	Testis			Uni-ZAP XR
H0039	Human Pancreas Tumor	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0040	Human Testes Tumor	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0041	Human Fetal Bone	Human Fetal Bone	Bone			Uni-ZAP XR
H0042	Human Adult Pulmonary	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0045	Human Esophagus, Cancer	Human Esophagus, cancer	Esophagus		disease	Uni-ZAP XR
H0046	Human Endometrial Tumor	Human Endometrial Tumor	Uterus		disease	Uni-ZAP XR
H0048	Human Pineal Gland	Human Pineal Gland				Uni-ZAP XR
H0050	Human Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0051	Human Hippocampus	Human Hippocampus	Brain			Uni-ZAP XR
H0052	Human Cerebellum	Human Cerebellum	Brain			Uni-ZAP XR
H0053	Human Adult Kidney	Human Adult Kidney	Kidney			Uni-ZAP XR
H0056	Human Umbilical Vein, Endo. remake	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR
H0057	Human Fetal Spleen					Uni-ZAP XR
H0059	Human Uterine Cancer	Human Uterine Cancer	Uterus		disease	Lambda ZAP II
H0060	Human Macrophage	Human Macrophage	Blood	Cell Line		pBluescript
H0063	Human Thymus	Human Thymus	Thymus			Uni-ZAP XR
H0068	Human Skin Tumor	Human Skin Tumor	Skin		disease	Uni-ZAP XR
H0069	Human Activated T-Cells	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0076	Human Membrane Bound Polysomes	Human Membrane Bound Polysomes	Blood	Cell Line		Uni-ZAP XR
H0081	Human Fetal Epithelium (Skin)	Human Fetal Skin	Skin			Uni-ZAP XR
H0083	HUMAN JURKAT MEMBRANE BOUND POLYSOMES	Jurkat Cells				Uni-ZAP XR
H0085	Human Colon	Human Colon				Lambda ZAP II
H0086	Human epithelioid sarcoma	Epithelioid Sarcoma, muscle	Sk Muscle		disease	Uni-ZAP XR
H0087	Human Thymus	Human Thymus				pBluescript
H0090	Human T-Cell Lymphoma	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR
H0099	Human Lung Cancer, subtracted	Human Lung Cancer	Lung			pBluescript
H0100	Human Whole Six Week Old Embryo	Human Whole Six Week Old Embryo	Embryo			Uni-ZAP XR
H0101	Human 7 Weeks Old Embryo, subtracted	Human Whole 7 Week Old Embryo	Embryo			Lambda ZAP II



H0102	Human Whole 6 Week Old Embryo (II), subt	Human Whole Six Week Old Embryo	Embryo			pBluescript
H0105	Human Fetal Heart, subtracted	Human Fetal Heart	Heart			pBluescript
H0109	Human Macrophage, subtracted	Macrophage	Blood	Cell Line		pBluescript
H0111	Human Placenta, subtracted	Human Placenta	Placenta			pBluescript
H0112	Human Parathyroid Tumor, subtracted	Human Parathyroid Tumor	Parathyroid			pBluescript
H0116	Human Thymus Tumor, subtracted	Human Thymus Tumor	Thymus			pBluescript
H0123	Human Fetal Dura Mater	Human Fetal Dura Mater	Brain			Uni-ZAP XR
H0124	Human Rhabdomyosarcoma	Human Rhabdomyosarcoma	Sk Muscle		disease	Uni-ZAP XR
H0125	Cem cells cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0130	LNCAP untreated	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0131	LNCAP + 0.3nM R1881	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
H0134	Raji Cells, cyclohexamide treated	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0135	Human Synovial Sarcoma	Human Synovial Sarcoma	Synovium			Uni-ZAP XR
H0139	Activated T-Cells, 4 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0141	Activated T-Cells, 12 hrs.	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0144	Nine Week Old Early Stage Human	9 Wk Old Early Stage Human	Embryo			Uni-ZAP XR
H0149	7 Week Old Early Stage Human, subtracted	Human Whole 7 Week Old Embryo	Embryo			Uni-ZAP XR
H0150	Human Epididymus	Epididymis	Testis			Uni-ZAP XR
H0156	Human Adrenal Gland Tumor	Human Adrenal Gland Tumor	Adrenal Gland		disease	Uni-ZAP XR
H0159	Activated T-Cells, 8 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0161	Activated T-Cells, 24 hrs., ligation 2	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0163	Human Synovium	Human Synovium	Synovium			Uni-ZAP XR
H0165	Human Prostate Cancer, Stage B2	Human Prostate Cancer, stage B2	Prostate		disease	Uni-ZAP XR
H0169	Human Prostate Cancer, Stage C fraction	Human Prostate Cancer, stage C	Prostate		disease	Uni-ZAP XR
H0170	12 Week Old Early Stage Human	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0171	12 Week Old Early Stage Human, II	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0178	Human Fetal Brain	Human Fetal Brain	Brain			Uni-ZAP XR
H0179	Human Neutrophil	Human Neutrophil	Blood	Cell Line		Uni-ZAP XR
H0180	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0181	Human Primary Breast	Human Primary	Breast		disease	Uni-ZAP XR

	Cancer	Breast Cancer				
H0182	Human Primary Breast Cancer	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0184	Human Colon Cancer, metastasized to liver	Human Colon Cancer, metastasized to liver	Liver		disease	Lambda ZAP II
H0187	Resting T-Cell	T-Cells	Blood	Cell Line		Lambda ZAP II
H0188	Human Normal Breast	Human Normal Breast	Breast			Uni-ZAP XR
H0189	Human Resting Macrophage	Human Macrophage/Monocytes	Blood	Cell Line		Uni-ZAP XR
H0191	Human Activated Macrophage (LPS), thior	Human Macrophage/Monocytes	Blood	Cell Line		Uni-ZAP XR
H0192	Cem Cells, cyclohexamide treated, subtra	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		Uni-ZAP XR
H0194	Human Cerebellum, subtracted	Human Cerebellum	Brain			pBluescript
H0196	Human Cardiomyopathy, subtracted	Human Cardiomyopathy	Heart			Uni-ZAP XR
H0204	Human Colon Cancer, subtracted	Human Colon Cancer	Colon			pBluescript
H0205	Human Colon Cancer, differential	Human Colon Cancer	Colon			pBluescript
H0208	Early Stage Human Lung, subtracted	Human Fetal Lung	Lung			pBluescript
H0212	Human Prostate, subtracted	Human Prostate	Prostate			pBluescript
H0213	Human Pituitary, subtracted	Human Pituitary				Uni-ZAP XR
H0214	Raji cells, cyclohexamide treated, subtracted	Cyclohexamide Treated Cem, Jurkat, Raji, and Supt	Blood	Cell Line		pBluescript
H0224	Activated T-Cells, 12 hrs, subtracted	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0225	Activated T-Cells, 12hrs, differentially expressed	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0231	Human Colon, subtraction	Human Colon				pBluescript
H0235	Human colon cancer, metastasized to liver, subtraction	Human Colon Cancer, metastasized to liver	Liver			pBluescript
H0244	Human 8 Week Whole Embryo, subtracted	Human 8 Week Old Embryo	Embryo			Uni-ZAP XR
H0247	Human Membrane Bound Polysomes- Enzyme Subtraction	Human Membrane Bound Polysomes	Blood	Cell Line		Uni-ZAP XR
H0250	Human Activated Monocytes	Human Monocytes				Uni-ZAP XR
H0251	Human Chondrosarcoma	Human Chondrosarcoma	Cartilage		disease	Uni-ZAP XR
H0252	Human Osteosarcoma	Human	Bone		disease	Uni-ZAP XR

		Osteosarcoma				
H0253	Human adult testis, large inserts	Human Adult Testis	Testis			Uni-ZAP XR
H0254	Breast Lymph node cDNA library	Breast Lymph Node	Lymph Node			Uni-ZAP XR
H0255	breast lymph node CDNA library	Breast Lymph Node	Lymph Node			Lambda ZAP II
H0257	HL-60, PMA 4H	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0261	H. cerebellum, Enzyme subtracted	Human Cerebellum	Brain			Uni-ZAP XR
H0263	human colon cancer	Human Colon Cancer	Colon		disease	Lambda ZAP II
H0264	human tonsils	Human Tonsil	Tonsil			Uni-ZAP XR
H0265	Activated T-Cell (12hs)/Thiouridine labelledEco	T-Cells	Blood	Cell Line		Uni-ZAP XR
H0266	Human Microvascular Endothelial Cells, fract. A	HMEC	Vein	Cell Line		Lambda ZAP II
H0268	Human Umbilical Vein Endothelial Cells, fract. A	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0271	Human Neutrophil, Activated	Human Neutrophil - Activated	Blood	Cell Line		Uni-ZAP XR
H0274	Human Adult Spleen, fractionII	Human Adult Spleen	Spleen			Uni-ZAP XR
H0280	K562 + PMA (36 hrs)	K562 Cell line	cell line	Cell Line		ZAP Express
H0284	Human OB MG63 control fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0286	Human OB MG63 treated (10 nM E2) fraction I	Human Osteoblastoma MG63 cell line	Bone	Cell Line		Uni-ZAP XR
H0290	Human OB HOS treated (1 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0292	Human OB HOS treated (10 nM E2) fraction I	Human Osteoblastoma HOS cell line	Bone	Cell Line		Uni-ZAP XR
H0294	Amniotic Cells - TNF induced	Amniotic Cells - TNF induced	Placenta	Cell Line		Uni-ZAP XR
H0300	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0305	CD34 positive cells (Cord Blood)	CD34 Positive Cells	Cord Blood			ZAP Express
H0306	CD34 depleted Buffy Coat (Cord Blood)	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0309	Human Chronic Synovitis	Synovium, Chronic Synovitis/ Osteoarthritis	Synovium		disease	Uni-ZAP XR
H0316	HUMAN STOMACH	Human Stomach	Stomach			Uni-ZAP XR
H0318	HUMAN B CELL LYMPHOMA	Human B Cell Lymphoma	Lymph Node		disease	Uni-ZAP XR



H0327	human corpus colosum	Human Corpus Callosum	Brain			Uni-ZAP XR
H0328	human ovarian cancer	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0329	Dermatofibrosarcoma Protuberance	Dermatofibrosarcoma Protuberans	Skin		disease	Uni-ZAP XR
H0331	Hepatocellular Tumor	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0333	Hemangiopericytoma	Hemangiopericytoma	Blood vessel		disease	Lambda ZAP II
H0334	Kidney cancer	Kidney Cancer	Kidney		disease	Uni-ZAP XR
H0341	Bone Marrow Cell Line (RS4;11)	Bone Marrow Cell Line RS4;11	Bone Marrow	Cell Line		Uni-ZAP XR
H0342	Lingual Gyrus	Lingual Gyrus	Brain			Uni-Zap XR
H0343	stomach cancer (human)	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0344	Adipose tissue (human)	Adipose - 6825A (human)				Uni-ZAP XR
H0345	SKIN	Skin - 4000868H	Skin			Uni-ZAP XR
H0349	human adult liver cDNA library	Human Adult Liver	Liver			pCMVSPORT 1
H0351	Glioblastoma	Glioblastoma	Brain		disease	Uni-ZAP XR
H0352	wilm's tumor	Wilm's Tumor			disease	Uni-ZAP XR
H0354	Human Leukocytes	Human Leukocytes	Blood	Cell Line		pCMVSPORT 1
H0355	Human Liver	Human Liver, normal Adult				pCMVSPORT 1
H0361	Human rejected kidney	Human Rejected Kidney			disease	pBluescript
H0366	L428 cell line	L428				ZAP Express
H0369	H. Atrophic Endometrium	Atrophic Endometrium and myometrium				Uni-ZAP XR
H0370	H. Lymph node breast Cancer	Lymph node with Met. Breast Cancer			disease	Uni-ZAP XR
H0372	Human Testes	Human Testes	Testis			pCMVSPORT 1
H0373	Human Heart	Human Adult Heart	Heart			pCMVSPORT 1
H0375	Human Lung	Human Lung				pCMVSPORT 1
H0376	Human Spleen	Human Adult Spleen	Spleen			pCMVSPORT 1
H0388	Human Rejected Kidney, 704 re-excision	Human Rejected Kidney			disease	pBluescript
H0390	Human Amygdala Depression, re-excision	Human Amygdala Depression			disease	pBluescript
H0391	H. Meningioma, M6	Human Meningioma	brain			pSport1
H0392	H. Meningioma, M1	Human Meningioma	brain			pSport1
H0393	Fetal Liver, subtraction II	Human Fetal Liver	Liver			pBluescript
H0394	A-14 cell line	Redd-Sternberg cell				ZAP Express
H0395	A1-CELL LINE	Redd-Sternberg cell				ZAP Express
H0396	L1 Cell line	Redd-Sternberg cell				ZAP Express
H0402	CD34 depleted Buffy Coat (Cord Blood), re-excision	CD34 Depleted Buffy Coat (Cord Blood)	Cord Blood			ZAP Express
H0403	H. Umbilical Vein	HUVE Cells	Umbilical	Cell Line		Uni-ZAP XR

	Endothelial Cells, IL4 induced		vein			
H0409	H. Striatum Depression, subtracted	Human Brain, Striatum Depression	Brain			pBluescript
H0411	H Female Bladder, Adult	Human Female Adult Bladder	Bladder			pSport1
H0412	Human umbilical vein endothelial cells, IL-4 induced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0413	Human Umbilical Vein Endothelial Cells, uninduced	HUVE Cells	Umbilical vein	Cell Line		pSport1
H0415	H. Ovarian Tumor, II, OV5232	Ovarian Tumor, OV5232	Ovary		disease	pCMVSPORT 2.0
H0416	Human Neutrophils, Activated, re-excision	Human Neutrophil - Activated	Blood	Cell Line		pBluescript
H0421	Human Bone Marrow, re-excision	Bone Marrow				pBluescript
H0422	T-Cell PHA 16 hrs	T-Cells	Blood	Cell Line		pSport1
H0423	T-Cell PHA 24 hrs	T-Cells	Blood	Cell Line		pSport1
H0424	Human Pituitary, subt IX	Human Pituitary				pBluescript
H0427	Human Adipose	Human Adipose, left hiplipoma				pSport1
H0428	Human Ovary	Human Ovary Tumor	Ovary			pSport1
H0431	H. Kidney Medulla, re-excision	Kidney medulla	Kidney			pBluescript
H0433	Human Umbilical Vein Endothelial cells, frac B, re-excision	HUVE Cells	Umbilical vein	Cell Line		pBluescript
H0434	Human Brain, striatum, re-excision	Human Brain, Striatum				pBluescript
H0435	Ovarian Tumor 10-3-95	Ovarian Tumor, OV350721	Ovary			pCMVSPORT 2.0
H0436	Resting T-Cell Library,II	T-Cells	Blood	Cell Line		pSport1
H0437	H Umbilical Vein Endothelial Cells, frac A, re-excision	HUVE Cells	Umbilical vein	Cell Line		Lambda ZAP II
H0438	H. Whole Brain #2, re-excision	Human Whole Brain #2				ZAP Express
H0439	Human Eosinophils	Eosinophils				pBluescript
H0441	H. Kidney Cortex, subtracted	Kidney cortex	Kidney			pBluescript
H0442	H. Striatum Depression, subt II	Human Brain, Striatum Depression	Brain			pBluescript
H0444	Spleen metastatic melanoma	Spleen, Metastatic malignant melanoma	Spleen		disease	pSport1
H0445	Spleen, Chronic lymphocytic leukemia	Human Spleen, CLL	Spleen		disease	pSport1
H0455	H. Striatum Depression, subt	Human Brain, Striatum Depression	Brain			pBluescript
H0457	Human Eosinophils	Human Eosinophils				pSport1

H0459	CD34+ cells, II, FRACTION 2	CD34 positive cells				pCMVSPORT 2.0
H0477	Human Tonsil, Lib 3	Human Tonsil	Tonsil			pSport1
H0478	Salivary Gland, Lib 2	Human Salivary Gland	Salivary gland			pSport1
H0483	Breast Cancer cell line, MDA 36	Breast Cancer Cell line, MDA 36				pSport1
H0484	Breast Cancer Cell line, angiogenic	Breast Cancer Cell line, Angiogenic, 36T3				pSport1
H0485	Hodgkin's Lymphoma I	Hodgkin's Lymphoma I			disease	pCMVSPORT 2.0
H0486	Hodgkin's Lymphoma II	Hodgkin's Lymphoma II			disease	pCMVSPORT 2.0
H0487	Human Tonsils, lib I	Human Tonsils				pCMVSPORT 2.0
H0488	Human Tonsils, Lib 2	Human Tonsils				pCMVSPORT 2.0
H0489	Crohn's Disease	Ileum	Intestine		disease	pSport1
H0492	HL-60, RA 4h, Subtracted	HL-60 Cells, RA stimulated for 4H	Blood	Cell Line		Uni-ZAP XR
H0494	Keratinocyte	Keratinocyte				pCMVSPORT 2.0
H0497	HEL cell line	HEL cell line		HEL 92.1.7		pSport1
H0505	Human Astrocyte	Human Astrocyte				pSport1
H0506	Ulcerative Colitis	Colon	Colon			pSport1
H0509	Liver, Hepatoma	Human Liver, Hepatoma, patient 8	Liver		disease	pCMVSPORT 3.0
H0510	Human Liver, normal	Human Liver, normal, Patient # 8	Liver			pCMVSPORT 3.0
H0518	pBMC stimulated w/ poly I/C	pBMC stimulated with poly I/C				pCMVSPORT 3.0
H0519	NTERA2, control	NTERA2, Teratocarcinoma cell line				pCMVSPORT 3.0
H0520	NTERA2 + retinoic acid, 14 days	NTERA2, Teratocarcinoma cell line				pSport1
H0521	Primary Dendritic Cells, lib 1	Primary Dendritic cells				pCMVSPORT 3.0
H0522	Primary Dendritic cells, frac 2	Primary Dendritic cells				pCMVSPORT 3.0
H0529	Myeloid Progenitor Cell Line	TF-1 Cell Line; Myeloid progenitor cell line				pCMVSPORT 3.0
H0538	Merkel Cells	Merkel cells	Lymph node			pSport1
H0539	Pancreas Islet Cell Tumor	Pancreas Islet Cell Tumour	Pancreas		disease	pSport1
H0542	T Cell helper I	Helper T cell				pCMVSPORT 3.0
H0543	T cell helper II	Helper T cell				pCMVSPORT 3.0
H0544	Human endometrial stromal cells	Human endometrial stromal cells				pCMVSPORT 3.0
H0545	Human endometrial stromal cells-treated with progesterone	Human endometrial stromal cells-treated with proge				pCMVSPORT 3.0



