CLAIMS

1. A bispecific fusion protein comprising a ligand specific for CTLA-4 and a ligand specific for a pMHC complex, wherein the ligand specific for CTLA-4 and the ligand specific for the pMHC complex are spaced apart by a linker.

2. A bispecific fusion protein according to claim 1, wherein the ligand specific for CTLA-4 is selected from CD80 (B7-1) or CD86 (B7-2), or an antibody specific for CTLA-4.

3. A bispecific fusion protein according to claim 1 or claim 2, wherein the ligand specific for the pMHC complex is selected from an anti-MHC antibody and LAG-3.

4. A bispecific fusion protein according to any preceding claim, wherein the linker is one or more of a polyamino acid sequence and an antibody Fc domain.

5. A bispecific fusion protein according to claim 4, wherein the polyamino acid sequence is G9 (Gly-9).

6. A bispecific fusion protein according to claim 2, wherein the ligand specific for CTLA-4 is CD80, preferably a CD80 mutated to increase specificity for CTLA-4.

7. A bispecific fusion protein according to claim 6, wherein CD80 is human CD80 comprising at least one of mutations W84A, K71G, K71V, S109G, R123S, R123D, G124L, S190A, S201A, R63A, M81A, N97A and E196A, preferably W84A or E196A.

8. A bispecific fusion protein according to claim 3, wherein the ligand specific for the pMHC complex is LAG-3, preferably mutated to increase specificity for pMHCII.

9. A bispecific fusion protein according to claim 8, wherein LAG-3 is human LAG-3 comprising at least one of mutations R73E, R75A, R75E and R76E, preferably R75A or R75E.

10. A bispecific fusion protein according to any one of claims 1-9, wherein the fusion protein comprises a sequence selected from the group consisting of SEQ ID NO: 6, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12 and SEQ ID NO: 14.

11. The bispecific fusion protein of any of claims 1-10 for use in tolerising a T-cell, when the T-cell is contacted with an antigen-presenting cell which presents an antigen via a MHC molecule and the bispecific fusion protein.

12. The bispecific fusion protein of any of claims 1-10 for use in the treatment of a disease selected from an autoimmune disease and transplant rejection.

13. The bispecific fusion protein for use according to claim 12, wherein the bispecific fusion protein is to be administered in combination with an immune suppressant or modulator.

14. The bispecific fusion protein for use according to claim 12 or claim 13, wherein the autoimmune disease is selected from type 1 diabetes (T1D), Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA), inflammatory bowel disease (IBD), ulcerative colitis (UC), Crohn's disease (CD), multiple sclerosis (MS), scleroderma, pemphigus vulgaris (PV), psoriasis, atopic dermatitis, celiac disease, Chronic Obstructive Lung disease, Hashimoto's thyroiditis, Graves' disease (thyroid), Sjögren's syndrome, Guillain-Barré syndrome, Goodpasture's syndrome, Addison's disease, Wegener's granulomatosis, primary biliary sclerosis, sclerosing cholangitis, autoimmune hepatitis, polymyalgia rheumatica, Raynaud's phenomenon, temporal arteritis, giant cell arteritis, autoimmune hemolytic anemia, pernicious anemia, polyarteritis nodosa, Behçet's disease, primary biliary cirrhosis, uveitis, myocarditis, rheumatic fever, ankylosing spondylitis, glomerulonephritis, sarcoidosis, dermatomyositis, myasthenia gravis, polymyositis, alopecia areata, and vitiligo.

15. The bispecific fusion protein for use according to claim 14, wherein the autoimmune disease is type 1 diabetes (T1D).