

Claims

1. A binding agent comprising at least three binding domains, wherein a first binding domain binds to the T cell-specific antigen CD3 and a second binding domain and a third binding domain bind to a claudin 6, wherein the first binding domain has the format of a Fab molecule and the second binding domain and the third binding domain have the format of an scFv molecule, wherein the binding agent comprises
- (a) a first polypeptide comprising a variable domain of a heavy chain of an immunoglobulin (VH) with a specificity for the T cell-specific antigen (VH(T)), a VH domain with a specificity for the claudin (VH(CLDN)) and a variable domain of a light chain of an immunoglobulin (VL) with a specificity for the claudin (VL(CLDN)); and
- (b) a second polypeptide comprising a VL domain with a specificity for the T cell-specific antigen (VL(T)), a VH domain with a specificity for the claudin (VH(CLDN)) and a VL domain with a specificity for the claudin (VL(CLDN)),
- wherein the first polypeptide and the second polypeptide are associated so as to form the binding agent,
- wherein VH(T) comprises or consists of an amino acid sequence represented by SEQ ID NO: 5, VL(T) comprises or consists of an amino acid sequence represented by SEQ ID NO: 6, VH(CLDN) comprises or consists of an amino acid sequence represented by SEQ ID NO: 8 and VL(CLDN) comprises or consists of an amino acid sequence represented by SEQ ID NO: 10.
2. The binding agent of claim 1, wherein the first polypeptide further comprises a constant domain 1 of a heavy chain of an immunoglobulin (CH1) and the second polypeptide further comprises a constant domain of a light chain of an immunoglobulin (CL), wherein both domains are able to associate.
3. The binding agent of claim 2, wherein the first polypeptide and the second polypeptide are covalently linked via a disulfide bridge between the CH1 domain and the CL domain.
4. The binding agent of claim 2 or 3, wherein, in the first polypeptide and the second polypeptide, the VH domain(s), the VL domain(s), the CH1 domain and the CL domain are arranged, from N-terminus to C-terminus, in the order
- VH(T)-CH1-VH(CLDN)-VL(CLDN) and VL(T)-CL-VH(CLDN)-VL(CLDN); or
- VH(T)-CH1-VL(CLDN)-VH(CLDN) and VL(T)-CL-VL(CLDN)-VH(CLDN).

5. The binding agent of claim 4, wherein the VH-VL or VL-VH domains are connected to the CH1 domain or CL domain via a peptide linker such as a peptide linker comprising the amino acid sequence DVP_{G2}S or SGPG₃RS(G₄S)₂.

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6. The binding agent of any one of claims 1 to 5, wherein the first binding domain preferably binds to the epsilon-chain of CD3.

7. The binding agent of any one of claims 1 to 6, wherein the binding agent induces T cell-mediated cytotoxicity against cancer cells expressing the claudin, wherein the binding agent preferably induces T cell-mediated cytotoxicity against cancer cells expressing the claudin with an EC₅₀ of ≤ 10 nM or ≤ 1 nM or ≤ 500 pM or ≤ 250 pM or ≤ 100 pM or ≤ 50 pM.

8. The binding agent of any one of claims 1 to 7, wherein

15 (i) the first polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 14 and the second polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 16;

(ii) the first polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 15 and the second polypeptide comprises or consists of an amino acid sequence represented

20 by SEQ ID NO: 16;

(iii) the first polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 17 and the second polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 19; or

(iv) the first polypeptide comprises or consists of an amino acid sequence represented by SEQ ID

25 NO: 18 and the second polypeptide comprises or consists of an amino acid sequence represented by SEQ ID NO: 19.

9. A nucleic acid encoding the binding agent of any one of claims 1 to 8 wherein said nucleic acid is preferably in the form of a vector or in the form of RNA.

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10. A host cell comprising nucleic acid sequences encoding the binding agent of any one of claims 1 to 8.

11. A binding agent as defined in any one of claims 1 to 8, a nucleic acid as defined in claim 9

35 or a host cell as defined in claim 10 for use as a medicament.

12. A binding agent as defined in any one of claims 1 to 8, a nucleic acid as defined in claim 9 or a host cell as defined in claim 10 for use in treating or preventing cancer.

5 13. A pharmaceutical composition comprising the binding agent as defined in any one of claims 1 to 8, a nucleic acids encoding the binding agent of any one of claims 1 to 8 or a host cell as defined in claim 10.

10 14. The binding agent for use of claim 12, the nucleic acid for use of claim 12, or the host cell for use of claim 12, wherein the cancer is characterized by cancer cells expressing claudin 6 and the cancer is selected from the group consisting of urinary bladder cancer, ovarian cancer, in particular ovarian adenocarcinoma and ovarian teratocarcinoma, lung cancer, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma, gastric cancer, breast cancer, hepatic cancer, pancreatic cancer, 15 skin cancer, in particular basal cell carcinoma and squamous cell carcinoma, malignant melanoma, head and neck cancer, in particular malignant pleomorphic adenoma, sarcoma, in particular synovial sarcoma and carcinosarcoma, bile duct cancer, cancer of the urinary bladder, in particular transitional cell carcinoma and papillary carcinoma, kidney cancer, in particular renal cell carcinoma including clear cell renal cell carcinoma and papillary renal cell carcinoma, colon 20 cancer, small bowel cancer, including cancer of the ileum, in particular small bowel adenocarcinoma and adenocarcinoma of the ileum, testicular embryonal carcinoma, placental choriocarcinoma, cervical cancer, testicular cancer, in particular testicular seminoma, testicular teratoma and embryonic testicular cancer, uterine cancer, germ cell tumors such as a teratocarcinoma or an embryonal carcinoma, in particular germ cell tumors of the testis, and the 25 metastatic forms thereof.