expanding T cells directly in patients would have several benefits, including saving production cost and time and reducing process-mediated differentiation of the T cells. However, until to date, there is no clinically validated procedure established by which CAR-T cells can be specifically expanded in patients.

Conventional IL-2 therapy suffers from dose-limiting systemic side effects mediated by e.g. regulatory T cells or endothelial cells. To overcome this limitation, researchers have developed novel IL-2-based therapies. For example it has been shown that cis-targeting IL-2 to the desired tumor-reactive T cell population has a significantly improved toxicity profile. Different strategies for the cis-targeting have been reported, including e.g., CD8 (Sultan et al. (2021)) or PD1 targeting (Deak et al. (2022)).

Summary

The disclosure comprises the combination therapy of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex with a membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex for use as a combination therapy, in particular in the treatment of cancer, for the use as a combination therapy in the prevention or treatment of metastasis, or for use as a combination therapy in stimulating an immune response or function, such as T cell activity.

In one aspect, provided is a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in combination with a recombinant membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex, for use in the treatment of cancer, for use in the prevention or treatment of metastasis, or for use in stimulating an immune response or function, such as T cell activity,
wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, wherein the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety, and
wherein the MAB polypeptide or MAB polypeptide complex comprises an antigen-binding moiety, or a component thereof, and a transmembrane domain, wherein the antigen-binding moiety binds to a variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind.

In another aspect, provided is a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex, comprising:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide

comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, wherein the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety.

Provided is a method for treatment or prevention of cancer or for stimulating and immune response or function, such as T cell activity in an individual, wherein said method comprises

(a) administration of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex to the individual, wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering; and

(b) administration of a recombinant membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex, wherein the MAB polypeptide or MAB polypeptide complex comprises an antigen-binding moiety, or a component thereof, and a transmembrane domain, wherein the antigen-binding moiety binds to a variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering, relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind.

In another aspect, provided is use of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in the manufacture of a medicament for treatment or prevention of cancer or for stimulating and immune response or function, such as T cell activity in an individual, wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering.

In another aspect, provided is use of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in the manufacture of a medicament for the treatment or prevention of cancer or for stimulating and immune response or function, such as T cell activity in an individual, wherein the treatment comprises:

(a) administration of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex to the individual, wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering; and

(b) administration of a recombinant membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex, wherein the MAB polypeptide or MAB polypeptide complex comprises an antigen-binding moiety, or a component thereof, and a transmembrane domain, wherein the antigen-binding moiety binds to a variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering, relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind.

In some examples, the antigen-binding moiety that binds to the Fc-IL2v comprises the heavy chain variable (VH) region and light chain variable (VL) region of an antibody that binds to the variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering.

In some examples, the antigen-binding moiety is or comprises an Fv, scFv, Fab, Fab‘, Fab‘-SH, $F(ab')_2$, crossFab, scFab or dAb moiety.

In some examples, the antigen-binding moiety comprises:

(a) (i) a VH region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:11;

HC-CDR2 having the amino acid sequence of SEQ ID NO:19; and

HC-CDR3 having the amino acid sequence of SEQ ID NO:13;

and

(ii) a VL region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:24;

LC-CDR2 having the amino acid sequence of SEQ ID NO:25; and

LC-CDR3 having the amino acid sequence of SEQ ID NO:26;

or

(b) (i) a VH region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:11;

HC-CDR2 having the amino acid sequence of SEQ ID NO:12; and

HC-CDR3 having the amino acid sequence of SEQ ID NO:13;

and

(ii) a VL region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:24;

LC-CDR2 having the amino acid sequence of SEQ ID NO:25; and

LC-CDR3 having the amino acid sequence of SEQ ID NO:26.

In some examples, the mutant IL-2 polypeptide further comprises the amino acid substitution Q126T.

In some examples, the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety, in particular wherein the recombinant Fc-IL2v polypeptide complex does not comprise a scFv, Fab or crossFab.

In some examples, the recombinant MAB polypeptide comprises an amino acid sequence derived from IL2Ra, IL15Ra or CD8a.

In some examples, the recombinant MAP polypeptide is a chimeric antigen receptor (CAR).