H0546	Human endometrial stromal cells-treated with estradiol	Human endometrial stromal cells-treated with estra				pCMV Sport 3.0
H0547	NTERA2 teratocarcinoma cell line+retinoic acid (14 days)	NTERA2, Teratocarcinoma cell line				pSport1
H0549	H. Epididymus, caput & corpus	Human Epididymus, caput and corpus				Uni-ZAP XR
H0550	H. Epididymus, cauda	Human Epididymus, cauda				Uni-ZAP XR
H0551	Human Thymus Stromal Cells	Human Thymus Stromal Cells				pCMV Sport 3.0
H0553	Human Placenta	Human Placenta				pCMV Sport 3.0
H0555	Rejected Kidney, lib 4	Human Rejected Kidney	Kidney		disease	pCMV Sport 3.0
H0556	Activated T-cell(12h)/Thiouridine-re-excision	T-Cells	Blood	Cell Line		Uni-ZAP XR
H0559	HL-60, PMA 4H, re-excision	HL-60 Cells, PMA stimulated 4H	Blood	Cell Line		Uni-ZAP XR
H0560	KMH2	KMH2				pCMV Sport 3.0
H0561	L428	L428				pCMV Sport 3.0
H0567	Human Fetal Brain, normalized A5002F	Human Fetal Brain				pCMV Sport 2.0
H0570	Human Fetal Brain, normalized C500H	Human Fetal Brain				pCMV Sport 2.0
H0571	Human Fetal Brain, normalized C500HE	Human Fetal Brain				pCMV Sport 2.0
H0574	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver		disease	Lambda ZAP II
H0575	Human Adult Pulmonary;re-excision	Human Adult Pulmonary	Lung			Uni-ZAP XR
H0576	Resting T-Cell; re-excision	T-Cells	Blood	Cell Line		Lambda ZAP II
H0579	Pericardium	Pericardium	Heart			pSport1
H0580	Dendritic cells, pooled	Pooled dendritic cells				pCMV Sport 3.0
H0581	Human Bone Marrow, treated	Human Bone Marrow	Bone Marrow			pCMV Sport 3.0
H0583	B Cell lymphoma	B Cell Lymphoma	B Cell		disease	pCMV Sport 3.0
H0584	Activated T-cells, 24 hrs,re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0585	Activated T-Cells,12 hrs,re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0586	Healing groin wound, 6.5 hours post incision	healing groin wound, 6.5 hours post incision - 2/	groin		disease	pCMV Sport 3.0
H0587	Healing groin wound; 7.5 hours post incision	Groin-2/19/97	groin		disease	pCMV Sport 3.0
H0590	Human adult small intestine,re-excision	Human Adult Small Intestine	Small Int.			Uni-ZAP XR
H0591	Human T-cell	T-Cell Lymphoma	T-Cell		disease	Uni-ZAP XR

	lymphoma;re-excision					
H0592	Healing groin wound - zero hr post-incision (control)	HGS wound healing project; abdomen			disease	pCMVSPORT 3.0
H0593	Olfactory epithelium;nasalcavity	Olfactory epithelium from roof of left nasal cavity				pCMVSPORT 3.0
H0594	Human Lung Cancer;re-excision	Human Lung Cancer	Lung		disease	Lambda ZAP II
H0595	Stomach cancer (human);re-excision	Stomach Cancer - 5383A (human)			disease	Uni-ZAP XR
H0596	Human Colon Cancer;re-excision	Human Colon Cancer	Colon			Lambda ZAP II
H0597	Human Colon; re-excision	Human Colon				Lambda ZAP II
H0598	Human Stomach;re-excision	Human Stomach	Stomach			Uni-ZAP XR
H0599	Human Adult Heart;re-excision	Human Adult Heart	Heart			Uni-ZAP XR
H0600	Healing Abdomen wound;70&90 min post incision	Abdomen			disease	pCMVSPORT 3.0
H0601	Healing Abdomen Wound;15 days post incision	Abdomen			disease	pCMVSPORT 3.0
H0604	Human Pituitary, re-excision	Human Pituitary				pBluescript
H0606	Human Primary Breast Cancer;re-excision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0608	H. Leukocytes, control	H.Leukocytes				pCMVSPORT 1
H0615	Human Ovarian Cancer Reexcision	Ovarian Cancer	Ovary		disease	Uni-ZAP XR
H0616	Human Testes, Reexcision	Human Testes	Testis			Uni-ZAP XR
H0617	Human Primary Breast Cancer Reexcision	Human Primary Breast Cancer	Breast		disease	Uni-ZAP XR
H0618	Human Adult Testes, Large Inserts, Reexcision	Human Adult Testis	Testis			Uni-ZAP XR
H0619	Fetal Heart	Human Fetal Heart	Heart			Uni-ZAP XR
H0620	Human Fetal Kidney; Reexcision	Human Fetal Kidney	Kidney			Uni-ZAP XR
H0622	Human Pancreas Tumor; Reexcision	Human Pancreas Tumor	Pancreas		disease	Uni-ZAP XR
H0623	Human Umbilical Vein; Reexcision	Human Umbilical Vein Endothelial Cells	Umbilical vein			Uni-ZAP XR
H0624	12 Week Early Stage Human II; Reexcision	Twelve Week Old Early Stage Human	Embryo			Uni-ZAP XR
H0625	Ku 812F Basophils Line	Ku 812F Basophils				pSport1
H0626	Saos2 Cells; Untreated	Saos2 Cell Line; Untreated				pSport1
H0628	Human Pre-Differentiated Adipocytes	Human Pre-Differentiated Adipocytes				Uni-ZAP XR
H0629	Human Leukocyte, control	Human Normalized				pCMVSPORT 1

	#2	leukocyte				
H0630	Human Leukocytes, normalized control #4	Human Normalized leukocyte				pCMVSPORT 1
H0631	Saos2, Dexamethosome Treated	Saos2 Cell Line; Dexamethosome Treated				pSport1
H0632	Hepatocellular Tumor; re-excision	Hepatocellular Tumor	Liver			Lambda ZAP II
H0633	Lung Carcinoma A549 TNFalpha activated	TNFalpha activated A549--Lung Carcinoma			disease	pSport1
H0634	Human Testes Tumor, re-excision	Human Testes Tumor	Testis		disease	Uni-ZAP XR
H0635	Human Activated T-Cells, re-excision	Activated T-Cells	Blood	Cell Line		Uni-ZAP XR
H0638	CD40 activated monocyte dendritic cells	CD40 activated monocyte dendritic cells				pSport1
H0640	Ficoll Human Stromal Cells, Untreated	Ficoll Human Stromal Cells, Untreated				Other
H0641	LPS activated derived dendritic cells	LPS activated monocyte derived dendritic cells				pSport1
H0642	Hep G2 Cells, lambda library	Hep G2 Cells				Other
H0643	Hep G2 Cells, PCR library	Hep G2 Cells				Other
H0644	Human Placenta (re-excision)	Human Placenta	Placenta			Uni-ZAP XR
H0645	Fetal Heart, re-excision	Human Fetal Heart	Heart			Uni-ZAP XR
H0646	Lung, Cancer (4005313 A3): Invasive Poorly Differentiated Lung Adenocarcinoma,	Metastatic squamous cell lung carcinoma, poorly di				pSport1
H0647	Lung, Cancer (4005163 B7): Invasive, Poorly Diff. Adenocarcinoma, Metastatic	Invasive poorly differentiated lung adenocarcinoma			disease	pSport1
H0648	Ovary, Cancer: (4004562 B6) Papillary Serous Cystic Neoplasm, Low Malignant Pot	Papillary Cstic neoplasm of low malignant potentia			disease	pSport1
H0649	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0650	B-Cells	B-Cells				pCMVSPORT 3.0
H0651	Ovary, Normal: (9805C040R)	Normal Ovary				pSport1
H0652	Lung, Normal: (4005313 B1)	Normal Lung				pSport1
H0653	Stromal Cells	Stromal Cells				pSport1
H0654	Lung, Cancer: (4005313 A3) Invasive Poorly-	Metastatic Squamous cell lung				Other



	differentiated Metastatic lung adenoc	Carcinoma poorly dif				
H0656	B-cells (unstimulated)	B-cells (unstimulated)				pSport1
H0657	B-cells (stimulated)	B-cells (stimulated)				pSport1
H0658	Ovary, Cancer (9809C332): Poorly differentiated adenocarcinoma	9809C332- Poorly differentiate	Ovary & Fallopian Tubes		disease	pSport1
H0659	Ovary, Cancer (15395A1F): Grade II Papillary Carcinoma	Grade II Papillary Carcinoma, Ovary	Ovary		disease	pSport1
H0660	Ovary, Cancer: (15799A1F) Poorly differentiated carcinoma	Poorly differentiated carcinoma, ovary			disease	pSport1
H0661	Breast, Cancer: (4004943 A5)	Breast cancer			disease	pSport1
H0662	Breast, Normal: (4005522B2)	Normal Breast - #4005522(B2)	Breast			pSport1
H0663	Breast, Cancer: (4005522 A2)	Breast Cancer - #4005522(A2)	Breast		disease	pSport1
H0664	Breast, Cancer: (9806C012R)	Breast Cancer	Breast		disease	pSport1
H0665	Stromal cells 3.88	Stromal cells 3.88				pSport1
H0666	Ovary, Cancer: (4004332 A2)	Ovarian Cancer, Sample #4004332A2			disease	pSport1
H0667	Stromal cells(HBM3.18)	Stromal cell(HBM 3.18)				pSport1
H0668	stromal cell clone 2.5	stromal cell clone 2.5				pSport1
H0670	Ovary, Cancer(4004650 A3): Well-Differentiated Micropapillary Serous Carcinoma	Ovarian Cancer - 4004650A3				pSport1
H0671	Breast, Cancer: (9802C020E)	Breast Cancer- Sample # 9802C020E				pSport1
H0672	Ovary, Cancer: (4004576 A8)	Ovarian Cancer(4004576A8)	Ovary			pSport1
H0673	Human Prostate Cancer, Stage B2; re-excision	Human Prostate Cancer, stage B2	Prostate			Uni-ZAP XR
H0674	Human Prostate Cancer, Stage C; re-excision	Human Prostate Cancer, stage C	Prostate			Uni-ZAP XR
H0675	Colon, Cancer: (9808C064R)	Colon Cancer 9808C064R				pCMVSPORT 3.0
H0677	TNFR degenerate oligo	B-Cells				PCR II
H0682	Serous Papillary Adenocarcinoma	serous papillary adenocarcinoma (9606G304SPA3B)				pCMVSPORT 3.0
H0683	Ovarian Serous Papillary Adenocarcinoma	Serous papillary adenocarcinoma, stage 3C (9804G01				pCMVSPORT 3.0

H0684	Serous Papillary Adenocarcinoma	Ovarian Cancer-9810G606	Ovaries			pCMV Sport 3.0
H0685	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-3	Adenocarcinoma of Ovary, Human Cell Line, # OVCAR-				pCMV Sport 3.0
H0686	Adenocarcinoma of Ovary, Human Cell Line	Adenocarcinoma of Ovary, Human Cell Line, # SW-626				pCMV Sport 3.0
H0687	Human normal ovary(#9610G215)	Human normal ovary(#9610G215)	Ovary			pCMV Sport 3.0
H0688	Human Ovarian Cancer(#9807G017)	Human Ovarian cancer(#9807G017), mRNA from Maura Ru				pCMV Sport 3.0
H0689	Ovarian Cancer	Ovarian Cancer, #9806G019				pCMV Sport 3.0
H0690	Ovarian Cancer, #9702G001	Ovarian Cancer, #9702G001				pCMV Sport 3.0
H0691	Normal Ovary, #9710G208	normal ovary, #9710G208				pCMV Sport 3.0
H0693	Normal Prostate #ODQ3958EN	Normal Prostate Tissue # ODQ3958EN				pCMV Sport 3.0
H0694	Prostate gland adenocarcinoma	Prostate gland, adenocarcinoma, mod/diff, gleason	prostate gland			pCMV Sport 3.0
H0695	mononucleocytes from patient	mononucleocytes from patient at Shady Grove Hospit				pCMV Sport 3.0
N0006	Human Fetal Brain	Human Fetal Brain				
N0009	Human Hippocampus, prescreened	Human Hippocampus				
S0002	Monocyte activated	Monocyte-activated	blood	Cell Line		Uni-ZAP XR
S0003	Human Osteoclastoma	Osteoclastoma	bone		disease	Uni-ZAP XR
S0005	Heart	Heart-left ventricle	Heart			pCDNA
S0007	Early Stage Human Brain	Human Fetal Brain				Uni-ZAP XR
S0010	Human Amygdala	Amygdala				Uni-ZAP XR
S0011	STROMAL - OSTEOCLASTOMA	Osteoclastoma	bone		disease	Uni-ZAP XR
S0022	Human Osteoclastoma Stromal Cells - unamplified	Osteoclastoma Stromal Cells				Uni-ZAP XR
S0024	Human Kidney Medulla - unamplified	Human Kidney Medulla				
S0026	Stromal cell TF274	stromal cell	Bone marrow	Cell Line		Uni-ZAP XR
S0027	Smooth muscle, serum treated	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0028	Smooth muscle, control	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0029	brain stem	Brain stem	brain			Uni-ZAP XR
S0031	Spinal cord	Spinal cord	spinal cord			Uni-ZAP XR
S0032	Smooth muscle-ILb induced	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR



