Claims

~~1. A mutant interleukin-2 (IL-2) polypeptide comprising at a first amino acid mutation that abolishes or reduces affinity of the mutant IL-2 polypeptide to the high-affinity IL-2 receptor and preserves affinity of the mutant IL-2 polypeptide to the intermediate-affinity IL-2 receptor, each compared to a wild-type IL-2 polypeptide, characterized in that said first amino acid mutation is at a position corresponding to residue 72 of human IL-2.~~

~~2. The mutant interleukin-2 polypeptide of claim 1, wherein said first amino acid mutation is an amino acid substitution, selected from the group of L72G, L72A, L72S, L72T, L72Q, L72E, L72N, L72D, L72R, and L72K.~~

~~3. The mutant interleukin-2 polypeptide of claim 1 or 2, comprising a second amino acid mutation that abolishes or reduces affinity of the mutant IL-2 polypeptide to the high-affinity IL-2 receptor and preserves affinity of the mutant IL-2 polypeptide to the intermediate-affinity IL-2 receptor, each compared to a wild-type IL-2 polypeptide.~~

~~4. The mutant interleukin-2 polypeptide of claim 3, wherein said second amino acid mutation is at a position selected from the positions corresponding to residue 35, 38, 42, 43, and 45 of human IL-2.~~

~~5. The mutant interleukin-2 polypeptide of claims 3 or 4, wherein said second amino acid mutation is at a position corresponding to residue 42 of human IL-2.~~

~~6. The mutant interleukin-2 polypeptide of claim 5, wherein said second amino acid mutation is an amino acid substitution, selected from the group of F42A, F42G, F42S, F42T, F42Q, F42E, F42N, F42D, F42R, and F42K.~~

~~7. The mutant interleukin-2 polypeptide of any one of claims 3 to 6, comprising a third amino acid mutation that abolishes or reduces affinity of the mutant IL-2 polypeptide to the high-affinity IL-2 receptor and preserves affinity of the mutant IL-2 polypeptide to the intermediate-affinity IL-2 receptor, each compared to a wild-type IL-2 polypeptide.~~

~~8~~1. ~~The~~ A mutant interleukin-2 (IL-2) polypeptide ~~of any one of claims 1 to 7~~, comprising three amino acid mutations that abolish or reduce affinity of the mutant IL-2 polypeptide to the high-affinity IL-2 receptor and preserve affinity of the mutant IL-2 polypeptide to the

intermediate-affinity IL-2 receptor, each compared to a wild-type IL-2 polypeptide, wherein said three amino acid mutations are at positions corresponding to residue 42, 45, and 72 of human IL-2 (SEQ ID NO: 1).

~~92~~. The mutant interleukin-2 polypeptide of claim ~~81~~, wherein said three amino acid mutations are amino acid substitutions selected from the group of F42A, F42G, F42S, F42T, F42Q, F42E, F42N, F42D, F42R, F42K, Y45A, Y45G, Y45S, Y45T, Y45Q, Y45E, Y45N, Y45D, Y45R, Y45K, L72G, L72A, L72S, L72T, L72Q, L72E, L72N, L72D, L72R, and L72K.

~~103~~. The mutant interleukin-2 polypeptide of any one of claims 1 ~~to or~~ ~~92~~, wherein said amino acid mutation at the position corresponding to position 72 of human IL-2 is the amino acid substitution L72G.

~~114~~. The mutant interleukin-2 polypeptide of any one of claims ~~4~~ 1 to ~~103~~, wherein said amino acid mutation at the position corresponding to position 42 of human IL-2 is the amino acid substitution F42A.

~~125~~. The mutant interleukin-2 polypeptide of any one of claims ~~4 or 81~~ to ~~114~~, wherein said amino acid mutation at the position corresponding to position 45 of human IL-2 is the amino acid substitution Y45A.

~~136~~. The mutant interleukin-2 polypeptide of any one of claims ~~8~~ 1 to ~~125~~, wherein said three amino acid mutations are the amino acid substitutions F42A, Y45A and L72G.

7. The mutant interleukin-2 polypeptide of claim 6, additionally comprising the amino acid substitution C125A.

~~148~~. The mutant interleukin-2 polypeptide of any one of claims 1 to ~~137~~, further comprising an amino acid mutation which eliminates the O-glycosylation site of IL-2 at a position corresponding to residue 3 of human IL-2.

~~159~~. The mutant interleukin-2 polypeptide of claim ~~148~~, wherein said amino acid mutation which eliminates the O-glycosylation site of IL-2 at a position corresponding to residue 3 of human IL-2 is an amino acid substitution selected from the group of T3A, T3G, T3Q, T3E, T3N, T3D, T3R, T3K, and T3P.

~~1610~~. The mutant interleukin-2 polypeptide of claim ~~14~~ 8 or ~~159~~, wherein said amino acid mutation which eliminates the O-glycosylation site of IL-2 at a position corresponding to residue 3 of human IL-2 is the amino acid substitution T3A.

~~17~~11. The mutant interleukin-2 polypeptide of any one of claims 1 to ~~16~~10, wherein said mutant IL-2 polypeptide comprises the sequence of SEQ ID NO: 19.

~~18~~12. The mutant interleukin-2 polypeptide of any one of claims 1 to ~~17~~11, wherein said mutant IL-2 polypeptide is linked to a non-IL-2 moiety.

~~19~~13. The mutant interleukin-2 polypeptide of any one of claims 1 to ~~18~~12, wherein said mutant IL-2 polypeptide is linked to a first and a second non-IL-2 moiety.

~~20~~14. The mutant interleukin-2 polypeptide of claim ~~19~~13, wherein said mutant IL-2 polypeptide shares a carboxy-terminal peptide bond with said first non-IL-2 moiety and an amino-terminal peptide bond with said second non-IL-2 moiety.

