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(54) **Human Fc-gamma receptor III**

Menschlicher Fc-gamma-Rezeptor III

Récepteur du Fc-gamma III humain

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(56) References cited:
WO-A-88/06733

- **NATURE, JUN 9 1988, 333 (6173) P568-70, ENGLAND, XP002032511 SIMMONS D ET AL: "The Fc gamma receptor of natural killer cells is a phospholipid-linked membrane protein [published erratum appears in Nature 1989 Aug 24;340(6235):662]"**
- **J IMMUNOL METHODS, JUN 26 1987, 100 (1-2) P235-41, NETHERLANDS, XP002032512 KHAYAT D ET AL: "Soluble circulating Fc gamma receptors in human serum. A new ELISA assay for specific and quantitative detection."**

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Description

Field of the Invention

[0001] The invention relates generally to therapeutic compounds, and more particularly to soluble and membrane-bound forms of a low-affinity receptor for human immunoglobulin G, nucleic acids encoding the same, and diagnostic.and therapeutic uses of such receptors.

BACKGROUND

[0002] Receptors for the Fc portion of immunoglobulin G (IgG) play a central role in cellular immune defenses. Three types of such receptors have been identified: A 72 kilodalton (kD) receptor with high affinity for monomeric IgG is found on monocytes and some macrophages, a 40 kD receptor with low affinity for monomeric IgG is found on monocytes, neutrophils, eosinophils, platelets and certain human tumor-cell lines, and a 50-70 kD receptor with low affinity for monomeric IgG is found on neutrophils, eosinophils, natural killer cells, and macrophages. These three types of Fcγ receptor are referred to as FcγRI, FcγRII, and FcγRIII, respectively: Unkeless et al., Ann. Rev. Immunol., Vol. 6, pgs. 251-281 (1988).

[0003] It is believed that FCγRIII-mediated removal IgG-coated platelets plays an important part in the pathogenesis of immune thrombocytopenic purpura (ITP), a platelet-deficiency condition characterized by excessive bleeding: von dem Borne, pgs. 222-256, in Immunohaematology, Engelfriet et al., eds. (Elsevier, Amsterdam, 1984). Clarkson et al., New England J. Med., Vol. 314, pgs. 1236-1239 (1986), report that the infusion of ligand-blocking anti-FcγRIII antibody into a patient with refractory ITP resulted in a transient increase in platelet count. This observation suggests that the most deleterious manifestation of ITP could be temporarily ameliorated by the administration of agents that block or compete with FCγRIII for binding sites on IgG-coated platelets.

[0004] In a separate area of clinical immunology, elevated serum levels of aggregates consisting of immunoglobulin and antigen (so-called "immune complexes") have been correlated with a wide variety of disorders, particularly autoimmune diseases, such as systemic lupus erythematosus (SLE), and rheumatoid arthritis. The level of such complexes has become an important diagnostic for presence of autoimmune disorders; e.g. Theofilopoulos et al., Am.J. Pathol., Col. 100, pgs. 531-591 (1980).

[0005] Present assays for the serum level of immune complexes include solid-phase assays which take advantage of the affinity of the complexes for certain complement or rheumatoid factor proteins, and cellular assays which take advantage of the property of Raji cells to preferentially bind immune complexes; Theofilopoulos et al., chapter 28, and Toth et al., chapter 29, in Rose et al., eds. Manual of Clinical Immunology, 3rd Ed. (American Society for Microbiology, Washington, D.C., 1986). Unfortunately, like many mammalian-cell based assays, the Raji-cell assay is difficult to perform, and requires elaborate controls and standards because of the inherent variability of Raji-cell binding to immune complexes.

[0006] Nature, vol. 333, 9 June 1988, pp 568 - 570 describes a receptor for the Fc region of human IgG and being 283 amino acids in length.

[0007] WO 88/06733 describes soluble forms of low affinity Fc gamma receptors, without providing any sequence information for the receptors.

[0008] In light of the foregoing, it would be advantageous for the medical community to have alternative assay methods for immune complexes utilizing well characterized, widely available, and conveniently cultured cell lines. It would also be advantageous if soluble FcγRs could be produced in sufficient quantity to permit practical emergency therapy for refactory cases of ITP.

SUMMARY OF THE INVENTION

[0009] The present invention is directed to soluble and membrane-bound human FcγRIII polypeptides, their muteins, nucleic acids capable of encoding the same, and diagnostic and therapeutic uses of such polypeptides and muteins.

[0010] The invention is based on the discovery of a cDNA encoding a human FcγRIII. A cDNA clone, pcD(SRα) containing the FcγRIII-encoding insert (illustrated in Figure 1) is deposited in E. coli K12 strain MC1061 with the American Type Culture Collection (ATCC), Rockville, Maryland, USA, under accession number 67707.

[0011] Accordingly, the invention provides a polypeptide capable of binding to the Fc portion of human IgG and comprising the amino acid sequence:-

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225                 230
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(b)

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Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60
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Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
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(c)

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Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225                 230                 235                 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
                245                 250
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(d)

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Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

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Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60
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Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
            180                 185
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or

(f)

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Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

Brief Description of The Drawings

[0012]

Figure 1, parts A and B (on two sheets to be read side-by-side) illustrates the nucleotide sequence of the cDNA insert of pcD(SRα)-GP5;
Figure 2 illustrates the relative location of the stop codon inserted to produce a soluble human FcγRIII, secreted as an FCγRIII mutant; ***[deletion(s)]*** and
Figure 3 parts A and B (on two sheets to be read side-by-side) illustrates the nucleotide sequence of the cDNA insert of pcD(SRα)-NL10.

DETAILED DESCRIPTION OF THE INVENTION

[0013] The present invention includes nucleic acids encoding polypeptides capable of binding to the Fc portion of human IgG. These polypeptides are derived from human FcγRIII. The invention includes soluble and membrane-bound polypeptides for human FcγRIII. These and other modified versions of the polypeptides are readily produced using standard protein engineering techniques.

[0014] Once nucleic acid sequence and/or amino acid sequence information is available for a native protein, a variety of techniques become available for producing virtually any mutation in the native sequence. Shortle, in Science, Vol. 229, pgs. 1193-1201 (1985), reviews techniques for mutating nucleic acids which are applicable to the present invention. Preferably, mutants of the protein of the present invention are produced by site-specific oligonucleotide-directed mutagenesis, e.g. Zoller and Smith, Methods in Enzymology, Vol. 100, pgs. 468-500 (1983), and Mark et al., U.S. Patent 4,518,584 entitled "Human Recombinant Interleukin-2 Muteins", which are incorporated by reference; or by so-called "cassette" mutagenesis described by Wells et al. in Gene, Vol. 34, pgs. 315-323 (1985), by Estell et al. in Science, Vol.

233, pgs. 659-663 (1986), and also essentially by Mullenbach et al. in J. Biol. Chem., Vol. 261, pgs. 719-722 (1986), and by Feretti et al. in Proc. Natl. Acad. Sci., Vol. 83, pgs. 597-603 (1986).

