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(54) Title: IL28 AND IL29 TRUNCATED CYSTEINE MUTANTS AND ANTIVIRAL METHODS OF USING SAME

(57) Abstract: IL-28A, IL-28B, IL-29, and certain mutants thereof have been shown to have antiviral activity on a spectrum of viral species. Of particular interest is the antiviral activity demonstrated on viruses that infect liver, such as hepatitis B virus and hepatitis C virus. In addition, IL-28A, IL-28B, IL-29, and mutants thereof do not exhibit some of the antiproliferative activity on hematopoietic cells that is observed with interferon treatment. Without the immunosuppressive effects accompanying interferon treatment, IL-28A, IL-28B, and IL-29 will be useful in treating immunocompromised patients for viral infections.

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PATENT APPLICATION
05-22PC

IL28 AND IL29 TRUNCATED CYSTEINE MUTANTS AND ANTIVIRAL METHODS OF USING SAME

BACKGROUND OF THE INVENTION

[1] Strategies for treating infectious disease often focus on ways to enhance immunity. For instance, the most common method for treating viral infection involves prophylactic vaccines that induce immune-based memory responses. Another method for treating viral infection includes passive immunization via immunoglobulin therapy (Meissner, J. Pediatr. 124:S17-21, 1994). Administration of Interferon alpha (IFN-α) is another method for treating viral infections such as genital warts (Reichman et al., Ann. Intern. Med. 108:675-9, 1988) and chronic viral infections like hepatitis C virus (HCV) (Davis et al., New Engl. J. Med. 339:1493-9, 1998) and hepatitis B virus (HBV). For instance, IFN-α and IFN-β are critical for inhibiting virus replication (reviewed by Vilcek et al., (Eds.), Interferons and other cytokines. In Fields Fundamental Virology., 3rd ed., Lippincott-Raven Publishers Philadelphia, PA, 1996, pages 341-365). In response to viral infection, CD4+ T cells become activated and initiate a T-helper type I (TH1) response and the subsequent cascade required for cell-mediated immunity. That is, following their expansion by specific growth factors like the cytokine IL-2, T-helper cells stimulate antigen-specific CD8+ T-cells, macrophages, and NK cells to kill virally infected host cells. Although oftentimes efficacious, these methods have limitations in clinical use. For instance, many viral infections are not amenable to vaccine development, nor are they treatable with antibodies alone. In addition, IFN's are not extremely effective and they can cause significant toxicities; thus, there is a need for improved therapies.

[2] Not all viruses and viral diseases are treated identically because factors, such as whether an infection is acute or chronic and the patient's underlying health, influence the type of treatment that is recommended. Generally, treatment of acute infections in immunocompetent patients should reduce the disease's severity, decrease complications, and decrease the rate of transmission. Safety, cost, and convenience are essential considerations in recommending an acute antiviral agent. Treatments for chronic infections should prevent viral damage to organs such as liver, lungs, heart, central nervous system, and gastrointestinal sytem, making efficacy the primary consideration.

[3] Chronic hepatitis is one of the most common and severe viral infections of humans worldwide belonging to the *Hepadnaviridae* family of viruses. Infected individuals are at high risk for developing liver cirrhosis, and eventually, hepatic cancer. Chronic hepatitis is characterized as an inflammatory liver disease continuing for at least six months without improvement. The majority of patients suffering from chronic hepatitis are infected with either chronic HBV, HCV or are suffering

from autoimmune disease. The prevalence of HCV infection in the general population exceeds 1% in the United States, Japan, China and Southeast Asia.

[4] Chronic HCV can progress to cirrhosis and extensive necrosis of the liver. Although chronic HCV is often associated with deposition of type I collagen leading to hepatic fibrosis, the mechanisms of fibrogenesis remain unknown. Liver (hepatic) fibrosis occurs as a part of the wound-healing response to chronic liver injury. Fibrosis occurs as a complication of haemochromatosis, Wilson's disease, alcoholism, schistosomiasis, viral hepatitis, bile duct obstruction, toxin exposure, and metabolic disorders. This formation of scar tissue is believed to represent an attempt by the body to encapsulate the injured tissue. Liver fibrosis is characterized by the accumulation of extracellular matrix that can be distinguished qualitatively from that in normal liver. Left unchecked, hepatic fibrosis progresses to cirrhosis (defined by the presence of encapsulated nodules), liver failure, and death.

[5] There are few effective treatments for hepatitis. For example, treatment of autoimmune chronic hepatitis is generally limited to immunosuppressive treatment with corticosteroids. For the treatment of HBV and HCV, the FDA has approved administration of recombinant IFN-α. However, IFN-α is associated with a number of dose-dependent adverse effects, including thrombocytopenia, leukopenia, bacterial infections, and influenza-like symptoms. Other agents used to treat chronic HBV or HCV include the nucleoside analog RIBAVIRIN™ and ursodeoxycholic acid; however, neither has been shown to be very effective. RIBAVIRIN™ + IFN combination therapy for results in 47% rate of sustained viral clearance (Lanford, R.E. and Bigger, C. Virology 293: 1-9 (2002). (See Medicine, (D. C. Dale and D. D. Federman, eds.) (Scientific American, Inc., New York), 4:VIII:1-8 (1995)).

[6] Respiratory syncytial virus is the major cause of pneumonia and bronchiolitis in infancy. RSV infects more than half of infants during their first year of exposure, and nearly all are infected after a second year. During seasonal epidemics most infants, children, and adults are at risk for infection or reinfection. Other groups at risk for serious RSV infections include premature infants, immune compromised children and adults, and the elderly. Symptoms of RSV infection range from a mild cold to severe bronchiolitis and pneumonia. Respiratory syncytial virus has also been associated with acute otitis media and RSV can be recovered from middle ear fluid. Herpes simplex virus-1 (HSV-1) and herpes simplex virus-2 (HSV-2) may be either lytic or latent, and are the causative agents in cold sores (HSV-1) and genital herpes, typically associated with lesions in the region of the eyes, mouth, and genitals (HSV-2). These viruses are a few examples of the many viruses that infect humans for which there are few adequate treatments available once infection has occurred.

[7] The demonstrated activities of the IL-28 and IL-29 cytokine family provide methods for treating specific virual infections, for example, liver specific viral infections. The activity of IL-

28 and IL-29 also demonstrate that these cytokines provide methods for treating immunocompromised patients. The methods for these and other uses should be apparent to those skilled in the art from the teachings herein.

DESCRIPTION OF THE INVENTION

DEFINITIONS

[8] In the description that follows, a number of terms are used extensively. The following definitions are provided to facilitate understanding of the invention.

[9] Unless otherwise specified, "a," "an," "the," and "at least one" are used interchangeably and mean one or more than one.

[10] The term "affinity tag" is used herein to denote a polypeptide segment that can be attached to a second polypeptide to provide for purification or detection of the second polypeptide or provide sites for attachment of the second polypeptide to a substrate. In principal, any peptide or protein for which an antibody or other specific binding agent is available can be used as an affinity tag. Affinity tags include a poly-histidine tract, protein A (Nilsson et al., EMBO J. 4:1075, 1985; Nilsson et al., Methods Enzymol. 198:3, 1991), glutathione S transferase (Smith and Johnson, Gene 67:31, 1988), Glu-Glu affinity tag (Grussenmeyer et al., Proc. Natl. Acad. Sci. USA 82:7952-4, 1985), substance P, Flag™ peptide (Hopp et al., Biotechnology 6:1204-10, 1988), streptavidin binding peptide, or other antigenic epitope or binding domain. See, in general, Ford et al., Protein Expression and Purification 2: 95-107, 1991. DNAs encoding affinity tags are available from commercial suppliers (e.g., Pharmacia Biotech, Piscataway, NJ).

[11] The term "allelic variant" is used herein to denote any of two or more alternative forms of a gene occupying the same chromosomal locus. Allelic variation arises naturally through mutation, and may result in phenotypic polymorphism within populations. Gene mutations can be silent (no change in the encoded polypeptide) or may encode polypeptides having altered amino acid sequence. The term allelic variant is also used herein to denote a protein encoded by an allelic variant of a gene.

[12] The terms "amino-terminal" and "carboxyl-terminal" are used herein to denote positions within polypeptides. Where the context allows, these terms are used with reference to a particular sequence or portion of a polypeptide to denote proximity or relative position. For example, a certain sequence positioned carboxyl-terminal to a reference sequence within a polypeptide is located proximal to the carboxyl terminus of the reference sequence, but is not necessarily at the carboxyl terminus of the complete polypeptide.

[13] The term "complement/anti-complement pair" denotes non-identical moieties that form a non-covalently associated, stable pair under appropriate conditions. For instance, biotin and

avidin (or streptavidin) are prototypical members of a complement/anti-complement pair. Other exemplary complement/anti-complement pairs include receptor/ligand pairs, antibody/antigen (or hapten or epitope) pairs, sense/antisense polynucleotide pairs, and the like. Where subsequent dissociation of the complement/anti-complement pair is desirable, the complement/anti-complement pair preferably has a binding affinity of $<10^9$ M^{-1}.

[14] The term "degenerate nucleotide sequence" denotes a sequence of nucleotides that includes one or more degenerate codons (as compared to a reference polynucleotide molecule that encodes a polypeptide). Degenerate codons contain different triplets of nucleotides, but encode the same amino acid residue (i.e., GAU and GAC triplets each encode Asp).

[15] The term "expression vector" is used to denote a DNA molecule, linear or circular, that comprises a segment encoding a polypeptide of interest operably linked to additional segments that provide for its transcription. Such additional segments include promoter and terminator sequences, and may also include one or more origins of replication, one or more selectable markers, an enhancer, a polyadenylation signal, etc. Expression vectors are generally derived from plasmid or viral DNA, or may contain elements of both.

[16] The term "isolated", when applied to a polynucleotide, denotes that the polynucleotide has been removed from its natural genetic milieu and is thus free of other extraneous or unwanted coding sequences, and is in a form suitable for use within genetically engineered protein production systems. Such isolated molecules are those that are separated from their natural environment and include cDNA and genomic clones. Isolated DNA molecules of the present invention are free of other genes with which they are ordinarily associated, but may include naturally occurring 5' and 3' untranslated regions such as promoters and terminators. The identification of associated regions will be evident to one of ordinary skill in the art (see for example, Dynan and Tijan, Nature 316:774-78, 1985).

[17] An "isolated" polypeptide or protein is a polypeptide or protein that is found in a condition other than its native environment, such as apart from blood and animal tissue. In a preferred form, the isolated polypeptide is substantially free of other polypeptides, particularly other polypeptides of animal origin. It is preferred to provide the polypeptides in a highly purified form, i.e. greater than 95% pure, more preferably greater than 99% pure. When used in this context, the term "isolated" does not exclude the presence of the same polypeptide in alternative physical forms, such as dimers or alternatively glycosylated or derivatized forms.

[18] The term "level" when referring to immune cells, such as NK cells, T cells, in particular cytotoxic T cells, B cells and the like, an increased level is either increased number of cells or enhanced activity of cell function.

[19] The term "level" when referring to viral infections refers to a change in the level of viral infection and includes, but is not limited to, a change in the level of CTLs or NK cells (as described above), a decrease in viral load, an increase antiviral antibody titer, decrease in serological levels of alanine aminotransferase, or improvement as determined by histological examination of a target tissue or organ. Determination of whether these changes in level are significant differences or changes is well within the skill of one in the art.

[20] The term "operably linked", when referring to DNA segments, indicates that the segments are arranged so that they function in concert for their intended purposes, e.g., transcription initiates in the promoter and proceeds through the coding segment to the terminator.

[21] The term "ortholog" denotes a polypeptide or protein obtained from one species that is the functional counterpart of a polypeptide or protein from a different species. Sequence differences among orthologs are the result of speciation.

[22] "Paralogs" are distinct but structurally related proteins made by an organism. Paralogs are believed to arise through gene duplication. For example, α-globin, β-globin, and myoglobin are paralogs of each other.

[23] A "polynucleotide" is a single- or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases read from the 5' to the 3' end. Polynucleotides include RNA and DNA, and may be isolated from natural sources, synthesized *in vitro*, or prepared from a combination of natural and synthetic molecules. Sizes of polynucleotides are expressed as base pairs (abbreviated "bp"), nucleotides ("nt"), or kilobases ("kb"). Where the context allows, the latter two terms may describe polynucleotides that are single-stranded or double-stranded. When the term is applied to double-stranded molecules it is used to denote overall length and will be understood to be equivalent to the term "base pairs". It will be recognized by those skilled in the art that the two strands of a double-stranded polynucleotide may differ slightly in length and that the ends thereof may be staggered as a result of enzymatic cleavage; thus all nucleotides within a double-stranded polynucleotide molecule may not be paired.

[24] A "polypeptide" is a polymer of amino acid residues joined by peptide bonds, whether produced naturally or synthetically. Polypeptides of less than about 10 amino acid residues are commonly referred to as "peptides".

[25] The term "promoter" is used herein for its art-recognized meaning to denote a portion of a gene containing DNA sequences that provide for the binding of RNA polymerase and initiation of transcription. Promoter sequences are commonly, but not always, found in the 5' non-coding regions of genes.

[26] A "protein" is a macromolecule comprising one or more polypeptide chains. A protein may also comprise non-peptidic components, such as carbohydrate groups. Carbohydrates

and other non-peptidic substituents may be added to a protein by the cell in which the protein is produced, and will vary with the type of cell. Proteins are defined herein in terms of their amino acid backbone structures; substituents such as carbohydrate groups are generally not specified, but may be present nonetheless.

[27] The term "receptor" denotes a cell-associated protein that binds to a bioactive molecule (i.e., a ligand) and mediates the effect of the ligand on the cell. Membrane-bound receptors are characterized by a multi-peptide structure comprising an extracellular ligand-binding domain and an intracellular effector domain that is typically involved in signal transduction. Binding of ligand to receptor results in a conformational change in the receptor that causes an interaction between the effector domain and other molecule(s) in the cell. This interaction in turn leads to an alteration in the metabolism of the cell. Metabolic events that are linked to receptor-ligand interactions include gene transcription, phosphorylation, dephosphorylation, increases in cyclic AMP production, mobilization of cellular calcium, mobilization of membrane lipids, cell adhesion, hydrolysis of inositol lipids and hydrolysis of phospholipids. In general, receptors can be membrane bound, cytosolic or nuclear; monomeric (e.g., thyroid stimulating hormone receptor, beta-adrenergic receptor) or multimeric (e.g., PDGF receptor, growth hormone receptor, IL-3 receptor, GM-CSF receptor, G-CSF receptor, erythropoietin receptor and IL-6 receptor).

[28] The term "secretory signal sequence" denotes a DNA sequence that encodes a polypeptide (a "secretory peptide") that, as a component of a larger polypeptide, directs the larger polypeptide through a secretory pathway of a cell in which it is synthesized. The larger polypeptide is commonly cleaved to remove the secretory peptide during transit through the secretory pathway.

[29] The term "splice variant" is used herein to denote alternative forms of RNA transcribed from a gene. Splice variation arises naturally through use of alternative splicing sites within a transcribed RNA molecule, or less commonly between separately transcribed RNA molecules, and may result in several mRNAs transcribed from the same gene. Splice variants may encode polypeptides having altered amino acid sequence. The term splice variant is also used herein to denote a protein encoded by a splice variant of an mRNA transcribed from a gene.

[30] Molecular weights and lengths of polymers determined by imprecise analytical methods (e.g., gel electrophoresis) will be understood to be approximate values. When such a value is expressed as "about" X or "approximately" X, the stated value of X will be understood to be accurate to ±10%.

[31] "zcyto20", "zcyto21", "zcyto22" are the previous designations for human IL-28A, IL-29, and IL-28B, respectively and are used interchangeably herein. IL-28A polypeptides of the present invention are shown in SEQ ID NOs:2, 18, 24, 26, 28, 30, 36, 138 and 140, which are encoded by polynucleotide sequences as shown in SEQ ID NOs:1, 17, 23, 25, 27, 29, 35, 137 and 139,

respectively. IL-28B polypeptides of the present invention are shown in SEQ ID NOs:6, 22, 40, 86, 88, 90, 92, 94, 96, 98, 100, 142 and 144, which are encoded by polynucleotide sequences as shown in SEQ ID NOs:5, 21, 39, 85, 87, 89, 91, 93, 95, 97, 99, 141 and 143, respectively. IL-29 polypeptides of the present invention are shown in SEQ ID NOs:4, 20, 32, 34, 38, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 146, 148 and 150, which are encoded by polynucleotide sequences as shown in SEQ ID NOs:3, 19, 31, 33, 37, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 145, 147 and 149, respectively.

[32] "zcyto24" and "zcyto25" are the previous designations for mouse IL-28A and IL-28B, and are shown in SEQ ID NOs:7, 8, 9, 10, respectively. The polynucleotide and polypeptides are fully described in PCT application WO 02/086087 commonly assigned to ZymoGenetics, Inc., incorporated herein by reference.

[33] "zcytor19" is the previous designation for IL-28 receptor α-subunit, and is shown in SEQ ID NOs:11, 12, 13, 14, 15, 16. The polynucleotides and polypeptides are described in PCT application WO 02/20569 on behalf of Schering, Inc., and WO 02/44209 assigned to ZymoGenetics, Inc and incorporated herein by reference. "IL-28 receptor" denotes the IL-28 α-subunit and CRF2-4 subunit forming a heterodimeric receptor.

[34] In one aspect, the present invention provides methods for treating viral infections comprising administering to a mammal with a viral infection a therapeutically effective amount of a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, wherein after administration of the polypeptide the viral infection level is reduced. In other embodiments, the methods comprise administering a polypeptide comprising an amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. In another aspect, the viral infection can optionally cause liver inflammation, wherein administering a therapeutically effective amount of a polypeptide reduces the liver inflammation. In other embodiments, the polypeptide is conjugated to a polyalkyl oxide moiety, such as polyethylene glycol (PEG), or F_c, or

human albumin. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, a reduction in the viral infection level is measured as a decrease in viral load, an increase in antiviral antibodies, a decrease in serological levels of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B viral infection and/or a hepatitis C viral infection. In another embodiment, the polypeptide may be given prior to, concurrent with, or subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The polypeptide may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[35] In one aspect, the present invention provides methods for treating viral infections comprising administering to a mammal with a viral infection a therapeutically effective amount of a composition comprising a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, and a pharmaceutically acceptable vehicle, wherein after administration of the composition the viral infection level is reduced. In other embodiments, the methods comprise administering composition comprising the polypeptide comprising an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In other embodiments, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or F_c, or human albumin. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, a reduction in the viral infection level is measured as a decrease in viral load, an increase in antiviral antibodies, a decrease in serological levels of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B virus infection or a hepatitis C virus infection. In another embodiment, the composition may further include or, be given prior to or, be given concurrent with, or be given subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase

inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The composition may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[36] In one aspect, the present invention provides methods for treating viral infections comprising administering to a mammal with a viral infection causing liver inflammation a therapeutically effective amount of a composition comprising a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, and a pharmaceutically acceptable vehicle, wherein after administration of the composition the viral infection level or liver inflammation is reduced. In other embodiments, the methods comprise administering composition comprising the polypeptide comprising an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In other embodiments, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or F_c, or human albumin. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, a reduction in the viral infection level is measured as a decrease in viral load, an increase in antiviral antibodies, a decrease in serological levels of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B virus infection or a hepatitis C virus infection. In another embodiment, the composition may further include or, be given prior to or, be given concurrent with, or be given subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The composition may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[37] In another aspect, the present invention provides methods for treating liver inflammation comprising administering to a mammal in need thereof a therapeutically effective amount of a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, wherein after administration of the polypeptide the liver inflammation is reduced. In one embodiment, the invention provides that the polypeptide comprises

an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In another embodiment, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or human albumin, or F_c. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, the present invention provides that the reduction in the liver inflammation is measured as a decrease in serological level of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the liver inflammation is associated with a hepatitis C viral infection or a hepatitis B viral infection. In another embodiment, the polypeptide may be given prior to, concurrent with, or subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The polypeptide may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[38] In another aspect, the present invention provides methods for treating liver inflammation comprising administering to a mammal in need thereof a therapeutically effective amount of a composition comprising a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, wherein after administration of the polypeptide the liver inflammation is reduced. In one embodiment, the invention provides that the polypeptide comprises an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In another embodiment, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or human albumin, or F_c. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for

instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, the present invention provides that the reduction in the liver inflammation is measured as a decrease in serological level of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the liver inflammation is associated with a hepatitis C virus infection or a hepatitis B virus infection. In another embodiment, the composition may further include or, be given prior to or, be given concurrent with, or be given subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The composition may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[39] In another aspect, the present invention provides methods of treating a viral infection comprising administering to an immunocompromised mammal with an viral infection a therapeutically effective amount of a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, wherein after administration of the polypeptide the viral infection is reduced. In another embodiment, the polypeptide comprises an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In another embodiment, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or human albumin, or F_c. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, a reduction in the viral infection level is measured as a decrease in viral load, an increase in antiviral antibodies, a decrease in serological levels of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B virus infection or a hepatitis C virus infection. In another embodiment, the polypeptide may be given prior to, concurrent with, or subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The polypeptide may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[40] In another aspect, the present invention provides methods of treating liver inflammation comprising administering to an immunocompromised mammal with liver inflammation a therapeutically effective amount of a polypeptide comprising an amino acid sequence that has at least 95% identity to amino acid residues of SEQ ID NO:134, wherein after administration of the polypeptide the liver inflammation is reduced. In another embodiment, the polypeptide comprises an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. The polypeptide may optionally comprise at least 15, at least 30, at least 45, or at least 60 sequential amino acids of an amino acid sequence as shown in SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and/or 150. In another embodiment, the polypeptide is conjugated to a polyalkyl oxide moiety, such as PEG, or human albumin, or F_c. The PEG may be N-terminally conjugated to the polypeptide and may comprise, for instance, a 20kD or 30kD monomethoxy-PEG propionaldehyde. In another embodiment, a reduction in the liver inflammation level is measured as a decrease in serological levels of alanine aminotransferase or histological improvement. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B virus infection or a hepatitis C virus infection. In another embodiment, the mammal is a human. In another embodiment, the present invention provides that the viral infection is a hepatitis B virus infection or a hepatitis C virus infection. In another embodiment, the polypeptide may be given prior to, concurrent with, or subsequent to, at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The polypeptide may be administered intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, orally, intranasally, or by inhalation.

[41] The discovery of a new family of interferon-like molecules was previously described in PCT applications, PCT/US01/21087 and PCT/US02/12887, and Sheppard et al., Nature Immunol. 4:63-68, 2003; U.S. Patent Application Serial Nos. 60/493,194 and 60/551,841; all incorporated by reference herein. This new family includes molecules designated zcyto20, zcyto21, zcyto22, zcyto24, zcyto25, where zcyto20, 21, and 22 are human sequences, and zcyto24 and 25 are mouse sequences. HUGO designations have been assigned to the interferon-like proteins. Zcyto20 has been designated IL-28A, zycto22 has been designated IL-28B, zycto21 has been designated IL-29. Kotenko et al., Nature Immunol. 4:69-77, 2003, have identified IL-28A as IFNλ2, IL-28B as IFNλ3, and IL-29 as

IFNλ1. The receptor for these proteins, originally designated zcytor19 (SEQ ID NOs:11 and 12), has been designated as IL-28RA by HUGO. When referring to "IL-28", the term shall mean both IL-28A and IL-28B.

[42] The present invention provides methods for using IL-28 and IL-29 as an antiviral agent in a broad spectrum of viral infections. In certain embodiments, the methods include using IL-28 and IL-29 in viral infections that are specific for liver, such as hepatitis. Furthermore, data indicate that IL-28 and IL-29 exhibit these antiviral activities without some of the toxicities associated with the use of IFN therapy for viral infection. One of the toxicities related to type I interferon therapy is myelosuppression. This is due to type I interferons suppression of bone marrow progenitor cells. Because IL-29 does not significantly suppress bone marrow cell expansion or B cell proliferation as is seen with IFN-α, IL-29 will have less toxicity associated with treatment. Similar results would be expected with IL-28A and IL-28B.

[43] IFN-α may be contraindicated in some patients, particularly when doses sufficient for efficacy have some toxicity or myelosuppressive effects. Examples of patients for which IFN is contraindicated can include (1) patients given previous immunosuppressive medication, (2) patients with HIV or hemophilia, (3) patients who are pregnant, (4) patients with a cytopenia, such as leukocyte deficiency, neutropenia, thrombocytopenia, and (5) patients exhibiting increased levels of serum liver enzymes. Moreover, IFN therapy is associated with symptoms that are characterized by nausea, vomiting, diarrhea and anorexia. The result being that some populations of patients will not tolerate IFN therapy, and IL-28A, IL-28B, and IL-29 can provide an alternative therapy for some of those patients.

[44] The methods of the present invention comprise administering a therapeutically effective amount of an IL-28A, IL-28B, and/or IL-29 polypeptide of the present invention that have retained some biological activity associated with IL-28A, IL-28B or IL-29, alone or in combination with other biologics or pharmaceuticals. The present invention provides methods of treating a mammal with a chronic or acute viral infection, causing liver inflammation, thereby reducing the viral infection or liver inflammation. In another aspect, the present invention provides methods of treating liver specific diseases, in particular liver disease where viral infection is in part an etiologic agent. These methods are based on the discovery that IL-28 and IL-29 have antiviral activity on hepatic cells.

[45] As stated above, the methods of the present invention provide administering a therapeutically effective amount of an IL-28A, IL-28B, and/or IL-29 polypeptide of the present invention that have retained some biological activity associated with IL-28A, IL-28B or IL-29, alone or in combination with other biologics or pharmaceuticals. The present invention provides methods of treatment of a mammal with a viral infection selected from the group consisting of hepatitis A,

hepatitis B, hepatitis C, and hepatitis D. Other aspects of the present invention provide methods for using IL-28 or IL-29 as an antiviral agent in viral infections selected from the group consisting of respiratory syncytial virus, herpes virus, Epstein-Barr virus, norovirus, influenza virus (e.g., avian influenza A virus, for instance the H5N1 virus), adenovirus, parainfluenza virus, rhino virus, coxsackie virus, vaccinia virus, west nile virus, severe acute respiratory syndrome, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus. In certain embodiments, the mammal can have either a chronic or acute viral infection.

[46] In another aspect, the methods of the present invention also include a method of treating a viral infection comprising administering a therapeutically effective amount of IL-28A, IL-28B, and/or IL-29 polypeptide of the present invention that have retained some biological activity associated with IL-28A, IL-28B or IL-29, alone or in combination with other biologics or pharmaceuticals, to an immunompromised mammal with a viral infection, thereby reducing the viral infection, such as is described above. All of the above methods of the present invention can also comprise the administration of zcyto24 or zcyto25 as well.

[47] IL-28 and IL-29 are known to have an odd number of cysteines (PCT application WO 02/086087 and Sheppard et al., supra.) Expression of recombinant IL-28 and IL-29 can result in a heterogeneous mixture of proteins composed of intramolecular disulfide bonding in multiple conformations. The separation of these forms can be difficult and laborious. It is therefore desirable to provide IL-28 and IL-29 molecules having a single intramolecular disulfide bonding pattern upon expression and methods for refolding and purifying these preparations to maintain homogeneity. Thus, the present invention provides for compositions and methods to produce homogeneous preparations of IL-28 and IL-29.

[48] The present invention provides polynucleotide molecules, including DNA and RNA molecules, that encode Cysteine mutants of IL-28 and IL-29 that result in expression of a recombinant IL-28 or IL-29 preparation that is a homogeneous preparation. For the purposes of this invention, a homogeneous preparation of IL-28 and IL-29 is a preparation in which comprises at least 98% of a single intramolecular disulfide bonding pattern in the purified polypeptide. In other embodiments, the single disulfide conformation in a preparation of purified polypeptide is at 99% homogeneous. In general, these Cysteine mutants will maintain some biological activity of the wildtype IL-28 or IL-29, as described herein. For example, the molecules of the present invention can bind to the IL-28 receptor with some specificity. Generally, a ligand binding to its cognate receptor is specific when the K_D falls within the range of 100 nM to 100 pM. Specific binding in the range of 100 mM to 10 nM K_D is low affinity binding. Specific binding in the range of 2.5 pM to 100 pM K_D is high affinity binding. In another example, biological activity of IL-28 or IL-29 Cysteine

mutants is present when the molecules are capable of some level of antiviral activity associated with wildtype IL-28 or IL-29. Determination of the level of antiviral activity is described in detail herein.

[49] An IL-28A gene encodes a polypeptide of 200 amino acids, as shown in SEQ ID NO:2. The signal sequence for IL-28A comprises amino acid residue 1 (Met) through amino acid residue 21 (Ala) of SEQ ID NO:2. The mature peptide for IL-28A begins at amino acid residue 22 (Val). A variant IL-28A gene encodes a polypeptide of 200 amino acids, as shown in SEQ ID NO:18. The signal sequence for IL-28A can be predicted as comprising amino acid residue -25 (Met) through amino acid residue -1 (Ala) of SEQ ID NO:18. The mature peptide for IL-28A begins at amino acid residue 1 (Val). IL-28A helices are predicted as follow: helix A is defined by amino acid residues 31 (Ala) to 45 (Leu); helix B by amino acid residues 58 (Thr) to 65 (Gln); helix C by amino acid residues 69 (Arg) to 86 (Ala); helix D by amino acid residues 95 (Val) to 114 (Ala); helix E by amino acid residues 126 (Thr) to 142 (Lys); and helix F by amino acid residues 148 (Cys) to 169 (Ala); as shown in SEQ ID NO:18. When a polynucleotide sequence encoding the mature polypeptide is expressed in a prokaryotic system, such as *E. coli*, a secretory signal sequence may not be required and an N-terminal Met may be present, resulting in expression of a polypeptide such as, for instance, as shown in SEQ ID NO:36.

[50] IL-28A polypeptides of the present invention also include a mutation at the second cysteine, C2, of the mature polypeptide. For example, C2 from the N-terminus of the polypeptide of SEQ ID NO:18 is the cysteine at amino acid position 48 (position 49, additional N-terminal Met, if expressed in *E coli*, see, for example, SEQ ID NO:36). This second cysteine (of which there are seven, like IL-28B) or C2 of IL-28A can be mutated, for example, to a serine, alanine, threonine, valine, or asparagine. IL-28A C2 mutant molecules of the present invention include, for example, polynucleotide molecules as shown in SEQ ID NOs:23 and 25, including DNA and RNA molecules, that encode IL-28A C2 mutant polypeptides as shown in SEQ ID NOs:24 and 26, respectively.

[51] The present invention also includes biologically active mutants of IL-28A C2 cysteine mutants which provide, at least partially, an antiviral activity as provided here, e.g., anti-hepatitis C activity. The second cysteine or C2 from the N-terminus of IL-28A can mutated to any amino acid that does not form a disulfide bond with another cysteine, e.g., serine, alanine, threonine, valine or aspargine. The biologically active mutants of IL-28A C2 cysteine mutants of the present invention include N-, C-, and N- and C-terminal deletions of IL-28A, e.g., the polypeptide of SEQ ID NO:138 encoded by the polynucleotide of SEQ ID NO:137.

[52] N-terminally modified biologically active mutants of IL-28A C2 mutants include, for example, amino acid residues 3-176 of SEQ ID NO:138 which is encoded by nucleotides 7-528 of SEQ ID NO:137; amino acid residues 4-176 of SEQ ID NO:138 which is encoded by nucleotides 10-528 of SEQ ID NO:137; amino acid residues 5-176 of SEQ ID NO:138 which is encoded by

nucleotides 13-528 of SEQ ID NO:137; amino acid residues 6-176 of SEQ ID NO:138 which is encoded by nucleotides 16-528 of SEQ ID NO:137; amino acid residues 7-176 of SEQ ID NO:138 which is encoded by nucleotidies 19-528 of SEQ ID NO:137; amino acid residues 8-176 of SEQ ID NO:138 which is encoded by nucleotides 22-528 of SEQ ID NO:137; amino acid residues 9-176 of SEQ ID NO:138 which is encoded by nucleotides 25-528 of SEQ ID NO:137; amino acid residues 10-176 of SEQ ID NO:138 which is encoded by nucleotides 28-528 of SEQ ID NO:137; amino acid residues 11-176 of SEQ ID NO:138 which is encoded by nucleotides 31-528 of SEQ ID NO:137; amino acid residues 12-176 of SEQ ID NO:138 which is encoded by nucleotides 34-528 of SEQ ID NO:137; amino acid residues 13-176 of SEQ ID NO:138 which is encoded by nucleotides 37-528 of SEQ ID NO:137; amino acid residues 14-176 of SEQ ID NO:138 which is encoded by nucleotides 40-528 of SEQ ID NO:137; amino acid residues 15-176 of SEQ ID NO:138 which is encoded by nucleotides 43-528 of SEQ ID NO:137; and amino acid residues 16-176 of SEQ ID NO:138 which is encoded by nucleotides 46-528 of SEQ ID NO:137. The N-terminally modified biologically active mutants of IL-28A C2 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[53] C-terminally modified biologically active mutants of IL-28A C2 mutants include, for example, amino acid residues 1-175 of SEQ ID NO:138 which is encoded by nucleotides 1-525 of SEQ ID NO:137.

[54] N-terminally and C-terminally modified biologically active mutants of IL-28A C2 mutants include, for example, amino acid residues 2-175 of SEQ ID NO:138 which is encoded by nucleotides 4-525 of SEQ ID NO:137; amino acid residues 3-175 of SEQ ID NO:138 which is encoded by nucleotides 7-525 of SEQ ID NO:137; amino acid residues 4-175 of SEQ ID NO:138 which is encoded by nucleotides 10-525 of SEQ ID NO:137; amino acid residues 5-175 of SEQ ID NO:138 which is encoded by nucleotides 13-525 of SEQ ID NO:137; amino acid residues 6-175 of SEQ ID NO:138 which is encoded by nucleotides 16-525 of SEQ ID NO:137; amino acid residues 7-175 of SEQ ID NO:138 which is encoded by nucleotides 19-525 of SEQ ID NO:137; amino acid residues 8-175 of SEQ ID NO:138 which is encoded by nucleotides 22-525 of SEQ ID NO:137; amino acid residues 9-175 of SEQ ID NO:138 which is encoded by nucleotides 25-525 of SEQ ID NO:137; amino acid residues 10-175 of SEQ ID NO:138 which is encoded by nucleotides 28-525 of SEQ ID NO:137; amino acid residues 11-175 of SEQ ID NO:138 which is encoded by nucleotides 31-525 of SEQ ID NO:137; amino acid residues 12-175 of SEQ ID NO:138 which is encoded by nucleotides 34-525 of SEQ ID NO:137; amino acid residues 13-175 of SEQ ID NO:138 which is encoded by nucleotides 37-525 of SEQ ID NO:137; amino acid residues 14-175 of SEQ ID NO:138 which is encoded by nucleotides 40-525 of SEQ ID NO:137; amino acid residues 15-175 of SEQ ID NO:138 which is encoded by nucleotides 43-525 of SEQ ID NO:137; amino acid residues 16-175 of

SEQ ID NO:138 which is encoded by nucleotides 46-525 of SEQ ID NO:137; and amino acid residues 17-175 of SEQ ID NO:138 which is encoded by nucleotides 49-525 of SEQ ID NO:137. The N-terminally and C-terminally modified biologically active mutants of IL-28A C2 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[55] In addition to the IL-28A C2 mutants, the present invention also includes IL-28A polypeptides comprising a mutation at the third cysteine position, C3, of the mature polypeptide. For example, C3 from the N-terminus of the polypeptide of SEQ ID NO:18, is the cysteine at position 50, (position 51, additional N-terminal Met, if expressed in *E coli*, see, for example, SEQ ID NO:36). IL-28A C3 mutant molecules of the present invention include, for example, polynucleotide molecules as shown in SEQ ID NOs:27 and 29, including DNA and RNA molecules, that encode IL-28A C3 mutant polypeptides as shown in SEQ ID NOs:28 and 30, respectively (PCT publication WO 03/066002 (Kotenko et al.)).

[56] The present invention also includes biologically active mutants of IL-28A C3 cysteine mutants which provide, at least partially, an antiviral activity as provided here, e.g., anti-hepatitis C activity. The third cysteine or C3 from the N-terminus of IL-28A can mutated to any amino acid that does not form a disulfide bond with another cysteine, e.g., serine, alanine, threonine, valine or aspargine. The biologically active mutants of IL-28A C3 cysteine mutants of the present invention include N-, C-, and N- and C-terminal deletions of IL-28A, e.g., the polypeptide of SEQ ID NO:140 encoded by the polynucleotide of SEQ ID NO:139.

[57] N-terminally modified biologically active mutants of IL-28A C3 mutants include, for example, amino acid residues 2-176 of SEQ ID NO:140 which is encoded by nucleotides 4-528 of SEQ ID NO:139; amino acid residues 3-176 of SEQ ID NO:140 which is encoded by nucleotides 7-528 of SEQ ID NO:139; amino acid residues 4-176 of SEQ ID NO:140 which is encoded by nucleotides 10-528 of SEQ ID NO:139; amino acid residues 5-176 of SEQ ID NO:140 which is encoded by nucleotides 13-528 of SEQ ID NO:139; amino acid residues 6-176 of SEQ ID NO:140 which is encoded by nucleotides 16-528 of SEQ ID NO:139; amino acid residues 7-176 of SEQ ID NO:140 which is encoded by nucleotidies 19-528 of SEQ ID NO:139; amino acid residues 8-176 of SEQ ID NO:140 which is encoded by nucleotides 22-528 of SEQ ID NO:139; amino acid residues 9-176 of SEQ ID NO:140 which is encoded by nucleotides 25-528 of SEQ ID NO:139; amino acid residues 10-176 of SEQ ID NO:140 which is encoded by nucleotides 28-528 of SEQ ID NO:139; amino acid residues 11-176 of SEQ ID NO:140 which is encoded by nucleotides 31-528 of SEQ ID NO:139; amino acid residues 12-176 of SEQ ID NO:140 which is encoded by nucleotides 34-528 of SEQ ID NO:139; amino acid residues 13-176 of SEQ ID NO:140 which is encoded by nucleotides 37-528 of SEQ ID NO:139; amino acid residues 14-176 of SEQ ID NO:140 which is encoded by nucleotides 40-528 of SEQ ID NO:139; amino acid residues 15-176 of SEQ ID NO:140 which is

encoded by nucleotides 43-528 of SEQ ID NO:139; and amino acid residues 16-176 of SEQ ID NO:140 which is encoded by nucleotides 46-528 of SEQ ID NO:139. The N-terminally modified biologically active mutants of IL-28A C3 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[58] C-terminally modified biologically active mutants of IL-28A C3 mutants include, for example, amino acid residues 1-175 of SEQ ID NO:140 which is encoded by nucleotides 1-525 of SEQ ID NO:139.

[59] N-terminally and C-terminally modified biologically active mutants of IL-28A C3 mutants include, for example, amino acid residues 2-175 of SEQ ID NO:140 which is encoded by nucleotides 4-525 of SEQ ID NO:139; amino acid residues 3-175 of SEQ ID NO:140 which is encoded by nucleotides 7-525 of SEQ ID NO:139; amino acid residues 4-175 which is encoded by nucleotides 10-525 of SEQ ID NO:139; amino acid residues 5-175 of SEQ ID NO:140 which is encoded by nucleotides 13-525 of SEQ ID NO:139; amino acid residues 6-175 of SEQ ID NO:140 which is encoded by nucleotides 16-525 of SEQ ID NO:139; amino acid residues 7-175 of SEQ ID NO:140 which is encoded by nucleotides 19-525 of SEQ ID NO:139; amino acid residues 8-175 of SEQ ID NO:140 which is encoded by nucleotides 22-525 of SEQ ID NO:139; amino acid residues 9-175 of SEQ ID NO:140 which is encoded by nucleotides 25-525 of SEQ ID NO:139; amino acid residues 10-175 of SEQ ID NO:140 which is encoded by nucleotides 28-525 of SEQ ID NO:139; amino acid residues 11-175 of SEQ ID NO:140 which is encoded by nucleotides 31-525 of SEQ ID NO:139; amino acid residues 12-175 of SEQ ID NO:140 which is encoded by nucleotides 34-525 of SEQ ID NO:139; amino acid residues 13-175 of SEQ ID NO:140 which is encoded by nucleotides 37-525 of SEQ ID NO:139; amino acid residues 14-175 of SEQ ID NO:140 which is encoded by nucleotides 40-525 of SEQ ID NO:139; amino acid residues 15-175 of SEQ ID NO:140 which is encoded by nucleotides 43-525 of SEQ ID NO:139; amino acid residues 16-175 of SEQ ID NO:140 which is encoded by nucleotides 46-525 of SEQ ID NO:139; and amino acid residues 17-175 of SEQ ID NO:140 which is encoded by nucleotides 49-525 of SEQ ID NO:139. The N-terminally and C-terminally modified biologically active mutants of IL-28A C3 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[60] The IL-28A polypeptides of the present invention include, for example, SEQ ID NOs:2, 18, 24, 26, 28, 30, 36, 138 and 140, and biologically active mutants, fusions, variants and fragments thereof which are encoded by IL-28A polynucleotide molecules as shown in SEQ ID NOs:1, 17, 23, 25, 27, 29, 35, 137 and 139, respectively.

[61] An IL-29 gene encodes a polypeptide of 200 amino acids, as shown in SEQ ID NO:4. The signal sequence for IL-29 comprises amino acid residue 1 (Met) through amino acid residue 19 (Ala) of SEQ ID NO:4. The mature peptide for IL-29 begins at amino acid residue 20 (Gly). IL-29

has been described in published PCT application WO 02/02627. A variant IL-29 gene encodes a polypeptide of 200 amino acids, as shown in, for example, SEQ ID NO:20, where amino acid residue 188 (or amino acid residue 169 of the mature polypeptide which begins from amino acid residue 20 (Gly)) is Asn instead of Asp. The present invention also provides a variant IL-29 gene wherein the mature polypeptide has a Thr at amino acid residue 10 substituted with a Pro, such as, for instance, SEQ ID NOs:54, 56, 58, 60, 62, 64, 66, 68, 146, 148 and 150 which are encoded by the polynucleotide sequences as shown in SEQ ID NOs:53, 55, 57, 59, 61, 63, 65, 67, 145, 147 and 149, respectively. The present invention also provides a variant IL-29 gene wherein the mature polypeptide has a Gly at amino acid residue 18 substituted with an Asp, such as, for instance, SEQ ID NOs:70, 72, 74, 76, 78, 80, 82, 84, 146 and 148, which are encoded by the polynucleotide sequences as shown in SEQ ID NOs:69, 71, 73, 75, 77, 79, 81, 83, 145 and 147, respectively. The signal sequence for IL-29 can be predicted as comprising amino acid residue -19 (Met) through amino acid residue -1 (Ala) of SEQ ID NO:20. The mature peptide for IL-29 begins at amino acid residue 1 (Gly) of SEQ ID NO:20. IL-29 has been described in PCT application WO 02/02627. IL-29 helices are predicted as follows: helix A is defined by amino acid residues 30 (Ser) to 44 (Leu); helix B by amino acid residues 57 (Asn) to 65 (Val); helix C by amino acid residues 70 (Val) to 85 (Ala); helix D by amino acid residues 92 (Glu) to 114 (Gln); helix E by amino acid residues 118 (Thr) to 139 (Lys); and helix F by amino acid residues 144 (Gly) to 170 (Leu); as shown in SEQ ID NO:20. When a polynucleotide sequence encoding the mature polypeptide is expressed in a prokaryotic system, such as *E. coli*, a secretory signal sequence may not be required and an N-terminal Met may be present, resulting in expression of an IL-29 polypeptide such as, for instance, as shown in SEQ ID NO:38.

[62] IL-29 polypeptides of the present invention also include a mutation at the fifth cysteine, C5, of the mature polypeptide. For example, C5 from the N-terminus of the polypeptide of SEQ ID NO:20, is the cysteine at position 171, or position 172 (additional N-terminal Met) if expressed in *E. coli*. (see, for example, SEQ ID NO:38). This fifth cysteine or C5 of IL-29 can be mutated, for example, to a serine, alanine, threonine, valine, or asparagine. These IL-29 C5 mutant polypeptides have a disulfide bond pattern of C1(Cys15 of SEQ ID NO:20)/C3(Cys112 of SEQ ID NO:20) and C2(Cys49 of SEQ ID NO:20)/C4(Cys145 of SEQ ID NO:20). IL-29 C5 mutant molecules of the present invention include, for example, polynucleotide molecules as shown in SEQ ID NOs:31, 33, 49, 51, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 147 and 149, including DNA and RNA molecules, that encode IL-29 C5 mutant polypeptides as shown in SEQ ID NOs:32, 34, 50, 52, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 148 and 150, respectively. Additional IL-29 C5 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:53, 55, 61, and 63, including DNA and RNA

molecules, that encode IL-29 C5 mutant polypeptides as shown in SEQ ID NOs:54, 55, 62, and 64, respectively (PCT publication WO 03/066002 (Kotenko et al.)). Additional, IL-29 C5 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:69, 71, 77, and 79, including DNA and RNA molecules, that encode IL-29 C5 mutant polypeptides as shown in SEQ ID NOs:70, 72, 78, and 80, respectively (PCT publication WO 02/092762 (Baum et al.)).

[63] The present invention also includes biologically active mutants of IL-29 C5 cysteine mutants which provide, at least partially, an antiviral activity as provided here, e.g., anti-hepatitis C activity. The fifth cysteine or C5 from the N-terminus of IL-29 can mutated to any amino acid that does not form a disulfide bond with another cysteine, e.g., serine, alanine, threonine, valine or aspargine. The biologically active mutants of IL-29 C5 cysteine mutants of the present invention include N-, C-, and N- and C-terminal deletions of IL-29, e.g., the polypeptides of SEQ ID NOs:148 and 150 encoded by the polynucleotides of SEQ ID NOs:147 and 149, respectively.

[64] N-terminally modified biologically active mutants of IL-29 C5 mutants include, for example, amino acid residues 2-182 of SEQ ID NO:148 which is encoded by nucleotides 4-546 of SEQ ID NO:147; amino acid residues 3-182 of SEQ ID NO:148 which is encoded by nucleotides 7-546 of SEQ ID NO:147; amino acid residues 4-182 of SEQ ID NO:148 which is encoded by nucleotides 10-546 of SEQ ID NO:147; amino acid residues 5-182 of SEQ ID NO:148 which is encoded by nucleotides 13-546 of SEQ ID NO:147; amino acid residues 6-182 of SEQ ID NO:148 which is encoded by nucleotides 16-546 of SEQ ID NO:147; amino acid residues 7-182 of SEQ ID NO:148 which is encoded by nucleotides 19-546 of SEQ ID NO:147; amino acid residues 8-182 of SEQ ID NO:148 which is encoded by nucleotides 22-546 of SEQ ID NO:147; amino acid residues 9-182 of SEQ ID NO:148 which is encoded by nucleotides 25-546 of SEQ ID NO:147; amino acid residues 10-182 of SEQ ID NO:148 which is encoded by nucleotides 28-546 of SEQ ID NO:147; amino acid residues 11-182 of SEQ ID NO:148 which is encoded by nucleotides 31-546 of SEQ ID NO:147; amino acid residues 12-182 of SEQ ID NO:148 which is encoded by nucleotides 34-546 of SEQ ID NO:147; amino acid residues 13-182 of SEQ ID NO:148 which is encoded by nucleotides 37-546 of SEQ ID NO:147; amino acid residues 14-182 of SEQ ID NO:148 which is encoded by nucleotides 40-546 of SEQ ID NO:147; amino acid residues 15-182 of SEQ ID NO:148 which is encoded by nucleotides 43-546 of SEQ ID NO:147; amino acid residues 2-176 of SEQ ID NO:150 which is encoded by nucleotides 4-528 of SEQ ID NO:149; amino acid residues 3-176 of SEQ ID NO:150 which is encoded by nucleotides 7-528 of SEQ ID NO:149; amino acid residues 4-176 of SEQ ID NO:150 which is encoded by nucleotides 10-528 of SEQ ID NO:149; amino acid residues 5-176 of SEQ ID NO:150 which is encoded by nucleotides 13-528 of SEQ ID NO:149; amino acid residues 6-176 of SEQ ID NO:150 which is encoded by nucleotides 16-528 of SEQ ID NO:149;

amino acid residues 7-176 of SEQ ID NO:150 which is encoded by nucleotides 19-528 of SEQ ID NO:149; amino acid residues 8-176 of SEQ ID NO:150 which is encoded by nucleotides 22-528 of SEQ ID NO:149; and amino acid residues 9-176 of SEQ ID NO:150 which is encoded by nucleotides 25-528 of SEQ ID NO:149. The N-terminally modified biologically active mutants of IL-29 C5 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[65] C-terminally modified biologically active mutants of IL-29 C5 mutants include, for example, amino acid residues 1-181 of SEQ ID NO:148 which is encoded by nucleotides 1-543 of SEQ ID NO:147; amino acid residues 1-180 of SEQ ID NO:148 which is encoded by nucleotides 1-540 of SEQ ID NO:147; amino acid residues 1-179 of SEQ ID NO:148 which is encoded by nucleotides 1-537 of SEQ ID NO:147; amino acid residues 1-178 of SEQ ID NO:148 which is encoded by nucleotides 1-534 of SEQ ID NO:147; amino acid residues 1-177 of SEQ ID NO:148 which is encoded by nucleotides 1-531 of SEQ ID NO:147; amino acid residues 1-176 of SEQ ID NO:148 which is encoded by nucleotides 1-528 of SEQ ID NO:147; amino acid residues 1-175 of SEQ ID NO:148 which is encoded by nucleotides 1-525 of SEQ ID NO:147; amino acid residues 1-174 of SEQ ID NO:148 which is encoded by nucleotides 1-522 of SEQ ID NO:147; amino acid residues 1-173 of SEQ ID NO:148 which is encoded by nucleotides 1-519 of SEQ ID NO:147; amino acid residues 1-172 of SEQ ID NO:148 which is encoded by nucleotides 1-516 of SEQ ID NO:147; amino acid residues 1-175 of SEQ ID NO:150 which is encoded by nucleotides 1-525 of SEQ ID NO:149; amino acid residues 1-174 of SEQ ID NO:150 which is encoded by nucleotides 1-522 of SEQ ID NO:149; amino acid residues 1-173 of SEQ ID NO:150 which is encoded by nucleotides 1-519 of SEQ ID NO:149; amino acid residues 1-172 of SEQ ID NO:150 which is encoded by nucleotides 1-516 of SEQ ID NO:149; amino acid residues 1-171 of SEQ ID NO:150 which is encoded by nucleotides 1-513 of SEQ ID NO:149; amino acid residues 1-170 of SEQ ID NO:150 which is encoded by nucleotides 1-510 of SEQ ID NO:149; amino acid residues 1-169 of SEQ ID NO:150 which is encoded by nucleotides 1-507 of SEQ ID NO:149; amino acid residues 1-168 of SEQ ID NO:150 which is encoded by nucleotides 1-504 of SEQ ID NO:149; amino acid residues 1-167 of SEQ ID NO:150 which is encoded by nucleotides 1-501 of SEQ ID NO:149; and amino acid residues 1-166 of SEQ ID NO:150 which is encoded by nucleotides 1-498 of SEQ ID NO:149.

