

therapy and other immunotherapy in that it can work with any CD3-positive T cell, independent of a costimulatory activating signal (Klinger et al., Immunol Reviews 2016).

[11] The expression of CLDN6 on the cell surface of germ cell tumors, ovarian cancer, and non-small cell lung cancer provides a basis for targeting these tumor types with CLDN6 x CD3 polypeptides/polypeptide constructs. Furthermore, CLDN6 x CD3 polypeptides/polypeptide constructs has the potential to target additional tumor types that express CLDN6, and particularly to any type of cancer that expresses CLDN6, more particularly for the treatment of cancer patients in second line treatment or higher, such as patients that have previously received chemotherapy or immunotherapy and who have relapsing disease.

Summary

[11a] In one aspect, the present disclosure provides a polypeptide or a polypeptide construct comprising

- a domain which binds to human CLDN6 (SEQ ID NO: 1), and
- a domain which binds to human CD3, and
- a domain extending the half-life of the polypeptide, wherein the domain, which binds to human CLDN6, binds to amino acids 29-39 of SEQ ID NO: 1 in the extracellular loop 1 (ECL1) of CLDN6, depicted in SEQ ID NO: 9, and/or to amino acids 151-160 of SEQ ID NO: 1 in the extracellular loop 2 (ECL2) of CLDN6, depicted in SEQ ID NO: 10.

[11b] In another aspect, the present disclosure provides a polypeptide or a polypeptide construct comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18. In another aspect, the present disclosure provides a polypeptide or polypeptide construct comprising a VH region and a VL region having amino acid sequences as depicted in SEQ ID NOs: 11+12. In another aspect, the present disclosure provides a polypeptide or polypeptide construct comprising an amino acid sequence as depicted in SEQ ID NO: 19.

[11c] In another aspect, the present disclosure provides a polypeptide or polypeptide construct comprising an amino acid sequence depicted in SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, or SEQ ID NO: 24. In yet another aspect, the present disclosure provides a polypeptide or a polypeptide construct comprising a domain which binds to human CLDN6 (SEQ ID NO: 1), and a domain which binds to human CD3, and a domain extending the half-life of the polypeptide, wherein the domain that binds to CLDN6 comprises a VH region comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in

SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18. In yet another aspect, the present disclosure provides a polypeptide or polypeptide construct as defined herein, wherein the domain binding to CLDN6 comprises a pair of a VH region and a VL region having amino acid sequences as depicted in SEQ ID NOs: 11+12.

[11d] In a further aspect, the present disclosure provides a polynucleotide encoding a polypeptide or polypeptide construct as defined herein. In a further aspect, the present disclosure provides a vector comprising a polynucleotide as defined herein. In a further aspect, the present disclosure provides a host cell transformed or transfected with the polynucleotide as defined herein or with the vector as defined herein. In a further aspect, the present disclosure provides a process for producing a polypeptide or polypeptide construct as defined herein, said process comprising culturing a host cell as defined herein under conditions allowing the expression of said polypeptide construct and recovering the produced polypeptide or polypeptide construct from the culture.

[11e] In a further aspect, the present disclosure provides a pharmaceutical composition comprising a polypeptide or polypeptide construct as defined herein, or that is produced according to the process as described herein. In a further aspect, the present disclosure provides the polypeptide or polypeptide construct as defined herein or that is produced according to the process as defined herein for the use as a medicament, particularly for the use in the prevention, treatment or amelioration of a disease, preferably a neoplasm. In a further aspect, the present disclosure provides a kit comprising a polypeptide or polypeptide construct as defined herein, a polypeptide or polypeptide construct produced as defined herein, a polynucleotide as defined herein, a vector as defined herein, and/or a host cell as defined herein.

[11f] In a further aspect, the present disclosure provides a use of the polypeptide or polypeptide construct as defined herein, or produced as defined herein in the manufacture of a medicament for the treatment or amelioration of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, wherein the disease preferably is selected from the group consisting of germ cell cancer, ovarian cancer, in particular ovarian adenocarcinoma and ovarian teratocarcinoma, uterine cancer, more particularly from ovarian serous cystadenocarcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, and lung cancer, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma or a pediatric neoplasm selected from Wilms tumor, extracranial rhabdoid or desmoplastic small round cell tumors.