[0015] Polypeptides with amino acid modifications (i.e. muteins) may be desirable in a variety of circumstances. For example, undesirable side effects might be reduced by certain muteins, particularly if the side effect is associated with a different part of the polypeptide from that of the desired activity. In some expression systems, the native polypeptide may be susceptible to degradation by proteases. In such cases, selected substitutions and/or deletions of amino acids which change the susceptible sequences can significantly enhance yields, e.g. British patent application 2173-804-A where Arg at position 275 of human tissue plasminogen activator is replaced by Gly or Glu. Muteins may also increase yields in purification procedures and/or increase shelf lives of proteins by eliminating amino acids susceptible to oxidation, acylation, alkylation, or other chemical modifications. For example, methionine readily undergoes oxidation to form a sulfoxide, which in many proteins is associated with loss of biological activity: e.g. Brot and Weissbach, Arch. Biochem. Biophys., Vol. 223, pg. 271 (1983). Methionines can often be replaced by more inert amino acids with little or no loss of biological activity, e.g. Australian patent application AU-A-52451/86. In bacterial expression systems, yields can sometimes be increased by eliminating or replacing conformationally inessential cysteine residues, e.g. Mark et al., U.S. Patent 4,518,584.

[0016] Preferably, soluble forms of the FcγRIII of the invention are produced by introducing a stop codon prior to (i.e. in the 5'- or "upstream" direction of) the coding region for the transmembrane and intracellular portions of the FcγRIII cDNA. This is conveniently done by site-specific mutagenesis. Transmembrane regions are readily identified by the presence of an amino acid segment containing from about 20-25 residues having high average hydrophobicity, e.g. Wickner, Science, Vol. 210, pgs. 861-868 (1980), and Greene et al., Ann. Rev. Immunol., Vol. 4, pgs. 69-95 (1986).

[0017] Plasmid pcD(SRα)-GP5 is similar to the pcD shuttle vector described by Okayama and Berg, Mol. Cell. Biol., Vol. 2, pgs. 161-170 (1983), and Vol. 3, pgs. 280-289 (1983), except that the SV40 promoter has been modified to improve expression by the downstream insertion of a portion of the long terminal repeat (LTR) from a HTLV(I) retrovirus, described by Takebe et al., Mol. Cell. Biol., Vol. 8, pgs. 466-472 (1988). The plasmid is conveniently propagated in E. coli K12 strain MC1061, or like host.

[0018] The immunoglobulin G binding property of the FcγRIIIs of the invention is measured by standard techniques, e.g. (1) in the case of membrane-bound FcγRIII: the ability of cells transfected with the FcγRIII cDNA to form rosettes in the presence of IgG-coated red blood cells (RBCs) or to preferentially bind human IgG aggregated by heat treatment; or (2) in the case of soluble FcγRIII: the ability to preferentially remove FcγRIII from solution by an immunoadsorbent column comprising human IgG, or to inhibit rosette formation between IgG-coated RBCs and cells known to have FcγRIIIs. The former measurements can be made with fluorescently labeled human IgG molecules, e.g. Haugland, Handbook of Fluorescent Probes (Molecular Probes, Inc., Junction City, OR, 1985). The latter measurements can be made by constructing an IgG column from isolated human IgG and a commercially available activated sepharose column, e.g, from Bio-Rad Laboratories (Richmond, CA).

[0019] Rosette assays are standard in the art, e.g. Winchester et al., chapter 31, in Rose et al., eds., Manual of Clinical Laboratory Immunology, 3rd Ed. (American Society for Microbiology, Washington, D.C., 1986).

[0020] Once the cDNA of the invention has been cloned, a wide range of expression systems (i.e. combinations of host and expression vector) can be used to produce the proteins of the invention. Possible types of host cells include, but are not limited to, bacterial, yeast, insect, mammalian, and the like. Selecting an expression system, and optimizing protein production thereby, involves the consideration and balancing of many factors, including (1) the nature of the protein to be expressed, e.g. the protein may be poisonous to some host organisms, it may be susceptible to degradation by host proteases, or it may be expressed in inactive conformations or in insoluble form in some hosts, (2) the nature of the messenger RNA (mRNA) corresponding to the protein of interest, e.g. the mRNA may have sequences particularly susceptible to host endonucleases, which drastically reduce the functional lifetime of the mRNA, or the mRNA may form secondary structures that mask the start codon or ribosome binding site, thereby inhibiting initiation of translation in some hosts, (3) the selection, availability, and arrangement of host-compatible expression-control sequences in the 3'- and 5'-regions flanking the coding region -- these include promoters, 5'- and 3'-protector sequences, ribosome binding sites, transcription terminators, enhancers, polyadenylate addition sites, cap sites, intron-splice sites, and the like, (4) whether the protein has a secretion-signal sequence which can be processed by the host, or whether an expression-control sequence encoding a signal sequence endogenous to the host must be spliced onto the region encoding the mature protein, (5) the available modes and efficiencies of transfection or transformation of the host, and whether transient or stable expression is desired, (6) the scale and cost of the host culture system desired for expressing the protein, (7) whether, and what type of, posttranslational modifications are desired, e.g. the extent and kind of glycosylation desired may affect the choice of host, (8) the ease with which the expressed protein can be separated from proteins and other materials of the host cells and/or culture medium e.g. in some cases it may be desirable to express a fusion protein with a specialized signal sequence to aid in later purification steps, e.g. Sassenfeld et al., Biotechnology, January 1984, (9) the stability and copy number of a particular vector in a selected host, e.g. Hofschneider et al., eds. Gene Cloning in Organisms other than E. coli (Springer Verlag, Berlin, 1982), and (10) like factors known to those skilled in the art.

[0021] Many reviews are available which provide guidance for making choices and/or modifications of specific expression systems in light of the recited factors, e.g., de Boer and Shepard, "Strategies for optimizing Foreign Gene Expression in Escherichia coli" pgs. 205-247, in Kroon, ed. Genes: Structure and Expression (John Wiley & Sons, New York, 1983), review several E. coli expression systems; Kucherlapati et al., Critical Reviews in Biochemistry, Vol. 16, Issue 4, pgs. 349-379 (1984), and Banerji et al., Genetic Engineering, Vol. 5, pgs. 19-31 (1983) review methods for transfecting and transforming mammalian cells; Reznikoff and Gold, eds., Maximizing Gene Expression (Butterworths, Boston, 1986) review selected topics in gene expression in E. coli, yeast, and mammalian cells; and Thilly, Mammalian Cell Technology (Butterworths, Boston, 1986) reviews mammalian expression systems.

[0022] Likewise, many reviews are available which describe techniques and conditions for linking and/or manipulating specific cDNAs and expression control sequences to create and/or modify expression vectors suitable for use with the present invention: e.g. Maniatis et al., Molecular Cloning: A Laboratory Manual (Cold Spring Harbor Laboratory, N.Y., 1982); Glover, DNA Cloning: A Practical Approach, Vol. I and II (IRL Press, Oxford, 1985), and Perbal, A Practical Guide to Molecular Cloning (John Wiley & Sons, N.Y., 1984).

[0023] Suitable expression systems for the invention include those disclosed by Itakura and Riggs, U.S. patent 4,704,362 (bacterial expression), by Clark et al., U.S. patent 4,675,285 and by Hamer U.S. patent 4,599,308 (mammalian expression), and by Kurjan et al., U.S. patent 4,546,082 (yeast expression). Accordingly, the above patents are incorporated by reference.

