Claims

1. An EphA3 binding agent, comprising six complementarity determining regions (CDRs) having an amino acid sequence set forth in the table below:

Ab Clone	**Region**	**SEQ ID NOs:**	**Region**	**SEQ ID NOs:**
3C3-1	CDR-H1	13-17	CDR-L1	28-32
	CDR-H2	18-22	CDR-L2	33-37
	CDR-H3	23-27	CDR-L3	38-42
2D4-1	CDR-H1	43-47	CDR-L1	58-62
	CDR-H2	48-52	CDR-L2	63-67
	CDR-H3	53-57	CDR-L3	68-72

2. The EphA3 binding agent of claim 1, wherein the agent is isolated.

3. The EphA3 binding agent of Claim 1 or claim 2, wherein:
    a. the VH polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 153; and/or
    b. the VL polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 154.

4. The EphA3 binding agent of Claim 1 or claim 2, wherein:
    a. the VH polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 155; and/or
    b. the VL polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 156.

5. The EphA3 binding agent of any one of the preceding claims, wherein the EphA3 binding agent is an antibody or antibody fragment.

6. The EphA3 binding agent of claim 5, wherein the EphA3 binding agent is a recombinant, human or humanized antibody or antibody fragment.

7. A chimeric antigen receptor (CAR) comprising an antigen-binding agent according to any one of claims 1-6.

8. A CAR comprising an antigen binding domain including six CDRs having a nucleotide sequence set forth in SEQ ID NOs:1-12, a transmembrane domain, preferably wherein the transmembrane

domain comprises a CD8 transmembrane domain, preferably wherein the CD8 transmembrane domain comprises an amino acid sequence set forth in SEQ ID NO:159, and an intracellular T-cell signalling domain, preferably wherein the intracellular signalling domain comprises a CD3 zeta intracellular signalling domain, preferably wherein the intracellular signalling domain comprises a CD3 zeta amino acid sequence set forth in SEQ ID NO:162.

9. The CAR of Claim 8, wherein the antigen binding domain comprises, consists or consists essentially of:

(a) a heavy chain immunoglobulin variable region (VH) polypeptide comprising a CDR 1 having an amino acid sequence set forth in SEQ ID NOs:13 to 17; a CDR 2 having an amino acid sequence set forth in SEQ ID NOs: 18 to 22; and a CDR 3 having an amino acid sequence set forth in SEQ ID NO: 23 to 27; and/or

(b) a light chain immunoglobulin variable region (VL) polypeptide comprising a CDR 1 having an amino acid sequence set forth in SEQ ID NOs: 28 to 32; a CDR 2 having an amino acid sequence set forth in SEQ ID NOs: 33 to 37; and a CDR 3 having an amino acid sequence set forth in SEQ ID NOs: 38 to 42.

10. The CAR of Claim 9, wherein:

(a) the VH polypeptide comprises an amino acid sequence set forth in SEQ ID NO:153; and/or

(b) the VL polypeptide comprises an amino acid sequence set forth in SEQ ID NO:154.

11. The CAR of Claim 8, wherein the antigen binding domain comprises, consists or consists essentially of:

(a) a heavy chain immunoglobulin variable region (VH) polypeptide comprising a CDR 1 having an amino acid sequence set forth in SEQ ID NOs: 43 to 47; a CDR 2 having an amino acid sequence set forth in SEQ ID NOs: 48 to 52; and a CDR 3 having an amino acid sequence set forth in SEQ ID NO: 53 to 57; and/or

(b) a light chain immunoglobulin variable region (VL) polypeptide comprising a CDR 1 having an amino acid sequence set forth in SEQ ID NOs: 58 to 62; a CDR 2 having an amino acid sequence set forth in SEQ ID NOs: 63 to 67; and a CDR 3 having an amino acid sequence set forth in SEQ ID NOs: 68 to 72.

12. The CAR of Claim 11, wherein:

(a) the VH polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 155; and/or

(b) the VL polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 156.

13. The CAR according to any one of Claims 7 to 12, wherein the antigen binding domain comprises a linker, such as the linker having an amino acid sequence set forth in SEQ ID NO: 158, optionally further comprising a leader sequence, preferably wherein the leader sequence comprises, consists or consists essentially of an amino acid sequence set forth in SEQ ID NO: 157.

14. The CAR according to any one of Claims 7 to 12, further comprising one or more co-stimulatory domains, such as a CD28 co-stimulatory domain having the amino acid sequence set forth in SEQ ID NO:161 and/or a CD137 co-stimulatory domain having the amino acid sequence set forth in SEQ ID NO:160.

15. An isolated nucleic acid encoding the EphA3 binding agent according to any one of Claims 1 to 6, or the CAR according to any one of Claims 7 to 14.

16. A genetic construct comprising the isolated nucleic acid of Claim 15.

17. An expression vector, or a plurality of expression vectors, comprising a nucleic acid or a plurality of nucleic acids according to claim 15.

18. A host cell comprising the nucleic acid of Claim 15 and/or the genetic construct of Claim 16, wherein the host cell is or comprises a T cell.

19. A method of producing an isolated EphA3 binding agent or a CAR, said method comprising; (i) culturing the host cell of Claim 18; and (ii) isolating said EphA3 binding agent or CAR from said host cell cultured in step (i).

20. An antibody or antibody fragment which binds and/or is raised against:

    (i) the EphA3 binding agent according to any one of Claims 1 to 6; and/or (ii) the CAR according to any one of Claims 7 to 12.

21. A composition comprising the EphA3 binding agent according to any one of Claims 1 to 6, the CAR according to any one of Claims 7 to 12, the isolated nucleic acid according to Claim 15, the genetic construct according to Claim 16 and/or the host cell according to Claim 18 and a pharmaceutically acceptable carrier diluent or excipient.

22. Use of the EphA3 binding agent according to any one of Claims 1 to 6, the CAR according to any one of Claims 7 to 12, the isolated nucleic acid according to Claim 15, the genetic construct according to Claim 16, the host cell according to Claim 18, and/or the composition of Claim 21, in the manufacture of a medicament for the treatment or prevention of an EphA3-expressing cancer.

23. An *ex vivo* method of detecting EphA3 or a cell expressing EphA3, said method including the step of forming a complex between the EphA3 binding agent according to any one of Claims 1 to 6, or the CAR according to any one of Claims 7 to 12 and EphA3 to thereby detect EphA3 or the cell expressing EphA3, preferably wherein the cell is or comprises a cancer cell.