CLAIMS

1. Use of an IL-2 agent in the manufacture of a medicament for treating or preventing a skin transplantation rejection in a subject,

wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5.

2. The use of claim 1, wherein the subject has received, is receiving, or will receive a skin transplantation.

3. The use of claim 1, wherein the skin transplantation rejection is graft-vs-host disease (GVHD).

4. Use of an IL-2 agent in the manufacture of a medicament for conditioning a subject prior to a skin transplantation,

wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5.

5. The use of claim 4, wherein:

(i) conditioning a subject prior to the skin transplantation comprises increasing the number of T regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample);

(ii) conditioning a subject prior to the skin transplantation comprises increasing the ratio of T regulatory cells over non-T-regulatory T cells and/or NK cells in the subject or in a sample from the subject (e.g., a peripheral blood sample), optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more; and/or

(iii) the IL-2 agent is used during the skin transplantation and/or after the skin transplantation.

6. Use of an IL-2 agent in the manufacture of a medicament for inducing and/or modulating (*e.g.*, increasing) immunosuppression in a subject,

wherein the subject has undergone, is undergoing, or will receive a skin transplantation,

wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5.

7. The use of claim 6, wherein:

(i) increasing immunosuppression in a subject comprises increasing the number of T-regulatory cells in the subject, or in a sample from the subject (*e.g.*, a peripheral blood sample); and/or

(ii) increasing immunosuppression in a subject prior to skin transplantation comprises increasing the ratio of T regulatory cells over non-T regulatory T cells and/or NK cells in the subject or in a sample from the subject (e.g., a peripheral blood sample), optionally wherein the ratio is increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more.

8. Use of an IL-2 agent in the manufacture of a medicament for selectively increasing T regulatory cells in a subject,

wherein the subject has undergone, is undergoing, or will receive a skin transplantation, and

wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5.

9. The use of claim 8, wherein the T regulatory cells are increased by about 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100%, or more, or about 2, 3, 4, 5, 6, 7, 8, 9, 10-fold or more, relative to non-T regulatory T cells, NK cells, non-T regulatory CD4+ cells, and/or CD8+ cells.

10. An IL-2 agent for use as a medicament in combination with a skin transplantation, wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5.

11. Use of an IL-2 agent in the manufacture of a medicament for:

(i) preventing a skin transplantation rejection in a subject;

(ii) inducing and/or modulating (e.g., increasing) immunosuppression in a subject; or

(iii) selectively increasing T regulatory cells in a subject,

wherein the IL-2 agent is an IL-2 fusion protein comprising an IL-2 variant, and wherein the IL-2 variant comprises the amino acid sequence of SEQ ID NO: 5, and wherein the medicament is to be used in combination with a skin transplantation.

12. The use of claim 11, wherein the skin transplantation rejection is graft versus host disease (GVHD).

13. The use of claim 11 or 12, wherein the IL-2 agent is to be administered to the subject prior to, during, and/or after the skin transplantation.

14. The use of any one of claims 1-9 or 11-13, or the IL-2 agent for use of claim 10, wherein the medicament is to be used in combination with one or more additional immunosuppressive agents chosen from cyclosporine, tacrolimus, mycophenolate mofetil, prednisone, azathioprine, sirolimus, daclizumab, or basiliximab.

15. The use of any one of claims 1-9 or 11-14, or the IL-2 agent for use of claim 10 or 14, wherein the IL-2 fusion protein further comprises an Fc region.

16. The use of claim 15, or the IL-2 agent for use of claim 15, wherein the Fc region:

(i) comprises an Fc region of IgG1 allotype m3 comprising an N297G substitution according to EU numbering;

(ii) comprises the amino acid sequence of SEQ ID NO: 1003, or an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof; and/or

(iii) is fused to the C-terminus of the IL-2 variant.

17. The use of any one of claims 1-9 or 11-16, or the IL-2 agent for use of any one of claims 10 or 14-16, wherein the IL-2 fusion protein further comprises a linker.

18. The use of claim 17 or the IL-2 agent for use of claim 17, wherein the linker comprises the amino acid sequence $(G_4S)_4$ (SEQ ID NO: 48).

19. The use of any one of claims 1-9 or 11-18, or the IL-2 agent for use of any one of claims 10 or 14-18, wherein the IL-2 fusion protein comprises an amino acid sequence of SEQ ID NO: 1008, an amino acid sequence that is at least 95% identical thereto or differs by no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids therefrom, or a functional fragment thereof.

20. The use of any one of claims 1-9 or 11-19, or the IL-2 agent for use of any one of claims 10 or 14-19, wherein the fusion protein comprises an amino acid sequence of SEQ ID NO: 1008.

21. The use of any one of claims 1-9 or 11-20, or the IL-2 agent for use of any one of claims 10 or 14-20, wherein the fusion protein forms a dimer.

22. The use of any one of claims 1-9 or 11-21, wherein the subject is a human, a non-human primate, or a mouse.

23. The use of any one of claims 1-9 or 11-22, or the IL-2 agent for use of any one of claims 10 or 14-22, wherein the use further comprises determining the activity of T regulatory cells, *e.g.*, by an *ex vivo* suppression assay.