[0024] Whenever SV40-based vectors are used, e.g. pcD vectors, a preferred host is the COS7 cell line, described by Gluzman, Cell, Vol. 23, pgs. 175-182 (1981) and available from the ATCC under accession number CRL1651.

[0025] Soluble FcγRIIIs of the invention are administered as a pharmaceutical composition for treating ITP. Such compositions contain an effective amount of the FcγRIII in a pharmaceutical carrier. A pharmaceutical carrier can be any compatible, non-toxic substance suitable for delivering the compositions of the invention to a patient. Generally, compositions useful for parenteral administration of such drugs are well known, e.g. Remington's Pharmaceutical Science, 15th Ed. (Mack Publishing Company, Easton, PA 1980). Alternatively, compositions of the invention may be introduced into a patient's body by an implantable drug delivery system, e.g. Urquhart et al., Ann. Rev. Pharmacol. Toxicol., Vol. 24, pgs. 199-236 (1984).

[0026] When administered parenterally, the soluble FcγRIIIs will be formulated in a unit dosage injectable form (solution, suspension, emulsion) in association with a pharmaceutical carrier. Such carriers are inherently non-toxic and non-therapeutic. Examples of such carriers are normal saline, Ringer's solution, dextrose solution, and Hank's solution. Nonaqueous carriers such as fixed oils and ethyl oleate may also be used. A preferred carrier is 5% dextrose/saline. The carrier.may contain minor amounts of additives such as substances that enhance isotonicity and chemical stability, e.g., buffers and preservatives. The soluble Fc-yRIII is preferably formulated in purified form substantially free of aggregates and other proteins at a concentration in the range of about 5 to 30 mg/ml, and preferably at a concentration in the range of about 10 to 20 mg/ml.

[0027] Selecting an administration regimen to deliver to a patient an amount of soluble FCγRIII which is effective in ameliorating the thrombopenia associated with ITP depends on several factors, including the serum turnover rate of the soluble FcγRIII, the serum level of competing endogenous FcγRIII associated with the immune disorder, the possible immunogenicity of the soluble FcγRIII, and the like. Preferably, an administration regimen maximizes the amount of soluble FcγRIII delivered to the patient consistent with an acceptable level of side effects. Accordingly, the amount of soluble FcγRIII delivered depends in part on the particular soluble FcγRIII employed and the severity of the disease being treated. Guidance in selecting appropriate doses is found in the literature on therapeutic uses of antibodies and antibody fragments, which are polypeptides of roughly the same size as the soluble FcγRIIIs, e.g. Bach et al., chapter 22, in Ferrone et al., eds., Handbook of Monoclonal Antibodies (Noges Publications, Park Ridge, NJ, 1985); and Russell, pgs. 303-357, and Smith et al., pgs. 365-389, in Haber et al., eds. Antibodies in Human Diagnosis and Therapy (Raven Press, New York, 1977). Preferably, the dose is in the range of about 1-20 mg/kg per day, more preferably about 1-10 mg/kg per day.

EXAMPLES

[0028] The following examples serve to illustrate the present invention. Selection of vectors and hosts as well as the concentration of reagents, temperatures, and the values of other variables are only to exemplify application of the present invention and are not to be considered limitations thereof.

Example I. Construction of stable mammalian cell transformants which express human FCγRIII

[0029] Preferably, mammalian cell lines capable of stable expression of the FcγRIII are produced by cotransfecting a host mammalian cell with a vector carrying a selectable marker and a vector carrying a host-compatible promoter and the FcγRIII cDNA insert. For pcD(SRα)-GP5, suitable hosts include Chinese hamster ovary cells, COS monkey cells,

and mouse L cells, such as a thymidine kinase deficient mutant (tk^-) L cell available from the American Type culture Collection under accession number CCL 1.3. The selectable marker allows one to select host cells which have a high probability of containing the FcγRIII gene fully integrated into the host genome. Typically, the ratio of pcD(SRα)-GP5 to the marker-containing vector in the transfection solution is about 10:1. Thus, if the marker gene is integrated into the host genome, it is very likely that pcD(SRα)-GP5- will also be integrated by virtue of its higher concentration. The selectable marker also provides a means of preventing the cultures of desired transformants from being overgrown by revertant cells.

[0030] tk^- mouse L cells are cotransfected with pcD(SRα)-GP5 and pSV2tk, a pSV2 plasmid carrying a thymidine kinase gene under control of the SV40 early promoter. The pSV2 plasmid is described by Mulligan et al., Science, Vol. 209, pgs. 1422-1427 (1980), and by Subramani et al., Mol. Cell. Biol., Vol. 1, pgs. 854-864 (1981), and is available from the American Type Culture Collection under accession number 37146. Both plasmids are amplified in E. coli, e.g. strain HB101 available from the ATCC under accession number 33694, and purified by cesium chloride equilibrium centrifugation. A suspension of about 1×10^5 of tk^- L cells in 10 ml of Dulbecco's Modified Eagle Medium (DME) with 10% fetal bovine serum is placed in a Falcon 3003 dish and cultured at 37°C for 20 hours in a 5% carbon dioxide gas incubator, after which the medium is replaced by 10 ml of fresh DME with 10% fetal bovine serum. The culture is incubated for an additional 4 hours. After incubation, 0.5 ml of solution A (50 mM Hepes, 280 mM NaCl, 1.5 mM sodium phosphate buffer, pH 7.22) and 0.5 ml of solution B (2M $CaCl_2$, 10 μg pcD(SRα)-GP5, 1 μg pSV2tk) are added to the culture medium, and the culture is incubated at 37°C for 24 hours in a 5% CO_2 atmosphere, after which the cells are placed in a selective medium with HAT (e.g. Sigma Chemical Co., St. Louis, MO). After two weeks the surviving colonies are subcloned by limiting dilution, and clones are assayed for expression of FcγRIII.

Example II. Use of stable L cell transformant expressing membrane-bound FcγRIII to measure serum levels of immune complex

[0031] A stably transformed mammalian cell expressing the FcγRIII of the invention can replace the Raji cell line in assays for immune complexes, e.g. Theofilopoulos et al., chapter 28, Manual of Clinical Laboratory Immunology, 3rd Ed. (American Society for Microbiology, Washington, D.C. 1986).

