CLAIMS

1. An antibody cytokine engrafted protein comprising:

   (a) a heavy chain variable region (VH), comprising Complementarity Determining Regions (CDR) HCDR1, HCDR2, HCDR3; and

   (b) a light chain variable region (VL), comprising LCDR1, LCDR2, LCDR3; and

   (c) an Interleukin 2 (IL2) molecule engrafted into HCDR1 or a CDR of the VL.

2. The antibody cytokine engrafted protein of any one of claim 1, wherein the IL2 molecule contains a mutation that reduces the affinity of the IL2 molecule to a low affinity IL2 receptor.

3. The antibody cytokine engrafted protein of claim 1 or 2, wherein the antibody cytokine engrafted protein stimulates Treg cell proliferation greater than native IL2 or Proleukin®.

4. The antibody cytokine engrafted protein of any one of claims 1-3, wherein the antibody cytokine engrafted protein stimulates CD8 T effector cell proliferation less than native IL2 or Proleukin®.

5. The antibody cytokine engrafted protein of any one of claims 1-4, wherein the antibody cytokine engrafted protein has a longer half life than native IL2 or Proleukin®.

6. The antibody cytokine engrafted protein of any one of claims 1-5, wherein the IL2 molecule consists of SEQ ID NO:4.

7. The antibody cytokine engrafted protein of any one of claims 1-5, wherein the IL2 molecule consists of SEQ ID NO:6.

8. The antibody cytokine engrafted protein of any one of claims 1-7, further comprising an IgG class antibody heavy chain.

9. The antibody cytokine engrafted protein of claim 8, wherein the IgG class antibody heavy chain is selected from IgG1, IgG2, or IgG4.

10. The antibody cytokine engrafted protein of any one of claims 1-9, wherein the binding specificity of the CDRs to target is reduced by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98%, 99%, or 100%, by the engrafted IL2 molecule.

11. The antibody cytokine engrafted protein of any one of claims 1-9, wherein the binding specificity of the CDRs to target is retained by 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 98%, 99%, or 100%, in the presence of the engrafted IL2 molecule.

12. The antibody cytokine engrafted protein of any one of claims 1-11, wherein the binding specificity of the CDRs is distinct from the binding specificity of the IL2 molecule.

13. The antibody cytokine engrafted protein of any one of claims 1-12, wherein the binding specificity of the CDRs is to a non-human antigen.

14. The antibody cytokine engrafted protein of claim 13, wherein the non-human antigen is a virus.

15. The antibody cytokine engrafted protein of claim 14, wherein the virus is respiratory syncytial virus (RSV).

16. The antibody cytokine engrafted protein of claim 15, wherein the RSV is selected from RSV subgroup A and RSV subgroup B.

17. The antibody cytokine engrafted protein of any one of claims 1-16, wherein the antibody scaffold portion of the antibody cytokine engrafted protein is humanized or human.

18. An antibody cytokine engrafted protein comprising:

(i) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO: 17, (b) a HCDR2 of SEQ ID NO:18, (c) a HCDR3 of SEQ ID NO:19 and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:30, (e) a LCDR2 of SEQ ID NO:31, and (f) a LCDR3 of SEQ ID NO:32;

(ii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:43, (b) a HCDR2 of SEQ ID NO:44, (c) a HCDR3 of SEQ ID NO:45; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:56, (e) a LCDR2 of SEQ ID NO:57, and (f) a LCDR3 of SEQ ID NO:58;

(iii) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:69, (b) a HCDR2 of SEQ ID NO:70, (c) a HCDR3 of SEQ ID NO:71; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:82, (e) a LCDR2 of SEQ ID NO:83, and (f) a LCDR3 of SEQ ID NO:84; or

(iv) a heavy chain variable region that comprises (a) a HCDR1 of SEQ ID NO:95, (b) a HCDR2 of SEQ ID NO:96, (c) a HCDR3 of SEQ ID NO:97; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:108, (e) a LCDR2 of SEQ ID NO:109, and (f) a LCDR3 of SEQ ID NO:110.

19. An antibody cytokine engrafted protein comprising:

(i) a heavy chain variable region (VH) that comprises SEQ ID NO:20, and a light chain variable region (VL) that comprises SEQ ID NO: 33;

(ii) a heavy chain variable region (VH) that comprises SEQ ID NO: 46, and a light chain variable region (VL) that comprises SEQ ID NO: 59;

(iii) a heavy chain variable region (VH) that comprises SEQ ID NO:72, and a light chain variable region (VL) that comprises SEQ ID NO:85; or

(iv) a heavy chain variable region (VH) that comprises SEQ ID NO:98, and a light chain variable region (VL) that comprises SEQ ID NO:111.

20. The antibody cytokine engrafted protein of any one of claims 1-19, further comprising a modified Fc region corresponding with reduced effector function.

