Claims

1. A tolerance-inducing construct comprising:
   i) a polynucleotide comprising a nucleotide sequence encoding a targeting unit targeting or capable of targeting antigen-presenting cells, a multimerization unit, such as a dimerization unit and an antigenic unit; or
   ii) a polypeptide encoded by the nucleotide sequence as defined in (i); or
   iii) a multimeric protein, such as a dimeric protein consisting of multiple polypeptides as defined in (ii), such as two polypeptides;

   wherein the antigenic unit comprises one or more T cell epitopes of a self-antigen, an allergen, an alloantigen or a xenoantigen.

2. The tolerance-inducing construct according to claim 1, wherein the targeting unit interacts with a surface molecules on the antigen-presenting cell, without activating the cell.

3. The tolerance-inducing construct according to any of the preceding claims, wherein said construct comprises a multimerization unit,
   preferably wherein said construct comprises a dimerization unit and/or wherein said multimeric protein is a dimeric protein.

4. The tolerance-inducing construct according to any of the preceding claims, wherein the targeting unit comprises or consists of a moiety that binds to a receptor selected from the group consisting of TGFβR1, TGFβR2, TGFβR3, IL10R, IL-10RA and IL10-RB, IL2R, IL4R, IL6R, IL11R and IL13R, IL27R, IL35R, IL37R, CCR7, CD11b, CD11c, CD103, CD14, CD36, CD205, CD109, VISTA, MARCO, MHCII, MHCII, CD83, SIGLEC, MGL, CD80, CD86, Clec9A, Clec12A, Clec12B, DCIR2, Langerin, MR, DC-Sign, Treml4, Dectin-1, PDL1, PDL2 and HVEM.

5. The tolerance-inducing construct according to claim 4, wherein the moiety is an antibody or part thereof, such as a scFv,

preferably wherein the moiety is an antibody with specificity for CD205, or a part of an antibody with specificity for CD205, such as a scFv.

6. The tolerance-inducing construct according to claim 4, wherein the moiety is a synthetic ligand or a natural ligand.

7. The tolerance-inducing construct according to claim 6, wherein the natural ligand is selected from the group consisting of TGFβ, IL-10, IL2, IL4, IL6, IL11, IL13, IL27, IL35, IL37, CCL19, CCL21, ICAM-1, keratin, VSIG-3, SCGB3A2, CTLA-4, preferably an extracellular domain of CTLA4, PD-1, preferably an extracellular domain of PD-1 and BTLA, preferably an extracellular domain of BLTA.

8. The tolerance-inducing construct according to claim 7, wherein the natural ligand is selected from the group consisting of IL-10, TGFβ, SCGB3A2 and VSIG-3.

9. The tolerance-inducing construct according to any of the preceding claims, wherein the antigenic unit comprises one T cell epitope of one self-antigen or one allergen or one alloantigen or one xenoantigen,
or wherein the antigenic unit comprises multiple T cell epitopes of one self-antigen or one allergen or one alloantigen or one xenoantigen,
or wherein the antigenic unit comprises multiple T cell epitopes of multiple different self-antigens or multiple different allergens or multiple different alloantigens or multiple different xenoantigens.

10. The tolerance-inducing construct according to any of the preceding claims, wherein the antigenic unit comprises 1 to 10 T cell epitopes such as 1, 2, 3, 4, 5, 6, 7, 8 or 9 or 10 T cell epitopes or 11 to 20 T cell epitopes, such as 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 T cell epitopes or 21 to 30 T cell epitopes, such as 21, 22, 23, 24, 25, 26, 27, 28, 29 or 30 T cell epitopes or 31 to 40 T cell epitopes, such as 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40 T cell epitopes or 41 to 50 T cell epitopes, such as 41, 42, 43, 44, 45, 46, 47, 48, 49 or 50 T cell epitopes.

11. The tolerance-inducing construct according to any of the preceding claims, wherein the antigenic unit comprises multiple T cell epitopes, which are separated by T cell epitope linkers,
preferably wherein the T cell epitope linkers are non-immunogenic and are more preferably also flexible.

12. The tolerance-inducing construct according to any of the preceding claims, wherein the construct is an individualized tolerance-inducing construct or an off-the-shelf tolerance-inducing construct.

13. The tolerance-inducing construct according to any of the preceding claims, wherein the antigenic unit comprises one or more T cell epitopes of an allergen,

such as an allergen selected from the group consisting of food allergen, bee venom allergen, latex allergen, dust mite allergen, cockroach allergen, mold allergen, fungal allergen, furry animal allergen, pollen allergen and allergen comprised in a drug.