[0032] Antiserum to human IgG is prepared in rabbits, and the IgG fraction is isolated by ammonium sulfate precipitation followed by fractionation on an anion-exchange chromatography column (DEAE-cellulose 52; Whatman Chemical Separation Ltd., Maidstone, England). Antiserum from commercial sources may also be used. The IgG fraction of the antiserum is brought to 5 mg/ml, and 1ml is labeled with ^{125}I. After iodination and dialysis, the antiserum is diluted to 1 mg/ml with phosphate-buffered saline (PBS) to give a specific activity of about 3×10^5 cpm/μg. Cells transformed with the FcγRIII cDNA are harvested after 72 hours of culture, and portions of 2×10^6 cells in 200 μl of medium are placed in 1.5-ml plastic Eppendorf conical tubes (Brinkmann Instruments, Inc., Westbury, N.Y.; catalog no. 22-36-411-1). One ml. of Spinner medium (Eagle minimal medium without Ca^{2+} and Mg^{2+}) is added to each tube, and the cells are centrifuged at 800 x g for 8 min. Supernatant fluids are aspirated, and the cell pellets are resuspended in 50 μl of Spinner medium. Serum to be tested is diluted fourfold in 0.15 M NaCl (physiological saline), and 25 μl is added to the transformed cells. After a 45-min incubation period at 37°C with gentle shaking by hand every 5 to 10 min, the cells are washed three times with Spinner medium. After the final wash, the cells, gently shaken every 5 to 10 minutes, are allowed to react for 30 min at 4°C with ^{125}I-labeled rabbit anti-human IgG diluted with Spinner medium containing 10 g of human serum albumin (HSA) per liter. After incubation, the cells are washed three times, supernatant fluids are completely aspirated, and radioactivity of the cell pellet is determined in a gamma counter. All assays are done in duplicate. The amount of uptake, expressed as absolute counts, percentage of the input, or micrograms of antibody, is referred to a standard curve of radioactive antibody uptake by cells incubated with normal human serum (complement source) containing various amounts of aggregated human IgG (AHG). The quantity of immune complex in serum is equated to an amount of AHG after correction for the dilution factor and is expressed as micrograms of AHG equivalent per milliliter of serum. The soluble AHG is formed from a solution of 6.5 mg of Cohn fraction II or isolated human IgG per ml of physiological saline, heated at 63°C for 30 min, and centrifuged (1,500 x g, 15 min) to remove insoluble large aggregates. The supernatant is then diluted with buffer to yield a final concentration of approximately 1.6 mg/ml. Portions (0.5 ml) of this preparation are stored at -70°C and can be used for as long as 1 month.

[0033] The standard curve of radioactive antibody uptake is constructed as follows. Fifty-microliter portions of AHG (80 μg of protein) are serially diluted (11 twofold dilutions) in saline. Subsequently, 50 μl of a twofold dilution of normal human serum (source of complement), freshly obtained or stored at -70°C, is added to each dilution of AHG, mixed carefully, and incubated at 37°C for 30 min. Thereafter, 25 μl of each mixture is added to 2×10^6 cells in duplicate (fourfold final dilutions of serum containing from 20 μg to about 20 ng of AHG); the mixture is incubated, washed, and reacted with radiolabeled antibody. Radioactivity is then counted as with the test sera. A base line of radioactive antibody uptake (background) by cells incubated with 25 μl of a fourfold dilution of normal human serum, used as a source of complement in the reference curve, is also established.

[0034] Standard preparation of IgG aggregates and of tetanus toxoid-human anti-tetanus toxoid immune complexes have recently been developed under the auspices of the International Union of Immunologists and are available through the Swiss Red Cross Blood Transfusion Service, e.g. Nydegger et al., Clin. Exp. Immunol., Vol. 58, pgs. 502-509 (1984).

Example III. Construction of a soluble human FcγRIII

[0035] Soluble FcγRIII was constructed using site-specific oligonucleotide-directed mutagenesis of the FcγRIII cDNA insert of pcD(SRa)-CP5. The entire cDNA insert of pcD(SRα)-GP5 was subcloned as a 2.4 kilobase Bam HI fragment into the Bluescript KS plasmid (Stratagene, San Diego, CA) and single-stranded.DNA was then prepared.

[0036] A synthetic oligonucleotide (minimum size about 18 nucleotides) encoding a TAA stop codon and a Bam HI site (with mutations' shown in boldface in Figure 2) was used as a primer for complementary strand synthesis using DNA polymerase I large fragment (Amersham, Arlington Heights, IL). Figure 2 indicates the position of the stop codon and Sam HI site relative to the major domains encoded by the FcγRIII cDNA: S represents the region encoding the signal peptide, EC represents the region encoding the extracellular domain of FcγRIII, H represents the region encoding the hydrophobic, or transmembrane, domain of FcγRIII, and C represents the region encoding the cytoplasmic domain. Introducing the stop codon as indicated by Figure 2 produces a mutant FcγRIII lacking both the cytoplasmic and transmembrane domains; it is soluble as shown by the designation "sFcγRIII" beside the modified DNA sequence. After the identity of the mutant was confirmed by DNA sequence analysis, it was subcloned back into the Bam HI site of the pcD (SRα) vector, amplified in E. coli, and transfected into COS 7 cells by electroporation. One day prior to transfection, approximately (1.5-2.0) x 10^6 COS 7 monkey cells were seeded onto individual 100 mm plates in Dulbecco's modified Eagle's medium (DME) containing 6% fetal calf serum and 2 mM glutamine. To perform the transfection, cells were harvested by trypsinization and counted, washed twice in serum-free DME, and suspended to (1-7) x 10^6 cells per ml in serum-free DME. DNA was added to 25 μg/ml and the mixture was allowed to stand at room temperature for 10 minutes, after which 0.8 ml was pulsed in a 0.4 cm sterile cuvette with a Bio Rad (Richmond, CA) Gene Pulser at 250 volts and 960 microfarads. After pulsing, cells were allowed to stand for 10 minutes and then were plated at (1.5-2.0) x 10^6 per 100 mm plate in DME plus 6% fetal calf serum. Supernatants were harvested and assayed for soluble FcγRIII after 72 hours.

[0037] The soluble FcγRIII in the COS7 culture supernatants was analyzed further by gel electrophoresis, and immunoprecipitated. The results of this will now be described. Lanes 1, 3 and 6 each contain proteins from culture supernatants of COS7 cells transfected with the pcD carrying the soluble FcγRIII cDNA. Lane 1 proteins were immunoprecipitated with a non-specific mouse IgG_2 antibody; Lane 3 proteins were immunoprecipitated with human IgG, presumably by the binding of the Fc portion of the antibody with the soluble FcγRIII; and Lane 6 proteins were immunoprecipitated with the monoclonal antibody 3G8 which is specific for the extracellular domain of FcγRIII. Size markers adjacent to the Control lane (lane 1) are in kilodaltons. The soluble FcγRIII corresponds to the broad band at about 40 kilodaltons. Lanes 4 and 7 contain proteins from culture supernatants of COS7 cells transfected with the pcD carrying the soluble FcγRIII cDNA and cultured in the presence of tunicamycin. Tunicamycin inhibits the posttranslational attachment of N-linked carbohydrates to proteins. It was applied in an attempt to determine the nature of the apparent heterogeneity of the 40 kilodalton band. ***[deletion(s)]*** The tunicamycin causes the appearance of two bands of lower molecular weight, which is consistent with the deglycosylation of the soluble FcγRIII. Tunicamycin was added to the cultures as disclosed by Martens et al., PNAS 84: 809-813 (1987). Lanes 2 and 5 contain proteins from culture supernatants of COS7 cells which had undergone the same manipulations as the COS cells of lanes 3 and 4 and lanes 6 and 7, respectively, with the excepticn that no plasmid DNA was included in the transfection protocol.

Example IV Isolation of a Variant human FcγRIII from Natural Killer Cells.

[0038] A cDNA library was constructed from mRNA extracted from a human natural killer (NK) cell line using the pcD (SRα) expression vector. The library was screened with a probe constructed from the cDNA insert of pcD(SRα)-GP5, which was radiolabeled with ^{31}P by random-primed DNA labeling (Boehringer Mannheim, Indianapolis, IN). A clone pcD (SRα)-NL10 was obtained that exhibited human IgG binding activity. The sequence of the cDNA insert of pcD(SRα)-NL10 is illustrated in Figure 3. It can be seen that the amino acid sequence of this FcγRIII and that encoded by pcD(SRα)-GP5 are very similar, differing in the extracellular domain by only six amino acids.

