**Claims**

1. A TGF-β complex comprising a first polypeptide and a second polypeptide as a heterodimer, wherein:
(i) the first polypeptide comprises

a) a scaffold polypeptide sequence comprising an interspecific dimerization sequence,

b) a masking polypeptide sequence comprising a TGF-β receptor polypeptide sequence or an anti-TGF-β polypeptide sequence,

c) optionally, one or more independently selected immunomodulatory polypeptide sequences, and

d) optionally, one or more independently selected linker polypeptide sequences interposed between one or more sequences of the first polypeptide; and

(ii) the second polypeptide comprises

a) a scaffold polypeptide sequence comprising a counterpart interspecific dimerization sequence to the interspecific dimerization sequence in the first polypeptide,

b) a TGF-β polypeptide sequence,

c) optionally one or more independently selected immunomodulatory polypeptide sequences, and

d) optionally, one or more independently selected linker polypeptide sequences interposed between one or more sequences of the second polypeptide;

a complex comprising these elements being collectively referred to as a masked TGF-β complex,
wherein the masking polypeptide sequence and the TGF-β polypeptide sequence bind to each other; and
wherein the interspecific dimerization sequence and the counterpart interspecific dimerization sequence interact with each other.

2. The masked TGF-β complex heterodimer of claim 1, wherein:
the first polypeptide comprises, from N-terminus to C-terminus,

a) one or more independently selected immunomodulatory sequences, the scaffold polypeptide sequence comprising the interspecific dimerization sequence, and the masking polypeptide sequence; or

b) the scaffold polypeptide sequence comprising an interspecific dimerization sequence, and the masking polypeptide sequence; and

the second polypeptide comprises, from N-terminus to C-terminus one or more independently selected immunomodulatory sequences, the scaffold polypeptide sequence comprising the counterpart interspecific dimerization sequence, and the TGF-β polypeptide sequence; and
wherein one or more independently selected linker polypeptide sequences may be interposed between one or more sequences of the first polypeptide and/or the second polypeptide.

3. A construct comprising a first polypeptide, wherein the first polypeptide comprises:

i) a scaffold polypeptide sequence;

ii) a TGF-β polypeptide sequence;

iii) a masking polypeptide sequence comprising a TGF-β receptor polypeptide sequence or an anti-TGF-β polypeptide sequence;

iv) optionally, one or more independently selected immunomodulatory polypeptide sequences; and

v) optionally, one or more independently selected linker polypeptide sequences interposed between one or more sequences of the first polypeptide;

a construct comprising these elements being collectively referred to as a masked TGF-β construct, and wherein the masking polypeptide sequence and the TGF-β polypeptide sequence bind to each other.

4. The masked TGF-β construct of claim 3, wherein the first polypeptide comprises, in order from N-terminus to C-terminus:

i) the scaffold polypeptide sequence, the masking polypeptide sequence, and the TGF-β polypeptide sequence;

ii) a first immunomodulatory polypeptide sequence, the scaffold polypeptide sequence, the masking polypeptide sequence, and the TGF-β polypeptide sequence; or

iii) a first independently selected immunomodulatory polypeptide sequence, a second independently selected immunomodulatory polypeptide sequence, the scaffold polypeptide sequence, the masking polypeptide sequence, and the TGF-β polypeptide sequence;

wherein the masked TGF-β construct optionally comprises one or more independently selected linker polypeptide sequences interposed between one or more sequences of the first polypeptide.

5. The masked TGF-β construct of claim 3 or claim 4, wherein the scaffold polypeptide comprises a dimerization sequence.

6. The masked TGF-β construct of any one of claims 3 to 5, further comprising a second polypeptide that is dimerized with the first polypeptide to form a masked TGF-β complex heterodimer**;**

wherein the second polypeptide comprises:

i) a scaffold polypeptide sequence;

ii) a TGF-β polypeptide sequence;

iii) a masking polypeptide sequence comprising a TGF-β receptor polypeptide sequence or an anti-TGF-β polypeptide sequence;

iv) optionally, one or more independently selected immunomodulatory polypeptide sequences; and

v) optionally, one or more independently selected linker polypeptide sequences interposed between one or more components of the second polypeptide.

7. The masked TGF-β construct of claim 6,
wherein the first polypeptide comprises a scaffold polypeptide that comprises an interspecific dimerization sequence,
wherein the second polypeptide comprises a scaffold polypeptide sequence that comprises a counterpart interspecific dimerization sequence to the interspecific dimerization sequence of the first polypeptide; and
wherein the interspecific dimerization sequence and the counterpart interspecific dimerization sequence interact with each other in the heterodimer.