S0036	Human Substantia Nigra	Human Substantia Nigra				Uni-ZAP XR
S0037	Smooth muscle, IL1b induced	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0038	Human Whole Brain #2 - Oligo dT > 1.5Kb	Human Whole Brain #2				ZAP Express
S0040	Adipocytes	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0044	Prostate BPH	prostate BPH	Prostate		disease	Uni-ZAP XR
S0045	Endothelial cells-control	Endothelial cell	endothelial cell-lung	Cell Line		Uni-ZAP XR
S0046	Endothelial-induced	Endothelial cell	endothelial cell-lung	Cell Line		Uni-ZAP XR
S0049	Human Brain, Striatum	Human Brain, Striatum				Uni-ZAP XR
S0050	Human Frontal Cortex, Schizophrenia	Human Frontal Cortex, Schizophrenia			disease	Uni-ZAP XR
S0051	Human Hypothalamus, Schizophrenia	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0052	neutrophils control	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0053	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0106	STRIATUM DEPRESSION		BRAIN		disease	Uni-ZAP XR
S0114	Anergic T-cell	Anergic T-cell		Cell Line		Uni-ZAP XR
S0116	Bone marrow	Bone marrow	Bone marrow			Uni-ZAP XR
S0118	Smooth muscle control 2	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0122	Osteoclastoma-normalized A	Osteoclastoma	bone		disease	pBluescript
S0126	Osteoblasts	Osteoblasts	Knee	Cell Line		Uni-ZAP XR
S0132	Epithelial-TNF $\alpha$ and INF induced	Airway Epithelial				Uni-ZAP XR
S0134	Apoptotic T-cell	apoptotic cells		Cell Line		Uni-ZAP XR
S0140	eosinophil-IL5 induced	eosinophil	lung	Cell Line		Uni-ZAP XR
S0142	Macrophage-oxLDL	macrophage-oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0144	Macrophage (GM-CSF treated)	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0146	prostate-edited	prostate BPH	Prostate			Uni-ZAP XR
S0148	Normal Prostate	Prostate	prostate			Uni-ZAP XR
S0150	LNCAP prostate cell line	LNCAP Cell Line	Prostate	Cell Line		Uni-ZAP XR
S0152	PC3 Prostate cell line	PC3 prostate cell line				Uni-ZAP XR
S0174	Prostate-BPH subtracted II	Human Prostate BPH				pBluescript
S0182	Human B Cell 8866	Human B- Cell 8866				Uni-ZAP XR
S0188	Prostate,BPH, Lib 2	Human Prostate BPH			disease	pSport1
S0190	Prostate BPH,Lib 2,	Human Prostate				pSport1



	subtracted	BPH				
S0192	Synovial Fibroblasts (control)	Synovial Fibroblasts				pSport1
S0194	Synovial hypoxia	Synovial Fibroblasts				pSport1
S0196	Synovial IL-1/TNF stimulated	Synovial Fibroblasts				pSport1
S0206	Smooth Muscle- HASTE normalized	Smooth muscle	Pulmonary artery	Cell Line		pBluescript
S0210	Messangial cell, frac 2	Messangial cell				pSport1
S0212	Bone Marrow Stromal Cell, untreated	Bone Marrow Stromal Cell, untreated				pSport1
S0214	Human Osteoclastoma, re-excision	Osteoclastoma	bone		disease	Uni-ZAP XR
S0216	Neutrophils IL-1 and LPS induced	human neutrophil induced	blood	Cell Line		Uni-ZAP XR
S0218	Apoptotic T-cell, re-excision	apoptotic cells		Cell Line		Uni-ZAP XR
S0222	H. Frontal cortex, epileptic; re-excision	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S0242	Synovial Fibroblasts (II1/TNF), subt	Synovial Fibroblasts				pSport1
S0250	Human Osteoblasts II	Human Osteoblasts	Femur		disease	pCMV Sport 2.0
S0260	Spinal Cord, re-excision	Spinal cord	spinal cord			Uni-ZAP XR
S0276	Synovial hypoxia-RSF subtracted	Synovial fibroblasts (rheumatoid)	Synovial tissue			pSport1
S0278	H Macrophage (GM-CSF treated), re-excision	Macrophage (GM-CSF treated)				Uni-ZAP XR
S0280	Human Adipose Tissue, re-excision	Human Adipose Tissue				Uni-ZAP XR
S0282	Brain Frontal Cortex, re-excision	Brain frontal cortex	Brain			Lambda ZAP II
S0294	Larynx tumor	Larynx tumor	Larynx, vocal cord		disease	pSport1
S0300	Frontal lobe, dementia; re-excision	Frontal Lobe dementia/Alzheimer's	Brain			Uni-ZAP XR
S0306	Larynx normal #10 261-273	Larynx normal				pSport1
S0308	Spleen/normal	Spleen normal				pSport1
S0312	Human osteoarthritic; fraction II	Human osteoarthritic cartilage			disease	pSport1
S0314	Human osteoarthritis; fraction I	Human osteoarthritic cartilage			disease	pSport1
S0316	Human Normal Cartilage, Fraction I	Human Normal Cartilage				pSport1
S0322	Siebben Polyposis	Siebben Polyposis				pSport1
S0328	Palate carcinoma	Palate carcinoma	Uvula		disease	pSport1
S0330	Palate normal	Palate normal	Uvula			pSport1
S0332	Pharynx carcinoma	Pharynx carcinoma	Hypopharynx			pSport1

S0342	Adipocytes;re-excision	Human Adipocytes from Osteoclastoma				Uni-ZAP XR
S0344	Macrophage-oxLDL; re- excision	macrophage- oxidized LDL treated	blood	Cell Line		Uni-ZAP XR
S0346	Human Amygdala;re- excision	Amygdala				Uni-ZAP XR
S0350	Pharynx Carcinoma	Pharynx carcinoma	Hypopharynx		disease	pSport1
S0352	Larynx Carcinoma	Larynx carcinoma			disease	pSport1
S0354	Colon Normal II	Colon Normal	Colon			pSport1
S0356	Colon Carcinoma	Colon Carcinoma	Colon		disease	pSport1
S0358	Colon Normal III	Colon Normal	Colon			pSport1
S0360	Colon Tumor II	Colon Tumor	Colon		disease	pSport1
S0364	Human Quadriceps	Quadriceps muscle				pSport1
S0366	Human Soleus	Soleus Muscle				pSport1
S0370	Larynx carcinoma II	Larynx carcinoma			disease	pSport1
S0372	Larynx carcinoma III	Larynx carcinoma			disease	pSport1
S0374	Normal colon	Normal colon				pSport1
S0376	Colon Tumor	Colon Tumor			disease	pSport1
S0378	Pancreas normal PCA4 No	Pancreas Normal PCA4 No				pSport1
S0380	Pancreas Tumor PCA4 Tu	Pancreas Tumor PCA4 Tu			disease	pSport1
S0382	Larynx carcinoma IV	Larynx carcinoma			disease	pSport1
S0384	Tongue carcinoma	Tongue carcinoma			disease	pSport1
S0388	Human Hypothalamus,schizophre nia, re-excision	Human Hypothalamus, Schizophrenia			disease	Uni-ZAP XR
S0390	Smooth muscle, control; re-excision	Smooth muscle	Pulmonary artery	Cell Line		Uni-ZAP XR
S0392	Salivary Gland	Salivary gland; normal				pSport1
S0400	Brain; normal	Brain; normal				pSport1
S0402	Adrenal Gland,normal	Adrenal gland; normal				pSport1
S0404	Rectum normal	Rectum, normal				pSport1
S0406	Rectum tumour	Rectum tumour				pSport1
S0408	Colon, normal	Colon, normal				pSport1
S0410	Colon, tumour	Colon, tumour				pSport1
S0414	Hippocampus, Alzheimer Subtracted	Hippocampus, Alzheimer Subtracted				Other
S0418	CHME Cell Line;treated 5 hrs	CHME Cell Line; treated				pCMV Sport 3.0
S0420	CHME Cell Line,untreated	CHME Cell line, untreated				pSport1
S0422	Mo7e Cell Line GM-CSF treated (1ng/ml)	Mo7e Cell Line GM-CSF treated (1ng/ml)				pCMV Sport 3.0
S0424	TF-1 Cell Line GM-CSF Treated	TF-1 Cell Line GM-CSF Treated				pSport1
S0426	Monocyte activated; re-	Monocyte-activated	blood	Cell Line		Uni-ZAP XR



	excision					
S0428	Neutrophils control; re-excision	human neutrophils	blood	Cell Line		Uni-ZAP XR
S0432	Sinus piniformis Tumour	Sinus piniformis Tumour				pSport1
S0434	Stomach Normal	Stomach Normal			disease	pSport1
S0436	Stomach Tumour	Stomach Tumour			disease	pSport1
S0438	Liver Normal Met5No	Liver Normal Met5No				pSport1
S0440	Liver Tumour Met 5 Tu	Liver Tumour				pSport1
S0442	Colon Normal	Colon Normal				pSport1
S0444	Colon Tumor	Colon Tumour			disease	pSport1
S0446	Tongue Tumour	Tongue Tumour				pSport1
S0452	Thymus	Thymus				pSport1
S0456	Tongue Normal	Tongue Normal				pSport1
S0458	Thyroid Normal (SDCA2 No)	Thyroid normal				pSport1
S0460	Thyroid Tumour	Thyroid Tumour				pSport1
S0462	Thyroid Thyroiditis	Thyroid Thyroiditis				pSport1
S0466	Larynx Tumor	Larynx Tumor			disease	pSport1
S0468	Ea.hy.926 cell line	Ea.hy.926 cell line				pSport1
S0470	Adenocarcinoma	PYFD			disease	pSport1
S0474	Human blood platelets	Platelets	Blood platelets			Other
S0665	Human Amygdala; re-excision	Amygdala				Uni-ZAP XR
S3012	Smooth Muscle Serum Treated, Norm	Smooth muscle	Pulmonary artery	Cell Line		pBluescript
S3014	Smooth muscle, serum induced, re-exc	Smooth muscle	Pulmonary artery	Cell Line		pBluescript
S6016	H. Frontal Cortex, Epileptic	H. Brain, Frontal Cortex, Epileptic	Brain		disease	Uni-ZAP XR
S6024	Alzheimers, spongy change	Alzheimer's/Spongy change	Brain		disease	Uni-ZAP XR
S6026	Frontal Lobe, Dementia	Frontal Lobe dementia/Alzheimer's	Brain			Uni-ZAP XR
S6028	Human Manic Depression Tissue	Human Manic depression tissue	Brain		disease	Uni-ZAP XR
T0002	Activated T-cells	Activated T-Cell, PBL fraction	Blood	Cell Line		pBluescript SK-
T0003	Human Fetal Lung	Human Fetal Lung				pBluescript SK-
T0004	Human White Fat	Human White Fat				pBluescript SK-
T0006	Human Pineal Gland	Human Pineal Gland				pBluescript SK-
T0008	Colorectal Tumor	Colorectal Tumor			disease	pBluescript SK-
T0010	Human Infant Brain	Human Infant Brain				Other
T0023	Human Pancreatic Carcinoma	Human Pancreatic Carcinoma			disease	pBluescript SK-
T0040	HSC172 cells	SA172 Cells				pBluescript SK-
T0041	Jurkat T-cell G1 phase	Jurkat T-cell				pBluescript SK-
T0042	Jurkat T-Cell, S phase	Jurkat T-Cell Line				pBluescript SK-



T0048	Human Aortic Endothelium	Human Aortic Endothelium				pBluescript SK-
T0049	Aorta endothelial cells + TNF-a	Aorta endothelial cells				pBluescript SK-
T0060	Human White Adipose	Human White Fat				pBluescript SK-
T0067	Human Thyroid	Human Thyroid				pBluescript SK-
T0068	Normal Ovary, Premenopausal	Normal Ovary, Premenopausal				pBluescript SK-
T0069	Human Uterus, normal	Human Uterus, normal				pBluescript SK-
T0071	Human Bone Marrow	Human Bone Marrow				pBluescript SK-
T0082	Human Adult Retina	Human Adult Retina				pBluescript SK-
T0109	Human (HCC) cell line liver (mouse) metastasis, remake					pBluescript SK-
T0110	Human colon carcinoma (HCC) cell line, remake					pBluescript SK-
T0114	Human (Caco-2) cell line, adenocarcinoma, colon, remake					pBluescript SK-
L0002	Atrium cDNA library Human heart					
L0004	ClonTech HL 1065a					
L0005	Clontech human aorta polyA+ mRNA (#6572)					
L0021	Human adult (K.Okubo)					
L0022	Human adult lung 3" directed MboI cDNA					
L0040	Human colon mucosa					
L0055	Human promyelocyte					
L0065	Liver HepG2 cell line.					
L0105	Human aorta polyA+ (TFujiwara)	aorta				
L0109	Human brain cDNA	brain				
L0142	Human placenta cDNA (TFujiwara)	placenta				
L0157	Human fetal brain (TFujiwara)		brain			
L0163	Human heart cDNA (YNakamura)		heart			
L0194	Human pancreatic cancer cell line Patu 8988t	pancreatic cancer		Patu 8988t		
L0351	Infant brain, Bento Soares					BA, M13-derived
L0352	Normalized infant brain, Bento Soares					BA, M13-derived
L0361	Stratagene ovary (#937217)		ovary			Bluescript SK
L0362	Stratagene ovarian cancer (#937219)					Bluescript SK-
L0364	NCI_CGAP_GC5	germ cell tumor				Bluescript SK-
L0366	Stratagene schizo brain	schizophrenic brain				Bluescript SK-

	S11	S-11 frontal lobe				
L0369	NCI_CGAP_AA1	adrenal adenoma	adrenal gland			Bluescript SK-
L0370	Johnston frontal cortex	pooled frontal lobe	brain			Bluescript SK-
L0371	NCI_CGAP_Br3	breast tumor	breast			Bluescript SK-
L0372	NCI_CGAP_Co12	colon tumor	colon			Bluescript SK-
L0373	NCI_CGAP_Co11	tumor	colon			Bluescript SK-
L0374	NCI_CGAP_Co2	tumor	colon			Bluescript SK-
L0375	NCI_CGAP_Kid6	kidney tumor	kidney			Bluescript SK-
L0376	NCI_CGAP_Lar1	larynx	larynx			Bluescript SK-
L0378	NCI_CGAP_Lu1	lung tumor	lung			Bluescript SK-
L0381	NCI_CGAP_HN4	squamous cell carcinoma	pharynx			Bluescript SK-
L0382	NCI_CGAP_Pr25	epithelium (cell line)	prostate			Bluescript SK-
L0383	NCI_CGAP_Pr24	invasive tumor (cell line)	prostate			Bluescript SK-
L0384	NCI_CGAP_Pr23	prostate tumor	prostate			Bluescript SK-
L0385	NCI_CGAP_Gas1	gastric tumor	stomach			Bluescript SK-
L0386	NCI_CGAP_HN3	squamous cell carcinoma from base of tongue	tongue			Bluescript SK-
L0387	NCI_CGAP_GCB0	germinal center B-cells	tonsil			Bluescript SK-
L0393	B, Human Liver tissue					gt11
L0415	b4HB3MA Cot8-HAP-Ft					Lafmid BA
L0438	normalized infant brain cDNA	total brain	brain			lafmid BA
L0439	Soares infant brain 1NIB		whole brain			Lafmid BA
L0455	Human retina cDNA randomly primed sublibrary	retina	eye			lambda gt10
L0462	WATM1					lambda gt11
L0471	Human fetal heart, Lambda ZAP Express					Lambda ZAP Express
L0475	KG1-a Lambda Zap Express cDNA library			KG1-a		Lambda Zap Express (Stratagene)
L0477	HPLA CCLee	placenta				Lambda ZAP II
L0480	Stratagene cat#937212 (1992)					Lambda ZAP, pBluescript SK(-)
L0483	Human pancreatic islet					Lambda ZAPII
L0485	STRATAGENE Human skeletal muscle cDNA library, cat. #936215.	skeletal muscle	leg muscle			Lambda ZAPII
L0499	NCI_CGAP_HSC2	stem cell 34+/38+	bone marrow			pAMP1
L0512	NCI_CGAP_Ov36	borderline ovarian carcinoma	ovary			pAMP1
L0517	NCI_CGAP_Pr1					pAMP10
L0518	NCI_CGAP_Pr2					pAMP10
L0519	NCI_CGAP_Pr3					pAMP10
L0520	NCI_CGAP_Alv1	alveolar rhabdomyosarcoma				pAMP10

L0521	NCI_CGAP_Ew1	Ewing's sarcoma				pAMP10
L0526	NCI_CGAP_Pr12	metastatic prostate bone lesion				pAMP10
L0527	NCI_CGAP_Ov2	ovary				pAMP10
L0528	NCI_CGAP_Pr5	prostate				pAMP10
L0529	NCI_CGAP_Pr6	prostate				pAMP10
L0533	NCI_CGAP_HSC1	stem cells	bone marrow			pAMP10
L0534	Chromosome 7 Fetal Brain cDNA Library	brain	brain			pAMP10
L0535	NCI_CGAP_Br5	infiltrating ductal carcinoma	breast			pAMP10
L0540	NCI_CGAP_Pr10	invasive prostate tumor	prostate			pAMP10
L0542	NCI_CGAP_Pr11	normal prostatic epithelial cells	prostate			pAMP10
L0543	NCI_CGAP_Pr9	normal prostatic epithelial cells	prostate			pAMP10
L0545	NCI_CGAP_Pr4.1	prostatic intraepithelial neoplasia - high grade	prostate			pAMP10
L0546	NCI_CGAP_Pr18	stroma	prostate			pAMP10
L0547	NCI_CGAP_Pr16	tumor	prostate			pAMP10
L0549	NCI_CGAP_HN10	carcinoma in situ from retromolar trigone				pAMP10
L0551	NCI_CGAP_HN7	normal squamous epithelium, floor of mouth				pAMP10
L0558	NCI_CGAP_Ov40	endometrioid ovarian metastasis	ovary			pAMP10
L0564	Jia bone marrow stroma	bone marrow stroma				pBluescript
L0565	Normal Human Trabecular Bone Cells	Bone	Hip			pBluescript
L0581	Stratagene liver (#937224)		liver			pBluescript SK
L0586	HTCDL1					pBluescript SK(-)
L0588	Stratagene endothelial cell 937223					pBluescript SK-
L0590	Stratagene fibroblast (#937212)					pBluescript SK-
L0591	Stratagene HeLa cell s3 937216					pBluescript SK-
L0592	Stratagene hNT neuron (#937233)					pBluescript SK-
L0593	Stratagene neuroepithelium (#937231)					pBluescript SK-
L0594	Stratagene neuroepithelium NT2RAMI 937234					pBluescript SK-
L0595	Stratagene NT2 neuronal precursor 937230	neuroepithelial cells	brain			pBluescript SK-