[0039] The descriptions of the foregoing embodiments of the invention have been presented for purpose of illustration and description. They are not intended to be exhaustive or to limit the invention to the precise forms disclosed, and obviously many modifications and variations are possible in light of the above teaching. The embodiments are chosen and described in order to best explain the principles of the invention and its practical application to thereby enable others skilled in the art to best utilize the invention in various embodiments and with such modifications as are suited to the particular use contemplated. It is intended that the scope of the invention be defined by the claims appended hereto.

[0040] Applicants have deposited pcD(SRα)-GP5 with the American Type Culture Collection Rockville, MD, USA

(ATCC), under accession number 67707. This deposit is made under the Budapest Treaty for the Deposit of Microorganisms; and also under conditions as provided under ATCC's agreement for culture Deposit for Patent Purposes, which assures that the deposit will be made available to the US Commissioner of Patents and Trademarks pursuant to 35 U.S.C. 122 and 37 C.F.R. 1.14, and will be made available to the public upon issue of a U.S. patent, which requires that the deposit be maintained. Availability of the deposited strain is not to be contrued as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

Claims

Claims for the following Contracting State(s): AT, BE, CH, DE, FR, GB, IT, LI ,LU, NL, SE

1. A polypeptide capable of binding to the Fc portion of human IgG and comprising the amino acid sequence

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

                    Leu Tyr Phe Ser Val Lys Thr Asn Ile
                    225                 230
```

(b)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
```

(c)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30
```

```
Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225                 230                 235                 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
                245                 250
```

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1 5 10 15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
20 25 30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
35 40 45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
50 55 60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65 70 75 80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
85 90 95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
100 105 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
115 120 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
130 135 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145 150 155 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
165 170 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
180 185

or

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. A polypeptide according to Claim 1 which is glycosylated.

3. A pharmaceutical composition comprising a polypeptide according to Claim 1 or 2 and a pharmaceutically acceptably carrier.

4. A pharmaceutical composition according to Claim 3 for treatment of immune thrombocytopenic purpura (ITP).

5. A pharmaceutical composition according to Claim 3 or 4 comprising 5-30 mg/ml of said polypeptide.

6. A pharmaceutical composition according to Claim 5 comprising 10-20 mg/ml of said polypeptide.

7. Use of a polypeptide according to Claim 1 or 2 in manufacture of a medicament for treatment of ITP.

Claims for the following Contracting State(s): ES, GR

1. A process which comprises making a polypeptide capable of binding to the Fc portion of human IgG and comprising the amino acid sequence

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220
```

```
Leu Tyr Phe Ser Val Lys Thr Asn Ile
225                 230
```

(b)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                   10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
```

(c)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225                 230                 235                 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
                245                 250
```

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
            180                 185
```

or

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. The process according to claim 1 in which the polypeptide glycosylated.

3. A process comprising making a pharmaceutical composition comprising the polypeptide defined in Claim 1 or 2 and a phannaceutically acceptable carrier.

4. The process of claim 3 wherein said pharmaceutical composition is for treatment of immune thrombocytopenic purpura (ITP).

5. The process of claim 4 wherein said pharmaceutical composition comprises 5-30 mg/ml of said polypeptide.

6. The process of claim 5 wherein said pharmaceutical composition comprises 10-20 mg/ml of said polypeptide.

7. Use of a polypeptide defined in Claim 1 or 2 in manufacture of a medicament for treatment of ITP.

Revendications

Revendications pour l'(les) Etat(s) contractant(s) suivant(s): AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

1. Polypeptide capable de se lier à la partie Fc d'une IgG humaine et comprenant la séquence d'amiaoacides

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220
```

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225 230

(b)

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
165 170 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
180 185 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
195 200 205

(c)

Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1 5 10 15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
20 25 30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
165 170 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
180 185 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
195 200 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
210 215 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225 230 235 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
245 250

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
            180                 185
```

ou

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. Polypeptide selon la revendication 1 qui est glycosylé.

3. Composition pharmaceutique comprenant un polypeptide selon la revendication 1 ou 2 et un support pharmaceutiquement accepable.

4. Composition pharmaceutique selon la revendication 3 pour le traitement du purpura thrombocytopénique immun (PTI).

5. Composition pharmaceutique selon la revendication 3 ou 4 comprenant 5-30 mg/ml dudit polypeptide.

6. Composition pharmaceutique selon la revendication 5 comprenant 10-20 mg/ml dudit polypeptide,

7. Utilisation d'un polypeptide selon la revendication 1 ou 2 dans la fabrication d'un médicament pour le traitement du PTI.

Revendications pour l'(les) Etat(s) contractant(s) suivant(s): ES, Gr

1. Procédé qui comprend la production d'un polypeptide capable de se fier à la partie Fe d'une IgG humaine et comprenant la séquence d'aminoacides

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225                 230
```

(b)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
```

(c)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30
```

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
35 40 45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
50 55 60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65 70 75 80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
85 90 95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
100 105 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
115 120 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
130 135 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145 150 155 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
165 170 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
180 185 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
195 200 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
210 215 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225 230 235 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
245 250

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1 5 10 15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
20 25 30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
35 40 45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
50 55 60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65 70 75 80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
85 90 95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
100 105 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
115 120 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
130 135 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145 150 155 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
165 170 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
180 185

ou

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. Procédé selon la revendication 1 dans lequel le polypeptide est glycosylé.

3. Procédé comprenant la production d'une composition pharmaceutique comprenant le polypeptide défini dans la revendication 1 ou 2 et un support pharmaceutiquement acceptable.

4. Procédé selon la revendication 3 où ladite composition pharmaceutique est pour le traitement du purpura thrombocytopénique immun (PTI).

5. Procédé selon la revendication 4 où ladite composition pharmaceutique comprend 5-30 mg/ml dudit polypeptide.

6. Procédé selon la revendication 5 où ladite composition pharmaceutique comprend 10-20 mg/ml dudit polypeptide.

7. Utilisation d'un polypeptide défini dans la revendication 1 ou 2 dans la fabrication d'un médicament pour le traitement du PU

Patentansprüche

Patentansprüche für folgende(n) Vertragsstaat(en): AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE.

1. Polypeptid, das an den Fc-Teil eines humanen IgG binden kann und die Aminosäuresequenz umfasst:

   (a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225                 230
```

(b)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
```

(c)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30
```

```
Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225                 230                 235                 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
                245                 250
```

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
            180                 185
```

oder

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. Polypeptid nach Anspruch 1, das glycosyliert ist.

3. Pharmazeutische Zubereitung, umfassend ein Polypeptid nach Anspruch 1 oder 2 und einen pharmazeutisch annehmbaren Träger.

4. Phamiazeutische Zubereitung nach Anspruch 3, welche für die Behandlung der idiopatischen trombocytopenischen Purpura (ITP) bestimmt ist.