[66] N-terminally and C-terminally modified biologically active mutants of IL-29 C5 mutants include, for example, amino acid residues 2-182 of SEQ ID NO:148 which is encoded by nucleotides 4-546 of SEQ ID NO:147; amino acid residues 2-181 of SEQ ID NO:148 which is encoded by nucleotides 4-543 of SEQ ID NO:147; amino acid residues 2-180 of SEQ ID NO:148 which is encoded by nucleotides 4-540 of SEQ ID NO:147; amino acid residues 2-179 of SEQ ID NO:148 which is encoded by nucleotides 4-537 of SEQ ID NO:147; amino acid residues 2-178 of

SEQ ID NO:148 which is encoded by nucleotides 4-534 of SEQ ID NO:147; amino acid residues 2-177 of SEQ ID NO:148 which is encoded by nucleotides 4-531 of SEQ ID NO:147; amino acid residues 2-176 of SEQ ID NO:148 which is encoded by nucleotides 4-528 of SEQ ID NO:147; amino acid residues 2-175 of SEQ ID NO:148 which is encoded by nucleotides 4-525 of SEQ ID NO:147; amino acid residues 2-174 of SEQ ID NO:148 which is encoded by nucleotides 4-522 of SEQ ID NO:147; amino acid residues 2-173 of SEQ ID NO:148 which is encoded by nucleotides 4-519 of SEQ ID NO:147; amino acid residues 2-172 of SEQ ID NO:148 which is encoded by nucleotides 4-516 of SEQ ID NO:147; amino acid residues 3-182 of SEQ ID NO:148 which is encoded by nucleotides 7-546 of SEQ ID NO:147; amino acid residues 3-181 of SEQ ID NO:148 which is encoded by nucleotides 7-543 of SEQ ID NO:147; amino acid residues 3-180 of SEQ ID NO:148 which is encoded by nucleotides 7-540 of SEQ ID NO:147; amino acid residues 3-179 of SEQ ID NO:148 which is encoded by nucleotides 7-537 of SEQ ID NO:147; amino acid residues 3-178 of SEQ ID NO:148 which is encoded by nucleotides 7-534 of SEQ ID NO:147; amino acid residues 3-177 of SEQ ID NO:148 which is encoded by nucleotides 7-531 of SEQ ID NO:147; amino acid residues 3-176 of SEQ ID NO:148 which is encoded by nucleotides 7-528 of SEQ ID NO:147; amino acid residues 3-175 of SEQ ID NO:148 which is encoded by nucleotides 7-525 of SEQ ID NO:147; amino acid residues 3-174 of SEQ ID NO:148 which is encoded by nucleotides 7-522 of SEQ ID NO:147; amino acid residues 3-173 of SEQ ID NO:148 which is encoded by nucleotides 7-519 of SEQ ID NO:147; amino acid residues 3-172 of SEQ ID NO:148 which is encoded by nucleotides 7-516 of SEQ ID NO:147; amino acid residues 4-182 of SEQ ID NO:148 which is encoded by nucleotides 10-546 of SEQ ID NO:147; amino acid residues 4-181 of SEQ ID NO:148 which is encoded by nucleotides 10-543 of SEQ ID NO:147; amino acid residues 4-180 of SEQ ID NO:148 which is encoded by nucleotides 10-540 of SEQ ID NO:147; amino acid residues 4-179 of SEQ ID NO:148 which is encoded by nucleotides 10-537 of SEQ ID NO:147; amino acid residues 4-178 of SEQ ID NO:148 which is encoded by nucleotides 10-534 of SEQ ID NO:147; amino acid residues 4-177 of SEQ ID NO:148 which is encoded by nucleotides 10-531 of SEQ ID NO:147; amino acid residues 4-176 of SEQ ID NO:148 which is encoded by nucleotides 10-528 of SEQ ID NO:147; amino acid residues 4-175 of SEQ ID NO:148 which is encoded by nucleotides 10-525 of SEQ ID NO:147; amino acid residues 4-174 of SEQ ID NO:148 which is encoded by nucleotides 10-522 of SEQ ID NO:147; amino acid residues 4-173 of SEQ ID NO:148 which is encoded by nucleotides 10-519 of SEQ ID NO:147; amino acid residues 4-172 of SEQ ID NO:148 which is encoded by nucleotides 10-516 of SEQ ID NO:147; amino acid residues 5-182 of SEQ ID NO:148 which is encoded by nucleotides 13-546 of SEQ ID NO:147; amino acid residues 5-181 of SEQ ID NO:148 which is encoded by nucleotides 13-543 of SEQ ID NO:147; amino acid residues 5-180 of SEQ ID NO:148 which is encoded by nucleotides 13-540 of SEQ ID NO:147; amino acid residues 5-179 of

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37-516 of SEQ ID NO:147; amino acid residues 14-182 of SEQ ID NO:148 which is encoded by nucleotides 40-546 of SEQ ID NO:147; amino acid residues 14-181 of SEQ ID NO:148 which is encoded by nucleotides 40-543 of SEQ ID NO:147; amino acid residues 14-180 of SEQ ID NO:148 which is encoded by nucleotides 40-540 of SEQ ID NO:147; amino acid residues 14-179 of SEQ ID NO:148 which is encoded by nucleotides 40-537 of SEQ ID NO:147; amino acid residues 14-178 of SEQ ID NO:148 which is encoded by nucleotides 40-534 of SEQ ID NO:147; amino acid residues 14-177 of SEQ ID NO:148 which is encoded by nucleotides 40-531 of SEQ ID NO:147; amino acid residues 14-176 of SEQ ID NO:148 which is encoded by nucleotides 40-528 of SEQ ID NO:147; amino acid residues 14-175 of SEQ ID NO:148 which is encoded by nucleotides 40-525 of SEQ ID NO:147; amino acid residues 14-174 of SEQ ID NO:148 which is encoded by nucleotides 40-522 of SEQ ID NO:147; amino acid residues 40-173 of SEQ ID NO:148 which is encoded by nucleotides 40-519 of SEQ ID NO:147; amino acid residues 14-172 of SEQ ID NO:148 which is encoded by nucleotides 40-516 of SEQ ID NO:147; amino acid residues 15-182 of SEQ ID NO:148 which is encoded by nucleotides 43-546 of SEQ ID NO:147; amino acid residues 15-181 of SEQ ID NO:148 which is encoded by nucleotides 43-543 of SEQ ID NO:147; amino acid residues 15-180 of SEQ ID NO:148 which is encoded by nucleotides 43-540 of SEQ ID NO:147; amino acid residues 15-179 of SEQ ID NO:148 which is encoded by nucleotides 43-537 of SEQ ID NO:147; amino acid residues 15-178 of SEQ ID NO:148 which is encoded by nucleotides 43-534 of SEQ ID NO:147; amino acid residues 15-177 of SEQ ID NO:148 which is encoded by nucleotides 43-531 of SEQ ID NO:147; amino acid residues 15-176 of SEQ ID NO:148 which is encoded by nucleotides 43-528 of SEQ ID NO:147; amino acid residues 15-175 of SEQ ID NO:148 which is encoded by nucleotides 43-525 of SEQ ID NO:147; amino acid residues 15-174 of SEQ ID NO:148 which is encoded by nucleotides 43-522 of SEQ ID NO:147; amino acid residues 15-173 of SEQ ID NO:148 which is encoded by nucleotides 43-519 of SEQ ID NO:147; amino acid residues 15-172 of SEQ ID NO:148 which is encoded by nucleotides 43-516 of SEQ ID NO:147; amino acid residues 16-182 of SEQ ID NO:148 which is encoded by nucleotides 46-546 of SEQ ID NO:147; amino acid residues 16-181 of SEQ ID NO:148 which is encoded by nucleotides 46-543 of SEQ ID NO:147; amino acid residues 16-180 of SEQ ID NO:148 which is encoded by nucleotides 46-540 of SEQ ID NO:147; amino acid residues 16-179 of SEQ ID NO:148 which is encoded by nucleotides 46-537 of SEQ ID NO:147; amino acid residues 16-178 of SEQ ID NO:148 which is encoded by nucleotides 46-534 of SEQ ID NO:147; amino acid residues 16-177 of SEQ ID NO:148 which is encoded by nucleotides 46-531 of SEQ ID NO:147; amino acid residues 16-176 of SEQ ID NO:148 which is encoded by nucleotides 46-528 of SEQ ID NO:147; amino acid residues16-175 of SEQ ID NO:148 which is encoded by nucleotides 46-525 of SEQ ID NO:147; amino acid residues 16-174 of SEQ ID NO:148 which is encoded by nucleotides 46-522 of SEQ ID NO:147; amino acid residues 16-173 of SEQ ID NO:148 which is

encoded by nucleotides 46-519 of SEQ ID NO:147; and amino acid residues 16-172 of SEQ ID NO:148 which is encoded by nucleotides 46-516 of SEQ ID NO:147. The N-terminally and C-terminally modified biologically active mutants of IL-29 C5 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[67] Additional IL-29 C5 N-terminally and C-terminally biologically active mutants include, for example, amino acid residues 2-176 of SEQ ID NO:150 which is encoded by nucleotides 4-528 of SEQ ID NO:149; amino acid residues 2-175 of SEQ ID NO:150 which is encoded by nucleotides 4-525 of SEQ ID NO:149; amino acid residues 2-174 of SEQ ID NO:150 which is encoded by nucleotides 4-522 of SEQ ID NO:149; amino acid residues 2-173 of SEQ ID NO:150 which is encoded by nucleotides 4-519 of SEQ ID NO:149; amino acid residues 2-172 of SEQ ID NO:150 which is encoded by nucleotides 4-516 of SEQ ID NO:149; amino acid residues 2-171 of SEQ ID NO:150 which is encoded by nucleotides 4-513 of SEQ ID NO:149; amino acid residues 2-170 of SEQ ID NO:150 which is encoded by nucleotides 4-510 of SEQ ID NO:149; amino acid residues 2-169 of SEQ ID NO:150 which is encoded by nucleotides 4-507 of SEQ ID NO:149; amino acid residues 2-168 of SEQ ID NO:150 which is encoded by nucleotides 4-504 of SEQ ID NO:149; amino acid residues 2-167 of SEQ ID NO:150 which is encoded by nucleotides 4-501 of SEQ ID NO:149; amino acid residues 2-166 of SEQ ID NO:150 which is encoded by nucleotides 4-498 of SEQ ID NO:149; amino acid residues 3-176 of SEQ ID NO:150 which is encoded by nucleotides 7-528 of SEQ ID NO:149; amino acid residues 3-175 of SEQ ID NO:150 which is encoded by nucleotides 7-525 of SEQ ID NO:149; amino acid residues 3-174 of SEQ ID NO:150 which is encoded by nucleotides 7-522 of SEQ ID NO:149; amino acid residues 3-173 of SEQ ID NO:150 which is encoded by nucleotides 7-519 of SEQ ID NO:149; amino acid residues 3-172 of SEQ ID NO:150 which is encoded by nucleotides 7-516 of SEQ ID NO:149; amino acid residues 3-171 of SEQ ID NO:150 which is encoded by nucleotides 7-513 of SEQ ID NO:149; amino acid residues 3-170 of SEQ ID NO:150 which is encoded by nucleotides 7-510 of SEQ ID NO:149; amino acid residues 3-169 of SEQ ID NO:150 which is encoded by nucleotides 7-507 of SEQ ID NO:149; amino acid residues 3-168 of SEQ ID NO:150 which is encoded by nucleotides 7-504 of SEQ ID NO:149; amino acid residues 3-167 of SEQ ID NO:150 which is encoded by nucleotides 7-501 of SEQ ID NO:149; amino acid residues 3-166 of SEQ ID NO:150 which is encoded by nucleotides 7-498 of SEQ ID NO:149; amino acid residues 4-176 of SEQ ID NO:150 which is encoded by nucleotides 10-528 of SEQ ID NO:149; amino acid residues 4-175 of SEQ ID NO:150 which is encoded by nucleotides 10-525 of SEQ ID NO:149; amino acid residues 4-174 of SEQ ID NO:150 which is encoded by nucleotides 10-522 of SEQ ID NO:149; amino acid residues 4-173 of SEQ ID NO:150 which is encoded by nucleotides 10-519 of SEQ ID NO:149; amino acid residues 4-172 of SEQ ID NO:150 which is encoded by nucleotides 10-516 of SEQ ID NO:149; amino acid residues 4-171 of

SEQ ID NO:150 which is encoded by nucleotides 10-513 of SEQ ID NO:149; amino acid residues 4-170 of SEQ ID NO:150 which is encoded by nucleotides 10-510 of SEQ ID NO:149; amino acid residues 4-169 of SEQ ID NO:150 which is encoded by nucleotides 10-507 of SEQ ID NO:149; amino acid residues 4-168 of SEQ ID NO:150 which is encoded by nucleotides 10-504 of SEQ ID NO:149; amino acid residues 4-167 of SEQ ID NO:150 which is encoded by nucleotides 10-501 of SEQ ID NO:149; amino acid residues 4-166 of SEQ ID NO:150 which is encoded by nucleotides 10-498 of SEQ ID NO:149; amino acid residues 5-176 of SEQ ID NO:150 which is encoded by nucleotides 13-528 of SEQ ID NO:149; amino acid residues 5-175 of SEQ ID NO:150 which is encoded by nucleotides 13-525 of SEQ ID NO:149; amino acid residues 5-174 of SEQ ID NO:150 which is encoded by nucleotides 13-522 of SEQ ID NO:149; amino acid residues 5-173 of SEQ ID NO:150 which is encoded by nucleotides 13-519 of SEQ ID NO:149; amino acid residues 5-172 of SEQ ID NO:150 which is encoded by nucleotides 13-516 of SEQ ID NO:149; amino acid residues 5-171 of SEQ ID NO:150 which is encoded by nucleotides 13-513 of SEQ ID NO:149; amino acid residues 5-170 of SEQ ID NO:150 which is encoded by nucleotides 13-510 of SEQ ID NO:149; amino acid residues 5-169 of SEQ ID NO:150 which is encoded by nucleotides 13-507 of SEQ ID NO:149; amino acid residues 5-168 of SEQ ID NO:150 which is encoded by nucleotides 13-504 of SEQ ID NO:149; amino acid residues 5-167 of SEQ ID NO:150 which is encoded by nucleotides 13-501 of SEQ ID NO:149; amino acid residues 5-166 of SEQ ID NO:150 which is encoded by nucleotides 13-498 of SEQ ID NO:149; amino acid residues 6-176 of SEQ ID NO:150 which is encoded by nucleotides 16-528 of SEQ ID NO:149; amino acid residues 6-175 of SEQ ID NO:150 which is encoded by nucleotides 16-525 of SEQ ID NO:149; amino acid residues 6-174 of SEQ ID NO:150 which is encoded by nucleotides 16-522 of SEQ ID NO:149; amino acid residues 6-173 of SEQ ID NO:150 which is encoded by nucleotides 16-519 of SEQ ID NO:149; amino acid residues 6-172 of SEQ ID NO:150 which is encoded by nucleotides 16-516 of SEQ ID NO:149; amino acid residues 6-171 of SEQ ID NO:150 which is encoded by nucleotides 16-513 of SEQ ID NO:149; amino acid residues 6-170 of SEQ ID NO:150 which is encoded by nucleotides 16-510 of SEQ ID NO:149; amino acid residues 6-169 of SEQ ID NO:150 which is encoded by nucleotides 16-507 of SEQ ID NO:149; amino acid residues 6-168 of SEQ ID NO:150 which is encoded by nucleotides 16-504 of SEQ ID NO:149; amino acid residues 6-167 of SEQ ID NO:150 which is encoded by nucleotides 16-501 of SEQ ID NO:149; amino acid residues 6-166 of SEQ ID NO:150 which is encoded by nucleotides 16-498 of SEQ ID NO:149; amino acid residues 7-176 of SEQ ID NO:150 which is encoded by nucleotides 19-528 of SEQ ID NO:149; amino acid residues 7-175 of SEQ ID NO:150 which is encoded by nucleotides 19-525 of SEQ ID NO:149; amino acid residues 7-174 of SEQ ID NO:150 which is encoded by nucleotides 19-522 of SEQ ID NO:149; amino acid residues 7-173 of SEQ ID NO:150 which is encoded by nucleotides 19-519 of SEQ ID NO:149; amino acid

residues 7-172 of SEQ ID NO:150 which is encoded by nucleotides 19-516 of SEQ ID NO:149; amino acid residues 7-171 of SEQ ID NO:150 which is encoded by nucleotides 19-513 of SEQ ID NO:149; amino acid residues 7-170 of SEQ ID NO:150 which is encoded by nucleotides 19-510 of SEQ ID NO:149; amino acid residues 7-169 of SEQ ID NO:150 which is encoded by nucleotides 19-507 of SEQ ID NO:149; amino acid residues 7-168 of SEQ ID NO:150 which is encoded by nucleotides 19-504 of SEQ ID NO:149; amino acid residues 7-167 of SEQ ID NO:150 which is encoded by nucleotides 19-501 of SEQ ID NO:149; amino acid residues 7-166 of SEQ ID NO:150 which is encoded by nucleotides 19-498 of SEQ ID NO:149; amino acid residues 8-176 of SEQ ID NO:150 which is encoded by nucleotides 22-528 of SEQ ID NO:149; amino acid residues 8-175 of SEQ ID NO:150 which is encoded by nucleotides 22-525 of SEQ ID NO:149; amino acid residues 8-174 of SEQ ID NO:150 which is encoded by nucleotides 22-522 of SEQ ID NO:149; amino acid residues 8-173 of SEQ ID NO:150 which is encoded by nucleotides 22-519 of SEQ ID NO:149; amino acid residues 8-172 of SEQ ID NO:150 which is encoded by nucleotides 22-516 of SEQ ID NO:149; amino acid residues 8-171 of SEQ ID NO:150 which is encoded by nucleotides 22-513 of SEQ ID NO:149; amino acid residues 8-170 of SEQ ID NO:150 which is encoded by nucleotides 22-510 of SEQ ID NO:149; amino acid residues 8-169 of SEQ ID NO:150 which is encoded by nucleotides 22-507 of SEQ ID NO:149; amino acid residues 8-168 of SEQ ID NO:150 which is encoded by nucleotides 22-504 of SEQ ID NO:149; amino acid residues 8-167 of SEQ ID NO:150 which is encoded by nucleotides 22-501 of SEQ ID NO:149; amino acid residues 8-166 of SEQ ID NO:150 which is encoded by nucleotides 22-498 of SEQ ID NO:149; amino acid residues 9-176 of SEQ ID NO:150 which is encoded by nucleotides 25-528 of SEQ ID NO:149; amino acid residues 9-175 of SEQ ID NO:150 which is encoded by nucleotides 25-525 of SEQ ID NO:149; amino acid residues 9-174 of SEQ ID NO:150 which is encoded by nucleotides 25-522 of SEQ ID NO:149; amino acid residues 9-173 of SEQ ID NO:150 which is encoded by nucleotides 25-519 of SEQ ID NO:149; amino acid residues 9-172 of SEQ ID NO:150 which is encoded by nucleotides 25-516 of SEQ ID NO:149; amino acid residues 9-171 of SEQ ID NO:150 which is encoded by nucleotides 25-513 of SEQ ID NO:149; amino acid residues 9-170 of SEQ ID NO:150 which is encoded by nucleotides 25-510 of SEQ ID NO:149; amino acid residues 9-169 of SEQ ID NO:150 which is encoded by nucleotides 25-507 of SEQ ID NO:149; amino acid residues 9-168 of SEQ ID NO:150 which is encoded by nucleotides 25-504 of SEQ ID NO:149; amino acid residues 9-167 of SEQ ID NO:150 which is encoded by nucleotides 25-501 of SEQ ID NO:149; amino acid residues 9-166 of SEQ ID NO:150 which is encoded by nucleotides 25-498 of SEQ ID NO:149; amino acid residues 10-176 of SEQ ID NO:150 which is encoded by nucleotides 28-528 of SEQ ID NO:149; amino acid residues 10-175 of SEQ ID NO:150 which is encoded by nucleotides 28-525 of SEQ ID NO:149; amino acid residues 10-174 of SEQ ID NO:150 which is encoded by nucleotides 28-522 of SEQ ID

NO:149; amino acid residues 10-173 of SEQ ID NO:150 which is encoded by nucleotides 28-519 of SEQ ID NO:149; amino acid residues 10-172 of SEQ ID NO:150 which is encoded by nucleotides 28-516 of SEQ ID NO:149; amino acid residues 10-171 of SEQ ID NO:150 which is encoded by nucleotides 28-513 of SEQ ID NO:149; amino acid residues 10-170 of SEQ ID NO:150 which is encoded by nucleotides 28-510 of SEQ ID NO:149; amino acid residues 10-169 of SEQ ID NO:150 which is encoded by nucleotides 28-507 of SEQ ID NO:149; amino acid residues 10-168 of SEQ ID NO:150 which is encoded by nucleotides 28-504 of SEQ ID NO:149; amino acid residues 10-167 of SEQ ID NO:150 which is encoded by nucleotides 28-501 of SEQ ID NO:149; and amino acid residues 10-166 of SEQ ID NO:150 which is encoded by nucleotides 28-498 of SEQ ID NO:149. The N-terminally and C-terminally modified biologically active mutants of IL-29 C5 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[68] In addition to the IL-29 C5 mutants, the present invention also includes IL-29 polypeptides comprising a mutation at the first cysteine position, C1, of the mature polypeptide. For example, C1 from the N-terminus of the polypeptide of SEQ ID NO:20, is the cysteine at position 15, or position 16 (additional N-terminal Met) if expressed in *E. coli* (see, for example, SEQ ID NO:38). This first cysteine or C1 of IL-29 can be mutated, for example, to a serine, alanine, threonine, valine, or asparagines. These IL-29 C1 mutant polypeptides will thus have a predicted disulfide bond pattern of C2(Cys49 of SEQ ID NO:20)/C4(Cys145 of SEQ ID NO:20) and C3(Cys112 of SEQ ID NO:20)/C5(Cys171 of SEQ ID NO:20). Additional IL-29 C1 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:41, 43, 45, 47, and 145, including DNA and RNA molecules, that encode IL-29 C1 mutant polypeptides as shown in SEQ ID NOs:42, 44, 46, 48 and 146, respectively. Additional IL-29 C1 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:57, 59, 65, and 67, including DNA and RNA molecules, that encode IL-29 C1 mutant polypeptides as shown in SEQ ID NOs:58, 60, 66, and 68, respectively (PCT publication WO 03/066002 (Kotenko et al.)). Additional, IL-29 C1 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:73, 75, 81, and 83, including DNA and RNA molecules, that encode IL-29 C1 mutant polypeptides as shown in SEQ ID NOs:74, 76, 82, and 84, respectively (PCT publication WO 02/092762 (Baum et al.)).

[69] The present invention also includes biologically active mutants of IL-29 C1 cysteine mutants which provide, at least partially, an antiviral activity as provided here, e.g., anti-hepatitis C activity. The first cysteine or C1 from the N-terminus of IL-29 can mutated to any amino acid that does not form a disulfide bond with another cysteine, e.g., serine, alanine, threonine, valine or aspargine. The biologically active mutants of IL-29 C1 cysteine mutants of the present invention

include N-, C-, and N- and C-terminal deletions of IL-29, e.g., the polypeptide of SEQ ID NOs:146 encoded by the polynucleotide of SEQ ID NO:145.

[70] N-terminally modified biologically active mutants of IL-29 C1 mutants include, for example, amino acid residues 2-182 of SEQ ID NO:146 which is encoded by nucleotides 4-546 of SEQ ID NO:145; amino acid residues 3-182 of SEQ ID NO:146 which is encoded by nucleotides 7-546 of SEQ ID NO:145; amino acid residues 4-182 of SEQ ID NO:146 which is encoded by nucleotides 10-546 of SEQ ID NO:145; amino acid residues 5-182 of SEQ ID NO:146 which is encoded by nucleotides 13-546 of SEQ ID NO:145; amino acid residues 6-182 of SEQ ID NO:146 which is encoded by nucleotides 16-546 of SEQ ID NO:145; amino acid residues 7-182 of SEQ ID NO:146 which is encoded by nucleotides 19-546 of SEQ ID NO:145; amino acid residues 8-182 of SEQ ID NO:146 which is encoded by nucleotides 22-546 of SEQ ID NO:145; amino acid residues 9-182 of SEQ ID NO:146 which is encoded by nucleotides 25-546 of SEQ ID NO:145; amino acid residues 10-182 of SEQ ID NO:146 which is encoded by nucleotides 28-546 of SEQ ID NO:145; amino acid residues 11-182 of SEQ ID NO:146 which is encoded by nucleotides 31-546 of SEQ ID NO:145; amino acid residues 12-182 of SEQ ID NO:146 which is encoded by nucleotides 34-182 of SEQ ID NO:145; amino acid residues 13-182 of SEQ ID NO:146 which is encoded by nucleotides 37-546 of SEQ ID NO:145; amino acid residues 14-182 of SEQ ID NO:146 which is encoded by nucleotides 40-546 of SEQ ID NO:145; amino acid residues 15-182 of SEQ ID NO:146 which is encoded by nucleotides 43-546 of SEQ ID NO:145; and amino acid residues 16-182 of SEQ ID NO:146 which is encoded by nucleotides 46-546 of SEQ ID NO:145. The N-terminally modified biologically active mutants of IL-29 C1 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[71] C-terminally modified biologically active mutants of IL-29 C1 mutants include, for example, amino acid residues 1-181 of SEQ ID NO:146 which is encoded by nucleotides 1-543 of SEQ ID NO:145; amino acid residues 1-180 of SEQ ID NO:146 which is encoded by nucleotides 1-540 of SEQ ID NO:145; amino acid residues 1-179 of SEQ ID NO:146 which is encoded by nucleotides 1-537 of SEQ ID NO:145; amino acid residues 1-178 of SEQ ID NO:146 which is encoded by nucleotides 1-534 of SEQ ID NO:145; amino acid residues 1-177 of SEQ ID NO:146 which is encoded by nucleotides 1-531 of SEQ ID NO:145; amino acid residues 1-176 of SEQ ID NO:146 which is encoded by nucleotides 1-528 of SEQ ID NO:145; amino acid residues 1-175 of SEQ ID NO:146 which is encoded by nucleotides 1-525 of SEQ ID NO:145; amino acid residues 1-174 of SEQ ID NO:146 which is encoded by nucleotides 1-522 of SEQ ID NO:145; amino acid residues 1-173 of SEQ ID NO:146 which is encoded by nucleotides 1-519 of SEQ ID NO:145; and amino acid residues 1-172 of SEQ ID NO:146 which is encoded by nucleotides 1-516 of SEQ ID NO:145.

[72] N-terminally and C-terminally modified biologically active mutants of IL-29 C1 mutants include, for example, amino acid residues 2-181 of SEQ ID NO:146 which is encoded by nucleotides 4-543 of SEQ ID NO:145; amino acid residues 2-180 of SEQ ID NO:146 which is encoded by nucleotides 4-540 of SEQ ID NO:145; amino acid residues 2-179 of SEQ ID NO:146 which is encoded by nucleotides 4-537 of SEQ ID NO:145; amino acid residues 2-178 of SEQ ID NO:146 which is encoded by nucleotides 4-534 of SEQ ID NO:145; amino acid residues 2-177 of SEQ ID NO:146 which is encoded by nucleotides 4-531 of SEQ ID NO:145; amino acid residues 2-176 of SEQ ID NO:146 which is encoded by nucleotides 4-528 of SEQ ID NO:145; amino acid residues 2-175 of SEQ ID NO:146 which is encoded by nucleotides 4-525 of SEQ ID NO:145; amino acid residues 2-174 of SEQ ID NO:146 which is encoded by nucleotides 4-522 of SEQ ID NO:145; amino acid residues 2-173 of SEQ ID NO:146 which is encoded by nucleotides 4-519 of SEQ ID NO:145; amino acid residues 2-172 of SEQ ID NO:146 which is encoded by nucleotides 4-516 of SEQ ID NO:145; amino acid residues 3-181 of SEQ ID NO:146 which is encoded by nucleotides 7-543 of SEQ ID NO:145; amino acid residues 3-180 of SEQ ID NO:146 which is encoded by nucleotides 7-540 of SEQ ID NO:145; amino acid residues 3-179 of SEQ ID NO:146 which is encoded by nucleotides 7-537 of SEQ ID NO:145; amino acid residues 3-178 of SEQ ID NO:146 which is encoded by nucleotides 7-534 of SEQ ID NO:145; amino acid residues 3-177 of SEQ ID NO:146 which is encoded by nucleotides 7-531 of SEQ ID NO:145; amino acid residues 3-176 of SEQ ID NO:146 which is encoded by nucleotides 7-528 of SEQ ID NO:145; amino acid residues 3-175 of SEQ ID NO:146 which is encoded by nucleotides 7-525 of SEQ ID NO:145; amino acid residues 3-174 of SEQ ID NO:146 which is encoded by nucleotides 7-522 of SEQ ID NO:145; amino acid residues 3-173 of SEQ ID NO:146 which is encoded by nucleotides 7-519 of SEQ ID NO:145; amino acid residues 3-172 of SEQ ID NO:146 which is encoded by nucleotides 7-516 of SEQ ID NO:145; amino acid residues 4-181 of SEQ ID NO:146 which is encoded by nucleotides 10-543 of SEQ ID NO:145; amino acid residues 4-180 of SEQ ID NO:146 which is encoded by nucleotides 10-540 of SEQ ID NO:145; amino acid residues 4-179 of SEQ ID NO:146 which is encoded by nucleotides 10-537 of SEQ ID NO:145; amino acid residues 4-178 of SEQ ID NO:146 which is encoded by nucleotides 10-534 of SEQ ID NO:145; amino acid residues 4-177 of SEQ ID NO:146 which is encoded by nucleotides 10-531 of SEQ ID NO:145; amino acid residues 4-176 of SEQ ID NO:146 which is encoded by nucleotides 10-528 of SEQ ID NO:145; amino acid residues 4-175 of SEQ ID NO:146 which is encoded by nucleotides 10-525 of SEQ ID NO:145; amino acid residues 4-174 of SEQ ID NO:146 which is encoded by nucleotides 10-522 of SEQ ID NO:145; amino acid residues 4-173 of SEQ ID NO:146 which is encoded by nucleotides 10-519 of SEQ ID NO:145; amino acid residues 4-172 of SEQ ID NO:146 which is encoded by nucleotides 10-516 of SEQ ID NO:145; amino acid residues 5-181 of SEQ ID NO:146 which is encoded by nucleotides 13-543 of

SEQ ID NO:145; amino acid residues 5-180 of SEQ ID NO:146 which is encoded by nucleotides 13-540 of SEQ ID NO:145; amino acid residues 5-179 of SEQ ID NO:146 which is encoded by nucleotides 13-537 of SEQ ID NO:145; amino acid residues 5-178 of SEQ ID NO:146 which is encoded by nucleotides 13-534 of SEQ ID NO:145; amino acid residues 5-177 of SEQ ID NO:146 which is encoded by nucleotides 13-531 of SEQ ID NO:145; amino acid residues 5-176 of SEQ ID NO:146 which is encoded by nucleotides 13-528 of SEQ ID NO:145; amino acid residues 5-175 of SEQ ID NO:146 which is encoded by nucleotides 13-525 of SEQ ID NO:145; amino acid residues 5-174 of SEQ ID NO:146 which is encoded by nucleotides 13-522 of SEQ ID NO:145; amino acid residues 5-173 of SEQ ID NO:146 which is encoded by nucleotides 13-519 of SEQ ID NO:145; amino acid residues 5-172 of SEQ ID NO:146 which is encoded by nucleotides 13-516 of SEQ ID NO:145; amino acid residues 6-181 of SEQ ID NO:146 which is encoded by nucleotides 16-543 of SEQ ID NO:145; amino acid residues 6-180 of SEQ ID NO:146 which is encoded by nucleotides 16-540 of SEQ ID NO:145; amino acid residues 6-179 of SEQ ID NO:146 which is encoded by nucleotides 16-537 of SEQ ID NO:145; amino acid residues 6-178 of SEQ ID NO:146 which is encoded by nucleotides 16-534 of SEQ ID NO:145; amino acid residues 6-177 of SEQ ID NO:146 which is encoded by nucleotides 16-531 of SEQ ID NO:145; amino acid residues 6-176 of SEQ ID NO:146 which is encoded by nucleotides 16-528 of SEQ ID NO:145; amino acid residues 6-175 of SEQ ID NO:146 which is encoded by nucleotides 16-525 of SEQ ID NO:145; amino acid residues 6-174 of SEQ ID NO:146 which is encoded by nucleotides 16-522 of SEQ ID NO:145; amino acid residues 6-173 of SEQ ID NO:146 which is encoded by nucleotides 16-519 of SEQ ID NO:145; amino acid residues 6-172 of SEQ ID NO:146 which is encoded by nucleotides 16-516 of SEQ ID NO:145; amino acid residues 7-181 of SEQ ID NO:146 which is encoded by nucleotides 19-543 of SEQ ID NO:145; amino acid residues 7-180 of SEQ ID NO:146 which is encoded by nucleotides 19-540 of SEQ ID NO:145; amino acid residues 7-179 of SEQ ID NO:146 which is encoded by nucleotides 19-537 of SEQ ID NO:145; amino acid residues 7-178 of SEQ ID NO:146 which is encoded by nucleotides 19-534 of SEQ ID NO:145; amino acid residues 7-177 of SEQ ID NO:146 which is encoded by nucleotides 19-531 of SEQ ID NO:145; amino acid residues 7-176 of SEQ ID NO:146 which is encoded by nucleotides 19-528 of SEQ ID NO:145; amino acid residues 7-175 of SEQ ID NO:146 which is encoded by nucleotides 19-525 of SEQ ID NO:145; amino acid residues 7-174 of SEQ ID NO:146 which is encoded by nucleotides 19-522 of SEQ ID NO:145; amino acid residues 7-173 of SEQ ID NO:146 which is encoded by nucleotides 19-519 of SEQ ID NO:145; amino acid residues 7-172 of SEQ ID NO:146 which is encoded by nucleotides 19-516 of SEQ ID NO:145; amino acid residues 8-181 of SEQ ID NO:146 which is encoded by nucleotides 22-543 of SEQ ID NO:145; amino acid residues 8-180 of SEQ ID NO:146 which is encoded by nucleotides 22-540 of SEQ ID NO:145; amino acid residues 8-179 of SEQ ID NO:146 which is encoded by

nucleotides 22-537 of SEQ ID NO:145; amino acid residues 8-178 of SEQ ID NO:146 which is encoded by nucleotides 22-534 of SEQ ID NO:145; amino acid residues 8-177 of SEQ ID NO:146 which is encoded by nucleotides 22-531 of SEQ ID NO:145; amino acid residues 8-176 of SEQ ID NO:146 which is encoded by nucleotides 22-528 of SEQ ID NO:145; amino acid residues 8-175 of SEQ ID NO:146 which is encoded by nucleotides 22-525 of SEQ ID NO:145; amino acid residues 8-174 of SEQ ID NO:146 which is encoded by nucleotides 22-522 of SEQ ID NO:145; amino acid residues 8-173 of SEQ ID NO:146 which is encoded by nucleotides 22-519 of SEQ ID NO:145; amino acid residues 8-172 of SEQ ID NO:146 which is encoded by nucleotides 22-516 of SEQ ID NO:145; amino acid residues 9-181 of SEQ ID NO:146 which is encoded by nucleotides 25-543 of SEQ ID NO:145; amino acid residues 9-180 of SEQ ID NO:146 which is encoded by nucleotides 25-540 of SEQ ID NO:145; amino acid residues 9-179 of SEQ ID NO:146 which is encoded by nucleotides 25-537 of SEQ ID NO:145; amino acid residues 9-178 of SEQ ID NO:146 which is encoded by nucleotides 25-534 of SEQ ID NO:145; amino acid residues 9-177 of SEQ ID NO:146 which is encoded by nucleotides 25-531 of SEQ ID NO:145; amino acid residues 9-176 of SEQ ID NO:146 which is encoded by nucleotides 25-528 of SEQ ID NO:145; amino acid residues 9-175 of SEQ ID NO:146 which is encoded by nucleotides 25-525 of SEQ ID NO:145; amino acid residues 9-174 of SEQ ID NO:146 which is encoded by nucleotides 25-522 of SEQ ID NO:145; amino acid residues 9-173 of SEQ ID NO:146 which is encoded by nucleotides 25-519 of SEQ ID NO:145; amino acid residues 9-172 of SEQ ID NO:146 which is encoded by nucleotides 25-516 of SEQ ID NO:145; amino acid residues 10-181 of SEQ ID NO:146 which is encoded by nucleotides 28-543 of SEQ ID NO:145; amino acid residues 10-180 of SEQ ID NO:146 which is encoded by nucleotides 28-540 of SEQ ID NO:145; amino acid residues 10-179 of SEQ ID NO:146 which is encoded by nucleotides 28-537 of SEQ ID NO:145; amino acid residues 10-178 of SEQ ID NO:146 which is encoded by nucleotides 28-534 of SEQ ID NO:145; amino acid residues 10-177 of SEQ ID NO:146 which is encoded by nucleotides 28-531 of SEQ ID NO:145; amino acid residues 10-176 of SEQ ID NO:146 which is encoded by nucleotides 28-528 of SEQ ID NO:145; amino acid residues 10-175 of SEQ ID NO:146 which is encoded by nucleotides 28-525 of SEQ ID NO:145; amino acid residues 10-174 of SEQ ID NO:146 which is encoded by nucleotides 28-522 of SEQ ID NO:145; amino acid residues 10-173 of SEQ ID NO:146 which is encoded by nucleotides 28-519 of SEQ ID NO:145; amino acid residues 10-172 of SEQ ID NO:146 which is encoded by nucleotides 28-516 of SEQ ID NO:145; amino acid residues 11-181 of SEQ ID NO:146 which is encoded by nucleotides 31-543 of SEQ ID NO:145; amino acid residues 11-180 of SEQ ID NO:146 which is encoded by nucleotides 31-540 of SEQ ID NO:145; amino acid residues 11-179 of SEQ ID NO:146 which is encoded by nucleotides 31-537 of SEQ ID NO:145; amino acid residues 11-178 of SEQ ID NO:146 which is encoded by nucleotides 31-534 of SEQ ID NO:145; amino acid residues 11-177 of SEQ ID NO:146

which is encoded by nucleotides 31-531 of SEQ ID NO:145; amino acid residues 11-176 of SEQ ID NO:146 which is encoded by nucleotides 31-528 of SEQ ID NO:145; amino acid residues 11-175 of SEQ ID NO:146 which is encoded by nucleotides 31-525 of SEQ ID NO:145; amino acid residues 11-174 of SEQ ID NO:146 which is encoded by nucleotides 31-522 of SEQ ID NO:145; amino acid residues 11-173 of SEQ ID NO:146 which is encoded by nucleotides 31-519 of SEQ ID NO:145; amino acid residues 11-172 of SEQ ID NO:146 which is encoded by nucleotides 31-516 of SEQ ID NO:145; amino acid residues 12-181 of SEQ ID NO:146 which is encoded by nucleotides 34-543 of SEQ ID NO:145; amino acid residues 12-180 of SEQ ID NO:146 which is encoded by nucleotides 34-540 of SEQ ID NO:145; amino acid residues 12-179 of SEQ ID NO:146 which is encoded by nucleotides 34-537 of SEQ ID NO:145; amino acid residues 12-178 of SEQ ID NO:146 which is encoded by nucleotides 34-534 of SEQ ID NO:145; amino acid residues 12-177 of SEQ ID NO:146 which is encoded by nucleotides 34-531 of SEQ ID NO:145; amino acid residues 12-176 of SEQ ID NO:146 which is encoded by nucleotides 34-528 of SEQ ID NO:145; amino acid residues 12-175 of SEQ ID NO:146 which is encoded by nucleotides 34-525 of SEQ ID NO:145; amino acid residues 12-174 of SEQ ID NO:146 which is encoded by nucleotides 34-522 of SEQ ID NO:145; amino acid residues 12-173 of SEQ ID NO:146 which is encoded by nucleotides 34-519 of SEQ ID NO:145; amino acid residues 12-172 of SEQ ID NO:146 which is encoded by nucleotides 34-516 of SEQ ID NO:145; amino acid residues 13-181 of SEQ ID NO:146 which is encoded by nucleotides 37-543 of SEQ ID NO:145; amino acid residues 13-180 of SEQ ID NO:146 which is encoded by nucleotides 37-540 of SEQ ID NO:145; amino acid residues 13-179 of SEQ ID NO:146 which is encoded by nucleotides 37-537 of SEQ ID NO:145; amino acid residues 13-178 of SEQ ID NO:146 which is encoded by nucleotides 37-534 of SEQ ID NO:145; amino acid residues 13-177 of SEQ ID NO:146 which is encoded by nucleotides 37-531 of SEQ ID NO:145; amino acid residues 13-176 of SEQ ID NO:146 which is encoded by nucleotides 37-528 of SEQ ID NO:145; amino acid residues 13-175 of SEQ ID NO:146 which is encoded by nucleotides 37-525 of SEQ ID NO:145; amino acid residues 13-174 of SEQ ID NO:146 which is encoded by nucleotides 37-522 of SEQ ID NO:145; amino acid residues 13-173 of SEQ ID NO:146 which is encoded by nucleotides 37-519 of SEQ ID NO:145; amino acid residues 13-172 of SEQ ID NO:146 which is encoded by nucleotides 37-516 of SEQ ID NO:145; amino acid residues 14-181 of SEQ ID NO:146 which is encoded by nucleotides 40-543 of SEQ ID NO:145; amino acid residues 14-180 of SEQ ID NO:146 which is encoded by nucleotides 40-540 of SEQ ID NO:145; amino acid residues 14-179 of SEQ ID NO:146 which is encoded by nucleotides 40-537 of SEQ ID NO:145; amino acid residues 14-178 of SEQ ID NO:146 which is encoded by nucleotides 40-534 of SEQ ID NO:145; amino acid residues 14-177 of SEQ ID NO:146 which is encoded by nucleotides 40-531 of SEQ ID NO:145; amino acid residues 14-176 of SEQ ID NO:146 which is encoded by nucleotides 40-528 of SEQ ID NO:145; amino acid residues 14-175 of

SEQ ID NO:146 which is encoded by nucleotides 40-525 of SEQ ID NO:145; amino acid residues 14-174 of SEQ ID NO:146 which is encoded by nucleotides 40-522 of SEQ ID NO:145; amino acid residues 14-173 of SEQ ID NO:146 which is encoded by nucleotides 40-519 of SEQ ID NO:145; amino acid residues 14-172 of SEQ ID NO:146 which is encoded by nucleotides 40-516 of SEQ ID NO:145; amino acid residues 15-181 of SEQ ID NO:146 which is encoded by nucleotides 43-543 of SEQ ID NO:145; amino acid residues 15-180 of SEQ ID NO:146 which is encoded by nucleotides 43-540 of SEQ ID NO:145; amino acid residues 15-179 of SEQ ID NO:146 which is encoded by nucleotides 43-537 of SEQ ID NO:145; amino acid residues 15-178 of SEQ ID NO:146 which is encoded by nucleotides 43-534 of SEQ ID NO:145; amino acid residues 15-177 of SEQ ID NO:146 which is encoded by nucleotides 43-531 of SEQ ID NO:145; amino acid residues 15-176 of SEQ ID NO:146 which is encoded by nucleotides 43-528 of SEQ ID NO:145; amino acid residues 15-175 of SEQ ID NO:146 which is encoded by nucleotides 43-525 of SEQ ID NO:145; amino acid residues 15-174 of SEQ ID NO:146 which is encoded by nucleotides 43-522 of SEQ ID NO:145; amino acid residues 15-173 of SEQ ID NO:146 which is encoded by nucleotides 43-519 of SEQ ID NO:145; amino acid residues 15-172 of SEQ ID NO:146 which is encoded by nucleotides 43-516 of SEQ ID NO:145; amino acid residues 16-181 of SEQ ID NO:146 which is encoded by nucleotides 46-543 of SEQ ID NO:145; amino acid residues 16-180 of SEQ ID NO:146 which is encoded by nucleotides 46-540 of SEQ ID NO:145; amino acid residues 16-179 of SEQ ID NO:146 which is encoded by nucleotides 46-537 of SEQ ID NO:145; amino acid residues 16-178 of SEQ ID NO:146 which is encoded by nucleotides 46-534 of SEQ ID NO:145; amino acid residues 16-177 of SEQ ID NO:146 which is encoded by nucleotides 46-531 of SEQ ID NO:145; amino acid residues 16-176 of SEQ ID NO:146 which is encoded by nucleotides 46-528 of SEQ ID NO:145; amino acid residues 16-175 of SEQ ID NO:146 which is encoded by nucleotides 46-525 of SEQ ID NO:145; amino acid residues 16-174 of SEQ ID NO:146 which is encoded by nucleotides 46-522 of SEQ ID NO:145; amino acid residues 16-173 of SEQ ID NO:146 which is encoded by nucleotides 46-519 of SEQ ID NO:145; and amino acid residues 16-172 of SEQ ID NO:146 which is encoded by nucleotides 46-516 of SEQ ID NO:145. The N-terminally and C-terminally modified biologically active mutants of IL-29 C1 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[73] The IL-29 polypeptides of the present invention include, for example, SEQ ID NOs:4, 20, 32, 34, 38, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 146, 148, 150, and biologically active mutants, fusions, variants and fragments thereof which are encoded by IL-29 polynucleotide molecules as shown in SEQ ID NOs:3, 19, 31, 33, 37, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127,

129, 131, 133, 135, 145, 147 and 149, respectively, may further include a signal sequence as shown in SEQ ID NOs:102, 104, 106, or 108. A polynucleotide molecule encoding the signal sequence polypeptides of SEQ ID NOs:102, 104, 106, and 108 are are shown as SEQ ID NOs:101, 103, 105, and 107, respectively.

[74] An IL-28B gene encodes a polypeptide of 205 amino acids, as shown in SEQ ID NO:6. The signal sequence for IL-28B comprises amino acid residue 1 (Met) through amino acid residue 21 (Ala) of SEQ ID NO:6. The mature peptide for IL-28B begins at amino acid residue 22 (Val). A variant IL-28B gene encodes a polypeptide of 200 amino acids, as shown in SEQ ID NO:22. The signal sequence for IL-28B can be predicted as comprising amino acid residue -25 (Met) through amino acid residue -1 (Ala) of SEQ ID NO:22. The mature peptide for IL-28B begins at amino acid residue 1 (Val) of SEQ ID NO:22. IL-28B helices are predicted as follow: helix A is defined by amino acid residues 31 (Ala) to 45 (Leu); helix B by amino acid residues 58 (Thr) to 65 (Gln); helix C by amino acid residues 69 (Arg) to 86 (Ala); helix D by amino acid residues 95 (Gly) to 114 (Ala); helix E by amino acid residues 126 (Thr) to 142 (Lys); and helix F by amino acid residues 148 (Cys) to 169 (Ala); as shown in SEQ ID NO:22. When a polynucleotide sequence encoding the mature polypeptide is expressed in a prokaryotic system, such as *E. coli*, a secretory signal sequence may not be required and an N-terminal Met may present, resulting in expression of a polypeptide such as is shown in SEQ ID NO:40.

[75] IL-28B polypeptides of the present invention also include a mutation at the second cysteine, C2, of the mature polypeptide. For example, C2 from the N-terminus of the polypeptide of SEQ ID NO:22 is the cysteine at amino acid position 48, or position 49 (additional N-terminal Met) if expressed in *E coli* (see, for example, SEQ ID NO:40). This second cysteine (of which there are seven, like IL-28A) or C2 of IL-28B can be mutated, for example, to a serine, alanine, threonine, valine, or asparagine. IL-28B C2 mutant molecules of the present invention include, for example, polynucleotide molecules as shown in SEQ ID NOs:85, 87 and 141, including DNA and RNA molecules, that encode IL-28B C2 mutant polypeptides as shown in SEQ ID NOs:86, 88 and 142, respectively. Additional IL-28B C2 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:93 and 95 including DNA and RNA molecules, that encode IL-28 C2 mutant polypeptides as shown in SEQ ID NOs:94 and 96, respectively (PCT publication WO 03/066002 (Kotenko et al.)).

[76] The present invention also includes biologically active mutants of IL-28B C2 cysteine mutants which provide, at least partially, an antiviral activity as provided here, e.g., anti-hepatitis C activity. The second cysteine or C2 from the N-terminus of IL-28B can mutated to any amino acid that does not form a disulfide bond with another cysteine, e.g., serine, alanine, threonine, valine or aspargine. The biologically active mutants of IL-28B C2 cysteine mutants of the present

invention include N-, C-, and N- and C-terminal deletions of IL-28B, e.g., the polypeptide of SEQ ID NO:142 encoded by the polynucleotide of SEQ ID NO:141.

