**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.

~~1~~3. A construct comprising ~~as~~ 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 ~~MOD~~ 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.

~~2~~4. The masked TGF-β construct of claim ~~1~~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 ~~MOD~~ immunomodulatory polypeptide sequence, the scaffold polypeptide sequence, the masking polypeptide sequence, and the TGF-β polypeptide sequence; or

iii) a first independently selected immunomodulatory ~~MOD~~ polypeptide sequence, a second independently selected immunomodulatory ~~MOD~~ 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.

~~3~~5. The masked TGF-β construct of claim 3 or claim ~~2~~4, wherein the scaffold polypeptide comprises a dimerization sequence~~, optionally wherein the scaffold polypeptide comprises an interspecific dimerization sequence~~.

~~4~~6. The masked TGF-β construct of any one of claims 3 to ~~3~~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 ~~optionally~~ comprising a TGF-β receptor polypeptide sequence or an anti-TGF-β polypeptide sequence;

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

and

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

~~5~~7. The masked TGF-β construct of claim ~~4~~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 ~~binding~~ dimerization sequence of the first polypeptide; and

wherein the interspecific ~~binding~~ dimerization sequence and the counterpart interspecific ~~binding~~ dimerization sequence interact with each other in the heterodimer.

~~6. 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 MOD polypeptide sequences, and~~

~~d) optionally, one or more independently selected linker polypeptide sequences; 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) one or more independently selected MOD polypeptide sequences, and~~

~~d) optionally, one or more independently selected linker polypeptide sequences;~~

~~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;~~

wherein the interspecific binding sequence and the counterpart interspecific binding sequence interact with each other (e.g., bind covalently or non-covalently) in the heterodimer; and

wherein the masked TGF-β first polypeptide and/or the second polypeptide optionally comprise one or more independently selected linker polypeptide sequences.

7. The masked TGF-β complex heterodimer of claim 6, wherein:

the first polypeptide comprises, from N-terminus to C-terminus,

a) one or two (or more) independently selected MOD 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 (e.g., TGF-β receptor polypeptide sequence); and

the second polypeptide comprises, from N-terminus to C-terminus one or two (or more) independently selected MOD sequences, the scaffold polypeptide sequence comprising the counterpart interspecific dimerization sequence, and the TGF-β polypeptide sequence.

8. The masked TGF-β construct or the complex of any one of claims 1-7, wherein the scaffold polypeptide sequence(s) are selected from the group consisting of variant Ig Fc polypeptide sequences, and variants thereof, optionally wherein the variant Ig Fc polypeptide sequences include mutations that reduce binding of the polypeptide to complement component 1q (C1q) and/or Fc lambda receptor (FcλR) and/or substantially reduce or eliminate the ability of the variant Ig Fc polypeptide to induce cell lysis, e.g., though complement-dependent cytotoxicity (CDC) and antibody-dependent cellular cytotoxicity (ADCC).

9. The masked TGF-β construct or complex of any one of claims 1 to 87, wherein the one or more independently selected MOD 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 MOD polypeptide sequences, and variants of any thereof.

1010. The masked TGF-β construct or complex of any one of claims 1 to 87, wherein at least one of the immunomodulatory MOD polypeptide sequences is a wt. IL-2 MOD polypeptide sequence or variant IL-2 MOD immunomodulatory polypeptide sequence

(i) having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% aa sequence identity to at least 80, 90, 100, 110, 120, 130 or 133 contiguous aas of SEQ ID NO:9.; or

~~(ii) having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99% or 100% aa sequence identity to at least 80, 90, 100, 110, 120, 130 or 133 contiguous aas of one of SEQ ID NOs: 13-27.~~

~~11~~11. The masked TGF-β construct or complex of any one of claims 1 to 10~~7~~, 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~~12. The masked TGF-β complex of claim ~~7~~2, wherein the complex ~~is formed from the combination of polypeptide~~ comprises polypeptide construct 4033 (SEQ~~.~~ ID~~.~~ NO~~.~~:191) and polypeptide construct 4039 (SEQ~~.~~ ID~~.~~ NO~~.~~:192).

~~13~~13. One or more nucleic acids encoding a masked TGF-β construct or complex of any one of claims 1 ~~-~~ to 12~~7~~.

~~14~~14. ~~A method of inducing Treg cells in a mammalian subject or treating a disease or condition in a subject comprising administering to the subject~~ Use of one or more masked TGF-β constructs or complexes according to any one of claims 1~~-~~ to 12~~7~~ or ~~a~~ one or more nucleic acid~~s~~ ~~encoding a masked TGF-β complex of~~according to ~~any of claims 1-7~~claim 13, in the manufacture of a medicament for the treatment of an autoimmune condition or disease.

~~15~~15. The ~~method~~ use of claim ~~14~~14~~9~~, wherein the ~~method is for the treatment of an~~ 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~~7~~, or one or more nucleic acids according to claim 13.

21. The pharmaceutical composition of claim 20~~5~~ 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).