21. The antibody cytokine engrafted protein of claim 20, wherein the modified Fc region comprises a mutation selected from one or more of D265A, P329A, P329G, N297A, L234A, and L235A.

22. The antibody cytokine engrafted protein of claim 21, wherein the modified Fc region comprises a combination of mutations selected from one or more of D265A/P329A, D265A/N297A, L234/L235A, P329A/L234A/L235A, and P329G/L234A/L235A.

23. An antibody cytokine engrafted protein comprising a HCDR1 of SEQ ID NO: 17, a HCDR2 of SEQ ID NO:18, a HCDR3 of SEQ ID NO:19, a LCDR1 of SEQ ID NO:30, a LCDR2 of SEQ ID NO:31, a LCDR3 of SEQ ID NO:32, a modified Fc region containing the mutation D265A/P329A, wherein the antibody cytokine engrafted protein stimulates less expansion of NK cells when compared to Proleukin®.

24. An antibody cytokine engrafted protein comprising a HCDR1 of SEQ ID NO:43, a HCDR2 of SEQ ID NO:44, a HCDR3 of SEQ ID NO:45, a LCDR1 of SEQ ID NO:56, a LCDR2 of SEQ ID NO:57, a LCDR3 of SEQ ID NO:58, a modified Fc region containing the mutation D265A/P329A, wherein the antibody cytokine engrafted protein stimulates less expansion of NK cells when compared to Proleukin®.

25. An antibody cytokine engrafted protein comprising a HCDR1 of SEQ ID NO:69, a HCDR2 of SEQ ID NO:70, a HCDR3 of SEQ ID NO:71, a LCDR1 of SEQ ID NO:82, a LCDR2 of SEQ ID NO:83, a LCDR3 of SEQ ID NO:84, a modified Fc region containing the mutation D265A/P329A, wherein the

antibody cytokine engrafted protein stimulates less expansion of NK cells when compared to Proleukin®.

26. An antibody cytokine engrafted protein comprising a HCDR1 of SEQ ID NO:95, a HCDR2 of SEQ ID NO:96, a HCDR3 of SEQ ID NO:97, a LCDR1 of SEQ ID NO:108, a LCDR2 of SEQ ID NO:109, a LCDR3 of SEQ ID NO:110, a modified Fc region containing the mutation D265A/P329A, wherein the antibody cytokine engrafted protein stimulates less expansion of NK cells when compared to Proleukin®.

27. An isolated nucleic acid encoding an antibody cytokine engrafted protein comprising:

(i) SEQ ID NO:23 and SEQ ID NO:36;

(ii) SEQ ID NO:49 and SEQ ID NO:62;

(iii) SEQ ID NO:75 and SEQ ID NO:88; or

(iv) SEQ ID NO:101 and SEQ ID NO:114.

28. A recombinant host cell suitable for the production of an antibody cytokine engrafted protein, comprising the nucleic acids of claim 27 encoding the heavy and light chain polypeptides of the protein, and optionally, a secretion signal.

29. The recombinant host cell of claim 28, which is a mammalian cell line.

30. The recombinant host cell of claim 29, wherein the mammalian cell line is a CHO cell line.

31. A pharmaceutical composition comprising the antibody cytokine engrafted protein of any one of claims 1-26 and a pharmaceutically acceptable carrier.

32. Use of an antibody cytokine engrafted protein in the manufacture of a medicament for treatment of an immune related disorder, the protein comprising:

(i) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO: 17, (b) a HCDR2 of SEQ ID NO:18, (c) a HCDR3 of SEQ ID NO:19 and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:30, (e) a LCDR2 of SEQ ID NO:31, and (f) a LCDR3 of SEQ ID NO:32; or

(ii) a heavy chain variable region that comprises: (a) a HCDR1 of SEQ ID NO:43, (b) a HCDR2 of SEQ ID NO:44, (c) a HCDR3 of SEQ ID NO:45; and a light chain variable region that comprises: (d) a LCDR1 of SEQ ID NO:56, (e) a LCDR2 of SEQ ID NO:57, and (f) a LCDR3 of SEQ ID NO:58,

wherein the immune related disorder is associated with IL-2.

33. The use of claim 32, wherein the immune related disorder is selected from the group consisting of Type 1 diabetes, System Lupus Erythematosus, Vitiligo, chronic graft versus host disease (cGvHD), prophylactic acute graft versus host disease (pGvHD), HIV-induced vasculitis, Alopecia areata, Systemic sclerosis morphoea, and primary anti-phospholipid syndrome.

34. Use of the antibody cytokine engrafted protein of any one of claims 1-26, or the pharmaceutical composition of claim 31, in the manufacture of a medicament for treating an immune related disorder, wherein the immune related disorder is associated with IL-2.