

WHAT IS CLAIMED IS:

1. A polypeptide complex comprising a human interleukin 15 (IL-15) polypeptide and a human interleukin 15 receptor alpha (IL-15R α) polypeptide, wherein the polypeptide complex comprises N-linked glycans comprising FA2G2, FA2G2S1, FA2G2S2, FA3G3S1, FA2F1G2S2, FA3G2S2, and FA3G3S3.
2. The polypeptide complex of claim 1, wherein IL-15 polypeptide has the sequence of SEQ ID NO: 1 or 5, and IL-15R α has the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21.
3. The polypeptide complex of claim 1, wherein the N-linked glycans comprise at least 10%, 12.5%, 15%, 17.5%, 20% or 22.5% of FA2G2S1.
4. The polypeptide complex of claim 1, wherein the N-linked glycans comprise at least 10%, 20%, 30%, or 40% of FA2G2S2.
5. A polypeptide complex comprising a human interleukin 15 (IL-15) polypeptide and a human interleukin 15 receptor alpha (IL-15R α) polypeptide, wherein the polypeptide complex comprises O-linked glycans, and wherein at least 80%, 85%, 90% or 95% of the glycans is core-1 O-linked glycan.
6. The polypeptide complex of claim 5, wherein IL-15 polypeptide has the sequence of SEQ ID NO: 1 or 5, and IL-15R α has the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21.
7. The polypeptide complex of claim 5, wherein the core-1 O-linked glycan is monosialylated and/or disialylated.
8. A polypeptide complex comprising a human interleukin 15 (IL-15) polypeptide and a human interleukin 15 receptor alpha (IL-15R α) polypeptide,
wherein the polypeptide complex comprises O-linked glycans, and wherein at least 80%, 85%, 90% or 95% of the glycans has core-1 O-linked glycan structures; and
wherein the polypeptide complex comprises N-linked glycans comprising FA2G2, FA2G2S1, FA2G2S2, FA3G3S1, FA2F1G2S2, FA3G2S2, and FA3G3S3.
9. The polypeptide complex of claim 8, wherein IL-15 polypeptide has the sequence of SEQ ID NO: 1 or 5, and IL-15R α has the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21.

10. The polypeptide complex of claim 8, wherein the N-linked glycans comprise at least 10%, 12.5%, 15%, 17.5%, 20% or 22.5% of FA2G2S1.

11. The polypeptide complex of claim 8, wherein the N-linked glycans comprise at least 10%, 20%, 30%, or 40% of FA2G2S2.

12. The polypeptide complex of claim 8, wherein the core-1 O-linked glycan is predominantly monosialylated and/or disialylated.

13. An isolated IL-15/IL-15R α heterodimer produced in a non-human cell, wherein the IL-15/IL-15R α heterodimer comprises α (2,6) O-linked sialylation.

14. The isolated IL-15/IL-15R α heterodimer of claim 13, wherein the non-human cell is a recombinant Chinese hamster ovary (CHO) cell.

15. The isolated IL-15/IL-15R α heterodimer of claim 14, wherein the CHO cell is altered to impair the function of matriptase.

16. The isolated IL-15/IL-15R α heterodimer of claim 13, wherein the isolated IL-15/IL-15R α heterodimer comprises O-linked glycans, and wherein at least 80%, 85%, 90% or 95% of the glycans is core-1 O-linked glycan.

17. The isolated IL-15/IL-15R α heterodimer of claim 16, wherein about 15% of the O-glycans has α (2,6)-linked sialylation.

18. A pharmaceutical composition comprising the polypeptide complex or the isolated IL-15/IL-15R α heterodimer of claim 13.

19. The pharmaceutical composition of claim 18, further comprising a pharmaceutically acceptable carrier.

20. A non-human cell comprising nucleic acids encoding a human interleukin 15 (IL-15) polypeptide and a human interleukin 15 receptor alpha (IL-15R α) polypeptide, wherein the IL-15 and IL-15 R α expressed by the cell form a heterodimer, and wherein the heterodimer comprises α (2,6)-linked sialylation.

21. The non-human cell of claim 20, wherein the non-human cell is a recombinant Chinese hamster ovary (CHO) cell.

22. The non-human cell of claim 20, wherein the CHO cell is altered to impair the function of matriptase.

23. A method of treating cancer, comprising administering to a subject in need of the pharmaceutical composition of claim 18.

24. A method of producing cells that express IL-15/IL-15 α heterodimer, comprising:

(a) providing non-human cells;

(b) transfecting the non-human cells with two vectors at the same time, wherein the two vectors comprises a first vector encoding both IL-15R α and IL-15, and a second vector encoding a portion of IL-15R α and culturing the transfected cells;

(c) transfecting the cells from step b) with a third vector encoding IL-15 and culturing the transfected cells; and

(d) isolating individual clones that express IL-15/IL-15 α heterodimer.

25. The method of claim 24, wherein the non-human cell is a recombinant Chinese hamster ovary (CHO) cell.

26. The method of claim 25, wherein the CHO cell is modified to impair the function of the matriptase gene.

27. The method of claim 24, wherein the IL-15R α has the sequence of SEQ ID NO: 6, 12 or 14.

28. The method of claim 24, wherein the IL-15 has the sequence of SEQ ID NO: 1 or 5.

29. The method of claim 24, wherein the portion of IL-15 R α is a soluble portion of IL-15R α .

30. The method of claim 29, wherein the soluble portion of IL-15R α has the sequence of SEQ ID NO:7, 10 or 21.

31. A method of producing IL-15/IL-15 R α heterodimer, comprising

(a) culturing the cells produced by claim 24 under a condition that allow for expression of a IL-15/IL-15R α heterodimer and secretion of the IL-15/IL-15R α heterodimer, and

(b) isolating the IL-15/IL-15 α heterodimer from the cell culture.

32. A polypeptide complex comprising a human interleukin 15 (IL-15) polypeptide and a human interleukin 15 receptor alpha (IL-15R α) polypeptide, wherein the polypeptide complex is produced by a recombinant Chinese hamster ovary (CHO) cell, and wherein the polypeptide complex does not have a IL-15R α chain splicing variant.

33. The polypeptide complex according to claim 32, wherein the CHO cell is altered to impair the function of matriptase.

34. The polypeptide complex of claim 32, wherein the IL-15R α chain splicing variant comprise 159 residues spanning from I1 to G159.