14. The tolerance-inducing construct according to any of claims 1 to 12, wherein the antigenic unit comprises one or more T cell epitopes of a self-antigen,

such as a self-antigen selected from the group consisting of multiple sclerosis self-antigen, type 1 diabetes mellitus self-antigen, celiac disease self-antigen, rheumatoid arthritis self-antigen, chronic inflammatory demyelinating polyradiculoneuropathy self-antigen, Hashimoto's thyroiditis self-antigen, pemphigus foliaceus self-antigen, pemphigus vulgaris self-antigen, thyroid eye disease self-antigen, Grave's disease self-antigen, primary biliary cirrhosis the self-antigen, myasthenia gravis self-antigen, insulin-resistant diabetes self-antigen and hemolytic anemia self-antigen..

15. The tolerance-inducing construct according to any of the preceding claims comprising a dimerization unit, wherein the dimerization unit comprises hinge exon h1 and hinge exon h4, a dimerization unit linker and a CH3 domain of human IgG3.

16. The tolerance-inducing construct according to any of claims 1 to 14 comprising a multimerization unit, wherein the multimerization unit is a trimerization unit, such as a collagen-derived trimerization unit, such as a human collagen-derived trimerization domain, such as human collagen derived XVIII trimerization domain or human collagen XV trimerization domain.

17. The tolerance-inducing construct according to any of the preceding claims, wherein the construct is the polynucleotide (i),

such as an RNA or DNA,

optionally wherein the polynucleotide further comprises a nucleotide sequence encoding a signal peptide.

18. A polynucleotide as defined in any of the claims 1 to 17.

19. A vector comprising the polynucleotide according to claim 18.

20. A host cell comprising the polynucleotide according to claim 18 or the vector according to claim 19.

21. A polypeptide encoded by the polynucleotide as defined in any of the claims 1 to 17 or a multimeric protein consisting of multiple of such polypeptides, such as a dimeric protein consisting of two of such polypeptides.

22. The polypeptide or the multimeric protein, such as dimeric protein according to claim 21, wherein said targeting unit, mulitimerization unit, such as dimerization unit and antigenic unit in said polypeptide or multimeric protein such as dimeric protein are in the N-terminal to C-terminal order of targeting unit, multimerization unit, such as dimerization unit, and antigenic unit.

23. Use of the tolerance-inducing construct according to any of claims 1 to 17, the polynucleotide according to claim 18, the vector according to claim 19, the polypeptide or multimeric protein, such as dimeric protein, according to claim 21 in the manufacture of a medicament.

24. A pharmaceutical composition comprising the tolerance-inducing construct according to any of claims 1 to 17 or the polynucleotide according to claim 18 or the vector according to claim 19 or the polypeptide or multimeric protein, such as dimeric protein, according to claim 21 and a pharmaceutically acceptable carrier,

optionally wherein the pharmaceutically acceptable carrier is selected from the group consisting of saline, buffered saline, PBS, dextrose, water, glycerol, ethanol, sterile isotonic aqueous buffers, and combinations thereof.

25. Use of the tolerance-inducing construct according to any of claims 1 to 17 or the polynucleotide according to claim 18 or the vector according to claim 19 or the polypeptide or multimeric protein, such as dimeric protein, according to claim 21 in the manufacture of a medicament for prophylactic or therapeutic treatment of conditions involving undesirable immune reactions, such as in the treatment of autoimmune diseases, allergic disease and graft rejection.

26. A method for preparing the pharmaceutical composition according to claim 24, wherein the pharmaceutical composition comprises the polypeptide or multimeric protein, such as dimeric protein according to claim 21, wherein the method comprises the steps of:

a) transfecting cells with the polynucleotide according to claim 18;

b) culturing the cells;

c) collecting and purifying the dimeric protein or the polypeptide expressed from the cells; and

d) mixing the dimeric protein or polypeptide obtained from step c) with a pharmaceutically acceptable carrier.

27. A method for preparing the pharmaceutical composition according to claim 24, wherein the pharmaceutical composition comprises the polynucleotide according to claim 18, wherein the method comprises the steps of:

a) preparing the polynucleotide;

b) optionally cloning the polynucleotide into an expression vector; and

c) mixing the polynucleotide obtained from step a) or the vector obtained from step b) with the pharmaceutically acceptable carrier.

28. A method for improving tolerance to a self-antigen, an allergen, an alloantigen or a xenoantigen using the tolerance-inducing construct according to any of claims 1 to 17.

29. A method for improving tolerance to a self-antigen, an allergen, an alloantigen or a xenoantigen in a subject, the method comprising administering to the subject the tolerance-inducing construct according to any of claims 1 to 17 or the pharmaceutical composition according to claim 24.