Detailed description of the invention

[12] The present invention provides new polypeptides/polypeptide construct as compounds that selectively and, preferably, specifically bind to CLDN6 (SEQ ID NO: 1) or any isoforms thereof, compositions comprising such compounds, methods of treatment and prevention of neoplastic diseases using the herein disclosed products, kits comprising the herein disclosed products, products for the use as

a medicament, particularly for the use in the treatment and prevention of neoplastic diseases. The amino acid sequence of human CLDN6 and related information may be found in the UniProt database under accession number P56747.

Compounds of the invention

[13] In one aspect, the present invention provides a polypeptide/polypeptide construct comprising, or consisting of, a domain, which binds to CLDN6 (SEQ ID NO: 1 or a fragment thereof or a variant of the amino acid sequence) on the surface of a target cell and a domain, which binds to CD3 on the surface of a T cell, the binding to both, CLDN6 and CD3, allow the T cell's activation. The binding of the polypeptide construct according to the invention engages T cells, i.e., binds to CD3, and brings a T cell and the target cell into close contact to allow activated T cells to induce cytotoxic/cytolytic mechanisms resulting in the destruction of the target cell (T cell-dependent cytotoxicity).

[14] Further, the present invention provides a polypeptide/polypeptide construct comprising, or consisting of, a domain, which comprises a paratope (i.e., an antigen-binding domain, more particularly an epitope-binding structure), which binds to CLDN6, wherein optionally the domain comprising a paratope (i.e., an antigen-binding (epitope-binding) structure) of the polypeptides/polypeptide constructs of the invention is capable of binding CLDN6 on the surface of a cell that expresses CLDN6 binds to the E1A and/or the E2B regions of CLDN6 (SEQ ID NO: 1). Thus, the present invention provides a polypeptide/polypeptide construct comprising, or consisting of, a domain which binds to CLDN6, wherein optionally the domain is capable of binding CLDN6 on the surface of a cell that expresses

Claims

1. A polypeptide or a polypeptide construct comprising
 - a domain which binds to human CLDN6 (SEQ ID NO: 1), and
 - a domain which binds to human CD3, and
 - a domain extending the half-life of the polypeptide, wherein the domain, which binds to human CLDN6, binds to amino acids 29-39 of SEQ ID NO: 1 in the extracellular loop 1 (ECL1) of CLDN6, depicted in SEQ ID NO: 9, and/or to amino acids 151-160 of SEQ ID NO: 1 in the extracellular loop 2 (ECL2) of CLDN6, depicted in SEQ ID NO: 10.
2. The polypeptide or polypeptide construct according to claim 1, wherein said polypeptide construct is a T-cell activating construct.
3. The polypeptide or polypeptide construct according to any one of claim 1 and 2, wherein said polypeptide construct is a T-cell activating polypeptide as determined in a T cell activation assay selected from the group comprising determining the expression quantity of CD69, determining the expression quantity of CD25, determining the quantity of secreted IL-2, and determining the cytolytic activity of the T cells.
4. The polypeptide or polypeptide construct according to any one of claims 1 to 3, wherein the domain which extends the half-life of the polypeptide comprises two polypeptide monomers, each comprising a hinge, a CH2 domain and a CH3 domain.
5. The polypeptide or polypeptide construct according to any one of claims 1 to 4, wherein said domain binding to CD3 binds to an extracellular epitope of the human and the Macaca CD3 ϵ chain.
6. The polypeptide or polypeptide construct according to any one of claims 1 to 5, wherein the domain that binds CLDN6 binds to the same epitope on CLDN6 as a polypeptide construct or an antibody or derivative or fragment thereof that comprise a domain binding to CLDN6, wherein the domain comprises complementarity determining regions CDR-H1, CDR-H2, and CDR-H3 of a variable heavy (VH) chain and/or complementarity determining regions CDR-L1, CDR-L2, and CDR-L3 of a variable light (VL) chain selected from the groups depicted in a) to s) below, a) to d), n) and s) being preferred, a) to c), e) and s) being particularly preferred:
 - a) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18;