~~21~~15. The mutant interleukin-2 polypeptide of any one of claims ~~18~~-12 to ~~20~~14, wherein said non-IL-2 moiety is an antigen binding moiety.

~~22~~16. An immunoconjugate comprising a mutant IL-2 polypeptide according to any one of claims 1 to ~~17~~-11 and an antigen binding moiety.

~~23~~17. The immunoconjugate of claim ~~22~~16, wherein said mutant IL-2 polypeptide shares an amino- or carboxy-terminal peptide bond with said antigen binding moiety.

~~24~~18. The immunoconjugate of claims ~~22~~-16 or ~~23~~17, wherein said immunoconjugate comprises as first and a second antigen binding moiety.

~~25~~19. The immunoconjugate of claim ~~24~~18, wherein said mutant IL-2 polypeptide shares an amino- or carboxy-terminal peptide bond with said first antigen binding moiety and said

second antigen binding moiety shares an amino- or carboxy-terminal peptide bond with either i) said mutant IL-2 polypeptide or ii) said first antigen binding moiety.

~~26~~20. The mutant interleukin-2 polypeptide of claim ~~21~~15 or the immunoconjugate of any one of claims ~~22~~16 to ~~25~~19, wherein said antigen binding moiety is an antibody or an antibody fragment.

~~27~~21. The mutant interleukin-2 polypeptide of claim ~~21~~15 or the immunoconjugate of any one of claims ~~22~~16 to ~~25~~19, wherein said antigen binding moiety is selected from a Fab molecule and a scFv molecule.

~~28~~22. The mutant interleukin-2 polypeptide of claim ~~21~~15 or the immunoconjugate of any one of claims ~~22~~16 to ~~25~~19, wherein said antigen binding moiety is an immunoglobulin molecule, particularly an IgG molecule.

~~29~~23. The mutant interleukin-2 polypeptide of claim ~~21~~15 or the immunoconjugate of any one of claims ~~22~~16 to ~~25~~19, wherein said antigen binding moiety is directed to an antigen presented on a tumor cell or in a tumor cell environment.

~~30~~24. The mutant interleukin-2 polypeptide or immunoconjugate of claim ~~29~~23, wherein said antigen is selected from the group of Fibroblast Activation Protein (FAP), the A1 domain of Tenascin-C (TNC A1), the A2 domain of Tenascin-C (TNC A2), the Extra Domain B of Fibronectin (EDB), Carcinoembryonic Antigen (CEA) and the Melanoma-associated Chondroitin Sulfate Proteoglycan (MCSP).

~~31~~25. The mutant interleukin-2 polypeptide or immunoconjugate of claim ~~30~~24, wherein said antigen is FAP.

~~32~~26. The mutant interleukin-2 polypeptide or immunoconjugate of claim ~~31~~25, wherein said antigen binding moiety directed to FAP comprises (i) the heavy chain variable region sequence of SEQ ID NO: 41 and the light chain variable region sequence of SEQ ID NO: 39; (ii) the heavy chain variable region sequence of SEQ ID NO: 51 and the light chain variable region sequence of SEQ ID NO: 49; (iii) the heavy chain variable region sequence of SEQ ID NO: 111 and the light chain variable region sequence of SEQ ID NO: 109; (iv) the heavy chain variable region sequence of SEQ ID NO: 143 and the light chain variable region sequence of SEQ ID NO: 141; or (v) the heavy chain variable region

sequence of SEQ ID NO: 151 and the light chain variable region sequence of SEQ ID NO: 149.

~~33~~27. The mutant interleukin-2 polypeptide or immunoconjugate of claim ~~32~~26, comprising (i) a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 297, a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 299, and a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 233; (ii) a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 301, a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 303, and a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 231; or (iii) a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 315, a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 317, and a polypeptide sequence that is at least about 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identical to SEQ ID NO: 233.

~~34~~28. An isolated polynucleotide encoding the mutant IL-2 polypeptide or immunoconjugate of any one of claims 1 to ~~33~~27.

~~35~~29. An expression vector comprising the polynucleotide of claim ~~34~~28.

~~36~~30. A host cell comprising the polynucleotide of claim ~~34~~28 or the expression vector of claim ~~35~~29.

~~37~~31. A method of producing a mutant IL-2 polypeptide or an immunoconjugate thereof, comprising culturing the host cell of claim ~~36~~30 under conditions suitable for the expression of the mutant IL-2 polypeptide or the immunoconjugate.

~~38~~32. A mutant IL-2 polypeptide or immunoconjugate produced by the method of claim ~~37~~31.

~~39~~33. A pharmaceutical composition comprising the mutant IL-2 polypeptide or immunoconjugate of any one of claims 1 to ~~33~~ 27 or ~~38~~ 32 and a pharmaceutically acceptable carrier.

~~40~~34. The mutant IL-2 polypeptide or immunoconjugate of any one of claims 1 to ~~33~~ 27 or ~~38~~ 32 for use in the treatment of a disease in an individual in need thereof.

~~41~~35. The mutant IL-2 polypeptide or immunoconjugate of claim ~~40~~34, wherein said disease is cancer.

~~42~~36. Use of the mutant IL-2 polypeptide or immunoconjugate of any one of claims 1 to ~~33~~ 27 or ~~38~~ 32 for manufacture of a medicament for treating a disease in an individual in need thereof.

~~43~~37. The mutant IL-2 polypeptide or immunoconjugate of any one of claims 1 to ~~33~~ 27 or ~~38~~ 32 for use in stimulating the immune system of an individual, comprising administering to said individual an effective amount of a composition comprising the mutant IL-2 polypeptide or immunoconjugate in a pharmaceutically acceptable form.