first target-binding domain and the second target-binding domain bind to a receptor for IL-2.

In a **first aspect**, the present disclosure refers to a method of stimulating or increasing the proliferation of a T_{reg} cell, wherein the method comprises:

culturing a T_{reg} cell in a liquid culture medium over a period of time, wherein at the beginning of the period of time, the liquid culture medium comprises:

a CD3/CD28-binding agent; and

a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1,

wherein the CD3/CD28-binding agent is:

(A) an anti-CD3/anti-CD28 bead;

(B) an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

(C) a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94; and

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains..

In an example, the present disclosure refers to a population of T_{reg} cells generated by any one of the methods of the first aspect.

In an example, the present disclosure refers to a composition comprising the population of T_{reg} cells of the previous example and a pharmaceutically acceptable carrier.

In an example, the present disclosure refers to use of the composition of the previous example in the manufacture of a medicament for treating a subject in need thereof.

In a **second aspect**, the present disclosure refers to a kit comprising:

(i) a CD3/CD28-binding agent;

(ii) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1; and

(iii) an mTOR inhibitor,

wherein the CD3/CD28-binding agent is:

(A) an anti-CD3/anti-CD28 bead;

(B) an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

(C) a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

In a **third aspect**, the present disclosure refers to method of stimulating or increasing the proliferation of a T_{reg} cell, wherein the method comprises:

culturing a T_{reg} cell in a liquid culture medium over a period of time, wherein at the beginning of the period of time, the liquid culture medium comprises:

(a) interleukin-2; and

(b) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94.

In an example, the present disclosure refers to a population of T_{reg} cells generated by any one of the methods of the third aspect.

In an example, the present disclosure refers to a composition comprising the population of T_{reg} cells of the previous example and a pharmaceutically acceptable carrier.

In an example, the present disclosure refers to use of the composition of the previous example in the manufacture of a medicament for treating a subject in need thereof.

In a **fourth aspect**, the present disclosure refers to a kit comprising:

(i) interleukin-2;

(ii) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains; and

(iii) an mTOR inhibitor.

In an example, the present disclosure refers to a method of stimulating or increasing the proliferation of a T_{reg} cell, wherein the method comprises:

culturing a T_{reg} cell in a liquid culture medium over a period of time, wherein at the beginning of the period of time, the liquid culture medium comprises:

a CD3/CD28-binding agent; and

a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a first domain of a pair of affinity domains; and

(b) a second chimeric polypeptide comprising:

(i) a second domain of a pair of affinity domains; and

(ii) a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

In an example, the present disclosure refers to population of T_{reg} cells generated by any one of the methods of the previous example.

In an xample, the present disclosure refers to a composition comprising the population of T_{reg} cells of the previous example and a pharmaceutically acceptable carrier.

In an example, the present disclosure refers to use of the composition of the previous example in the manufacture of a medicament for treating a subject in need thereof.

In an example, the present disclosure refers to a kit comprising:

a CD3/CD28-binding agent;

a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising:

(i) a first target-binding domain;

(ii) a soluble tissue factor domain; and

(iii) a first domain of a pair of affinity domains;

(b) a second chimeric polypeptide comprising:

(i) a second domain of a pair of affinity domains; and

(ii) a second target-binding domain,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains; and

an mTOR inhibitor.

In an example, the present disclosure refers to a method of isolating a T_{reg} cell from a sample obtained from a subject, wherein the method comprises separating the T_{reg} cell from the sample based on its expression of CD39, thereby isolating the T_{reg} cell.

In an example, the present disclosure refers to a population of isolated T_{reg} cells generated by the method of the previous example.

In an example, the present disclosure refers to method of expanding a population of isolated T_{reg} cells of the previous example, comprising culturing the population of isolated T_{reg} cells under conditions that allow for proliferation of the isolated T_{reg} cells.

In an example, the present disclosure refers to a composition comprising the population of isolated T_{reg} cells of the invention and a pharmaceutically acceptable carrier.

In an example, the present disclosure refers to use of the composition of the previous example in the manufacture of a medicament for treating a subject in need thereof.

