Claims

1. An *ex vivo* method of modulating gamma variable 4 (Vγ4) T cells comprising administering to a cell population comprising Vγ4 T cells an anti-Vγ4 antibody or fragment thereof comprising:

(a) a VH comprising a HCDR1 having SEQ ID NO: 79, a HCDR2 having SEQ ID NO: 56 and a HCDR3 having SEQ ID NO: 10; and

(b) a VL comprising a LCDR1 having SEQ ID NO: 102, a LCDR2 having SEQUENCE A9 (of Figure 1) and a LCDR3 having SEQ ID NO: 33

2. The method of claim 1, wherein:

(a) the VH comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 125;

(b) the VL comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 148 or 269; or

(c) both (a) and (b).

3. The method of claim 1 or 2, wherein

(a) the VH comprises SEQ ID NO: 125;

(b) the VL comprises SEQ ID NO: 148 or 269; or

(c) both (a) and (b).

4. The method of any one of claims 1 to 3, wherein the anti-Vγ4 antibody or fragment thereof comprises:

(a) a heavy chain amino acid sequence having at least 80% sequence identity with SEQ ID NO: 292;

(b) a light chain amino acid sequence having at least 80% sequence identity with SEQ ID NO: 315; or

(c) both (a) and (b).

5. The method of any one of claims 1 to 4, wherein the anti-Vγ4 antibody or fragment thereof comprises:

(a) a heavy chain amino acid sequence comprising SEQ ID NO: 292;

(b) a light chain amino acid sequence comprising SEQ ID NO: 315; or

(c) both (a) and (b).

6. The method of any one of claims 1 to 3, wherein the anti-Vγ4 antibody comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 241, optionally wherein the amino acid sequence comprises SEQ ID NO: 241.

7. The method of any one of claims 1 to 3, wherein the anti-Vγ4 antibody or fragment thereof comprises an amino acid sequence having at least 80% sequence identity with SEQ ID NO: 171, optionally wherein the amino acid sequence comprises SEQ ID NO: 171.

8. The method of any one of claims 1 to 7, wherein the anti-Vγ4 antibody or fragment thereof binds to an epitope of the Vγ4 chain of the γδ TCR comprising one or more amino acid residues within amino acid region 67-82 of SEQ ID NO: 1, optionally wherein the epitope comprises or consists of K76 and/or M80 of SEQ ID NO: 1.

9. The method of claim 8, wherein the epitope is an activating epitope of a γδ T cell, optionally wherein binding of the activating epitope: (i) downregulates the γδ TCR; (ii) activates degranulation of the γδ T cell; (iii) activates γδ T cell-mediated killing; and/or (iv) activates or increases Vγ4 chain-mediated cell signalling.

10. The method as defined in any one of claims 1 to 9, wherein the anti-Vγ4 antibody or fragment thereof is:

(i) an scFv or a full length antibody; and/or

(ii) a human antibody or fragment thereof.

11. The method as defined in any one of claims 1 to 10, wherein the modulation comprises expansion of Vγ4 T cells.

12. The method as defined in claim 11, wherein the method provides an expanded population of Vγ4 T cells which contains greater than about 60% Vγ4 T cells.

13. The method as defined in any one of claims 1 to 12, wherein the method comprises:

(i) culturing the cell population for at least 5 days after administering the anti-Vγ4 antibody or fragment thereof;

(ii) culturing the cell population in the presence of IL-2 and/or IL-15; or

(iii) both (i) and (ii).

14. The method as defined in any one of claims 1 to 13, wherein the cell population is obtained from:

(i) a haematopoietic sample or a fraction thereof, optionally wherein the haematopoietic sample consists of peripheral blood mononuclear cells (PBMCs) or low density mononuclear cells (LDMCs); or

(ii) a non-haematopoietic tissue sample, such as a skin, colon, gut, mammary gland, lung, prostate, liver, spleen, pancreas, uterus, vagina or other cutaneous, mucosal or serous membrane sample.

15. The method as defined in any one of claims 1 to 14, wherein the cell population is obtained from human or non-human animal tissue.