CLAIMS

1. A composition for immunomodulation to achieve antigen-specific tolerance, the composition comprising:

an antigen to which tolerance is desired;

wherein the antigen is selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein, proteolipid protein, and immunogenic fragments thereof;

an erythrocyte-binding moiety,

wherein the erythrocyte-binding moiety comprises an antibody, antibody fragment, or a single chain variable fragment (scFv) that has the ability to non-covalently, specifically bind an exterior erythrocyte surface *in situ* in blood,

wherein the antigen to which tolerance is desired is recombinantly fused or chemically conjugated to the erythrocyte-binding moiety, and

wherein, upon administration to a human in which tolerance to the antigen is desired:

the composition binds to CD45 negative cells, but not to CD45 positive cells, and the composition reduces, fails to induce, or prevents inflammatory responses in antigen-specific T cells as compared to when the human is exposed to the antigen alone.

2. The composition of Claim 1, wherein the erythrocyte-binding moiety is derived from a 10F7 clone, wherein the antibody fragment is affinity matured, and wherein the composition reduces the number of resident lymph node and spleen cells expressing interferon-gamma (IFNγ), as compared to the number of resident lymph node and spleen cells expressing IFNγ when the human is exposed to the antigen alone.

3. The composition of Claim 1 or 2, wherein the erythrocyte-binding moiety comprises an antibody fragment directed against Glycophorin A.

4. The composition according to any one of Claims 1 to 3, wherein the erythrocyte-binding moiety is derived from a 10F7 clone.

5. The composition of Claim 3, wherein the antibody fragment is affinity matured.

6. The composition according to any one of Claims 1 to 5, wherein the erythrocyte-binding moiety is fused via a linker, to the N- or C-terminus of the antigen.

7. The composition according to any one of Claims 1 to 6, wherein the administration of the composition ameliorates multiple sclerosis, and wherein the antigen is an immunogenic fragment of myelin basic protein, myelin oligodendrocyte glycoprotein or proteolipid protein.

8. A composition for immunomodulation to achieve antigen-specific tolerance, the composition comprising:

an antigen recombinantly fused or chemically conjugated with an erythrocyte-binding moiety;

said antigen being recognizable by an immune system of a subject, the immune system of the subject being able to respond to the antigen with an unwanted immune response;

wherein said erythrocyte-binding moiety comprises a polypeptide;

wherein upon administration of the composition, said erythrocyte-binding moiety non-covalently and specifically binds an erythrocyte *in situ* in blood and presents said antigen to the immune system of the subject;

wherein the erythrocyte-binding moiety does not specifically bind to other blood components, wherein the other blood components comprises blood proteins, albumin, fibronectin, platelets, and white blood cells;

wherein said composition elicits a tolerogenic response upon administration to said subject; and

wherein said antigen is associated with multiple sclerosis.

9. The composition of Claim 8, wherein the antigen is selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein, proteolipid protein, and immunogenic fragments thereof.

10. The composition of Claim 8 or 9, wherein the erythrocyte-binding moiety is chemically conjugated to the antigen.

11. The composition of Claim 8 or 9, wherein the erythrocyte-binding moiety is fused to the antigen via recombinant DNA technology.

12. The composition of Claim 8 or 9, wherein the erythrocyte-binding moiety is fused, optionally via a linker, to the N- or C-terminus of the antigen.

13. The composition according to any one of Claims 8 to 12, wherein the erythrocyte-binding moiety comprises an antibody fragment, wherein the antibody fragment is derived from a 10F7 clone, and wherein the antibody fragment has undergone affinity maturation.

14. The composition of Claim 12, wherein the linker is a peptide, a polymer, an aptamer, a nucleic acid, or a particle.

15. A composition for immunomodulation to achieve antigen-specific tolerance, the composition comprising:

one or more antigens antigen fused or chemically conjugated with an erythrocyte-binding moiety;

wherein said one or more antigens is selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein, proteolipid protein, immunogenic fragments thereof, and combinations thereof;

said one or more antigens being recognizable by an immune system of a subject, the immune system of the subject being able to respond to or previously having responded to the one or more antigens with an unwanted immune response,

said erythrocyte-binding moiety having the ability to non-covalently, specifically bind an erythrocyte surface *in situ* in blood and present said one or more antigens to the immune system of the subject,

wherein said erythrocyte-binding moiety comprises at least one peptide, an antibody, or an antibody fragment, and

wherein, upon administration to a human, the composition:

(i) binds to CD45 negative cells, but not to CD45 positive cells,

(ii) induces greater proliferation of antigen-specific CD8+ T cells, as compared to the proliferation of antigen-specific CD8+ T cells induced by the antigen alone, or

(iii) reduces the number of resident lymph node and spleen cells expressing interferon-gamma (IFNγ), as compared to the number of resident lymph node and spleen cells expressing IFNγ when the human is exposed to the antigen alone.

16. The composition of Claim 15, wherein the erythrocyte-binding moiety has the ability to bind Band 3 (CD233), glycophorin-A, glycophorin B (CD235b), glycophorin C(CD235c), or glycophorin D (CD235d) with an affinity generating a dissociation constant of between about 10 μM and 0.1 nM as determined by equilibrium binding measurements between the erythrocyte-binding moiety and erythrocytes.

17. The composition of Claim 15 or 16, comprising two or more antigens selected from the group consisting of myelin basic protein, myelin oligodendrocyte glycoprotein, proteolipid protein, immunogenic fragments thereof, and combinations thereof.

18. The composition of Claim 17, wherein said antigens are optionally antigens are conjugated to a multimeric branched polymer.

19. The composition according to any one of Claims 15 to 18, wherein the one or more antigens is fused with the erythrocyte-binding moiety, wherein the erythrocyte-binding moiety is derived from a 10F7 clone, and wherein the erythrocyte-binding moiety is affinity-matured.

20. The composition according to any one of Claims 15 to 19, wherein the administration of the composition ameliorates multiple sclerosis.