[77] N-terminally modified biologically active mutants of IL-28B C2 mutants include, for example, amino acid residues 2-176 of SEQ ID NO:142 which is encoded by nucleotides 4-528 of SEQ ID NO:141; amino acid residues 3-176 of SEQ ID NO:142 which is encoded by nucleotides 7-528 of SEQ ID NO:141; amino acid residues 4-176 of SEQ ID NO:142 which is encoded by nucleotides 10-528 of SEQ ID NO:141; amino acid residues 5-176 of SEQ ID NO:142 which is encoded by nucleotides 13-528 of SEQ ID NO:141; amino acid residues 6-176 of SEQ ID NO:142 which is encoded by nucleotides 16-528 of SEQ ID NO:141; amino acid residues 7-176 of SEQ ID NO:142 which is encoded by nucleotides 19-528 of SEQ ID NO:141; amino acid residues 8-176 of SEQ ID NO:142 which is encoded by nucleotides 22-528 of SEQ ID NO:141; amino acid residues 9-176 of SEQ ID NO:142 which is encoded by nucleotides 25-528 of SEQ ID NO:141; amino acid residues 10-176 of SEQ ID NO:142 which is encoded by nucleotides 28-528 of SEQ ID NO:141; amino acid residues 11-176 of SEQ ID NO:142 which is encoded by nucleotides 31-528 of SEQ ID NO:141; amino acid residues 12-176 of SEQ ID NO:142 which is encoded by nucleotides 34-528 of SEQ ID NO:141; amino acid residues 13-176 of SEQ ID NO:142 which is encoded by nucleotides 37-528 of SEQ ID NO:141; amino acid residues 14-176 of SEQ ID NO:142 which is encoded by nucleotides 40-528 of SEQ ID NO:141; amino acid residues 15-176 of SEQ ID NO:142 which is encoded by nucleotides 43-528 of SEQ ID NO:141; amino acid residues 16-176 of SEQ ID NO:142 which is encoded by nucleotides 46-528 of SEQ ID NO:141; and amino acid residues 17-176 of SEQ ID NO:142 which is encoded by nucleotides 49-528 of SEQ ID NO:141. The N-terminally modified biologically active mutants of IL-28 C2 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[78] C-terminally modified biologically active mutants of IL-28B C2 mutants include, for example, amino acid residues 1-175 of SEQ ID NO:142 which is encoded by nucleotides 1-525 of SEQ ID NO:141.

[79] N-terminally and C-terminally biologically active mutants of IL-28B C2 mutants include, for example, amino acid residues 2-175 of SEQ ID NO:142 which is encoded by nucleotides 4-525 of SEQ ID NO:141; amino acid residues 3-175 of SEQ ID NO:142 which is encoded by nucleotides 7-525 of SEQ ID NO:141; amino acid residues 4-175 of SEQ ID NO:142 which is encoded by nucleotides 10-525 of SEQ ID NO:141; amino acid residues 5-175 of SEQ ID NO:142 which is encoded by nucleotides 13-525 of SEQ ID NO:141; amino acid residues 6-175 of SEQ ID NO:142 which is encoded by nucleotides 16-525 of SEQ ID NO:141; amino acid residues 7-175 of SEQ ID NO:142 which is encoded by nucleotides 19-525 of SEQ ID NO:141; amino acid residues 8-175 of SEQ ID NO:142 which is encoded by nucleotides 22-525 of SEQ ID NO:141; amino acid

residues 9-175 of SEQ ID NO:142 which is encoded by nucleotides 25-525 of SEQ ID NO:141; amino acid residues 10-175 of SEQ ID NO:142 which is encoded by nucleotides 28-525 of SEQ ID NO:141; amino acid residues 11-175 of SEQ ID NO:142 which is encoded by nucleotides 31-525 of SEQ ID NO:141; amino acid residues 12-175 of SEQ ID NO:142 which is encoded by nucleotides 34-525 of SEQ ID NO:141; amino acid residues 13-175 of SEQ ID NO:142 which is encoded by nucleotides 37-525 of SEQ ID NO:141; amino acid residues 14-175 of SEQ ID NO:142 which is encoded by nucleotides 40-525 of SEQ ID NO:141; amino acid residues 15-175 of SEQ ID NO:142 which is encoded by nucleotides 43-525 of SEQ ID NO:141; amino acid residues 16-175 of SEQ ID NO:142 which is encoded by nucleotides 46-525 of SEQ ID NO:141; and amino acid residues 17-175 of SEQ ID NO:142 which is encoded by nucleotides 49-525 of SEQ ID NO:141. The N-terminally and C-terminally modified biologically active mutants of IL-28 C2 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[80] In addition to the IL-28B C2 mutants, the present invention also includes IL-28B polypeptides comprising a mutation at the third cysteine position, C3, of the mature polypeptide. For example, C3 from the N-terminus of the polypeptide of SEQ ID NO:22, is the cysteine at position 50, or position 51 (additional N-terminal Met) if expressed in *E. coli* (see, for example, SEQ ID NO:40). IL-28B C3 mutant molecules of the present invention include, for example, polynucleotide molecules as shown in SEQ ID NOs:89, 91 and 143, including DNA and RNA molecules, that encode IL-28B C3 mutant polypeptides as shown in SEQ ID NOs:90, 92 and 144, respectively. Additional IL-28B C3 mutant molecules of the present invention include polynucleotide molecules as shown in SEQ ID NOs:97 and 99 including DNA and RNA molecules, that encode IL-28B C3 mutant polypeptides as shown in SEQ ID NOs:98 and 100, respectively (PCT publication WO 03/066002 (Kotenko et al.)).

[81] N-terminally biologically active mutants of IL-28B C3 mutants include, for example, amino acid residues 2-176 of SEQ ID NO:144 which is encoded by nucleotides 4-528 of SEQ ID NO:143; amino acid residues 3-176 of SEQ ID NO:144 which is encoded by nucleotides 7-528 of SEQ ID NO:143; amino acid residues 4-176 of SEQ ID NO:144 which is encoded by nucleotides 10-528 of SEQ ID NO:143; amino acid residues 5-176 of SEQ ID NO:144 which is encoded by nucleotides 13-528 of SEQ ID NO:143; amino acid residues 6-176 of SEQ ID NO:144 which is encoded by nucleotides 16-528 of SEQ ID NO:143; amino acid residues 7-176 of SEQ ID NO:144 which is encoded by nucleotides 19-528 of SEQ ID NO:143; amino acid residues 8-176 of SEQ ID NO:144 which is encoded by nucleotides 22-528 of SEQ ID NO:143; amino acid residues 9-176 of SEQ ID NO:144 which is encoded by nucleotides 25-528 of SEQ ID NO:143; amino acid residues 10-176 of SEQ ID NO:144 which is encoded by nucleotides 28-528 of SEQ ID NO:143; amino acid residues 11-176 of SEQ ID NO:144 which is encoded by nucleotides 31-528 of SEQ ID NO:143; amino acid residues 12-176 of SEQ ID NO:144 which is encoded by nucleotides 34-528 of SEQ ID

NO:143; amino acid residues 13-176 of SEQ ID NO:144 which is encoded by nucleotides 37-528 of SEQ ID NO:143; amino acid residues 14-176 of SEQ ID NO:144 which is encoded by nucleotides 40-528 of SEQ ID NO:143; amino acid residues 15-176 of SEQ ID NO:144 which is encoded by nucleotides 43-528 of SEQ ID NO:143; amino acid residues 16-176 of SEQ ID NO:144 which is encoded by nucleotides 46-528 of SEQ ID NO:143; and amino acid residues 17-176 of SEQ ID NO:144 which is encoded by nucleotides 49-528 of SEQ ID NO:143. The N-terminally modified biologically active mutants of IL-28 C3 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[82] C-terminally modified biologically active mutants of IL-28B C3 mutants include, for example, amino acid residues 1-175 of SEQ ID NO:144 which is encoded by nucleotides 1-525 of SEQ ID NO:143.

[83] N-terminally and C-terminally biologically active mutants of IL-28B C3 mutants include, for example, amino acid residues 2-175 of SEQ ID NO:144 which is encoded by nucleotides 4-525 of SEQ ID NO:143; amino acid residues 3-175 of SEQ ID NO:144 which is encoded by nucleotides 7-525 of SEQ ID NO:143; amino acid residues 4-175 of SEQ ID NO:144 which is encoded by nucleotides 10-525 of SEQ ID NO:143; amino acid residues 5-175 of SEQ ID NO:144 which is encoded by nucleotides 13-525 of SEQ ID NO:143; amino acid residues 6-175 of SEQ ID NO:144 which is encoded by nucleotides 16-525 of SEQ ID NO:143; amino acid residues 7-175 of SEQ ID NO:144 which is encoded by nucleotides 19-525 of SEQ ID NO:143; amino acid residues 8-175 of SEQ ID NO:144 which is encoded by nucleotides 22-525 of SEQ ID NO:143; amino acid residues 9-175 of SEQ ID NO:144 which is encoded by nucleotides 25-525 of SEQ ID NO:143; amino acid residues 10-175 of SEQ ID NO:144 which is encoded by nucleotides 28-525 of SEQ ID NO:143; amino acid residues 11-175 of SEQ ID NO:144 which is encoded by nucleotides 31-525 of SEQ ID NO:143; amino acid residues 12-175 of SEQ ID NO:144 which is encoded by nucleotides 34-525 of SEQ ID NO:143; amino acid residues 13-175 of SEQ ID NO:144 which is encoded by nucleotides 37-525 of SEQ ID NO:143; amino acid residues 14-175 of SEQ ID NO:144 which is encoded by nucleotides 40-525 of SEQ ID NO:143; amino acid residues 15-175 of SEQ ID NO:144 which is encoded by nucleotides 43-525 of SEQ ID NO:143; amino acid residues 16-175 of SEQ ID NO:144 which is encoded by nucleotides 46-525 of SEQ ID NO:143; and amino acid residues 17-175 of SEQ ID NO:144 which is encoded by nucleotides 49-525 of SEQ ID NO:143. The N-terminally and C-terminally modified biologically active mutants of IL-28 C3 mutants of the present invention may also include an N-terminal Methione if expressed, for instance, in *E. coli*.

[84] The IL-28B polypeptides of the present invention include, for example, SEQ ID NOs:6, 22, 40, 86, 88, 90, 92, 94, 96, 98, 100, 142, 144, and biologically active mutants, fusions,

variants and fragments thereof which are encoded by IL-28B polynucleotide molecules as shown in SEQ ID NOs:5, 21, 39, 85, 87, 89, 91, 93, 95, 97, 99, 141 and 143, respectively.

[85] Zcyto24 gene encodes a polypeptide of 202 amino acids, as shown in SEQ ID NO:8. Zcyto24 secretory signal sequence comprises amino acid residue 1 (Met) through amino acid residue 28 (Ala) of SEQ ID NO:8. An alternative site for cleavage of the secretory signal sequence can be found at amino acid residue 24 (Thr). The mature polypeptide comprises amino acid residue 29 (Asp) to amino acid residue 202 (Val).

[86] Zcyto25 gene encodes a polypeptide of 202 amino acids, as shown in SEQ ID NO:10. Zcyto25 secretory signal sequence comprises amino acid residue 1 (Met) through amino acid residue 28 (Ala) of SEQ ID NO:10. An alternative site for cleavage of the secretory signal sequence can be found at amino acid residue 24 (Thr). The mature polypeptide comprises amino acid residue 29 (Asp) to amino acid residue 202 (Val).

[87] The IL-28 and IL-29 cysteine mutant polypeptides of the present invention provided for the expression of a single-disulfide form of the IL-28 or IL-29 molecule. When IL-28 and IL-29 are expressed in *E. coli*, an N-terminal Methionine is present. SEQ ID NOs:26, and 34, for instance, show the amino acid residue numbering for IL-28A and IL-29 mutants, respectively, when the N-terminal Met is present. Table 1 shows the possible combinations of intramolecular disulfide bonded cysteine pairs for wildtype IL-28A, IL-28B, and IL-29.

Table 1

IL-28A SEQ ID NO:18	C_{16}-C_{115}	C_{48}-C_{148}	C_{50}-C_{148}	C_{167}-C_{174}	C_{16}-C_{48}	C_{16}-C_{50}	C_{48}-C_{115}	C_{50}-C_{115}	C_{115}-C_{148}
Met IL-28A SEQ ID NO:36	C_{17}-C_{116}	C_{49}-C_{149}	C_{51}-C_{1498}	C_{168}-C_{175}	C_{17}-C_{49}	C_{17}-C_{51}	C_{49}-C_{116}	C_{51}-C_{116}	C_{116}-C_{149}
IL-29 SEQ ID NO:20	C_{15}-C_{112}	C_{49}-C_{145}	C_{112}-C_{171}						
Met IL-29 SEQ ID NO:38	C_{16}-C_{113}	C_{50}-C_{146}	C_{113}-C_{172}						
IL-28B SEQ ID NO:22	C_{16}-C_{115}	C_{48}-C_{148}	C_{50}-C_{148}	C_{167}-C_{174}	C_{16}-C_{48}	C_{16}-C_{50}	C_{48}-C_{115}	C_{50}-C_{115}	C_{115}-C_{148}
Met IL-28B SEQ ID NO:40	C_{17}-C_{116}	C_{49}-C_{149}	C_{51}-C_{1498}	C_{168}-C_{175}	C_{17}-C_{49}	C_{17}-C_{51}	C_{49}-C_{116}	C_{51}-C_{116}	C_{116}-C_{149}

[88] Using methods known in the art, IL-28 or IL-29 polypeptides of the present invention can be prepared as monomers or multimers; glycosylated or non-glycosylated; pegylated or non-pegylated; fusion proteins; and may or may not include an initial methionine amino acid residue. IL-28 or IL-29 polypeptides can be conjugated to acceptable water-soluble polymer moieties for use in therapy. Conjugation of interferons, for example, with water-soluble polymers has been shown to enhance the circulating half-life of the interferon, and to reduce the immunogenicity of the polypeptide (see, for example, Nieforth *et al.*, Clin. Pharmacol. Ther. 59:636 (1996), and Monkarsh *et al.*, Anal. Biochem. 247:434 (1997)).

[89] Suitable water-soluble polymers include polyethylene glycol (PEG), monomethoxy-PEG, mono-(C1-C10)alkoxy-PEG, aryloxy-PEG, poly-(N-vinyl pyrrolidone)PEG, tresyl monomethoxy PEG, monomethoxy-PEG propionaldehyde, PEG propionaldehyde, *bis*-succinimidyl carbonate PEG, propylene glycol homopolymers, a polypropylene oxide/ethylene oxide co-polymer, polyoxyethylated polyols (*e.g.*, glycerol), monomethoxy-PEG butyraldehyde, PEG butyraldehyde, monomethoxy-PEG acetaldehyde, PEG acetaldehyde, methoxyl PEG-succinimidyl propionate, methoxyl PEG-succinimidyl butanoate, polyvinyl alcohol, dextran, cellulose, or other carbohydrate-based polymers. Suitable PEG may have a molecular weight from about 600 to about 60,000,

including, for example, 5,000, 12,000, 20,000, 30,000, 40,000, and 50,000, which can be linear or branched. A IL-28 or IL-29 conjugate can also comprise a mixture of such water-soluble polymers.

[90] One example of an IL-28 or IL-29 conjugate comprises an IL-28 or IL-29 moiety and a polyalkyl oxide moiety attached to the *N*-terminus of the IL-28 or IL-29 moiety. PEG is one suitable polyalkyl oxide. As an illustration, IL-28 or IL-29 can be modified with PEG, a process known as "PEGylation." PEGylation of an IL-28 or IL-29 can be carried out by any of the PEGylation reactions known in the art (see, for example, EP 0 154 316, Delgado *et al.*, Critical Reviews in Therapeutic Drug Carrier Systems 9:249 (1992), Duncan and Spreafico, Clin. Pharmacokinet. 27:290 (1994), and Francis *et al.*, Int J Hematol 68:1 (1998)). For example, PEGylation can be performed by an acylation reaction or by an alkylation reaction with a reactive polyethylene glycol molecule. In an alternative approach, IL-28 or IL-29 conjugates are formed by condensing activated PEG, in which a terminal hydroxy or amino group of PEG has been replaced by an activated linker (see, for example, Karasiewicz *et al.*, U.S. Patent No. 5,382,657).

[91] PEGylation by acylation typically requires reacting an active ester derivative of PEG with an IL-28 or IL-29 polypeptide. An example of an activated PEG ester is PEG esterified to *N*-hydroxysuccinimide. As used herein, the term "acylation" includes the following types of linkages between IL-28 or IL-29 and a water-soluble polymer: amide, carbamate, urethane, and the like. Methods for preparing PEGylated IL-28 or IL-29 by acylation will typically comprise the steps of (a) reacting an IL-28 or IL-29 polypeptide with PEG (such as a reactive ester of an aldehyde derivative of PEG) under conditions whereby one or more PEG groups attach to IL-28 or IL-29, and (b) obtaining the reaction product(s). Generally, the optimal reaction conditions for acylation reactions will be determined based upon known parameters and desired results. For example, the larger the ratio of PEG: IL-28 or IL-29, the greater the percentage of polyPEGylated IL-28 or IL-29 product.

[92] PEGylation by alkylation generally involves reacting a terminal aldehyde, e.g., propionaldehyde, butyraldehyde, acetaldehyde, and the like, derivative of PEG with IL-28 or IL-29 in the presence of a reducing agent. PEG groups are preferably attached to the polypeptide via a $-CH_2-NH_2$ group.

[93] Derivatization via reductive alkylation to produce a monoPEGylated product takes advantage of the differential reactivity of different types of primary amino groups available for derivatization. Typically, the reaction is performed at a pH that allows one to take advantage of the pKa differences between the ε-amino groups of the lysine residues and the α-amino group of the *N*-terminal residue of the protein. By such selective derivatization, attachment of a water-soluble polymer that contains a reactive group such as an aldehyde, to a protein is controlled. The conjugation with the polymer occurs predominantly at the *N*-terminus of the protein without significant modification of other reactive groups such as the lysine side chain amino groups.

[94] Reductive alkylation to produce a substantially homogenous population of monopolymer IL-28 or IL-29 conjugate molecule can comprise the steps of: (a) reacting an IL-28 or IL-29 polypeptide with a reactive PEG under reductive alkylation conditions at a pH suitable to permit selective modification of the α-amino group at the amino terminus of the IL-28 or IL-29, and (b) obtaining the reaction product(s). The reducing agent used for reductive alkylation should be stable in aqueous solution and preferably be able to reduce only the Schiff base formed in the initial process of reductive alkylation. Preferred reducing agents include sodium borohydride, sodium cyanoborohydride, dimethylamine borane, trimethylamine borane, and pyridine borane.

[95] For a substantially homogenous population of monopolymer IL-28 or IL-29 conjugates, the reductive alkylation reaction conditions are those that permit the selective attachment of the water-soluble polymer moiety to the *N*-terminus of IL-28 or IL-29. Such reaction conditions generally provide for pKa differences between the lysine amino groups and the α-amino group at the *N*-terminus. The pH also affects the ratio of polymer to protein to be used. In general, if the pH is lower, a larger excess of polymer to protein will be desired because the less reactive the *N*-terminal α-group, the more polymer is needed to achieve optimal conditions. If the pH is higher, the polymer: IL-28 or IL-29 need not be as large because more reactive groups are available. Typically, the pH will fall within the range of 3 - 9, or 3 - 6. Another factor to consider is the molecular weight of the water-soluble polymer. Generally, the higher the molecular weight of the polymer, the fewer number of polymer molecules which may be attached to the protein. For PEGylation reactions, the typical molecular weight is about 2 kDa to about 100 kDa, about 5 kDa to about 50 kDa, or about 12 kDa to about 40 kDa. The molar ratio of water-soluble polymer to IL-28 or IL-29 will generally be in the range of 1:1 to 100:1. Typically, the molar ratio of water-soluble polymer to IL-28 or IL-29 will be 1:1 to 20:1 for polyPEGylation, and 1:1 to 5:1 for monoPEGylation.

[96] General methods for producing conjugates comprising interferon and water-soluble polymer moieties are known in the art. See, for example, Karasiewicz *et al.*, U.S. Patent No. 5,382,657, Greenwald *et al.*, U.S. Patent No. 5,738, 846, Nieforth *et al.*, Clin. Pharmacol. Ther. 59:636 (1996), Monkarsh *et al.*, Anal. Biochem. 247:434 (1997). PEGylated species can be separated from unconjugated IL-28 or IL-29 polypeptides using standard purification methods, such as dialysis, ultrafiltration, ion exchange chromatography, affinity chromatography, size exclusion chromatography, and the like.

[97] The IL-28 or IL-29 polypeptides of the present invention are capable of specifically binding the IL-28 receptor and/or acting as an antiviral agent. The binding of IL-28 or Il-29 polypeptides to the IL-28 receptor can be assayed using established approaches. IL-28 or IL-29 polypeptides can be iodinated using an iodobead (Pierce, Rockford, IL) according to manufacturer's directions, and the ^{125}I-IL-28 or ^{125}I-IL-29 can then be used as described below.

[98] In a first approach fifty nanograms of ^{125}I-IL-28 or ^{125}I-IL-29 can be combind with 1000ng of IL-28 receptor human IgG fusion protein, in the presence or absence of possible binding competitors including unlabeled cysteine mutant IL-28, cysteine mutant IL-29, IL-28, or IL-29. The same binding reactions would also be performed substituting other cytokine receptor human IgG fusions as controlsfor specificity. Following incubation at 4°C, protein–G (Zymed, SanFransisco, CA) is added to the reaction, to capture the receptor-IgG fusions and any proteins bound to them, and the reactions are incubated another hour at 4°C. The protein-G sepharose is then collected, washed three times with PBS and ^{125}I-IL-28 or ^{125}I-IL-29 bound is measure by gamma counter (Packard Instruments, Downers Grove, IL).

[99] In a second approach, the ability of molecules to inhibit the binding of ^{125}I-IL-28 or ^{125}I-IL-29 to plate bound receptors can be assayed. A fragment of the IL-28 receptor, representing the extracellular, ligand binding domain, can be adsorbed to the wells of a 96 well plate by incubating 100 μl of 1 g/mL solution of receptor in the plate overnight. In a second form, a receptor-human IgG fusion can be bound to the wells of a 96 well plate that has been coated with an antibody directed against the human IgG portion of the fusion protein. Following coating of the plate with receptor the plate is washed, blocked with SUPERBLOCK (Pierce, Rockford, IL) and washed again. Solutions containing a fixed concentration of ^{125}I-IL-28 or ^{125}I-IL-29 with or without increasing concentrations of potential binding competitors including, Cysteine mutant IL-28, cysteine mutant IL-29, IL-28 and IL-29, and 100 μl of the solution added to appropriate wells of the plate. Following a one hour incubation at 4°C the plate is washed and the amount ^{125}I-IL-28 or ^{125}I-IL-29 bound determined by counting (Topcount, Packard Instruments, Downers grove, IL). The specificity of binding of ^{125}I-IL-28 or ^{125}I-IL-29 can be defined by receptor molecules used in these binding assays as well as by the molecules used as inhibitors.

[100] In addition to pegylation, human albumin can be coupled to an IL-28 or IL-29 polypeptide of the present invention to prolong its half-life. Human albumin is the most prevalent naturally occurring blood protein in the human circulatory system, persisting in circulation in the body for over twenty days. Research has shown that therapeutic proteins genetically fused to human albumin have longer half-lives. An IL28 or IL29 albumin fusion protein, like pegylation, may provide patients with long-acting treatment options that offer a more convenient administration schedule, with similar or improved efficacy and safety compared to currently available treatments (U.S. Patent No. 6,165,470; Syed et al., Blood, 89(9):3243-3253 (1997); Yeh et al., Proc. Natl. Acad. Sci. USA, 89:1904-1908 (1992); and Zeisel et al., Horm. Res., 37:5-13 (1992)).

[101] Like the aforementioned peglyation and human albumin, an Fc portion of the human IgG molecule can be fused to a polypeptide of the present invention. The resultant fusion protein may have an increased circulating half-life due to the Fc moiety (U.S. Patent No. 5,750,375, U.S.

Patent No. 5843,725, U.S. Patent No. 6,291,646; Barouch et al., Journal of Immunology, 61:1875-1882 (1998); Barouch et al., Proc. Natl. Acad. Sci. USA, 97(8):4192-4197 (April 11, 2000); and Kim et al., Transplant Proc., 30(8):4031-4036 (Dec. 1998)).

[102] IL-28A, IL-29, IL-28B, zcyto24 and zcyto25, each have been shown to form a complex with the orphan receptor designated zcytor19 (IL-28RA). IL-28RA is described in a commonly assigned patent application PCT/US01/44808. IL-28B, IL-29, zcyto24, and zcyto25 have been shown to bind or signal through IL-28RA as well, further supporting that IL-28A, IL-29, IL-28B, zcyto24 and zcyto25 are members of the same family of cytokines. IL-28RA receptor is a class II cytokine receptor. Class II cytokine receptors usually bind to four-helix-bundle cytokines. For example, interleukin-10 and the interferons bind receptors in this class (e.g., interferon-gamma receptor, alpha and beta chains and the interferon-alpha/beta receptor alpha and beta chains).

[103] Class II cytokine receptors are characterized by the presence of one or more cytokine receptor modules (CRM) in their extracellular domains. Other class II cytokine receptors include zcytor11 (commonly owned US Patent No. 5,965,704), CRF2-4 (Genbank Accession No. Z17227), IL-10R (Genbank Accession No.s U00672 and NM_001558), DIRS1, zcytor7 (commonly owned US Patent No. 5,945,511), and tissue factor. IL-28RA, like all known class II receptors except interferon-alpha/beta receptor alpha chain, has only a single class II CRM in its extracellular domain.

[104] Analysis of a human cDNA clone encoding IL-28RA (SEQ ID NO:11) revealed an open reading frame encoding 520 amino acids (SEQ ID NO:12) comprising a secretory signal sequence (residues 1 (Met) to 20 (Gly) of SEQ ID NO:12) and a mature IL-28RA cytokine receptor polypeptide (residues 21 (Arg) to 520 (Arg) of SEQ ID NO:12) an extracellular ligand-binding domain of approximately 206 amino acid residues (residues 21 (Arg) to 226 (Asn) of SEQ ID NO:12), a transmembrane domain of approximately 23 amino acid residues (residues 227 (Trp) to 249 (Trp) of SEQ ID NO:12), and an intracellular domain of approximately 271 amino acid residues (residues 250 (Lys) to 520 (Arg) of SEQ ID NO:12). Within the extracellular ligand-binding domain, there are two fibronectin type III domains and a linker region. The first fibronectin type III domain comprises residues 21 (Arg) to 119 (Tyr) of SEQ ID NO:12, the linker comprises residues 120 (Leu) to 124 (Glu) of SEQ ID NO:12, and the second fibronectin type III domain comprises residues 125 (Pro) to 223 (Pro) of SEQ ID NO:12.

[105] In addition, a human cDNA clone encoding a IL-28RA variant with a 29 amino acid deletion was identified. This IL-28RA variant (as shown in SEQ ID NO:13) comprises an open reading frame encoding 491 amino acids (SEQ ID NO:14) comprising a secretory signal sequence (residues 1 (Met) to 20 (Gly) of SEQ ID NO:14) and a mature IL-28RA cytokine receptor polyptide (residues 21 (Arg) to 491 (Arg) of SEQ ID NO:14) an extracellular ligand-binding domain of approximately 206 amino acid residues (residues 21 (Arg) to 226 (Asn) of SEQ ID NO:14, a

transmembrane domain of approximately 23 amino acid residues (residues 227 (Trp) to 249 (Trp) of SEQ ID NO:14), and an intracellular domain of approximately 242 amino acid residues (residues 250 (Lys) to 491 (Arg) of SEQ ID NO:14).

[106] A truncated soluble form of the IL-28RA receptor mRNA appears to be naturally expressed. Analysis of a human cDNA clone encoding the truncated soluble IL-28RA (SEQ ID NO:15) revealed an open reading frame encoding 211 amino acids (SEQ ID NO:16) comprising a secretory signal sequence (residues 1 (Met) to 20 (Gly) of SEQ ID NO:16) and a mature truncated soluble IL-28RA receptor polyptide (residues 21 (Arg) to 211 (Ser) of SEQ ID NO:16) a truncated extracellular ligand-binding domain of approximately 143 amino acid residues (residues 21 (Arg) to 163 (Trp) of SEQ ID NO:16), no transmembrane domain, but an additional domain of approximately 48 amino acid residues (residues 164 (Lys) to 211 (Ser) of SEQ ID NO:16).

[107] IL-28RA is a member of the same receptor subfamily as the class II cytokine receptors, and receptors in this subfamily may associate to form homodimers that transduce a signal. Several members of the subfamily (e.g., receptors that bind interferon, IL-10, IL-19, and IL-TIF) combine with a second subunit (termed a β-subunit) to bind ligand and transduce a signal. However, in many cases, specific β-subunits associate with a plurality of specific cytokine receptor subunits. For example, class II cytokine receptors, such as, zcytor11 (US Patent No. 5,965,704) and CRF2-4 receptor heterodimerize to bind the cytokine IL-TIF (See, WIPO publication WO 00/24758; Dumontier et al., J. Immunol. 164:1814-1819, 2000; Spencer, SD et al., J. Exp. Med. 187:571-578, 1998; Gibbs, VC and Pennica Gene 186:97-101, 1997 (CRF2-4 cDNA); Xie, MH et al., J. Biol. Chem. 275: 31335-31339, 2000). IL-10β receptor is believed to be synonymous with CRF2-4 (Dumoutier, L. et al., Proc. Nat'l. Acad. Sci. 97:10144-10149, 2000; Liu Y et al, J Immunol. 152; 1821-1829, 1994 (IL-10R cDNA). Therefore, one could expect that IL-28, IL-29, zcyto24 and zcyto25 would bind either monomeric, homodimeric, heterodimeric and multimeric zcytor19 receptors. Experimental evidence has identified CRF2-4 as the putative binding partner for IL-28RA.

[108] Examples of biological activity for molecules used to identify IL-28 or IL-29 molecules that are useful in the methods of the present invention include molecules that can bind to the IL-28 receptor with some specificity. Generally, a ligand binding to its cognate receptor is specific when the K_D falls within the range of 100 nM to 100 pM. Specific binding in the range of 100 mM to 10 nM K_D is low affinity binding. Specific binding in the range of 2.5 pM to 100 pM K_D is high affinity binding. In another example, biologically active IL-28 or IL-29 molecules are capable of some level of antiviral activity associated with wildtype IL-28 or IL-29.

[109] The various codons that encode for a given amino acid are set forth below in Table 2.

TABLE 2

Amino Acid	One Letter Code	Codons	Degenerate Codon
Cys	C	TGC TGT	TGY
Ser	S	AGC AGT TCA TCC TCG TCT	WSN
Thr	T	ACA ACC ACG ACT	ACN
Pro	P	CCA CCC CCG CCT	CCN
Ala	A	GCA GCC GCG GCT	GCN
Gly	G	GGA GGC GGG GGT	GGN
Asn	N	AAC AAT	AAY
Asp	D	GAC GAT	GAY
Glu	E	GAA GAG	GAR
Gln	Q	CAA CAG	CAR
His	H	CAC CAT	CAY
Arg	R	AGA AGG CGA CGC CGG CGT	MGN
Lys	K	AAA AAG	AAR
Met	M	ATG	ATG
Ile	I	ATA ATC ATT	ATH
Leu	L	CTA CTC CTG CTT TTA TTG	YTN
Val	V	GTA GTC GTG GTT	GTN
Phe	F	TTC TTT	TTY
Tyr	Y	TAC TAT	TAY
Trp	W	TGG	TGG
Ter	.	TAA TAG TGA	TRR
Asn|Asp	B		RAY
Glu|Gln	Z		SAR
Any	X		NNN

[110] One of ordinary skill in the art will appreciate that some ambiguity is introduced in determining a degenerate codon, representative of all possible codons encoding each amino acid. For example, the degenerate codon for serine (WSN) can, in some circumstances, encode arginine (AGR), and the degenerate codon for arginine (MGN) can, in some circumstances, encode serine (AGY). A similar relationship exists between codons encoding phenylalanine and leucine. Thus, some polynucleotides encompassed by the degenerate sequence may encode variant amino acid sequences, but one of ordinary skill in the art can easily identify such variant sequences by referencing the sequences disclosed herein. Variant sequences can be readily tested for functionality as described herein.

[111] One of ordinary skill in the art will also appreciate that different species can exhibit "preferential codon usage." In general, see, Grantham, et al., Nuc. Acids Res. 8:1893-912, 1980; Haas, et al. Curr. Biol. 6:315-24, 1996; Wain-Hobson, et al., Gene 13:355-64, 1981; Grosjean and Fiers, Gene 18:199-209, 1982; Holm, Nuc. Acids Res. 14:3075-87, 1986; Ikemura, J. Mol. Biol. 158:573-97, 1982. As used herein, the term "preferential codon usage" or "preferential codons" is a term of art referring to protein translation codons that are most frequently used in cells of a certain species, thus favoring one or a few representatives of the possible codons encoding each amino acid (See Table 2). For example, the amino acid Threonine (Thr) may be encoded by ACA, ACC, ACG, or ACT, but in mammalian cells ACC is the most commonly used codon; in other species, for example, insect cells, yeast, viruses or bacteria, different Thr codons may be preferential. Preferential codons for a particular species can be introduced into the polynucleotides of the present invention by a variety of methods known in the art. Introduction of preferential codon sequences into recombinant DNA can, for example, enhance production of the protein by making protein translation more efficient within a particular cell type or species. Sequences containing preferential codons can be tested and optimized for expression in various species, and tested for functionality as disclosed herein.

[112] As previously noted, the isolated polynucleotides of the present invention include DNA and RNA. Methods for preparing DNA and RNA are well known in the art. In general, RNA is isolated from a tissue or cell that produces large amounts of IL-28 or IL-29 RNA. Such tissues and cells are identified by Northern blotting (Thomas, Proc. Natl. Acad. Sci. USA 77:5201, 1980), or by screening conditioned medium from various cell types for activity on target cells or tissue. Once the activity or RNA producing cell or tissue is identified, total RNA can be prepared using guanidinium isothiocyanate extraction followed by isolation by centrifugation in a CsCl gradient (Chirgwin et al., Biochemistry 18:52-94, 1979). Poly $(A)^+$ RNA is prepared from total RNA using the method of Aviv and Leder (Proc. Natl. Acad. Sci. USA 69:1408-12, 1972). Complementary DNA (cDNA) is prepared from poly$(A)^+$ RNA using known methods. In the alternative, genomic DNA can be isolated. Polynucleotides encoding IL-28 or IL-29 polypeptides are then identified and isolated by, for example, hybridization or PCR.

[113] A full-length clones encoding IL-28 or IL-29 can be obtained by conventional cloning procedures. Complementary DNA (cDNA) clones are preferred, although for some applications (e.g., expression in transgenic animals) it may be preferable to use a genomic clone, or to modify a cDNA clone to include at least one genomic intron. Methods for preparing cDNA and genomic clones are well known and within the level of ordinary skill in the art, and include the use of the sequence disclosed herein, or parts thereof, for probing or priming a library. Expression libraries can be probed with antibodies to IL-28 receptor fragments, or other specific binding partners.

[114] Those skilled in the art will recognize that the sequence disclosed in, for example, SEQ ID NOs:17, 19 and 21, represent a single allele of human IL-28A, IL-29, and IL28B, respectively, and that allelic variation and alternative splicing are expected to occur. For example, an IL-29 variant has been identified where amino acid residue 169 as shown in SEQ ID NO:19 is an Asn residue whereas its corresponding amino acid residue in SEQ ID NO:4 is an Arg residue, as described in WO 02/086087. Such allelic variants are included in the present invention. Allelic variants of IL-28 and IL-29 molecules of the present invention can be cloned by probing cDNA or genomic libraries from different individuals according to standard procedures. Allelic variants of the DNA sequence shown in SEQ ID NOs:17, 19, and 21, including those containing silent mutations and those in which mutations result in amino acid sequence changes, in addition to the cysteine mutations, are within the scope of the present invention, as are proteins which are allelic variants of SEQ ID NO:18, 20, and 22. cDNAs generated from alternatively spliced mRNAs, which retain the properties of IL-28 or IL-29 polypeptides, are included within the scope of the present invention, as are polypeptides encoded by such cDNAs and mRNAs. Allelic variants and splice variants of these sequences can be cloned by probing cDNA or genomic libraries from different individuals or tissues according to standard procedures known in the art, and mutations to the polynucleotides encoding cysteines or cysteine residues can be introduced as described herein.

[115] Within embodiments of the invention, isolated IL-28 and IL-29-encoding nucleic acid molecules can hybridize under stringent conditions to nucleic acid molecules having the nucleotide sequence selected from the group of SEQ ID NOs:1, 3, 5, 17, 19, 21, 23, 25, 27, 29, 31, 33, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, or to its complement thereof. In general, stringent conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength and pH) at which 50% of the target sequence hybridizes to a perfectly matched probe.

[116] A pair of nucleic acid molecules, such as DNA-DNA, RNA-RNA and DNA-RNA, can hybridize if the nucleotide sequences have some degree of complementarity. Hybrids can tolerate mismatched base pairs in the double helix, but the stability of the hybrid is influenced by the degree of mismatch. The T_m of the mismatched hybrid decreases by 1°C for every 1-1.5% base pair mismatch. Varying the stringency of the hybridization conditions allows control over the degree of mismatch that will be present in the hybrid. The degree of stringency increases as the hybridization temperature increases and the ionic strength of the hybridization buffer decreases.

[117] It is well within the abilities of one skilled in the art to adapt these conditions for use with a particular polynucleotide hybrid. The T_m for a specific target sequence is the temperature

(under defined conditions) at which 50% of the target sequence will hybridize to a perfectly matched probe sequence. Those conditions which influence the T_m include, the size and base pair content of the polynucleotide probe, the ionic strength of the hybridization solution, and the presence of destabilizing agents in the hybridization solution. Numerous equations for calculating T_m are known in the art, and are specific for DNA, RNA and DNA-RNA hybrids and polynucleotide probe sequences of varying length (see, for example, Sambrook *et al.*, Molecular Cloning: A Laboratory Manual, Second Edition (Cold Spring Harbor Press 1989); Ausubel *et al.*, (eds.), Current Protocols in Molecular Biology (John Wiley and Sons, Inc. 1987); Berger and Kimmel (eds.), Guide to Molecular Cloning Techniques, (Academic Press, Inc. 1987); and Wetmur, Crit. Rev. Biochem. Mol. Biol. 26:227 (1990)). Sequence analysis software such as OLIGO 6.0 (LSR; Long Lake, MN) and *Primer Premier 4.0* (Premier Biosoft International; Palo Alto, CA), as well as sites on the Internet, are available tools for analyzing a given sequence and calculating T_m based on user defined criteria. Such programs can also analyze a given sequence under defined conditions and identify suitable probe sequences. Typically, hybridization of longer polynucleotide sequences, >50 base pairs, is performed at temperatures of about 20-25°C below the calculated T_m. For smaller probes, <50 base pairs, hybridization is typically carried out at the T_m or 5-10°C below the calculated T_m. This allows for the maximum rate of hybridization for DNA-DNA and DNA-RNA hybrids.

[118] Following hybridization, the nucleic acid molecules can be washed to remove non-hybridized nucleic acid molecules under stringent conditions, or under highly stringent conditions. Typical stringent washing conditions include washing in a solution of 0.5x - 2x SSC with 0.1% sodium dodecyl sulfate (SDS) at 55 - 65°C. That is, nucleic acid molecules encoding an IL-28 or IL-29 polypeptide hybridize with a nucleic acid molecule having the nucleotide sequence selected from the group of SEQ ID NOs:1, 3, 5, 17, 19, 21, 23, 25, 27, 29, 31, 33, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149 or its complement thereof, under stringent washing conditions, in which the wash stringency is equivalent to 0.5x - 2x SSC with 0.1% SDS at 55 - 65°C, including 0.5x SSC with 0.1% SDS at 55°C, or 2x SSC with 0.1% SDS at 65°C. One of skill in the art can readily devise equivalent conditions, for example, by substituting SSPE for SSC in the wash solution.

[119] Typical highly stringent washing conditions include washing in a solution of 0.1x - 0.2x SSC with 0.1% sodium dodecyl sulfate (SDS) at 50 - 65°C. In other words, nucleic acid molecules encoding a variant of an IL-28 or IL-29 polypeptide hybridize with a nucleic acid molecule having the nucleotide sequence selected from the group of SEQ ID NOs:1, 3, 5, 17, 19, 21, 23, 25, 27, 29, 31, 33, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135,

137, 139, 141, 143, 145, 147, 149, or its complement thereof, under highly stringent washing conditions, in which the wash stringency is equivalent to 0.1x - 0.2x SSC with 0.1% SDS at 50 - 65°C, including 0.1x SSC with 0.1% SDS at 50°C, or 0.2x SSC with 0.1% SDS at 65°C.

[120] The present invention also provides isolated IL-28 or IL-29 polypeptides that have a substantially similar sequence identity to the polypeptides of the present invention, for example, selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. The term "substantially similar sequence identity" is used herein to denote polypeptides comprising at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 97.5 %, at least 98%, at least 98.5%, at least 99%, at least 99.5%, or greater than 99.5% sequence identity to the amino acid sequences selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. The present invention also includes polypeptides that comprise an amino acid sequence having at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 97.5%, at least 98%, at least 98.5%, at least 99%, at least 99.5%, or greater than 99.5% sequence identity to a polypeptide or fragment thereof of the present invention. The present invention further includes nucleic acid molecules that encode such polypeptides. The IL-28 and IL-29 polypeptides of the present invention are preferably recombinant polypeptides. In another aspect, the IL-28 and IL-29 polypeptides of the present invention have at least 15, at least 30, at least 45, or at least 60 sequential amino acids. For example, an IL-29 polypeptide of the present invention relates to a polypeptide having at least 15, at least 30, at least 45, or at least 60 sequential amino acids to an amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. Methods for determining percent identity are herein.

[121] The present invention also contemplates variant nucleic acid molecules that can be identified using two criteria: a determination of the similarity between the encoded polypeptide with the amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150 and/or a hybridization assay, as described above. Such variants include nucleic acid molecules: (1) that hybridize with a nucleic acid molecule having the nucleotide sequence selected from the group of SEQ ID NOs:1, 3, 5, 17, 19, 21, 23, 25, 27, 29, 31, 33, 37, 39,

41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, or complement thereof, under stringent washing conditions, in which the wash stringency is equivalent to 0.5x - 2x SSC with 0.1% SDS at 55 - 65°C; or (2) that encode a polypeptide having at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 97.5%, at least 98%, at least 98.5%, at least 99%, at least 99.5%, or greater than 99.5% sequence identity to the amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. Alternatively, variants can be characterized as nucleic acid molecules: (1) that hybridize with a nucleic acid molecule having the nucleotide sequence selected from the group of SEQ ID NOs:1, 3, 5, 17, 19, 21, 23, 25, 27, 29, 31, 33, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, 77, 79, 81, 83, 85, 87, 89, 91, 93, 95, 97, 99, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149 or its complement thereof, under highly stringent washing conditions, in which the wash stringency is equivalent to 0.1x - 0.2x SSC with 0.1% SDS at 50 - 65°C; and (2) that encode a polypeptide having at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, at least 99.5%, or greater than 99.5% sequence identity to the amino acid sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150.

[122] Percent sequence identity is determined by conventional methods. See, for example, Altschul et al., Bull. Math. Bio. 48:603 (1986), and Henikoff and Henikoff, Proc. Natl. Acad. Sci. USA 89:10915 (1992). Briefly, two amino acid sequences are aligned to optimize the alignment scores using a gap opening penalty of 10, a gap extension penalty of 1, and the "BLOSUM62" scoring matrix of Henikoff and Henikoff (*ibid.*) as shown in Table 2 (amino acids are indicated by the standard one-letter codes).

$$\frac{\text{Total number of identical matches}}{\text{[length of the longer sequence plus the number of gaps introduced into the longer sequence in order to align the two sequences]}} \times 100$$

Table 3

	A	R	N	D	C	Q	E	G	H	I	L	K	M	F	P	S	T	W	Y	V
A	4																			
R	-1	5																		
N	-2	0	6																	
D	-2	-2	1	6																
C	0	-3	-3	-3	9															
Q	-1	1	0	0	-3	5														
E	-1	0	0	2	-4	2	5													
G	0	-2	0	-1	-3	-2	-2	6												
H	-2	0	1	-1	-3	0	0	-2	8											
I	-1	-3	-3	-3	-1	-3	-3	-4	-3	4										
L	-1	-2	-3	-4	-1	-2	-3	-4	-3	2	4									
K	-1	2	0	-1	-3	1	1	-2	-1	-3	-2	5								
M	-1	-1	-2	-3	-1	0	-2	-3	-2	1	2	-1	5							
F	-2	-3	-3	-3	-2	-3	-3	-3	-1	0	0	-3	0	6						
P	-1	-2	-2	-1	-3	-1	-1	-2	-2	-3	-3	-1	-2	-4	7					
S	1	-1	1	0	-1	0	0	0	-1	-2	-2	0	-1	-2	-1	4				
T	0	-1	0	-1	-1	-1	-1	-2	-2	-1	-1	-1	-1	-2	-1	1	5			
W	-3	-3	-4	-4	-2	-2	-3	-2	-2	-3	-2	-3	-1	1	-4	-3	-2	11		
Y	-2	-2	-2	-3	-2	-1	-2	-3	2	-1	-1	-2	-1	3	-3	-2	-2	2	7	
V	0	-3	-3	-3	-1	-2	-2	-3	-3	3	1	-2	1	-1	-2	-2	0	-3	-1	4

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[123] Those skilled in the art appreciate that there are many established algorithms available to align two amino acid sequences. The "FASTA" similarity search algorithm of Pearson and Lipman is a suitable protein alignment method for examining the level of identity shared by an amino acid sequence disclosed herein and the amino acid sequence of a putative variant IL-28 or IL-29. The FASTA algorithm is described by Pearson and Lipman, Proc. Nat'l Acad. Sci. USA 85:2444 (1988), and by Pearson, Meth. Enzymol. 183:63 (1990).

[124] Briefly, FASTA first characterizes sequence similarity by identifying regions shared by the query sequence (*e.g.*, SEQ ID NO:2) and a test sequence that have either the highest density of identities (if the ktup variable is 1) or pairs of identities (if ktup=2), without considering conservative amino acid substitutions, insertions, or deletions. The ten regions with the highest density of identities are then rescored by comparing the similarity of all paired amino acids using an amino acid substitution matrix, and the ends of the regions are "trimmed" to include only those residues that contribute to the highest score. If there are several regions with scores greater than the "cutoff" value (calculated by a predetermined formula based upon the length of the sequence and the ktup value), then the trimmed initial regions are examined to determine whether the regions can be joined to form an approximate alignment with gaps. Finally, the highest scoring regions of the two amino acid sequences are aligned using a modification of the Needleman-Wunsch-Sellers algorithm (Needleman and Wunsch, J. Mol. Biol. 48:444 (1970); Sellers, SIAM J. Appl. Math. 26:787 (1974)), which allows for amino acid insertions and deletions. Preferred parameters for FASTA analysis are: ktup=1, gap opening penalty=10, gap extension penalty=1, and substitution matrix=BLOSUM62. These parameters can be introduced into a FASTA program by modifying the scoring matrix file ("SMATRIX"), as explained in Appendix 2 of Pearson, Meth. Enzymol. 183:63 (1990).

[125] FASTA can also be used to determine the sequence identity of nucleic acid molecules using a ratio as disclosed above. For nucleotide sequence comparisons, the ktup value can range between one to six, preferably from three to six, most preferably three, with other parameters set as default.

[126] IL-28 or IL-29 polypeptides with substantially similar sequence identity are characterized as having one or more amino acid substitutions, deletions or additions. These changes are preferably of a minor nature, that is conservative amino acid substitutions (see Table 4) and other substitutions that do not significantly affect the folding or activity of the polypeptide; small deletions, typically of one to about 30 amino acids; and amino- or carboxyl-terminal extensions, such as an amino-terminal methionine residue, a small linker peptide of up to about 20-25 residues, or an affinity tag. The present invention thus includes polypeptides that comprise a sequence that is at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 97.5%, at least 98%, at least 98.5%, at least 99%, at least 99.5%, or greater than 99.5% identical to the corresponding region of SEQ ID

NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150. Polypeptides comprising affinity tags can further comprise a proteolytic cleavage site between the IL-28 and IL-29 polypeptide and the affinity tag. Preferred such sites include thrombin cleavage sites and factor Xa cleavage sites.

Table 4

Conservative amino acid substitutions

Basic:	arginine
	lysine
	histidine
Acidic:	glutamic acid
	aspartic acid
Polar:	glutamine
	asparagine
Hydrophobic:	leucine
	isoleucine
	valine
Aromatic:	phenylalanine
	tryptophan
	tyrosine
Small:	glycine
	alanine
	serine
	threonine
	methionine

[127] Determination of amino acid residues that comprise regions or domains that are critical to maintaining structural integrity can be determined. Within these regions one can determine specific residues that will be more or less tolerant of change and maintain the overall tertiary structure of the molecule. Methods for analyzing sequence structure include, but are not limited to alignment of multiple sequences with high amino acid or nucleotide identity, secondary structure propensities, binary patterns, complementary packing and buried polar interactions (Barton, Current Opin. Struct. Biol. 5:372-376, 1995 and Cordes et al., Current Opin. Struct. Biol. 6:3-10, 1996). In general, when designing modifications to molecules or identifying specific fragments determination of structure will be accompanied by evaluating activity of modified molecules.

