

CLAIMS

1. A human interleukin 2 (IL-2) mutein,
wherein the IL2 mutein has an amino acid sequence identical to the polypeptide of SEQ ID NO: 1, except for:
 - (A) amino acid substitutions L18R and Q22E; and
 - (B) an amino acid substitution at position 126 selected from the group consisting of Q126A, Q126C, Q126D, Q126E, Q126G, Q126H, Q126I, Q126K, Q126M, Q126R and Q126S, wherein the substitutions are numbered in accordance with the amino acid sequence of SEQ ID NO: 1.
2. The IL-2 mutein of claim 1, wherein the mutein comprises the deletion of 1, 2, or 3 amino acids from the N-terminus.
3. The IL-2 mutein of claim 1, wherein the mutein comprises the amino acid substitution Q126H, Q126K, or Q126M.
4. The IL-2 mutein of claim 1, wherein the mutein comprises an amino acid substitution Q126K.
5. The IL-2 mutein of any one of claims 1-4, wherein the mutein is structurally modified to increase half-life, wherein said modification to increase half-life comprises one or more modifications selected from the group consisting of fusion to a human Fc antibody fragment, fusion to albumin, and PEGylation.
6. The IL-2 mutein of any one of claims 1-5, wherein said mutein increases proliferation of regulatory T (T_{reg}).
7. The IL-2 mutein of any one of claims 1-6, wherein said mutein causes expansion of T_{reg} cells.
8. The IL-2 mutein of any one of claims 1-7, wherein the mutein has 70-95% E_{max} as compared to the polypeptide encoded by SEQ ID NO: 1.
9. A nucleic acid encoding the IL-2 mutein of any one of claims 1-8.
10. A vector comprising the nucleic acid of claim 9.
11. A host cell comprising the nucleic acid of claim 9 or the vector of claim 10.
12. A sterile pharmaceutical composition comprising the IL-2 mutein of any one of claims 1-8 and a pharmaceutically acceptable excipient.

13. A syringe comprising (a) the IL-2 mutein of any one of claims 1-8; (b) the nucleic acid of claim 9; (c) the vector of claim 10; (d) the host cell of claim 11; and/or (e) the pharmaceutical composition of claim 12.
14. A kit comprising:
 - (a) one or more of (i) the IL-2 mutein of any one of claims 1-8 or 24-29; (ii) the nucleic acid of claim 9; (iii) the vector of claim 10; (iv) the host cell of claim 11; (v) the sterile pharmaceutical composition of claim 12; and (vi) the syringe of claim 13; and
 - (b) written instructions for using the (i) the IL-2 mutein of any one of claims 1-8 or 24-29; (ii) the nucleic acid of claim 9; (iii) the vector of claim 10; (iv) the host cell of claim 11; (v) the sterile pharmaceutical composition of claim 12; and (vi) the syringe of claim 13.
15. Use of the (a) a therapeutically effective amount of the IL-2 mutein of any one of claims 1-8 or 24-29; (b) the nucleic acid of claim 9; (c) the vector of claim 10; (d) the host cell of claim 11; and/or (e) the pharmaceutical composition of claim 12 in the preparation of a medicament for the treatment of an autoimmune disease in an individual in need thereof, wherein the IL-2 mutein comprises the amino acid substitution Q126H or Q126K.
16. The use of claim 15, wherein the autoimmune disease is selected from the group consisting of rheumatoid arthritis, insulin-dependent diabetes mellitus, hemolytic anemias, rheumatic fever, thyroiditis, Crohn's disease, myasthenia gravis, glomerulonephritis, autoimmune hepatitis, multiple sclerosis, alopecia areata, psoriasis, vitiligo, dystrophic epidermolysis bullosa, systemic lupus erythematosus, and graft vs. host disease.
17. The use of claim 15, wherein the autoimmune disease is graft vs. host disease.
18. The use of any one of claims 15-17, wherein the IL-2 mutein of any one of claims 1-8 or the pharmaceutical composition of claim 12 is to be administered in combination with an antibody that targets the mutein to a specific cell type.
19. The use of claim 18, wherein the cell type is a regulatory T (T_{reg}) cell.
20. The use of claim 18 or claim 19, wherein the antibody is covalently or non-covalently linked to the IL-2 mutein.
21. A method for producing the IL-2 mutein of any one of claims 1-8 comprising culturing the host cell of claim 11 under suitable conditions for the production of the mutein.
22. The method of claim 21 further comprising isolating and/or purifying the produced IL-2 mutein.

23. The method of claim 21 or 22, further comprising structurally modifying the IL-2 mutein to increase half-life, wherein said modification comprises one or more alterations selected from the group consisting of fusion to a human Fc antibody fragment, fusion to albumin, and PEGylation.
24. The IL2 mutein of claim 6 wherein the IL2 mutein is PEGylated.
25. The IL2 mutein of claim 24 wherein PEGylation occurs at the N-terminus.
26. The IL2 mutein of claim 24 or 25 wherein the PEG has a molecular weight of approximately 10,000, 20,000, 30,000, or 40,000 daltons average molecular weight.
27. The IL2 mutein of any one of claims 24-26 wherein the PEG is a branched PEG.
28. The IL2 mutein of any one of claims 24-27 wherein the PEG has a molecular weight of 40,000 daltons average molecular weight.
29. The IL2 mutein of any one of claims 24-28 wherein the IL2 mutein comprises an N-terminal deletion of one amino acid residue (Ala1).