8. The masked TGF-β construct or the complex of any one of claims 1-7, wherein the scaffold polypeptide sequence(s) are variant Ig Fc polypeptide sequences, and wherein the variant Ig Fc polypeptide sequences include mutations that substantially reduce or eliminate the ability of the variant Ig Fc polypeptide to induce cell lysis.

9. The masked TGF-β construct or complex of any one of claims 1 to 8, wherein the one or more independently selected immunomodulatory polypeptide sequences are wild-type or variant immunomodulatory polypeptide sequences selected from the group consisting of: PD-L1, FAS-L, IL-1, IL-2, IL-4, IL-6, IL-7, IL-10, IL-15, IL-21, and IL-23.

10. The masked TGF-β construct or complex of any one of claims 1 to 8, wherein at least one of the immunomodulatory polypeptide sequences is a variant IL-2 immunomodulatory polypeptide sequence having at least 95% aa sequence identity to SEQ ID NO:9.

11. The masked TGF-β construct or complex of any one of claims 1 to 10, wherein the masking polypeptide sequence is a TGF-β receptor ("TβR") polypeptide sequence that comprises an ectodomain fragment of a type I (TβRI), type II (TβRII) or type III (TβRIII) TβR.

12. The masked TGF-β complex of claim 2, wherein the complex comprises polypeptide construct 4033 (SEQ ID NO:191) and polypeptide construct 4039 (SEQ ID NO:192).

13. One or more nucleic acids encoding a masked TGF-β construct or complex of any one of claims 1 to 12.

14. Use of one or more masked TGF-β constructs or complexes according to any one of claims 1 to 12 or one or more nucleic acids according to claim 13, in the manufacture of a medicament for the treatment of an autoimmune condition or disease.

15. The use of claim 14, wherein the autoimmune condition or disease is selected from the group consisting of: Addison's disease, alopecia areata, ankylosing spondylitis, autoimmune encephalomyelitis, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune-associated infertility, autoimmune thrombocytopenic purpura, bullous pemphigoid, celiac disease, Crohn's disease, Goodpasture's syndrome, glomerulonephritis, Grave's disease, Hashimoto's thyroiditis, mixed connective tissue disease, multiple sclerosis, myasthenia gravis (MG), pemphigus, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic lupus erythematosus (SLE), type 1 diabetes (T1D), celiac disease, vasculitis, and vitiligo.

16. The use of claim 14 or claim 15, wherein the pharmaceutical composition comprises polypeptide construct 4033 (SEQ ID NO:191) and polypeptide construct 4039 (SEQ ID NO:192).

17. A composition comprising one or more genetically modified host cells, wherein the genetically modified host cells individually or collectively comprise one or more nucleic acids according to claim 13.

18. A method of producing a masked TGF-β construct or complex, the method comprising culturing a composition of genetically modified host cells according to claim 17 under conditions such that the genetically modified host cells produce the TGF-β construct or complex.

19. The method of claim 18, wherein the TGF-β complex produced by the cells comprises polypeptide construct 4033 (SEQ ID NO:191) and polypeptide construct 4039 (SEQ ID NO:192).

20. A pharmaceutical composition comprising one or more masked TGF-β constructs or complexes according to any one of claims 1 to 12, or one or more nucleic acids according to claim 13.

21. The pharmaceutical composition of claim 20 for use in the treatment of an autoimmune condition or disease.

22. The pharmaceutical composition of claim 21, wherein the autoimmune condition or disease is selected from the group consisting of: Addison's disease, alopecia areata, ankylosing spondylitis, autoimmune encephalomyelitis, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune-associated infertility, autoimmune thrombocytopenic purpura, bullous pemphigoid, celiac disease, Crohn's disease, Goodpasture's syndrome, glomerulonephritis, Grave's disease, Hashimoto's thyroiditis, mixed connective tissue disease, multiple sclerosis, myasthenia gravis (MG), pemphigus, pernicious anemia, polymyositis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleroderma, Sjögren's syndrome, systemic lupus erythematosus (SLE), type 1 diabetes (T1D), celiac disease, vasculitis, and vitiligo.

23. The pharmaceutical composition of any one of claims 20 to 22, wherein the TGF-β complex comprises polypeptide construct 4033 (SEQ ID NO:191) and polypeptide construct 4039 (SEQ ID NO:192).