L0596	Stratagene colon (#937204)		colon			pBluescript SK-
L0597	Stratagene corneal stroma (#937222)		cornea			pBluescript SK-
L0598	Morton Fetal Cochlea	cochlea	ear			pBluescript SK-
L0599	Stratagene lung (#937210)		lung			pBluescript SK-
L0600	Weizmann Olfactory Epithelium	olfactory epithelium	nose			pBluescript SK-
L0601	Stratagene pancreas (#937208)		pancreas			pBluescript SK-
L0602	Pancreatic Islet	pancreatic islet	pancreas			pBluescript SK-
L0603	Stratagene placenta (#937225)		placenta			pBluescript SK-
L0604	Stratagene muscle 937209	muscle	skeletal muscle			pBluescript SK-
L0605	Stratagene fetal spleen (#937205)	fetal spleen	spleen			pBluescript SK-
L0606	NCI_CGAP_Lym5	follicular lymphoma	lymph node			pBluescript SK-
L0607	NCI_CGAP_Lym6	mantle cell lymphoma	lymph node			pBluescript SK-
L0608	Stratagene lung carcinoma 937218	lung carcinoma	lung	NCI-H69		pBluescript SK-
L0611	Schiller meningioma	meningioma	brain			pBluescript SK- (Stratagene)
L0617	Chromosome 22 exon					pBluescriptIIKS +
L0619	Chromosome 9 exon II					pBluescriptIIKS +
L0622	HM1					pcDNAII (Invitrogen)
L0623	HM3	pectoral muscle (after mastectomy)				pcDNAII (Invitrogen)
L0627	NCI_CGAP_Co1	bulk tumor	colon			pCMV-SPORT2
L0628	NCI_CGAP_Ov1	ovary bulk tumor	ovary			pCMV-SPORT2
L0629	NCI_CGAP_Mel3	metastatic melanoma to bowel	bowel (skin primary)			pCMV-SPORT4
L0630	NCI_CGAP_CNS1	substantia nigra	brain			pCMV-SPORT4
L0631	NCI_CGAP_Br7		breast			pCMV-SPORT4
L0635	NCI_CGAP_PNS1	dorsal root ganglion	peripheral nervous system			pCMV-SPORT4
L0636	NCI_CGAP_Pit1	four pooled pituitary adenomas	brain			pCMV-SPORT6
L0637	NCI_CGAP_Brn53	three pooled meningiomas	brain			pCMV-SPORT6
L0638	NCI_CGAP_Brn35	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0639	NCI_CGAP_Brn52	tumor, 5 pooled (see description)	brain			pCMV-SPORT6
L0640	NCI_CGAP_Br18	four pooled high-grade tumors, including two prima	breast			pCMV-SPORT6
L0641	NCI_CGAP_Co17	juvenile granulosa	colon			pCMV-SPORT6

		tumor			
L0642	NCI_CGAP_Co18	moderately differentiated adenocarcinoma	colon		pCMV-SPORT6
L0643	NCI_CGAP_Co19	moderately differentiated adenocarcinoma	colon		pCMV-SPORT6
L0644	NCI_CGAP_Co20	moderately differentiated adenocarcinoma	colon		pCMV-SPORT6
L0646	NCI_CGAP_Co14	moderately-differentiated adenocarcinoma	colon		pCMV-SPORT6
L0647	NCI_CGAP_Sar4	five pooled sarcomas, including myxoid liposarcoma	connective tissue		pCMV-SPORT6
L0648	NCI_CGAP_Eso2	squamous cell carcinoma	esophagus		pCMV-SPORT6
L0649	NCI_CGAP_GU1	2 pooled high-grade transitional cell tumors	genitourinary tract		pCMV-SPORT6
L0650	NCI_CGAP_Kid13	2 pooled Wilms' tumors, one primary and one metast	kidney		pCMV-SPORT6
L0651	NCI_CGAP_Kid8	renal cell tumor	kidney		pCMV-SPORT6
L0652	NCI_CGAP_Lu27	four pooled poorly-differentiated adenocarcinomas	lung		pCMV-SPORT6
L0653	NCI_CGAP_Lu28	two pooled squamous cell carcinomas	lung		pCMV-SPORT6
L0654	NCI_CGAP_Lu31		lung, cell line		pCMV-SPORT6
L0655	NCI_CGAP_Lym12	lymphoma, follicular mixed small and large cell	lymph node		pCMV-SPORT6
L0656	NCI_CGAP_Ov38	normal epithelium	ovary		pCMV-SPORT6
L0657	NCI_CGAP_Ov23	tumor, 5 pooled (see description)	ovary		pCMV-SPORT6
L0658	NCI_CGAP_Ov35	tumor, 5 pooled (see description)	ovary		pCMV-SPORT6
L0659	NCI_CGAP_Pan1	adenocarcinoma	pancreas		pCMV-SPORT6
L0661	NCI_CGAP_Mel15	malignant melanoma, metastatic to lymph node	skin		pCMV-SPORT6
L0662	NCI_CGAP_Gas4	poorly differentiated adenocarcinoma with signet r	stomach		pCMV-SPORT6
L0663	NCI_CGAP_Ut2	moderately-differentiated endometrial adenocarcino	uterus		pCMV-SPORT6
L0664	NCI_CGAP_Ut3	poorly-differentiated	uterus		pCMV-SPORT6

		endometrial adenocarcinoma,				
L0665	NCL_CGAP_Ut4	serous papillary carcinoma, high grade, 2 pooled t	uterus			pCMV-SPORT6
L0666	NCL_CGAP_Ut1	well-differentiated endometrial adenocarcinoma, 7	uterus			pCMV-SPORT6
L0667	NCL_CGAP_CML1	myeloid cells, 18 pooled CML cases, BCR/ABL rearra	whole blood			pCMV-SPORT6
L0717	Gessler Wilms tumor					pSPORT1
L0718	Testis 5					pSPORT1
L0720	PN001-Normal Human Prostate		prostate			pSport1
L0731	Soares_pregnant_uterus_NbHPU		uterus			pT7T3-Pac
L0738	Human colorectal cancer					pT7T3D
L0740	Soares melanocyte 2NbHM	melanocyte				pT7T3D (Pharmacia) with a modified polylinker
L0741	Soares adult brain N2b4HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0742	Soares adult brain N2b5HB55Y		brain			pT7T3D (Pharmacia) with a modified polylinker
L0743	Soares breast 2NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0744	Soares breast 3NbHBst		breast			pT7T3D (Pharmacia) with a modified polylinker
L0745	Soares retina N2b4HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0746	Soares retina N2b5HR	retina	eye			pT7T3D (Pharmacia) with a modified polylinker
L0747	Soares_fetal_heart_NbHH 19W		heart			pT7T3D (Pharmacia) with a modified polylinker
L0748	Soares fetal liver spleen 1NFLS		Liver and Spleen			pT7T3D (Pharmacia) with a modified



						polylinker
L0749	Soares_fetal_liver_spleen _1NFLS_S1		Liver and Spleen			pT7T3D (Pharmacia) with a modified polylinker
L0750	Soares_fetal_lung_NbHL1 9W		lung			pT7T3D (Pharmacia) with a modified polylinker
L0751	Soares ovary tumor NbHOT	ovarian tumor	ovary			pT7T3D (Pharmacia) with a modified polylinker
L0752	Soares_parathyroid_tumor _NbHPA	parathyroid tumor	parathyroid gland			pT7T3D (Pharmacia) with a modified polylinker
L0753	Soares_pineal_gland_N3H PG		pineal gland			pT7T3D (Pharmacia) with a modified polylinker
L0754	Soares placenta Nb2HP		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0755	Soares_placenta_8to9wee ks_2NbHP8to9W		placenta			pT7T3D (Pharmacia) with a modified polylinker
L0756	Soares_multiple_sclerosis _2NbHMSP	multiple sclerosis lesions				pT7T3D (Pharmacia) with a modified polylinker V_TYPE
L0757	Soares_senescent_fibrobla sts_NbHSF	senescent fibroblast				pT7T3D (Pharmacia) with a modified polylinker V_TYPE
L0758	Soares_testis_NHT					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0759	Soares_total_fetus_Nb2H F8_9w					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0761	NCI_CGAP_CLL1	B-cell, chronic lymphocytic leukemia				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0762	NCI_CGAP_Br1.1	breast				pT7T3D-Pac (Pharmacia) with a modified

						polylinker
L0763	NCI_CGAP_Br2	breast				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0764	NCI_CGAP_Co3	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0765	NCI_CGAP_Co4	colon				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0766	NCI_CGAP_GCB1	germinal center B cell				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0767	NCI_CGAP_GC3	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0768	NCI_CGAP_GC4	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0769	NCI_CGAP_Brn25	anaplastic oligodendroglioma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0770	NCI_CGAP_Brn23	glioblastoma (pooled)	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0771	NCI_CGAP_Co8	adenocarcinoma	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0772	NCI_CGAP_Co10	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0773	NCI_CGAP_Co9	colon tumor RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0774	NCI_CGAP_Kid3		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0775	NCI_CGAP_Kid5	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker

L0776	NCI_CGAP_Lu5	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0777	Soares_NhHMPu_S1	Pooled human melanocyte, fetal heart, and pregnant	mixed (see below)			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0778	Barstead pancreas HPLRB1		pancreas			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0779	Soares_NFL_T_GBC_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0780	Soares_NSF_F8_9W_OT _PA_P_S1		pooled			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0782	NCI_CGAP_Pr21	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0783	NCI_CGAP_Pr22	normal prostate	prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0785	Barstead spleen HPLRB2		spleen			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0786	Soares_NbHFB		whole brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0787	NCI_CGAP_Sub1					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0788	NCI_CGAP_Sub2					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0789	NCI_CGAP_Sub3					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0790	NCI_CGAP_Sub4					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0791	NCI_CGAP_Sub5					pT7T3D-Pac (Pharmacia)



						with a modified polylinker
L0792	NCI_CGAP_Sub6					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0793	NCI_CGAP_Sub7					pT7T3D-Pac (Pharmacia) with a modified polylinker
L0794	NCI_CGAP_GC6	pooled germ cell tumors				pT7T3D-Pac (Pharmacia) with a modified polylinker
L0796	NCI_CGAP_Brn50	medulloblastoma	brain			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0800	NCI_CGAP_Co16	colon tumor, RER+	colon			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0803	NCI_CGAP_Kid11		kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0804	NCI_CGAP_Kid12	2 pooled tumors (clear cell type)	kidney			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0805	NCI_CGAP_Lu24	carcinoid	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0806	NCI_CGAP_Lu19	squamous cell carcinoma, poorly differentiated (4	lung			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0807	NCI_CGAP_Ov18	fibrotheoma	ovary			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0808	Barstead prostate BPH HPLRB4 I		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L0809	NCI_CGAP_Pr28		prostate			pT7T3D-Pac (Pharmacia) with a modified polylinker
L2251	Human fetal lung	Fetal lung				

**TABLE 5**

<b>OMIM Reference</b>	<b>Description</b>
106300	Ankylosing spondylitis
108800	Atrial septal defect, secundum type
120160	Osteogenesis imperfecta, 4 clinical forms, 166200, 166210, 259420, 166220
120160	Osteoporosis, idiopathic, 166710
120160	Ehlers-Danlos syndrome, type VIIA2, 130060
120160	Marfan syndrome, atypical
120290	OSMED syndrome, 215150
120290	Stickler syndrome, type II, 184840
120810	C4 deficiency
120820	C4 deficiency
126650	Chloride diarrhea, congenital, Finnish type, 214700
126650	Colon cancer
129900	EEC syndrome-1
142857	Pemphigoid, susceptibility to
142858	Beryllium disease, chronic, susceptibility to
145001	Hyperparathyroidism-jaw tumor syndrome
150270	Laryngeal adductor paralysis
150292	Epidermolysis bullosa, Herlitz junctional type, 226700
154276	Malignant hyperthermia susceptibility 3
154705	Marfan syndrome, type II
167250	Paget disease of bone
170261	Bare lymphocyte syndrome, type I, due to TAP2 deficiency
173360	Thrombophilia due to excessive plasminogen activator inhibitor
173360	Hemorrhagic diathesis due to PAI1 deficiency
177900	Psoriasis susceptibility-1
179450	Ragweed sensitivity
183600	Split hand/foot malformation, type 1
187680	6-mercaptopurine sensitivity
193300	Renal cell carcinoma
193300	von Hippel-Lindau syndrome
201910	Adrenal hyperplasia, congenital, due to 21-hydroxylase deficiency
208250	Jacobs syndrome
217000	C2 deficiency
222100	Diabetes mellitus, insulin-dependent-1
227646	Fanconi anemia, type D
233100	[Renal glucosuria]
235200	Hemochromatosis
248611	Maple syrup urine disease, type Ib
253260	Biotinidase deficiency
256550	Sialidosis, type I
256550	Sialidosis, type II
278720	Xeroderma pigmentosum, group C



600202	Dyslexia, specific, 2
600261	Ehlers-Danlos-like syndrome
600995	Nephrotic syndrome, idiopathic, steroid-resistant
601154	Cardiomyopathy, dilated, 1E
601253	Muscular dystrophy, limb-girdle, type IC
601652	Glaucoma 1A, primary open angle, juvenile-onset, 137750
601868	Deafness, autosomal dominant 13
602011	Pancreatic endocrine tumors
602136	Refsum disease, infantile, 266510
602136	Zellweger syndrome-1, 214100
602136	Adrenoleukodystrophy, neonatal, 202370
602280	Retinitis pigmentosa-14, 600132
602447	Coronary artery disease, susceptibility to
602475	Ossification of posterior longitudinal ligament of spine

*Polynucleotide and Polypeptide Variants*

[84] The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X or the complementary strand thereto, nucleotide sequences encoding the polypeptide of SEQ ID NO:Y, the nucleotide sequence of SEQ ID NO:X encoding the polypeptide sequence as defined in column 7 of Table 1A, nucleotide sequences encoding the polypeptide as defined in column 7 of Table 1A, the nucleotide sequence as defined in columns 8 and 9 of Table 2, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, the nucleotide sequence as defined in column 6 of Table 1B, nucleotide sequences encoding the polypeptide encoded by the nucleotide sequence as defined in column 6 of Table 1B, the cDNA sequence contained in Clone ID NO:Z, and/or nucleotide sequences encoding the polypeptide encoded by the cDNA sequence contained in Clone ID NO:Z.

[85] The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y, the polypeptide sequence as defined in column 7 of Table 1A, a polypeptide sequence encoded by the polynucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the nucleotide sequence as defined in columns 8 and 9 of Table 2, a polypeptide sequence encoded by the nucleotide sequence as defined in column 6 of Table 1B, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a polypeptide sequence encoded by the cDNA sequence contained in Clone ID NO:Z.



[86] "Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

[87] Thus, one aspect of the invention provides an isolated nucleic acid molecule comprising, or alternatively consisting of, a polynucleotide having a nucleotide sequence selected from the group consisting of: (a) a nucleotide sequence described in SEQ ID NO:X or contained in the cDNA sequence of Clone ID NO:Z; (b) a nucleotide sequence in SEQ ID NO:X or the cDNA in Clone ID NO:Z which encodes the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (c) a nucleotide sequence in SEQ ID NO:X or the cDNA in Clone ID NO:Z which encodes a mature polypeptide; (d) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes a biologically active fragment of a polypeptide; (e) a nucleotide sequence in SEQ ID NO:X or the cDNA sequence of Clone ID NO:Z, which encodes an antigenic fragment of a polypeptide; (f) a nucleotide sequence encoding a polypeptide comprising the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (g) a nucleotide sequence encoding a mature polypeptide of the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (h) a nucleotide sequence encoding a biologically active fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (i) a nucleotide sequence encoding an antigenic fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; and (j) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), or (i) above.

[88] The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j) above, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence of the cDNA contained in Clone ID NO:Z or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding a polypeptide

sequence encoded by the nucleotide sequence in SEQ ID NO:X, a polypeptide sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z, the nucleotide coding sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto, the nucleotide coding sequence in SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto, a nucleotide sequence encoding the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto, the nucleotide sequence in SEQ ID NO:X encoding the polypeptide sequence as defined in column 7 of Table 1A or the complementary strand thereto, nucleotide sequences encoding the polypeptide as defined in column 7 of Table 1A or the complementary strand thereto, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides and nucleic acids.

[89] In a preferred embodiment, the invention encompasses nucleic acid molecules which comprise, or alternatively, consist of a polynucleotide which hybridizes under stringent hybridization conditions, or alternatively, under lower stringency conditions, to a polynucleotide in (a), (b), (c), (d), (e), (f), (g), (h), or (i), above, as are polypeptides encoded by these polynucleotides. In another preferred embodiment, polynucleotides which hybridize to the complement of these nucleic acid molecules under stringent hybridization conditions, or alternatively, under lower stringency conditions, are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[90] In another embodiment, the invention provides a purified protein comprising, or alternatively consisting of, a polypeptide having an amino acid sequence selected from the group consisting of: (a) the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; (b) the amino acid sequence of a mature form of a polypeptide having the amino acid sequence of SEQ ID NO:Y or the amino acid sequence encoded by the cDNA in Clone ID NO:Z; (c) the amino acid sequence of a biologically active fragment of a polypeptide having the complete amino



acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z; and (d) the amino acid sequence of an antigenic fragment of a polypeptide having the complete amino acid sequence of SEQ ID NO:Y or the complete amino acid sequence encoded by the cDNA in Clone ID NO:Z.

[91] The present invention is also directed to proteins which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100%, identical to, for example, any of the amino acid sequences in (a), (b), (c), or (d), above, the amino acid sequence shown in SEQ ID NO:Y, the amino acid sequence encoded by the cDNA contained in Clone ID NO:Z, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X as defined in columns 8 and 9 of Table 2, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B, the amino acid sequence as defined in column 7 of Table 1A, an amino acid sequence encoded by the nucleotide sequence in SEQ ID NO:X, and an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X. Fragments of these polypeptides are also provided (e.g., those fragments described herein). Further proteins encoded by polynucleotides which hybridize to the complement of the nucleic acid molecules encoding these amino acid sequences under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention, as are the polynucleotides encoding these proteins.

