

Claims

1. A polypeptide comprising a mutein of human interleukin-2 (IL2) or of a functional variant of human IL2, wherein the human IL2 or the functional variant thereof is substituted at at least position 80 (leucine), position 81 (arginine), position 85 (leucine) and position 92 (isoleucine) relative to wild type human IL2 and numbered in accordance with wild type human IL2, wherein the substitution enhances the affinity for the $\beta\gamma$ IL2 receptor complex (IL2R $\beta\gamma$) and wherein the human IL2 or the functional variant thereof is not substituted at position 86 (isoleucine) relative to wild type human IL2 and numbered in accordance with wild type human IL2.
2. The polypeptide of claim 1, wherein position 80 (leucine) is substituted by phenylalanine, position 81 (arginine) is substituted by glutamic acid, position 85 (leucine) is substituted by valine and position 92 (isoleucine) is substituted by phenylalanine relative to wild type human IL2 and numbered in accordance with wild type human IL2.
3. The polypeptide of claim 1 or 2, wherein the human IL2 or the functional variant thereof is further substituted at position 74 (glutamine) relative to wild type human IL2 and numbered in accordance with wild type human IL2.
4. The polypeptide of claim 3, wherein position 74 (glutamine) is substituted by histidine relative to wild type human IL2 and numbered in accordance with wild type human IL2.
5. A polypeptide comprising a mutein of human IL2 or of a functional variant of human IL2, wherein the human IL2 or the functional variant thereof is substituted at at least position 80 (leucine) by phenylalanine, position 81 (arginine) by glutamic acid, position 85 (leucine) by valine and position 92 (isoleucine) by phenylalanine relative to wild type human IL2 and numbered in accordance with wild type human IL2.
6. The polypeptide of claim 5, wherein the human IL2 or the functional variant thereof is further substituted at position 74 (glutamine) by histidine relative to wild type human IL2 and numbered in accordance with wild type human IL2.
7. A polypeptide comprising a mutein of human IL2 or of a functional variant of human IL2, wherein the human IL2 or the functional variant thereof is substituted at at least position 74 (glutamine) by histidine,

position 80 (leucine) by phenylalanine, position 81 (arginine) by glutamic acid, position 85 (leucine) by valine and position 92 (isoleucine) by phenylalanine relative to wild type human IL2 and numbered in accordance with wild type human IL2.

8. The polypeptide of any one of claims 5 to 7, wherein the substitution enhances the affinity for IL2R $\beta\gamma$.

9. The polypeptide of any one of claims 1 to 8, wherein the human IL2 or the functional variant thereof further comprises one or more amino acid substitutions which reduce the affinity for the alpha subunit of the $\alpha\beta\gamma$ IL2 receptor complex (IL2R $\alpha\beta\gamma$).

10. The polypeptide of claim 9, wherein the one or more amino acid substitutions which reduce the affinity for the alpha subunit of IL2R $\alpha\beta\gamma$ reduce the affinity for IL2R $\alpha\beta\gamma$ to a greater extent than for IL2R $\beta\gamma$.

11. The polypeptide of claim 9 or 10, wherein the one or more amino acid substitutions which reduce the affinity for the alpha subunit of IL2R $\alpha\beta\gamma$ comprise substitutions of the human IL2 or the functional variant thereof at position 43 (lysine) and position 61 (glutamic acid) relative to wild type human IL2 and numbered in accordance with wild type human IL2.

12. The polypeptide of claim 11, wherein position 43 (lysine) is substituted by glutamic acid and position 61 (glutamic acid) is substituted by lysine.

13. A polypeptide comprising a mutein of human IL2 or of a functional variant of human IL2, wherein the human IL2 or the functional variant thereof is substituted at at least position 43 (lysine) by glutamic acid, position 61 (glutamic acid) by lysine, position 74 (glutamine) by histidine, position 80 (leucine) by phenylalanine, position 81 (arginine) by glutamic acid, position 85 (leucine) by valine and position 92 (isoleucine) by phenylalanine relative to wild type human IL2 and numbered in accordance with wild type human IL2.

14. The polypeptide of any one of claims 5 to 13, wherein the human IL2 or the functional variant thereof is not substituted at position 86 (isoleucine) relative to wild type human IL2 and numbered in accordance with wild type human IL2.