- b) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 27, a CDR-H2 depicted in SEQ ID NO: 28, and a CDR-H3 depicted in SEQ ID NO: 29, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 30, a CDR-L2 depicted in SEQ ID NO: 31 and a CDR-L3 depicted in SEQ ID NO: 32;
- c) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 41, a CDR-H2 depicted in SEQ ID NO: 42, and a CDR-H3 depicted in SEQ ID NO: 43, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 44, a CDR-L2 depicted in SEQ ID NO: 45 and a CDR-L3 depicted in SEQ ID NO: 46;
- d) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 55, a CDR-H2 depicted in SEQ ID NO: 56, and a CDR-H3 depicted in SEQ ID NO: 57, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 58, a CDR-L2 depicted in SEQ ID NO: 59 and a CDR-L3 depicted in SEQ ID NO: 60;
- e) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 69, a CDR-H2 depicted in SEQ ID NO: 70, and a CDR-H3 depicted in SEQ ID NO: 71, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 72, a CDR-L2 depicted in SEQ ID NO: 73 and a CDR-L3 depicted in SEQ ID NO: 74;
- f) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 83, a CDR-H2 depicted in SEQ ID NO: 84, and a CDR-H3 depicted in SEQ ID NO: 85, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 86, a CDR-L2 depicted in SEQ ID NO: 87 and a CDR-L3 depicted in SEQ ID NO: 88;
- g) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 97, a CDR-H2 depicted in SEQ ID NO: 98, and a CDR-H3 depicted in SEQ ID NO: 99, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 100, a CDR-L2 depicted in SEQ ID NO: 101 and a CDR-L3 depicted in SEQ ID NO: 102;
- h) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 111, a CDR-H2 depicted in SEQ ID NO: 112, and a CDR-H3 depicted in SEQ ID NO: 113, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 114, a CDR-L2 depicted in SEQ ID NO: 115 and a CDR-L3 depicted in SEQ ID NO: 116;
- i) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 125, a CDR-H2 depicted in SEQ ID NO: 126, and a CDR-H3 depicted in SEQ ID NO: 127, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 128, a CDR-L2 depicted in SEQ ID NO: 129 and a CDR-L3 depicted in SEQ ID NO: 130;
- j) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 139, a CDR-H2 depicted in SEQ ID NO: 140, and a CDR-H3 depicted in SEQ ID NO: 141, and a VL region comprising a CDR-L1

- depicted in SEQ ID NO: 142, a CDR-L2 depicted in SEQ ID NO: 143 and a CDR-L3 depicted in SEQ ID NO: 144;
- k) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 153, a CDR-H2 depicted in SEQ ID NO: 154, and a CDR-H3 depicted in SEQ ID NO: 155, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 156, a CDR-L2 depicted in SEQ ID NO: 157 and a CDR-L3 depicted in SEQ ID NO: 158;
 - l) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 167, a CDR-H2 depicted in SEQ ID NO: 168, and a CDR-H3 depicted in SEQ ID NO: 169, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 170, a CDR-L2 depicted in SEQ ID NO: 171 and a CDR-L3 depicted in SEQ ID NO: 172;
 - m) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 181, a CDR-H2 depicted in SEQ ID NO: 182, and a CDR-H3 depicted in SEQ ID NO: 183, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 184, a CDR-L2 depicted in SEQ ID NO: 185 and a CDR-L3 depicted in SEQ ID NO: 186;
 - n) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 195, a CDR-H2 depicted in SEQ ID NO: 196, and a CDR-H3 depicted in SEQ ID NO: 197, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 198, a CDR-L2 depicted in SEQ ID NO: 199 and a CDR-L3 depicted in SEQ ID NO: 200;
 - o) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 209, a CDR-H2 depicted in SEQ ID NO: 210, and a CDR-H3 depicted in SEQ ID NO: 211, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 212, a CDR-L2 depicted in SEQ ID NO: 213 and a CDR-L3 depicted in SEQ ID NO: 214;
 - p) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 223, a CDR-H2 depicted in SEQ ID NO: 224, and a CDR-H3 depicted in SEQ ID NO: 225, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 226, a CDR-L2 depicted in SEQ ID NO: 227 and a CDR-L3 depicted in SEQ ID NO: 228;
 - q) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 237, a CDR-H2 depicted in SEQ ID NO: 238, and a CDR-H3 depicted in SEQ ID NO: 239, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 240, a CDR-L2 depicted in SEQ ID NO: 241 and a CDR-L3 depicted in SEQ ID NO: 242;
 - r) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 251, a CDR-H2 depicted in SEQ ID NO: 252, and a CDR-H3 depicted in SEQ ID NO: 253, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 254, a CDR-L2 depicted in SEQ ID NO: 255 and a CDR-L3 as depicted in SEQ ID NO: 256,