[92] By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each 100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence referred to in Table 1A or 2 as the ORF (open reading frame), or any fragment specified as described herein.

[93] As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a



nucleotide sequence of the present invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245 (1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identity are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the length of the subject nucleotide sequence, whichever is shorter.

[94] If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

[95] For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example,

a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

[96] By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference sequence or in one or more contiguous groups within the reference sequence.

[97] As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, the amino acid sequence of a polypeptide referred to in Table 1A (e.g., the amino acid sequence identified in column 6) or Table 2 (e.g., the amino acid sequence of the polypeptide encoded by the polynucleotide sequence defined in columns 8 and 9 of Table 2) or a fragment thereof; the amino acid sequence of the polypeptide encoded by the polynucleotide sequence in SEQ ID NO:B as defined in column 6 of Table 1B or a fragment thereof, the amino acid sequence of the polypeptide encoded by the nucleotide sequence in SEQ ID NO:X or a fragment thereof, or the amino acid sequence of the polypeptide encoded by cDNA contained in Clone ID NO:Z, or a fragment thereof, can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci.6:237-245 (1990)). In a sequence



alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is expressed as percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

[98] If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal residues of the subject sequence.

[99] For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C-termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity\_\_\_\_\_



calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to be made for the purposes of the present invention.

[100] The polynucleotide variants of the invention may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, polypeptide variants in which less than 50, less than 40, less than 30, less than 20, less than 10, or 5-50, 5-25, 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as *E. coli*).

[101] Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985)). These allelic variants can vary at either the polynucleotide and/or polypeptide level and are included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

[102] Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the polypeptide of the present invention without substantial loss of biological function. As an example, Ron et al. (*J. Biol. Chem.* 268: 2984-2988 (1993)) reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., *J. Biotechnology* 7:199-216 (1988).)

[103] Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (*J. Biol. Chem.* 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500

individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

[104] Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

[105] Thus, the invention further includes polypeptide variants which show a functional activity (e.g., biological activity) of the polypeptides of the invention. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity.

[106] The present application is directed to nucleic acid molecules at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, (e.g., encoding a polypeptide having the amino acid sequence of an N and/or C terminal deletion), irrespective of whether they encode a polypeptide having functional activity. This is because even where a particular nucleic acid molecule does not encode a polypeptide having functional activity, one of skill in the art would still know how to use the nucleic acid molecule, for instance, as a hybridization probe or a polymerase chain reaction (PCR) primer. Uses of the nucleic acid molecules of the present invention that do not encode a polypeptide having functional activity include, inter alia, (1) isolating a gene or allelic or splice variants thereof in a cDNA library; (2) *in situ* hybridization (e.g., "FISH") to metaphase chromosomal spreads to provide precise chromosomal location of the gene, as described in Verma et al., Human Chromosomes: A Manual of Basic Techniques, Pergamon Press, New York (1988); (3) Northern Blot analysis for detecting mRNA expression in specific tissues (e.g., normal or diseased tissues); and (4) *in situ* hybridization (e.g., histochemistry) for detecting mRNA expression in specific tissues (e.g., normal or



diseased tissues).

[107] Preferred, however, are nucleic acid molecules having sequences at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to the nucleic acid sequences disclosed herein, which do, in fact, encode a polypeptide having functional activity. By a polypeptide having "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) protein of the invention. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide of the invention for binding) to an anti-polypeptide of the invention antibody], immunogenicity (ability to generate antibody which binds to a specific polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention.

[108] The functional activity of the polypeptides, and fragments, variants and derivatives of the invention, can be assayed by various methods.

[109] For example, in one embodiment where one is assaying for the ability to bind or compete with a full-length polypeptide of the present invention for binding to an anti-polypeptide antibody, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

[110] In another embodiment, where a ligand is identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography,



and affinity blotting. See generally, Phizicky et al., *Microbiol. Rev.* 59:94-123 (1995). In another embodiment, the ability of physiological correlates of a polypeptide of the present invention to bind to a substrate(s) of the polypeptide of the invention can be routinely assayed using techniques known in the art.

[111] In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the present invention and fragments, variants and derivatives thereof to elicit polypeptide related biological activity (either *in vitro* or *in vivo*). Other methods will be known to the skilled artisan and are within the scope of the invention.

[112] Of course, due to the degeneracy of the genetic code, one of ordinary skill in the art will immediately recognize that a large number of the nucleic acid molecules having a sequence at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99%, or 100% identical to, for example, the nucleic acid sequence of the cDNA contained in Clone ID NO:Z, the nucleic acid sequence referred to in Table 1A (SEQ ID NO:X), the nucleic acid sequence disclosed in Table 2 (e.g., the nucleic acid sequence delineated in columns 8 and 9) or fragments thereof, will encode polypeptides "having functional activity." In fact, since degenerate variants of any of these nucleotide sequences all encode the same polypeptide, in many instances, this will be clear to the skilled artisan even without performing the above described comparison assay. It will be further recognized in the art that, for such nucleic acid molecules that are not degenerate variants, a reasonable number will also encode a polypeptide having functional activity. This is because the skilled artisan is fully aware of amino acid substitutions that are either less likely or not likely to significantly effect protein function (e.g., replacing one aliphatic amino acid with a second aliphatic amino acid), as further described below.

[113] For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions," *Science* 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

[114] The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions

have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

[115] The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. See Cunningham and Wells, *Science* 244:1081-1085 (1989). The resulting mutant molecules can then be tested for biological activity.

[116] As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly. Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitutions with one or more of the amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, serum albumin (preferably human serum albumin) or a fragment thereof, or leader or secretory sequence, or a sequence facilitating purification, or (v) fusion of the polypeptide with another compound, such as albumin (including but not limited to recombinant albumin (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)).



Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

[117] For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. See Pinckard et al., *Clin. Exp. Immunol.* 2:331-340 (1967); Robbins et al., *Diabetes* 36: 838-845 (1987); Cleland et al., *Crit. Rev. Therapeutic Drug Carrier Systems* 10:307-377 (1993).

[118] A further embodiment of the invention relates to polypeptides which comprise the amino acid sequence of a polypeptide having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions from a polypeptide sequence disclosed herein. Of course it is highly preferable for a polypeptide to have an amino acid sequence which comprises the amino acid sequence of a polypeptide of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X, an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, an amino acid sequence encoded by the complement of SEQ ID NO:X, and/or an amino acid sequence encoded by cDNA contained in Clone ID NO:Z which contains, in order of ever-increasing preference, at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions.

[119] In specific embodiments, the polypeptides of the invention comprise, or alternatively, consist of, fragments or variants of a reference amino acid sequence selected from: (a) the amino acid sequence of SEQ ID NO:Y or fragments thereof (e.g., the mature form and/or other fragments described herein); (b) the amino acid sequence encoded by SEQ ID NO:X or fragments thereof; (c) the amino acid sequence encoded by the complement of SEQ ID NO:X or fragments thereof; (d) the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or fragments thereof; and (e) the amino acid sequence encoded by cDNA contained in Clone ID NO:Z or fragments thereof; wherein the fragments or variants have 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, amino acid residue additions, substitutions, and/or deletions when compared to the reference amino acid sequence. In preferred embodiments, the amino acid substitutions are



conservative. Polynucleotides encoding these polypeptides are also encompassed by the invention.

*Polynucleotide and Polypeptide Fragments*

[120] The present invention is also directed to polynucleotide fragments of the polynucleotides (nucleic acids) of the invention. In the present invention, a "polynucleotide fragment" refers to a polynucleotide having a nucleic acid sequence which, for example: is a portion of the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of the polynucleotide sequence encoding the polypeptide encoded by the cDNA contained in Clone ID NO:Z or the complementary strand thereto; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence of SEQ ID NO:X as defined in columns 8 and 9 of Table 2 or the complementary strand thereto; is a portion of the polynucleotide sequence in SEQ ID NO:X or the complementary strand thereto; is a polynucleotide sequence encoding a portion of the polypeptide of SEQ ID NO:Y; is a polynucleotide sequence encoding a portion of a polypeptide encoded by SEQ ID NO:X; is a polynucleotide sequence encoding a portion of a polypeptide encoded by the complement of the polynucleotide sequence in SEQ ID NO:X; is a portion of a polynucleotide sequence encoding the amino acid sequence encoded by the region of SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto; or is a portion of the polynucleotide sequence of SEQ ID NO:B as defined in column 6 of Table 1B or the complementary strand thereto.

[121] The polynucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in Clone ID NO:Z, or the nucleotide sequence shown in SEQ ID NO:X or the complementary strand thereto. In this context "about" includes the particularly recited value or a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., at least 160, 170, 180, 190,

200, 250, 500, 600, 1000, or 2000 nucleotides in length ) are also encompassed by the invention.

[122] Moreover, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 601-650, 651-700, 701-750, 751-800, 801-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of SEQ ID NO:X, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[123] Further representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a sequence from about nucleotide number 1-50, 51-



100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 601-650, 651-700, 701-750, 751-800, 801-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, 2001-2050, 2051-2100, 2101-2150, 2151-2200, 2201-2250, 2251-2300, 2301-2350, 2351-2400, 2401-2450, 2451-2500, 2501-2550, 2551-2600, 2601-2650, 2651-2700, 2701-2750, 2751-2800, 2801-2850, 2851-2900, 2901-2950, 2951-3000, 3001-3050, 3051-3100, 3101-3150, 3151-3200, 3201-3250, 3251-3300, 3301-3350, 3351-3400, 3401-3450, 3451-3500, 3501-3550, 3551-3600, 3601-3650, 3651-3700, 3701-3750, 3751-3800, 3801-3850, 3851-3900, 3901-3950, 3951-4000, 4001-4050, 4051-4100, 4101-4150, 4151-4200, 4201-4250, 4251-4300, 4301-4350, 4351-4400, 4401-4450, 4451-4500, 4501-4550, 4551-4600, 4601-4650, 4651-4700, 4701-4750, 4751-4800, 4801-4850, 4851-4900, 4901-4950, 4951-5000, 5001-5050, 5051-5100, 5101-5150, 5151-5200, 5201-5250, 5251-5300, 5301-5350, 5351-5400, 5401-5450, 5451-5500, 5501-5550, 5551-5600, 5601-5650, 5651-5700, 5701-5750, 5751-5800, 5801-5850, 5851-5900, 5901-5950, 5951-6000, 6001-6050, 6051-6100, 6101-6150, 6151-6200, 6201-6250, 6251-6300, 6301-6350, 6351-6400, 6401-6450, 6451-6500, 6501-6550, 6551-6600, 6601-6650, 6651-6700, 6701-6750, 6751-6800, 6801-6850, 6851-6900, 6901-6950, 6951-7000, 7001-7050, 7051-7100, 7101-7150, 7151-7200, 7201-7250, 7251-7300 or 7301 to the end of the cDNA sequence contained in Clone ID NO:Z, or the complementary strand thereto. In this context "about" includes the particularly recited range or a range larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has a functional activity (e.g., biological activity). More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to one or more of these polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

[124] Moreover, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one, two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence delineated in Table 1B column 6. Additional, representative examples of polynucleotide fragments of the invention comprise, or alternatively consist of, a nucleic acid sequence comprising one,



two, three, four, five, six, seven, eight, nine, ten, or more of the above described polynucleotide fragments of the invention in combination with a polynucleotide sequence that is the complementary strand of a sequence delineated in column 6 of Table 1B. In further embodiments, the above-described polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that of the BAC fragment having the sequence disclosed in SEQ ID NO:B (see Table 1B, column 5). In additional embodiments, the above-described polynucleotide fragments of the invention comprise, or alternatively consist of, sequences delineated in Table 1B, column 6, and have a nucleic acid sequence which is different from that published for the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). In additional embodiments, the above-described polynucleotides of the invention comprise, or alternatively consist of, sequences delineated Table 1B, column 6, and have a nucleic acid sequence which is different from that contained in the BAC clone identified as BAC ID NO:A (see Table 1B, column 4). Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides and polypeptides are also encompassed by the invention.

[125] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1B, column 2) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[126] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in column 6 of Table 1B which correspond to the same Clone ID NO:Z (see Table 1B, column 1), and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[127] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, or more fragments of the sequences delineated in the same row of column 6 of Table 1B, and the polynucleotide sequence of SEQ ID NO:X (e.g., as defined in Table 1A or 1B) or fragments or variants thereof. Polypeptides encoded by these polynucleotides, other polynucleotides that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention.

[128] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of the sequence of SEQ ID NO:X are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids that encode these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[129] In additional specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X (e.g., as described herein) are directly contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[130] In further specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of a fragment or variant of the sequence of SEQ ID NO:X and the 5' 10 polynucleotides of the sequence of one of the sequences delineated in column 6 of Table 1B are directly



contiguous. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[131] In specific embodiments, polynucleotides of the invention comprise, or alternatively consist of a polynucleotide sequence in which the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B and the 5' 10 polynucleotides of another sequence in column 6 are directly contiguous. In preferred embodiments, the 3' 10 polynucleotides of one of the sequences delineated in column 6 of Table 1B is directly contiguous with the 5' 10 polynucleotides of the next sequential exon delineated in Table 1B, column 6. Nucleic acids which hybridize to the complement of these 20 contiguous polynucleotides under stringent hybridization conditions or alternatively, under lower stringency conditions, are also encompassed by the invention. Polypeptides encoded by these polynucleotides and/or nucleic acids, other polynucleotides and/or nucleic acids encoding these polypeptides, and antibodies that bind these polypeptides are also encompassed by the invention. Additionally, fragments and variants of the above-described polynucleotides, nucleic acids, and polypeptides are also encompassed by the invention.

[132] In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y, a portion of an amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a portion of an amino acid sequence encoded by the polynucleotide sequence of SEQ ID NO:X, a portion of an amino acid sequence encoded by the complement of the polynucleotide sequence in SEQ ID NO:X, and/or a portion of an amino acid sequence encoded by the cDNA contained in Clone ID NO:Z. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 101-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-



480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of cDNA and SEQ ID NO: Y. In a preferred embodiment, polypeptide fragments of the invention include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 101-120, 121-140, 141-160, 161-180, 181-200, 201-220, 221-240, 241-260, 261-280, 281-300, 301-320, 321-340, 341-360, 361-380, 381-400, 401-420, 421-440, 441-460, 461-480, 481-500, 501-520, 521-540, 541-560, 561-580, 581-600, 601-620, 621-640, 641-660, 661-680, 681-700, 701-720, 721-740, 741-760, 761-780, 781-800, 801-820, 821-840, 841-860, 861-880, 881-900, 901-920, 921-940, 941-960, 961-980, 981-1000, 1001-1020, 1021-1040, 1041-1060, 1061-1080, 1081-1100, 1101-1120, 1121-1140, 1141-1160, 1161-1180, 1181-1200, 1201-1220, 1221-1240, 1241-1260, 1261-1280, 1281-1300, 1301-1320, 1321-1340, 1341-1360, 1361-1380, 1381-1400, 1401-1420, 1421-1440, or 1441 to the end of the coding region of SEQ ID NO:Y. Moreover, polypeptide fragments of the invention may be at least about 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, or ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

[133] Even if deletion of one or more amino acids from the N-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example, the ability of shortened muteins to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptides generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the N-terminus. Whether a particular polypeptide lacking N-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutein with a large number of deleted N-terminal amino acid

residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[134] Accordingly, polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

[135] The present invention further provides polypeptides having one or more residues deleted from the amino terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X or the complement thereof, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, a polypeptide encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1B, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, N-terminal deletions may be described by the general formula m-q, where q is a whole integer representing the total number of amino acid residues in a polypeptide of the invention (e.g., the polypeptide disclosed in SEQ ID NO:Y, or the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), and m is defined as any integer ranging from 2 to q-6. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[136] The present invention further provides polypeptides having one or more residues from the carboxy terminus of the amino acid sequence of a polypeptide disclosed herein (e.g., a polypeptide of SEQ ID NO:Y, a polypeptide encoded by the polynucleotide sequence contained in SEQ ID NO:X, a polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or a polypeptide encoded by the cDNA contained in Clone ID NO:Z). In particular, C-terminal deletions may be described by the general formula 1-n, where n is any whole integer ranging from 6 to q-1, and where n corresponds to the position of amino acid residue in a polypeptide of the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.



[137] In addition, any of the above described N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides having one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of a polypeptide encoded by SEQ ID NO:X (e.g., including, but not limited to, the preferred polypeptide disclosed as SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2), the cDNA contained in Clone ID NO:Z, and/or the complement thereof, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[138] Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification or loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind a ligand) may still be retained. For example the ability of the shortened mutin to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a mutin with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

[139] The present application is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[140] Any polypeptide sequence encoded by, for example, the polynucleotide sequences set forth as SEQ ID NO:X or the complement thereof, (presented, for example, in Tables 1A and 2), the cDNA contained in Clone ID NO:Z, or the polynucleotide sequence as defined in column 6 of Table 1B, may be analyzed to determine certain preferred regions of the polypeptide. For example, the amino acid sequence of a polypeptide encoded by a



polynucleotide sequence of SEQ ID NO:X (e.g., the polypeptide of SEQ ID NO:Y and the polypeptide encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2) or the cDNA contained in Clone ID NO:Z may be analyzed using the default parameters of the DNASTAR computer algorithm (DNASTAR, Inc., 1228 S. Park St., Madison, WI 53715 USA; <http://www.dnastar.com/>).