5. Pharmazeutische Zubereitung nach Anspruch 4, die 5 bis 30 mg/ml des Polypeptids enthält.

6. Pharmazeutische Zubereitung nach Anspruch 5, die 10 bis 20 mg/ml des Polypeptids enthält.

7. Verwendung eines Polypeptids nach Anspruch 1 oder 2 bei der Herstellung eines Medikaments zur Behandlung der ITP.

Patentansprüche für folgende(n) Vertragsstaat(en): ES, GR

1. Verfahren, welches das Herstellen eines Polypeptids umfasst, das an den Fc-Teil eines humanen IgG binden kann und die Aminosäuresequenz umfasst:

(a)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220
```

Leu Tyr Phe Ser Val Lys Thr Asn Ile
225 230

(b)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Asn Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
        195                 200                 205
```

(c)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30
```

```
Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly Tyr Gln
        195                 200                 205

Val Ser Phe Cys Leu Val Met Val Leu Leu Phe Ala Val Asp Thr Gly
    210                 215                 220

Leu Tyr Phe Ser Val Lys Thr Asn Ile Arg Ser Ser Thr Arg Asp Trp
225                 230                 235                 240

Lys Asp His Lys Phe Lys Trp Arg Lys Asp Pro Gln Asp Lys
                245                 250
```

(d)

```
Met Trp Gln Leu Leu Leu Pro Thr Ala Leu Leu Leu Leu Val Ser Ala
1               5                  10                  15

Gly Met Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro
            20                  25                  30

Gln Trp Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln
        35                  40                  45

Gly Ala Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu
    50                  55                  60

Ser Leu Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr
65                  70                  75                  80

Val Asp Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu
                85                  90                  95

Ser Asp Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln
            100                 105                 110

Ala Pro Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys
        115                 120                 125

His Ser Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn
    130                 135                 140

Gly Lys Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro
145                 150                 155                 160

Lys Ala Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe
                165                 170                 175

Gly Ser Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln
            180                 185                 190

Gly Leu Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
        195                 200                 205
```

(e)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Asn Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

 Pro Val Gln Leu Glu Val His Val Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

 Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

 Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

 Asp Arg Lys Tyr Phe His His Asn Ser Asp Phe His Ile Pro Lys Ala
    130                 135                 140

 Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Val Gly Ser
145                 150                 155                 160

 Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

 Ala Val Ser Thr Ile Ser Ser Phe Ser Pro Pro Gly
            180                 185
```

oder

(f)

```
Arg Thr Glu Asp Leu Pro Lys Ala Val Val Phe Leu Glu Pro Gln Trp
1               5                  10                  15

Tyr Arg Val Leu Glu Lys Asp Ser Val Thr Leu Lys Cys Gln Gly Ala
            20                  25                  30

Tyr Ser Pro Glu Asp Asn Ser Thr Gln Trp Phe His Asn Glu Ser Leu
        35                  40                  45

Ile Ser Ser Gln Ala Ser Ser Tyr Phe Ile Asp Ala Ala Thr Val Asp
    50                  55                  60

Asp Ser Gly Glu Tyr Arg Cys Gln Thr Asn Leu Ser Thr Leu Ser Asp
65                  70                  75                  80

Pro Val Gln Leu Glu Val His Ile Gly Trp Leu Leu Leu Gln Ala Pro
                85                  90                  95

Arg Trp Val Phe Lys Glu Glu Asp Pro Ile His Leu Arg Cys His Ser
            100                 105                 110

Trp Lys Asn Thr Ala Leu His Lys Val Thr Tyr Leu Gln Asn Gly Lys
        115                 120                 125

Gly Arg Lys Tyr Phe His His Asn Ser Asp Phe Tyr Ile Pro Lys Ala
    130                 135                 140

Thr Leu Lys Asp Ser Gly Ser Tyr Phe Cys Arg Gly Leu Phe Gly Ser
145                 150                 155                 160

Lys Asn Val Ser Ser Glu Thr Val Asn Ile Thr Ile Thr Gln Gly Leu
                165                 170                 175

Ala Val Ser Thr Ile Ser Ser Phe Phe Pro Pro Gly
            180                 185
```

2. Verfahren nach Anspruch 1, worin das Polypeptid glycosyliert ist.

3. Verfahren zur Herstellung einer pharmazeutischen Zubereitung, umfassend das Polypeptid, wie es in Anspruch 1 oder 2 definiert ist, und einen pharmazeutisch annehmbaren Träger.

4. Verfahren nach Anspruch 3, worin die pharmazeutische Zubereitung für die Behandlung der idiopatischen thrombocytopenischen Purpura (ITP) bestimmt ist.

5. Verfahren nach Anspruch 4, worin die pharmazeutische Zubereitung 5 bis 30 mg/ml des Polypeptids enthält.

6. Verfahren nach Anspruch 5, worin die pharmazeutische Zubereitung 10 bis 20 mg/ml des Polypeptids enthält.

7. Verwendung eines Polypeptids, wie in Anspruch 1 oder 2 definiert, bei der Herstellung eines Medikaments zur Behandlung der ITP.

```
          10                  30                  50
CACTCCAGTGTGGCATCATGTGGCAGCTGCTCCTCCCAACTGCTCTGCTACTT
                  MetTrpGlnLeuLeuLeuProThrAlaLeuLeuLeu
         110                 130                 150
GTTCCTGGAGCCTCAATGGTACAGGGTGCTCGAGAAGGACAGTGTGACTCTG
lPheLeuGluProGlnTrpTyrArgValLeuGluLysAspSerValThrLeu
         210                 230                 250
CACAATGAGAACCTCATCTCAAGCCAGGCCTCGAGCTACTTCATTGACGCTGCC
HisAsnGluAsnLeuIleSerSerGlnAlaSerSerTyrPheIleAspAlaAla
         310                 330                 350
CCCTCAGTGACCCGGTGCAGCTAGAAGTCCATGTCGGCTGGCTGTTGCTCCAG
hrLeuSerAspProValGlnLeuGluValHisValGlyTrpLeuLeuLeuGln
         410                 430                 450
TCACAGCTGGAAGAACACTGCTCTGCATAAGGTCACATATTTACAGAATGGC
sHisSerTrpLysAsnThrAlaLeuHisLysValThrTyrLeuGlnAsnGly
         510                 530                 550
GCCACACTCAAAGATAGCGGCTCCTACTTCTGCAGGGGGCTTGTTGGGAGTAAA
AlaThrLeuLysAspSerGlySerTyrPheCysArgGlyLeuValGlySerLys
         610                 630                 650
CAGTGTCAACCATCTCATCATTCTCTCCACCTGGGTACCAAGTCTCTTTCTGC
laValSerThrIleSerSerPheSerProProGlyTyrGlnValSerPheCys
         710                 730                 750
TGTGAAGACAAACATTTGAAGCTCAACAAGAGACTGGAAGGACCATAAACTTA
rValLysThrAsnIleEnd

AATAAGAGCAGTGGCAGCAGCATCTCTGAACATTTCTCTGGATTTGCAACCCC
GCCAGATCCTTTATCCAACTCTCGATTTTTCCTTGGTCTCCAGTGGAAGGGAA
CTAGAAATTGAAGTTTCAGAGCTACACAAACACTTTTTCTGTCCCAACCATTC
CATACAAAAATTGCTCGTATTATAAATTACCCAGTTTAGAGGGGAAAAAAGAA
AGGACCCTACAGAGTGTGGGAACTGCTGGGGATCTAGAGAATTCAGTGGGACC
GGGAGGTGTTCCCATCTGAGCCCAGAGATAAGGGTGTCTTCCTAGAACATTAG
CTTCCAGGGGACTCTATCAGAACTGGACCATTTCCAAGTATATAACGATGAGC
TTGGGGTGGGGGTGGGGTGGAAAAGAAAGTACAGAACAAACCCTGTGTCACTG
AATGAGAAAGCCTGAGAAGAAAGAACCAACCACAAGCACACAGGAAGGAAAGC
TTAATGCAGGGACTGTAAAACCACCTTTTCTGCTTCAATGTCTAGTTCCTGTA
TAAATGTACTACTGAGCTTCACTGAGTTACGCTGTGAAACTTTCAAATCCTTC
ATGAAAAAAAGCTTTAGCTGTCTCCTGTTTTGTAAGCTTTCAGTGCAACATTT
```