- s) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 265, a CDR-H2 depicted in SEQ ID NO: 266, and a CDR-H3 depicted in SEQ ID NO: 267, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 268, a CDR-L2 depicted in SEQ ID NO: 269, and a CDR-L3 as depicted in SEQ ID NO: 270.
7. The polypeptide or polypeptide construct according to any one of claims 1 to 6, wherein the domain binding to human CD3 epsilon also binds to *Callithrix jacchus* or *Saimiri sciureus* CD3 epsilon.
 8. The polypeptide or polypeptide construct according to any one of claims 1 to 7, wherein
 - a) the polypeptide is a single chain construct,
 - b) the domain binding to CLDN6 is in the format of an scFv,
 - c) the domain binding to CD3 is in the format of an scFv,
 - d) the domains are connected via a linker, and/or
 - e) the polypeptide or polypeptide construct comprises a domain providing an extended serum half-life.
 9. The polypeptide or polypeptide construct according to any one of claims 1 to 8, wherein the domain binding to CLDN6 does not bind to CLDN1, CLDN2, CLDN3, CLDN4, CLDN9, and/or CLDN18.1/CLDN18.2.
 10. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises a VH region comprising a CDR-H1, a CDR-H2 and a CDR-H3 and a VL region comprising a CDR-L1, a CDR-L2 and a CDR-L3 selected from the groups depicted in in a) to s) below, a) to d), n) and s) being preferred, a) to c), e) and s) being particularly preferred):
 - a) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18;
 - b) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 27, a CDR-H2 depicted in SEQ ID NO: 28, and a CDR-H3 depicted in SEQ ID NO: 29, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 30, a CDR-L2 depicted in SEQ ID NO: 31 and a CDR-L3 depicted in SEQ ID NO: 32;
 - c) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 41, a CDR-H2 depicted in SEQ ID NO: 42, and a CDR-H3 depicted in SEQ ID NO: 43, and a VL region comprising a CDR-L1

- depicted in SEQ ID NO: 44, a CDR-L2 depicted in SEQ ID NO: 45 and a CDR-L3 depicted in SEQ ID NO: 46;
- d) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 55, a CDR-H2 depicted in SEQ ID NO: 56, and a CDR-H3 depicted in SEQ ID NO: 57, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 58, a CDR-L2 depicted in SEQ ID NO: 59 and a CDR-L3 depicted in SEQ ID NO: 60;
 - e) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 69, a CDR-H2 depicted in SEQ ID NO: 70, and a CDR-H3 depicted in SEQ ID NO: 71, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 72, a CDR-L2 depicted in SEQ ID NO: 73 and a CDR-L3 depicted in SEQ ID NO: 74;
 - f) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 83, a CDR-H2 depicted in SEQ ID NO: 84, and a CDR-H3 depicted in SEQ ID NO: 85, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 86, a CDR-L2 depicted in SEQ ID NO: 87 and a CDR-L3 depicted in SEQ ID NO: 88;
 - g) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 97, a CDR-H2 depicted in SEQ ID NO: 98, and a CDR-H3 depicted in SEQ ID NO: 99, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 100, a CDR-L2 depicted in SEQ ID NO: 101 and a CDR-L3 depicted in SEQ ID NO: 102;
 - h) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 111, a CDR-H2 depicted in SEQ ID NO: 112, and a CDR-H3 depicted in SEQ ID NO: 113, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 114, a CDR-L2 depicted in SEQ ID NO: 115 and a CDR-L3 depicted in SEQ ID NO: 116;
 - i) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 125, a CDR-H2 depicted in SEQ ID NO: 126, and a CDR-H3 depicted in SEQ ID NO: 127, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 128, a CDR-L2 depicted in SEQ ID NO: 129 and a CDR-L3 depicted in SEQ ID NO: 130;
 - j) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 139, a CDR-H2 depicted in SEQ ID NO: 140, and a CDR-H3 depicted in SEQ ID NO: 141, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 142, a CDR-L2 depicted in SEQ ID NO: 143 and a CDR-L3 depicted in SEQ ID NO: 144;
 - k) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 153, a CDR-H2 depicted in SEQ ID NO: 154, and a CDR-H3 depicted in SEQ ID NO: 155, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 156, a CDR-L2 depicted in SEQ ID NO: 157 and a CDR-L3 depicted in SEQ ID NO: 158;