[128] Amino acid sequence changes are made in IL-28 or IL-29 polypeptides so as to minimize disruption of higher order structure essential to biological activity. For example, where the IL-28 or IL-29 polypeptide comprises one or more helices, changes in amino acid residues will be made so as not to disrupt the helix geometry and other components of the molecule where changes in

conformation abate some critical function, for example, binding of the molecule to its binding partners. The effects of amino acid sequence changes can be predicted by, for example, computer modeling as disclosed above or determined by analysis of crystal structure (see, e.g., Lapthorn et al., Nat. Struct. Biol. 2:266-268, 1995). Other techniques that are well known in the art compare folding of a variant protein to a standard molecule (e.g., the native protein). For example, comparison of the cysteine pattern in a variant and standard molecules can be made. Mass spectrometry and chemical modification using reduction and alkylation provide methods for determining cysteine residues which are associated with disulfide bonds or are free of such associations (Bean et al., Anal. Biochem. 201:216-226, 1992; Gray, Protein Sci. 2:1732-1748, 1993; and Patterson et al., Anal. Chem. 66:3727-3732, 1994). It is generally believed that if a modified molecule does not have the same cysteine pattern as the standard molecule folding would be affected. Another well known and accepted method for measuring folding is circular dichrosism (CD). Measuring and comparing the CD spectra generated by a modified molecule and standard molecule is routine (Johnson, Proteins 7:205-214, 1990). Crystallography is another well known method for analyzing folding and structure. Nuclear magnetic resonance (NMR), digestive peptide mapping and epitope mapping are also known methods for analyzing folding and structurally similarities between proteins and polypeptides (Schaanan et al., Science 257:961-964, 1992).

[129] A Hopp/Woods hydrophilicity profile of an IL-28 or IL-29 polypeptide sequence selected from the group of SEQ ID NOs:2, 4, 6, 18, 20, 22, 24, 26, 28, 30, 32, 34, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, 78, 80, 82, 84, 86, 88, 90, 92, 94, 96, 98, 100, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148 and 150 can be generated (Hopp et al., Proc. Natl. Acad. Sci.78:3824-3828, 1981; Hopp, J. Immun. Meth. 88:1-18, 1986 and Triquier et al., Protein Engineering 11:153-169, 1998). The profile is based on a sliding six-residue window. Buried G, S, and T residues and exposed H, Y, and W residues were ignored. Those skilled in the art will recognize that hydrophilicity or hydrophobicity will be taken into account when designing modifications in the amino acid sequence of an IL-28 or IL-29 polypeptide, so as not to disrupt the overall structural and biological profile. Of particular interest for replacement are hydrophobic residues selected from the group consisting of Val, Leu and Ile or the group consisting of Met, Gly, Ser, Ala, Tyr and Trp.

[130] The identities of essential amino acids can also be inferred from analysis of sequence similarity between IFN-α and members of the family of IL-28A, IL-28B, and IL-29 (as shown in Tables 1 and 2). Using methods such as "FASTA" analysis described previously, regions of high similarity are identified within a family of proteins and used to analyze amino acid sequence for conserved regions. An alternative approach to identifying a variant polynucleotide on the basis of

structure is to determine whether a nucleic acid molecule encoding a potential variant IL-28 or IL-29 gene can hybridize to a nucleic acid molecule as discussed above.

[131] Other methods of identifying essential amino acids in the polypeptides of the present invention are procedures known in the art, such as site-directed mutagenesis or alanine-scanning mutagenesis (Cunningham and Wells, Science 244:1081 (1989), Bass et al., Proc. Natl Acad. Sci. USA 88:4498 (1991), Coombs and Corey, "Site-Directed Mutagenesis and Protein Engineering," in Proteins: Analysis and Design, Angeletti (ed.), pages 259-311 (Academic Press, Inc. 1998)). In the latter technique, single alanine mutations are introduced at every residue in the molecule, and the resultant IL-28 and IL-29 molecules are tested for biological or biochemical activity as disclosed below to identify amino acid residues that are critical to the activity of the molecule. See also, Hilton *et al.*, J. Biol. Chem. 271:4699 (1996).

[132] The present invention also includes functional fragments of IL-28 or IL-29 polypeptides and nucleic acid molecules encoding such functional fragments. A "functional" IL-28 or IL-29 or fragment thereof as defined herein is characterized by its proliferative or differentiating activity, by its ability to induce or inhibit specialized cell functions, or by its ability to bind specifically to an anti- IL-28 or IL-29 antibody or IL-28 receptor (either soluble or immobilized). The specialized activities of IL-28 or IL-29 polypeptides and how to test for them are disclosed herein. As previously described herein, IL-28 and IL-29 polypeptides are characterized by a six-helical-bundle. Thus, the present invention further provides fusion proteins encompassing: (a) polypeptide molecules comprising one or more of the helices described above; and (b) functional fragments comprising one or more of these helices. The other polypeptide portion of the fusion protein may be contributed by another helical-bundle cytokine or interferon, such as IFN-α, or by a non-native and/or an unrelated secretory signal peptide that facilitates secretion of the fusion protein.

[133] The IL-28 or IL-29 polypeptides of the present invention, including full-length polypeptides, biologically active fragments, and fusion polypeptides can be produced according to conventional techniques using cells into which have been introduced an expression vector encoding the polypeptide. As used herein, "cells into which have been introduced an expression vector" include both cells that have been directly manipulated by the introduction of exogenous DNA molecules and progeny thereof that contain the introduced DNA. Suitable host cells are those cell types that can be transformed or transfected with exogenous DNA and grown in culture, and include bacteria, fungal cells, and cultured higher eukaryotic cells. Techniques for manipulating cloned DNA molecules and introducing exogenous DNA into a variety of host cells are disclosed by Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1989, and Ausubel et al., eds., Current Protocols in Molecular Biology, John Wiley and Sons, Inc., NY, 1987.

[134] In general, a DNA sequence encoding an IL-28 or IL-29 polypeptide is operably linked to other genetic elements required for its expression, generally including a transcription promoter and terminator, within an expression vector. The vector will also commonly contain one or more selectable markers and one or more origins of replication, although those skilled in the art will recognize that within certain systems selectable markers may be provided on separate vectors, and replication of the exogenous DNA may be provided by integration into the host cell genome. Selection of promoters, terminators, selectable markers, vectors and other elements is a matter of routine design within the level of ordinary skill in the art. Many such elements are described in the literature and are available through commercial suppliers.

[135] To direct an IL-28 or IL-29 polypeptide into the secretory pathway of a host cell, a secretory signal sequence (also known as a leader sequence, prepro sequence or pre sequence) is provided in the expression vector. The secretory signal sequence may be that of IL-28 or IL-29, e.g., SEQ ID NO:119 or SEQ ID NO:121, or may be derived from another secreted protein (e.g., t-PA; see, U.S. Patent No. 5,641,655) or synthesized *de novo*. The secretory signal sequence is operably linked to an IL-28 or IL-29 DNA sequence, i.e., the two sequences are joined in the correct reading frame and positioned to direct the newly synthesized polypeptide into the secretory pathway of the host cell. Secretory signal sequences are commonly positioned 5' to the DNA sequence encoding the polypeptide of interest, although certain signal sequences may be positioned elsewhere in the DNA sequence of interest (see, e.g., Welch et al., U.S. Patent No. 5,037,743; Holland et al., U.S. Patent No. 5,143,830).

[136] A wide variety of suitable recombinant host cells includes, but is not limited to, gram-negative prokaryotic host organisms. Suitable strains of *E. coli* include W3110 and mutants-strains thereof (e.g, an *OmpT* protease deficient W3110 strain, and an *OmpT* protease and *fhuA* deficient W3110 strain), K12-derived strains MM294, TG-1, JM-107, BL21, and UT5600. Other suitable strains include: BL21(DE3), BL21(DE3)pLysS, BL21(DE3)pLysE, DH1, DH4I, DH5, DH5I, DH5IF', DH5IMCR, DH10B, DH10B/p3, DH11S, C600, HB101, JM101, JM105, JM109, JM110, K38, RR1, Y1088, Y1089, CSH18, ER1451, ER1647, *E. coli* K12, *E. coli* K12 RV308, *E. coli* K12 C600, *E. coli*HB101, *E. coli* K12 C600 R.sub.k-M.sub.k-, *E. coli* K12 RR1 (see, for example, Brown (ed.), Molecular Biology Labfax (Academic Press 1991)). Other gram-negative prokaryotic hosts can include *Serratia*, *Pseudomonas*, *Caulobacter*. Prokaryotic hosts can include gram-positive organisms such as *Bacillus*, for example, *B. subtilis* and *B. thuringienesis*, and *B. thuringienesis* var. *israelensis*, as well as *Streptomyces*, for example, *S. lividans*, *S. ambofaciens*, *S. fradiae*, and *S. griseofuscus*. Suitable strains of *Bacillus subtilus* include BR151, YB886, MI119, MI120, and B170 (see, for example, Hardy, "Bacillus Cloning Methods," in DNA Cloning: A Practical Approach, Glover (ed.) (IRL Press 1985)). Standard techniques for propagating vectors in prokaryotic hosts are well-known

to those of skill in the art (see, for example, Ausubel *et al.* (eds.), Short Protocols in Molecular Biology, *3rd Edition* (John Wiley & Sons 1995); Wu *et al.*, Methods in Gene Biotechnology (CRC Press, Inc. 1997)). In one embodiment, the methods of the present invention use Cysteine mutant IL-28 or IL-29 expressed in the W3110 strain, which has been deposited at the American Type Culture Collection (ATCC) as ATCC # 27325.

[137] When large scale production of an IL-28 or IL-29 polypeptide using the expression system of the present invention is required, batch fermentation can be used. Generally, batch fermentation comprises that a first stage seed flask is prepared by growing *E. coli* strains expressing an IL-28 or IL-29 polypeptide in a suitable medium in shake flask culture to allow for growth to an optical density (OD) of between 5 and 20 at 600 nm. A suitable medium would contain nitrogen from a source(s) such as ammonium sulfate, ammonium phosphate, ammonium chloride, yeast extract, hydrolyzed animal proteins, hydrolyzed plant proteins or hydrolyzed caseins. Phosphate will be supplied from potassium phosphate, ammonium phosphate, phosphoric acid or sodium phosphate. Other components would be magnesium chloride or magnesium sulfate, ferrous sulfate or ferrous chloride, and other trace elements. Growth medium can be supplemented with carbohydrates, such as fructose, glucose, galactose, lactose, and glycerol, to improve growth. Alternatively, a fed batch culture is used to generate a high yield of IL-28 or IL-29 polypeptide. The IL-28 or IL-29 polypeptide producing *E. coli* strains are grown under conditions similar to those described for the first stage vessel used to inoculate a batch fermentation.

[138] Following fermentation the cells are harvested by centrifugation, re-suspended in homogenization buffer and homogenized, for example, in an APV-Gaulin homogenizer (Invensys APV, Tonawanda, New York) or other type of cell disruption equipment, such as bead mills or sonicators. Alternatively, the cells are taken directly from the fermentor and homogenized in an APV-Gaulin homogenizer. The washed inclusion body prep can be solubilized using guanidine hydrochloride (5-8 M) or urea (7 – 8 M) containing a reducing agent such as beta mercaptoethanol (10 – 100 mM) or dithiothreitol (5-50 mM). The solutions can be prepared in Tris, phopshate, HEPES or other appropriate buffers. Inclusion bodies can also be solubilized with urea (2-4 M) containing sodium lauryl sulfate (0.1-2%). In the process for recovering purified IL-28 or IL-29 from transformed *E. coli* host strains in which the IL-28 or IL-29 is accumulates as refractile inclusion bodies, the cells are disrupted and the inclusion bodies are recovered by centrifugation. The inclusion bodies are then solubilized and denatured in 6 M guanidine hydrochloride containing a reducing agent. The reduced IL-28 or IL-29 is then oxidized in a controlled renaturation step. Refolded IL-28 or IL-29 can be passed through a filter for clarification and removal of insoluble protein. The solution is then passed through a filter for clarification and removal of insoluble protein. After the IL-28 or IL-29 protein is refolded and concentrated, the refolded IL-28 or IL-29 protein is captured in

dilute buffer on a cation exchange column and purified using hydrophobic interaction chromatography.

[139] Cultured mammalian cells are suitable hosts within the present invention. Methods for introducing exogenous DNA into mammalian host cells include calcium phosphate-mediated transfection (Wigler et al., Cell 14:725, 1978; Corsaro and Pearson, Somatic Cell Genetics 7:603, 1981: Graham and Van der Eb, Virology 52:456, 1973), electroporation (Neumann et al., EMBO J. 1:841-5, 1982), DEAE-dextran mediated transfection (Ausubel et al., ibid.), and liposome-mediated transfection (Hawley-Nelson et al., Focus 15:73, 1993; Ciccarone et al., Focus 15:80, 1993, and viral vectors (Miller and Rosman, BioTechniques 7:980-90, 1989; Wang and Finer, Nature Med. 2:714-6, 1996). The production of recombinant polypeptides in cultured mammalian cells is disclosed, for example, by Levinson et al., U.S. Patent No. 4,713,339; Hagen et al., U.S. Patent No. 4,784,950; Palmiter et al., U.S. Patent No. 4,579,821; and Ringold, U.S. Patent No. 4,656,134. Suitable cultured mammalian cells include the COS-1 (ATCC No. CRL 1650), COS-7 (ATCC No. CRL 1651), BHK (ATCC No. CRL 1632), BHK 570 (ATCC No. CRL 10314), 293 (ATCC No. CRL 1573; Graham et al., J. Gen. Virol. 36:59-72, 1977) and Chinese hamster ovary (e.g. CHO-K1; ATCC No. CCL 61) cell lines. Additional suitable cell lines are known in the art and available from public depositories such as the American Type Culture Collection, Manassas, VA. In general, strong transcription promoters are preferred, such as promoters from SV-40 or cytomegalovirus. See, e.g., U.S. Patent No. 4,956,288. Other suitable promoters include those from metallothionein genes (U.S. Patent Nos. 4,579,821 and 4,601,978) and the adenovirus major late promoter.

[140] Drug selection is generally used to select for cultured mammalian cells into which foreign DNA has been inserted. Such cells are commonly referred to as "transfectants". Cells that have been cultured in the presence of the selective agent and are able to pass the gene of interest to their progeny are referred to as "stable transfectants." A preferred selectable marker is a gene encoding resistance to the antibiotic neomycin. Selection is carried out in the presence of a neomycin-type drug, such as G-418 or the like. Selection systems can also be used to increase the expression level of the gene of interest, a process referred to as "amplification." Amplification is carried out by culturing transfectants in the presence of a low level of the selective agent and then increasing the amount of selective agent to select for cells that produce high levels of the products of the introduced genes. A preferred amplifiable selectable marker is dihydrofolate reductase, which confers resistance to methotrexate. Other drug resistance genes (e.g. hygromycin resistance, multi-drug resistance, puromycin acetyltransferase) can also be used. Alternative markers that introduce an altered phenotype, such as green fluorescent protein, or cell surface proteins such as CD4, CD8, Class I MHC, placental alkaline phosphatase may be used to sort transfected cells from untransfected cells by such means as FACS sorting or magnetic bead separation technology.

[141] Other higher eukaryotic cells can also be used as hosts, including plant cells, insect cells and avian cells. The use of *Agrobacterium rhizogenes* as a vector for expressing genes in plant cells has been reviewed by Sinkar et al., J. Biosci. (Bangalore) 11:47-58, 1987. Transformation of insect cells and production of foreign polypeptides therein is disclosed by Guarino et al., U.S. Patent No. 5,162,222 and WIPO publication WO 94/06463. Insect cells can be infected with recombinant baculovirus, commonly derived from *Autographa californica nuclear polyhedrosis virus* (AcNPV). See, King, L.A. and Possee, R.D., The Baculovirus Expression System: A Laboratory Guide, London, Chapman & Hall; O'Reilly, D.R. et al., Baculovirus Expression Vectors: A Laboratory Manual, New York, Oxford University Press., 1994; and, Richardson, C. D., Ed., Baculovirus Expression Protocols. Methods in Molecular Biology, Totowa, NJ, Humana Press, 1995. The second method of making recombinant baculovirus utilizes a transposon-based system described by Luckow (Luckow, V.A, et al., J Virol 67:4566-79, 1993). This system is sold in the Bac-to-Bac kit (Life Technologies, Rockville, MD). This system utilizes a transfer vector, pFastBac1™ (Life Technologies) containing a Tn7 transposon to move the DNA encoding the Cysteine mutant IL-28 or IL-29 polypeptide into a baculovirus genome maintained in *E. coli* as a large plasmid called a "bacmid." The pFastBac1™ transfer vector utilizes the AcNPV polyhedrin promoter to drive the expression of the gene of interest, in this case IL-28 or IL-29. However, pFastBac1™ can be modified to a considerable degree. The polyhedrin promoter can be removed and substituted with the baculovirus basic protein promoter (also known as P*cor*, p6.9 or MP promoter) which is expressed earlier in the baculovirus infection, and has been shown to be advantageous for expressing secreted proteins. See, Hill-Perkins, M.S. and Possee, R.D., J. Gen. Virol. 71:971-6, 1990; Bonning, B.C. et al., J. Gen. Virol. 75:1551-6, 1994; and, Chazenbalk, G.D., and Rapoport, B., J. Biol. Chem. 270:1543-9, 1995. In such transfer vector constructs, a short or long version of the basic protein promoter can be used. Moreover, transfer vectors can be constructed which replace the native IL-28 or IL-29 secretory signal sequences with secretory signal sequences derived from insect proteins. For example, a secretory signal sequence from Ecdysteroid Glucosyltransferase (EGT), honey bee Melittin (Invitrogen, Carlsbad, CA), or baculovirus gp67 (PharMingen, San Diego, CA) can be used in constructs to replace the native IL-28 or IL-29 secretory signal sequence. In addition, transfer vectors can include an in-frame fusion with DNA encoding an epitope tag at the C- or N-terminus of the expressed Cysteine mutant IL-28 or IL-29 polypeptide, for example, a Glu-Glu epitope tag (Grussenmeyer, T. et al., Proc. Natl. Acad. Sci. 82:7952-4, 1985). Using techniques known in the art, a transfer vector containing IL-28 or IL-29 is transformed into *E. Coli*, and screened for bacmids which contain an interrupted lacZ gene indicative of recombinant baculovirus. The bacmid DNA containing the recombinant baculovirus genome is isolated, using common techniques, and used to

transfect *Spodoptera frugiperda* cells, e.g. Sf9 cells. Recombinant virus that expresses IL-28 or IL-29 is subsequently produced. Recombinant viral stocks are made by methods commonly used the art.

[142] The recombinant virus is used to infect host cells, typically a cell line derived from the fall armyworm, *Spodoptera frugiperda.* See, in general, Glick and Pasternak, Molecular Biotechnology: Principles and Applications of Recombinant DNA, ASM Press, Washington, D.C., 1994. Another suitable cell line is the High FiveO™ cell line (Invitrogen) derived from *Trichoplusia ni* (U.S. Patent No. 5,300,435).

[143] Fungal cells, including yeast cells, can also be used within the present invention. Yeast species of particular interest in this regard include *Saccharomyces cerevisiae*, *Pichia pastoris*, and *Pichia methanolica.* Methods for transforming *S. cerevisiae* cells with exogenous DNA and producing recombinant polypeptides therefrom are disclosed by, for example, Kawasaki, U.S. Patent No. 4,599,311; Kawasaki et al., U.S. Patent No. 4,931,373; Brake, U.S. Patent No. 4,870,008; Welch et al., U.S. Patent No. 5,037,743; and Murray et al., U.S. Patent No. 4,845,075. Transformed cells are selected by phenotype determined by the selectable marker, commonly drug resistance or the ability to grow in the absence of a particular nutrient (e.g., leucine). A preferred vector system for use in *Saccharomyces cerevisiae* is the *POT1* vector system disclosed by Kawasaki et al. (U.S. Patent No. 4,931,373), which allows transformed cells to be selected by growth in glucose-containing media. Suitable promoters and terminators for use in yeast include those from glycolytic enzyme genes (see, e.g., Kawasaki, U.S. Patent No. 4,599,311; Kingsman et al., U.S. Patent No. 4,615,974; and Bitter, U.S. Patent No. 4,977,092) and alcohol dehydrogenase genes. See also U.S. Patents Nos. 4,990,446; 5,063,154; 5,139,936 and 4,661,454. Transformation systems for other yeasts, including *Hansenula polymorpha, Schizosaccharomyces pombe, Kluyveromyces lactis, Kluyveromyces fragilis, Ustilago maydis, Pichia pastoris, Pichia methanolica, Pichia guillermondii* and *Candida maltosa* are known in the art. See, for example, Gleeson et al., J. Gen. Microbiol. 132:3459-65, 1986 and Cregg, U.S. Patent No. 4,882,279. *Aspergillus* cells may be utilized according to the methods of McKnight et al., U.S. Patent No. 4,935,349. Methods for transforming *Acremonium chrysogenum* are disclosed by Sumino et al., U.S. Patent No. 5,162,228. Methods for transforming *Neurospora* are disclosed by Lambowitz, U.S. Patent No. 4,486,533. The use of *Pichia methanolica* as host for the production of recombinant proteins is disclosed in U.S. Patent Nos. 5,955,349, 5,888,768 and 6,001,597, U.S. Patent No. 5,965,389, U.S. Patent No. 5,736,383, and U.S. Patent No. 5,854,039.

[144] It is preferred to purify the polypeptides and proteins of the present invention to ≥80% purity, more preferably to ≥90% purity, even more preferably ≥95% purity, and particularly preferred is a pharmaceutically pure state, that is greater than 99.9% pure with respect to contaminating macromolecules, particularly other proteins and nucleic acids, and free of infectious

and pyrogenic agents. Preferably, a purified polypeptide or protein is substantially free of other polypeptides or proteins, particularly those of animal origin.

[145] Expressed recombinant IL-28 or IL-29 proteins (including chimeric polypeptides and multimeric proteins) are purified by conventional protein purification methods, typically by a combination of chromatographic techniques. See, in general, Affinity Chromatography: Principles & Methods, Pharmacia LKB Biotechnology, Uppsala, Sweden, 1988; and Scopes, Protein Purification: Principles and Practice, Springer-Verlag, New York, 1994. Proteins comprising a polyhistidine affinity tag (typically about 6 histidine residues) are purified by affinity chromatography on a nickel chelate resin. See, for example, Houchuli et al., Bio/Technol. 6: 1321-1325, 1988. Proteins comprising a glu-glu tag can be purified by immunoaffinity chromatography according to conventional procedures. See, for example, Grussenmeyer et al., supra. Maltose binding protein fusions are purified on an amylose column according to methods known in the art.

[146] IL-28 or IL-29 polypeptides can also be prepared through chemical synthesis according to methods known in the art, including exclusive solid phase synthesis, partial solid phase methods, fragment condensation or classical solution synthesis. See, for example, Merrifield, J. Am. Chem. Soc. 85:2149, 1963; Stewart et al., Solid Phase Peptide Synthesis (2nd edition), Pierce Chemical Co., Rockford, IL, 1984; Bayer and Rapp, Chem. Pept. Prot. 3:3, 1986; and Atherton et al., Solid Phase Peptide Synthesis: A Practical Approach, IRL Press, Oxford, 1989. In vitro synthesis is particularly advantageous for the preparation of smaller polypeptides.

[147] Generally, the dosage of administered IL-28 or IL29 polypeptide of the present invention will vary depending upon such factors as the patient's age, weight, height, sex, general medical condition and previous medical history. Typically, it is desirable to provide the recipient with a dosage of IL-28 or IL29 polypeptide which is in the range of from about 1 pg/kg to 10 mg/kg (amount of agent/body weight of patient), although a lower or higher dosage also may be administered as circumstances dictate. One skilled in the art can readily determine such dosages, and adjustments thereto, using methods known in the art.

[148] Administration of an IL-28 or IL29 polypeptide to a subject can be topical, inhalant, intravenous, intraarterial, intraperitoneal, intramuscular, subcutaneous, intrapleural, intrathecal, by perfusion through a regional catheter, or by direct intralesional injection. When administering therapeutic proteins by injection, the administration may be by continuous infusion or by single or multiple boluses.

[149] Additional routes of administration include oral, mucosal-membrane, pulmonary, and transcutaneous. Oral delivery is suitable for polyester microspheres, zein microspheres, proteinoid microspheres, polycyanoacrylate microspheres, and lipid-based systems (see, for example, DiBase and Morrel, "Oral Delivery of Microencapsulated Proteins," in *Protein Delivery: Physical Systems*,

Sanders and Hendren (eds.), pages 255-288 (Plenum Press 1997)). The feasibility of an intranasal delivery is exemplified by such a mode of insulin administration (see, for example, Hinchcliffe and Illum, *Adv. Drug Deliv. Rev. 35*:199 (1999)). Dry or liquid particles comprising IL-28 or IL29 polypeptide can be prepared and inhaled with the aid of dry-powder dispersers, liquid aerosol generators, or nebulizers (*e.g.*, Pettit and Gombotz, *TIBTECH 16*:343 (1998); Patton *et al., Adv. Drug Deliv. Rev. 35*:235 (1999)). This approach is illustrated by the AERX diabetes management system, which is a hand-held electronic inhaler that delivers aerosolized insulin into the lungs. Studies have shown that proteins as large as 48,000 kDa have been delivered across skin at therapeutic concentrations with the aid of low-frequency ultrasound, which illustrates the feasibility of trascutaneous administration (Mitragotri *et al., Science 269*:850 (1995)). Transdermal delivery using electroporation provides another means to administer a molecule having IL-28 or IL29 polypeptide activity (Potts *et al., Pharm. Biotechnol. 10*:213 (1997)).

[150] A pharmaceutical composition comprising a protein, polypeptide, or peptide having IL-28 or IL29 polypeptide activity can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the therapeutic proteins are combined in a mixture with a pharmaceutically acceptable vehicle. A composition is said to be in a "pharmaceutically acceptable vehicle" if its administration can be tolerated by a recipient patient. Sterile phosphate-buffered saline is one example of a pharmaceutically acceptable vehicle. Other suitable vehicles are well-known to those in the art. See, for example, Gennaro (ed.), *Remington's Pharmaceutical Sciences*, 19th Edition (Mack Publishing Company 1995).

[151] For purposes of therapy, molecules having IL-28 or IL29 polypeptide activity and a pharmaceutically acceptable vehicle are administered to a patient in a therapeutically effective amount. A combination of a protein, polypeptide, or peptide having IL-28 or IL29 polypeptide activity and a pharmaceutically acceptable vehicle is said to be administered in a "therapeutically effective amount" or "effective amount" if the amount administered is physiologically significant. An agent is physiologically significant if its presence results in a detectable change in the physiology of a recipient patient. For example, an agent used to treat inflammation is physiologically significant if its presence alleviates at least a portion of the inflammatory response.

[152] A pharmaceutical composition comprising IL-28 or IL29 polypeptide of the present invention can be furnished in liquid form, in an aerosol, or in solid form. Liquid forms, are illustrated by injectable solutions, aerosols, droplets, topological solutions and oral suspensions. Exemplary solid forms include capsules, tablets, and controlled-release forms. The latter form is illustrated by miniosmotic pumps and implants (Bremer *et al., Pharm. Biotechnol. 10*:239 (1997); Ranade, "Implants in Drug Delivery," in *Drug Delivery Systems*, Ranade and Hollinger (eds.), pages 95-123 (CRC Press 1995); Bremer *et al.*, "Protein Delivery with Infusion Pumps," in *Protein Delivery:*

Physical Systems, Sanders and Hendren (eds.), pages 239-254 (Plenum Press 1997); Yewey *et al.*, "Delivery of Proteins from a Controlled Release Injectable Implant," in *Protein Delivery: Physical Systems*, Sanders and Hendren (eds.), pages 93-117 (Plenum Press 1997)). Other solid forms include creams, pastes, other topological applications, and the like.

[153] Liposomes provide one means to deliver therapeutic polypeptides to a subject intravenously, intraperitoneally, intrathecally, intramuscularly, subcutaneously, or via oral administration, inhalation, or intranasal administration. Liposomes are microscopic vesicles that consist of one or more lipid bilayers surrounding aqueous compartments (see, generally, Bakker-Woudenberg *et al., Eur. J. Clin. Microbiol. Infect. Dis. 12 (Suppl. 1)*:S61 (1993), Kim, *Drugs 46*:618 (1993), and Ranade, "Site-Specific Drug Delivery Using Liposomes as Carriers," in *Drug Delivery Systems*, Ranade and Hollinger (eds.), pages 3-24 (CRC Press 1995)). Liposomes are similar in composition to cellular membranes and as a result, liposomes can be administered safely and are biodegradable. Depending on the method of preparation, liposomes may be unilamellar or multilamellar, and liposomes can vary in size with diameters ranging from 0.02 μm to greater than 10 μm. A variety of agents can be encapsulated in liposomes: hydrophobic agents partition in the bilayers and hydrophilic agents partition within the inner aqueous space(s) (see, for example, Machy *et al., Liposomes In Cell Biology And Pharmacology* (John Libbey 1987), and Ostro *et al., American J. Hosp. Pharm. 46*:1576 (1989)). Moreover, it is possible to control the therapeutic availability of the encapsulated agent by varying liposome size, the number of bilayers, lipid composition, as well as the charge and surface characteristics of the liposomes.

[154] Liposomes can adsorb to virtually any type of cell and then slowly release the encapsulated agent. Alternatively, an absorbed liposome may be endocytosed by cells that are phagocytic. Endocytosis is followed by intralysosomal degradation of liposomal lipids and release of the encapsulated agents (Scherphof *et al., Ann. N.Y. Acad. Sci. 446*:368 (1985)). After intravenous administration, small liposomes (0.1 to 1.0 μm) are typically taken up by cells of the reticuloendothelial system, located principally in the liver and spleen, whereas liposomes larger than 3.0 μm are deposited in the lung. This preferential uptake of smaller liposomes by the cells of the reticuloendothelial system has been used to deliver chemotherapeutic agents to macrophages and to tumors of the liver.

[155] The reticuloendothelial system can be circumvented by several methods including saturation with large doses of liposome particles, or selective macrophage inactivation by pharmacological means (Claassen *et al., Biochim. Biophys. Acta 802*:428 (1984)). In addition, incorporation of glycolipid- or polyethelene glycol-derivatized phospholipids into liposome membranes has been shown to result in a significantly reduced uptake by the reticuloendothelial system (Allen *et al., Biochim. Biophys. Acta 1068*:133 (1991); Allen *et al., Biochim. Biophys. Acta*

1150:9 (1993)).

[156] Liposomes can also be prepared to target particular cells or organs by varying phospholipid composition or by inserting receptors or ligands into the liposomes. For example, liposomes, prepared with a high content of a nonionic surfactant, have been used to target the liver (Hayakawa *et al.*, Japanese Patent 04-244,018; Kato *et al., Biol. Pharm. Bull. 16*:960 (1993)). These formulations were prepared by mixing soybean phospatidylcholine, α-tocopherol, and ethoxylated hydrogenated castor oil (HCO-60) in methanol, concentrating the mixture under vacuum, and then reconstituting the mixture with water. A liposomal formulation of dipalmitoylphosphatidylcholine (DPPC) with a soybean-derived sterylglucoside mixture (SG) and cholesterol (Ch) has also been shown to target the liver (Shimizu *et al., Biol. Pharm. Bull. 20*:881 (1997)).

[157] Alternatively, various targeting ligands can be bound to the surface of the liposome, such as antibodies, antibody fragments, carbohydrates, vitamins, and transport proteins. For example, liposomes can be modified with branched type galactosyllipid derivatives to target asialoglycoprotein (galactose) receptors, which are exclusively expressed on the surface of liver cells (Kato and Sugiyama, *Crit. Rev. Ther. Drug Carrier Syst. 14*:287 (1997); Murahashi *et al., Biol. Pharm. Bull.20*:259 (1997)). Similarly, Wu *et al., Hepatology 27*:772 (1998), have shown that labeling liposomes with asialofetuin led to a shortened liposome plasma half-life and greatly enhanced uptake of asialofetuin-labeled liposome by hepatocytes. On the other hand, hepatic accumulation of liposomes comprising branched type galactosyllipid derivatives can be inhibited by preinjection of asialofetuin (Murahashi *et al., Biol. Pharm. Bull.20*:259 (1997)). Polyaconitylated human serum albumin liposomes provide another approach for targeting liposomes to liver cells (Kamps *et al., Proc. Nat'l Acad. Sci. USA 94*:11681 (1997)). Moreover, Geho, *et al.* U.S. Patent No. 4,603,044, describe a hepatocyte-directed liposome vesicle delivery system, which has specificity for hepatobiliary receptors associated with the specialized metabolic cells of the liver.

[158] In a more general approach to tissue targeting, target cells are prelabeled with biotinylated antibodies specific for a ligand expressed by the target cell (Harasym *et al., Adv. Drug Deliv. Rev. 32*:99 (1998)). After plasma elimination of free antibody, streptavidin-conjugated liposomes are administered. In another approach, targeting antibodies are directly attached to liposomes (Harasym *et al., Adv. Drug Deliv. Rev. 32*:99 (1998)).

[159] Polypeptides having IL-28 or IL29 polypeptide activity can be encapsulated within liposomes using standard techniques of protein microencapsulation (see, for example, Anderson *et al., Infect. Immun. 31*:1099 (1981), Anderson *et al., Cancer Res. 50*:1853 (1990), and Cohen *et al., Biochim. Biophys. Acta 1063*:95 (1991), Alving *et al.* "Preparation and Use of Liposomes in Immunological Studies," in *Liposome Technology,* 2nd Edition, Vol. III, Gregoriadis (ed.), page 317 (CRC Press 1993), Wassef *et al., Meth. Enzymol. 149*:124 (1987)). As noted above, therapeutically

useful liposomes may contain a variety of components. For example, liposomes may comprise lipid derivatives of poly(ethylene glycol) (Allen *et al., Biochim. Biophys. Acta 1150*:9 (1993)).

[160] Degradable polymer microspheres have been designed to maintain high systemic levels of therapeutic proteins. Microspheres are prepared from degradable polymers such as poly(lactide-co-glycolide) (PLG), polyanhydrides, poly (ortho esters), nonbiodegradable ethylvinyl acetate polymers, in which proteins are entrapped in the polymer (Gombotz and Pettit, *Bioconjugate Chem. 6*:332 (1995); Ranade, "Role of Polymers in Drug Delivery," in *Drug Delivery Systems*, Ranade and Hollinger (eds.), pages 51-93 (CRC Press 1995); Roskos and Maskiewicz, "Degradable Controlled Release Systems Useful for Protein Delivery," in *Protein Delivery: Physical Systems*, Sanders and Hendren (eds.), pages 45-92 (Plenum Press 1997); Bartus *et al., Science 281*:1161 (1998); Putney and Burke, *Nature Biotechnology 16*:153 (1998); Putney, *Curr. Opin. Chem. Biol. 2*:548 (1998)). Polyethylene glycol (PEG)-coated nanospheres can also provide vehicles for intravenous administration of therapeutic proteins (see, for example, Gref *et al., Pharm. Biotechnol. 10*:167 (1997)).

[161] Other dosage forms can be devised by those skilled in the art, as shown, for example, by Ansel and Popovich, *Pharmaceutical Dosage Forms and Drug Delivery Systems,* 5th Edition (Lea & Febiger 1990), Gennaro (ed.), *Remington's Pharmaceutical Sciences*, 19th Edition (Mack Publishing Company 1995), and by Ranade and Hollinger, *Drug Delivery Systems* (CRC Press 1996).

[162] As an illustration, pharmaceutical compositions may be supplied as a kit comprising a container that comprises an IL-28 or IL29 polypeptide of the present invention. Therapeutic polypeptides can be provided in the form of an injectable solution for single or multiple doses, or as a sterile powder that will be reconstituted before injection. Alternatively, such a kit can include a dry-powder disperser, liquid aerosol generator, or nebulizer for administration of a therapeutic polypeptide. Such a kit may further comprise written information on indications and usage of the pharmaceutical composition. Moreover, such information may include a statement that the IL-28 or IL29 polypeptide composition is contraindicated in patients with known hypersensitivity to IL-28 or IL29 polypeptide. The kit may further comprise at least one additional antiviral agent selected from the group of Interferon alpha, Interferon beta, Interferon gamma, Interferon omega, protease inhibitor, RNA or DNA polymerase inhibitor, nucleoside analog, antisense inhibitor, and combinations thereof. The additional antiviral agent included in the kit, for example, can be RIBAVIRIN™, PEG-INTRON®, PEGASYS®, or a combination thereof. It can also be advantageous for patients with a viral infection, such as hepatitis C, to take their medicine consistently and get the appropriate dose for their individualized therapy. Thus, a kit may optionally also include a small needle, with a self-priming feature and a large, easy-to-read dosing knob. This will help patients feel confident that they are getting an accurate dose and offers an easy-to-use alternative for people who may be intimidated

by a traditional needle and syringe system. For example, the kit may include a disposable, one-time use precision dosing system that allows patients to administer an IL-28 or IL-29 molecule of the present invention in three easy steps: Mix, Dial and Deliver. (1) Mixing occurs by simply pushing down on the pen to combine the IL-28 or IL-29 molecule powder with sterile water, both of which are stored in the body of the pen; (2) Dialing allows patients to accurately select their predetermined individualized dose; and (3) Delivery allows patients to inject their individualized dose of the medication (See, for example, Schering Plough's PEG-INTRON REDIPEN).

[163] IL-28 and IL-29 polypeptides of the present invention can be used in treating, ablating, curing, preventing, inhibiting, reducing, or delaying onset of liver specific diseases, in particular liver disease where viral infection is in part an etiologic agent. In particular IL-28 and IL-29 polypeptides will be used to treat a mammal with a viral infection selected from the group consisting of hepatitis A, hepatitis B, hepatitis C, and hepatitis D. When liver disease is inflammatory and continuing for at least six months, it is generally considered chronic hepatitis. Hepatitis C virus (HCV) patients actively infected will be positive for HCV-RNA in their blood, which is detectable by reverse transcriptase/polymerase chain reaction (RT-PCR) assays. The methods of the present invention will slow the progression of the liver disease. Clinically, diagnostic tests for HCV include serologic assays for antibodies and molecular tests for viral particles. Enzyme immunoassays are available (Vrielink et al., Transfusion 37:845-849, 1997), but may require confirmation using additional tests such as an immunoblot assay (Pawlotsky et al., Hepatology 27:1700-1702, 1998). Qualitative and quantitative assays generally use polymerase chain reaction techniques, and are preferred for assessing viremia and treatment response (Poynard et al., Lancet 352:1426-1432, 1998; McHutchinson et al., N. Engl. J. Med. 339:1485-1492, 1998). Several commercial tests are available, such as, quantitative RT-PCR (Amplicor HCV Monitor™, Roche Molecular Systems, Branchburg, NJ) and a branched DNA (deoxyribonucleic acid) signal amplification assay (Quantiplex™ HCV RNA Assay [bDNA], Chiron Corp., Emeryville, CA). A non-specific laboratory test for liver inflammation or necrosis measures alanine aminotransferase level (ALT) and is inexpensive and readily available (National Institutes of Health Consensus Development Conference Panel, Hepatology 26 (Suppl. 1):2S-10S, 1997). Histologic evaluation of liver biopsy is generally considered the most accurate means for determining hepatitis progression (Yano et al., Hepatology 23:1334-1340, 1996.) For a review of clinical tests for HCV, see, Lauer et al., N. Engl. J. Med. 345:41-52, 2001.

[164] There are several *in vivo* models for testing HBV and HCV that are known to those skilled in art. For example, the effects of IL-28 or IL-29 on mammals infected with HBV can be accessed using a woodchuck model. Briefly, woodchucks chronically infected with woodchuck hepatitis virus (WHV) develop hepatitis and hepatocellular carcinoma that is similar to disease in

humans chronically infected with HBV. The model has been used for the preclinical assessment of antiviral activity. A chronically infected WHV strain has been established and neonates are inoculated with serum to provide animals for studying the effects of certain compounds using this model. (For a review, see, Tannant et al., ILAR J. 42 (2):89-102, 2001). Chimpanzees may also be used to evaluate the effect of IL-28 and IL-29 on HBV infected mammals. Using chimpanzees, characterization of HBV was made and these studies demonstrated that the chimpanzee disease was remarkably similar to the disease in humans (Barker et al., J. Infect. Dis. 132:451-458, 1975 and Tabor et al., J. Infect. Dis. 147:531-534, 1983.) The chimpanzee model has been used in evaluating vaccines (Prince et al., In: Vaccines 97, Cold Spring Harbor Laboratory Press, 1997.) Therapies for HIV are routinely tested using non-human primates infected with simian immunodeficiency viruses (for a review, see, Hirsch et al., Adv. Pharmcol. 49:437-477, 2000 and Nathanson et al., AIDS 13 (suppl. A):S113-S120, 1999.) For a review of use of non-human primates in HIV, hepatitis, malaria, respiratory syncytial virus, and other diseases, see, Sibal et al., ILAR J. 42 (2):74-84, 2001.

[165] Other examples of the types of viral infections for which an IL-28 or IL-29 molecule of the present invention can be used in treating, ablating, curing, preventing, inhibiting, reducing, or delaying onset of viral symptoms include, but are not limited to: infections caused by DNA Viruses (e.g., Herpes Viruses such as Herpes Simplex viruses, Epstein-Barr virus, Cytomegalovirus; Pox viruses such as Variola (small pox) virus; Hepadnaviruses (e.g, Hepatitis B virus); Papilloma viruses; Adenoviruses); RNA Viruses (e.g., HIV I, II; HTLV I, II; Poliovirus; Hepatitis A; Orthomyxoviruses (e.g., Influenza viruses, e.g., avian influenza A virus, for instance the H5N1 virus); Paramyxoviruses (e.g., Measles virus); Rabies virus; Hepatitis C); Coronavirus (causes Severe Acute Respiratory Syndrome (SARS)); Rhinovirus, Respiratory Syncytial Virus, Norovirus, West Nile Virus, Yellow Fever, Rift Vallley Virus, Lassa Fever Virus, Ebola Virus, Lymphocytic Choriomeningitis Virus, which replicates in tissues including liver, and the like. Moreover, examples of the types of diseases for which IL-28 and IL-29 could be used include, but are not limited to: Acquired immunodeficiency; Hepatitis; Gastroenteritis; Hemorrhagic diseases; Enteritis; Carditis; Encephalitis; Paralysis; Brochiolitis; Upper and lower respiratory disease; Respiratory Papillomatosis; Arthritis; Disseminated disease, hepatocellular carcinoma resulting rom chronic Hepatitis C infection. In addition, viral disease in other tissues may be treated with IL-28A, IL-28B, and IL-29, for example viral meningitis, and HIV-related disease. For example, a transgenic model for testing the activity of a therapeutic sample is described in the following examples and described in Morrey, et al., Antiviral Ther., 3 (Suppl 3):59-68, 1998.

[166] Animal models that are used to test for efficacy in specific viruses are known. For example, Dengue Virus can be tested using a model as such as described in Huang et al., J. Gen. Virol. Sep;81(Pt 9):2177-82, 2000. West Nile Virus can be tested using the model as described in

Xiao et al., Emerg. Infect. Dis. Jul-Aug;7(4):714-21, 2001or Mashimo et al., Proc. Natl. Acad. Sci. U S A. Aug 20;99(17):11311-6, 2002. Venezuelan equine encephalitis virus model is described in Jackson et al., Veterinary Pathology, 28 (5): 410-418, 1991; Vogel et al., Arch. Pathol. Lab. Med. Feb;120(2):164-72, 1996; Lukaszewski and Brooks, J. of Virology, 74(11):5006-5015, 2000. Rhinoviruses models are described in Yin and Lomax, J. Gen. Virol. 67 (Pt 11):2335-40, 1986. Models for respiratory syncytial virus are described in Byrd and Prince, Clin. Infect. Dis. 25(6):1363-8, 1997. Other models are known in the art and it is well within the skill of those ordinarily skilled in the art to know how to use such models.

[167] Noroviruses (genus *Norovirus*, family *Caliciviridae*) are a group of related, single-stranded RNA, nonenveloped viruses that cause acute gastroenteritis in humans. Norovirus was recently approved as the official genus name for the group of viruses provisionally described as "Norwalk-like viruses" (NLV). Noroviruses are estimated to cause 23 million cases of acute gastroenteritis in the United States per year, and are the leading cause of gastroenteritis in the United States.

[168] The symptoms of norovirus illness usually include nausea, vomiting, diarrhea, and some stomach cramping. Sometimes people additionally have a low-grade fever, chills, headache, muscle aches, and a general sense of tiredness. The illness often begins suddenly, and the infected person may feel very sick. The illness is usually brief, with symptoms lasting only about 1 or 2 days. In general, children experience more vomiting than adults. Most people with norovirus illness have both of these symptoms. Currently, there is no antiviral medication that works against norovirus and there is no vaccine to prevent infection.

[169] Therapeutics to Noroviruses have been difficult to identify in part because of a lack of good cell culture systems and animal models of disease. The recent identification of a murine norovirus now allows testing of therapeutics such as IL-28 and IL-29 polypeptides of the present invention in a cell culture system (Wobus, Karst et al., "Replication of Norovirus in Cell Culture Reveals a Tropism for Dendritic Cells and Macrophages," PLoS Biol, 2(12):e432, (2004)) and a mouse model of disease (Karst, Wobus et al., "STAT1-dependent innate immunity to a Norwalk-like virus," Science, 299(5612):1575-8 (2003)).

[170] Karst, S. M., C. E. Wobus, et al. (2003). "STAT1-dependent innate immunity to a Norwalk-like virus." Science, 299(5612): 1575-8.

[171] Norwalk-like caliciviruses (Noroviruses) cause over 90% of nonbacterial epidemic gastroenteritis worldwide, but the pathogenesis of norovirus infection is poorly understood because these viruses do not grow in cultured cells and there is no small animal model. Here, we report a previously unknown murine norovirus. Analysis of Murine Norovirus 1 infection revealed that signal transducer and activator of transcription 1-dependent innate immunity, but not T and B cell-

dependent adaptive immunity, is essential for norovirus resistance. The identification of host molecules essential for murine norovirus resistance may provide targets for prevention or control of an important human disease.

[172] Wobus, C. E., S. M. Karst, et al. (2004). "Replication of Norovirus in Cell Culture Reveals a Tropism for Dendritic Cells and Macrophages." PLoS Biol, 2(12): e432.

[173] Noroviruses are understudied because these important enteric pathogens have not been cultured to date. We found that the norovirus murine norovirus 1 (MNV-1) infects macrophage-like cells in vivo and replicates in cultured primary dendritic cells and macrophages. MNV-1 growth was inhibited by the interferon-alphabeta receptor and STAT-1, and was associated with extensive rearrangements of intracellular membranes. An amino acid substitution in the capsid protein of serially passaged MNV-1 was associated with virulence attenuation in vivo. This is the first report of replication of a norovirus in cell culture. The capacity of MNV-1 to replicate in a STAT-1-regulated fashion and the unexpected tropism of a norovirus for cells of the hematopoietic lineage provide important insights into norovirus biology.

[174] IL-28 and IL-29 polypeptides of the present invention can be used in combination with antiviral agents, including those described above. Some of the more common treatments for viral infection include drugs that inhibit viral replication such as ACYCLOVIR™. In addition, the combined use of some of these agents form the basis for highly active antiretroviral therapy (HAART) used for the treatment of AIDS. Examples in which the combination of immunotherapy (i.e., cytokines) and antiviral drugs shows improved efficacy include the use of interferon plus RIBAVIRIN™ for the treatment of chronic hepatitis C infection (Maddrey, Semin. Liver. Dis.19 Suppl 1:67-75, 1999) and the combined use of IL-2 and HAART (Ross, et al, ibid..) Thus, as IL-28 and IL-29 can stimulate the immune system against disease, it can similarly be used in HAART applications.

[175] In particular, IL-28 and IL-29 polypeptides of the present invention may be useful in monotherapy or combination therapy with IFN-α, e.g., PEGASYS® or PEG-INTRON® (with or without a nucleoside analog, such as RIBAVIRIN™, lamivudine, entecavir, emtricitabine, telbivudine and tenofovir) or with a nucleoside analog, such as RIBAVIRIN™, lamivudine, entecavir, emtricitabine, telbivudine and tenofovir in patients who do not respond well to IFN therapy.

[176] These patients may not respond to IFN therapy due to having less type I interferon receptor on the surface of their cells (Yatsuhashi H, et al., J Hepatol. Jun.30(6):995-1003, 1999; Mathai et al., J Interferon Cytokine Res. Sep.19(9):1011-8, 1999; Fukuda et al., J Med. Virol. 63(3):220-7, 2001). IL-28A, IL-28B, and IL-29 may also be useful in monotherapy or combination therapy with IFN-α (with or without a nucleoside analog, such as RIBAVIRIN™, lamivudine,

entecavir, emtricitabine, and telbivudine and tenofovir) or with a nucleoside analog, such as RIBAVIRIN™ in patients who have less type I interferon receptor on the surface of their cells due to down-regulation of the type I interferon receptor after type I interferon treatment (Dupont et al., J. Interferon Cytokine Res. 22(4):491-501, 2002).

[177] IL-28 or IL-29 polylpeptide may be used in combination with other immunotherapies including cytokines, immunoglobulin transfer, and various co-stimulatory molecules. In addition to antiviral drugs, IL-28 and IL-29 polypeptides of the present invention can be used in combination with any other immunotherapy that is intended to stimulate the immune system. Thus, IL-28 and IL-29 polypeptides could be used with other cytokines such as Interferon, IL-21, or IL-2. IL-28 and IL-29 can also be added to methods of passive immunization that involve immunoglobulin transfer, one example bring the use of antibodies to treat RSV infection in high risk patients (Meissner HC, ibid.). In addition, IL-28 and IL-29 polypeptides can be used with additional co-stimulatory molecules such as 4-1BB ligand that recognize various cell surface molecules like CD137 (Tan, JT et al., J Immunol. 163:4859-68, 1999).