[141] Polypeptide regions that may be routinely obtained using the DNASTAR computer algorithm include, but are not limited to, Garnier-Robson alpha-regions, beta-regions, turn-regions, and coil-regions; Chou-Fasman alpha-regions, beta-regions, and turn-regions; Kyte-Doolittle hydrophilic regions and hydrophobic regions; Eisenberg alpha- and beta-amphipathic regions; Karplus-Schulz flexible regions; Emini surface-forming regions; and Jameson-Wolf regions of high antigenic index. Among highly preferred polynucleotides of the invention in this regard are those that encode polypeptides comprising regions that combine several structural features, such as several (e.g., 1, 2, 3 or 4) of the features set out above.

[142] Additionally, Kyte-Doolittle hydrophilic regions and hydrophobic regions, Emini surface-forming regions, and Jameson-Wolf regions of high antigenic index (i.e., containing four or more contiguous amino acids having an antigenic index of greater than or equal to 1.5, as identified using the default parameters of the Jameson-Wolf program) can routinely be used to determine polypeptide regions that exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from data by DNASTAR analysis by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

[143] Preferred polypeptide fragments of the invention are fragments comprising, or alternatively, consisting of, an amino acid sequence that displays a functional activity (e.g. biological activity) of the polypeptide sequence of which the amino acid sequence is a fragment. By a polypeptide displaying a "functional activity" is meant a polypeptide capable of one or more known functional activities associated with a full-length protein, such as, for example, biological activity, antigenicity, immunogenicity, and/or multimerization, as described herein.

[144] Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity

of the fragments may include an improved desired activity, or a decreased undesirable activity.

[145] In preferred embodiments, polypeptides of the invention comprise, or alternatively consist of, one, two, three, four, five or more of the antigenic fragments of the polypeptide of SEQ ID NO:Y, or portions thereof. Polynucleotides encoding these polypeptides are also encompassed by the invention.

[146] The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of: the polypeptide sequence shown in SEQ ID NO:Y; a polypeptide sequence encoded by SEQ ID NO:X or the complementary strand thereto; the polypeptide sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2; the polypeptide sequence encoded by the portion of SEQ ID NO:B as defined in column 6 of Table 1B or the complement thereto; the polypeptide sequence encoded by the cDNA contained in Clone ID NO:Z; or the polypeptide sequence encoded by a polynucleotide that hybridizes to the sequence of SEQ ID NO:X, the complement of the sequence of SEQ ID NO:X, the complement of a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, or the cDNA sequence contained in Clone ID NO:Z under stringent hybridization conditions or alternatively, under lower stringency hybridization as defined *supra*. The present invention further encompasses polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X, or a fragment thereof), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under stringent hybridization conditions or alternatively, under lower stringency hybridization conditions defined *supra*.

[147] The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described *infra*. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998-4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can



immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross-reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

[148] Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, R. A., Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985) further described in U.S. Patent No. 4,631,211.)

[149] In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies, that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

[150] Non-limiting examples of epitopes of polypeptides that can be used to generate antibodies of the invention include a polypeptide comprising, or alternatively consisting of, at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y specified in column 7 of Table 1A. These polypeptide fragments have been determined to bear antigenic epitopes of the proteins of the invention by the analysis of the Jameson-Wolf antigenic index which is included in the DNASTar suite of computer programs. By "comprise" it is intended that a polypeptide contains at least one, two, three, four, five, six or more of the portion(s) of SEQ ID NO:Y shown in column 7 of Table 1A, but it may contain additional flanking residues on either the amino or carboxyl termini of the recited portion. Such additional flanking sequences are preferably sequences naturally found adjacent to the portion; i.e., contiguous sequence shown in SEQ ID NO:Y. The flanking sequence may, however, be sequences from a heterologous polypeptide, such as from another protein described herein or from a heterologous polypeptide not described herein.



In particular embodiments, epitope portions of a polypeptide of the invention comprise one, two, three, or more of the portions of SEQ ID NO:Y shown in column 7 of Table 1A.

[151] Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. See, for instance, Sutcliffe et al., *supra*; Wilson et al., *supra*; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

[152] Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, *in vivo* immunization, *in vitro* immunization, and phage display methods. See, e.g., Sutcliffe et al., *supra*; Wilson et al., *supra*, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If *in vivo* immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl-N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier-coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 µg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

[153] As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof, resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1 – 585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) which is herein incorporated by reference in its entirety. In another preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with polypeptide fragments comprising, or alternatively consisting of, amino acid residues 1-z of human serum albumin, where z is an integer from 369 to 419, as described in U.S. Patent 5,766,883 herein incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous protein (e.g., immunoglobulin Fc polypeptide or human serum albumin polypeptide). Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

[154] Such fusion proteins as those described above may facilitate purification and may increase half-life *in vivo*. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion disulfide bonds have also been found to be



more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., *J. Biochem.*, 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin (HA) tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, *Proc. Natl. Acad. Sci. USA* 88:8972-897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni<sup>2+</sup> nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

#### *Fusion Proteins*

[155] Any polypeptide of the present invention can be used to generate fusion proteins. For example, the polypeptide of the present invention, when fused to a second protein, can be used as an antigenic tag. Antibodies raised against the polypeptide of the present invention can be used to indirectly detect the second protein by binding to the polypeptide. Moreover, because secreted proteins target cellular locations based on trafficking signals, polypeptides of the present invention which are shown to be secreted can be used as targeting molecules once fused to other proteins.

[156] Examples of domains that can be fused to polypeptides of the present invention include not only heterologous signal sequences, but also other heterologous functional regions. The fusion does not necessarily need to be direct, but may occur through linker sequences.

[157] In certain preferred embodiments, proteins of the invention are fusion proteins comprising an amino acid sequence that is an N and/or C-terminal deletion of a polypeptide of the invention. In preferred embodiments, the invention is directed to a fusion protein comprising an amino acid sequence that is at least 90%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence of the invention. Polynucleotides encoding these proteins are also encompassed by the invention.



[158] Moreover, fusion proteins may also be engineered to improve characteristics of the polypeptide of the present invention. For instance, a region of additional amino acids, particularly charged amino acids, may be added to the N-terminus of the polypeptide to improve stability and persistence during purification from the host cell or subsequent handling and storage. Also, peptide moieties may be added to the polypeptide to facilitate purification. Such regions may be removed prior to final preparation of the polypeptide. The addition of peptide moieties to facilitate handling of polypeptides are familiar and routine techniques in the art.

[159] As one of skill in the art will appreciate that, as discussed above, polypeptides of the present invention, and epitope-bearing fragments thereof, can be combined with heterologous polypeptide sequences. For example, the polypeptides of the present invention may be fused with heterologous polypeptide sequences, for example, the polypeptides of the present invention may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM) or portions thereof (CH1, CH2, CH3, and any combination thereof, including both entire domains and portions thereof), or albumin (including, but not limited to, native or recombinant human albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)), resulting in chimeric polypeptides. For example, EP-A-O 464 533 (Canadian counterpart 2045869) discloses fusion proteins comprising various portions of constant region of immunoglobulin molecules together with another human protein or part thereof. In many cases, the Fc part in a fusion protein is beneficial in therapy and diagnosis, and thus can result in, for example, improved pharmacokinetic properties (EP-A 0232 262). Alternatively, deleting the Fc part after the fusion protein has been expressed, detected, and purified, would be desired. For example, the Fc portion may hinder therapy and diagnosis if the fusion protein is used as an antigen for immunizations. In drug discovery, for example, human proteins, such as hIL-5, have been fused with Fc portions for the purpose of high-throughput screening assays to identify antagonists of hIL-5. See, D. Bennett et al., *J. Molecular Recognition* 8:52-58 (1995); K. Johanson et al., *J. Biol. Chem.* 270:9459-9471 (1995).

[160] Moreover, the polypeptides of the present invention can be fused to marker sequences, such as a polypeptide which facilitates purification of the fused polypeptide. In preferred embodiments, the marker amino acid sequence is a hexa-histidine peptide, such as

the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, CA, 91311), among others, many of which are commercially available. As described in Gentz et al., Proc. Natl. Acad. Sci. USA 86:821-824 (1989), for instance, hexa-histidine provides for convenient purification of the fusion protein. Another peptide tag useful for purification, the "HA" tag, corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., Cell 37:767 (1984)).

[161] Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33 (1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308-13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

[162] Thus, any of these above fusions can be engineered using the polynucleotides or the polypeptides of the present invention.

#### Recombinant and Synthetic Production of Polypeptides of the Invention

[163] The present invention also relates to vectors containing the polynucleotide of the present invention, host cells, and the production of polypeptides by synthetic and recombinant techniques. The vector may be, for example, a phage, plasmid, viral, or



retroviral vector. Retroviral vectors may be replication competent or replication defective. In the latter case, viral propagation generally will occur only in complementing host cells.

[164] The polynucleotides of the invention may be joined to a vector containing a selectable marker for propagation in a host. Generally, a plasmid vector is introduced in a precipitate, such as a calcium phosphate precipitate, or in a complex with a charged lipid. If the vector is a virus, it may be packaged in vitro using an appropriate packaging cell line and then transduced into host cells.

[165] The polynucleotide insert should be operatively linked to an appropriate promoter, such as the phage lambda PL promoter, the E. coli lac, trp, phoA and tac promoters, the SV40 early and late promoters and promoters of retroviral LTRs, to name a few. Other suitable promoters will be known to the skilled artisan. The expression constructs will further contain sites for transcription initiation, termination, and, in the transcribed region, a ribosome binding site for translation. The coding portion of the transcripts expressed by the constructs will preferably include a translation initiating codon at the beginning and a termination codon (UAA, UGA or UAG) appropriately positioned at the end of the polypeptide to be translated.

[166] As indicated, the expression vectors will preferably include at least one selectable marker. Such markers include dihydrofolate reductase, G418, glutamine synthase, or neomycin resistance for eukaryotic cell culture, and tetracycline, kanamycin or ampicillin resistance genes for culturing in E. coli and other bacteria. Representative examples of appropriate hosts include, but are not limited to, bacterial cells, such as E. coli, Streptomyces and Salmonella typhimurium cells; fungal cells, such as yeast cells (e.g., Saccharomyces cerevisiae or Pichia pastoris (ATCC Accession No. 201178)); insect cells such as Drosophila S2 and Spodoptera Sf9 cells; animal cells such as CHO, COS, 293, and Bowes melanoma cells; and plant cells. Appropriate culture mediums and conditions for the above-described host cells are known in the art.

[167] Among vectors preferred for use in bacteria include pQE70, pQE60 and pQE-9, available from QIAGEN, Inc.; pBluescript vectors, Phagescript vectors, pNH8A, pNH16a, pNH18A, pNH46A, available from Stratagene Cloning Systems, Inc.; and ptrc99a, pKK223-3, pKK233-3, pDR540, pRIT5 available from Pharmacia Biotech, Inc. Among preferred eukaryotic vectors are pWLNEO, pSV2CAT, pOG44, pXT1 and pSG available from Stratagene; and pSVK3, pBPV, pMSG and pSVL available from Pharmacia. Preferred expression vectors for use in yeast systems include, but are not limited to pYES2, pYD1,



pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalph, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, pPIC9K, and PAO815 (all available from Invitrogen, Carlsbad, CA). Other suitable vectors will be readily apparent to the skilled artisan.

[168] Vectors which use glutamine synthase (GS) or DHFR as the selectable markers can be amplified in the presence of the drugs methionine sulphoximine or methotrexate, respectively. An advantage of glutamine synthase based vectors are the availability of cell lines (e.g., the murine myeloma cell line, NS0) which are glutamine synthase negative. Glutamine synthase expression systems can also function in glutamine synthase expressing cells (e.g., Chinese Hamster Ovary (CHO) cells) by providing additional inhibitor to prevent the functioning of the endogenous gene. A glutamine synthase expression system and components thereof are detailed in PCT publications: WO87/04462; WO86/05807; WO89/01036; WO89/10404; and WO91/06657, which are hereby incorporated in their entireties by reference herein. Additionally, glutamine synthase expression vectors can be obtained from Lonza Biologics, Inc. (Portsmouth, NH). Expression and production of monoclonal antibodies using a GS expression system in murine myeloma cells is described in Bebbington *et al.*, *Bio/technology* 10:169(1992) and in Biblia and Robinson *Biotechnol. Prog.* 11:1 (1995) which are herein incorporated by reference.

[169] The present invention also relates to host cells containing the above-described vector constructs described herein, and additionally encompasses host cells containing nucleotide sequences of the invention that are operably associated with one or more heterologous control regions (e.g., promoter and/or enhancer) using techniques known of in the art. The host cell can be a higher eukaryotic cell, such as a mammalian cell (e.g., a human derived cell), or a lower eukaryotic cell, such as a yeast cell, or the host cell can be a prokaryotic cell, such as a bacterial cell. A host strain may be chosen which modulates the expression of the inserted gene sequences, or modifies and processes the gene product in the specific fashion desired. Expression from certain promoters can be elevated in the presence of certain inducers; thus expression of the genetically engineered polypeptide may be controlled. Furthermore, different host cells have characteristics and specific mechanisms for the translational and post-translational processing and modification (e.g., phosphorylation, cleavage) of proteins. Appropriate cell lines can be chosen to ensure the desired modifications and processing of the foreign protein expressed.

[170] Introduction of the nucleic acids and nucleic acid constructs of the invention into the host cell can be effected by calcium phosphate transfection, DEAE-dextran mediated

transfection, cationic lipid-mediated transfection, electroporation, transduction, infection, or other methods. Such methods are described in many standard laboratory manuals, such as Davis et al., *Basic Methods In Molecular Biology* (1986). It is specifically contemplated that the polypeptides of the present invention may in fact be expressed by a host cell lacking a recombinant vector.

[171] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., the coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., US Patent Number 5,641,670, issued June 24, 1997; International Publication Number WO 96/29411; International Publication Number WO 94/12650; Koller *et al.*, *Proc. Natl. Acad. Sci. USA* 86:8932-8935 (1989); and Zijlstra *et al.*, *Nature* 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

[172] Polypeptides of the invention can be recovered and purified from recombinant cell cultures by well-known methods including ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification.

[173] Polypeptides of the present invention can also be recovered from: products purified from natural sources, including bodily fluids, tissues and cells, whether directly isolated or cultured; products of chemical synthetic procedures; and products produced by recombinant techniques from a prokaryotic or eukaryotic host, including, for example, bacterial, yeast, higher plant, insect, and mammalian cells. Depending upon the host employed in a recombinant production procedure, the polypeptides of the present invention may be glycosylated or may be non-glycosylated. In addition, polypeptides of the invention may also include an initial modified methionine residue, in some cases as a result of host-mediated processes. Thus, it is well known in the art that the N-terminal methionine



encoded by the translation initiation codon generally is removed with high efficiency from any protein after translation in all eukaryotic cells. While the N-terminal methionine on most proteins also is efficiently removed in most prokaryotes, for some proteins, this prokaryotic removal process is inefficient, depending on the nature of the amino acid to which the N-terminal methionine is covalently linked.

[174] In one embodiment, the yeast *Pichia pastoris* is used to express polypeptides of the invention in a eukaryotic system. *Pichia pastoris* is a methylotrophic yeast which can metabolize methanol as its sole carbon source. A main step in the methanol metabolism pathway is the oxidation of methanol to formaldehyde using O<sub>2</sub>. This reaction is catalyzed by the enzyme alcohol oxidase. In order to metabolize methanol as its sole carbon source, *Pichia pastoris* must generate high levels of alcohol oxidase due, in part, to the relatively low affinity of alcohol oxidase for O<sub>2</sub>. Consequently, in a growth medium depending on methanol as a main carbon source, the promoter region of one of the two alcohol oxidase genes (*AOX1*) is highly active. In the presence of methanol, alcohol oxidase produced from the *AOX1* gene comprises up to approximately 30% of the total soluble protein in *Pichia pastoris*. See Ellis, S.B., et al., *Mol. Cell. Biol.* 5:1111-21 (1985); Koutz, P.J., et al., *Yeast* 5:167-77 (1989); Tschopp, J.F., et al., *Nucl. Acids Res.* 15:3859-76 (1987). Thus, a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, under the transcriptional regulation of all or part of the *AOX1* regulatory sequence is expressed at exceptionally high levels in *Pichia* yeast grown in the presence of methanol.

[175] In one example, the plasmid vector pPIC9K is used to express DNA encoding a polypeptide of the invention, as set forth herein, in a *Pichea* yeast system essentially as described in "*Pichia* Protocols: Methods in Molecular Biology," D.R. Higgins and J. Cregg, eds. The Humana Press, Totowa, NJ, 1998. This expression vector allows expression and secretion of a polypeptide of the invention by virtue of the strong *AOX1* promoter linked to the *Pichia pastoris* alkaline phosphatase (PHO) secretory signal peptide (i.e., leader) located upstream of a multiple cloning site.