In some examples, the recombinant MAP polypeptide comprises at least one recombinant CD3-TCR complex polypeptide.

In some examples, the recombinant CD3-TCR complex polypeptide comprises:

(i) an antigen-binding moiety, or a component thereof, wherein the antigen-binding moiety binds to the variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering, relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind; and

(ii) a CD3-TCR complex association domain having an amino acid sequence derived from a CD3-TCR complex polypeptide.

In some examples, the recombinant CD3-TCR complex polypeptide is capable of associating through its CD3-TCR complex association domain with one or more CD3-TCR complex polypeptides to form a CD3-TCR complex.

In some examples, the amino acid sequence derived from a CD3-TCR complex polypeptide is derived from CD3ε, TCRα or TCRβ.

In another aspect, provided is a cell comprising a recombinant MAB polypeptide or MAB polypeptide complex as hereinbefore described.

In another aspect, provided is a method of producing an enriched pool of cells comprising contacting a starting pool of cells comprising at least one cell as hereinbefore described with the recombinant Fc-IL2v polypeptide complex as hereinbefore described and incubating the cells until the fraction of cells comprising the recombinant MAB polypeptide or MAB polypeptide complex reaches a desired fraction of the total pool of cells to produce the enriched pool of cells.

In another aspect, provided is a nucleic acid, or a plurality of nucleic acids, encoding a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex as hereinbefore described, or a recombinant MAB polypeptide or MAB polypeptide complex as hereinbefore described.

In another aspect, provided is an expression vector, or a plurality of expression vectors, comprising a nucleic acid as hereinbefore described.

In another aspect, provided is a cell comprising a recombinant MAB polypeptide or MAB polypeptide complex as hereinbefore described, a nucleic acid or a plurality of nucleic acids as hereinbefore described, or an expression vector or a plurality of expression vectors as hereinbefore described.

In some examples, cells expressing the recombinant MAB polypeptide and/or the recombinant MAB polypeptide complex cells are specifically expanded, in particular wherein the cells are specifically expanded by contacting the cells with the recombinant Fc-IL2v polypeptide complex as hereinbefore described.

In some examples, cells expressing the recombinant MAB polypeptide and/or the recombinant MAB polypeptide complex cells are enriched, in particular wherein the cells are enriched by contacting the cells with the recombinant Fc-IL2v polypeptide complex as hereinbefore described.

In some examples, cells expressing the recombinant MAB polypeptide and/or the recombinant MAB polypeptide complex cells are enriched to >90% of a total cell pool.

In another aspect, provided is a method of producing an enriched pool of cells comprising contacting a starting pool of cells comprising at least one cell as hereinbefore described with the recombinant Fc-IL2v polypeptide complex as hereinbefore described and incubating the cells until the fraction of cells comprising the recombinant MAB polypeptide or MAB polypeptide complex reaches a desired fraction of the total pool of cells to produce the enriched pool of cells.

In another aspect, provided is a pharmaceutical composition comprising a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex as hereinbefore described, a cell as hereinbefore described or an enriched pool of cells produced as hereinbefore described.

Provided is the disclosure as hereinbefore described with reference to the Figures and Examples.

Brief description of the Figures

Figure 1A-1D. Schematic representation of exemplary recombinant membrane-anchored antigen bining (MAB) polypeptides and MAB polypeptide complexes according to the present disclosure. Depicted are (from left to right) a recombinant CD3ε-TCR complex polypeptide in a TCR complex, a recombinant TCRαβ based MAB polypeptide complex, recombinant first or second generation CARs and recombinant non-signaling tags with a binding moiety in form of a scFv (1A). Schematic representation of the gene constructs corresponding to the P329G-CARs (1B), TCR-based MAB polypeptide complexes (P329G-CD3ε and P329G-Cαβ) (1C) and non-signaling MAB polypeptide (P329G-tag, 1D).

Figure 2. Schematic representation of exemplary recombinant Fc-IL2v polypeptide complexes according to the present disclosure. An IL2 variant is fused via a linker to a variant Fc containing an orthogonal

Claims

1. A recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in combination with a recombinant membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex, for use in the treatment of cancer, for use in the prevention or treatment of metastasis, or for use in stimulating an immune response or function, such as T cell activity,
wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, wherein the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety, and

wherein the MAB polypeptide or MAB polypeptide complex comprises an antigen-binding moiety, or a component thereof, and a transmembrane domain, wherein the antigen-binding moiety binds to a variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind.