[178] IL-28 and IL-29 can be used as a monotherapy for acute and chronic viral infections and for immunocompromised patients. Methods that enhance immunity can accelerate the recovery time in patients with unresolved infections. Immunotherapies can have an even greater impact on subsets of immunocompromised patients such as the very young or elderly as well as patients that suffer immunodeficiencies acquired through infection, or induced following medical interventions such as chemotherapy or bone marrow ablation. Examples of the types of indications being treated via immune-modulation include; the use of IFN-α for chronic hepatitis (Perry CM, and Jarvis B, Drugs 61:2263-88, 2001), the use of IL-2 following HIV infection (Mitsuyasu R., J. Infect. Dis. 185 Suppl 2:S115-22, 2002; and Ross RW et al., Expert Opin. Biol. Ther. 1:413-24, 2001), and the use of IFN-α (Faro A, Springer Semin. Immunopathol.20:425-36, 1998) for treating Epstein Barr Virus infections following transplantation. Experiments performed in animal models indicate that IL-2 and GM-CSF may also be efficacious for treating EBV related diseases (Baiocchi RA et al., .J Clin. Invest. 108:887-94, 2001).

[179] IL-28 and IL-29 molecules of the present invention can be used as a monotherapy for acute and chronic viral infections and for immunocompromised patients. Methods that enhance immunity can accelerate the recovery time in patients with unresolved infections. In addition, IL-28 and IL-29 molecules of the present invention can be administered to a mammal in combination with other antiviral agents such as ACYCLOVIR™, RIBAVIRIN™, Interferons (e.g., PEGINTRON® and PEGASYS®), Serine Protease Inhibitors, Polymerase Inhibitors, Nucleoside Analogs, Antisense Inhibitors, and combinations thereof, to treat, ablate, cure, prevent, inhibit, reduce, or delay the onset of a viral infection selected from the group of hepatitis A, hepatitis B, hepatitis C, hepatitis D,

respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus (e.g., avian influenza A virus, for instance the H5N1 virus), adenovirus, parainfluenza virus, Severe Acute Respiratory Syndrome, rhino virus, coxsackie virus, vaccinia virus, west nile virus, dengue virus, venezuelan equine encephalitis virus, pichinde virus, and polio virus. IL-28 and IL-29 polypeptides of the present invention can also be used in combination with other immunotherapies including cytokines, immunoglobulin transfer, and various co-stimulatory molecules. In addition, IL-28 and IL-29 molecules of the present invention can be used to treat a mammal with a chronic or acute viral infection that has resulted liver inflammation, thereby reducing the viral infection and/or liver inflammation. In particular IL-28 and IL-29 will be used to treat a mammal with a viral infection selected from the group of hepatitis A, hepatitis B, hepatitis C, and/or hepatitis D. IL-28 and IL-29 molecules of the present invention can also be used as an antiviral agent in viral infections selected from the group consisting of respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus (e.g., avian influenza A virus, for instance the H5N1 virus), adenovirus, parainfluenza virus, Severe Acute Respiratory Syndrome, rhino virus, coxsackie virus, vaccinia virus, west nile virus, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus.

[180] The present invention is further illustrated by the following non-limiting examples.

EXAMPLES

Example 1

Induction of IL-28A, IL-29 and IL-28B by poly I:C and viral infection

[181] Freshly isolated human peripheral blood mononuclear cells were grown in the presence of polyinosinic acid-polycytidylic acid (poly I:C; 100 μg/ml) (SIGMA; St. Louis, MO), encephalomyocarditis virus (EMCV) with an MOI of 0.1, or in medium alone. After a 15h incubation, total RNA was isolated from cells and treated with RNase-free DNase. 100 ng total RNA was used as template for one-step RT-PCR using the Superscript One-Step RT-PCR with Platinum Taq kit and gene-specific primers as suggested by the manufacturer (Invitrogen).

[182] Low to undetectable amounts of human IL-28A, IL-28B, and IL-29, IFN-α and IFN-β RNA were seen in untreated cells. In contrast, the amount of IL-28A, IL-29, IL-28B RNA was increased by both poly I:C treatment and viral infection, as was also seen for the type I interferons. These experiments indicate that IL-28A, IL-29, IL-28B, like type I interferons, can be induced by double-stranded RNA or viral infection.

Example 2

IL-28 and IL-29 signaling activity compared to IFNα in HepG2 cells

A. Cell Transfections

[183] HepG2 cells were transfected as follows: 700,000 HepG2 cells/well (6 well plates) were plated approximately 18h prior to transfection in 2 milliliters DMEM + 10% fetal bovine serum. Per well, 1 microgram pISRE-Luciferase DNA (Stratagene) and 1 microgram pIRES2-EGFP DNA (Clontech,) were added to 6 microliters Fugene 6 reagent (Roche Biochemicals) in a total of 100 microliters DMEM. This transfection mix was added 30 minutes later to the pre-plated HepG2 cells. Twenty-four hours later the transfected cells were removed from the plate using trypsin-EDTA and replated at approximately 25,000 cells/well in 96 well microtiter plates. Approximately 18 h prior to ligand stimulation, media was changed to DMEM + 0.5%FBS.

B. Signal Transduction Reporter Assays

[184] The signal transduction reporter assays were done as follows: Following an 18h incubation at 37°C in DMEM + 0.5%FBS, transfected cells were stimulated with 100 ng/ml IL-28A, IL-29, IL-28B, zcyto24, zcyto25 and huIFN-α2a ligands. Following a 4-hour incubation at 37° degrees, the cells were lysed, and the relative light units (RLU) were measured on a luminometer after addition of a luciferase substrate. The results obtained are shown as the fold induction of the RLU of the experimental samples over the medium alone control (RLU of experimental samples/RLU of medium alone = fold induction). Table 5 shows that IL-28A, IL-29, IL-28B, zcyto24 and zcyto25 induce ISRE signaling in human HepG2 liver cells transfected with ISRE-luciferase.

[185] Table 5: Fold Induction of Cytokine-dependent ISRE Signaling in HepG2 Cells

Cytokine	Fold Induction
IL-28A	5.6
IL-29	4
IL-28B	5.8
Zcyto24	4.7
Zcyto25	3
HuIFN-a2a	5.8

Example 3

IL-29 antiviral activity compared to IFNα in HepG2 cells

[186] An antiviral assay was adapted for EMCV (American Type Culture Collection # VR-129B, Manassas, VA) with human cells (Familletti, P., et al., Methods Enzym. 78: 387-394, 1981). Cells were plated with cytokines and incubated 24 hours prior to challenge by EMCV at a multiplicity of infection of 0.1 to 1. The cells were analyzed for viability with a dye-uptake bioassay 24 hours after infection (Berg, K., et al., Apmis 98: 156-162, 1990). Target cells were given MTT and incubated at 37°C for 2 hours. A solubiliser solution was added, incubated overnight at 37°C and the optical density at 570 nm was determined. OD570 is directly proportional to antiviral activity.

[187] The results show the antiviral activity when IL-29 and IFN on were tested with HepG2 cells: IL-29, IFN-β and IFN α-2a were added at varying concentration to HepG2 cells prior to EMCV infection and dye-uptake assay. The mean and standard deviation of the OD570 from triplicate wells is plotted. OD570 is directly proportional to antiviral activity. For IL-29, the EC50 was 0.60 ng/ml; for IFN-α2a, the EC50 was 0.57 ng/ml; and for IFN-β, the EC50 was 0.46ng/ml.

Example 4

IL-28RA mRNA expression in liver and lymphocyte subsets

[188] In order to further examine the mRNA distribution for IL-28RA, semi-quantitative RT-PCR was performed using the SDS 7900HT system (Applied Biosystems, CA). One-step RT-PCR was performed using 100ng total RNA for each sample and gene-specific primers. A standard curve was generated for each primer set using Bjab RNA and all sample values were normalized to HPRT. The normalized results are summarized in Tables 6-8. The normalized values for IFNAR2 and CRF2-4 are also shown.

[189] Table 6: B and T cells express significant levels of IL-28RA mRNA. Low levels are seen in dendritic cells and most monocytes.

Table 6

Cell/Tissue	IL-28RA	IFNAR2	CRF2-4
Dendritic Cells unstim	.04	5.9	9.8
Dendritic Cells +IFNg	.07	3.6	4.3
Dendritic Cells	.16	7.85	3.9
CD14+ stim'd with LPS/IFNg	.13	12	27
CD14+ monocytes resting	.12	11	15.4
Hu CD14+ Unact.	4.2	TBD	TBD
Hu CD14+ 1 ug/ml LPS act.	2.3	TBD	TBD
H. Inflamed tonsil	3	12.4	9.5
H. B-cells+PMA/Iono 4 & 24 hrs	3.6	1.3	1.4
Hu CD19+ resting	6.2	TBD	TBD
Hu CD19+ 4 hr. PMA/Iono	10.6	TBD	TBD
Hu CD19+ 24 hr Act. PMA/Iono	3.7	TBD	TBD
IgD+ B-cells	6.47	13.15	6.42
IgM+ B-cells	9.06	15.4	2.18
IgD- B-cells	5.66	2.86	6.76
NKCells + PMA/Iono	0	6.7	2.9
Hu CD3+ Unactivated	2.1	TBD	TBD
CD4+ resting	.9	8.5	29.1
CD4+ Unstim 18 hrs	1.6	8.4	13.2
CD4+ +Poly I/C	2.2	4.5	5.1
CD4+ + PMA/Iono	.3	1.8	.9
CD3 neg resting	1.6	7.3	46
CD3 neg unstim 18 hrs	2.4	13.2	16.8
CD3 neg+Poly I/C 18 hrs	5.7	7	30.2
CD3 neg+LPS 18 hrs	3.1	11.9	28.2
CD8+ unstim 18 hrs	1.8	4.9	13.1
CD8+ stim'd with PMA/Ion 18 hrs	.3	.6	1.1

[190] As shown in Table 7, normal liver tissue and liver derived cell lines display substantial levels of IL-28RA and CRF2-4 mRNA.

Table 7

Cell/Tissue	IL-28RA	IFNAR2	CRF2-4
HepG2	1.6	3.56	2.1
HepG2 UGAR 5/10/02	1.1	1.2	2.7
HepG2, CGAT HKES081501C	4.3	2.1	6
HuH7 5/10/02	1.63	16	2
HuH7 hepatoma - CGAT	4.2	7.2	3.1
Liver, normal - CGAT #HXYZ020801K	11.7	3.2	8.4
Liver, NAT - Normal adjacent tissue	4.5	4.9	7.7
Liver, NAT - Normal adjacent tissue	2.2	6.3	10.4
Hep SMVC hep vein	0	1.4	6.5
Hep SMCA hep. Artery	0	2.1	7.5
Hep. Fibro	0	2.9	6.2

Hep. Ca.	3.8	2.9	5.8
Adenoca liver	8.3	4.2	10.5
SK-Hep-1 adenoca. Liver	.1	1.3	2.5
AsPC-1 Hu. Pancreatic adenocarc.	.7	.8	1.3
Hu. Hep. Stellate cells	.025	4.4	9.7

[191] As shown in Table 8, primary airway epithelial cells contain abundant levels of IL-28RA and CRF2-4.

Table 8

Cell/Tissue	**IL-28RA**	**IFNAR2**	**CRF2-4**
U87MG - glioma	0	.66	.99
NHBE unstim	1.9	1.7	8.8
NHBE + TNF-alpha	2.2	5.7	4.6
NHBE + poly I/C	1.8	nd	nd
Small Airway Epithelial Cells	3.9	3.3	27.8
NHLF - Normal human lung fibroblasts	0	nd	nd

[192] As shown in Table 8, IL-28RA is present in normal and diseased liver specimens, with increased expression in tissue from Hepatitis C and Hepatitis B infected specimens.

Table 8

Cell/Tissue	IL-28RA	CRF2-4	IFNAR2
Liver with Coagulation Necrosis	8.87	15.12	1.72
Liver with Autoimmune Hepatitis	6.46	8.90	3.07
Neonatal Hepatitis	6.29	12.46	6.16
Endstage Liver disease	4.79	17.05	10.58
Fulminant Liver Failure	1.90	14.20	7.69
Fulminant Liver failure	2.52	11.25	8.84
Cirrhosis, primary biliary	4.64	12.03	3.62
Cirrhosis Alcoholic (Laennec's)	4.17	8.30	4.14
Cirrhosis, Cryptogenic	4.84	7.13	5.06
Hepatitis C+, with cirrhosis	3.64	7.99	6.62
Hepatitis C+	6.32	11.29	7.43
Fulminant hepatitis secondary to Hep A	8.94	21.63	8.48
Hepatitis C+	7.69	15.88	8.05
Hepatitis B+	1.61	12.79	6.93
Normal Liver	8.76	5.42	3.78
Normal Liver	1.46	4.13	4.83
Liver NAT	3.61	5.43	6.42
Liver NAT	1.97	10.37	6.31
Hu Fetal Liver	1.07	4.87	3.98
Hepatocellular Carcinoma	3.58	3.80	3.22
Adenocarcinoma Liver	8.30	10.48	4.17
hep. SMVC, hep. Vein	0.00	6.46	1.45
Hep SMCA hep. Artery	0.00	7.55	2.10
Hep. Fibroblast	0.00	6.20	2.94
HuH7 hepatoma	4.20	3.05	7.24
HepG2 Hepatocellular carcinoma	3.40	5.98	2.11
SK-Hep-1 adenocar. Liver	0.03	2.53	1.30
HepG2 Unstim	2.06	2.98	2.28
HepG2+zcyto21	2.28	3.01	2.53
HepG2+IFNα	2.61	3.05	3.00
Normal Female Liver - degraded	1.38	6.45	4.57
Normal Liver - degraded	1.93	4.99	6.25
Normal Liver - degraded	2.41	2.32	2.75
Disease Liver - degraded	2.33	3.00	6.04
Primary Hepatocytes from Clonetics	9.13	7.97	13.30

[193] As shown in Tables 9-13, IL-28RA is detectable in normal B cells, B lymphoma cell lines, T cells, T lymphoma cell lines (Jurkat), normal and transformed lymphocytes (B cells and T cells) and normal human monocytes.

Table 9

	HPRT Mean	IL-28RA Mean	IL-28RA norm	IFNAR2	IFNR2 norm	CRF2-4	CRF2-4 Norm
CD14+ 24hr unstim #A38	13.1	68.9	5.2	92.3	7.0	199.8	15.2
CD14+ 24 hr stim #A38	6.9	7.6	1.1	219.5	31.8	276.6	40.1
CD14+ 24 hr unstim #A112	17.5	40.6	2.3	163.8	9.4	239.7	13.7
CD14+ 24 hr stim #A112	11.8	6.4	0.5	264.6	22.4	266.9	22.6
CD14+ rest #X	32.0	164.2	5.1	1279.7	39.9	699.9	21.8
CD14+ +LPS #X	21.4	40.8	1.9	338.2	15.8	518.0	24.2
CD14+ 24 hr unstim #A39	26.3	86.8	3.3	297.4	11.3	480.6	18.3
CD14+ 24 hr stim #A39	16.6	12.5	0.8	210.0	12.7	406.4	24.5
HL60 Resting	161.2	0.2	0.0	214.2	1.3	264.0	1.6
HL60+PMA	23.6	2.8	0.1	372.5	15.8	397.5	16.8
U937 Resting	246.7	0.0	0.0	449.4	1.8	362.5	1.5
U937+PMA	222.7	0.0	0.0	379.2	1.7	475.9	2.1
Jurkat Resting	241.7	103.0	0.4	327.7	1.4	36.1	0.1
Jurkat Activated	130.7	143.2	1.1				
Colo205	88.8	43.5	0.5				
HT-29	26.5	30.5	1.2				

Table 10

	HPRT SD	IL-28RA SD
Mono 24hr unstim #A38	0.6	2.4
Mono 24 hr stim #A38	0.7	0.2
Mono 24 hr unstim #A112	2.0	0.7
Mono 24 hr stim #A112	0.3	0.1
Mono rest #X	5.7	2.2
Mono+LPS #X	0.5	1.0
Mono 24 hr unstim #A39	0.7	0.8
Mono 24 hr stim #A39	0.1	0.7
HL60 Resting	19.7	0.1
HL60+PMA	0.7	0.4
U937 Resting	7.4	0.0
U937+PMA	7.1	0.0
Jurkat Resting	3.7	1.1
Jurkat Activated	2.4	1.8
Colo205	1.9	0.7
HT-29	2.3	1.7

Table 11

	Mean Hprt	Mean IFNAR2	Mean IL-28RA	Mean CRF
CD3+/CD4+ 0	10.1	85.9	9.0	294.6
CD4/CD3+ Unstim 18 hrs	12.9	108.7	20.3	170.4
CD4+/CD3+ +Poly I/C 18 hrs	24.1	108.5	52.1	121.8
CD4+/CD3+ + PMA/Iono 18 hrs	47.8	83.7	16.5	40.8
CD3 neg 0	15.4	111.7	24.8	706.1
CD3 neg unstim 18 hrs	15.7	206.6	37.5	263.0
CD3 neg +Poly I/C 18 hrs	9.6	67.0	54.7	289.5
CD3 neg +LPS 18 hrs	14.5	173.2	44.6	409.3
CD8+ Unstim. 18 hrs	6.1	29.7	11.1	79.9
CD8+ + PMA/Iono 18 hrs	78.4	47.6	26.1	85.5
12.8.1 - NHBE Unstim	47.4	81.1	76.5	415.6
12.8.2 - NHBE+TNF-alpha	42.3	238.8	127.7	193.9
SAEC	15.3	49.9	63.6	426.0

Table 12

	IL-28RA Norm	CRF Norm	IFNAR2 Norm	IL-28RA SD	CRF SD	IFNAR2 SD
CD3+/CD4+ 0	0.9	29.1	8.5	0.1	1.6	0.4
CD4/CD3+ Unstim 18 hrs	1.6	13.2	8.4	0.2	1.6	1.4
CD4+/CD3+ +Poly I/C 18 hrs	2.2	5.1	4.5	0.1	0.3	0.5
CD4+/CD3+ + PMA/Iono 18 hrs	0.3	0.9	1.8	0.0	0.1	0.3
CD3 neg 0	1.6	46.0	7.3	0.2	4.7	1.3
CD3 neg unstim 18 hrs	2.4	16.8	13.2	0.4	2.7	2.3
CD3 neg +Poly I/C 18 hrs	5.7	30.2	7.0	0.3	1.7	0.8
CD3 neg +LPS 18 hrs	3.1	28.2	11.9	0.4	5.4	2.9
CD8+ Unstim. 18 hrs	1.8	13.1	4.9	0.1	1.1	0.3
CD8+ + PMA/Iono 18 hrs	0.3	1.1	0.6	0.0	0.1	0.0
12.8.1 - NHBE Unstim	1.6	8.8	1.7	0.1	0.4	0.1
12.8.2 - NHBE+TNF-alpha	3.0	4.6	5.7	0.1	0.1	0.1
SAEC	4.1	27.8	3.3	0.2	1.1	0.3

Table 13

	SD Hprt	SD IFNAR2	SD IL-28RA	SD CRF
CD3+/CD4+ 0	0.3	3.5	0.6	12.8
CD4/CD3+ Unstim 18 hrs	1.4	13.7	1.1	8.5
CD4+/CD3+ +Poly I/C 18 hrs	1.3	9.8	1.6	3.4
CD4+/CD3+ + PMA/Iono 18 hrs	4.0	10.3	0.7	3.7
CD3 neg 0	1.4	16.6	1.6	28.6
CD3 neg unstim 18 hrs	2.4	16.2	2.7	12.6
CD3 neg +Poly I/C 18 hrs	0.5	7.0	1.0	8.3
CD3 neg +LPS 18 hrs	1.0	39.8	5.6	73.6
CD8+ Unstim. 18 hrs	0.2	1.6	0.5	6.1
CD8+ + PMA/Iono 18 hrs	1.3	1.7	0.2	8.1
12.8.1 - NHBE Unstim	2.4	5.6	2.7	2.8
12.8.2 - NHBE+TNF-alpha	0.5	3.4	3.5	3.4
SAEC	0.5	4.8	1.8	9.9

Example 5

Mouse IL-28 Does Not Effect Daudi Cell Proliferation

[194] Human Daudi cells were suspended in RPMI + 10%FBS at 50,000 cells/milliliter and 5000 cells were plated per well in a 96 well plate. IL-29-CEE (IL-29 conjugated with glu tag), IFN-γ or IFN-α2a was added in 2-fold serial dilutions to each well. IL-29-CEE was used at a concentration range of from 1000 ng/ml to 0.5 ng/ml. IFN-γ was used at a concentration range from 125 ng/ml to 0.06 ng/ml. IFN-α2a was used at a concentration range of from 62 ng/ml to 0.03 ng/ml. Cells were incubated for 72 h at 37°C. After 72 hours Alamar Blue (Accumed, Chicago, IL) was added at 20

microliters/well. Plates were further incubated at 37°C., 5% CO, for 24 hours. Plates were read on the Fmax™ plate reader (Molecular Devices, Sunnyvale, CA) using the SoftMax™ Pro program, at wavelengths 544 (Excitation) and 590 (Emission). Alamar Blue gives a fluourometric readout based on the metabolic activity of cells, and is thus a direct measurement of cell proliferation in comparison to a negative control. The results indicate that IL-29-CEE, in contrast to IFN-α2a, has no significant effect on proliferation of Daudi cells.

Example 6

Mouse IL-28 Does Not Have Antiproliferative Effect on Mouse B cells

[195] Mouse B cells were isolated from 2 Balb/C spleens (7 months old) by depleting CD43+ cells using MACS magnetic beads. Purified B cells were cultured in vitro with LPS, anti-IgM or anti-CD40 monoclonal antibodies. Mouse IL-28 or mouse IFNα was added to the cultures and ^{3}H-thymidine was added at 48 hrs. and ^{3}H-thymidine incorporation was measured after 72 hrs. culture.

[196] IFNα at 10 ng/ml inhibited ^{3}H-thymidine incorporation by mouse B cells stimulated with either LPS or anti-IgM. However mouse IL-28 did not inhibit ^{3}H-thymidine incorporation at any concentration tested including 1000 ng/ml. In contrast, both mIFNα and mouse IL-28 increased ^{3}H thymidine incorporation by mouse B cells stimulated with anti-CD40 MAb.

[197] These data demonstrate that mouse IL-28 unlike IFNa displays no antiproliferative activity even at high concentrations. In addition, zcyto24 enhances proliferation in the presence of anti-CD40 MAbs. The results illustrate that mouse IL-28 differs from IFNα in that mouse IL-28 does not display antiproliferative activity on mouse B cells, even at high concentrations. In addition, mouse IL-28 enhances proliferation in the presence of anti-CD40 monoclonal antibodies.

Example 7

Bone marrow expansion assay

[198] Fresh human marrow mononuclear cells (Poietic Technologies, Gaithersburg, Md.) were adhered to plastic for 2 hrs in αMEM, 10% FBS, 50 micromolar β–mercaptoethanol, 2 ng/ml FLT3L at 37ºC. Non adherent cells were then plated at 25,000 to 45,000 cells/well (96 well tissue culture plates) in αMEM, 10% FBS, 50 micromolar β–mercaptoethanol, 2 ng/ml FLT3L in the presence or absence of 1000 ng/ml IL-29-CEE, 100 ng/ml IL-29-CEE, 10 ng/ml IL-29-CEE, 100 ng/ml IFN-α2a, 10 ng/ml IFN- α2a or 1 ng/ml IFN- α2a. These cells were incubated with a variety of cytokines to test for expansion or differentiation of hematopoietic cells from the marrow (20 ng/ml IL-2, 2 ng/ml IL-3, 20 ng/ml IL-4, 20 ng/ml IL-5, 20 ng/ml IL-7, 20 ng/ml IL-10, 20 ng/ml IL-12, 20 ng/ml IL-15, 10 ng/ml IL-21 or no added cytokine). After 8 to 12 days Alamar Blue (Accumed,

Chicago, Ill.) was added at 20 microliters/well. Plates were further incubated at 37°C, 5% CO, for 24 hours. Plates were read on the Fmax™ plate reader (Molecular Devices Sunnyvale, Calif.) using the SoftMax™ Pro program, at wavelengths 544 (Excitation) and 590 (Emission). Alamar Blue gives a fluourometric readout based on the metabolic activity of cells, and is thus a direct measurement of cell proliferation in comparison to a negative control.

[199] IFN-α2a caused a significant inhibition of bone marrow expansion under all conditions tested. In contrast, IL-29 had no significant effect on expansion of bone marrow cells in the presence of IL-3, IL-4, IL-5, IL-7, IL-10, IL-12, IL-21 or no added cytokine. A small inhibition of bone marrow cell expansion was seen in the presence of IL-2 or IL-15.

Example 8

Inhibition of IL-28 and IL-29 signaling with soluble receptor (zcytoR19/CRF2-4)

A. Signal Transduction Reporter Assay

[200] A signal transduction reporter assay can be used to show the inhibitor properties of zcytor19-Fc4 homodimeric and zcytor19-Fc/CRF2-4-Fc heterodimeric soluble receptors on zcyto20, zcyto21 and zcyto24 signaling. Human embryonal kidney (HEK) cells overexpressing the zcytor19 receptor are transfected with a reporter plasmid containing an interferon-stimulated response element (ISRE) driving transcription of a luciferase reporter gene. Luciferase activity following stimulation of transfected cells with ligands (including zcyto20 (SEQ ID NO:18), zcyto21 (SEQ ID NO:20), zcyto24 (SEQ ID NO:8)) reflects the interaction of the ligand with soluble receptor.

B. Cell Transfections

[201] 293 HEK cells overexpressing zcytor19 were transfected as follows: 700,000 293 cells/well (6 well plates) were plated approximately 18h prior to transfection in 2 milliliters DMEM + 10% fetal bovine serum. Per well, 1 microgram pISRE-Luciferase DNA (Stratagene) and 1 microgram pIRES2-EGFP DNA (Clontech,) were added to 6 microliters Fugene 6 reagent (Roche Biochemicals) in a total of 100 microliters DMEM. This transfection mix was added 30 minutes later to the pre-plated 293 cells. Twenty-four hours later the transfected cells were removed from the plate using trypsin-EDTA and replated at approximately 25,000 cells/well in 96 well microtiter plates. Approximately 18 h prior to ligand stimulation, media was changed to DMEM + 0.5%FBS.

C. Signal Transduction Reporter Assays

[202] The signal transduction reporter assays were done as follows: Following an 18h incubation at 37°C in DMEM + 0.5%FBS, transfected cells were stimulated with 10 ng/ml zcyto20,

zcyto21 or zcyto24 and 10 micrograms/ml of the following soluble receptors; human zcytor19-Fc homodimer, human zcytor19-Fc/human CRF2-4-Fc heterodimer, human CRF2-4-Fc homodimer, murine zcytor19-Ig homodimer. Following a 4-hour incubation at 37°C, the cells were lysed, and the relative light units (RLU) were measured on a luminometer after addition of a luciferase substrate. The results obtained are shown as the percent inhibition of ligand-induced signaling in the presence of soluble receptor relative to the signaling in the presence of PBS alone. Table 13 shows that the human zcytor19-Fc/human CRF2-4 heterodimeric soluble receptor is able to inhibit zcyto20, zcyto21 and zcyto24-induced signaling between 16 and 45% of control. The human zcytor19-Fc homodimeric soluble receptor is also able to inhibit zcyto21-induced signaling by 45%. No significant effects were seen with huCRF2-4-Fc or muzcytor19-Ig homodimeric soluble receptors.

[203] Table 14: Percent Inhibition of Ligand-induced Interferon Stimulated Response Element (ISRE) Signaling by Soluble Receptors

Ligand	Huzcytor19-Fc/huCRF2-4-Fc	Huzcytor19-Fc	HuCRF2-4-Fc	Muzcytor19-Ig
Zcyto20	16%	92%	80%	91%
Zcyto21	16%	45%	79%	103%
Zcyto24	47%	90%	82%	89%

Example 9

IL-28 and IL-29 inhibit HIV replication in fresh human PBMCs

[204] Human immunodeficiency virus (HIV) is a pathogenic retrovirus that infects cells of the immune system. CD4 T cells and monocytes are the primary infected cell types. To test the ability of IL-28 and IL-29 to inhibit HIV replication *in vitro*, PBMCs from normal donors were infected with the HIV virus in the presence of IL-28, IL-29 and MetIL-29C172S-PEG.

[205] Fresh human peripheral blood mononuclear cells (PBMCs) were isolated from whole blood obtained from screened donors who were seronegative for HIV and HBV. Peripheral blood cells were pelleted/washed 2-3 times by low speed centrifugation and resuspended in PBS to remove contaminating platelets. The washed blood cells were diluted 1:1 with Dulbecco's phosphate buffered saline (D-PBS) and layered over 14 mL of Lymphocyte Separation Medium ((LSM; cellgro™ by Mediatech, Inc. Herndon, VA); density 1.078 +/-0.002 g/ml) in a 50 mL centrifuge tube and centrifuged for 30 minutes at 600 x G. Banded PBMCs were gently aspirated from the resulting interface and subsequently washed 2X in PBS by low speed centrifugation. After the final wash, cells were counted by trypan blue exclusion and resuspended at 1 x 10^7 cells/mL in RPMI 1640 supplemented with 15% Fetal Bovine Serum (FBS), 2 mM L-glutamine, 4 μg/mL PHA-P. The cells

were allowed to incubate for 48-72 hours at 37°C. After incubation, PBMCs were centrifuged and resuspended in RPMI 1640 with 15% FBS, 2 mM L-glutamine, 100 U/mL penicillin, 100 μg/mL streptomycin, 10 μg/mL gentamycin, and 20 U/mL recombinant human IL-2. PBMCs were maintained in the medium at a concentration of 1-2 x 10^6 cells/mL with biweekly medium changes until used in the assay protocol. Monocytes were depleted from the culture as the result of adherence to the tissue culture flask.

[206] For the standard PBMC assay, PHA-P stimulated cells from at least two normal donors were pooled, diluted in fresh medium to a final concentration of 1 x 10^6 cells/mL, and plated in the interior wells of a 96 well round bottom microplate at 50 μL/well (5 x 10^4 cells/well). Test dilutions were prepared at a 2X concentration in microtiter tubes and 100 μL of each concentration was placed in appropriate wells in a standard format. IL-28, IL-29 and MetIL-29C172S-PEG were added at concentrations from 0-10 μg/ml, usually in 1/2 log dilutions. 50 μL of a predetermined dilution of virus stock was placed in each test well (final MOI of 0.1). Wells with only cells and virus added were used for virus control. Separate plates were prepared identically without virus for drug cytotoxicity studies using an MTS assay system. The PBMC cultures were maintained for seven days following infection, at which time cell-free supernatant samples were collected and assayed for reverse transcriptase activity and p24 antigen levels.

[207] A decrease in reverse transcriptase activity or p24 antigen levels with IL-28, IL-29 and MetIL-29C172S-PEG would be indicators of antiviral activity. Result would demonstrate that IL-28 and IL-29 may have therapeutic value in treating HIV and AIDS.

Example 10

IL-28 and IL-29 inhibit GBV-B replication in marmoset liver cells

[208] HCV is a member of the *Flaviviridae* family of RNA viruses. HCV does not replicate well in either *ex-vivo* or *in vitro* cultures and therefore, there are no satisfactory systems to test the anti-HCV activity of molecules *in vitro.* GB virus B (GBV-B) is an attractive surrogate model for use in the development of anti-HCV antiviral agents since it has a relatively high level of sequence identity with HCV and is a hepatotropic virus. To date, the virus can only be grown in the primary hepatocytes of certain non-human primates. This is accomplished by either isolating hepatocytes *in vitro* and infecting them with GBV-B, or by isolating hepatocytes from GBV-B infected marmosets and directly using them with antiviral compounds.

[209] The effects of IL-28, IL-29 and MetIL-29C172S-PEG are assayed on GBV-B extracellular RNA production by TaqMan RT-PCR and on cytotoxicity using CellTiter96® reagent (Promega, Madison, WI) at six half-log dilutions IL-28, IL-29 or MetIL-29C172S-PEG polypeptide in triplicate. Untreated cultures serve as the cell and virus controls. Both RIBAVIRIN® (200 μg/ml

at the highest test concentration) and IFN-α (5000 IU/ml at the highest test) are included as positive control compounds. Primary hepatocyte cultures are isolated and plated out on collagen-coated plates. The next day the cultures are treated with the test samples (IL-28, IL-29, MetIL-29C172S-PEG, IFNα, or RIBAVIRIN®) for 24hr before being exposed to GBV-B virions or treated directly with test samples when using *in vivo* infected hepatocytes. Test samples and media are added the next day, and replaced three days later. Three to four days later (at day 6-7 post test sample addition) the supernatant is collected and the cell numbers quantitated with CellTiter96®. Viral RNA is extracted from the supernatant and quantified with triplicate replicates in a quantitative TaqMan RT-PCR assay using an *in vitro* transcribed RNA containing the RT-PCR target as a standard. The average of replicate samples is computed. Inhibition of virus production is assessed by plotting the average RNA and cell number values of the triplicate samples relative to the untreated virus and cell controls. The inhibitory concentration of drug resulting in 50% inhibition of GBV-B RNA production (IC50) and the toxic concentration resulting in destruction of 50% of cell numbers relative to control values (TC50) are calculated by interpolation from graphs created with the data.

[210] Inhibition of the GBV-B RNA production by IL-28 and 29 is an indication of the antiviral properties of IL-28 and IL-29 on this Hepatitis C-like virus on hepatocytes, the primary organ of infection of Hepatitis C, and positive results suggest that IL-28 or IL-29 may be useful in treating HCV infections in humans.

Example 11

IL-28, IL-29 and MetIL-29C172S-PEG inhibit HBV replication in WT10 cells

[211] Chronic hepatitis B (HBV) is one of the most common and severe viral infections of humans belonging to the *Hepadnaviridae* family of viruses. To test the antiviral activities of IL-28 and IL-29 against HBV, IL-28, IL-29 and MetIL-29C172S-PEG were tested against HBV in an *in vitro* infection system using a variant of the human liver line HepG2. IL-28, IL-29 and MetIL-29C172S-PEG inhibited viral replication in this system, suggesting therapeutic value in treating HBV in humans.

[212] WT10 cells are a derivative of the human liver cell line HepG2 2.2.15. WT10 cells are stably transfected with the HBV genome, enabling stable expression of HBV transcripts in the cell line (Fu and Cheng, Antimicrobial Agents Chemother. 44(12):3402-3407, 2000). In the WT10 assay the drug in question and a 3TC control will be assayed at five concentrations each, diluted in a half-log series. The endpoints are TaqMan PCR for extracellular HBV DNA (IC50) and cell numbers using CellTiter96 reagent (TC50). The assay is similar to that described by Korba et al. Antiviral Res. 15(3):217-228, 1991 and Korba et al., Antiviral Res. 19(1):55-70, 1992. Briefly, WT10 cells are plated in 96-well microtiter plates. After 16-24 hours the confluent monolayer of HepG2-2.2.15 cells

is washed and the medium is replaced with complete medium containing varying concentrations of a test samples in triplicate. 3TC is used as the positive control, while media alone is added to cells as a negative control (virus control, VC). Three days later the culture medium is replaced with fresh medium containing the appropriately diluted test samples. Six days following the initial addition of the test compound, the cell culture supernatant is collected, treated with pronase and DNAse, and used in a real-time quantitative TaqMan PCR assay. The PCR-amplified HBV DNA is detected in real-time by monitoring increases in fluorescence signals that result from the exonucleolytic degradation of a quenched fluorescent probe molecule that hybridizes to the amplified HBV DNA. For each PCR amplification, a standard curve is simultaneously generated using dilutions of purified HBV DNA. Antiviral activity is calculated from the reduction in HBV DNA levels (IC_{50}). A dye uptake assay is then employed to measure cell viability which is used to calculate toxicity (TC_{50}). The therapeutic index (TI) is calculated as TC_{50}/IC_{50}.

[213] IL-28, IL-29 and MetIL-29C172S-PEG inhibited HepB viral replication in WT10 cells with an IC50 < 0.032ug/ml. This demonstrates antiviral activity of IL-28 and IL-29 against HBV grown in liver cell lines, providing evidence of therapeutic value for treating HBV in human patients.

Example 12

IL-28, IL-29 and MetIL-29C172S-PEG inhibit BVDV replication in bovine kidney cells

[214] HCV is a member of the *Flaviviridae* family of RNA viruses. Other viruses belonging to this family are the bovine viral diarrhea virus (BVDV) and yellow fever virus (YFV). HCV does not replicate well in either *ex vivo* or *in vitro* cultures and therefore there are no systems to test anti-HCV activity in vitro. The BVDV and YFV assays are used as surrogate viruses for HCV to test the antiviral activities against the *Flavivirida* family of viruses.

[215] The antiviral effects of IL-28, IL-29 and MetIL-29C172S-PEG were assessed in inhibition of cytopathic effect assays (CPE). The assay measured cell death using Madin-Darby bovine kidney cells (MDBK) after infection with cytopathic BVDV virus and the inhibition of cell death by addition of IL-28, IL-29 and MetIL-29C172S-PEG. The MDBK cells were propagated in Dulbecco's modified essential medium (DMEM) containing phenol red with 10% horse serum, 1% glutamine and 1% penicillin-streptomycin. CPE inhibition assays were performed in DMEM without phenol red with 2% FBS, 1% glutamine and 1% Pen-Strep. On the day preceding the assays, cells were trypsinized (1% trypsin-EDTA), washed, counted and plated out at 10^4 cells/well in a 96-well flat-bottom BioCoat® plates (Fisher Scientific, Pittsburgh, PA) in a volume of 100 µl/well. The next day, the medium was removed and a pre-titered aliquot of virus was added to the cells. The amount of virus was the maximum dilution that would yield complete cell killing (>80%) at the time of maximal CPE development (day 7 for BVDV). Cell viability was determined using a CellTiter96® reagent

(Promega) according to the manufacturer's protocol, using a Vmax plate reader (Molecular Devices, Sunnyvale, CA). Test samples were tested at six concentrations each, diluted in assay medium in a half-log series. IFNα and RIBAVIRIN® were used as positive controls. Test sample were added at the time of viral infection. The average background and sample color-corrected data for percent CPE reduction and percent cell viability at each concentration were determined relative to controls and the IC_{50} calculated relative to the TC_{50}.

[216] IL-28, IL-29 and MetIL-29C172S-PEG inhibited cell death induced by BVDV in MDBK bovine kidney cells. IL-28 inhibited cell death with an IC_{50} of 0.02 μg/ml, IL-29 inhibited cell death with an IC_{50} of 0.19 μg/ml, and MetIL-29C172S-PEG inhibited cell death with an IC_{50} of 0.45 μg/ml. This demonstrated that IL-28 and IL-29 have antiviral activity against the *Flavivirida* family of viruses.

Example 13

Induction of Interferon Stimulated Genes by IL-28 and IL-29

A. Human Peripheral Blood Mononuclear Cells

[217] Freshly isolated human peripheral blood mononuclear cells were grown in the presence of IL-29 (20 ng/mL), IFNα2a (2 ng/ml) (PBL Biomedical Labs, Piscataway, NJ), or in medium alone. Cells were incubated for 6, 24, 48, or 72 hours, and then total RNA was isolated and treated with RNase-free DNase. 100 ng total RNA was used as a template for One-Step Semi-Quantitative RT-PCR® using Taqman One-Step RT-PCR Master Mix® Reagents and gene specific primers as suggested by the manufacturer. (Applied Biosystems, Branchburg, NJ) Results were normalized to HPRT and are shown as the fold induction over the medium alone control for each time-point. Table 15 shows that IL-29 induces Interferon Stimulated Gene Expression in human peripheral blood mononuclear cells at all time-points tested.

Table 15

	MxA Fold induction	Pkr Fold Induction	OAS Fold Induction
6 hr IL29	3.1	2.1	2.5
6 hr IFNα2a	17.2	9.6	16.2
24 hr IL29	19.2	5.0	8.8
24 hr IFNα2a	57.2	9.4	22.3
48 hr IL29	7.9	3.5	3.3
48hr IFNα2a	18.1	5.0	17.3
72 hr IL29	9.4	3.7	9.6
72 hr IFNα2a	29.9	6.4	47.3

B. Activated Human T Cells

[218] Human T cells were isolated by negative selection from freshly harvested peripheral blood mononuclear cells using the Pan T-cell Isolation® kit according to manufacturer's instructions (Miltenyi, Auburn, CA). T cells were then activated and expanded for 5 days with plate-bound anti-CD3, soluble anti-CD28 (0.5ug/ml), (Pharmingen, San Diego, CA) and Interleukin 2 (IL-2; 100 U/ml) (R&D Systems, Minneapolis, MN), washed and then expanded for a further 5 days with IL-2. Following activation and expansion, cells were stimulated with IL-28A (20 ng/ml), IL-29 (20 ng/ml), or medium alone for 3, 6, or 18 hours. Total RNA was isolated and treated with RNase-Free DNase. One-Step Semi-Quantitative RT-PCR® was performed as described in the example above. Results were normalized to HPRT and are shown as the fold induction over the medium alone control for each time-point. Table 16 shows that IL-28 and IL-29 induce Interferon Stimulated Gene expression in activated human T cells at all time-points tested.

Table 16

	MxA Fold Induction	Pkr Fold Induction	OAS Fold Induction
Donor #1 3 hr IL28	5.2	2.8	4.8
Donor #1 3 hr IL29	5.0	3.5	6.0
Donor #1 6 hr IL28	5.5	2.2	3.0
Donor #1 6 hr IL29	6.4	2.2	3.7
Donor #1 18 hr IL28	4.6	4.8	4.0
Donor #1 18 hr IL29	5.0	3.8	4.1
Donor #2 3 hr IL28	5.7	2.2	3.5
Donor #2 3 hr IL29	6.2	2.8	4.7
Donor #2 6 hr IL28	7.3	1.9	4.4
Donor #2 6 hr IL29	8.7	2.6	4.9
Donor #2 18 hr IL28	4.7	2.3	3.6
Donor #2 18 hr IL29	4.9	2.1	3.8

C. Primary Human Hepatocytes

[219] Freshly isolated human hepatocytes from two separate donors (Cambrex, Baltimore, MD and CellzDirect, Tucson, AZ) were stimulated with IL-28A (50 ng/ml), IL-29 (50 ng/ml), IFNα2a (50 ng/ml), or medium alone for 24 hours. Following stimulation, total RNA was isolated and treated with RNase-Free DNase. One-step semi-quantitative RT-PCR was performed as described previously in the example above. Results were normalized to HPRT and are shown as the fold induction over the medium alone control for each time-point. Table 17 shows that IL-28 and IL-29 induce Interferon Stimulated Gene expression in primary human hepatocytes following 24-hour stimulation.

Table 17

	MxA Fold Induction	Pkr Fold Induction	OAS Fold Induction
Donor #1 IL28	31.4	6.4	30.4
Donor #1 IL29	31.8	5.2	27.8
Donor #1 IFN-α2a	63.4	8.2	66.7
Donor #2 IL28	41.7	4.2	24.3
Donor #2 IL29	44.8	5.2	25.2
Donor #2 IFN-α2a	53.2	4.8	38.3

D. HepG2 and HuH7: Human Liver Hepatoma Cell Lines

[220] HepG2 and HuH7 cells (ATCC NOS. 8065, Manassas, VA) were stimulated with IL-28A (10 ng/ml), IL-29 (10 ng/ml), IFNα2a (10 ng/ml), IFNB (1 ng/ml) (PBL Biomedical, Piscataway, NJ), or medium alone for 24 or 48 hours. In a separate culture, HepG2 cells were stimulated as described above with 20 ng/ml of MetIL-29C172S-PEG or MetIL-29-PEG. Total RNA was isolated and treated with RNase-Free DNase. 100 ng Total RNA was used as a template for one-step semi-quantitative RT-PCR as described previously. Results were normalized to HPRT and are shown as the fold induction over the medium alone control for each time-point. Table 18 shows that IL-28 and IL-29 induce ISG expression in HepG2 and HuH7 liver hepatoma cell lines after 24 and 48 hours.

Table 18

	MxA Fold Induction	Pkr Fold Induction	OAS Fold Induction
HepG2 24 hr IL28	12.4	0.7	3.3
HepG2 24 hr IL29	36.6	2.2	6.4
HepG2 24 hr IFNα2a	12.2	1.9	3.2
HepG2 24 hr IFNβ	93.6	3.9	19.0
HepG2 48hr IL28	2.7	0.9	1.1
HepG2 48hr IL29	27.2	2.1	5.3
HepG2 48 hr IFNα2a	2.5	0.9	1.2
HepG2 48hr IFNβ	15.9	1.8	3.3
HuH7 24 hr IL28	132.5	5.4	52.6
HuH7 24 hr IL29	220.2	7.0	116.6
HuH7 24 hr IFNα2a	157.0	5.7	67.0
HuH7 24 hr IFNβ	279.8	5.6	151.8
HuH7 48hr IL28	25.6	3.4	10.3
HuH7 48hr IL29	143.5	7.4	60.3
HuH7 48 hr IFNα2a	91.3	5.8	32.3
HuH7 48hr IFNβ	65.0	4.2	35.7

Table 19

	MxA Fold Induction	OAS Fold Induction	Pkr Fold Induction
MetIL-29-PEG	36.7	6.9	2.2
MetIL-29C172S-PEG	46.1	8.9	2.8

[221] Data shown is for 20 ng/ml metIL-29-PEG and metIL-29C172S-PEG versions of IL-29 after culture for 24 hours.

[222] Data shown is normalized to HPRT and shown as fold induction over unstimulated cells.

Example 14

Antiviral Activity of IL-28 and IL-29 in HCV Replicon System

[223] The ability of antiviral drugs to inhibit HCV replication can be tested *in vitro* with the HCV replicon system. The replicon system consists of the Huh7 human hepatoma cell line that has been transfected with subgenomic RNA replicons that direct constitutive replication of HCV genomic RNAs (Blight, K.J. et al. Science 290:1972-1974, 2000). Treatment of replicon clones with IFNα at 10 IU/ml reduces the amount of HCV RNA by 85% compared to untreated control cell lines. The ability of IL-28A and IL-29 to reduce the amount of HCV RNA produced by the replicon clones in 72 hours indicates the antiviral state conferred upon Huh7 cells by IL-28A/IL-29 treatment is effective in inhibiting HCV replicon replication, and thereby, very likely effective in inhibiting HCV replication.

[224] The ability of IL-28A and IL-29 to inhibit HCV replication as determined by Bayer Branched chain DNA kit, is be done under the following conditions:

[225] IL28 alone at increasing concentrations (6)* up to 1.0 μg/ml

[226] IL29 alone at increasing concentrations (6)* up to 1.0 μg/ml

[227] PEGIL29 alone at increasing concentrations (6)* up to 1.0 μg/ml

[228] IFNα2A alone at 0.3, 1.0, and 3.0 IU/ml

[229] Ribavirin alone.

[230] The positive control is IFNα and the negative control is ribavirin.

[231] The cells are stained after 72 hours with Alomar Blue to assess viablility.

[232] *The concentrations for conditions 1-3 are:

[233] μg/ml, 0.32 μg/ml, 0.10 μg/ml, 0.032 μg/ml, 0.010 μg/ml, 0.0032 μg/ml.

[234] The replicon clone (BB7) is treated 1X per day for 3 consecutive days with the doses listed above. Total HCV RNA is measured after 72 hours.

Example 15

IL-28 and IL-29 have antiviral activity against pathogenic viruses

[235] Two methods are used to assay *in vitro* antiviral activity of IL-28 and IL-29 against a panel of pathogenic viruses including, among others, adenovirus, parainfluenza virus. respiratory syncytial virus, rhino virus, coxsackie virus, influenza virus, vaccinia virus, west nile virus, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus. These two methods are inhibition of virus-induced cytopathic effect (CPE) determined by visual (microscopic) examination of the cells and increase in neutral red (NR) dye uptake into cells. In the CPE inhibition method, seven concentrations of test drug (log10 dilutions, such as 1000, 100, 10, 1, 0.1, 0.01, 0.001 ng/ml) are evaluated against each virus in 96-well flat-bottomed microplates containing host cells. The compounds are added 24 hours prior to virus, which is used at a concentration of approximately 5 to 100 cell culture infectious doses per well, depending upon the virus, which equates to a multiplicity of infection (MOI) of 0.01 to 0.0001 infectious particles per cell. The tests are read after incubation at 37°C for a specified time sufficient to allow adequate viral cytopathic effect to develop. In the NR uptake assay, dye (0.34% concentration in medium) is added to the same set of plates used to obtain the visual scores. After 2 h, the color intensity of the dye absorbed by and subsequently eluted from the cells is determined using a microplate autoreader. Antiviral activity is expressed as the 50% effective (virus-inhibitory) concentration (EC50) determined by plotting compound concentration versus percent inhibition on semilogarithmic graph paper. The EC50/IC50 data in some cases may be

determined by appropriate regression analysis software. In general, the EC50s determined by NR assay are two-to fourfold higher than those obtained by the CPE method.