FIGURE 1 PART A

```
                  70  +1                  90
 CTAGTTTCAGCTGGCATGCGGACTGAAGATCTCCCAAAGGCTGTGGT
 LeuValSerAlaGlyMetArgThrGluAspLeuProLysAlaValVa
                 170                 190
AAGTGCCAGGGAGCCTACTCCCCTGAGGACAATTCCACACAGTGGTTT
LysCysGlnGlyAlaTyrSerProGluAspAsnSerThrGlnTrpPhe
                 270                 290
  ACAGTCGACGACAGTGGAGAGTACAGGTGCCAGACAAACCTCTCCA
  ThrValAspAspSerGlyGluTyrArgCysGlnThrAsnLeuSerT
                 370                 390
 GCCCCTCGGTGGGTGTTCAAGGAGGAAGACCCTATTCACCTGAGGTG
 AlaProArgTrpValPheLysGluGluAspProIleHisLeuArgCy
                 470                 490
AAAGACAGGAAGTATTTTCATCATAATTCTGACTTCCACATTCCAAAA
LysAspArgLysTyrPheHisHisAsnSerAspPheHisIleProLys
                 570                 590
  AATGTGTCTTCAGAGACTGTGAACATCACCATCACTCAAGGTTTGG
  AsnValSerSerGluThrValAsnIleThrIleThrGlnGlyLeuA
                 670                 690
 TTGGTGATGGTACTCCTTTTTGCAGTGGACACAGGACTATATTTCTC
 LeuValMetValLeuLeuPheAlaValAspThrGlyLeuTyrPheSe
                 770                 790
 AATGGAGAAAGGACCCTCAAGACAAATGACCCCCATCCCATGGGAGT


 ATCATCCTCAGGCCTCTCTACAAGCAGCAGGAAACATAGAACTCAGA
 AAGCCCATGATCTTCAAGCAGGGAAGCCCCCAGTGAGTAGCTGCATTC   1000
 CCTCACAGTAAAACAACAATACAGGCTAGGGATGGTAATCCTTTAAA
 AATAATTATTCCTAAACAAATGGATAAGTAGAATTAATGATTGAGGC   1200
 AATGAAAGCATGGCTGAGAAATAGCAGGGTAGTCCAGGATAGTCTAA
 CCGTAGTGGAATTAACAGGAAATCATGAGGGTGACGTAGAATTGAGT   1400
 CCTCTAATGCTAGGAGTAGCAAATGGTCCTAGGAAGGGGACTGAGGA
 TCCCAAGTTAAGCTAAGTGAACAGAACTATCTCAGCATCAGAATGAG   1600
 GCAGGAGGTGAAAATGCTTTCTTGGCCAGGGTAGTAAGAATTAGAGG
 TAGCTTTGTTCATTGCATTTATTAAACAAATGTTGTATAACCAATAC   1800
 TTCAGTCAGTTCCAATGAGGTGGGGATGGAGAAGACAATTGTTGCTT
 CTTGGTTCCAATAAAGCATTTTACA (A)n
```

FIGURE 1 PART B

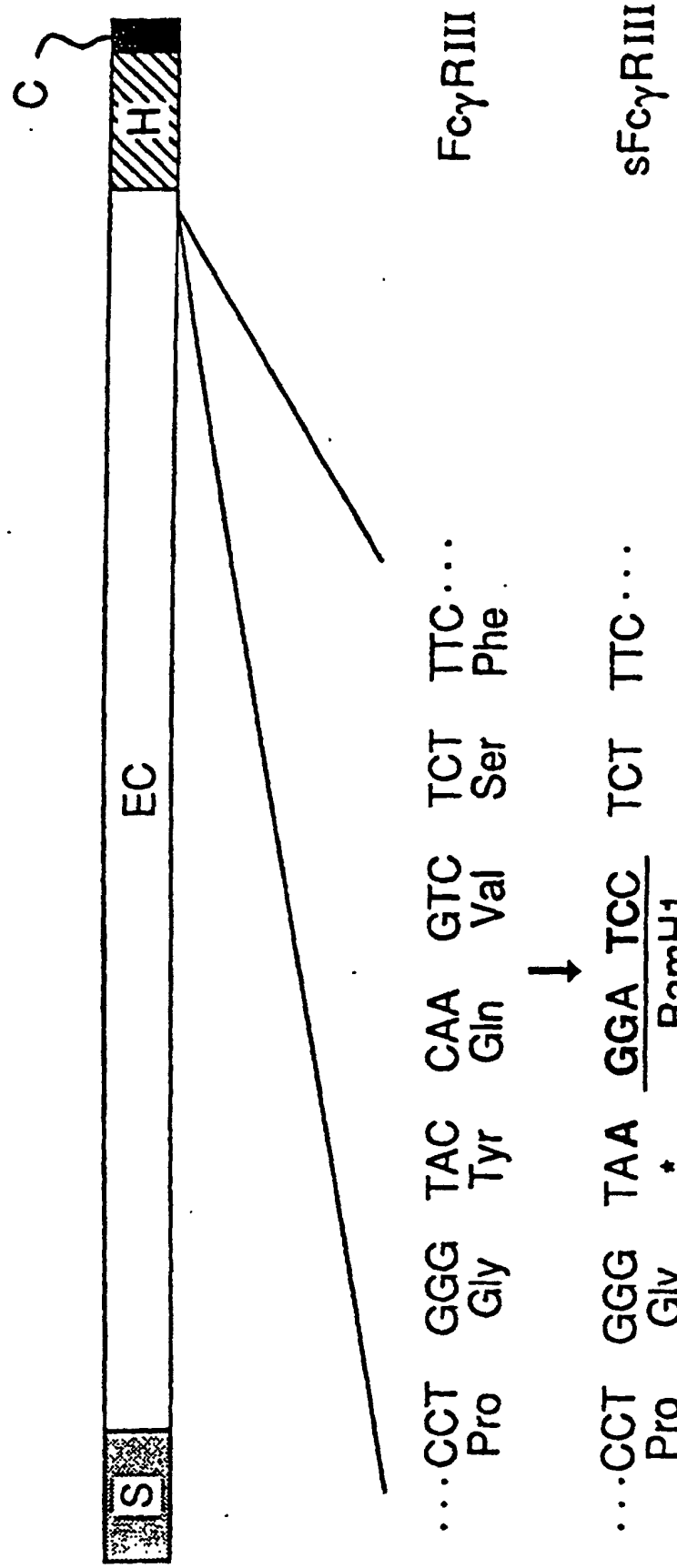
C
H
EC
S
FcγRIII
sFcγRIII
...CCT GGG TAC CAA GTC TCT TTC...
Pro Gly Tyr Gln Val Ser Phe
...CCT GGG TAA GGA TCC TCT TTC...
Pro Gly * BamH1