[176] Many other yeast vectors could be used in place of pPIC9K, such as, pYES2, pYD1, pTEF1/Zeo, pYES2/GS, pPICZ, pGAPZ, pGAPZalpha, pPIC9, pPIC3.5, pHIL-D2, pHIL-S1, pPIC3.5K, and PAO815, as one skilled in the art would readily appreciate, as



long as the proposed expression construct provides appropriately located signals for transcription, translation, secretion (if desired), and the like, including an in-frame AUG as required.

[177] In another embodiment, high-level expression of a heterologous coding sequence, such as, for example, a polynucleotide of the present invention, may be achieved by cloning the heterologous polynucleotide of the invention into an expression vector such as, for example, pGAPZ or pGAPZalpha, and growing the yeast culture in the absence of methanol.

[178] In addition to encompassing host cells containing the vector constructs discussed herein, the invention also encompasses primary, secondary, and immortalized host cells of vertebrate origin, particularly mammalian origin, that have been engineered to delete or replace endogenous genetic material (e.g., coding sequence), and/or to include genetic material (e.g., heterologous polynucleotide sequences) that is operably associated with polynucleotides of the invention, and which activates, alters, and/or amplifies endogenous polynucleotides. For example, techniques known in the art may be used to operably associate heterologous control regions (e.g., promoter and/or enhancer) and endogenous polynucleotide sequences via homologous recombination (see, e.g., U.S. Patent No. 5,641,670, issued June 24, 1997; International Publication No. WO 96/29411, published September 26, 1996; International Publication No. WO 94/12650, published August 4, 1994; Koller et al., Proc. Natl. Acad. Sci. USA 86:8932-8935 (1989); and Zijlstra et al., Nature 342:435-438 (1989), the disclosures of each of which are incorporated by reference in their entireties).

[179] In addition, polypeptides of the invention can be chemically synthesized using techniques known in the art (e.g., see Creighton, 1983, Proteins: Structures and Molecular Principles, W.H. Freeman & Co., N.Y., and Hunkapiller et al., Nature, 310:105-111 (1984)). For example, a polypeptide corresponding to a fragment of a polypeptide can be synthesized by use of a peptide synthesizer. Furthermore, if desired, nonclassical amino acids or chemical amino acid analogs can be introduced as a substitution or addition into the polypeptide sequence. Non-classical amino acids include, but are not limited to, to the D-isomers of the common amino acids, 2,4-diaminobutyric acid,  $\alpha$ -amino isobutyric acid, 4-aminobutyric acid, Abu, 2-amino butyric acid,  $\gamma$ -Abu,  $\epsilon$ -Ahx, 6-amino hexanoic acid, Aib, 2-amino isobutyric acid, 3-amino propionic acid, ornithine, norleucine, norvaline, hydroxyproline, sarcosine, citrulline, homocitrulline, cysteic acid, t-butylglycine, t-

butylalanine, phenylglycine, cyclohexylalanine, b-alanine, fluoro-amino acids, designer amino acids such as b-methyl amino acids, Ca-methyl amino acids, Na-methyl amino acids, and amino acid analogs in general. Furthermore, the amino acid can be D (dextrorotary) or L (levorotary).

[180] The invention encompasses polypeptides of the present invention which are differentially modified during or after translation, e.g., by glycosylation, acetylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to an antibody molecule or other cellular ligand, etc. Any of numerous chemical modifications may be carried out by known techniques, including but not limited, to specific chemical cleavage by cyanogen bromide, trypsin, chymotrypsin, papain, V8 protease, NaBH<sub>4</sub>; acetylation, formylation, oxidation, reduction; metabolic synthesis in the presence of tunicamycin; etc.

[181] Additional post-translational modifications encompassed by the invention include, for example, e.g., N-linked or O-linked carbohydrate chains, processing of N-terminal or C-terminal ends), attachment of chemical moieties to the amino acid backbone, chemical modifications of N-linked or O-linked carbohydrate chains, and addition or deletion of an N-terminal methionine residue as a result of procaryotic host cell expression. The polypeptides may also be modified with a detectable label, such as an enzymatic, fluorescent, isotopic or affinity label to allow for detection and isolation of the protein.

[182] Examples of suitable enzymes include horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin; and examples of suitable radioactive material include iodine (<sup>121</sup>I, <sup>123</sup>I, <sup>125</sup>I, <sup>131</sup>I), carbon (<sup>14</sup>C), sulfur (<sup>35</sup>S), tritium (<sup>3</sup>H), indium (<sup>111</sup>In, <sup>112</sup>In, <sup>113m</sup>In, <sup>115m</sup>In), technetium (<sup>99</sup>Tc, <sup>99m</sup>Tc), thallium (<sup>201</sup>Tl), gallium (<sup>68</sup>Ga, <sup>67</sup>Ga), palladium (<sup>103</sup>Pd), molybdenum (<sup>99</sup>Mo), xenon (<sup>133</sup>Xe), fluorine (<sup>18</sup>F), <sup>153</sup>Sm, <sup>177</sup>Lu, <sup>159</sup>Gd, <sup>149</sup>Pm, <sup>140</sup>La, <sup>175</sup>Yb, <sup>166</sup>Ho, <sup>90</sup>Y, <sup>47</sup>Sc, <sup>186</sup>Re, <sup>188</sup>Re, <sup>142</sup>Pr, <sup>105</sup>Rh, and <sup>97</sup>Ru.

[183] In specific embodiments, a polypeptide of the present invention or fragment or variant thereof is attached to macrocyclic chelators that associate with radiometal ions,



including but not limited to,  $^{177}\text{Lu}$ ,  $^{90}\text{Y}$ ,  $^{166}\text{Ho}$ , and  $^{153}\text{Sm}$ , to polypeptides. In a preferred embodiment, the radiometal ion associated with the macrocyclic chelators is  $^{111}\text{In}$ . In another preferred embodiment, the radiometal ion associated with the macrocyclic chelator is  $^{90}\text{Y}$ . In specific embodiments, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid (DOTA). In other specific embodiments, DOTA is attached to an antibody of the invention or fragment thereof via a linker molecule. Examples of linker molecules useful for conjugating DOTA to a polypeptide are commonly known in the art - see, for example, DeNardo et al., *Clin Cancer Res.* 4(10):2483-90 (1998); Peterson et al., *Bioconjug. Chem.* 10(4):553-7 (1999); and Zimmerman et al., *Nucl. Med. Biol.* 26(8):943-50 (1999); which are hereby incorporated by reference in their entirety.

[184] As mentioned, the proteins of the invention may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in a given polypeptide. Polypeptides of the invention may be branched, for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphatidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, *PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES*, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); *POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS*, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., *Meth. Enzymol.* 182:626-646 (1990); Rattan et al., *Ann. N.Y. Acad. Sci.* 663:48-62 (1992)).



[185] Also provided by the invention are chemically modified derivatives of the polypeptides of the invention which may provide additional advantages such as increased solubility, stability and circulating time of the polypeptide, or decreased immunogenicity (see U.S. Patent No. 4,179,337). The chemical moieties for derivitization may be selected from water soluble polymers such as polyethylene glycol, ethylene glycol/propylene glycol copolymers, carboxymethylcellulose, dextran, polyvinyl alcohol and the like. The polypeptides may be modified at random positions within the molecule, or at predetermined positions within the molecule and may include one, two, three or more attached chemical moieties.

[186] The polymer may be of any molecular weight, and may be branched or unbranched. For polyethylene glycol, the preferred molecular weight is between about 1 kDa and about 100 kDa (the term "about" indicating that in preparations of polyethylene glycol, some molecules will weigh more, some less, than the stated molecular weight) for ease in handling and manufacturing. Other sizes may be used, depending on the desired therapeutic profile (e.g., the duration of sustained release desired, the effects, if any on biological activity, the ease in handling, the degree or lack of antigenicity and other known effects of the polyethylene glycol to a therapeutic protein or analog). For example, the polyethylene glycol may have an average molecular weight of about 200, 500, 1000, 1500, 2000, 2500, 3000, 3500, 4000, 4500, 5000, 5500, 6000, 6500, 7000, 7500, 8000, 8500, 9000, 9500, 10,000, 10,500, 11,000, 11,500, 12,000, 12,500, 13,000, 13,500, 14,000, 14,500, 15,000, 15,500, 16,000, 16,500, 17,000, 17,500, 18,000, 18,500, 19,000, 19,500, 20,000, 25,000, 30,000, 35,000, 40,000, 45,000, 50,000, 55,000, 60,000, 65,000, 70,000, 75,000, 80,000, 85,000, 90,000, 95,000, or 100,000 kDa.

[187] As noted above, the polyethylene glycol may have a branched structure. Branched polyethylene glycols are described, for example, in U.S. Patent No. 5,643,575; Morpurgo *et al.*, *Appl. Biochem. Biotechnol.* 56:59-72 (1996); Vorobjev *et al.*, *Nucleosides Nucleotides* 18:2745-2750 (1999); and Caliceti *et al.*, *Bioconjug. Chem.* 10:638-646 (1999), the disclosures of each of which are incorporated herein by reference.

[188] The polyethylene glycol molecules (or other chemical moieties) should be attached to the protein with consideration of effects on functional or antigenic domains of the protein. There are a number of attachment methods available to those skilled in the art, such as, for example, the method disclosed in EP 0 401 384 (coupling PEG to G-CSF), herein incorporated by reference; see also Malik *et al.*, *Exp. Hematol.* 20:1028-1035 (1992),

reporting pegylation of GM-CSF using tresyl chloride. For example, polyethylene glycol may be covalently bound through amino acid residues via a reactive group, such as a free amino or carboxyl group. Reactive groups are those to which an activated polyethylene glycol molecule may be bound. The amino acid residues having a free amino group may include lysine residues and the N-terminal amino acid residues; those having a free carboxyl group may include aspartic acid residues glutamic acid residues and the C-terminal amino acid residue. Sulfhydryl groups may also be used as a reactive group for attaching the polyethylene glycol molecules. Preferred for therapeutic purposes is attachment at an amino group, such as attachment at the N-terminus or lysine group.

[189] As suggested above, polyethylene glycol may be attached to proteins via linkage to any of a number of amino acid residues. For example, polyethylene glycol can be linked to proteins via covalent bonds to lysine, histidine, aspartic acid, glutamic acid, or cysteine residues. One or more reaction chemistries may be employed to attach polyethylene glycol to specific amino acid residues (e.g., lysine, histidine, aspartic acid, glutamic acid, or cysteine) of the protein or to more than one type of amino acid residue (e.g., lysine, histidine, aspartic acid, glutamic acid, cysteine and combinations thereof) of the protein.

[190] One may specifically desire proteins chemically modified at the N-terminus. Using polyethylene glycol as an illustration of the present composition, one may select from a variety of polyethylene glycol molecules (by molecular weight, branching, etc.), the proportion of polyethylene glycol molecules to protein (polypeptide) molecules in the reaction mix, the type of pegylation reaction to be performed, and the method of obtaining the selected N-terminally pegylated protein. The method of obtaining the N-terminally pegylated preparation (i.e., separating this moiety from other monopegylated moieties if necessary) may be by purification of the N-terminally pegylated material from a population of pegylated protein molecules. Selective proteins chemically modified at the N-terminus modification may be accomplished by reductive alkylation which exploits differential reactivity of different types of primary amino groups (lysine versus the N-terminal) available for derivatization in a particular protein. Under the appropriate reaction conditions, substantially selective derivatization of the protein at the N-terminus with a carbonyl group containing polymer is achieved.

[191] As indicated above, pegylation of the proteins of the invention may be accomplished by any number of means. For example, polyethylene glycol may be attached to the protein either directly or by an intervening linker. Linkerless systems for attaching



polyethylene glycol to proteins are described in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992); Francis et al., Intern. J. of Hematol. 68:1-18 (1998); U.S. Patent No. 4,002,531; U.S. Patent No. 5,349,052; WO 95/06058; and WO 98/32466, the disclosures of each of which are incorporated herein by reference.

[192] One system for attaching polyethylene glycol directly to amino acid residues of proteins without an intervening linker employs tresylated MPEG, which is produced by the modification of monmethoxy polyethylene glycol (MPEG) using tresylchloride ( $\text{ClSO}_2\text{CH}_2\text{CF}_3$ ). Upon reaction of protein with tresylated MPEG, polyethylene glycol is directly attached to amine groups of the protein. Thus, the invention includes protein-polyethylene glycol conjugates produced by reacting proteins of the invention with a polyethylene glycol molecule having a 2,2,2-trifluoroethane sulphonyl group.

[193] Polyethylene glycol can also be attached to proteins using a number of different intervening linkers. For example, U.S. Patent No. 5,612,460, the entire disclosure of which is incorporated herein by reference, discloses urethane linkers for connecting polyethylene glycol to proteins. Protein-polyethylene glycol conjugates wherein the polyethylene glycol is attached to the protein by a linker can also be produced by reaction of proteins with compounds such as MPEG-succinimidylsuccinate, MPEG activated with 1,1'-carbonyldiimidazole, MPEG-2,4,5-trichloropenylcarbonate, MPEG-p-nitrophenolcarbonate, and various MPEG-succinate derivatives. A number of additional polyethylene glycol derivatives and reaction chemistries for attaching polyethylene glycol to proteins are described in International Publication No. WO 98/32466, the entire disclosure of which is incorporated herein by reference. Pegylated protein products produced using the reaction chemistries set out herein are included within the scope of the invention.

[194] The number of polyethylene glycol moieties attached to each protein of the invention (i.e., the degree of substitution) may also vary. For example, the pegylated proteins of the invention may be linked, on average, to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 15, 17, 20, or more polyethylene glycol molecules. Similarly, the average degree of substitution within ranges such as 1-3, 2-4, 3-5, 4-6, 5-7, 6-8, 7-9, 8-10, 9-11, 10-12, 11-13, 12-14, 13-15, 14-16, 15-17, 16-18, 17-19, or 18-20 polyethylene glycol moieties per protein molecule. Methods for determining the degree of substitution are discussed, for example, in Delgado et al., Crit. Rev. Thera. Drug Carrier Sys. 9:249-304 (1992).

[195] The polypeptides of the invention can be recovered and purified from chemical



synthesis and recombinant cell cultures by standard methods which include, but are not limited to, ammonium sulfate or ethanol precipitation, acid extraction, anion or cation exchange chromatography, phosphocellulose chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and lectin chromatography. Most preferably, high performance liquid chromatography ("HPLC") is employed for purification. Well known techniques for refolding protein may be employed to regenerate active conformation when the polypeptide is denatured during isolation and/or purification.

[196] The polypeptides of the invention may be in monomers or multimers (i.e., dimers, trimers, tetramers and higher multimers). Accordingly, the present invention relates to monomers and multimers of the polypeptides of the invention, their preparation, and compositions (preferably, Therapeutics) containing them. In specific embodiments, the polypeptides of the invention are monomers, dimers, trimers or tetramers. In additional embodiments, the multimers of the invention are at least dimers, at least trimers, or at least tetramers.

[197] Multimers encompassed by the invention may be homomers or heteromers. As used herein, the term homomer refers to a multimer containing only polypeptides corresponding to a protein of the invention (e.g., the amino acid sequence of SEQ ID NO:Y, an amino acid sequence encoded by SEQ ID NO:X or the complement of SEQ ID NO:X, the amino acid sequence encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or an amino acid sequence encoded by cDNA contained in Clone ID NO:Z (including fragments, variants, splice variants, and fusion proteins, corresponding to these as described herein)). These homomers may contain polypeptides having identical or different amino acid sequences. In a specific embodiment, a homomer of the invention is a multimer containing only polypeptides having an identical amino acid sequence. In another specific embodiment, a homomer of the invention is a multimer containing polypeptides having different amino acid sequences. In specific embodiments, the multimer of the invention is a homodimer (e.g., containing two polypeptides having identical or different amino acid sequences) or a homotrimer (e.g., containing three polypeptides having identical and/or different amino acid sequences). In additional embodiments, the homomeric multimer of the invention is at least a homodimer, at least a homotrimer, or at least a homotetramer.

[198] As used herein, the term heteromer refers to a multimer containing one or more heterologous polypeptides (i.e., polypeptides of different proteins) in addition to the polypeptides of the invention. In a specific embodiment, the multimer of the invention is a heterodimer, a heterotrimer, or a heterotetramer. In additional embodiments, the heteromeric multimer of the invention is at least a heterodimer, at least a heterotrimer, or at least a heterotetramer.