- l) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 167, a CDR-H2 depicted in SEQ ID NO: 168, and a CDR-H3 depicted in SEQ ID NO: 169, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 170, a CDR-L2 depicted in SEQ ID NO: 171 and a CDR-L3 depicted in SEQ ID NO: 172;
 - m) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 181, a CDR-H2 depicted in SEQ ID NO: 182, and a CDR-H3 depicted in SEQ ID NO: 183, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 184, a CDR-L2 depicted in SEQ ID NO: 185 and a CDR-L3 depicted in SEQ ID NO: 186;
 - n) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 195, a CDR-H2 depicted in SEQ ID NO: 196, and a CDR-H3 depicted in SEQ ID NO: 197, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 198, a CDR-L2 depicted in SEQ ID NO: 199 and a CDR-L3 depicted in SEQ ID NO: 200;
 - o) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 209, a CDR-H2 depicted in SEQ ID NO: 210, and a CDR-H3 depicted in SEQ ID NO: 211, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 212, a CDR-L2 depicted in SEQ ID NO: 213 and a CDR-L3 depicted in SEQ ID NO: 214;
 - p) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 223, a CDR-H2 depicted in SEQ ID NO: 224, and a CDR-H3 depicted in SEQ ID NO: 225, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 226, a CDR-L2 depicted in SEQ ID NO: 227 and a CDR-L3 depicted in SEQ ID NO: 228;
 - q) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 237, a CDR-H2 depicted in SEQ ID NO: 238, and a CDR-H3 depicted in SEQ ID NO: 239, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 240, a CDR-L2 depicted in SEQ ID NO: 241 and a CDR-L3 depicted in SEQ ID NO: 242;
 - r) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 251, a CDR-H2 depicted in SEQ ID NO: 252, and a CDR-H3 depicted in SEQ ID NO: 253, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 254, a CDR-L2 depicted in SEQ ID NO: 255 and a CDR-L3 as depicted in SEQ ID NO: 256,
 - s) a VH region comprising a CDR-H1 depicted in SEQ ID NO: 265, a CDR-H2 depicted in SEQ ID NO: 266, and a CDR-H3 depicted in SEQ ID NO: 267, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 268, a CDR-L2 depicted in SEQ ID NO: 269, and a CDR-L3 as depicted in SEQ ID NO: 270.
11. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises a VH region having an amino acid sequence selected from the group comprising the sequences depicted in SEQ ID NO: 11, SEQ ID NO: 25, SEQ ID NO: 39,

SEQ ID NO: 53, SEQ ID NO: 67, SEQ ID NO: 81, SEQ ID NO: 95, SEQ ID NO: 109, SEQ ID NO: 123, SEQ ID NO: 137, SEQ ID NO: 151, SEQ ID NO: 165, SEQ ID NO: 179, SEQ ID NO: 193, SEQ ID NO: 207, SEQ ID NO: 221, SEQ ID NO: 235, SEQ ID NO: 249, or SEQ ID NO: 263,

wherein said VH region amino acid sequence may have one or more modifications of one or several amino acid residues in the framework and/or hypervariable regions, provided said domain comprising said modified VH region selectively binds to CLDN6, and

optionally wherein said domain is part of a polypeptide or polypeptide construct that activates T cells and maintains the ability to induce T cell-dependent cytotoxicity,

further, optionally, wherein said domain is part of a polypeptide or polypeptide construct that activates T cells and maintains the ability to induce T cell-dependent cytotoxicity with more than 1000fold efficacy than in an identical cell type which expresses CLDN9, but does not express CLDN6, and

still further optionally, wherein said domain is part of a polypeptide or polypeptide construct that is not capable of activating T cells and inducing T cell-dependent cytotoxicity in CLDN6-negative cells of the same cell type, preferably when tested in an in vitro cytotoxicity assay.

12. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises a VL region having an amino acid sequence selected from the group comprising the sequences depicted in SEQ ID NO: 12, SEQ ID NO: 26, SEQ ID NO: 40, SEQ ID NO: 54, SEQ ID NO: 68, SEQ ID NO: 82, SEQ ID NO: 96, SEQ ID NO: 110, SEQ ID NO: 124, SEQ ID NO: 138, SEQ ID NO: 152, SEQ ID NO: 166, SEQ ID NO: 180, SEQ ID NO: 194, SEQ ID NO: 208, SEQ ID NO: 222, SEQ ID NO: 236, SEQ ID NO: 250, or SEQ ID NO: 264,

wherein said VL region amino acid sequence may have one or more modifications of one or several amino acid residues in the framework and/or hypervariable regions, provided said domain comprising said modified VL region selectively binds to CLDN6, and

optionally wherein said domain is part of a polypeptide or polypeptide construct that activates T cells and maintains the ability to induce T cell-dependent cytotoxicity in target cells,

further, optionally, wherein said domain is part of a polypeptide or polypeptide construct that activates T cells and maintains the ability to induce T cell-dependent cytotoxicity with more than 500fold efficacy than in control cells which do not express CLDN6, wherein these cells optionally express CLDN9, but

still further optionally, wherein said domain is part of a polypeptide or polypeptide construct that is not capable of activating T cells and inducing T cell-dependent cytotoxicity in

CLDN6-negative cells of the same cell type, preferably when tested in a in vitro cytotoxicity assay.

13. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises a pair of a VH region and a VL region having amino acid sequences as depicted in SEQ ID NOs: 11+12, SEQ ID NO: 25+26, SEQ ID NO: 39+40, SEQ ID NO: 53+54, SEQ ID NO: 67+68, SEQ ID NO: 81+82, SEQ ID NO: 95+96, SEQ ID NO: 109+110, SEQ ID NO: 123+124, SEQ ID NO: 137+138, SEQ ID NO: 151+152, SEQ ID NO: 165+166, SEQ ID NO: 179+180, SEQ ID NO: 193+194, SEQ ID NO: 207+208, SEQ ID NO: 221+222, SEQ ID NO: 235+236, SEQ ID NO: 249+250, or SEQ ID NO: 263+264.
14. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises an amino acid sequence as depicted in SEQ ID NO: 19, SEQ ID NO: 22, SEQ ID NO: 33, SEQ ID NO: 36, SEQ ID NO: 47, SEQ ID NO: 50, SEQ ID NO: 61, SEQ ID NO: 64, SEQ ID NO: 75, SEQ ID NO: 78, SEQ ID NO: 89, SEQ ID NO: 92, SEQ ID NO: 103, SEQ ID NO: 106, SEQ ID NO: 117, SEQ ID NO: 120, SEQ ID NO: 131, SEQ ID NO: 134, SEQ ID NO: 145, SEQ ID NO: 148, SEQ ID NO: 159, SEQ ID NO: 162, SEQ ID NO: 173, SEQ ID NO: 176, SEQ ID NO: 187, SEQ ID NO: 190, SEQ ID NO: 201, SEQ ID NO: 204, SEQ ID NO: 215, SEQ ID NO: 218, SEQ ID NO: 229, SEQ ID NO: 232, SEQ ID NO: 243, SEQ ID NO: 246, SEQ ID NO: 257, or SEQ ID NO: 260, SEQ ID NO: 271 or SEQ ID NO: 274.
15. The polypeptide or polypeptide construct according to any one of the preceding claims, comprising an amino acid sequence selected from the group of those depicted in SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, and SEQ ID NO: 38, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51, and SEQ ID NO: 52, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, and SEQ ID NO: 66, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, and SEQ ID NO: 80, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, and SEQ ID NO: 94, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, and SEQ ID NO: 108, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, and SEQ ID NO: 122, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, and SEQ ID NO: 136, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, and SEQ ID NO: 150, SEQ ID NO: 159, SEQ ID NO: 160, SEQ ID NO: 161, SEQ ID NO: 162, SEQ ID

NO: 163, and SEQ ID NO: 164, SEQ ID NO: 173, SEQ ID NO: 174, SEQ ID NO: 175, SEQ ID NO: 176, SEQ ID NO: 177, and SEQ ID NO: 178, SEQ ID NO: 187, SEQ ID NO: 188, SEQ ID NO: 189, SEQ ID NO: 190, SEQ ID NO: 191, and SEQ ID NO: 192, SEQ ID NO: 201, SEQ ID NO: 202, SEQ ID NO: 203, SEQ ID NO: 204, SEQ ID NO: 205, and SEQ ID NO: 206, SEQ ID NO: 215, SEQ ID NO: 216, SEQ ID NO: 217, SEQ ID NO: 218, SEQ ID NO: 219, and SEQ ID NO: 220, SEQ ID NO: 229, SEQ ID NO: 230, SEQ ID NO: 231, SEQ ID NO: 232, SEQ ID NO: 233, and SEQ ID NO: 234, SEQ ID NO: 243, SEQ ID NO: 244, SEQ ID NO: 245, SEQ ID NO: 246, SEQ ID NO: 247, and SEQ ID NO: 248, SEQ ID NO: 257, SEQ ID NO: 258, SEQ ID NO: 259, SEQ ID NO: 260, SEQ ID NO: 261, and SEQ ID NO: 262, SEQ ID NO: 271, SEQ ID NO: 272, SEQ ID NO: 273, SEQ ID NO: 274, SEQ ID NO: 275, and SEQ ID NO: 276, or from polypeptides/polypeptide constructs having an amino acid having at least 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identity to said sequences.