Table 20: Visual Assay

Virus	Cell line	Drug	EC50 Visual	IC50 Visual	SI Visual (IC50/ EC50)
Adenovirus	A549	IL-28A	>10 μg/ml	>10 μg/ml	0
Adenovirus	A549	IL-29	>10 μg/ml	>10 μg/ml	0
Adenovirus	A549	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	IL-28A	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	IL-29	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	IL-28A	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	IL-29	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Rhino 2	KB	IL-28A	>10 μg/ml	>10 μg/ml	0
Rhino 2	KB	IL-29	>10 μg/ml	>10 μg/ml	0
Rhino 2	KB	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Rhino 9	HeLa	IL-28A	>10 μg/ml	>10 μg/ml	0
Rhino 9	HeLa	IL-29	>10 μg/ml	>10 μg/ml	0
Rhino 9	HeLa	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Coxsackie B4 virus	KB	IL-28A	>10 μg/ml	>10 μg/ml	0
Coxsackie B4 virus	KB	IL-29	>10 μg/ml	>10 μg/ml	0
Coxsackie B4 virus	KB	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0

Influenza (type A [H3N2])	Maden-Darby Canine Kidney	IL-28A	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Maden-Darby Canine Kidney	IL-29	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Maden-Darby Canine Kidney	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Vero	IL-28A	0.1 μg/ml	>10 μg/ml	>100
Influenza (type A [H3N2])	Vero	IL-29	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Vero	MetIL-29 C172S-PEG	0.045 μg/ml	>10 μg/ml	>222
Vaccinia virus	Vero	IL-28A	>10 μg/ml	>10 μg/ml	0
Vaccinia virus	Vero	IL-29	>10 μg/ml	>10 μg/ml	0
Vaccinia virus	Vero	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
West Nile virus	Vero	IL-28A	0.00001 μg/ml	>10 μg/ml	>1,000,000
West Nile virus	Vero	IL-29	0.000032 μg/ml	>10 μg/ml	>300,000
West Nile virus	Vero	MetIL-29 C172S-PEG	0.001 μg/ml	>10 μg/ml	>10,000
Dengue virus	Vero	IL-28A	0.01 μg/ml	>10 μg/ml	>1000
Dengue virus	Vero	IL-29	0.032 μg/ml	>10 μg/ml	>312
Dengue virus	Vero	MetIL-29 C172S-PEG	0.0075 μg/ml	>10 μg/ml	>1330

Venezuelan equine encephalitis virus	Vero	IL-28A	0.01 μg/ml	>10 μg/ml	>1000
Venezuelan equine encephalitis virus	Vero	IL-29	0.012 μg/ml	>10 μg/ml	>833
Venezuelan equine encephalitis virus	Vero	MetIL-29 C172S-PEG	0.0065 μg/ml	>10 μg/ml	>1538
Pichinde virus	BSC-1	IL-28A	>10 μg/ml	>10 μg/ml	0
Pichinde virus	BSC-1	IL-29	>10 μg/ml	>10 μg/ml	0
Pichinde virus	BSC-1	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Polio virus	Vero	IL-28A	>10 μg/ml	>10 μg/ml	0
Polio virus	Vero	IL-29	>10 μg/ml	>10 μg/ml	0
Polio virus	Vero	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0

Table 21: Neutral Red Assay

Virus	Cell line	Drug	EC50 NR	IC50 NR	SI NR (IC50/ EC50)
Adenovirus	A549	IL-28A	>10 μg/ml	>10 μg/ml	0
Adenovirus	A549	IL-29	>10 μg/ml	>10 μg/ml	0
Adenovirus	A549	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	IL-28A	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	IL-29	>10 μg/ml	>10 μg/ml	0
Parainfluenza virus	MA-104	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	IL-28A	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	IL-29	>10 μg/ml	>10 μg/ml	0
Respiratory syncytial virus	MA-104	MetIL-29 C172S-	5.47 μg/ml	>10 μg/ml	>2

		PEG			
Rhino 2	KB	IL-28A	>10 μg/ml	>10 μg/ml	0
Rhino 2	KB	IL-29	>10 μg/ml	>10 μg/ml	0
Rhino 2	KB	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Rhino 9	HeLa	IL-28A	1.726 μg/ml	>10 μg/ml	>6
Rhino 9	HeLa	IL-29	0.982 μg/ml	>10 μg/ml	>10
Rhino 9	HeLa	MetIL-29 C172S-PEG	2.051 μg/ml	>10 μg/ml	>5
Coxsackie B4 virus	KB	IL-28A	>10 μg/ml	>10 μg/ml	0
Coxsackie B4 virus	KB	IL-29	>10 μg/ml	>10 μg/ml	0
Coxsackie B4 virus	KB	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Maden-Darby Canine Kidney	IL-28A	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Maden-Darby Canine Kidney	IL-29	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Maden-Darby Canine Kidney	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Influenza (type A [H3N2])	Vero	IL-28A	0.25 μg/ml	>10 μg/ml	>40
Influenza (type A [H3N2])	Vero	IL-29	2 μg/ml	>10 μg/ml	>5
Influenza (type A [H3N2])	Vero	MetIL-29 C172S-PEG	1.4 μg/ml	>10 μg/ml	>7
Vaccinia virus	Vero	IL-28A	>10 μg/ml	>10 μg/ml	0
Vaccinia virus	Vero	IL-29	>10 μg/ml	>10 μg/ml	0
Vaccinia virus	Vero	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
West Nile virus	Vero	IL-28A	0.0001 μg/ml	>10 μg/ml	>100,000
West Nile virus	Vero	IL-29	0.00025 μg/ml	>10 μg/ml	>40,000
West Nile virus	Vero	MetIL-29 C172S-PEG	0.00037 μg/ml	>10 μg/ml	>27,000
Dengue virus	Vero	IL-28A	0.1 μg/ml	>10 μg/ml	>100
Dengue virus	Vero	IL-29	0.05 μg/ml	>10 μg/ml	>200

Dengue virus	Vero	MetIL-29 C172S-PEG	0.06 μg/ml	>10 μg/ml	>166
Venezuelan equine encephalitis virus	Vero	IL-28A	0.035 μg/ml	>10 μg/ml	>286
Venezuelan equine encephalitis virus	Vero	IL-29	0.05 μg/ml	>10 μg/ml	>200
Venezuelan equine encephalitis virus	Vero	MetIL-29 C172S-PEG	0.02 μg/ml	>10 μg/ml	>500
Pichinde virus	BSC-1	IL-28A	>10 μg/ml	>10 μg/ml	0
Pichinde virus	BSC-1	IL-29	>10 μg/ml	>10 μg/ml	0
Pichinde virus	BSC-1	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0
Polio virus	Vero	IL-28A	>1.672 μg/ml	>10 μg/ml	>6
Polio virus	Vero	IL-29	>10 μg/ml	>10 μg/ml	0
Polio virus	Vero	MetIL-29 C172S-PEG	>10 μg/ml	>10 μg/ml	0

Example 16

IL-28, IL-29, metIL-29-PEG and metIL-29C172S-PEG Stimulate ISG induction in the Mouse Liver Cell line AML-12

[236] Interferon stimulated genes (ISGs) are genes that are induced by type I interferons (IFNs) and also by the IL-28 and IL-29 family molecules, suggesting that IFN and IL-28 and IL-29 induce similar pathways leading to antiviral activity. Human type I IFNs (IFNα1-4 and IFNβ) have little or no activity on mouse cells, which is thought to be caused by lack of species cross-reactivity. To test if human IL-28 and IL-29 have effects on mouse cells, ISG induction by human IL-28 and IL-29 was evaluated by real-time PCR on the mouse liver derived cell line AML-12.

[237] AML-12 cells were plated in 6-well plates in complete DMEM media at a concentration of 2 x 10^6 cells/well. Twenty-four hours after plating cells, human IL-28 and IL-29 were added to the culture at a concentration of 20 ng/ml. As a control, cells were either stimulated with mouse IFNα (positive control) or unstimulated (negative). Cells were harvested at 8, 24, 48 and 72 hours after addition of CHO-derived human IL-28A (SEQ ID NO:18) or IL-29 (SEQ ID NO:20) . RNA was isolated from cell pellets using RNAEasy-kit® (Qiagen, Valencia, CA). RNA was treated with DNase (Millipore, Billerica, MA) to clean RNA of any contaminating DNA. cDNA was generated using Perkin-Elmer RT mix. ISG gene induction was evaluated by real-time PCR using primers and probes specific for mouse OAS, Pkr and Mx1. To obtain quantitative data, HPRT real-time PCR was duplexed with ISG PCR. A standard curve was obtained using known amounts of RNA from IFN-stimulated mouse PBLs. All data are shown as expression relative to internal HPRT expression.

[238] Human IL-28A and IL-29 stimulated ISG induction in the mouse hepatocyte cell line AML-12 and demonstrated that unlike type I IFNs, the IL-28/29 family proteins showed cross-species reactivity.

Table 22

Stimulation	OAS	PkR	Mx1
None	0.001	0.001	0.001
Human IL-28	0.04	0.02	0.06
Human IL-29	0.04	0.02	0.07
Mouse IL-28	0.04	0.02	0.08
Mouse IFNα	0.02	0.02	0.01

[239] All data shown were expressed as fold relative to HPRT gene expression ng of OAS mRNA = normalized value of OAS mRNA amount relative to internal ng of HPRT mRNA housekeeping gene, HPRT

As an example, the data for the 48 hour time point is shown.

Table 23

AML12's

	Mx1 Fold Induction	OAS Fold Induction	Pkr Fold Induction
MetIL-29-PEG	728	614	8
MetIL-29C172S-PEG	761	657	8

[240] Cells were stimulated with 20 ng/ml metIL-29-PEG or metIL-29C172S-PEG for 24 hours.

[241] Data shown is normalized to HPRT and shown as fold induction over unstimulated cells.

Example 17

ISGs are Efficiently Induced in Spleens of Transgenic Mice Expressing Human IL-29

[242] Transgenic (Tg) mice were generated expressing human IL-29 under the control of the Eu-lck promoter. To study if human IL-29 has biological activity *in vivo* in mice, expression of ISGs was analyzed by real-time PCR in the spleens of Eu-lck IL-29 transgenic mice.

[243] Transgenic mice (C3H/C57BL/6) were generated using a construct that expressed the human IL-29 gene under the control of the Eu-lck promoter. This promoter is active in T cells and B cells. Transgenic mice and their non-transgenic littermates (n=2/gp) were sacrificed at about 10 weeks of age. Spleens of mice were isolated. RNA was isolated from cell pellets using RNAEasy-kit® (Qiagen). RNA was treated with DNase to clean RNA of any contaminating DNA. cDNA was generated using Perkin-Elmer RT® mix. ISG gene induction was evaluated by real-time PCR using primers and probes (5' FAM, 3' NFQ) specific for mouse OAS, Pkr and Mx1. To obtain quantitative data, HPRT real-time PCR was duplexed with ISG PCR. Furthermore, a standard curve was obtained

using known amounts of IFN stimulated mouse PBLs. All data are shown as expression relative to internal HPRT expression.

[244] Spleens isolated from IL-29 Tg mice showed high induction of ISGs OAS, Pkr and Mx1 compared to their non-Tg littermate controls suggesting that human IL-29 is biologically active in vivo in mice.

Table 24

Mice	**OAS**	**PkR**	**Mx1**
Non-Tg	4.5	4.5	3.5
IL-29 Tg	12	8	21

[245] All data shown are fold expression relative to HPRT gene expresssion. The average expression in two mice is shown

Example 18

Human IL-28 and IL-29 Protein Induce ISG Gene Expression In Liver, Spleen and Blood of Mice

[246] To determine whether human IL-28 and IL-29 induce interferon stimulated genes *in vivo*, CHO-derived human IL-28A and IL-29 protein were injected into mice. In addition, *E. coli* derived IL-29 was also tested in *in vivo* assays as described above using MetIL-29C172S-PEG and MetIL-29-PEG. At various time points and at different doses, ISG gene induction was measured in the blood, spleen and livers of the mice.

[247] C57BL/6 mice were injected i.p or i.v with a range of doses (10 μg – 250 μg) of CHO-derived human IL-28A and IL-29 or MetIL-29C172S-PEG and MetIL-29C16-C113-PEG. Mice were sacrificed at various time points (1hr – 48hr). Spleens and livers were isolated from mice, and RNA was isolated. RNA was also isolated from the blood cells. The cells were pelleted and RNA isolated from pellets using RNAEasy®-kit (Qiagen). RNA was treated with DNase (Amicon) to rid RNA of any contaminating DNA. cDNA was generated using Perkin-Elmer RT mix (Perkin-Elmer). ISG gene induction was measured by real-time PCR using primers and probes specific for mouse OAS, Pkr and Mx1. To obtain quantitative data, HPRT real-time PCR was duplexed with ISG PCR. A standard curve was calculated using known amounts of IFN-stimulated mouse PBLs. All data are shown as expression relative to internal HPRT expression.

[248] Human IL-29 induced ISG gene expression (OAS, Pkr, Mx1) in the livers, spleen and blood of mice in a dose dependent manner. Expression of ISGs peaked between 1-6 hours after injection and showed sustained expression above control mice upto 48 hours. In this experiment, human IL-28A did not induce ISG gene expression.

Table 25

Injection	OAS- 1hr	OAS-6hr	OAS-24hr	OAS-48hr
None - liver	1.6	1.6	1.6	1.6
IL-29 liver	2.5	4	2.5	2.8
None - spleen	1.8	1.8	1.8	1.8
IL-29 - spleen	4	6	3.2	3.2
None - blood	5	5	5	5

IL-29 blood	12	18	11	10

[249] Results shown are fold expression relative to HPRT gene expression. A sample data set for IL-29 induced OAS in liver at a single injection of 250 μg i.v. is shown. The data shown is the average expression from 5 different animals/group.

Table 26

Injection	OAS (24hr)
None	1.8
IL-29 10 μg	3.7
IL-29 50 μg	4.2
IL-29 250 μg	6

Table 27

	MetIL-29-PEG				MetIL-29C172S-PEG				Naive
	3hr	6hr	12hr	24hr	3hr	6hr	12hr	24hr	24hr
PKR	18.24	13.93	4.99	3.77	5.29	5.65	3.79	3.55	3.70
OAS	91.29	65.93	54.04	20.81	13.42	13.02	10.54	8.72	6.60
Mx1	537.51	124.99	33.58	35.82	27.89	29.34	16.61	0.00	10.98

[250] Mice were injected with 100 μg of proteins i.v. Data shown is fold expression over HPRT expression from livers of mice. Similar data was obtained from blood and spleens of mice.

Example 19

IL-28 and IL-29 Induce ISG Protein In Mice

[251] To analyze of the effect of human IL-28 and IL-29 on induction of ISG protein (OAS), serum and plasma from IL-28 and IL-29 treated mice were tested for OAS activity.

[252] C57BL/6 mice were injected i.v with PBS or a range of concentrations (10 μg-250 μg) of human IL-28 or IL-29. Serum and plasma were isolated from mice at varying time points, and OAS activity was measured using the OAS radioimmunoassay (RIA) kit from Eiken Chemicals (Tokyo, Japan).

[253] IL-28 and IL-29 induced OAS activity in the serum and plasma of mice showing that these proteins are biologically active *in vivo*.

Table 28

Injection	OAS-1hr	OAS-6hr	OAS-24hr	OAS-48hr
None	80	80	80	80
IL-29	80	80	180	200

[254] OAS activity is shown at pmol/dL of plasma for a single concentration (250 μg) of human IL-29.

Example 20

IL-28 and IL-29 inhibit Adenoviral pathology in mice

[255] To test the antiviral activities of IL-28 and IL-29 against viruses that infect the liver, the test samples were tested in mice against infectious adenoviral vectors expressing an internal green fluorescent protein (GFP) gene. When injected intravenously, these viruses primarily target the liver for gene expression. The adenoviruses are replication deficient, but cause liver damage due to inflammatory cell infiltrate that can be monitored by measurement of serum levels of liver enzymes like AST and ALT, or by direct examination of liver pathology.

[256] C57Bl/6 mice were given once daily intraperitoneal injections of 50 μg mouse IL-28 (zcyto24) or metIL-29C172S- PEG for 3 days. Control animals were injected with PBS. One hour following the 3rd dose, mice were given a single bolus intravenous tail vein injection of the adenoviral vector, AdGFP (1 X 10^9 plaque-forming units (pfu)). Following this, every other day mice were given an additional dose of PBS, mouse IL-28 or metIL-29C172S- PEG for 4 more doses (total of 7 doses). One hour following the final dose of PBS, mouse IL-28 or metIL-29C172S- PEG mice were terminally bleed and sacrificed. The serum and liver tissue were analyzed. Serum was analyzed for AST and ALT liver enzymes. Liver was isolated and analyzed for GFP expression and histology. For histology, liver specimens were fixed in formalin and then embedded in paraffin followed by H&E staining. Sections of liver that had been blinded to treat were examined with a light microscope. Changes were noted and scored on a scale designed to measure liver pathology and inflammation.

[257] Mouse IL-28 and IL-29 inhibited adenoviral infection and gene expression as measured by liver fluorescence. PBS-treated mice (n=8) had an average relative liver fluorescence of 52.4 (arbitrary units). In contrast, IL-28-treated mice (n=8) had a relative liver fluorescence of 34.5, and IL-29-treated mice (n=8) had a relative liver fluorescence of 38.9. A reduction in adenoviral infection and gene expression led to a reduced liver pathology as measured by serum ALT and AST levels and histology. PBS-treated mice (n=8) had an average serum AST of 234 U/L (units/liter) and serum ALT of 250 U/L. In contrast, IL-28-treated mice (n=8) had an average serum AST of 193 U/L and serum ALT of 216 U/L, and IL-29-treated mice (n=8) had an average serum AST of 162 U/L and serum ALT of 184 U/L. In addition, the liver histology indicated that mice given either mouse IL-28 or IL-29 had lower liver and inflammation scores than the PBS-treated group. The livers from the IL-29 group also had less proliferation of sinusoidal cells, fewer mitotic figures and fewer changes in the hepatocytes (e.g. vacuolation, presence of multiple nuclei, hepatocyte enlargement) than in the PBS treatment group. These data demonstrate that mouse IL-28 and IL-29 have antiviral properties against a liver-trophic virus.

Example 21

LCMV Models

[258] Lymphocytic choriomeningitis virus (LCMV) infections in mice mice are an excellent model of acture and chronic infection. These models are used to evaluate the effect of cytokines on the antiviral immune response and the effects IL-28 and IL-29 have viral load and the antiviral immune response. The two models used are: LCMV Armstrong (acute) infection and LCMV Clone 13 (chronic) infection. (See, e.g., Wherry et al., J. Virol. 77:4911-4927, 2003; Blattman et al., Nature Med. 9(5):540-547, 2003; Hoffman et al., J. Immunol. 170:1339-1353, 2003.) There are three stages of CD8 T cell development in response to virus: 1) expansion, 2) contraction, and 3) memory (acute model). IL-28 or IL-29 is injected during each stage for both acute and chronic models. In the chronic model, IL-28 or IL-29 is injected 60 days after infection to assess the effect of IL-28 or IL-29 on persistent viral load. For both acute and chronic models, IL-28 or IL-29 is injected, and the viral load in blood, spleen and liver is examined. Other paramenter that can be examined include: tetramer staining by flow to count the number of LCMV-specific CD8+ T cells; the ability of tetramer+ cells to produce cytokines when stimulated with their cognate LCMV antigen; and the ability of LCMV-specific CD8+ T cells to proliferate in response to their cognate LCMV antigen. LCMV-specific T cells are phenotyped by flow cytometry to assess the cells activation and differentiation state. Also, the ability of LCMV-specific CTL to lyse target cells bearing their cognate LCMV antigen is examined. The number and function of LCMV-specific CD4+ T cells is also assessed.

[259] A reduction in viral load after treatment with IL-28 or IL-29 is determined. A 50% reduction in viral load in any organ, especially liver, would be significant. For IL-28 or IL-29 treated mice, a 20% increase in the percentage of tetramer positive T cells that proliferate, make cytokine, or display a mature phenotype relative to untreated mice would also be considered significant.

[260] IL-28 or IL-29 injection leading to a reduction in viral load is due to more effective control of viral infection especially in the chronic model where untreated the viral titers remain elevated for an extended period of time. A two fold reduction in viral titer relative to untreated mice is considered significant.

Example 22

Influenza Model of Acute Viral Infection

A. Preliminary Experiment to test antiviral activity

[261] To determine the antiviral activity of IL-28 or IL-29 on acute infection by *Influenza* virus, an *in vivo* study using influenza infected c57B1/6 mice is performed using the following protocol:

[262] Animals: 6 weeks-old female BALB/c mice (Charles River) with 148 mice, 30 per group.

[263] Groups:

[264] Absolute control (not infected) to run in parallel for antibody titre and histopathology (2 animals per group)

[265] Vehicle (i.p.) saline

[266] Amantadine (positive control) 10 mg/day during 5 days (per os) starting 2 hours before infection

[267] IL-28 or IL-29 treated (5 μg, i.p. starting 2 hours after infection)

[268] IL-28 or IL-29 (25 μg, i.p. starting 2 hours after infection)

[269] IL-28 or IL-29 (125 μg, i.p. starting 2 hours after infection)

[270] Day 0 – Except for the absolute controls, all animals infected with Influenza virus

[271] For viral load (10 at LD50)

[272] For immunology workout (LD30)

[273] Day 0 – 9 – daily injections of IL-28 or IL-29 (i.p.)

[274] Body weight and general appearance recorded (3 times/week)

[275] Day 3 – sacrifice of 8 animals per group

[276] Viral load in right lung (TCID50)

[277] Histopathology in left lung

[278] Blood sample for antibody titration

[279] Day 10 – sacrifice of all surviving animals collecting blood samples for antibody titration, isolating lung lymphocytes (4 pools of 3) for direct CTL assay (in all 5 groups), and quantitative immunophenotyping for the following markers: CD3/CD4, CD3/CD8, CD3/CD8/CD11b, CD8/CD44/CD62L, CD3/DX5, GR-1/F480, and CD19.

[280] Study No.2

[281] Efficacy study of IL-28 or IL-29 in C57Bl/6 mice infected with mouse-adapted virus is done using 8 weeks-old female C57Bl/6 mice (Charles River).

[282] Group 1: Vehicle (i.p.)

[283] Group 2: Positive control: Anti-influenza neutralizing antibody (goat anti-influenza A/USSR (H1N1) (Chemicon International, Temecula, CA); 40 μg/mouse at 2 h and 4 h post infection (10 μl intranasal)

[284] Group 3: IL-28 or IL-29 (5 μg, i.p.)

[285] Group 4: IL-28 or IL-29 (25 μg, i.p.)

[286] Group 5: IL-28 or IL-29 (125 μg, i.p.)

[287] Following-life observations and immunological workouts are prepared:

[288] Day 0 – all animals infected with Influenza virus (dose determined in experiment 2)

[289] Day 0 – 9 – daily injections of IL-28 or IL-29 (i.p.)

[290] Body weight and general appearance recorded every other day

[291] Day 10 – sacrifice of surviving animals and perform viral assay to determine viral load in lung.

[292] Isolation of lung lymphocytes (for direct CTL assay in the lungs using EL-4 as targets and different E:T ratio (based on best results from experiments 1 and 2).

[293] Tetramer staining: The number of CD8+ T cells binding MHC Class I tetramers containing influenza A nucleoprotein (NP) epitope are assessed using complexes of MHC class I with viral peptides: FLU-$NP_{366-374}/D^b$ (ASNENMETM), (LMCV peptide/D^b).

[294] Quantitative immunophenotyping of the following: CD8, tetramer, intracellular IFNγ, NK1.1, CD8, tetramer, CD62L, CD44, CD3(+ or -), NK1.1(+), intracellular IFNγ, CD4, CD8, NK1.1, DX5, CD3 (+ or -), NK1.1, DX5, tetramer, Single colour samples for cytometer adjustment.

Survival/Re-challenge Study

[295] Day 30: Survival study with mice are treated for 9 days with different doses of IL-28 or IL-29 or with positive anti-influenza antibody control. Body weight and antibody production in individual serum samples (Total, IgG1, IgG2a, IgG2b) are measured.

Re-challenge study:

[296] Day 0: Both groups will be infected with A/PR virus (1LD30).

[297] Group 6 will not be treated.

[298] Group 7 will be treated for 9 days with 125 μg of IL-28 or IL-29.

[299] Day 30: Survival study

[300] Body weight and antibody production in individual serum samples (Total, IgG1, IgG2a, IgG2b) are measured.

[301] Day 60: Re-challenge study

[302] Survivors in each group will be divided into 2 subgroups

[303] Group 6A and 7A will be re-challenge with A/PR virus (1 LD30)

[304] Group 6B and 7B will be re-challenge with A/PR virus (1 LD30).

[305] Both groups will be followed up and day of sacrifice will be determined. Body weight and antibody production in individual serum samples (Total, IgG1, IgG2a, IgG2b) are measured.

Example 23

IL-28 and IL-29 have Antiviral Activity Against Hepatitis B virus (HBV) in vivo

[306] A transgenic mouse model (Guidotti et al., J. Virology 69:6158-6169, 1995) supports the replication of high levels of infectious HBV and has been used as a chemotherapeutic model for HBV infection. Transgenic mice are treated with antiviral drugs and the levels of HBV DNA and RNA are measured in the transgenic mouse liver and serum following treatment. HBV protein levels can also be measured in the transgenic mouse serum following treatment. This model has been used to evaluate the effectiveness of lamivudine and IFN-α in reducing HBV viral titers..

[307] HBV TG mice (male) are given intraperitoneal injections of 2.5, 25 or 250 micrograms IL-28 or IL-29 every other day for 14 days (total of 8 doses). Mice are bled for serum collection on day of treatment (day 0) and day 7. One hour following the final dose of IL-29 mice undergo a terminal bleed and are sacrificed. Serum and liver are analyzed for liver HBV DNA, liver HBV RNA, serum HBV DNA, liver HBc, serum Hbe and serum HBs.

[308] Reduction in liver HBV DNA, liver HBV RNA, serum HBV DNA, liver HBc, serum Hbe or serum HBs in response to IL-28 or IL-29 reflects antiviral activity of these compounds against HBV.

Example 24

IL-28 and IL-29 inhibit human herpesvirus-8 (HHV-8) replication in BCBL-1 cells

[309] The antiviral activities of IL-28 and IL-29 were tested against HHV-8 in an *in vitro* infection system using a B-lymphoid cell line, BCBL-1.

[310] In the HHV-8 assay the test compound and a ganciclovir control were assayed at five concentrations each, diluted in a half-log series. The endpoints were TaqMan PCR for extracellular HHV-8 DNA (IC50) and cell numbers using CellTiter96® reagent (TC50; Promega, Madison, WI). Briefly, BCBL-1 cells were plated in 96-well microtiter plates. After 16-24 hours the cells were washed and the medium was replaced with complete medium containing various concentrations of the test compound in triplicate. Ganciclovir was the positive control, while media alone was a negative control (virus control, VC). Three days later the culture medium was replaced with fresh medium containing the appropriately diluted test compound. Six days following the initial administration of the test compound, the cell culture supernatant was collected, treated with pronase and DNAse and then used in a real-time quantitative TaqMan PCR assay. The PCR-amplified HHV-8 DNA was detected in real-time by monitoring increases in fluorescence signals that result from the exonucleolytic degradation of a quenched fluorescent probe molecule that hybridizes to the amplified HHV-8 DNA. For each PCR amplification, a standard curve was simultaneously generated using dilutions of purified HHV-8 DNA. Antiviral activity was calculated from the reduction in HHV-8 DNA levels (IC_{50}). A novel dye uptake assay was then employed to measure cell viability which was used to calculate toxicity (TC_{50}). The therapeutic index (TI) is calculated as TC_{50}/IC_{50}.

[311] IL-28 and IL-29 inhibit HHV-8 viral replication in BCBL-1 cells. IL-28A had an IC_{50} of 1 μg/ml and a TC_{50} of >10 μg/ml (TI >10). IL-29 had an IC_{50} of 6.5 μg/ml and a TC_{50} of >10 μg/ml (TI >1.85). MetIL-29C172S-PEG had an IC_{50} of 0.14 μg/ml and a TC_{50} of >10 μg/ml (TI >100).

Example 25

IL-28 and IL-29 antiviral activity against Epstein Barr Virus (EBV)

[312] The antiviral activities of IL-28 and IL-29 are tested against EBV in an *in vitro* infection system in a B-lymphoid cell line, P3HR-1. In the EBV assay the test compound and a control are assayed at five concentrations each, diluted in a half-log series. The endpoints are TaqMan PCR for extracellular EBV DNA (IC50) and cell numbers using CellTiter96® reagent

(TC50; Promega). Briefly, P3HR-1 cells are plated in 96-well microtiter plates. After 16-24 hours the cells are washed and the medium is replaced with complete medium containing various concentrations of the test compound in triplicate. In addition to a positive control, media alone is added to cells as a negative control (virus control, VC). Three days later the culture medium is replaced with fresh medium containing the appropriately diluted test compound. Six days following the initial administration of the test compound, the cell culture supernatant is collected, treated with pronase and DNAse and then used in a real-time quantitative TaqMan PCR assay. The PCR-amplified EBV DNA is detected in real-time by monitoring increases in fluorescence signals that result from the exonucleolytic degradation of a quenched fluorescent probe molecule that hybridizes to the amplified EBV DNA. For each PCR amplification, a standard curve was simultaneously generated using dilutions of purified EBV DNA. Antiviral activity is calculated from the reduction in EBV DNA levels (IC_{50}). A novel dye uptake assay was then employed to measure cell viability which was used to calculate toxicity (TC_{50}). The therapeutic index (TI) is calculated as TC_{50}/IC_{50}.

Example 26

IL-28 and IL-29 antiviral activity against Herpes Simplex Virus-2 (HSV-2)

[313] The antiviral activities of IL-28 and IL-29 were tested against HSV-2 in an *in vitro* infection system in Vero cells. The antiviral effects of IL-28 and IL-29 were assessed in inhibition of cytopathic effect assays (CPE). The assay involves the killing of Vero cells by the cytopathic HSV-2 virus and the inhibition of cell killing by IL-28 and IL-29. The Vero cells are propagated in Dulbecco's modified essential medium (DMEM) containing phenol red with 10% horse serum, 1% glutamine and 1% penicillin-streptomycin, while the CPE inhibition assays are performed in DMEM without phenol red with 2% FBS, 1% glutamine and 1% Pen-Strep. On the day preceding the assays, cells were trypsinized (1% trypsin-EDTA), washed, counted and plated out at 10^4 cells/well in a 96-well flat-bottom BioCoat® plates (Fisher Scientific, Pittsburgh, PA) in a volume of 100 µl/well. The next morning, the medium was removed and a pre-titered aliquot of virus was added to the cells. The amount of virus used is the maximum dilution that would yield complete cell killing (>80%) at the time of maximal CPE development. Cell viability is determined using a CellTiter 96® reagent (Promega) according to the manufacturer's protocol, using a Vmax plate reader (Molecular Devices, Sunnyvale, CA). Compounds are tested at six concentrations each, diluted in assay medium in a half-log series. Acyclovir was used as a positive control. Compounds are added at the time of viral infection. The average background and drug color-corrected data for percent CPE reduction and percent cell viability at each concentration are determined relative to controls and the IC_{50} calculated relative to the TC_{50}.

[314] IL-28A, IL-29 and MetIL-29C172S-PEG did not inhibit cell death (IC_{50} of >10ug/ml) in this assay. There was also no antiviral activity of IFNα in the assay.

Example 27

PEG-rIL-29-C172S and PEG-rIL-29-d2-7 Antiviral Activity Against Hepatitis C Virus in the Hepatitis C Replicon Model

[315] In order to determine the effectiveness of PEG-rIL-29 in preventing viral replication of human hepatitis C virus two forms of PEG-rIL-29 (IL-29 C172S polypeptide N-terminally conjugated to a 20kD methoxy-polyethylene glycol propionaldehyde ("PEG-rIL-29-C172S") (SEQ ID NO:34) and IL-29 C172S d2-7 polypeptide N-terminally conjugated to a 20kD methoxy-polyethylene glycol propionaldehyde ("PEG-rIL-29-d2-7") (SEQ ID NO:134) were tested in the HCV Replicon model.

[316] In this model AVA5 cells (Huh7 cells containing the subgenomic HCV replicon, BB7) (Blight et al., Science, 290:1972-1974 (2000)) were used. Cultures were maintained in a sub-confluent state in DMEM with glutamine, non-essential amino acids, and 10% heat-inactivated fetal bovine serum (Biofluids, Inc.) as previously described (Blight et al., Science, 290:1972-1974 (2000)). Stock cultures were maintained in a sub-confluent state in this culture medium with 1mg/ml G418 (Invitrogen, Inc.) (Blight et al., Science, 290:1972-1974 (2000)). Cells for antiviral analysis were seeded into 24-well or 48-well tissue culture plates (Nunc, Inc.) and grown for three days in the presence of G418. G418 was then removed for the duration of the antiviral treatments to eliminate potential loss of cells due to the reduction of HCV replicon (and G418-resistance) copy number. Cultures (rapidly dividing, 3-4 cultures per concentration, per experiment) were treated for three consecutive days with the test compounds. Medium was replaced daily with fresh test compounds. Analysis of HCV RNA was performed 24 hours following the last addition of test compounds. Toxicity analyses using neutral red dye uptake were performed as previously described in Korba et al., Antiviral Res., 19(1):55-70 (1992). Cultures for the toxicity analyses were seeded from the same stock cultures and maintained on separate plates under conditions identical to those used for the corresponding antiviral assays.

[317] Daily aliquots of test compounds (PEG-rIL-29-C172S and PEG-rIL-29-d2-7, PEGASYS® (Roche) and PEG®-Intron (Schering-Plough)) were made from stock solutions in individual tubes. On each day of treatment, daily aliquots of the diluted test compounds were suspended into culture medium at room temperature, and immediately added to the cell cultures, thereby subjecting each aliquot of test compound to the same, limited, number of freeze-thaw cycles.

[318] HCV RNA levels were quantitatively measured using one of two methods. The first method used the application of commercial bDNA technology (Versant HCV™, Bayer Diagnostics,

Inc., Oakland CA) for the detection of intracellular HCV. For this assay, no RNA extraction is required. Cells are lysed in the culture wells, and the resulting solution is then directly quantitatively assayed for RNA. The bDNA assay uses the certified HCV international reference standards and has internal extraction controls included in each sample. The EC50 value for each test drug is calculated using linear regression analysis (MS Excel™).

[319] The second method for HCV RNA quantitation is a modification of a previously described dot blot hybridization assay (Korba et al., Antiviral Res., 19(1):55-70 (1992)). Whole cell RNA was extracted from cells using either RNeasy™ mini-columns (Qiagen, Inc.), or Purescript RNA Purification kits (Gentra Systems, Inc.). RNA samples were denatured in 10XSSC/18% deionized formaldehyde for 20 min. at 80°C, applied to nitrocellulose under vacuum, washed once with 20XSSC, baked for 15 min at 80°C. under vacuum, and hybridized against ^{32}P-labelled DNA probes. Following the denaturation step, each RNA sample was split onto two nitrocellulose membranes for hybridization with either HCV-specific or human β-actin-specific ^{32}P-labelled DNA probes (95% of the sample for HCV, 5% for β-actin). The HCV hybridization probe used was a gel-purified, 6600bp *Hind III* fragment isolated from the HCV replicon source plasmid, BB7 (Blight et al., Science, 290:1972-1974 (2000)). The β-actin probe was a gel-purified, 550bp PCR product generated from AVA5 cell RNA using a commercial PCR kit (Invitrogen, Inc.). Both probes were labeled with ^{32}P-dCTP using a commercial random priming procedure (Clonetech-BD Biosciences, Inc.). Hybridization was performed overnight at either 47°C (HCV), or 40°C (β-actin), and washing was performed at either 65°C (HCV), or 60°C (β-actin), as previously described (Korba et al., Antiviral Res., 19(1):55-70 (1992)). Quantitation against independently determined standards present on each hybridization membrane was achieved using a beta scanner (Packard Instruments, Inc.). The mean levels of β-actin RNA present in 6-8 untreated cultures contained in each experiment were used as the basis for determining the relative level of β-actin RNA in each individual sample. Levels of HCV RNA were normalized to the levels of β-actin RNA present in each individual sample. HCV RNA levels in treated cultures were then compared to the normalized mean levels of HCV RNA present in the 6-8 untreated cultures contained in each experiment. The EC50 value for each test drug is calculated using linear regression analysis (MS Excel™).

[320] Initial experiments tested PEG-rIL-29-C172S (SEQ ID NO:34), PEGASYS® and PEG®-Intron and used the Versant HCV™ method to measure HCV viral load. In these experiments the calculated EC50s were PEG-rIL-29-C172S, 0.117 ng/mL; PEGASYS®, 0.004 ng/mL; PEG®-Intron, 0.002 ng/mL. All cytokines tested reduced HCV viral load by greater than 99% at the maximum concentration tested (PEG-rIL-29-C172S, 99.9% HCV RNA reduction at 1000 ng/mL; PEGASYS®, 99.78% HCV RNA reduction at 1000 ng/mL; PEG®-Intron, 99.85% HCV RNA reduction at 1000 ng/mL).

[321] Additional experiments tested PEG-rIL-29-C172S, PEG-rIL-29-d2-7, PEGASYS® and PEG®-Intron and used the dot blot hybridization assay described above. In these experiments the calculated EC50s were PEG-rIL-29-C172S, 0.356 ng/mL; PEG-rIL-29-d2-7, 0.516 ng/mL; PEGASYS®, 0.004 ng/mL; PEG®-Intron, 0.002 ng/mL. All cytokines tested reduced HCV viral load by greater than 90% at 100 ng/mL, the maximum concentration tested.

[322] In conclusion, PEG-rIL-29-C172S and PEG-rIL-29-d2-7 are able to reduce HCV viral load in a dose-dependent manner in the HCV Replicon model similar to that of the marketed pegylated interferon alphas, PEGASYS® and PEG®-Intron.

[323] The complete disclosure of all patents, patent applications, and publications, and electronically available material (e.g., GenBank amino acid and nucleotide sequence submissions) cited herein are incorporated by reference. The foregoing detailed description and examples have been given for clarity of understanding only. No unnecessary limitations are to be understood therefrom. The invention is not limited to the exact details shown and described, for variations obvious to one skilled in the art will be included within the invention defined by the claims.

CLAIMS

What is claimed is:

1. A method of treating a viral infection in a mammal, the method comprising:

administering to the mammal a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150, wherein after administration of the polypeptide the viral load is reduced.

2. The method of claim 1 wherein the polypeptide is a recombinant polypeptide.

3. The method of claim 1 wherein the viral infection is a virus selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus, human immunodeficiency virus, respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus, avian influenza A virus, adenovirus, parainfluenza virus, rhino virus, coxsackie virus, vaccinia virus, west nile virus, severe acute respiratory syndrome, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus.

4. The method of claim 1 wherein the polypeptide is conjugated to a polyalkyl oxide moiety.

5. The method of claim 4 wherein the polyalkyl oxide moiety is polyethylene glycol.

6. The method of claim 5 wherein the polyethylene glycol is monomethoxy-PEG propionaldehyde.

7. The method of claim 6 wherein the monomethoxy-PEG propionaldehyde has a molecular weight of about 20 Kd or 30Kd.

8. The method of claim 6 wherein the monomethoxy-PEG propionaldehyde is linear or branched.

9. The method of claim 6 wherein the monomethoxy-PEG propionaldehyde is conjugated N-terminally to the polypeptide.

10. A method of treating liver inflammation in a mammal, the method comprising:

administering to the mammal a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150, wherein after administration the liver inflammation is reduced.

11. The method of claim 10 wherein the polypeptide is a recombinant polypeptide.

12. The method of claim 10 wherein the liver inflammation is associated with a viral infection.

13. The method of claim 12 wherein the viral infection is a virus selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus, human immunodeficiency virus, respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus, avian influenza A virus, adenovirus, parainfluenza virus, rhino virus, coxsackie virus, vaccinia virus, west nile virus, severe acute respiratory syndrome, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus.

14. The method of claim 10 wherein the polypeptide is conjugated to a polyalkyl oxide moiety.

15. The method of claim 14 wherein the polyalkyl oxide moiety is polyethylene glycol.

16. The method of claim 15 wherein the polyethylene glycol is monomethoxy-PEG propionaldehyde.

17. The method of claim 16 wherein the monomethoxy-PEG propionaldehyde has a molecular weight of about 20 Kd or 30Kd.

18. The method of claim 16 wherein the monomethoxy-PEG propionaldehyde is linear or branched.

19. The method of claim 16 wherein the monomethoxy-PEG propionaldehyde is conjugated N-terminally to the polypeptide.

20. A method of treating a viral infection in a mammal, the method comprising:

administering to the mammal a composition comprising:

a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150; and

a pharmaceutically acceptable vehicle; and

wherein after administration of the composition the viral load is reduced.

21. The method of claim 20 wherein the viral infection is a virus selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus, human immunodeficiency virus, respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus, avian influenza A virus, adenovirus, parainfluenza virus, rhino virus, coxsackie virus, vaccinia virus, west nile virus, severe acute respiratory syndrome, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus.

22. The method of claim 20 wherein the polypeptide is conjugated to a polyalkyl oxide moiety.

23. The method of claim 22 wherein the polyalkyl oxide moiety is polyethylene glycol.

24. The method of claim 23 wherein the polyethylene glycol is monomethoxy-PEG propionaldehyde.

25. The method of claim 24 wherein the monomethoxy-PEG propionaldehyde has a molecular weight of about 20 Kd or 30Kd.

26. The method of claim 24 wherein the monomethoxy-PEG propionaldehyde is linear or branched.

27. The method of claim 27 wherein the monomethoxy-PEG propionaldehyde is conjugated N-terminally to the polypeptide.

28. A method of treating liver inflammation in a mammal, the method comprising:

administering to the mammal a therapeutically effective amount of a composition comprising:

an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150; and

a pharmaceutically acceptable vehicle; and

wherein after administration of the composition the liver inflammation is reduced.

29. A method of treating a viral infection comprising administering to an immunocompromised mammal with a viral infection a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150, wherein after administration of the polypeptide the viral infection is reduced.

30. The method of claim 29 wherein the immunocompromised mammal is infected with a virus selected from the group consisting of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis D virus, human immunodeficiency virus, respiratory syncytial virus, herpes virus, Epstein-Barr virus, influenza virus, avian influenza A virus, adenovirus, parainfluenza virus, rhino virus, coxsackie virus, vaccinia virus, west nile virus, severe acute respiratory syndrome, dengue virus, venezuelan equine encephalitis virus, pichinde virus and polio virus.

31. A method of treating a viral infection in an immunocompromised mammal, the method comprising;

administering to the immunocompromised mammal a composition comprising:

a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150; and

a pharmaceutically acceptable vehicle; and

wherein after administration of the composition the viral infection is reduced.

32. A kit comprising:

a composition comprising:

a therapeutically effective amount of an isolated polypeptide comprising an amino acid sequence having at least 95% sequence identity to an amino acid sequence selected from the group consisting of SEQ ID NOs:138, 140, 142, 144, 146, 148 and 150; and

a pharmaceutically acceptable vehicle.

33. The kit of claim 32 further comprising an antiviral agent.

34. The kit of claim 33 wherein the antiviral agent is selected from the group of Interferon alpha, Interferon beta, Interferine gamma, Serine Protease Inhibitor, Polymerase Inhibitor, Antisense Inhibitor, and combinations thereof.

35. The kit of claim 34 wherein the antiviral agent is RIBAVIRIN.

36. The kit of claim 34 wherein the antiviral agent is PEG-INTRON.

37. The kit of claim 34 wherein the antiviral agent is PEGASYS.

SEQUENCE LISTING

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Ser Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
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Leu Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg
            180                 185                 190
Thr Ser Thr His Pro Glu Ser Thr
        195                 200


<210> 5
<211> 615
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)...(615)

<221> misc_feature
<222> (0)...(0)
<223> IL-28B

<400> 5
atg acc ggg gac tgc atg cca gtg ctg gtg ctg atg gcc gca gtg ctg   48
Met Thr Gly Asp Cys Met Pro Val Leu Val Leu Met Ala Ala Val Leu
 1               5                  10                  15

acc gtg act gga gca gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg   96
Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro
            20                  25                  30

gat gca agg ggc tgc cac ata gcc cag ttc aag tcc ctg tct cca cag   144
Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln
        35                  40                  45

gag ctg cag gcc ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt   192
Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu
    50                  55                  60

ctg ctg aag gac tgc aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg   240
Leu Leu Lys Asp Cys Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp
65                  70                  75                  80

gac ctg agg cag ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct   288
Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala
                85                  90                  95

gag ctg gcc ctg acg ctg aag gtt ctg gag gcc acc gct gac act gac   336
Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp
            100                 105                 110

cca gcc ctg ggg gat gtc ttg gac cag ccc ctt cac acc ctg cac cat   384
Pro Ala Leu Gly Asp Val Leu Asp Gln Pro Leu His Thr Leu His His
```

```
        115                 120                 125

atc ctc tcc cag ctc cgg gcc tgt gtg agt cgt cag ggc ccg ggc acc   432
Ile Leu Ser Gln Leu Arg Ala Cys Val Ser Arg Gln Gly Pro Gly Thr
    130                 135                 140

cag atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc cgc ctc   480
Gln Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly Arg Leu
145                 150                 155                 160

cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag gag tcc cct   528
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Pro
                165                 170                 175

ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   576
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
            180                 185                 190

cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc               615
Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
        195                 200                 205


<210> 6
<211> 205
<212> PRT
<213> Homo sapiens

<400> 6
Met Thr Gly Asp Cys Met Pro Val Leu Val Leu Met Ala Ala Val Leu
 1                5                  10                  15
Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro
            20                  25                  30
Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln
        35                  40                  45
Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu
    50                  55                  60
Leu Leu Lys Asp Cys Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp
65                  70                  75                  80
Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala
                85                  90                  95
Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp
            100                 105                 110
Pro Ala Leu Gly Asp Val Leu Asp Gln Pro Leu His Thr Leu His His
        115                 120                 125
Ile Leu Ser Gln Leu Arg Ala Cys Val Ser Arg Gln Gly Pro Gly Thr
    130                 135                 140
Gln Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly Arg Leu
145                 150                 155                 160
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Pro
                165                 170                 175
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
            180                 185                 190
Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
        195                 200                 205


<210> 7
<211> 633
<212> DNA
<213> Mus musculus

<220>
<221> CDS
<222> (22)...(630)
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<400> 7
tcacagaccc cggagagcaa c atg aag cca gaa aca gct ggg ggc cac atg 51
Met Lys Pro Glu Thr Ala Gly Gly His Met
1 5 10

ctc ctc ctg ctg ttg cct ctg ctg ctg gcc gca gtg ctg aca aga acc 99
Leu Leu Leu Leu Leu Pro Leu Leu Leu Ala Ala Val Leu Thr Arg Thr
15 20 25

caa gct gac cct gtc ccc agg gcc acc agg ctc cca gtg gaa gca aag 147
Gln Ala Asp Pro Val Pro Arg Ala Thr Arg Leu Pro Val Glu Ala Lys
30 35 40

gat tgc cac att gct cag ttc aag tct ctg tcc cca aaa gag ctg cag 195
Asp Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Lys Glu Leu Gln
45 50 55

gcc ttc aaa aag gcc aag gat gcc atc gag aag agg ctg ctt gag aag 243
Ala Phe Lys Lys Ala Lys Asp Ala Ile Glu Lys Arg Leu Leu Glu Lys
60 65 70

gac ctg agg tgc agt tcc cac ctc ttc ccc agg gcc tgg gac ctg aag 291
Asp Leu Arg Cys Ser Ser His Leu Phe Pro Arg Ala Trp Asp Leu Lys
75 80 85 90

cag ctg cag gtc caa gag cgc ccc aag gcc ttg cag gct gag gtg gcc 339
Gln Leu Gln Val Gln Glu Arg Pro Lys Ala Leu Gln Ala Glu Val Ala
95 100 105

ctg acc ctg aag gtc tgg gag aac atg act gac tca gcc ctg gcc acc 387
Leu Thr Leu Lys Val Trp Glu Asn Met Thr Asp Ser Ala Leu Ala Thr
110 115 120

atc ctg ggc cag cct ctt cat aca ctg agc cac att cac tcc cag ctg 435
Ile Leu Gly Gln Pro Leu His Thr Leu Ser His Ile His Ser Gln Leu
125 130 135

cag acc tgt aca cag ctt cag gcc aca gca gag ccc agg tcc ccg agc 483
Gln Thr Cys Thr Gln Leu Gln Ala Thr Ala Glu Pro Arg Ser Pro Ser
140 145 150

cgc cgc ctc tcc cgc tgg ctg cac agg ctc cag gag gcc cag agc aag 531
Arg Arg Leu Ser Arg Trp Leu His Arg Leu Gln Glu Ala Gln Ser Lys
155 160 165 170

gag acc cct ggc tgc ctg gag gcc tct gtc acc tcc aac ctg ttt cgc 579
Glu Thr Pro Gly Cys Leu Glu Ala Ser Val Thr Ser Asn Leu Phe Arg
175 180 185

ctg ctc acc cgg gac ctc aag tgt gtg gcc aat gga gac cag tgt gtc 627
Leu Leu Thr Arg Asp Leu Lys Cys Val Ala Asn Gly Asp Gln Cys Val
190 195 200

tga cct 633
*

<210> 8
<211> 202
<212> PRT
<213> Mus musculus

<400> 8
Met Lys Pro Glu Thr Ala Gly Gly His Met Leu Leu Leu Leu Leu Pro
1 5 10 15

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Leu Leu Leu Ala Ala Val Leu Thr Arg Thr Gln Ala Asp Pro Val Pro
            20                  25                  30
Arg Ala Thr Arg Leu Pro Val Glu Ala Lys Asp Cys His Ile Ala Gln
        35                  40                  45
Phe Lys Ser Leu Ser Pro Lys Glu Leu Gln Ala Phe Lys Lys Ala Lys
    50                  55                  60
Asp Ala Ile Glu Lys Arg Leu Leu Glu Lys Asp Leu Arg Cys Ser Ser
65                  70                  75                  80
His Leu Phe Pro Arg Ala Trp Asp Leu Lys Gln Leu Gln Val Gln Glu
                85                  90                  95
Arg Pro Lys Ala Leu Gln Ala Glu Val Ala Leu Thr Leu Lys Val Trp
            100                 105                 110
Glu Asn Met Thr Asp Ser Ala Leu Ala Thr Ile Leu Gly Gln Pro Leu
        115                 120                 125
His Thr Leu Ser His Ile His Ser Gln Leu Gln Thr Cys Thr Gln Leu
    130                 135                 140
Gln Ala Thr Ala Glu Pro Arg Ser Pro Ser Arg Arg Leu Ser Arg Trp
145                 150                 155                 160
Leu His Arg Leu Gln Glu Ala Gln Ser Lys Glu Thr Pro Gly Cys Leu
                165                 170                 175
Glu Ala Ser Val Thr Ser Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu
            180                 185                 190
Lys Cys Val Ala Asn Gly Asp Gln Cys Val
        195                 200
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<210> 9
<211> 632
<212> DNA
<213> Mus musculus

<220>
<221> CDS
<222> (22)...(630)