FIGURE 2

NL 10

```
        10                  30                  50
GGGGGGGGGGGGGGTAAATCCGCAGGACCTGGGTAACACGAGGAAGGGCTCCG

       110                 130                 150
TGCTCCTCCCAACTGCTCTGCTACTTCTAGTTTCAGCTGGCATGCGGACTGAA
euLeuLeuProThrAlaLeuLeuLeuLeuValSerAlaGlyMetArgThrGlu
       210                 230                 250
GCTCGAGAAGGACAGTGTGACTCTGAAGTGCCAGGGAGCCTACTCCCCTGAG
lLeuGluLysAspSerValThrLeuLysCysGlnGlyAlaTyrSerProGlu
       310                 330                 350
GCCTCGAGCTACTTCATTGACGCTGCCACAGTCGACGACAGTGGAGAGTACAGG
AlaSerSerTyrPheIleAspAlaAlaThrValAspAspSerGlyGluTyrArg
       410                 430                 450
TCCATATCGGCTGGCTGTTGCTCCAGGCCCCTCGGTGGGTGTTCAAGGAGGAA
alHisIleGlyTrpLeuLeuLeuGlnAlaProArgTrpValPheLysGluGlu
       510                 530                 550
TAAGGTCACATATTTACAGAATGGCAAAGGCAGGAAGTATTTTCATCATAAT
sLysValThrTyrLeuGlnAsnGlyLysGlyArgLysTyrPheHisHisAsn
       610                 630                 650
TTCTGCAGGGGGCTTTTTGGGAGTAAAAATGTGTCTTCAGAGACTGTGAACATC
PheCysArgGlyLeuPheGlySerLysAsnValSerSerGluThrValAsnIle
       710                 730                 750
CACCTGGGTACCAAGTCTCTTTCTGCTTGGTGATGGTACTCCTTTTTGCAGTG
roProGlyTyrGlnValSerPheCysLeuValMetValLeuLeuPheAlaVal
       810                 830                 850
AAGAGACTGGAAGGACCATAAATTTAAATGGAGAAAGGACCCTCAAGACAAATGA
rArgAspTrpLysAspHisLysPheLysTrpArgLysAspProGlnAspLysEnd

GAACATTTCTCTGGATTTGCAACCCCATCATCCTCAGGCCTCTCTACAAGCAGCA
TTTCCTTGGTCTCCAGTGGAAGGGAAAAGCCCATGATCTTCAAGCAGGGAAGCCC
AAACACTTTTTCTGTCCCAACCGTTCCCTCACAGCAAAGCAACAATACAGGCTAG
TACCCAGTTTAGAGGGGAAAAAAAAACAATTATTCCTAAATAAATGGATAAGTAG
GGCATCTAGGGAATTCAGTGGGACCAATGAAAGCATGGCTGAGAAATAGCAGGTA
AAGGGTGTCTTCCTAGAACATTAGCCGTAGTGGAATTAACAGGAAATCATGAGGG
ATCTCCAAGTATATAACGATGAGTCCTCTTAATGCTAGGAGTAGAAAATGGTCCT
AGTACAGAACAAACCCTGTGTCACTGTCCCAAGTTGCTAAGTGAACAGAACTATC
GCACACAGGAAGGGGGGCGCAGGAGGTCAAAATGCTTTCTTGGCCAGGGTAGTAA
CAATATCTAATTCCTGTGTAGCTTTGTTCATTGCATTTATTAAACAAATGTTGTA
GAAACTTTCAAATCCTTCATCATGTCAGTTCCAATGAGGTGGGGATGGAGAAGAC
GCTTTAAGCGCAACATTTCTTGGTTCCAATAAAGCATTTTACAAGATCTTGCATG
ATGATAAAAAAAAAAAAAAAAAAAA
```

FIGURE 3 PART A

NL 10

```
                    70                                  90
 GATATCTTTGGTGACTTGTCCACTCCAGTGTGGCATCATGTGGCAGC
                                                   MetTrpGlnL
                   170                                 190
 GATCTCCCAAAGGCTGTGGTGTTCCTGGAGCCTCAATGGTACAGGGT
 AspLeuProLysAlaValValPheLeuGluProGlnTrpTyrArgVa
                   270                                 290
GACAATTCCACACAGTGGTTTCACAATGAGAGCCTCATCTCAAGCCAG
AspAsnSerThrGlnTrpPheHisAsnGluSerLeuIleSerSerGln
                   370                                 390
 TGCCAGACAAACCTCTCCACCCTCAGTGACCCGGTGCAGCTAGAAG
 CysGlnThrAsnLeuSerThrLeuSerAspProValGlnLeuGluV
                   470                                 490
 GACCCTATTCACCTGAGGTGTCACAGCTGGAAGAACACTGCTCTGCA
 AspProIleHisLeuArgCysHisSerTrpLysAsnThrAlaLeuHi
                   570                                 590
TCTGACTTCTACATTCCAAAAGCCACACTCAAAGACAGCGGCTCCTAC
SerAspPheTyrIleProLysAlaThrLeuLysAspSerGlySerTyr
                   670                                 690
 ACCATCACTCAAGGTTTGGCAGTGTCAACCATCTCATCATTCTTTC
 ThrIleThrGlnGlyLeuAlaValSerThrIleSerSerPhePheP
                   770                                 790
 GACACAGGACTATATTTCTCTGTGAAGACAAACATTCGAAGCTCAAC
 AspThrGlyLeuTyrPheSerValLysThrAsnIleArgSerSerTh
                   870                                 890
  CCCCCATCCCATGGGGGTAATAAGAGCAGTAGCAGCAGCATCTCT
```

```
  GGAAACATAGAACTCAGAGCCAGATCCCTTATCCAACTCTCGACT    1000
  CAGTGAGTAGCTGCATTCCTAGAAATTGAAGTTTCAGAGCTACAC
  GGATGGTAATCCTTTAAACATACAAAAATTGCTCGTGTTATAAAT    1200
  AATTAATGGTTGAGGCcAGGACCATACAGAGTGTGGGAACTGCTG
  GTCCAGGATAGTCTAAGGGAGGTGTTCCCATCTGAGCCCAGAGAT    1400
  TGACGTAGAATTGAGTCTTCCAGGGGACTCTATCAGAACTGGACC
  AGGAAGGGGACTGAGGATTGCGGTGGGGGGTGGGGTGGAAAAGAA    1600
  TCAGCATCAGAATGAGAAAGCCTGAGAAGAAACAACCAACCACAA
  GAATTAGAGGTTAATGCAGGGACTGTAAAACCACCTTTTCTGCTT    1800
  TAACCAATACTAAATGTACTACTGAGCTTCGCTGAGTTAAGTTAT
  AATTGTTGCTTATGAAAGAAAGCTTTACGTGTCTCTGTTTTGTAA    2000
  CTACTCTTAGATAGAAGATGGGAAAACCATGGTAATAAAATATGA
```

FIGURE 3 PART B