CLAIMS

1. A pharmaceutically acceptable composition comprising an erythrocyte-binding moiety, a linker, and a tolerogenic antigen, which are recombinantly fused or chemically conjugated, wherein:

said erythrocyte-binding moiety is an antibody, an antibody fragment or a single chain antigen binding domain (scFv) moiety that specifically binds to Band3, glycophorin A, glycophorin B, glycophorin C, or glycophorin D on a human erythrocyte *in situ* in blood,

said linker is a peptide, a linear or branched polymer, a covalent bond, or an ionic bond;

said tolerogenic antigen is an antigen to which subjects exposed to the antigen develop an unwanted immune response,

wherein the tolerogenic antigen is a food antigen, a therapeutic agent, a self-antigen, a fragment of any of such antigens, or a mimotope of any such antigens; and

wherein upon administration to a subject, the composition is able to induce one or more of (i) proliferation of CD8+ T cells having an apoptotic- or exhausted-fate phenotype, (ii) deletion of CD4 and/or CD8+ T cells specific for the tolerogenic antigen, and (iii) the ability to induce regulatory cell phenotypes.

2. The pharmaceutically acceptable composition of claim 1 wherein said erythrocyte-binding moiety comprises an antibody fragment or scFv moiety that specifically binds glycophorin A.

3. The pharmaceutically acceptable composition of claim 1 wherein said erythrocyte-binding moiety is derived from a 10F7 clone.

4. The pharmaceutically acceptable composition of claim 1 wherein the tolerogenic antigen comprises:

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 (GAD-65), GAD-67, insulinoma-associated protein 2 (IA-2), insulinoma-associated protein 2β (IA-2β), ICA69, ICA12 (SOX-13), carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin-A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2, hepatocarcinoma-intestine-pancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific

glucose-6-phosphatase catalytic subunit-related protein, and SST G-protein coupled receptors 1-5;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: myelin basic protein, myelin oligodendrocyte glycoprotein and proteolipid protein; and

a food antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), a-lactalbumin (ALA), lactotransferrin, Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, gliadin, high molecular weight glutenin, low molecular weight glutenin, alpha- and gamma-gliadin, hordein, seclain, and avenin.

5. A pharmaceutically acceptable composition according to any one of Claims 1 to 4, wherein the tolerogenic antigen comprises a mimotope of the food antigen, the therapeutic agent, the self-antigen, or of fragments of any such antigens.

6. A pharmaceutically acceptable composition according to any one of claims 1 to 5, wherein said linker is a branched polymer that increases the affinity of erythrocyte binding by avidity effects.

7. The pharmaceutically acceptable composition of claim 6 wherein said branched polymer is conjugated to more than one erythrocyte-binding moiety.

8. A pharmaceutically acceptable composition according to any one of claims 1 to 3, wherein the tolerogenic antigen is a therapeutic agent selected from the group consisting of Factor VIII, Factor IX, asparaginase and uricase, a fragment of any such antigens, or a mimotope of any such antigens.

9. Use of a therapeutically effective amount of a pharmaceutically acceptable composition for the manufacture of a medicament for treating an unwanted immune response, the composition comprising an erythrocyte-binding moiety, a linker, and a tolerogenic antigen wherein the erythrocyte-binding moiety, the linker and the tolerogenic antigen are recombinantly fused or chemically conjugated, wherein:

said erythrocyte-binding moiety is an antibody, an antibody fragment or a single chain antigen binding domain (scFv) moiety that specifically binds to Band3, glycophorin A, glycophorin B, glycophorin C or glycophorin D on a human erythrocyte *in situ* in blood,

said linker is a peptide, a linear or branched polymer, a covalent bond, an ionic bond, an aptamer, a nucleic acid or a particle;

said tolerogenic antigen is an antigen to which patients develop subjects develop an unwanted immune response;

wherein the tolerogenic antigen is a food antigen, a therapeutic agent, a self-antigen, a fragment of any such antigens, or a mimotope of any such antigens; and

wherein, upon administration to a patient, the composition is able to induce one or more of (i) proliferation of CD8+ T cells having an apoptotic- or exhausted-fate phenotype, (ii) deletion of CD4 and/or CD8+ T cells specific for the tolerogenic antigen, and (iii) the ability to induce regulatory cell phenotypes.

10. The use of claim 9 wherein said erythrocyte-binding moiety comprises an antibody fragment or an scFv moiety that specifically binds glycophorin A.

11. The use of claim 9 wherein said erythrocyte-binding moiety is derived from a 10F7 clone.

12. A use according to any one of claims 9 to 11, wherein said composition is administered to a subject prior to an unwanted immune response to the antigen, wherein said composition prevents or reduces the unwanted immune response.

13. A use according to any one of claims 9 to 11, wherein said composition is administered to a subject having an unwanted immune response to the antigen, wherein said composition prevents or reduces the unwanted immune response.

14. A use according to any one of claims 9 to 13, where the unwanted immune response is associated with a disease selected from the group: type 1 diabetes mellitus; multiple sclerosis; rheumatoid arthritis; celiac disease; vitiligo; pemphigus vulgaris and variants; bullous pemphigoid; hemophilia and cancer.