In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the liquid culture medium further includes an IgG1 antibody construct that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the single-chain chimeric polypeptide. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the IgG1 antibody construct comprises a heavy chain variable domain comprising CDRs of SEQ ID NOs: 66, 67 or 74, and 68,
and a light chain variable domain comprising CDRs of SEQ ID NOs: 69, 70, and 71. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the heavy chain variable domain comprises a sequence that is at least 90% identical to SEQ ID NO: 72, and the light chain variable domain comprises a sequence that is at least 90% identical to SEQ ID NO: 73. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the heavy chain variable domain comprises SEQ ID NO: 72, and the light chain variable domain comprises SEQ ID NO: 73. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the first target-binding domain and the soluble tissue factor domain directly abut each other. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the single-chain chimeric polypeptide further comprises a linker

sequence between the first target-binding domain and the soluble tissue factor domain. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the soluble tissue factor domain and the second target-binding domain directly abut each other. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the single-chain chimeric polypeptide further comprises a linker sequence between the soluble tissue factor domain and the second target-binding domain. In some examples of any of the methods of stimulating or increasing the proliferation of a T_{reg} cell described herein, the first target-binding domain and the second target-binding domain comprise the same amino acid sequence. In some examples of any of the

WHAT IS CLAIMED IS:

1. A method of stimulating or increasing the proliferation of a T_{reg} cell, wherein the method comprises:

culturing a T_{reg} cell in a liquid culture medium over a period of time, wherein at the beginning of the period of time, the liquid culture medium comprises:

a CD3/CD28-binding agent; and

a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1,

wherein the CD3/CD28-binding agent is:

(A) an anti-CD3/anti-CD28 bead;

(B) an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

(C) a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94; and

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

2. The method of claim 1, wherein the liquid culture medium further includes an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the single-chain chimeric polypeptide.

3. The method of claim 1 or 2, wherein the CD3/CD28-binding agent is an anti-CD3/anti-CD28 bead.

4. The method of claim 1 or 2, wherein the CD3/CD28-binding agent is an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6.

5. The method of claim 4, wherein the additional single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6.

6. The method of claim 5, wherein the additional single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising SEQ ID NO: 5, a soluble tissue factor domain comprising SEQ ID NO: 2, and a second target-binding domain comprising SEQ ID NO: 6.

7. The method of any one of claims 4-6, wherein the liquid culture medium further includes an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the additional single-chain chimeric polypeptide.

8. The method of claim 1 or 2, wherein the CD3/CD28 binding agent is a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and:

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein:

the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

9. The method of claim 8, wherein:

the first chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 99; and

the second chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 94.

10. The method of claim 9, wherein:

the first chimeric polypeptide comprises in an N- to -C terminal direction:

(i) a first target-binding domain comprising SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising SEQ ID NO: 99; and

the second chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a second target-binding domain comprising SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising SEQ ID NO: 94.

11. The method of any one of claims 8-10, wherein the liquid culture medium further includes an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the multi-chain chimeric polypeptide.

12. The method of any one of claims 1-11, wherein the single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 1.

13. The method of claim 12, wherein the single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising SEQ

ID NO: 2, a soluble tissue factor domain comprising SEQ ID NO: 1, and a second target-binding domain comprising SEQ ID NO: 1.

14. The method of any one of claims 1-13, wherein the method further comprises, before the culturing step, a step of isolating the T_{reg} cell from a sample obtained from a subject.

15. The method of any one of claims 1-13, wherein the method further comprises, after the culturing step, a step of isolating the T_{reg} cell from a sample obtained from a subject.

16. The method of any one of claims 1-15, wherein the T_{reg} cells comprises a chimeric antigen receptor.

17. A kit comprising:

(i) a CD3/CD28-binding agent;

(ii) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 1; and

(iii) an mTOR inhibitor,

wherein the CD3/CD28-binding agent is:

(A) an anti-CD3/anti-CD28 bead;

(B) an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

(C) a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

18. The kit of claim 17, wherein the CD3/CD28-binding agent is an anti-CD3/anti-CD28 bead.

19. The kit of claim 17, wherein the CD3/CD28-binding agent is an additional single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6.

20. The kit of claim 19, wherein the additional single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6.

21. The kit of claim 20, wherein the additional single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising SEQ ID NO: 5, a soluble tissue factor domain comprising SEQ ID NO: 2, and a second target-binding domain comprising SEQ ID NO: 6.

22. The kit of claim 17, wherein the CD3/CD28 binding agent is a multi-chain chimeric polypeptide comprising:

(a) a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

(b) a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

23. The kit of claim 22, wherein:

the first chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 99; and

the second chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 94.