2. A recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex, comprising:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, wherein the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety.

3. Use of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in the manufacture of a medicament for treatment or prevention of cancer or for stimulating and immune response or function, such as T cell activity in an individual, wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering.

4. Use of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex in the manufacture of a medicament for the treatment or prevention of cancer or for stimulating and immune response or function, such as T cell activity in an individual, wherein the treatment comprises:

(a) administration of a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex to the individual, wherein the recombinant Fc-IL2v polypeptide complex comprises:

(i) a first polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering, and wherein the first polypeptide further comprises an IL-2 variant (IL2v) polypeptide comprising an IL-2 polypeptide comprising the amino acid substitutions F42A, Y45A and L72G wherein numbering is relative to the human IL-2 sequence SEQ ID NO: 40; and

(ii) a second polypeptide comprising a variant CH2-CH3 region comprising G329 according to EU numbering; and

(b) administration of a recombinant membrane-anchored antigen binding (MAB) polypeptide or MAB polypeptide complex, wherein the MAB polypeptide or MAB polypeptide complex comprises an antigen-binding moiety, or a component thereof, and a transmembrane domain, wherein the antigen-binding moiety binds to a variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering, relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind.

5. The recombinant Fc-IL2v polypeptide complex for use according to claim 1, the recombinant Fc-IL2v polypeptide complex according to claim 2, or the use according to claim 3 or 4, wherein the antigen-binding moiety that binds to the Fc-IL2v comprises the heavy chain variable (VH) region and light chain variable (VL) region of an antibody that binds to the variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering.

6. The recombinant Fc-IL2v polypeptide complex for use according to claim 1 or 5, the recombinant Fc-IL2v polypeptide complex according to claim 2 or 5, or the use according to any one of claims 3 to 5, wherein the antigen-binding moiety is or comprises an Fv, scFv, Fab, Fab‘, Fab‘-SH, $F(ab')_2$, crossFab, scFab or dAb moiety.

7. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1, 5 or 6, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2, 5 or 6, or the use according to any one of claims 3 to 6, wherein the antigen-binding moiety comprises:

(a) (i) a VH region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:11;

HC-CDR2 having the amino acid sequence of SEQ ID NO:19; and

HC-CDR3 having the amino acid sequence of SEQ ID NO:13;

and

(ii) a VL region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:24;

LC-CDR2 having the amino acid sequence of SEQ ID NO:25; and

LC-CDR3 having the amino acid sequence of SEQ ID NO:26;

or

(b) (i) a VH region incorporating the following CDRs:

HC-CDR1 having the amino acid sequence of SEQ ID NO:11;

HC-CDR2 having the amino acid sequence of SEQ ID NO:12; and

HC-CDR3 having the amino acid sequence of SEQ ID NO:13;

and

(ii) a VL region incorporating the following CDRs:

LC-CDR1 having the amino acid sequence of SEQ ID NO:24;

LC-CDR2 having the amino acid sequence of SEQ ID NO:25; and

LC-CDR3 having the amino acid sequence of SEQ ID NO:26.

8. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 7, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 7, or the use according to any one of claims 3 to 7, wherein the mutant IL-2 polypeptide further comprises the amino acid substitution Q126T.

9. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 8, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 8, or the use according to any one of claims 3 to 8, wherein the recombinant Fc-IL2v polypeptide complex does not comprise an antigen binding moiety, in particular wherein the recombinant Fc-IL2v polypeptide complex does not comprise a scFv, Fab or crossFab.

10. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 9, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 9, or the use according to any one of claims 3 to 9, wherein the recombinant MAB polypeptide comprises an amino acid sequence derived from IL2Ra, IL15Ra or CD8a.

11. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 10, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 10, or the use according to any one of claims 3 to 10, wherein the recombinant MAP polypeptide is a chimeric antigen receptor (CAR).

12. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 11, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 11, or the use according to any one of claims 3 to 11, wherein the recombinant MAP polypeptide comprises at least one recombinant CD3-TCR complex polypeptide.

