CLAIMS

1. A protein construct, comprising:

(i) a BTNL3/8 targeting moiety,

(ii) a payload, and

(iii) an optional linker linking the targeting moiety to the payload;

wherein the BTNL3/8 targeting moiety comprises a T cell receptor (TCR) Vγ domain and a paired T cell receptor (TCR) Vδ domain, the TCR Vγ domain include J region and complementarity-determining regions CDR1, CDR2, CDR3 and CDR4;

wherein the amino acid at sequence position number 87 of the TCR Vγ domain is aspartic acid or histidine, and the amino acid at sequence position number 90 of the TCR Vγ domain is glycine or glutamic acid;

wherein the remaining residues of the Vγ domain CDR4 are, at each position, independently selected from the corresponding residues of a human or murine Vγ domain;

wherein the payload is a protein payload fused in frame to the targeting moiety or is a small molecule linked to the targeting moiety; and

wherein the Vγ domain CDR4 is located between the CDR2 and the CDR3 regions of the TCR Vγ domain.

2. The protein construct of claim 1, wherein the remaining residues of the Vγ domain CDR4 are, at each residue position, independently selected from the corresponding residues of human Vγ4, human Vγ2, or mouse Vγ7, such as wherein the remaining residues of the Vγ domain CDR4 are all selected from the corresponding residues of human Vγ4, human Vγ2, or mouse Vγ7.

3. The protein construct of claim 1, wherein the amino acid sequence at positions numbers 87-90 of the Vγ domain is SEQ ID NO: 1 or SEQ ID NO: 2.

4. The protein construct of claim 1, wherein the TCR Vγ domain is a human Vγ2 domain in which the amino acids of the CDR4 are substituted with aspartic acid or histidine at amino acid sequence position number 87 and substituted with glycine or glutamic acid at amino acid sequence position number 90, or

wherein the TCR Vγ domain is a human Vγ4 domain.

5. The protein construct of any one of the preceding claims, wherein the Vγ domain CDR3 is a human or mouse Vγ CDR3 sequence.

6. The protein construct of any one of claims 1-5, wherein the J region is a Vγ J region, the J region includes a human Vγ J region or a mouse Vγ J region, or

wherein the J region comprises a SEQ ID NO selected from the group consisting of SEQ ID NOs: 15-18.

7. The protein construct of any one of the preceding claims, wherein the Vγ domain and the Vδ domain are covalently linked by at least one disulfide bond.

8. The protein construct of claim 7, wherein the Vγ domain and the Vδ domain are paired by a specific heterodimeric interaction, such as leucine zipper complementarity.

9. The protein construct of claim 8, wherein the targeting moiety comprises SEQ ID NO:9, SEQ ID NO:10 or SEQ ID NO:11.

10. The protein construct of claim 7, wherein the targeting moiety comprises a single chain in-frame fusion of the Vγ domain and the Vδ domain, optionally

wherein the Vγ domain is N terminal to the Vδ domain or C terminal to the Vδ domain.

11. The protein construct of claim 10, wherein the single chain in-frame fusion of the Vγ domain and the Vδ domain comprises an internal linker sequence.

12. The protein construct of any one of claims 7-11, wherein the Vδ domain is a human Vδ domain selected from Vδ1, Vδ2 or Vδ5.

13. The protein construct of any one of claims 1-12, further comprising:

a first T cell receptor constant region,

wherein the first T cell receptor constant region is fused in-frame to the C terminus of the Vγ domain.

14. The protein construct of claim 13, wherein the first T cell receptor constant region is a human T cell receptor β constant region, a human T cell receptor α constant region or a human T cell receptor γ constant region.

15. The protein construct of any one of claims 7-14, wherein the targeting moiety further comprises a second T cell receptor constant region,

wherein the second T cell receptor constant region is fused in-frame to the C terminus of the paired Vδ domain.

16. The protein construct of claim 15, wherein the second T cell receptor constant region is a human T cell receptor α constant region, a human T cell receptor β constant region or a human T cell receptor δ constant region.

17. The protein construct of any one of claims 15 or 16, wherein the in-frame fusion of the Vδ domain and the second T cell receptor constant region comprises an internal linker sequence between the Vδ domain and the second T cell receptor constant region.

18. The protein construct of any one of the preceding claims, wherein the payload is a protein payload fused in frame to the targeting moiety,

wherein the protein payload is a cytokine or an antibody.

19. The protein construct of any one of claims 1-16, wherein the payload is a small molecule, selected from a hormone, a nucleic acid and an inhibitory RNA (RNAi).

20. The protein construct of any one of the preceding claims, wherein the optional linker is a peptide fused in-frame to the targeting moiety or is a molecule conjugated to the targeting moiety.

21. A pharmaceutical composition comprising the protein construct of any one of the preceding claims and a pharmaceutically acceptable carrier, optionally

wherein the pharmaceutical composition is suitable for parenteral administration, such as intravenous administration, intramuscular administration or sub cutaneous administration.

22. Use of a therapeutically effective amount of the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating a condition of the gastrointestinal system in which gastrointestinal tissue expresses BTNL3/8, wherein the medicament is to be administered to a patient with the condition in which the gastrointestinal tissue expresses BTNL3/8.

23. The use of claim 22, wherein the payload of the protein construct is an anti-inflammatory agent, such as an aminosalicylate, a non-steroidal anti-inflammatory agent, an anti-inflammatory cytokine, an anti-proinflammatory agent or a steroid.

24. The use of claim 22, wherein the payload is an immunomodulator.

25. Use of a therapeutically effective amount of the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating an inflammatory bowel disease, wherein the medicament is to be administered to a patient with inflammatory bowel disease, optionally wherein the inflammatory bowel disease is ulcerative colitis or Crohn's disease.

26. Use of a therapeutically effective amount of the pharmaceutical composition of claim 21 in the manufacture of a medicament for treating irritable bowel syndrome, diverticulitis, celiac disease, a microbial infection, or a metabolic disorder or metabolic deficiency, in a patient, wherein the medicament is to be administered to the patient.

27. The use of any one of claims 22-26, wherein

(i) at least a portion of the BTNL3/8 targeting moiety and/or the payload is internalized into a cell, or

(ii) wherein the BTNL3/8 targeting moiety and/or the payload is not internalized into a cell.

28. A recombinant γδ TCR protein, comprising:

at least one sequence having at least 90% sequence identity to a sequence from the group consisting of SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, and SEQ ID NO: 13.