<400> 9

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tcacagaccc cggagagcaa c atg aag cca gaa aca gct ggg ggc cac atg   51
                        Met Lys Pro Glu Thr Ala Gly Gly His Met
                         1               5                  10

ctc ctc ctg ctg ttg cct ctg ctg ctg gcc gca gtg ctg aca aga acc   99
Leu Leu Leu Leu Leu Pro Leu Leu Leu Ala Ala Val Leu Thr Arg Thr
                15                  20                  25

caa gct gac cct gtc ccc agg gcc acc agg ctc cca gtg gaa gca aag   147
Gln Ala Asp Pro Val Pro Arg Ala Thr Arg Leu Pro Val Glu Ala Lys
            30                  35                  40

gat tgc cac att gct cag ttc aag tct ctg tcc cca aaa gag ctg cag   195
Asp Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Lys Glu Leu Gln
        45                  50                  55

gcc ttc aaa aag gcc aag ggt gcc atc gag aag agg ctg ctt gag aag   243
Ala Phe Lys Lys Ala Lys Gly Ala Ile Glu Lys Arg Leu Leu Glu Lys
    60                  65                  70

gac atg agg tgc agt tcc cac ctc atc tcc agg gcc tgg gac ctg aag   291
Asp Met Arg Cys Ser Ser His Leu Ile Ser Arg Ala Trp Asp Leu Lys
75                  80                  85                  90

cag ctg cag gtc caa gag cgc ccc aag gcc ttg cag gct gag gtg gcc   339
Gln Leu Gln Val Gln Glu Arg Pro Lys Ala Leu Gln Ala Glu Val Ala
                95                  100                 105

ctg acc ctg aag gtc tgg gag aac ata aat gac tca gcc ctg acc acc   387
Leu Thr Leu Lys Val Trp Glu Asn Ile Asn Asp Ser Ala Leu Thr Thr
```

```
            110                 115                 120

atc ctg ggc cag cct ctt cat aca ctg agc cac att cac tcc cag ctg   435
Ile Leu Gly Gln Pro Leu His Thr Leu Ser His Ile His Ser Gln Leu
        125                 130                 135

cag acc tgt aca cag ctt cag gcc aca gca gag ccc aag ccc ccg agt   483
Gln Thr Cys Thr Gln Leu Gln Ala Thr Ala Glu Pro Lys Pro Pro Ser
    140                 145                 150

cgc cgc ctc tcc cgc tgg ctg cac agg ctc cag gag gcc cag agc aag   531
Arg Arg Leu Ser Arg Trp Leu His Arg Leu Gln Glu Ala Gln Ser Lys
155                 160                 165                 170

gag act cct ggc tgc ctg gag gac tct gtc acc tcc aac ctg ttt caa   579
Glu Thr Pro Gly Cys Leu Glu Asp Ser Val Thr Ser Asn Leu Phe Gln
                175                 180                 185

ctg ctc ctc cgg gac ctc aag tgt gtg gcc agt gga gac cag tgt gtc   627
Leu Leu Leu Arg Asp Leu Lys Cys Val Ala Ser Gly Asp Gln Cys Val
            190                 195                 200

tga cc                                                            632
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```

<210> 10
<211> 202
<212> PRT
<213> Mus musculus

<400> 10

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Met Lys Pro Glu Thr Ala Gly Gly His Met Leu Leu Leu Leu Leu Pro
 1               5                  10                  15
Leu Leu Leu Ala Ala Val Leu Thr Arg Thr Gln Ala Asp Pro Val Pro
            20                  25                  30
Arg Ala Thr Arg Leu Pro Val Glu Ala Lys Asp Cys His Ile Ala Gln
        35                  40                  45
Phe Lys Ser Leu Ser Pro Lys Glu Leu Gln Ala Phe Lys Lys Ala Lys
    50                  55                  60
Gly Ala Ile Glu Lys Arg Leu Leu Glu Lys Asp Met Arg Cys Ser Ser
65                  70                  75                  80
His Leu Ile Ser Arg Ala Trp Asp Leu Lys Gln Leu Gln Val Gln Glu
                85                  90                  95
Arg Pro Lys Ala Leu Gln Ala Glu Val Ala Leu Thr Leu Lys Val Trp
            100                 105                 110
Glu Asn Ile Asn Asp Ser Ala Leu Thr Thr Ile Leu Gly Gln Pro Leu
        115                 120                 125
His Thr Leu Ser His Ile His Ser Gln Leu Gln Thr Cys Thr Gln Leu
    130                 135                 140
Gln Ala Thr Ala Glu Pro Lys Pro Pro Ser Arg Arg Leu Ser Arg Trp
145                 150                 155                 160
Leu His Arg Leu Gln Glu Ala Gln Ser Lys Glu Thr Pro Gly Cys Leu
                165                 170                 175
Glu Asp Ser Val Thr Ser Asn Leu Phe Gln Leu Leu Leu Arg Asp Leu
            180                 185                 190
Lys Cys Val Ala Ser Gly Asp Gln Cys Val
        195                 200
```

<210> 11
<211> 1563
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)...(1563)

<221> misc_feature
<222> (0)...(0)
<223> IL-28RA

<400> 11

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atg gcg ggg ccc gag cgc tgg ggc ccc ctg ctc ctg tgc ctg ctg cag   48
Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15

gcc gct cca ggg agg ccc cgt ctg gcc cct ccc cag aat gtg acg ctg   96
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
            20                  25                  30

ctc tcc cag aac ttc agc gtg tac ctg aca tgg ctc cca ggg ctt ggc   144
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
        35                  40                  45

aac ccc cag gat gtg acc tat ttt gtg gcc tat cag agc tct ccc acc   192
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
    50                  55                  60

cgt aga cgg tgg cgc gaa gtg gaa gag tgt gcg gga acc aag gag ctg   240
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65                  70                  75                  80

cta tgt tct atg atg tgc ctg aag aaa cag gac ctg tac aac aag ttc   288
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                85                  90                  95

aag gga cgc gtg cgg acg gtt tct ccc agc tcc aag tcc ccc tgg gtg   336
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110

gag tcc gaa tac ctg gat tac ctt ttt gaa gtg gag ccg gcc cca cct   384
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125

gtc ctg gtg ctc acc cag acg gag gag atc ctg agt gcc aat gcc acg   432
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140

tac cag ctg ccc ccc tgc atg ccc cca ctg gat ctg aag tat gag gtg   480
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Asp Leu Lys Tyr Glu Val
145                 150                 155                 160

gca ttc tgg aag gag ggg gcc gga aac aag acc cta ttt cca gtc act   528
Ala Phe Trp Lys Glu Gly Ala Gly Asn Lys Thr Leu Phe Pro Val Thr
                165                 170                 175

ccc cat ggc cag cca gtc cag atc act ctc cag cca gct gcc agc gaa   576
Pro His Gly Gln Pro Val Gln Ile Thr Leu Gln Pro Ala Ala Ser Glu
            180                 185                 190

cac cac tgc ctc agt gcc aga acc atc tac acg ttc agt gtc ccg aaa   624
His His Cys Leu Ser Ala Arg Thr Ile Tyr Thr Phe Ser Val Pro Lys
        195                 200                 205

tac agc aag ttc tct aag ccc acc tgc ttc ttg ctg gag gtc cca gaa   672
Tyr Ser Lys Phe Ser Lys Pro Thr Cys Phe Leu Leu Glu Val Pro Glu
    210                 215                 220

gcc aac tgg gct ttc ctg gtg ctg cca tcg ctt ctg ata ctg ctg tta   720
```

```
Ala Asn Trp Ala Phe Leu Val Leu Pro Ser Leu Leu Ile Leu Leu Leu
225                 230                 235                 240

gta att gcc gca ggg ggt gtg atc tgg aag acc ctc atg ggg aac ccc   768
Val Ile Ala Ala Gly Gly Val Ile Trp Lys Thr Leu Met Gly Asn Pro
                245                 250                 255

tgg ttt cag cgg gca aag atg cca cgg gcc ctg gac ttt tct gga cac   816
Trp Phe Gln Arg Ala Lys Met Pro Arg Ala Leu Asp Phe Ser Gly His
            260                 265                 270

aca cac cct gtg gca acc ttt cag ccc agc aga cca gag tcc gtg aat   864
Thr His Pro Val Ala Thr Phe Gln Pro Ser Arg Pro Glu Ser Val Asn
        275                 280                 285

gac ttg ttc ctc tgt ccc caa aag gaa ctg acc aga ggg gtc agg ccg   912
Asp Leu Phe Leu Cys Pro Gln Lys Glu Leu Thr Arg Gly Val Arg Pro
    290                 295                 300

acg cct cga gtc agg gcc cca gcc acc caa cag aca aga tgg aag aag   960
Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln Thr Arg Trp Lys Lys
305                 310                 315                 320

gac ctt gca gag gac gaa gag gag gag gat gag gag gac aca gaa gat  1008
Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp Thr Glu Asp
                325                 330                 335

ggc gtc agc ttc cag ccc tac att gaa cca cct tct ttc ctg ggg caa  1056
Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro Ser Phe Leu Gly Gln
            340                 345                 350

gag cac cag gct cca ggg cac tcg gag gct ggt ggg gtg gac tca ggg  1104
Glu His Gln Ala Pro Gly His Ser Glu Ala Gly Gly Val Asp Ser Gly
        355                 360                 365

agg ccc agg gct cct ctg gtc cca agc gaa ggc tcc tct gct tgg gat  1152
Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly Ser Ser Ala Trp Asp
    370                 375                 380

tct tca gac aga agc tgg gcc agc act gtg gac tcc tcc tgg gac agg  1200
Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp Ser Ser Trp Asp Arg
385                 390                 395                 400

gct ggg tcc tct ggc tat ttg gct gag aag ggg cca ggc caa ggg ccg  1248
Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly Pro Gly Gln Gly Pro
                405                 410                 415

ggt ggg gat ggg cac caa gaa tct ctc cca cca cct gaa ttc tcc aag  1296
Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro Pro Glu Phe Ser Lys
            420                 425                 430

gac tcg ggt ttc ctg gaa gag ctc cca gaa gat aac ctc tcc tcc tgg  1344
Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp Asn Leu Ser Ser Trp
        435                 440                 445

gcc acc tgg ggc acc tta cca ccg gag ccg aat ctg gtc cct ggg gga  1392
Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn Leu Val Pro Gly Gly
    450                 455                 460

ccc cca gtt tct ctt cag aca ctg acc ttc tgc tgg gaa agc agc cct  1440
Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys Trp Glu Ser Ser Pro
465                 470                 475                 480

gag gag gaa gag gag gcg agg gaa tca gaa att gag gac agc gat gcg  1488
Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile Glu Asp Ser Asp Ala
                485                 490                 495
```

```
ggc agc tgg ggg gct gag agc acc cag agg acc gag gac agg ggc cgg   1536
Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr Glu Asp Arg Gly Arg
            500                 505                 510

aca ttg ggg cat tac atg gcc agg tga                           1563
Thr Leu Gly His Tyr Met Ala Arg  *
        515                 520
```

<210> 12
<211> 520
<212> PRT
<213> Homo sapiens

<400> 12

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Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
            20                  25                  30
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
        35                  40                  45
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
    50                  55                  60
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65                  70                  75                  80
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                85                  90                  95
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Asp Leu Lys Tyr Glu Val
145                 150                 155                 160
Ala Phe Trp Lys Glu Gly Ala Gly Asn Lys Thr Leu Phe Pro Val Thr
                165                 170                 175
Pro His Gly Gln Pro Val Gln Ile Thr Leu Gln Pro Ala Ala Ser Glu
            180                 185                 190
His His Cys Leu Ser Ala Arg Thr Ile Tyr Thr Phe Ser Val Pro Lys
        195                 200                 205
Tyr Ser Lys Phe Ser Lys Pro Thr Cys Phe Leu Leu Glu Val Pro Glu
    210                 215                 220
Ala Asn Trp Ala Phe Leu Val Leu Pro Ser Leu Leu Ile Leu Leu Leu
225                 230                 235                 240
Val Ile Ala Ala Gly Gly Val Ile Trp Lys Thr Leu Met Gly Asn Pro
                245                 250                 255
Trp Phe Gln Arg Ala Lys Met Pro Arg Ala Leu Asp Phe Ser Gly His
            260                 265                 270
Thr His Pro Val Ala Thr Phe Gln Pro Ser Arg Pro Glu Ser Val Asn
        275                 280                 285
Asp Leu Phe Leu Cys Pro Gln Lys Glu Leu Thr Arg Gly Val Arg Pro
    290                 295                 300
Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln Thr Arg Trp Lys Lys
305                 310                 315                 320
Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp Thr Glu Asp
                325                 330                 335
Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro Ser Phe Leu Gly Gln
            340                 345                 350
Glu His Gln Ala Pro Gly His Ser Glu Ala Gly Gly Val Asp Ser Gly
        355                 360                 365
Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly Ser Ser Ala Trp Asp
    370                 375                 380
Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp Ser Ser Trp Asp Arg
385                 390                 395                 400
```

```
Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly Pro Gly Gln Gly Pro
                405                 410                 415
Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro Pro Glu Phe Ser Lys
            420                 425                 430
Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp Asn Leu Ser Ser Trp
        435                 440                 445
Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn Leu Val Pro Gly Gly
    450                 455                 460
Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys Trp Glu Ser Ser Pro
465                 470                 475                 480
Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile Glu Asp Ser Asp Ala
                485                 490                 495
Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr Glu Asp Arg Gly Arg
            500                 505                 510
Thr Leu Gly His Tyr Met Ala Arg
        515                 520


<210> 13
<211> 1476
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)...(1476)

<221> misc_feature
<222> (0)...(0)
<223> IL-28RA splice variant

<400> 13
atg gcg ggg ccc gag cgc tgg ggc ccc ctg ctc ctg tgc ctg ctg cag   48
Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15

gcc gct cca ggg agg ccc cgt ctg gcc cct ccc cag aat gtg acg ctg   96
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
            20                  25                  30

ctc tcc cag aac ttc agc gtg tac ctg aca tgg ctc cca ggg ctt ggc   144
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
        35                  40                  45

aac ccc cag gat gtg acc tat ttt gtg gcc tat cag agc tct ccc acc   192
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
    50                  55                  60

cgt aga cgg tgg cgc gaa gtg gaa gag tgt gcg gga acc aag gag ctg   240
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65                  70                  75                  80

cta tgt tct atg atg tgc ctg aag aaa cag gac ctg tac aac aag ttc   288
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                85                  90                  95

aag gga cgc gtg cgg acg gtt tct ccc agc tcc aag tcc ccc tgg gtg   336
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110

gag tcc gaa tac ctg gat tac ctt ttt gaa gtg gag ccg gcc cca cct   384
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125

gtc ctg gtg ctc acc cag acg gag gag atc ctg agt gcc aat gcc acg   432
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
```

```
    130                 135                 140

tac cag ctg ccc ccc tgc atg ccc cca ctg ttt ctg aag tat gag gtg   480
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Phe Leu Lys Tyr Glu Val
145                 150                 155                 160

gca ttt tgg ggg ggg ggg gcc gga acc aag acc cta ttt cca gtc act   528
Ala Phe Trp Gly Gly Gly Ala Gly Thr Lys Thr Leu Phe Pro Val Thr
                165                 170                 175

ccc cat ggc cag cca gtc cag atc act ctc cag cca gct gcc agc gaa   576
Pro His Gly Gln Pro Val Gln Ile Thr Leu Gln Pro Ala Ala Ser Glu
            180                 185                 190

cac cac tgc ctc agt gcc aga acc atc tac acg ttc agt gtc ccg aaa   624
His His Cys Leu Ser Ala Arg Thr Ile Tyr Thr Phe Ser Val Pro Lys
        195                 200                 205

tac agc aag ttc tct aag ccc acc tgc ttc ttg ctg gag gtc cca gaa   672
Tyr Ser Lys Phe Ser Lys Pro Thr Cys Phe Leu Leu Glu Val Pro Glu
    210                 215                 220

gcc aac tgg gct ttc ctg gtg ctg cca tcg ctt ctg ata ctg ctg tta   720
Ala Asn Trp Ala Phe Leu Val Leu Pro Ser Leu Leu Ile Leu Leu Leu
225                 230                 235                 240

gta att gcc gca ggg ggt gtg atc tgg aag acc ctc atg ggg aac ccc   768
Val Ile Ala Ala Gly Gly Val Ile Trp Lys Thr Leu Met Gly Asn Pro
                245                 250                 255

tgg ttt cag cgg gca aag atg cca cgg gcc ctg gaa ctg acc aga ggg   816
Trp Phe Gln Arg Ala Lys Met Pro Arg Ala Leu Glu Leu Thr Arg Gly
            260                 265                 270

gtc agg ccg acg cct cga gtc agg gcc cca gcc acc caa cag aca aga   864
Val Arg Pro Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln Thr Arg
        275                 280                 285

tgg aag aag gac ctt gca gag gac gaa gag gag gag gat gag gag gac   912
Trp Lys Lys Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp
    290                 295                 300

aca gaa gat ggc gtc agc ttc cag ccc tac att gaa cca cct tct ttc   960
Thr Glu Asp Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro Ser Phe
305                 310                 315                 320

ctg ggg caa gag cac cag gct cca ggg cac tcg gag gct ggt ggg gtg   1008
Leu Gly Gln Glu His Gln Ala Pro Gly His Ser Glu Ala Gly Gly Val
                325                 330                 335

gac tca ggg agg ccc agg gct cct ctg gtc cca agc gaa ggc tcc tct   1056
Asp Ser Gly Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly Ser Ser
            340                 345                 350

gct tgg gat tct tca gac aga agc tgg gcc agc act gtg gac tcc tcc   1104
Ala Trp Asp Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp Ser Ser
        355                 360                 365

tgg gac agg gct ggg tcc tct ggc tat ttg gct gag aag ggg cca ggc   1152
Trp Asp Arg Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly Pro Gly
    370                 375                 380

caa ggg ccg ggt ggg gat ggg cac caa gaa tct ctc cca cca cct gaa   1200
Gln Gly Pro Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro Pro Glu
385                 390                 395                 400
```

```
ttc tcc aag gac tcg ggt ttc ctg gaa gag ctc cca gaa gat aac ctc   1248
Phe Ser Lys Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp Asn Leu
                405                 410                 415

tcc tcc tgg gcc acc tgg ggc acc tta cca ccg gag ccg aat ctg gtc   1296
Ser Ser Trp Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn Leu Val
            420                 425                 430

cct ggg gga ccc cca gtt tct ctt cag aca ctg acc ttc tgc tgg gaa   1344
Pro Gly Gly Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys Trp Glu
        435                 440                 445

agc agc cct gag gag gaa gag gag gcg agg gaa tca gaa att gag gac   1392
Ser Ser Pro Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile Glu Asp
    450                 455                 460

agc gat gcg ggc agc tgg ggg gct gag agc acc cag agg acc gag gac   1440
Ser Asp Ala Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr Glu Asp
465                 470                 475                 480

agg ggc cgg aca ttg ggg cat tac atg gcc agg tga                   1476
Arg Gly Arg Thr Leu Gly His Tyr Met Ala Arg  *
                485                 490
```

<210> 14
<211> 491
<212> PRT
<213> Homo sapiens

<400> 14

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Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
            20                  25                  30
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
        35                  40                  45
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
    50                  55                  60
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65                  70                  75                  80
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                85                  90                  95
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Phe Leu Lys Tyr Glu Val
145                 150                 155                 160
Ala Phe Trp Gly Gly Gly Ala Gly Thr Lys Thr Leu Phe Pro Val Thr
                165                 170                 175
Pro His Gly Gln Pro Val Gln Ile Thr Leu Gln Pro Ala Ala Ser Glu
            180                 185                 190
His His Cys Leu Ser Ala Arg Thr Ile Tyr Thr Phe Ser Val Pro Lys
        195                 200                 205
Tyr Ser Lys Phe Ser Lys Pro Thr Cys Phe Leu Leu Glu Val Pro Glu
    210                 215                 220
Ala Asn Trp Ala Phe Leu Val Leu Pro Ser Leu Leu Ile Leu Leu Leu
225                 230                 235                 240
Val Ile Ala Ala Gly Gly Val Ile Trp Lys Thr Leu Met Gly Asn Pro
                245                 250                 255
Trp Phe Gln Arg Ala Lys Met Pro Arg Ala Leu Glu Leu Thr Arg Gly
            260                 265                 270
Val Arg Pro Thr Pro Arg Val Arg Ala Pro Ala Thr Gln Gln Thr Arg
```

```
        275                 280                 285
Trp Lys Lys Asp Leu Ala Glu Asp Glu Glu Glu Glu Asp Glu Glu Asp
    290                 295                 300
Thr Glu Asp Gly Val Ser Phe Gln Pro Tyr Ile Glu Pro Pro Ser Phe
305                 310                 315                 320
Leu Gly Gln Glu His Gln Ala Pro Gly His Ser Glu Ala Gly Gly Val
                325                 330                 335
Asp Ser Gly Arg Pro Arg Ala Pro Leu Val Pro Ser Glu Gly Ser Ser
            340                 345                 350
Ala Trp Asp Ser Ser Asp Arg Ser Trp Ala Ser Thr Val Asp Ser Ser
        355                 360                 365
Trp Asp Arg Ala Gly Ser Ser Gly Tyr Leu Ala Glu Lys Gly Pro Gly
    370                 375                 380
Gln Gly Pro Gly Gly Asp Gly His Gln Glu Ser Leu Pro Pro Pro Glu
385                 390                 395                 400
Phe Ser Lys Asp Ser Gly Phe Leu Glu Glu Leu Pro Glu Asp Asn Leu
                405                 410                 415
Ser Ser Trp Ala Thr Trp Gly Thr Leu Pro Pro Glu Pro Asn Leu Val
            420                 425                 430
Pro Gly Gly Pro Pro Val Ser Leu Gln Thr Leu Thr Phe Cys Trp Glu
        435                 440                 445
Ser Ser Pro Glu Glu Glu Glu Glu Ala Arg Glu Ser Glu Ile Glu Asp
    450                 455                 460
Ser Asp Ala Gly Ser Trp Gly Ala Glu Ser Thr Gln Arg Thr Glu Asp
465                 470                 475                 480
Arg Gly Arg Thr Leu Gly His Tyr Met Ala Arg
                485                 490
```

<210> 15
<211> 674
<212> DNA
<213> Homo sapiens

<220>
<221> CDS
<222> (1)...(636)

<221> misc_feature
<222> (0)...(0)
<223> IL-28RA soluble variant

<400> 15

```
atg gcg ggg ccc gag cgc tgg ggc ccc ctg ctc ctg tgc ctg ctg cag   48
Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15

gcc gct cca ggg agg ccc cgt ctg gcc cct ccc cag aat gtg acg ctg   96
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
             20                  25                  30

ctc tcc cag aac ttc agc gtg tac ctg aca tgg ctc cca ggg ctt ggc   144
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
         35                  40                  45

aac ccc cag gat gtg acc tat ttt gtg gcc tat cag agc tct ccc acc   192
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
     50                  55                  60

cgt aga cgg tgg cgc gaa gtg gaa gag tgt gcg gga acc aag gag ctg   240
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
 65                  70                  75                  80

cta tgt tct atg atg tgc ctg aag aaa cag gac ctg tac aac aag ttc   288
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                 85                  90                  95
```

```
aag gga cgc gtg cgg acg gtt tct ccc agc tcc aag tcc ccc tgg gtg   336
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110

gag tcc gaa tac ctg gat tac ctt ttt gaa gtg gag ccg gcc cca cct   384
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125

gtc ctg gtg ctc acc cag acg gag gag atc ctg agt gcc aat gcc acg   432
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140

tac cag ctg ccc ccc tgc atg ccc cca ctg gat ctg aag tat gag gtg   480
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Asp Leu Lys Tyr Glu Val
145                 150                 155                 160

gca ttc tgg aag gag ggg gcc gga aac aag gtg gga agc tcc ttt cct   528
Ala Phe Trp Lys Glu Gly Ala Gly Asn Lys Val Gly Ser Ser Phe Pro
                165                 170                 175

gcc ccc agg cta ggc ccg ctc ctc cac ccc ttc tta ctc agg ttc ttc   576
Ala Pro Arg Leu Gly Pro Leu Leu His Pro Phe Leu Leu Arg Phe Phe
            180                 185                 190

tca ccc tcc cag cct gct cct gca ccc ctc ctc cag gaa gtc ttc cct   624
Ser Pro Ser Gln Pro Ala Pro Ala Pro Leu Leu Gln Glu Val Phe Pro
        195                 200                 205

gta cac tcc tga cttctggcag tcagccctaa taaaatctga tcaaagta         674
Val His Ser  *
    210
```

<210> 16
<211> 211
<212> PRT
<213> Homo sapiens

<400> 16

```
Met Ala Gly Pro Glu Arg Trp Gly Pro Leu Leu Leu Cys Leu Leu Gln
 1               5                  10                  15
Ala Ala Pro Gly Arg Pro Arg Leu Ala Pro Pro Gln Asn Val Thr Leu
            20                  25                  30
Leu Ser Gln Asn Phe Ser Val Tyr Leu Thr Trp Leu Pro Gly Leu Gly
        35                  40                  45
Asn Pro Gln Asp Val Thr Tyr Phe Val Ala Tyr Gln Ser Ser Pro Thr
    50                  55                  60
Arg Arg Arg Trp Arg Glu Val Glu Glu Cys Ala Gly Thr Lys Glu Leu
65                  70                  75                  80
Leu Cys Ser Met Met Cys Leu Lys Lys Gln Asp Leu Tyr Asn Lys Phe
                85                  90                  95
Lys Gly Arg Val Arg Thr Val Ser Pro Ser Ser Lys Ser Pro Trp Val
            100                 105                 110
Glu Ser Glu Tyr Leu Asp Tyr Leu Phe Glu Val Glu Pro Ala Pro Pro
        115                 120                 125
Val Leu Val Leu Thr Gln Thr Glu Glu Ile Leu Ser Ala Asn Ala Thr
    130                 135                 140
Tyr Gln Leu Pro Pro Cys Met Pro Pro Leu Asp Leu Lys Tyr Glu Val
145                 150                 155                 160
Ala Phe Trp Lys Glu Gly Ala Gly Asn Lys Val Gly Ser Ser Phe Pro
                165                 170                 175
Ala Pro Arg Leu Gly Pro Leu Leu His Pro Phe Leu Leu Arg Phe Phe
            180                 185                 190
Ser Pro Ser Gln Pro Ala Pro Ala Pro Leu Leu Gln Glu Val Phe Pro
        195                 200                 205
```

```
Val His Ser
    210


<210> 17
<211> 734
<212> DNA
<213> Homo sapiens

<220>
<221> sig_peptide
<222> (53)...(127)

<221> mat_peptide
<222> (128)...(655)

<221> CDS
<222> (53)...(655)

<400> 17
tgggtgacag cctcagagtg tttcttctgc tgacaaagac cagagatcag ga atg aaa 58
                                                          Met Lys
                                                          -25

cta gac atg act ggg gac tgc acg cca gtg ctg gtg ctg atg gcc gca   106
Leu Asp Met Thr Gly Asp Cys Thr Pro Val Leu Val Leu Met Ala Ala
            -20                 -15                 -10

gtg ctg acc gtg act gga gca gtt cct gtc gcc agg ctc cac ggg gct   154
Val Leu Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu His Gly Ala
         -5                  1               5

ctc ccg gat gca agg ggc tgc cac ata gcc cag ttc aag tcc ctg tct   202
Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser Leu Ser
 10                  15                  20                  25

cca cag gag ctg cag gcc ttt aag agg gcc aaa gat gcc tta gaa gag   250
Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu
                30                  35                  40

tcg ctt ctg ctg aag gac tgc agg tgc cac tcc cgc ctc ttc ccc agg   298
Ser Leu Leu Leu Lys Asp Cys Arg Cys His Ser Arg Leu Phe Pro Arg
             45                  50                  55

acc tgg gac ctg agg cag ctg cag gtg agg gag cgc ccc atg gct ttg   346
Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Met Ala Leu
         60                  65                  70

gag gct gag ctg gcc ctg acg ctg aag gtt ctg gag gcc acc gct gac   394
Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr Ala Asp
     75                  80                  85

act gac cca gcc ctg gtg gac gtc ttg gac cag ccc ctt cac acc ctg   442
Thr Asp Pro Ala Leu Val Asp Val Leu Asp Gln Pro Leu His Thr Leu
 90                  95                  100                 105

cac cat atc ctc tcc cag ttc cgg gcc tgt atc cag cct cag ccc acg   490
His His Ile Leu Ser Gln Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr
                110                 115                 120

gca ggg ccc agg acc cgg ggc cgc ctc cac cat tgg ctg tac cgg ctc   538
Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu Tyr Arg Leu
            125                 130                 135

cag gag gcc cca aaa aag gag tcc cct ggc tgc ctc gag gcc tct gtc   586
Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu Ala Ser Val
```

```
        140                 145                 150

acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctg aat tgt gtt gcc   634
Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn Cys Val Ala
    155                 160                 165

agt ggg gac ctg tgt gtc tga ccctcccacc agtcatgcaa cctgagattt      685
Ser Gly Asp Leu Cys Val  *
170                 175

tatttataaa ttagccactt gtcttaattt attgccaccc agtcgctat             734

<210> 18
<211> 200
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> (1)...(25)

<400> 18
Met Lys Leu Asp Met Thr Gly Asp Cys Thr Pro Val Leu Val Leu Met
-25                 -20                 -15                 -10
Ala Ala Val Leu Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu His
                -5                   1                   5
Gly Ala Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser
        10                  15                  20
Leu Ser Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu
    25                  30                  35
Glu Glu Ser Leu Leu Leu Lys Asp Cys Arg Cys His Ser Arg Leu Phe
40                  45                  50                  55
Pro Arg Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Met
                60                  65                  70
Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr
            75                  80                  85
Ala Asp Thr Asp Pro Ala Leu Val Asp Val Leu Asp Gln Pro Leu His
        90                  95                  100
Thr Leu His His Ile Leu Ser Gln Phe Arg Ala Cys Ile Gln Pro Gln
    105                 110                 115
Pro Thr Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu Tyr
120                 125                 130                 135
Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu Ala
                140                 145                 150
Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn Cys
            155                 160                 165
Val Ala Ser Gly Asp Leu Cys Val
        170                 175


<210> 19
<211> 856
<212> DNA
<213> Homo sapiens

<220>
<221> sig_peptide
<222> (98)...(154)

<221> mat_peptide
<222> (155)...(700)

<221> CDS
<222> (98)...(700)

<400> 19
```

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aattaccttt tcactttaca cacatcatct tggattgccc attttgcgtg gctaaaaagc 60
agagccatgc cgctggggaa gcagttgcga tttagcc atg gct gca gct tgg acc  115
                                        Met Ala Ala Ala Trp Thr
                                                            -15

gtg gtg ctg gtg act ttg gtg cta ggc ttg gcc gtg gca ggc cct gtc   163
Val Val Leu Val Thr Leu Val Leu Gly Leu Ala Val Ala Gly Pro Val
            -10                 -5                  1

ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac att ggc agg   211
Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg
     5                  10                  15

ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg   259
Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg
 20                  25                  30                  35

gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct   307
Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser
                40                  45                  50

cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag   355
Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu
            55                  60                  65

cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg   403
Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu
        70                  75                  80

gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt   451
Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu
     85                  90                  95

cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct   499
His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro
100                 105                 110                 115

cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg   547
Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu
                120                 125                 130

cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag   595
His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu
            135                 140                 145

gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa   643
Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys
        150                 155                 160

tat gtg gcc gat ggg aac ctg tgt ctg aga acg tca acc cac cct gag   691
Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr His Pro Glu
    165                 170                 175

tcc acc tga caccccacac cttatttatg cgctgagccc tactccttcc          740
Ser Thr  *
180

ttaatttatt tcctctcacc ctttatttat gaagctgcag ccctgactga gacatagggc 800
tgagtttatt gttttacttt tatacattat gcacaaataa acaacaagga attgga     856
```

<210> 20
<211> 200
<212> PRT
<213> Homo sapiens

<220>

<221> SIGNAL
<222> (1)...(19)

<400> 20
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
-15 -10 -5
Ala Val Ala Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys
1 5 10
Gly Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala
15 20 25
Ser Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys
30 35 40 45
Asn Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg
50 55 60
Leu Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala
65 70 75
Leu Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp
80 85 90
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
95 100 105
Gln Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly
110 115 120 125
Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155
Leu Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg
160 165 170
Thr Ser Thr His Pro Glu Ser Thr
175 180

<210> 21
<211> 734
<212> DNA
<213> Homo sapiens

<220>
<221> sig_peptide
<222> (53)...(127)

<221> mat_peptide
<222> (128)...(655)

<221> CDS
<222> (53)...(655)

<400> 21
tgggtgacag cctcagagtg tttcttctgc tgacaaagac cagagatcag ga atg aaa 58
Met Lys
-25

cta gac atg acc ggg gac tgc atg cca gtg ctg gtg ctg atg gcc gca 106
Leu Asp Met Thr Gly Asp Cys Met Pro Val Leu Val Leu Met Ala Ala
-20 -15 -10

gtg ctg acc gtg act gga gca gtt cct gtc gcc agg ctc cgc ggg gct 154
Val Leu Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu Arg Gly Ala
-5 1 5

ctc ccg gat gca agg ggc tgc cac ata gcc cag ttc aag tcc ctg tct 202
Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser Leu Ser
10 15 20 25

cca cag gag ctg cag gcc ttt aag agg gcc aaa gat gcc tta gaa gag 250
Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu

```
                30                  35                  40

tcg ctt ctg ctg aag gac tgc aag tgc cgc tcc cgc ctc ttc ccc agg   298
Ser Leu Leu Leu Lys Asp Cys Lys Cys Arg Ser Arg Leu Phe Pro Arg
            45                  50                  55

acc tgg gac ctg agg cag ctg cag gtg agg gag cgc ccc gtg gct ttg   346
Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Val Ala Leu
        60                  65                  70

gag gct gag ctg gcc ctg acg ctg aag gtt ctg gag gcc acc gct gac   394
Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr Ala Asp
    75                  80                  85

act gac cca gcc ctg ggg gat gtc ttg gac cag ccc ctt cac acc ctg   442
Thr Asp Pro Ala Leu Gly Asp Val Leu Asp Gln Pro Leu His Thr Leu
90                  95                  100                 105

cac cat atc ctc tcc cag ctc cgg gcc tgt atc cag cct cag ccc acg   490
His His Ile Leu Ser Gln Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr
                110                 115                 120

gca ggg ccc agg acc cgg ggc cgc ctc cac cat tgg ctg cac cgg ctc   538
Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu His Arg Leu
            125                 130                 135

cag gag gcc cca aaa aag gag tcc cct ggc tgc ctc gag gcc tct gtc   586
Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu Ala Ser Val
        140                 145                 150

acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctg aat tgt gtt gcc   634
Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn Cys Val Ala
    155                 160                 165

agc ggg gac ctg tgt gtc tga cccttccgcc agtcatgcaa cctgagattt      685
Ser Gly Asp Leu Cys Val  *
170                 175

tatttataaa ttagccactt ggcttaattt attgccaccc agtcgctat             734
```

<210> 22
<211> 200
<212> PRT
<213> Homo sapiens

<220>
<221> SIGNAL
<222> (1)...(25)

<400> 22

```
Met Lys Leu Asp Met Thr Gly Asp Cys Met Pro Val Leu Val Leu Met
-25                 -20                 -15                 -10
Ala Ala Val Leu Thr Val Thr Gly Ala Val Pro Val Ala Arg Leu Arg
                -5                  1                   5
Gly Ala Leu Pro Asp Ala Arg Gly Cys His Ile Ala Gln Phe Lys Ser
        10                  15                  20
Leu Ser Pro Gln Glu Leu Gln Ala Phe Lys Arg Ala Lys Asp Ala Leu
    25                  30                  35
Glu Glu Ser Leu Leu Leu Lys Asp Cys Lys Cys Arg Ser Arg Leu Phe
40                  45                  50                  55
Pro Arg Thr Trp Asp Leu Arg Gln Leu Gln Val Arg Glu Arg Pro Val
                60                  65                  70
Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Thr
            75                  80                  85
Ala Asp Thr Asp Pro Ala Leu Gly Asp Val Leu Asp Gln Pro Leu His
        90                  95                  100
```

```
Thr Leu His His Ile Leu Ser Gln Leu Arg Ala Cys Ile Gln Pro Gln
    105                 110                 115
Pro Thr Ala Gly Pro Arg Thr Arg Gly Arg Leu His His Trp Leu His
120                 125                 130                 135
Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Pro Gly Cys Leu Glu Ala
                140                 145                 150
Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Asn Cys
            155                 160                 165
Val Ala Ser Gly Asp Leu Cys Val
        170                 175
```

<210> 23
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28A mutant C48S

<221> CDS
<222> (1)...(528)

<400> 23

```
gtt cct gtc gcc agg ctc cac ggg gct ctc ccg gat gca agg ggc tgc   48
Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt   96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac tcc   144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Ser
        35                  40                  45

agg tgc cac tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg   192
Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60

cag gtg agg gag cgc ccc atg gct ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg gtg gac   288
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val Asp
                85                  90                  95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ttc   336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Phe
            100                 105                 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc   384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125

cgc ctc cac cat tgg ctg tac cgg ctc cag gag gcc cca aaa aag gag   432
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc   480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160

ctc acg cga gac ctg aat tgt gtt gcc agt ggg gac ctg tgt gtc tga   528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val  *
```

165 170 175

<210> 24
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-28A mutant C48S

<400> 24
Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly Cys
1 5 10 15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
20 25 30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Ser
35 40 45
Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
50 55 60
Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val Asp
85 90 95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Phe
100 105 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 25
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-28A mutant C49S

<221> CDS
<222> (1)...(531)

<400> 25
atg gtt cct gtc gcc agg ctc cac ggg gct ctc ccg gat gca agg ggc 48
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac 144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45

tcc agg tgc cac tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag 192
Ser Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60

ctg cag gtg agg gag cgc ccc atg gct ttg gag gct gag ctg gcc ctg 240

```
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg gtg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95

gac gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ttc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg tac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agt ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 26
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-28A mutant C49S

<400> 26

```
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Ser Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 27

<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28A mutant C50S

<221> CDS
<222> (1)...(528)

<400> 27
gtt cct gtc gcc agg ctc cac ggg gct ctc ccg gat gca agg ggc tgc 48
Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly Cys
1 5 10 15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt 96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
20 25 30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac tgc 144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
35 40 45

agg tcc cac tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg 192
Arg Ser His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
50 55 60

cag gtg agg gag cgc ccc atg gct ttg gag gct gag ctg gcc ctg acg 240
Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80

ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg gtg gac 288
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val Asp
85 90 95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ttc 336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Phe
100 105 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc 384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125

cgc ctc cac cat tgg ctg tac cgg ctc cag gag gcc cca aaa aag gag 432
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc 480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160

ctc acg cga gac ctg aat tgt gtt gcc agt ggg gac ctg tgt gtc tga 528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val *
165 170 175

<210> 28
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-28A mutant C50S

<400> 28

```
Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
        35                  40                  45
Arg Ser His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val Asp
                85                  90                  95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Phe
            100                 105                 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 29
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-28A mutant C51S

<221> CDS
<222> (1)...(531)

<400> 29

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atg gtt cct gtc gcc agg ctc cac ggg gct ctc ccg gat gca agg ggc   48
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45

tgc agg tcc cac tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag   192
Cys Arg Ser His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60

ctg cag gtg agg gag cgc ccc atg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg gtg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95

gac gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ttc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
```

```
        115                 120                 125

ggc cgc ctc cac cat tgg ctg tac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agt ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 30
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-28A mutant C51S

<400> 30

```
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Arg Ser His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 31
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 mutant C171S

<221> CDS
<222> (1)...(546)

<400> 31

```
ggt ccg gtt ccg acc tct aaa cca acc acc act ggt aaa ggt tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
```

```
1               5                   10                  15

atc ggt cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc aaa   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg tct   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg gat   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct tgc   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct ggt   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc cgt   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gat ctg aaa tac gtt gct gat ggt aac ctg tct ctg cgt acc tct acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Ser Leu Arg Thr Ser Thr
                165                 170                 175

cat ccg gaa tct acc taa                                         546
His Pro Glu Ser Thr  *
            180
```

<210> 32
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 mutant C171S

```
<400> 32
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
```

```
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Ser Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 33
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-29 mutant C172S

<221> CDS
<222> (1)...(549)

<400> 33

```
atg ggt ccg gtt ccg acc tct aaa cca acc acc act ggt aaa ggt tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac atc ggt cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
             20                  25                  30

aaa aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
         35                  40                  45

tct tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                 85                  90                  95

gat cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgc att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
```

```
145                 150                 155                 160

cgt gat ctg aaa tac gtt gct gat ggt aac ctg tct ctg cgt acc tct   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Ser Leu Arg Thr Ser
                165                 170                 175

acc cat ccg gaa tct acc taa                                       549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 34
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-29 mutant C172S

<400> 34

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Ser Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 35
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-28A

<221> CDS
<222> (1)...(531)

<400> 35

```
atg gtt cct gtc gcc agg ctc cac ggg gct ctc ccg gat gca agg ggc   48
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
```

```
ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
         35                  40                  45

tgc agg tgc cac tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag   192
Cys Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
     50                  55                  60

ctg cag gtg agg gag cgc ccc atg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg gtg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                 85                  90                  95

gac gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ttc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg tac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agt ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                              531
 *
```

<210> 36
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-28A

<400> 36

```
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
```

```
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175


<210> 37
<211> 621
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-29

<221> CDS
<222> (1)...(549)

<400> 37
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aac ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga caccccacac cttatttatg cgctgagccc      579
Thr His Pro Glu Ser Thr  *
```

180

tactccttcc ttaatttatt tcctctcacc ctttatttat ga 621

<210> 38
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-29

<400> 38
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
1 5 10 15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
100 105 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
115 120 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
130 135 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145 150 155 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
165 170 175
Thr His Pro Glu Ser Thr
180

<210> 39
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> met IL-28B

<221> CDS
<222> (1)...(531)

<400> 39
atg gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc 48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac 144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45

tgc aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag 192
Cys Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60

```
ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg ggg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95

gat gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 40
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> met IL-28B

<400> 40

```
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 41
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant, Asn169

<221> CDS
<222> (1)...(546)

<221> variation
<222> (44)...(45)
<223> n = A, T, G, or C

<400> 41

```
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 42
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant, Asn169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 42
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
1 5 10 15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
20 25 30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
35 40 45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
50 55 60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65 70 75 80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
85 90 95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
100 105 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
115 120 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
130 135 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145 150 155 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
165 170 175
His Pro Glu Ser Thr
180

<210> 43
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant, Asn170

<221> CDS
<222> (1)...(549)

<221> variation
<222> (47)...(48)
<223> n = A, T, G, or C

<400> 43
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn 48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
1 5 10 15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg 144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45

```
agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 44
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant, Asn170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 44

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
```

```
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 45
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant, Asp169

<221> CDS
<222> (1)...(546)

<221> variation
<222> (44)...(45)
<223> n = A, T, G, or C

<400> 45

```
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
```

```
gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 46
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant, Asp169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 46

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 47
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant, Asp170

<221> CDS
<222> (1)...(549)

<221> variation
<222> (47)...(48)
<223> n = A, T, G, or C

<400> 47

```
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn   48
```

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 48
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant, Asp170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 48

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
```

```
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 49
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Asp169 Cys171 mutant

<221> CDS
<222> (1)...(546)

<221> variation
<222> (512)...(513)
<223> n = A, T, G, or C

<400> 49

```
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
```

```
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180


<210> 50
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Asp169 Cys171 mutant

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 50
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180


<210> 51
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Asp170 Cys172 mutant
```

<221> CDS
<222> (1)...(549)

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 51
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc 48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
1 5 10 15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg 144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc 192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg 240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta 288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc 336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
100 105 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc 384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
115 120 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct 432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
130 135 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg 480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145 150 155 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca 528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
165 170 175

acc cac cct gag tcc acc tga 549
Thr His Pro Glu Ser Thr *
180

<210> 52
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Asp170 Cys172 mutant

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 52
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
1 5 10 15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
100 105 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
115 120 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
130 135 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145 150 155 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
165 170 175
Thr His Pro Glu Ser Thr
180

<210> 53
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Asn169 Cys171 mutant

<221> CDS
<222> (1)...(546)

<221> variation
<222> (30)...(30)
<223> n = A, T, G, or C

<221> variation
<222> (512)...(513)
<223> n = A, T, G, or C

<400> 53
ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc tgc cac 48
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys His
1 5 10 15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag 96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
20 25 30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt 144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
35 40 45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag 192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
50 55 60

```
gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
 65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 54
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Asn169 Cys171 mutant

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 54

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
```

```
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 55
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Asn170 Cys172 mutant

<221> CDS
<222> (1)...(549)

<221> variation
<222> 33, 515, 516
<223> n = A, T, G, or C

<400> 55

```
atg ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys
 1               5                  10                  15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
             20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
         35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175
```

acc cac cct gag tcc acc tga 549
Thr His Pro Glu Ser Thr *
180

<210> 56
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Asn170 Cys172 mutant

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 56
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys
1 5 10 15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
100 105 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
115 120 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
130 135 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145 150 155 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
165 170 175
Thr His Pro Glu Ser Thr
180

<210> 57
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Cys15 mutant Asn169

<221> CDS
<222> (1)...(546)

<221> variation
<222> (30)...(30)
<223> n = A, T, G, or C

<221> variation
<222> (44)...(45)
<223> n = A, T, G, or C

<400> 57
ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc dnn cac 48

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180


<210> 58
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Cys15 mutant Asn169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 58
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
```

```
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180


<210> 59
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Cys16 mutant Asn170

<221> CDS
<222> (1)...(549)

<221> variation
<222> (33)...(33)
<223> n = A, T, G, or C

<221> variation
<222> (47)...(48)
<223> n = A, T, G, or C

<400> 59
atg ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc dnn   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa
 1               5                  10                  15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
```

```
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 60
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Cys16 mutant Asn170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 60

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 61
<211> 546
<212> DNA

<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Asp169 Cys171 mutant

<221> CDS
<222> (1)...(546)

<221> variation
<222> (30)...(30)
<223> n = A, T, G, or C

<221> variation
<222> (512)...(513)
<223> n = A, T, G, or C

<400> 61

```
ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                         546
His Pro Glu Ser Thr  *
            180
```

<210> 62
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Asp169 Cys171 mutant

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 62
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys His
1 5 10 15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
20 25 30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
35 40 45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
50 55 60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65 70 75 80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
85 90 95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
100 105 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
115 120 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
130 135 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145 150 155 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
165 170 175
His Pro Glu Ser Thr
180

<210> 63
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Asp170 Cys172 mutant

<221> CDS
<222> (1)...(549)

<221> variation
<222> (33)...(33)
<223> n = A, T, G, or C

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 63
atg ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc tgc 48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys
1 5 10 15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

```
aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
         35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                 85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 64
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Asp170 Cys172 mutant

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 64

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
```

```
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 65
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Cys15 mutant Asp169

<221> CDS
<222> (1)...(546)

<221> variation
<222> 30, 44, 45
<223> n = A, T, G, or C

<400> 65

```
ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc dnn cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa His
 1               5                  10                  15

att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
```

```
tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 66
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Pro10 Cys15 mutant Asp169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 66

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa His
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 67
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Cys16 mutant Asp170

<221> CDS
<222> (1)...(549)

<221> variation
<222> 33, 47, 48

<223> n = A, T, G, or C

<400> 67
atg ggc cct gtc ccc act tcc aag ccc acc ccn act ggg aag ggc dnn 48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa
1 5 10 15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg 144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc 192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg 240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta 288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc 336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
100 105 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc 384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
115 120 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct 432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
130 135 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg 480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145 150 155 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca 528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
165 170 175

acc cac cct gag tcc acc tga 549
Thr His Pro Glu Ser Thr *
180

<210> 68
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Pro11 Cys16 mutant Asp170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 68
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Pro Thr Gly Lys Gly Xaa

```
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 69
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Asp18 Asn169 Cys171 mutant

<221> CDS
<222> (1)...(546)

<221> variation
<222> (512)...(513)
<223> n = A, T, G, or C

<400> 69

```
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15

att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
```

```
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180


<210> 70
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Asp18 Asn169 Cys171 mutant

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 70
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180


<210> 71
<211> 549
<212> DNA
```

<213> Artificial Sequence

<220>
<223> Met IL-29 Asp19 Asn170 Cys172 mutant

<221> CDS
<222> (1)...(549)

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 71

```
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 72
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Asp19 Asn170 Cys172 mutant

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 72
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1   5   10   15
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20   25   30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35   40   45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50   55   60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65   70   75   80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85   90   95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100   105   110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115   120   125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130   135   140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145   150   155   160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165   170   175
Thr His Pro Glu Ser Thr
            180

<210> 73
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant Asp18 Asn169

<221> CDS
<222> (1)...(546)

<221> variation
<222> (44)...(45)
<223> n = A, T, G, or C

<400> 73
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
 1   5   10   15

att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20   25   30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35   40   45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50   55   60

```
gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
 65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 74
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant Asp18 Asn169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 74

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
 1               5                  10                  15
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
```

```
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 75
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant Asp19 Asn170

<221> CDS
<222> (1)...(549)

<221> variation
<222> (47)...(48)
<223> n = A, T, G, or C

<400> 75

```
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15

cac att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aay ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175
```

```
acc cac cct gag tcc acc tga                                          549
Thr His Pro Glu Ser Thr  *
            180


<210> 76
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant Asp19 Asn170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 76
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180


<210> 77
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Asp18 Asp169 Cys171 mutant

<221> CDS
<222> (1)...(546)

<221> variation
<222> (512)...(513)
<223> n = A, T, G, or C

<400> 77
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15

att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag   96
```

```
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
             20                  25                  30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt   144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
         35                  40                  45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag   192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
     50                  55                  60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg   240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
 65                  70                  75                  80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac   288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                 85                  90                  95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt   336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac   384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc   432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga   480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca acc   528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cac cct gag tcc acc tga                                          546
His Pro Glu Ser Thr  *
            180
```