13. The recombinant Fc-IL2v polypeptide complex, the use or the recombinant Fc-IL2v polypeptide complex for use according to claim 12, wherein the recombinant CD3-TCR complex polypeptide comprises:

(i) an antigen-binding moiety, or a component thereof, wherein the antigen-binding moiety binds to the variant CH2-CH3 region comprising the amino acid substitution P329G according to EU numbering, relative to the amino acid sequence of a reference CH2-CH3 region comprising P329 according to EU numbering, to which the antigen-binding moiety does not bind; and

(ii) a CD3-TCR complex association domain having an amino acid sequence derived from a CD3-TCR complex polypeptide.

14. The recombinant Fc-IL2v polypeptide complex, the use or the recombinant Fc-IL2v polypeptide complex for use according to claim 13, wherein the recombinant CD3-TCR complex polypeptide is capable of associating through its CD3-TCR complex association domain with one or more CD3-TCR complex polypeptides to form a CD3-TCR complex.

15. The recombinant Fc-IL2v polypeptide complex, the use or the recombinant Fc-IL2v polypeptide complex for use according to claim 13 or 14, wherein the amino acid sequence derived from a CD3-TCR complex polypeptide is derived from CD3ε, TCRα or TCRβ.

16. A cell comprising a recombinant MAB polypeptide or MAB polypeptide complex according to any one of claims 1 or 10 to 15.

17. A method of producing an enriched pool of cells comprising contacting a starting pool of cells comprising at least one cell according to claim 16 with the recombinant Fc-IL2v polypeptide complex of any one of claims 2 or 5 to 9 and incubating the cells until the fraction of cells comprising the recombinant MAB polypeptide or MAB polypeptide complex reaches a desired fraction of the total pool of cells to produce the enriched pool of cells.

18. A nucleic acid, or a plurality of nucleic acids, encoding a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex according to any one of claims 2 or 5 to 9, or a recombinant MAB polypeptide or MAB polypeptide complex according to any one of claims 1 or 10 to 15.

19. An expression vector, or a plurality of expression vectors, comprising a nucleic acid according to claim 18.

20. A cell comprising a recombinant MAB polypeptide or MAB polypeptide complex according to any one of claims 1 or 10 to 15, a nucleic acid or a plurality of nucleic acids according to claim 18, or an expression vector or a plurality of expression vectors according to claim 19.

21. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 15, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 15, or the use according to any one of claims 3 to 15, or the cell of claim 20, wherein cells expressing the recombinant MAB

polypeptide and/or the recombinant MAB polypeptide complex cells are specifically expanded, in particular wherein the cells are specifically expanded by contacting the cells with the recombinant Fc-IL2v polypeptide complex of any one of claims 2 or 5 to 9.

22. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 15, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 15, or the use according to any one of claims 3 to 15, or the cell of claim 20, wherein cells expressing the recombinant MAB polypeptide and/or the recombinant MAB polypeptide complex cells are enriched, in particular wherein the cells are enriched by contacting the cells with the recombinant Fc-IL2v polypeptide complex of any one of claims 2 or 5 to 9.

23. The recombinant Fc-IL2v polypeptide complex for use according to any one of claims 1 or 5 to 15, the recombinant Fc-IL2v polypeptide complex according to any one of claims 2 or 5 to 15, or the use according to any one of claims 3 to 15, or the cell of claim 20, wherein cells expressing the recombinant MAB polypeptide and/or the recombinant MAB polypeptide complex cells are enriched to >90% of a total cell pool.

24. A method of producing an enriched pool of cells comprising contacting a starting pool of cells comprising at least one cell according to claim 20 with the recombinant Fc-IL2v polypeptide complex of any one of claims 2 or 5 to 9 and incubating the cells until the fraction of cells comprising the recombinant MAB polypeptide or MAB polypeptide complex reaches a desired fraction of the total pool of cells to produce the enriched pool of cells.

25. A pharmaceutical composition comprising a recombinant Fc domain-IL2 variant (Fc-IL2v) polypeptide complex according to any one of claims 2 or 5 to 9, a cell according to claim 20 or an enriched pool of cells produced according to claim 24.