24. The kit of claim 23, wherein:

the first chimeric polypeptide comprises in an N- to -C terminal direction:

(i) a first target-binding domain comprising SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising SEQ ID NO: 99; and

the second chimeric polypeptide comprises in an N- to C-terminal direction:

(i) a second target-binding domain comprising SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising SEQ ID NO: 94.

25. The kit of any one of claims 17-24, wherein the single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 1, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 1.

26. The kit of claim 25, wherein the single-chain chimeric polypeptide comprises in an N- to C-terminal direction a first target-binding domain comprising SEQ ID NO: 1, a soluble tissue factor domain comprising SEQ ID NO: 2, and a second target-binding domain comprising SEQ ID NO: 1.

27. A method of stimulating or increasing the proliferation of a T_{reg} cell, wherein the method comprises:

culturing a T_{reg} cell in a liquid culture medium over a period of time, wherein at the beginning of the period of time, the liquid culture medium comprises:

(a) interleukin-2; and

(b) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94.

28. The method of claim 27, wherein the liquid culture medium comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6.

29. The method of claim 28, wherein the liquid culture medium comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence at least 90% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6.

30. The method of claim 29, wherein the liquid culture medium comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising SEQ ID NO: 5, a soluble tissue factor domain comprising SEQ ID NO: 2, and a second target-binding domain comprising SEQ ID NO: 6.

31. The method of any one of claims 28-30, wherein the liquid culture medium further includes an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the single-chain chimeric polypeptide.

32. The method of claim 27, wherein the liquid culture medium comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

33. The method of claim 32, wherein the liquid culture medium comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 94.

34. The method of claim 33, wherein the liquid culture medium comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising SEQ ID NO: 94.

35. The method of any one of claims 32-34, wherein the liquid culture medium further includes an IgG1 antibody that comprises at least one antigen-binding domain that binds specifically to the soluble tissue factor domain of the multi-chain chimeric polypeptide.

36. The method of any one of claims 27-35, wherein the liquid culture medium further comprises an mTOR inhibitor.

37. The method of any one of claims 27-36, wherein the method further comprises, before the culturing step, a step of isolating the T_{reg} cell from a sample obtained from a subject.

38. The method of any one of claims 27-36, wherein the method further comprises, after the culturing step, a step of isolating the Treg cell from a sample obtained from a subject.

39. The method of any one of claims 27-38, wherein the T_{reg} cells comprises a chimeric antigen receptor.

40. A kit comprising:

(i) interleukin-2;

(ii) a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; or

a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains; and

(iii) an mTOR inhibitor.

41. The kit of claim 40, wherein the kit comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6.

42. The kit of claim 41, wherein the kit comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5, a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2, and a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6.

43. The kit of claim 42, wherein the kit comprises a single-chain chimeric polypeptide comprising in an N- to C-terminal direction a first target-binding domain

comprising SEQ ID NO: 5, a soluble tissue factor domain comprising SEQ ID NO: 2, and a second target-binding domain comprising SEQ ID NO: 6.

44. The kit of claim 40, wherein the kit comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 80% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising a sequence that is at least 80% identical to SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising a sequence that is at least 80% identical to SEQ ID NO: 94,

wherein the first chimeric polypeptide and the second chimeric polypeptide associate through the binding of the first domain and the second domain of the pair of affinity domains.

45. The kit of claim 44, wherein the kit comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising a sequence that is at least 90% identical to SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(ii) a second target-binding domain comprising a sequence that is at least 90% identical to SEQ ID NO: 6; and

a second domain of a pair of affinity domains comprising a sequence that is at least 90% identical to SEQ ID NO: 94.

46. The kit of claim 45, wherein the kit comprises a multi-chain chimeric polypeptide comprising:

a first chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a first target-binding domain comprising SEQ ID NO: 5;

(ii) a soluble tissue factor domain comprising SEQ ID NO: 2; and

(iii) a first domain of a pair of affinity domains comprising SEQ ID NO: 99; and

a second chimeric polypeptide comprising in an N- to C-terminal direction:

(i) a second target-binding domain comprising SEQ ID NO: 6; and

(ii) a second domain of a pair of affinity domains comprising SEQ ID NO: 94.