<210> 78
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Asp18 Asp169 Cys171 mutant

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 78

```
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
```

```
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 79
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Asp19 Asp170 Cys172 mutant

<221> CDS
<222> (1)...(549)

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 79

```
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
             20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
         35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
```

```
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 80
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Asp19 Asp170 Cys172 mutant

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 80

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 81
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant Asp18 Asp169

<221> CDS
<222> (1)...(546)

<221> variation
<222> (44)...(45)
<223> n = A, T, G, or C

<400> 81
ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn cac 48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
1 5 10 15

att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag 96
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
20 25 30

aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt 144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
35 40 45

tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag 192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
50 55 60

gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg 240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65 70 75 80

aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac 288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
85 90 95

cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt 336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
100 105 110

atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac 384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
115 120 125

cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc 432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
130 135 140

tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga 480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145 150 155 160

gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca acc 528
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
165 170 175

cac cct gag tcc acc tga 546
His Pro Glu Ser Thr *
180

<210> 82
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Cys15 mutant Asp18 Asp169

<221> VARIANT
<222> (15)...(15)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 82
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa His
1 5 10 15
Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
20 25 30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
35 40 45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
50 55 60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65 70 75 80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
85 90 95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
100 105 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
115 120 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
130 135 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145 150 155 160
Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser Thr
165 170 175
His Pro Glu Ser Thr
180

<210> 83
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant Asp19 Asp170

<221> CDS
<222> (1)...(549)

<221> variation
<222> (47)...(48)
<223> n = A, T, G, or C

<400> 83
atg ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc dnn 48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
1 5 10 15

cac att gay agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg 144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc 192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg 240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta 288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95

```
gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg gay ctg tgt ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 84
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 Cys16 mutant Asp19 Asp170

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 84

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Asp Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asp Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 85

<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28B Cys48 mutant

<221> CDS
<222> (1)...(528)

<221> variation
<222> (143)...(144)
<223> n = A, T, G, or C

<400> 85

```
gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc tgc   48
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt   96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac dnn   144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Xaa
        35                  40                  45

aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg   192
Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60

cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg ggg gat   288
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly Asp
                85                  90                  95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ctc   336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
            100                 105                 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc   384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125

cgc ctc cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag gag   432
Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc   480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160

ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc tga   528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val  *
                165                 170                 175
```

<210> 86
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-28B Cys48 mutant

<221> VARIANT
<222> (48)...(48)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 86
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
1 5 10 15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
20 25 30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Xaa
35 40 45
Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly Asp
85 90 95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
100 105 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125
Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 87
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys49 mutant

<221> CDS
<222> (1)...(531)

<221> variation
<222> (146)...(147)
<223> n = A, T, G, or C

<400> 87
atg gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc 48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac 144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45

dnn aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag 192
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60

ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg 240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu

```
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg ggg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                 85                  90                  95

gat gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 88
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys49 mutant

<221> VARIANT
<222> (49)...(49)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 88

```
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 89
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28B Cys50 mutant

<221> CDS
<222> (1)...(528)

<221> variation
<222> (149)...(150)
<223> n = A, T, G, or C

<400> 89
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gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc tgc   48
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt   96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
             20                  25                  30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac tgc   144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
         35                  40                  45

aag dnn cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg   192
Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
     50                  55                  60

cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg ggg gat   288
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly Asp
                 85                  90                  95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ctc   336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
            100                 105                 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc   384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125

cgc ctc cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag gag   432
Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc   480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160

ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc tga   528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val  *
                165                 170                 175
```

<210> 90
<211> 175

<212> PRT
<213> Artificial Sequence

<220>
<223> IL-28B Cys50 mutant

<221> VARIANT
<222> (50)...(50)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 90
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
1 5 10 15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
20 25 30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
35 40 45
Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly Asp
85 90 95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
100 105 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125
Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 91
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys51 mutant

<221> CDS
<222> (1)...(531)

<221> variation
<222> (152)...(153)
<223> n = A, T, G, or C

<400> 91
atg gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc 48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac 144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45

tgc aag dnn cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag 192
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60

```
ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc acc gct gac act gac cca gcc ctg ggg   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95

gat gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg cac cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 92
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys51 mutant

<221> VARIANT
<222> (51)...(51)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 92

```
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
```

```
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175


<210> 93
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28B Cys48 mutant T87S H135Y

<221> CDS
<222> (1)...(528)

<221> variation
<222> 143, 144, 261
<223> n = A, T, G, or C

<400> 93
gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc tgc   48
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt   96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac dnn   144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Xaa
        35                  40                  45

aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg   192
Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60

cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtt ctg gag gcc wsn gct gac act gac cca gcc ctg ggg gat   288
Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly Asp
                85                  90                  95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ctc   336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
            100                 105                 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc   384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125

cgc ctc cac cat tgg ctg tay cgg ctc cag gag gcc cca aaa aag gag   432
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc   480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160

ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc tga   528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val  *
                165                 170                 175
```

<210> 94
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<221> VARIANT
<222> (48)...(48)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<221> VARIANT
<222> (87)...(87)
<223> Xaa = Ser

<223> IL-28B Cys48 mutant T87S H135Y

<400> 94
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
1 5 10 15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
20 25 30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Xaa
35 40 45
Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
50 55 60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80
Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly Asp
85 90 95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
100 105 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
115 120 125
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
130 135 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145 150 155 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 95
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys49 mutant T88S H136Y

<221> CDS
<222> (1)...(531)

<221> variation
<222> 146, 147, 264
<223> n = A, T, G, or C

<400> 95
atg gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc 48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

```
ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
          35                  40                  45

dnn aag tgc cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag   192
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
      50                  55                  60

ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtt ctg gag gcc wsn gct gac act gac cca gcc ctg ggg   288
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95

gat gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg tay cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 96
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<221> VARIANT
<222> (49)...(49)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<221> VARIANT
<222> (136)...(136)
<223> Xaa = Ser

<223> Met IL-28B Cys49 mutant T88S H136Y

<400> 96

```
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
```

```
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175


<210> 97
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-28B Cys50 mutant T87S H135Y

<221> CDS
<222> (1)...(528)

<221> variation
<222> 149, 150, 261
<223> n = A, T, G, or C

<400> 97
gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc tgc   48
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15

cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc ttt   96
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30

aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac tgc   144
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
        35                  40                  45

aag dnn cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag ctg   192
Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60

cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aag gtt ctg gag gcc wsn gct gac act gac cca gcc ctg ggg gat   288
Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly Asp
                85                  90                  95

gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag ctc   336
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
            100                 105                 110

cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg ggc   384
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125

cgc ctc cac cat tgg ctg tay cgg ctc cag gag gcc cca aaa aag gag   432
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
```

```
    130                 135                 140

tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc ctc   480
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160

ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc tga   528
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val  *
                165                 170                 175
```

<210> 98
<211> 175
<212> PRT
<213> Artificial Sequence

<220>
<221> VARIANT
<222> (50)...(50)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<221> VARIANT
<222> (87)...(87)
<223> Xaa = Ser

<223> IL-28B Cys50 mutant T87S H135Y

<400> 98

```
Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly Cys
 1               5                  10                  15
His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala Phe
            20                  25                  30
Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp Cys
        35                  40                  45
Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly Asp
                85                  90                  95
Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu
            100                 105                 110
Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg Gly
        115                 120                 125
Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys Glu
    130                 135                 140
Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu
145                 150                 155                 160
Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 99
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-28B Cys51 mutant T88S H136Y

<221> CDS
<222> (1)...(531)

<221> variation
<222> 152, 152, 264

<223> n = A, T, G, or C

<400> 99

```
atg gtt cct gtc gcc agg ctc cgc ggg gct ctc ccg gat gca agg ggc   48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac ata gcc cag ttc aag tcc ctg tct cca cag gag ctg cag gcc   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30

ttt aag agg gcc aaa gat gcc tta gaa gag tcg ctt ctg ctg aag gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45

tgc aag dnn cgc tcc cgc ctc ttc ccc agg acc tgg gac ctg agg cag   192
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60

ctg cag gtg agg gag cgc ccc gtg gct ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80

acg ctg aag gtt ctg gag gcc wsn gct gac act gac cca gcc ctg ggg   288
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95

gat gtc ttg gac cag ccc ctt cac acc ctg cac cat atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cgg gcc tgt atc cag cct cag ccc acg gca ggg ccc agg acc cgg   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggc cgc ctc cac cat tgg ctg tay cgg ctc cag gag gcc cca aaa aag   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc cct ggc tgc ctc gag gcc tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctg aat tgt gtt gcc agc ggg gac ctg tgt gtc   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175

tga                                                               531
 *
```

<210> 100
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<221> VARIANT
<222> (51)...(51)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<221> VARIANT
<222> (88)...(88)
<223> Xaa = Ser

<223> Met IL-28B Cys51 mutant T88S H136Y

<400> 100
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1   5   10   15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20   25   30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35   40   45
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50   55   60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65   70   75   80
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85   90   95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100   105   110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115   120   125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130   135   140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145   150   155   160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165   170   175

<210> 101
<211> 45
<212> DNA
<213> Artificial Sequence

<220>
<223> signal sequence

<221> CDS
<222> (1)...(45)

<221> variation
<222> 6, 9, 12, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45
<223> n = A, T, G, or C

<400> 101
atg gcn gcn gcn tgg acn gtn gtn ytn gtn acn ytn gtn ytn ggn 45
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly
 1   5   10   15

<210> 102
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> signal sequence

<400> 102
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly
 1   5   10   15

<210> 103
<211> 57
<212> DNA
<213> Artificial Sequence

<220>
<223> signal sequence

<221> CDS
<222> (1)...(57)

<221> variation
<222> 6, 9, 12, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57
<223> n = A, T, G, or C

<400> 103
atg gcn gcn gcn tgg acn gtn gtn ytn gtn acn ytn gtn ytn ggn ytn 48
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15

gcn gtn gcn 57
Ala Val Ala

<210> 104
<211> 19
<212> PRT
<213> Artificial Sequence

<220>
<223> signal sequence

<400> 104
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15
Ala Val Ala

<210> 105
<211> 63
<212> DNA
<213> Artificial Sequence

<220>
<223> signal sequence

<221> CDS
<222> (1)...(63)

<221> variation
<222> 6, 9, 12, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63
<223> n = A, T, G, or C

<400> 105
atg gcn gcn gcn tgg acn gtn gtn ytn gtn acn ytn gtn ytn ggn ytn 48
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15

gcn gtn gcn ggn ccn 63
Ala Val Ala Gly Pro
20

<210> 106
<211> 21
<212> PRT

<213> Artificial Sequence

<220>
<223> signal sequence

<400> 106
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15
Ala Val Ala Gly Pro
20

<210> 107
<211> 72
<212> DNA
<213> Artificial Sequence

<220>
<223> signal sequence

<221> CDS
<222> (1)...(72)

<221> variation
<222> 6, 9, 12, 18, 21, 24, 27, 30, 33, 36, 39, 42, 45, 48, 51, 54, 57, 60, 63, 66, 69, 72
<223> n = A, T, G, or C

<400> 107
atg gcn gcn gcn tgg acn gtn gtn ytn gtn acn ytn gtn ytn ggn ytn 48
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15

gcn gtn gcn ggn ccn gtn ccn acn 72
Ala Val Ala Gly Pro Val Pro Thr
20

<210> 108
<211> 24
<212> PRT
<213> Artificial Sequence

<220>
<223> signal sequence

<400> 108
Met Ala Ala Ala Trp Thr Val Val Leu Val Thr Leu Val Leu Gly Leu
1 5 10 15
Ala Val Ala Gly Pro Val Pro Thr
20

<210> 109
<211> 546
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C171X

<221> CDS
<222> (1)...(546)

<221> variation
<222> (512)...(513)

<223> n = A, T, G, or C

<400> 109

```
ggt ccg gtt ccg acc tct aaa cca acc acc act ggt aaa ggt tgc cac   48
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His
 1               5                  10                  15

atc ggt cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc aaa   96
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30

aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg tct  144
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45

tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg cag  192
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60

gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc ctg  240
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80

aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg gat  288
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95

cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct tgc  336
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110

att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg cac  384
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125

cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct ggt  432
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140

tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc cgt  480
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160

gat ctg aaa tac gtt gct gat ggt aac ctg dnn ctg cgt acc tct acc  528
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175

cat ccg gaa tct acc taa                                         546
His Pro Glu Ser Thr  *
            180
```

<210> 110
<211> 181
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C171X

<221> VARIANT
<222> (171)...(171)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 110
Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His

```
 1               5                  10                  15
Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys
            20                  25                  30
Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser
        35                  40                  45
Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln
    50                  55                  60
Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu
65                  70                  75                  80
Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp
                85                  90                  95
Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys
            100                 105                 110
Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His
        115                 120                 125
His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly
    130                 135                 140
Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg
145                 150                 155                 160
Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr
                165                 170                 175
His Pro Glu Ser Thr
            180
```

<210> 111
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Met IL-29 C172X

<221> CDS
<222> (1)...(549)

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 111

```
atg ggt ccg gtt ccg acc tct aaa cca acc acc act ggt aaa ggt tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac atc ggt cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aaa aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

tct tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gat cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct   336
```

```
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgc att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cgt gat ctg aaa tac gtt gct gat ggt aac ctg dnn ctg cgt acc tct   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cat ccg gaa tct acc taa                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 112
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Met IL-29 C172X

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 112

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 113
<211> 543
<212> DNA

<213> Artificial Sequence

<220>
<223> IL-29 C170X, truncated after N-terminal Methionine and Glycine

<221> CDS
<222> (1)...(543)

<221> variation
<222> (509)...(510)
<223> n = A, T, G, or C

<400> 113

```
cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac att   48
Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile
 1               5                  10                  15

ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag aag   96
Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys
            20                  25                  30

gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc   144
Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys
        35                  40                  45

agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg   192
Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val
    50                  55                  60

agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag   240
Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys
65                  70                  75                  80

gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac cag   288
Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln
                85                  90                  95

ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc   336
Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile
            100                 105                 110

cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac   384
Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His
        115                 120                 125

tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc   432
Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys
    130                 135                 140

ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac   480
Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp
145                 150                 155                 160

ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc cac   528
Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His
                165                 170                 175

cct gag tcc acc tga                                              543
Pro Glu Ser Thr  *
            180
```

<210> 114
<211> 180

<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C170X, truncated after N-terminal Methionine and Glycine

<221> VARIANT
<222> (170)...(170)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 114

Pro	Val	Pro	Thr	Ser	Lys	Pro	Thr	Thr	Thr	Gly	Lys	Gly	Cys	His	Ile
1				5					10					15	
Gly	Arg	Phe	Lys	Ser	Leu	Ser	Pro	Gln	Glu	Leu	Ala	Ser	Phe	Lys	Lys
			20					25					30		
Ala	Arg	Asp	Ala	Leu	Glu	Glu	Ser	Leu	Lys	Leu	Lys	Asn	Trp	Ser	Cys
		35					40					45			
Ser	Ser	Pro	Val	Phe	Pro	Gly	Asn	Trp	Asp	Leu	Arg	Leu	Leu	Gln	Val
	50					55					60				
Arg	Glu	Arg	Pro	Val	Ala	Leu	Glu	Ala	Glu	Leu	Ala	Leu	Thr	Leu	Lys
65					70					75					80
Val	Leu	Glu	Ala	Ala	Ala	Gly	Pro	Ala	Leu	Glu	Asp	Val	Leu	Asp	Gln
			85					90					95		
Pro	Leu	His	Thr	Leu	His	His	Ile	Leu	Ser	Gln	Leu	Gln	Ala	Cys	Ile
		100					105					110			
Gln	Pro	Gln	Pro	Thr	Ala	Gly	Pro	Arg	Pro	Arg	Gly	Arg	Leu	His	His
	115					120					125				
Trp	Leu	His	Arg	Leu	Gln	Glu	Ala	Pro	Lys	Lys	Glu	Ser	Ala	Gly	Cys
130					135					140					
Leu	Glu	Ala	Ser	Val	Thr	Phe	Asn	Leu	Phe	Arg	Leu	Leu	Thr	Arg	Asp
145					150					155					160
Leu	Lys	Tyr	Val	Ala	Asp	Gly	Asn	Leu	Xaa	Leu	Arg	Thr	Ser	Thr	His
			165					170					175		
Pro	Glu	Ser	Thr												
		180													

<210> 115
<211> 540
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C169X, truncated after N-terminal Methionine, Glycine, and Proline

<221> CDS
<222> (1)...(540)

<221> variation
<222> (506)...(507)
<223> n = A, T, G, or C

<400> 115

gtc	ccc	act	tcc	aag	ccc	acc	aca	act	ggg	aag	ggc	tgc	cac	att	ggc	48
Val	Pro	Thr	Ser	Lys	Pro	Thr	Thr	Thr	Gly	Lys	Gly	Cys	His	Ile	Gly	
1			5					10					15			
agg	ttc	aaa	tct	ctg	tca	cca	cag	gag	cta	gcg	agc	ttc	aag	aag	gcc	96
Arg	Phe	Lys	Ser	Leu	Ser	Pro	Gln	Glu	Leu	Ala	Ser	Phe	Lys	Lys	Ala	
		20					25					30				
agg	gac	gcc	ttg	gaa	gag	tca	ctc	aag	ctg	aaa	aac	tgg	agt	tgc	agc	144
Arg	Asp	Ala	Leu	Glu	Glu	Ser	Leu	Lys	Leu	Lys	Asn	Trp	Ser	Cys	Ser	
	35					40					45					

```
tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg   192
Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg
     50                  55                  60

gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc   240
Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val
 65                  70                  75                  80

ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc   288
Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro
                85                  90                  95

ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag   336
Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln
            100                 105                 110

cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg   384
Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp
        115                 120                 125

ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg   432
Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu
    130                 135                 140

gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc   480
Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu
145                 150                 155                 160

aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc cac cct   528
Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro
                165                 170                 175

gag tcc acc tga                                                   540
Glu Ser Thr  *
```

<210> 116
<211> 179
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C169X, truncated after N-terminal
Methionine, Glycine, and Proline

<221> VARIANT
<222> (169)...(169)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 116

```
Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly
 1               5                  10                  15
Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala
            20                  25                  30
Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser
        35                  40                  45
Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg
    50                  55                  60
Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val
65                  70                  75                  80
Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro
                85                  90                  95
Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln
            100                 105                 110
```

```
Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp
        115                 120                 125
Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu
    130                 135                 140
Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu
145                 150                 155                 160
Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro
                165                 170                 175
Glu Ser Thr
```

<210> 117
<211> 537
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C168X, truncated after N-terminal
Methionine, Glycine, Proline, and Valine

<221> CDS
<222> (1)...(537)

<221> variation
<222> (503)...(504)
<223> n = A, T, G, or C

<400> 117

```
ccc act tcc aag ccc acc aca act ggg aag ggc tgc cac att ggc agg   48
Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg
 1               5                  10                  15

ttc aaa tct ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg   96
Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg
            20                  25                  30

gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct   144
Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser
        35                  40                  45

cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag   192
Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu
    50                  55                  60

cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg   240
Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu
65                  70                  75                  80

gag gcc gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt   288
Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu
                85                  90                  95

cac acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct   336
His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro
            100                 105                 110

cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg   384
Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu
        115                 120                 125

cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag   432
His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu
    130                 135                 140

gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa   480
```

```
Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys
145                 150                 155                 160

tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc cac cct gag   528
Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu
                165                 170                 175

tcc acc tga                                                       537
Ser Thr  *
```

<210> 118
<211> 178
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C168X, truncated after N-terminal Methionine, Glycine, Proline, and Valine

<221> VARIANT
<222> (168)...(168)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 118

```
Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg
 1               5                  10                  15
Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg
            20                  25                  30
Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser
        35                  40                  45
Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu
    50                  55                  60
Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu
65                  70                  75                  80
Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu
                85                  90                  95
His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro
            100                 105                 110
Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu
        115                 120                 125
His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu
    130                 135                 140
Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys
145                 150                 155                 160
Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu
                165                 170                 175
Ser Thr
```

<210> 119
<211> 534
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C167X, truncated after N-terminal Methionine, Glycine, Proline, Valine, and Proline

<221> CDS
<222> (1)...(534)

<221> variation
<222> (500)...(501)

<223> n = A, T, G, or C

<400> 119

```
act tcc aag ccc acc aca act ggg aag ggc tgc cac att ggc agg ttc   48
Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe
 1               5                  10                  15

aaa tct ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg gac   96
Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp
            20                  25                  30

gcc ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct cct   144
Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro
        35                  40                  45

gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag cgc   192
Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg
    50                  55                  60

cct gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg gag   240
Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu
65                  70                  75                  80

gcc gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt cac   288
Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His
                85                  90                  95

acc ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct cag   336
Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln
            100                 105                 110

ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg cac   384
Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His
        115                 120                 125

cgg ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag gca   432
Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala
    130                 135                 140

tct gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa tat   480
Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr
145                 150                 155                 160

gtg gcc gat ggg aac ctg dnn ctg aga acg tca acc cac cct gag tcc   528
Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser
                165                 170                 175

acc tga                                                          534
Thr  *
```

<210> 120
<211> 177
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C167X, truncated after N-terminal
Methionine, Glycine, Proline, Valine, and Proline

<221> VARIANT
<222> (167)...(167)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 120

```
Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe
 1               5                  10                  15
Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp
            20                  25                  30
Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro
        35                  40                  45
Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg
    50                  55                  60
Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu
65                  70                  75                  80
Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His
                85                  90                  95
Thr Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln
            100                 105                 110
Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His
        115                 120                 125
Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala
    130                 135                 140
Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr
145                 150                 155                 160
Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser
                165                 170                 175
Thr
```

<210> 121
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C166X, truncated after N-terminal Methionine, Glycine, Proline, Valine, Proline, and Threonine

<221> CDS
<222> (1)...(531)

<221> variation
<222> (497)...(498)
<223> n = A, T, G, or C

<400> 121

```
tcc aag ccc acc aca act ggg aag ggc tgc cac att ggc agg ttc aaa   48
Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
 1               5                  10                  15

tct ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg gac gcc   96
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
            20                  25                  30

ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct cct gtc   144
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
        35                  40                  45

ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag cgc cct   192
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
    50                  55                  60

gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg gag gcc   240
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
65                  70                  75                  80

gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt cac acc   288
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
```

```
                85                  90                  95

ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct cag ccc   336
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
            100                 105                 110

aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg cac cgg   384
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
        115                 120                 125

ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag gca tct   432
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
    130                 135                 140

gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa tat gtg   480
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145                 150                 155                 160

gcc gat ggg aac ctg dnn ctg aga acg tca acc cac cct gag tcc acc   528
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
                165                 170                 175

tga                                                               531
 *
```

<210> 122
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C166X, truncated after N-terminal
Methionine, Glycine, Proline, Valine, Proline, and
Threonine

<221> VARIANT
<222> (166)...(166)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 122

```
Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
 1               5                  10                  15
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
            20                  25                  30
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
        35                  40                  45
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
    50                  55                  60
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
65                  70                  75                  80
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
                85                  90                  95
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
            100                 105                 110
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
        115                 120                 125
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
    130                 135                 140
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145                 150                 155                 160
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
                165                 170                 175
```

<210> 123
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 C165X, truncated after N-terminal
Methionine, Glycine, Proline, Valine, Proline,
Threonine, and Serine

<221> CDS
<222> (1)...(528)

<221> variation
<222> (494)...(495)
<223> n = A, T, G, or C

<400> 123

```
aag ccc acc aca act ggg aag ggc tgc cac att ggc agg ttc aaa tct   48
Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys Ser
 1               5                  10                  15

ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg gac gcc ttg   96
Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala Leu
            20                  25                  30

gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct cct gtc ttc   144
Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val Phe
        35                  40                  45

ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag cgc cct gtg   192
Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro Val
    50                  55                  60

gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg gag gcc gct   240
Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Ala
65                  70                  75                  80

gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt cac acc ctg   288
Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr Leu
                85                  90                  95

cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct cag ccc aca   336
His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro Thr
            100                 105                 110

gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg cac cgg ctc   384
Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg Leu
        115                 120                 125

cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag gca tct gtc   432
Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser Val
    130                 135                 140

acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa tat gtg gcc   480
Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val Ala
145                 150                 155                 160

gat ggg aac ctg dnn ctg aga acg tca acc cac cct gag tcc acc tga   528
Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr  *
                165                 170                 175
```

<210> 124
<211> 175

<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 C165X, truncated after N-terminal
Methionine, Glycine, Proline, Valine, Proline,
Threonine, and Serine

<221> VARIANT
<222> (165)...(165)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 124
Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys Ser
1 5 10 15
Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala Leu
20 25 30
Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val Phe
35 40 45
Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro Val
50 55 60
Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala Ala
65 70 75 80
Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr Leu
85 90 95
His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro Thr
100 105 110
Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg Leu
115 120 125
Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser Val
130 135 140
Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val Ala
145 150 155 160
Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
165 170 175

<210> 125
<211> 552
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Leu insert after N-terminal Met, C173X

<221> CDS
<222> (1)...(552)

<221> variation
<222> (6)...(6)
<223> n = A, T, G, or C

<221> variation
<222> (518)...(519)
<223> n = A, T, G, or C

<400> 125
atg ytn ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc 48
Met Leu Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly
1 5 10 15

tgc cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc 96
Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser
20 25 30

ttc aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac 144

```
Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn
          35                  40                  45

tgg agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt   192
Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu
      50                  55                  60

ctc cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acg ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc   288
Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val
                 85                  90                  95

cta gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag   336
Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln
            100                 105                 110

gcc tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc   384
Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg
        115                 120                 125

ctc cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc   432
Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser
    130                 135                 140

gct ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc   480
Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu
145                 150                 155                 160

acg cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg   528
Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr
                165                 170                 175

tca acc cac cct gag tcc acc tga                                  552
Ser Thr His Pro Glu Ser Thr  *
            180
```

<210> 126
<211> 183
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Leu insert after N-terminal Met, C173X

<221> VARIANT
<222> (173)...(173)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 126

```
Met Leu Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly
 1               5                  10                  15
Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser
            20                  25                  30
Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn
        35                  40                  45
Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val
                85                  90                  95
Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln
```

```
            100                 105                 110
Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg
        115                 120                 125
Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser
    130                 135                 140
Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu
145                 150                 155                 160
Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr
                165                 170                 175
Ser Thr His Pro Glu Ser Thr
            180


<210> 127
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 G2L C172X

<221> CDS
<222> (1)...(549)

<221> variation
<222> (6)...(6)
<223> n = A, T, G, or C

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 127
atg ytn cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc   48
Met Leu Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc   96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
             20                  25                  30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
         35                  40                  45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
     50                  55                  60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
 65                  70                  75                  80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                 85                  90                  95

gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
```

```
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                     549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 128
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 G2L C172X

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 128

```
Met Leu Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 129
<211> 552
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Ile insert after N-terminal Met, C173X

<221> CDS
<222> (1)...(552)

<221> variation
<222> (518)...(519)
<223> n = A, T, G, or C

<400> 129
atg ath ggc cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc 48
Met Ile Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly
1 5 10 15

tgc cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc 96
Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser
20 25 30

ttc aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac 144
Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn
35 40 45

tgg agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt 192
Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu
50 55 60

ctc cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg 240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65 70 75 80

acg ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc 288
Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val
85 90 95

cta gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag 336
Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln
100 105 110

gcc tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc 384
Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg
115 120 125

ctc cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc 432
Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser
130 135 140

gct ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc 480
Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu
145 150 155 160

acg cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg 528
Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr
165 170 175

tca acc cac cct gag tcc acc tga 552
Ser Thr His Pro Glu Ser Thr *
180

<210> 130
<211> 183
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Ile insert after N-terminal Met, C173X

<221> VARIANT
<222> (173)...(173)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 130
Met Ile Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly
1 5 10 15
Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser
20 25 30
Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn
35 40 45
Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu
50 55 60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65 70 75 80
Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val
85 90 95
Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln
100 105 110
Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg
115 120 125
Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser
130 135 140
Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu
145 150 155 160
Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr
165 170 175
Ser Thr His Pro Glu Ser Thr
180

<210> 131
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 G2I C172X

<221> CDS
<222> (1)...(549)

<221> variation
<222> (515)...(516)
<223> n = A, T, G, or C

<400> 131
atg ath cct gtc ccc act tcc aag ccc acc aca act ggg aag ggc tgc 48
Met Ile Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
1 5 10 15

cac att ggc agg ttc aaa tct ctg tca cca cag gag cta gcg agc ttc 96
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
20 25 30

aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg aaa aac tgg 144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
35 40 45

agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg agg ctt ctc 192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
50 55 60

cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg gcc ctg acg 240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65 70 75 80

ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag gac gtc cta 288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
85 90 95

```
gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag ctc cag gcc   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg ggc cgc ctc   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag gag tcc gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc ctc ctc acg   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg aga acg tca   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cac cct gag tcc acc tga                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 132
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 G2I C172X

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 132

```
Met Ile Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 133

<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 after N-terminal Met amino acid residues 2-7 deleted, C166X

<221> CDS
<222> (1)...(531)

<221> variation
<222> (497)...(498)
<223> n = A, T, G, or C

<400> 133

```
atg aag ccc acc aca act ggg aag ggc tgc cac att ggc agg ttc aaa   48
Met Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
 1               5                  10                  15

tct ctg tca cca cag gag cta gcg agc ttc aag aag gcc agg gac gcc   96
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
            20                  25                  30

ttg gaa gag tca ctc aag ctg aaa aac tgg agt tgc agc tct cct gtc   144
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
        35                  40                  45

ttc ccc ggg aat tgg gac ctg agg ctt ctc cag gtg agg gag cgc cct   192
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
    50                  55                  60

gtg gcc ttg gag gct gag ctg gcc ctg acg ctg aag gtc ctg gag gcc   240
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
65                  70                  75                  80

gct gct ggc cca gcc ctg gag gac gtc cta gac cag ccc ctt cac acc   288
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
                85                  90                  95

ctg cac cac atc ctc tcc cag ctc cag gcc tgt atc cag cct cag ccc   336
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
            100                 105                 110

aca gca ggg ccc agg ccc cgg ggc cgc ctc cac cac tgg ctg cac cgg   384
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
        115                 120                 125

ctc cag gag gcc ccc aaa aag gag tcc gct ggc tgc ctg gag gca tct   432
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
    130                 135                 140

gtc acc ttc aac ctc ttc cgc ctc ctc acg cga gac ctc aaa tat gtg   480
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145                 150                 155                 160

gcc gat ggg aac ctg dnn ctg aga acg tca acc cac cct gag tcc acc   528
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
                165                 170                 175

tga                                                               531
 *
```

<210> 134

<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 after N-terminal Met amino acid residues 2-7 deleted, C166X

<221> VARIANT
<222> (166)...(166)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 134
Met Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
1 5 10 15
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
20 25 30
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
35 40 45
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
50 55 60
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
65 70 75 80
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
85 90 95
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
100 105 110
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
115 120 125
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
130 135 140
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145 150 155 160
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
165 170 175

<210> 135
<211> 558
<212> DNA
<213> Artificial Sequence

<220>
<223> IL-29 Glu, Ala, and Glu inserted after N-terminal Met, C175X

<221> CDS
<222> (1)...(558)

<221> variation
<222> (524)...(525)
<223> n = A, T, G, or C

<400> 135
atg gar gcn gar ggc cct gtc ccc act tcc aag ccc acc aca act ggg 48
Met Glu Ala Glu Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly
1 5 10 15

aag ggc tgc cac att ggc agg ttc aaa tct ctg tca cca cag gag cta 96
Lys Gly Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu
20 25 30

gcg agc ttc aag aag gcc agg gac gcc ttg gaa gag tca ctc aag ctg 144
Ala Ser Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu
35 40 45

```
aaa aac tgg agt tgc agc tct cct gtc ttc ccc ggg aat tgg gac ctg   192
Lys Asn Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu
     50                  55                  60

agg ctt ctc cag gtg agg gag cgc cct gtg gcc ttg gag gct gag ctg   240
Arg Leu Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu
 65                  70                  75                  80

gcc ctg acg ctg aag gtc ctg gag gcc gct gct ggc cca gcc ctg gag   288
Ala Leu Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu
                85                  90                  95

gac gtc cta gac cag ccc ctt cac acc ctg cac cac atc ctc tcc cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctc cag gcc tgt atc cag cct cag ccc aca gca ggg ccc agg ccc cgg   384
Leu Gln Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg
        115                 120                 125

ggc cgc ctc cac cac tgg ctg cac cgg ctc cag gag gcc ccc aaa aag   432
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gag tcc gct ggc tgc ctg gag gca tct gtc acc ttc aac ctc ttc cgc   480
Glu Ser Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctc ctc acg cga gac ctc aaa tat gtg gcc gat ggg aac ctg dnn ctg   528
Leu Leu Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu
                165                 170                 175

aga acg tca acc cac cct gag tcc acc tga                           558
Arg Thr Ser Thr His Pro Glu Ser Thr  *
            180                 185
```

<210> 136
<211> 185
<212> PRT
<213> Artificial Sequence

<220>
<223> IL-29 Glu, Ala, and Glu inserted after N-terminal Met, C175X

<221> VARIANT
<222> (175)...(175)
<223> Xaa = Ser, Ala, Thr, Val, or Asn

<400> 136

```
Met Glu Ala Glu Gly Pro Val Pro Thr Ser Lys Pro Thr Thr Thr Gly
 1               5                  10                  15
Lys Gly Cys His Ile Gly Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu
            20                  25                  30
Ala Ser Phe Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu
        35                  40                  45
Lys Asn Trp Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu
    50                  55                  60
Arg Leu Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu
65                  70                  75                  80
Ala Leu Thr Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Gln Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg
```

```
        115                 120                 125
Gly Arg Leu His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Ala Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Lys Tyr Val Ala Asp Gly Asn Leu Xaa Leu
                165                 170                 175
Arg Thr Ser Thr His Pro Glu Ser Thr
            180                 185


<210> 137
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-28A C2 mutant for expression in E. coli

<221> CDS
<222> (1)...(528)

<221> variation
<222> (146)...(147)
<223> n = A, T, G or C

<400> 137
atg gtt ccg gtt gct cgt ctg cac ggt gct ctg ccg gac gct cgt ggt   48
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac atc gct cag ttc aaa tct ctg tct ccg cag gaa ctg cag gct   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30

ttc aaa cgt gct aaa gac gct ctg gaa gaa tct ctg ctg ctg aaa gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45

dnn cgt tgc cac tct cgt ctg ttc ccg cgt acc tgg gac ctg cgt cag   192
Xaa Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60

ctg cag gtt cgt gaa cgt ccg atg gct ctg gaa gct gaa ctg gct ctg   240
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80

acc ctg aaa gtt ctg gaa gct acc gct gac acc gac ccg gct ctg gtt   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95

gac gtt ctg gac cag ccg ctg cac acc ctg cac cac atc ctg tct cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ttc cgt gct tgc atc cag ccg cag ccg acc gct ggt ccg cgt acc cgt   384
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggt cgt ctg cac cac tgg ctg tac cgt ctg cag gaa gct ccg aaa aaa   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gaa tct ccg ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
```

```
ctg ctg acc cgt gac ctg aac tgc gtt gct tct ggt gac ctg tgc gtt   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 138
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-28A C2 mutant for expression in E. coli

<221> VARIANT
<222> (49)...(49)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<400> 138

```
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Xaa Arg Cys His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 139
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-28A C3 mutant for expression in E. coli

<221> CDS
<222> (1)...(528)

<221> variation
<222> (152)...(153)
<223> n = A, T, G or C

<400> 139

```
atg gtt ccg gtt gct cgt ctg cac ggt gct ctg ccg gac gct cgt ggt   48
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac atc gct cag ttc aaa tct ctg tct ccg cag gaa ctg cag gct   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
```

```
            20                  25                  30

ttc aaa cgt gct aaa gac gct ctg gaa gaa tct ctg ctg ctg aaa gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
         35                  40                  45

tgc cgt dnn cac tct cgt ctg ttc ccg cgt acc tgg gac ctg cgt cag   192
Cys Arg Xaa His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
     50                  55                  60

ctg cag gtt cgt gaa cgt ccg atg gct ctg gaa gct gaa ctg gct ctg   240
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
 65                  70                  75                  80

acc ctg aaa gtt ctg gaa gct acc gct gac acc gac ccg gct ctg gtt   288
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95

gac gtt ctg gac cag ccg ctg cac acc ctg cac cac atc ctg tct cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ttc cgt gct tgc atc cag ccg cag ccg acc gct ggt ccg cgt acc cgt   384
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggt cgt ctg cac cac tgg ctg tac cgt ctg cag gaa gct ccg aaa aaa   432
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gaa tct ccg ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160

ctg ctg acc cgt gac ctg aac tgc gtt gct tct ggt gac ctg tgc gtt   528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 140
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-28A C3 mutant for expression in E. coli

<221> VARIANT
<222> (51)...(51)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<400> 140

```
Met Val Pro Val Ala Arg Leu His Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Arg Xaa His Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Met Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Thr Ala Asp Thr Asp Pro Ala Leu Val
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
```

```
            100                 105                 110
Phe Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Tyr Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175


<210> 141
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-28B C2 mutant for expression in E. coli

<221> CDS
<222> (1)...(528)

<221> variation
<222> 146, 147, 264
<223> n = A, T, G or C

<400> 141
atg gtt ccg gtt gct cgt ctg cgt ggt gct ctg ccg gac gct cgt ggt   48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15

tgc cac atc gct cag ttc aaa tct ctg tct ccg cag gaa ctg cag gct   96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30

ttc aaa cgt gct aaa gac gct ctg gaa gaa tct ctg ctg ctg aaa gac   144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45

dnn aaa tgc cgt tct cgt ctg ttc ccg cgt acc tgg gac ctg cgt cag   192
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60

ctg cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg   240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80

acc ctg aaa gtt ctg gaa gct wsn gct gac acc gac ccg gct ctg ggt   288
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95

gac gtt ctg gac cag ccg ctg cac acc ctg cac cac atc ctg tct cag   336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110

ctg cgt gct tgc atc cag ccg cag ccg acc gct ggt ccg cgt acc cgt   384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125

ggt cgt ctg cac cac tgg ctg yay cgt ctg cag gaa gct ccg aaa aaa   432
Gly Arg Leu His His Trp Leu Xaa Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140

gaa tct ccg ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt   480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
```

ctg ctg acc cgt gac ctg aac tgc gtt gct tct ggt gac ctg tgc gtt 528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 142
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-28B C2 mutant for expression in E. coli

<221> VARIANT
<222> (49)...(49)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<221> VARIANT
<222> (88)...(88)
<223> Xaa = Thr or Ser

<221> VARIANT
<222> (136)...(136)
<223> Xaa = His or Tyr

<400> 142
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45
Xaa Lys Cys Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65 70 75 80
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
85 90 95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
100 105 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
115 120 125
Gly Arg Leu His His Trp Leu Xaa Arg Leu Gln Glu Ala Pro Lys Lys
130 135 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145 150 155 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 143
<211> 528
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-28B C3 mutant for expression in E. coli

<221> CDS
<222> (1)...(528)

<221> variation
<222> 152, 153, 264
<223> n = A, T, G or C

<400> 143
atg gtt ccg gtt gct cgt ctg cgt ggt gct ctg ccg gac gct cgt ggt 48
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
1 5 10 15

tgc cac atc gct cag ttc aaa tct ctg tct ccg cag gaa ctg cag gct 96
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
20 25 30

ttc aaa cgt gct aaa gac gct ctg gaa gaa tct ctg ctg ctg aaa gac 144
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
35 40 45

tgc aaa dnn cgt tct cgt ctg ttc ccg cgt acc tgg gac ctg cgt cag 192
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
50 55 60

ctg cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg 240
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65 70 75 80

acc ctg aaa gtt ctg gaa gct wsn gct gac acc gac ccg gct ctg ggt 288
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
85 90 95

gac gtt ctg gac cag ccg ctg cac acc ctg cac cac atc ctg tct cag 336
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
100 105 110

ctg cgt gct tgc atc cag ccg cag ccg acc gct ggt ccg cgt acc cgt 384
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
115 120 125

ggt cgt ctg cac cac tgg ctg yay cgt ctg cag gaa gct ccg aaa aaa 432
Gly Arg Leu His His Trp Leu Xaa Arg Leu Gln Glu Ala Pro Lys Lys
130 135 140

gaa tct ccg ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt 480
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145 150 155 160

ctg ctg acc cgt gac ctg aac tgc gtt gct tct ggt gac ctg tgc gtt 528
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
165 170 175

<210> 144
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-28B C3 mutant for expression in E. coli

<221> VARIANT
<222> (51)...(51)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<221> VARIANT
<222> (88)...(88)
<223> Xaa = Thr or Ser

<221> VARIANT
<222> (136)...(136)

<223> Xaa = His or Tyr

<400> 144

```
Met Val Pro Val Ala Arg Leu Arg Gly Ala Leu Pro Asp Ala Arg Gly
 1               5                  10                  15
Cys His Ile Ala Gln Phe Lys Ser Leu Ser Pro Gln Glu Leu Gln Ala
            20                  25                  30
Phe Lys Arg Ala Lys Asp Ala Leu Glu Glu Ser Leu Leu Leu Lys Asp
        35                  40                  45
Cys Lys Xaa Arg Ser Arg Leu Phe Pro Arg Thr Trp Asp Leu Arg Gln
    50                  55                  60
Leu Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu
65                  70                  75                  80
Thr Leu Lys Val Leu Glu Ala Xaa Ala Asp Thr Asp Pro Ala Leu Gly
                85                  90                  95
Asp Val Leu Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln
            100                 105                 110
Leu Arg Ala Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Thr Arg
        115                 120                 125
Gly Arg Leu His His Trp Leu Xaa Arg Leu Gln Glu Ala Pro Lys Lys
    130                 135                 140
Glu Ser Pro Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg
145                 150                 155                 160
Leu Leu Thr Arg Asp Leu Asn Cys Val Ala Ser Gly Asp Leu Cys Val
                165                 170                 175
```

<210> 145
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-29 C1 mutant for expression in E. coli

<221> CDS
<222> (1)...(549)

<221> variation
<222> 33, 47, 48, 57
<223> n = A, T, G or C

<400> 145

```
atg ggt ccg gtt ccg acc tct aaa cca acc mcn act ggt aaa ggt dnn   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Xaa Thr Gly Lys Gly Xaa
 1               5                  10                  15

cac atc grn cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc   96
His Ile Xaa Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aaa aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

tct tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
```

```
gat cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgc att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160

cgt gat ctg aaa tac gtt gct gat ggt ray ctg tgc ctg cgt acc tct   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Xaa Leu Cys Leu Arg Thr Ser
                165                 170                 175

acc cat ccg gaa tct acc taa                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 146
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-29 C1 mutant for expression in E. coli

<221> VARIANT
<222> (11)...(11)
<223> Xaa = Thr or Pro

<221> VARIANT
<222> (16)...(16)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<221> VARIANT
<222> (19)...(19)
<223> Xaa = Gly or Asp

<221> VARIANT
<222> (170)...(170)
<223> Xaa = Asn or Asp

<400> 146

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Xaa Thr Gly Lys Gly Xaa
 1               5                  10                  15
His Ile Xaa Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
```

```
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Xaa Leu Cys Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 147
<211> 549
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-29 C5 mutant for expression in E. coli

<221> CDS
<222> (1)...(549)

<221> variation
<222> 33, 57, 515, 516
<223> n = A, T, G or C

<400> 147

```
atg ggt ccg gtt ccg acc tct aaa cca acc mcn act ggt aaa ggt tgc   48
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Xaa Thr Gly Lys Gly Cys
 1               5                  10                  15

cac atc grn cgt ttc aaa tct ctg tct ccg cag gaa ctg gct tct ttc   96
His Ile Xaa Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30

aaa aaa gct cgt gac gct ctg gaa gaa tct ctg aaa ctg aaa aac tgg   144
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45

tct tgc tct tct ccg gtt ttc ccg ggt aac tgg gat ctg cgt ctg ctg   192
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60

cag gtt cgt gaa cgt ccg gtt gct ctg gaa gct gaa ctg gct ctg acc   240
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80

ctg aaa gtt ctg gaa gct gct gca ggt cct gct ctg gaa gat gtt ctg   288
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95

gat cag ccg ctg cac act ctg cac cac atc ctg tct cag ctg cag gct   336
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110

tgc att caa ccg caa ccg acc gct ggt ccg cgt ccg cgt ggt cgt ctg   384
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125

cac cac tgg ctg cat cgt ctg cag gaa gct ccg aaa aaa gaa tct gct   432
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140

ggt tgc ctg gaa gct tct gtt acc ttc aac ctg ttc cgt ctg ctg acc   480
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
```

```
cgt gat ctg aaa tac gtt gct gat ggt ray ctg dnn ctg cgt acc tct   528
Arg Asp Leu Lys Tyr Val Ala Asp Gly Xaa Leu Xaa Leu Arg Thr Ser
                165                 170                 175

acc cat ccg gaa tct acc taa                                      549
Thr His Pro Glu Ser Thr  *
            180
```

<210> 148
<211> 182
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-29 C5 mutant for expression in E. coli

<221> VARIANT
<222> (11)...(11)
<223> Xaa = Thr or Pro

<221> VARIANT
<222> (19)...(19)
<223> Xaa = Gly or Asp

<221> VARIANT
<222> (170)...(170)
<223> Xaa = Asp or Asn

<221> VARIANT
<222> (172)...(172)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<400> 148

```
Met Gly Pro Val Pro Thr Ser Lys Pro Thr Xaa Thr Gly Lys Gly Cys
 1               5                  10                  15
His Ile Xaa Arg Phe Lys Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe
            20                  25                  30
Lys Lys Ala Arg Asp Ala Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp
        35                  40                  45
Ser Cys Ser Ser Pro Val Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu
    50                  55                  60
Gln Val Arg Glu Arg Pro Val Ala Leu Glu Ala Glu Leu Ala Leu Thr
65                  70                  75                  80
Leu Lys Val Leu Glu Ala Ala Ala Gly Pro Ala Leu Glu Asp Val Leu
                85                  90                  95
Asp Gln Pro Leu His Thr Leu His His Ile Leu Ser Gln Leu Gln Ala
            100                 105                 110
Cys Ile Gln Pro Gln Pro Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu
        115                 120                 125
His His Trp Leu His Arg Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala
    130                 135                 140
Gly Cys Leu Glu Ala Ser Val Thr Phe Asn Leu Phe Arg Leu Leu Thr
145                 150                 155                 160
Arg Asp Leu Lys Tyr Val Ala Asp Gly Xaa Leu Xaa Leu Arg Thr Ser
                165                 170                 175
Thr His Pro Glu Ser Thr
            180
```

<210> 149
<211> 531
<212> DNA
<213> Artificial Sequence

<220>
<223> Human IL-29 d2/7 C5 mutant for expression in E. coli

<221> CDS
<222> (1)...(531)

<221> variation
<222> (497)...(498)
<223> n = A, T, G or C

<400> 149

```
atg aaa cca acc acc act ggt aaa ggt tgc cac atc ggt cgt ttc aaa   48
Met Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
 1               5                  10                  15

tct ctg tct ccg cag gaa ctg gct tct ttc aaa aaa gct cgt gac gct   96
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
             20                  25                  30

ctg gaa gaa tct ctg aaa ctg aaa aac tgg tct tgc tct tct ccg gtt   144
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
         35                  40                  45

ttc ccg ggt aac tgg gat ctg cgt ctg ctg cag gtt cgt gaa cgt ccg   192
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
     50                  55                  60

gtt gct ctg gaa gct gaa ctg gct ctg acc ctg aaa gtt ctg gaa gct   240
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
 65                  70                  75                  80

gct gca ggt cct gct ctg gaa gat gtt ctg gat cag ccg ctg cac act   288
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
                 85                  90                  95

ctg cac cac atc ctg tct cag ctg cag gct tgc att caa ccg caa ccg   336
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
            100                 105                 110

acc gct ggt ccg cgt ccg cgt ggt cgt ctg cac cac tgg ctg cat cgt   384
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
        115                 120                 125

ctg cag gaa gct ccg aaa aaa gaa tct gct ggt tgc ctg gaa gct tct   432
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
    130                 135                 140

gtt acc ttc aac ctg ttc cgt ctg ctg acc cgt gat ctg aaa tac gtt   480
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145                 150                 155                 160

gct gat ggt aac ctg dnn ctg cgt acc tct acc cat ccg gaa tct acc   528
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
                165                 170                 175

taa                                                              531
 *
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<210> 150
<211> 176
<212> PRT
<213> Artificial Sequence

<220>
<223> Human IL-29 d2/7 C5 mutant for expression in E. coli

<221> VARIANT
<222> (166)...(166)
<223> Xaa = Ser, Ala, Thr, Val or Asn

<400> 150

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Met Lys Pro Thr Thr Thr Gly Lys Gly Cys His Ile Gly Arg Phe Lys
 1               5                  10                  15
Ser Leu Ser Pro Gln Glu Leu Ala Ser Phe Lys Lys Ala Arg Asp Ala
            20                  25                  30
Leu Glu Glu Ser Leu Lys Leu Lys Asn Trp Ser Cys Ser Ser Pro Val
        35                  40                  45
Phe Pro Gly Asn Trp Asp Leu Arg Leu Leu Gln Val Arg Glu Arg Pro
    50                  55                  60
Val Ala Leu Glu Ala Glu Leu Ala Leu Thr Leu Lys Val Leu Glu Ala
65                  70                  75                  80
Ala Ala Gly Pro Ala Leu Glu Asp Val Leu Asp Gln Pro Leu His Thr
                85                  90                  95
Leu His His Ile Leu Ser Gln Leu Gln Ala Cys Ile Gln Pro Gln Pro
            100                 105                 110
Thr Ala Gly Pro Arg Pro Arg Gly Arg Leu His His Trp Leu His Arg
        115                 120                 125
Leu Gln Glu Ala Pro Lys Lys Glu Ser Ala Gly Cys Leu Glu Ala Ser
    130                 135                 140
Val Thr Phe Asn Leu Phe Arg Leu Leu Thr Arg Asp Leu Lys Tyr Val
145                 150                 155                 160
Ala Asp Gly Asn Leu Xaa Leu Arg Thr Ser Thr His Pro Glu Ser Thr
                165                 170                 175
```