[199] Multimers of the invention may be the result of hydrophobic, hydrophilic, ionic and/or covalent associations and/or may be indirectly linked by, for example, liposome formation. Thus, in one embodiment, multimers of the invention, such as, for example, homodimers or homotrimers, are formed when polypeptides of the invention contact one another in solution. In another embodiment, heteromultimers of the invention, such as, for example, heterotrimers or heterotetramers, are formed when polypeptides of the invention contact antibodies to the polypeptides of the invention (including antibodies to the heterologous polypeptide sequence in a fusion protein of the invention) in solution. In other embodiments, multimers of the invention are formed by covalent associations with and/or between the polypeptides of the invention. Such covalent associations may involve one or more amino acid residues contained in the polypeptide sequence (e.g., that recited in SEQ ID NO:Y, encoded by the portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or encoded by the cDNA contained in Clone ID NO:Z). In one instance, the covalent associations are cross-linking between cysteine residues located within the polypeptide sequences which interact in the native (i.e., naturally occurring) polypeptide. In another instance, the covalent associations are the consequence of chemical or recombinant manipulation. Alternatively, such covalent associations may involve one or more amino acid residues contained in the heterologous polypeptide sequence in a fusion protein. In one example, covalent associations are between the heterologous sequence contained in a fusion protein of the invention (see, e.g., US Patent Number 5,478,925). In a specific example, the covalent associations are between the heterologous sequence contained in a Fc fusion protein of the invention (as described herein). In another specific example, covalent associations of fusion proteins of the invention are between heterologous polypeptide sequence from another protein that is capable of forming covalently associated multimers, such as for example, osteoprotegerin (see, e.g., International Publication NO: WO 98/49305, the contents of which are herein incorporated by reference in its entirety). In another embodiment, two or more polypeptides of the invention are joined through peptide



linkers. Examples include those peptide linkers described in U.S. Pat. No. 5,073,627 (hereby incorporated by reference). Proteins comprising multiple polypeptides of the invention separated by peptide linkers may be produced using conventional recombinant DNA technology.

[200] Another method for preparing multimer polypeptides of the invention involves use of polypeptides of the invention fused to a leucine zipper or isoleucine zipper polypeptide sequence. Leucine zipper and isoleucine zipper domains are polypeptides that promote multimerization of the proteins in which they are found. Leucine zippers were originally identified in several DNA-binding proteins (Landschulz et al., *Science* 240:1759, (1988)), and have since been found in a variety of different proteins. Among the known leucine zippers are naturally occurring peptides and derivatives thereof that dimerize or trimerize. Examples of leucine zipper domains suitable for producing soluble multimeric proteins of the invention are those described in PCT application WO 94/10308, hereby incorporated by reference. Recombinant fusion proteins comprising a polypeptide of the invention fused to a polypeptide sequence that dimerizes or trimerizes in solution are expressed in suitable host cells, and the resulting soluble multimeric fusion protein is recovered from the culture supernatant using techniques known in the art.

[201] Trimeric polypeptides of the invention may offer the advantage of enhanced biological activity. Preferred leucine zipper moieties and isoleucine moieties are those that preferentially form trimers. One example is a leucine zipper derived from lung surfactant protein D (SPD), as described in Hoppe et al. (*FEBS Letters* 344:191, (1994)) and in U.S. patent application Ser. No. 08/446,922, hereby incorporated by reference. Other peptides derived from naturally occurring trimeric proteins may be employed in preparing trimeric polypeptides of the invention.

[202] In another example, proteins of the invention are associated by interactions between Flag® polypeptide sequence contained in fusion proteins of the invention containing Flag® polypeptide sequence. In a further embodiment, proteins of the invention are associated by interactions between heterologous polypeptide sequence contained in Flag® fusion proteins of the invention and anti-Flag® antibody.

[203] The multimers of the invention may be generated using chemical techniques known in the art. For example, polypeptides desired to be contained in the multimers of the invention may be chemically cross-linked using linker molecules and linker molecule length optimization techniques known in the art (see, e.g., US Patent Number 5,478,925,



which is herein incorporated by reference in its entirety). Additionally, multimers of the invention may be generated using techniques known in the art to form one or more inter-molecule cross-links between the cysteine residues located within the sequence of the polypeptides desired to be contained in the multimer (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Further, polypeptides of the invention may be routinely modified by the addition of cysteine or biotin to the C-terminus or N-terminus of the polypeptide and techniques known in the art may be applied to generate multimers containing one or more of these modified polypeptides (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). Additionally, techniques known in the art may be applied to generate liposomes containing the polypeptide components desired to be contained in the multimer of the invention (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

[204] Alternatively, multimers of the invention may be generated using genetic engineering techniques known in the art. In one embodiment, polypeptides contained in multimers of the invention are produced recombinantly using fusion protein technology described herein or otherwise known in the art (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In a specific embodiment, polynucleotides coding for a homodimer of the invention are generated by ligating a polynucleotide sequence encoding a polypeptide of the invention to a sequence encoding a linker polypeptide and then further to a synthetic polynucleotide encoding the translated product of the polypeptide in the reverse orientation from the original C-terminus to the N-terminus (lacking the leader sequence) (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety). In another embodiment, recombinant techniques described herein or otherwise known in the art are applied to generate recombinant polypeptides of the invention which contain a transmembrane domain (or hydrophobic or signal peptide) and which can be incorporated by membrane reconstitution techniques into liposomes (see, e.g., US Patent Number 5,478,925, which is herein incorporated by reference in its entirety).

#### Antibodies

[205] Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or

variant of the invention (e.g., a polypeptide or fragment or variant of the amino acid sequence of SEQ ID NO:Y or a polypeptide encoded by the cDNA contained in Clone ID No:Z, and/or an epitope, of the present invention) as determined by immunoassays well known in the art for assaying specific antibody-antigen binding. Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), intracellularly-made antibodies (i.e., intrabodies), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

[206] Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')<sub>2</sub>, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

[207] The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for



different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

[208] Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, or by size in contiguous amino acid residues, or listed in the Tables and Figures. Preferred epitopes of the invention include the predicted epitopes shown in column 7 of Table 1A, as well as polynucleotides that encode these epitopes. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

[209] Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide



of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or  $K_d$  less than  $5 \times 10^{-2}$  M,  $10^{-2}$  M,  $5 \times 10^{-3}$  M,  $10^{-3}$  M,  $5 \times 10^{-4}$  M,  $10^{-4}$  M,  $5 \times 10^{-5}$  M,  $10^{-5}$  M,  $5 \times 10^{-6}$  M,  $10^{-6}$  M,  $5 \times 10^{-7}$  M,  $10^{-7}$  M,  $5 \times 10^{-8}$  M,  $10^{-8}$  M,  $5 \times 10^{-9}$  M,  $10^{-9}$  M,  $5 \times 10^{-10}$  M,  $10^{-10}$  M,  $5 \times 10^{-11}$  M,  $10^{-11}$  M,  $5 \times 10^{-12}$  M,  $10^{-12}$  M,  $5 \times 10^{-13}$  M,  $10^{-13}$  M,  $5 \times 10^{-14}$  M,  $10^{-14}$  M,  $5 \times 10^{-15}$  M, or  $10^{-15}$  M.

[210] The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

[211] Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described *supra*). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

[212] The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from

binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No. 5,811,097; Deng et al., *Blood* 92(6):1981-1988 (1998); Chen et al., *Cancer Res.* 58(16):3668-3678 (1998); Harrop et al., *J. Immunol.* 161(4):1786-1794 (1998); Zhu et al., *Cancer Res.* 58(15):3209-3214 (1998); Yoon et al., *J. Immunol.* 160(7):3170-3179 (1998); Prat et al., *J. Cell. Sci.* 111(Pt2):237-247 (1998); Pitard et al., *J. Immunol. Methods* 205(2):177-190 (1997); Liautard et al., *Cytokine* 9(4):233-241 (1997); Carlson et al., *J. Biol. Chem.* 272(17):11295-11301 (1997); Taryman et al., *Neuron* 14(4):755-762 (1995); Muller et al., *Structure* 6(9):1153-1167 (1998); Bartunek et al., *Cytokine* 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

[213] Antibodies of the present invention may be used, for example, to purify, detect, and target the polypeptides of the present invention, including both *in vitro* and *in vivo* diagnostic and therapeutic methods. For example, the antibodies have utility in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); incorporated by reference herein in its entirety.

[214] As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalent and non-covalent conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387; the disclosures of which are incorporated herein by reference in their entireties.



[215] The antibodies of the invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

[216] The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of-interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

[217] Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., *Antibodies: A Laboratory Manual*, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: *Monoclonal Antibodies and T-Cell Hybridomas* 563-681 (Elsevier, N.Y., 1981). (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.



[218] Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples. In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

[219] Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

[220] Another well known method for producing both polyclonal and monoclonal human B cell lines is transformation using Epstein Barr Virus (EBV). Protocols for generating EBV-transformed B cell lines are commonly known in the art, such as, for example, the protocol outlined in Chapter 7.22 of Current Protocols in Immunology, Coligan et al., Eds., 1994, John Wiley & Sons, NY, which is hereby incorporated in its entirety by reference. The source of B cells for transformation is commonly human peripheral blood, but B cells for transformation may also be derived from other sources including, but not limited to, lymph nodes, tonsil, spleen, tumor tissue, and infected tissues. Tissues are generally made into single cell suspensions prior to EBV transformation. Additionally, steps may be taken to either physically remove or inactivate T cells (e.g., by treatment with cyclosporin A) in B cell-containing samples, because T cells from individuals seropositive for anti-EBV antibodies can suppress B cell immortalization by EBV.

[221] In general, the sample containing human B cells is inoculated with EBV, and cultured for 3-4 weeks. A typical source of EBV is the culture supernatant of the B95-8 cell

line (ATCC #VR-1492). Physical signs of EBV transformation can generally be seen towards the end of the 3-4 week culture period. By phase-contrast microscopy, transformed cells may appear large, clear, hairy and tend to aggregate in tight clusters of cells. Initially, EBV lines are generally polyclonal. However, over prolonged periods of cell cultures, EBV lines may become monoclonal or polyclonal as a result of the selective outgrowth of particular B cell clones. Alternatively, polyclonal EBV transformed lines may be subcloned (e.g., by limiting dilution culture) or fused with a suitable fusion partner and plated at limiting dilution to obtain monoclonal B cell lines. Suitable fusion partners for EBV transformed cell lines include mouse myeloma cell lines (e.g., SP2/0, X63-Ag8.653), heteromyeloma cell lines (human x mouse; e.g., SPAM-8, SBC-H20, and CB-F7), and human cell lines (e.g., GM 1500, SKO-007, RPMI 8226, and KR-4). Thus, the present invention also provides a method of generating polyclonal or monoclonal human antibodies against polypeptides of the invention or fragments thereof, comprising EBV-transformation of human B cells.

[222] Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')<sub>2</sub> fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')<sub>2</sub> fragments). F(ab')<sub>2</sub> fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

[223] For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., *J. Immunol. Methods* 182:41-50 (1995); Ames et al., *J. Immunol. Methods*



184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

[224] As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')<sub>2</sub> fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

[225] Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including *in vivo* use of antibodies in humans and *in vitro* detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol. Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816,397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter,



preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

[226] Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

[227] Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal

antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, *Int. Rev. Immunol.* 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; 5,939,598; 6,075,181; and 6,114,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

[228] Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., *Bio/technology* 12:899-903 (1988)).

[229] Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotypic antibodies that "mimic" polypeptides of the invention using techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, *FASEB J.* 7(5):437-444; (1989) and Nissinoff, *J. Immunol.* 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby block its biological activity. Alternatively, antibodies which bind to and enhance polypeptide multimerization and/or binding, and/or receptor/ligand multimerization,



binding and/or signaling can be used to generate anti-idiotypes that function as agonists of a polypeptide of the invention and/or its ligand/receptor. Such agonistic anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens as agonists of the polypeptides of the invention or its ligand(s)/receptor(s). For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligand(s)/receptor(s), and thereby promote or enhance its biological activity.

[230] Intrabodies of the invention can be produced using methods known in the art, such as those disclosed and reviewed in Chen et al., *Hum. Gene Ther.* 5:595-601 (1994); Marasco, W.A., *Gene Ther.* 4:11-15 (1997); Rondon and Marasco, *Annu. Rev. Microbiol.* 51:257-283 (1997); Proba et al., *J. Mol. Biol.* 275:245-253 (1998); Cohen et al., *Oncogene* 17:2445-2456 (1998); Ohage and Steipe, *J. Mol. Biol.* 291:1119-1128 (1999); Ohage et al., *J. Mol. Biol.* 291:1129-1134 (1999); Wirtz and Steipe, *Protein Sci.* 8:2245-2250 (1999); Zhu et al., *J. Immunol. Methods* 231:207-222 (1999); and references cited therein.

#### *Polynucleotides Encoding Antibodies*

[231] The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or alternatively, under lower stringency hybridization conditions, e.g., as defined *supra*, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y, to a polypeptide encoded by a portion of SEQ ID NO:X as defined in columns 8 and 9 of Table 2, and/or to a polypeptide encoded by the cDNA contained in Clone ID NO:Z.

[232] The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., *BioTechniques* 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

[233] Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a



particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

[234] Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, *Molecular Cloning, A Laboratory Manual*, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, *Current Protocols in Molecular Biology*, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

[235] In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well known in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described *supra*. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., *J. Mol. Biol.* 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed *supra*, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino acid

substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

[236] In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described *supra*, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

[237] Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423-42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in *E. coli* may also be used (Skerra et al., Science 242:1038-1041 (1988)).

#### *Methods of Producing Antibodies*

[238] The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques. Methods of producing antibodies include, but are not limited to, hybridoma technology, EBV transformation, and other methods discussed herein as well as through the use recombinant DNA technology, as discussed below.

[239] Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for



the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

[240] The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

[241] A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention *in situ*. These include but are not limited to microorganisms such as bacteria (e.g., *E. coli*, *B. subtilis*) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., *Saccharomyces*, *Pichia*) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus



expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as *Escherichia coli*, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., *Gene* 45:101 (1986); Cockett et al., *Bio/Technology* 8:2 (1990)).

[242] In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the *E. coli* expression vector pUR278 (Ruther et al., *EMBO J.* 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, *Nucleic Acids Res.* 13:3101-3109 (1985); Van Heeke & Schuster, *J. Biol. Chem.* 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

[243] In an insect system, *Autographa californica* nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions

(for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

[244] In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by *in vitro* or *in vivo* recombination. Insertion in a non-essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

[245] In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein. Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERO, BHK, HeLa, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

[246] For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be



engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

[247] A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., *Cell* 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, *Proc. Natl. Acad. Sci. USA* 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., *Cell* 22:817 (1980)) genes can be employed in tk-, hgp<sup>r</sup>t- or ap<sup>r</sup>t- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., *Natl. Acad. Sci. USA* 77:357 (1980); O'Hare et al., *Proc. Natl. Acad. Sci. USA* 78:1527 (1981)); gpt, which confers resistance to mycophenolic acid (Mulligan & Berg, *Proc. Natl. Acad. Sci. USA* 78:2072 (1981)); neo, which confers resistance to the aminoglycoside G-418 *Clinical Pharmacy* 12:488-505; Wu and Wu, *Biotherapy* 3:87-95 (1991); Tolstoshev, *Ann. Rev. Pharmacol. Toxicol.* 32:573-596 (1993); Mulligan, *Science* 260:926-932 (1993); and Morgan and Anderson, *Ann. Rev. Biochem.* 62:191-217 (1993); May, 1993, *TIB TECH* 11(5):155-215 (1993)); and hyg<sup>r</sup>, which confers resistance to hygromycin (Santerre et al., *Gene* 30:147 (1984)). Methods commonly known in the art of recombinant DNA technology may be routinely applied to select the desired recombinant clone, and such methods are described, for example, in Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, NY (1993); Kriegler, *Gene Transfer and Expression, A Laboratory Manual*, Stockton Press, NY (1990); and in Chapters 12 and 13, Dracopoli et al. (eds), *Current Protocols in Human Genetics*, John Wiley & Sons, NY (1994); Colberre-Garapin et al., *J. Mol. Biol.* 150:1 (1981), which are incorporated by reference herein in their entireties.



## DEMANDE OU BREVET VOLUMINEUX

LA PRÉSENTE PARTIE DE CETTE DEMANDE OU CE BREVET COMPREND PLUS D'UN TOME.

CECI EST LE TOME 1 DE 3  
CONTENANT LES PAGES 1 À 340

NOTE : Pour les tomes additionels, veuillez contacter le Bureau canadien des brevets

## JUMBO APPLICATIONS/PATENTS

THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

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NOM DU FICHER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

*What Is Claimed Is:*

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
  - (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence contained in Clone ID NO:Z, which is hybridizable to SEQ ID NO:X;
  - (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X;
  - (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X;
  - (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X;
  - (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X;
  - (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X, having biological activity;
  - (g) a polynucleotide which is a variant of SEQ ID NO:X;
  - (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
  - (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
  - (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.
2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence contained in cDNA Clone ID NO:Z, which is hybridizable to SEQ ID NO:X.

5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.

11. An isolated polypeptide comprising an amino acid sequence at least 90% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence contained in cDNA Clone ID NO:Z;

(b) a polypeptide fragment of SEQ ID NO:Y or the encoded sequence contained in cDNA Clone ID NO:Z, having biological activity;



- (c) a polypeptide domain of SEQ ID NO:Y or the encoded sequence contained in cDNA Clone ID NO:Z;
- (d) a polypeptide epitope of SEQ ID NO:Y or the encoded sequence contained in cDNA Clone ID NO:Z;
- (e) a full length protein of SEQ ID NO:Y or the encoded sequence contained in cDNA Clone ID NO:Z;
- (f) a variant of SEQ ID NO:Y;
- (g) an allelic variant of SEQ ID NO:Y; or
- (h) a species homologue of the SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:  
(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and  
(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:  
(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.

22. A method of identifying an activity in a biological assay, wherein the method comprises:

(a) expressing SEQ ID NO:X in a cell;

(b) isolating the supernatant;

(c) detecting an activity in a biological assay; and

identifying the protein in the supernatant having the activity.

23. The product produced by the method of claim 20.

24. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11.