15. A use according to any one of claims 9 to 13, where the tolerogenic antigen comprises:
a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 (GAD-65), GAD-67, insulinoma-associated protein 2 (IA-2), insulinoma-associated protein 2β (IA-2β), ICA69,

ICA12 (SOX-13), carboxypeptidase H, Imogen 38, GLIMA 38, chromogranin-A, HSP-60, caboxypeptidase E, peripherin, glucose transporter 2, hepatocarcinoma-intestine-pancreas/pancreatic associated protein, S100β, glial fibrillary acidic protein, regenerating gene II, pancreatic duodenal homeobox 1, dystrophia myotonica kinase, islet-specific glucose-6-phosphatase catalytic subunit-related protein, and SST G-protein coupled receptors 1-5;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: myelin basic protein, myelin oligodendrocyte glycoprotein and proteolipid protein;

collagen II, a fragment thereof, or a mimotope thereof;

tissue transglutaminase, a fragment thereof, or a mimotope thereof ~~and gliadin~~;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: tyrosinase, and tyrosinase related protein 1 and 2;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: desmoglein 3, desmoglein 1, desmoglein 4, pemphaxin, desmocollins, plakoglobin, perplakin, desmoplakins, and acetylcholine receptor;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: BP180, BP230, plectin and laminin 5;

a self-antigen, a fragment thereof, or a mimotope thereof selected from the group consisting of: conarachin (Ara h 1), allergen II (Ara h 2), arachis agglutinin, conglutin (Ara h 6), a-lactalbumin (ALA), lactotransferrin, Pen a 1 allergen (Pen a 1), allergen Pen m 2 (Pen m 2), tropomyosin fast isoform, gliadin, high molecular weight glutenin, low molecular weight glutenin, alpha- and gamma-gliadin, hordein, seclain, and avenin; or

a therapeutic agent, a fragment thereof, or a mimotope thereof selected from the group consisting of Factor VIII, Factor IX, asparaginase and uricase.

16. The use of claim 9 wherein the unwanted immune response is associated with celiac disease and wherein the tolerogenic antigen is tissue trans-glutaminase, high molecular weight glutenin, low molecular weight glutenin, alpha- or gamma-gliadin.

17. Use of a therapeutically effective amount of a pharmaceutically acceptable composition for the manufacture of a medicament for treating an unwanted immune response, the composition comprising:

an erythrocyte-binding moiety,

a linker, and

a tolerogenic antigen, wherein:

the erythrocyte-binding moiety, the linker and the tolerogenic antigen are recombinantly fused,

the erythrocyte-binding moiety is an antibody fragment or a single chain antigen binding domain (scFv) moiety that non-covalently and specifically binds to Band 3, glycophorin A, glycophorin B, glycophorin C or glycophorin D on a human erythrocyte *in situ* in blood,

said linker is a peptide, a linear or branched polymer, a covalent bond, an ionic bond, an aptamer, a nucleic acid or a particle; and

said tolerogenic antigen is a foreign antigen to which patients develop an unwanted immune response.

18. A pharmaceutically acceptable composition comprising an erythrocyte-binding moiety and a tolerogenic antigen, which are recombinantly fused or chemically conjugated, wherein:

said erythrocyte-binding moiety is an antibody, an antibody fragment or scFv moiety that specifically binds to glycophorin A on a human erythrocyte,

said tolerogenic antigen is an antigen to which patients develop an unwanted immune response; and

wherein the tolerogenic antigen is a food antigen, a therapeutic agent, a self-antigen, or a fragment of any of such antigens.

19. The pharmaceutically acceptable composition of claim 18, wherein said erythrocyte-binding moiety is a scFv.

20. The pharmaceutically acceptable composition of claim 18, wherein said erythrocyte-binding moiety is an antibody fragment.

21. A pharmaceutically acceptable composition according to any one of claims 18 to 20, wherein the food antigen is selected from the group of gliadin, alpha-gliadin, gamma-gliadin, a fragment of such antigens and a mimotope of any of such antigens.

22. A pharmaceutically acceptable composition according to any one of claims 18 to 20, wherein the self-antigen is selected from the group of insulin, proinsulin, preproinsulin, glutamic acid decarboxylase-65 (GAD-65), GAD-67, islet-specific glucose-6-phosphatase catalytic subunit-related protein, a fragment of such antigens and a mimotope of any of such antigens.

23. Use of the pharmaceutically acceptable composition according to any one of claims 18 to 22 for the manufacture of a medicament for treating an unwanted immune response.

24. Use of the pharmaceutically acceptable composition of claim 21 for the manufacture of a medicament for treating Celiac disease.

25. Use of the pharmaceutically acceptable composition of claim 22 for the manufacture of a medicament for treating type 1 diabetes mellitus.

26. A pharmaceutically acceptable composition according to any one of claims 18 to 20, wherein the self-antigen is selected from the group of myelin basic protein, myelin oligodendrocyte glycoprotein and proteolipid protein, a fragment of such antigens and a mimotope of any of such antigens.

27. Use of the pharmaceutically acceptable composition of claim 26 for the manufacture of a medicament for treating multiple sclerosis.