

WHAT IS CLAIMED IS:

1. An isolated human interleukin 15 and interleukin 15 receptor alpha (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.
2. The isolated IL-15/IL-15R α heterodimer of claim 1, wherein the non-human cell is a non-human mammalian cell.
3. The isolated IL-15/IL-15R α heterodimer of claim 1, wherein the non-human cell is a recombinant Chinese hamster ovary (CHO) cell.
4. The isolated IL-15/IL-15R α heterodimer of any one of claims 1-3, wherein the isolated IL-15/IL-15R α heterodimer comprises O-linked glycans, and wherein at least 80%, 85%, 90% or 95% of the O-linked glycans are core-1 O-linked glycan.
5. The isolated IL-15/IL-15R α heterodimer of claim 4, wherein about 15% of the O-glycans have α (2,6)-linked sialylation.
6. The isolated IL-15/IL-15R α heterodimer of any one of claims 1-5, wherein the IL-15 comprises the amino acid sequence of SEQ ID NO: 1 or 5, or a fragment thereof; and the IL-15R α comprises the amino acid sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21, or a fragment thereof.
7. The isolated IL-15/IL-15R α heterodimer of any one of claims 1-5, wherein the IL-15 comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1, and the IL-15R α comprises the amino acid sequence of SEQ ID NO: 10.
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 N-linked glycans comprising FA2G2, FA2G2S1, FA2G2S2, FA3G3S1, FA2F1G2S2, FA3G2S2, and FA3G3S3.

9. The polypeptide complex of claim 8, wherein the IL-15 polypeptide comprises the sequence of SEQ ID NO: 1 or 5, or a fragment thereof; and the IL-15R α comprises the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21, or a fragment thereof.

10. The polypeptide complex of claim 8, wherein the IL-15 polypeptide comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1, and the IL-15R α polypeptide comprises the amino acid sequence of SEQ ID NO: 10.

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

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

13. 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 O-linked glycans are core-1 O-linked glycans.

14. The polypeptide complex of claim 13, wherein the IL-15 polypeptide comprises the sequence of SEQ ID NO: 1 or 5, or a fragment thereof; and the IL-15R α comprises the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21, or a fragment thereof.

15. The polypeptide complex of claim 13, wherein the IL-15 polypeptide comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1, and the IL-15R α polypeptide comprises the amino acid sequence of SEQ ID NO: 10.

16. The polypeptide complex of any one of claims 13-15, wherein the core-1 O-linked glycans are predominantly monosialylated and/or disialylated.

17. 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 O-linked glycans have core-1 O-linked glycan structures; and

wherein the polypeptide complex comprises N-linked glycans comprising FA2G2, FA2G2S1, FA2G2S2, FA3G3S1, FA2F1G2S2, FA3G2S2, and FA3G3S3.

18. The polypeptide complex of claim 17, wherein the IL-15 polypeptide comprises the sequence of SEQ ID NO: 1 or 5, or a fragment thereof; and the IL-15R α comprises the sequence of SEQ ID NO: 6, 7, 10, 12, 14 or 21, or a fragment thereof.

19. The polypeptide complex of claim 18, wherein the IL-15 polypeptide comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1, and the IL-15R α polypeptide comprises the amino acid sequence of SEQ ID NO: 10.

20. The polypeptide complex of any one of claims 17-19, wherein at least 10%, 12.5%, 15%, 17.5%, 20% or 22.5% of the N-linked glycans comprise FA2G2S1.

21. The polypeptide complex of any one of claims 17-20, wherein at least 10%, 20%, 30%, or 40% of the N-linked glycans comprise FA2G2S2.

22. The polypeptide complex of any one of claims 17-21, wherein the core-1 O-linked glycans are predominantly monosialylated and/or disialylated.

23. A pharmaceutical composition comprising the isolated IL-15/IL-15R α heterodimer of any one of claims 1-7 or the polypeptide complex of any one of claims 8-22, and a pharmaceutically acceptable carrier.

24. A non-human cell comprising a nucleic acid sequence encoding a human interleukin 15 (IL-15) polypeptide and a nucleic acid sequence encoding a human interleukin 15 receptor alpha (IL-15R α) polypeptide, wherein the cell is effective to express the IL-15 and IL-15 R α

polypeptides, and wherein the IL-15 and IL-15 R α polypeptides are effective to form a heterodimer, and wherein the heterodimer comprises $\alpha(2,6)$ -linked sialylation.

25. The non-human cell of claim 24, wherein the non-human cell is a non-human mammalian cell.

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

27. Use of the isolated IL-15/IL-15R α heterodimer of any one of claims 1-7, the polypeptide complex of any one of claims 8-22, the pharmaceutical composition of claim 23, or the non-human cell of any one of claims 24-26 in the manufacture of a medicament for the treatment of cancer.

28. A method of producing cells that express an 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 the IL-15/IL-15 α heterodimer, wherein the IL-15/IL-15 α heterodimer comprises $\alpha(2,6)$ O-linked sialylation.

29. The method of claim 28, wherein the non-human cell is a non-human mammalian cell.

30. The method of claim 28, wherein the non-human cell is a recombinant Chinese hamster ovary (CHO) cell.

31. The method of any one of claims 28-30, wherein the IL-15R α comprises the sequence of SEQ ID NO: 6, 12 or 14, or a fragment thereof.

32. The method of any one of claims 28-31, wherein the IL-15 comprises the sequence of SEQ ID NO: 1 or 5, or a fragment thereof.

33. The method of any one of claims 28-31, wherein the IL-15 comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1.

34. The method of any one of claims 28-30, wherein the portion of IL-15 R α is a soluble portion of IL-15R α .

35. The method of claim 34, wherein the soluble portion of IL-15R α comprises the sequence of SEQ ID NO: 7, 10 or 21.

36. The method of any one of claims 28-30, wherein the IL-15 comprises residues 49-162 of the amino acid sequence of SEQ ID NO: 1, and the IL-15R α comprises the amino acid sequence of SEQ ID NO: 10.

37. A method of producing an IL-15/IL-15 R α heterodimer, comprising:

(a) culturing the cells produced by the method of any one of claims claim 28-36 under a condition that allows for expression of the 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.

38. 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 comprising 159 residues spanning from I1 to G159 of the amino acid sequence of SEQ ID NO: 29.