15. The polypeptide of any one of claims 1 to 14, wherein the human IL2 has the amino acid sequence according to SEQ ID NO: 1.
16. The polypeptide of any one of claims 1 to 15, wherein the mutein of human IL2 or the functional variant thereof has a decreased ability to stimulate regulatory T cells compared to wild type human IL2.
17. The polypeptide of any one of claims 1 to 16, wherein the mutein of human IL2 or the functional variant thereof has an increased ability to stimulate effector T cells compared to wild type human IL2.
18. The polypeptide of any one of claims 1 to 17, which is an extended pharmacokinetic (PK) polypeptide.
19. The polypeptide of claim 18, wherein the extended-PK polypeptide comprises a fusion protein.
20. The polypeptide of claim 19, wherein the fusion protein comprises a moiety of the mutein of human IL2 or the functional variant thereof and a moiety which is heterologous to human IL2 or the functional variant thereof.
21. The polypeptide of claim 19 or 20, wherein the fusion protein comprises a moiety of the mutein of human IL2 or the functional variant thereof and a moiety selected from the group consisting of serum albumin, an immunoglobulin fragment, transferrin, Fn3, and variants thereof.
22. The polypeptide of claim 21, wherein the serum albumin comprises mouse serum albumin or human serum albumin.
23. The polypeptide of claim 21, wherein the immunoglobulin fragment comprises an immunoglobulin Fc domain.
24. A polynucleotide encoding the polypeptide of any one of claims 1 to 23.
25. The polynucleotide of claim 24, which is RNA.
26. A host cell comprising the polynucleotide of claim 24 or 25.

27. The polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, or the host cell of claim 26 for pharmaceutical use.
28. The polypeptide, polynucleotide or host cell of claim 27, wherein the pharmaceutical use comprises a therapeutic or prophylactic treatment of a disease or disorder.
29. The polypeptide, polynucleotide or host cell of claim 27 or 28, for use in a method for treating or preventing cancer in a subject.
30. A pharmaceutical composition comprising the polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, or the host cell of claim 26.
31. A method of treating a subject comprising administering to the subject the polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, the host cell of claim 26, or the pharmaceutical composition of claim 30.
32. A method for inducing an immune response in a subject comprising administering to the subject the polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, the host cell of claim 26, or the pharmaceutical composition of claim 30.
33. The method of claim 31 or 32, which further comprises administering to the subject a peptide or protein comprising an epitope for inducing an immune response specific for an antigen in the subject or a polynucleotide encoding the peptide or protein.
34. The method of claim 33, wherein the polynucleotide encoding the peptide or protein is RNA.
35. The method of any one of claims 31 to 34, which is a method for treating or preventing cancer in a subject, wherein optionally the antigen is a tumor-associated antigen.
36. A method for treating or preventing cancer in a subject comprising administering to the subject the polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, the host cell of claim 26, or the pharmaceutical composition of claim 30.

37. The method of claim 36, which further comprises administering to the subject a peptide or protein comprising an epitope for inducing an immune response specific for a tumor-associated antigen in the subject or a polynucleotide encoding the peptide or protein.
38. The method of claim 37, wherein the polynucleotide encoding the peptide or protein is RNA.
39. A medical preparation comprising the polypeptide of any one of claims 1 to 23, the polynucleotide of claim 24 or 25, the host cell of claim 26, or the pharmaceutical composition of claim 30.
40. The medical preparation of claim 39, further comprising a peptide or protein comprising an epitope for inducing an immune response specific for an antigen in a subject or a polynucleotide encoding the peptide or protein.
41. The medical preparation of claim 40, wherein the polynucleotide encoding the peptide or protein is RNA.
42. The medical preparation of claim 40 or 41, which comprises the polypeptide, polynucleotide, host cell, or pharmaceutical composition and the peptide or protein comprising an epitope or polynucleotide encoding the peptide or protein, respectively, in separate containers.
43. The medical preparation of any one of claims 39 to 42, further comprising instructions for use of the medical preparation for treating or preventing cancer wherein optionally the antigen is a tumor-associated antigen.
44. The medical preparation of any one of claims 39 to 43 for pharmaceutical use.
45. The medical preparation of claim 44, wherein the pharmaceutical use comprises a therapeutic or prophylactic treatment of a disease or disorder.
46. The medical preparation of any one of claims 39 to 45 for use in a method for treating or preventing cancer in a subject, wherein optionally the antigen is a tumor-associated antigen.