16. A polypeptide or a polypeptide construct comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18.
17. A polypeptide or polypeptide construct comprising a VH region and a VL region having amino acid sequences as depicted in SEQ ID NOs: 11+12.
18. A polypeptide or polypeptide construct comprising an amino acid sequence as depicted in SEQ ID NO: 19.
19. A polypeptide or polypeptide construct comprising an amino acid sequence depicted in SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, or SEQ ID NO: 24.
20. A polypeptide or a polypeptide construct comprising a domain which binds to human CLDN6 (SEQ ID NO: 1), and a domain which binds to human CD3, and a domain extending the half-life of the polypeptide, wherein the domain that binds to CLDN6 comprises a VH region comprising a CDR-H1 depicted in SEQ ID NO: 13, a CDR-H2 depicted in SEQ ID NO: 14, and a CDR-H3 depicted in SEQ ID NO: 15, and a VL region comprising a CDR-L1 depicted in SEQ ID NO: 16, a CDR-L2 depicted in SEQ ID NO: 17 and a CDR-L3 depicted in SEQ ID NO: 18.
21. A polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises a pair of a VH region and a VL region having amino acid sequences as depicted in SEQ ID NOs: 11+12.

22. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 comprises an amino acid sequence as depicted in SEQ ID NO: 19.
23. The polypeptide or polypeptide construct according to any one of the preceding claims, comprising an amino acid sequence depicted in SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, and SEQ ID NO: 24.
24. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 induces at least 100fold, at least 250fold, at least 500fold lower cytotoxicity as determined in an in vitro assay using a cell that expresses a mutant of wild-type CLDN6 as depicted in SEQ ID NO: 1 that comprises at least one or more of the following mutations M29X, wherein X is preferably L, R145X, wherein X is preferably Q, and/or Q156X, wherein X is preferably L, as compared with the cytotoxicity measured in the in vitro assay using a cell that expresses CLDN6 as depicted in SEQ ID NO: 1.
25. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the domain binding to CLDN6 induces at least 100fold, at least 250fold, at least 500fold lower cytotoxicity as determined in an in vitro assay using a cell that expresses a mutant of wild-type CLDN6 as depicted in SEQ ID NO: 1 that comprises at least one or more of the following mutations M29X, wherein X is preferably L, R145X, wherein X is preferably Q, and/or Q156X, wherein X is preferably L, as compared with the cytotoxicity measured in the in vitro assay using a cell that expresses CLDN6 as depicted in SEQ ID NO: 1, wherein said construct is capable of activating T cells and inducing cytotoxicity in target cells expressing CLDN6, and wherein said construct has a heavy chain CDR3 sequence comprising: X1LIVX2APX3 (SEQ ID NO. 667), wherein X1 is either A or N; X2 is either V or E; and X3 is either V or A.
26. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct is a single chain construct.
27. The polypeptide or polypeptide construct according to one of the preceding claims, wherein said half-life extending domain comprising two polypeptide monomers comprises a hinge, a CH2 domain and a CH3 domain comprising in an amino to carboxyl order:

hinge-CH2-CH3-linker-hinge-CH2-CH3.
28. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the CH2 domain comprises an intra domain cysteine disulfide bridge.
29. The polypeptide or polypeptide construct according to one of the preceding claims, wherein

- (i) the antigen-binding (epitope-binding) domain binding CLDN6 comprises two antibody variable domains and the antigen-binding (epitope-binding) domain binding CD3 comprises two antibody variable domains;
 - (ii) the antigen-binding (epitope-binding) domain binding CLDN6 comprises one antibody variable domain and the antigen-binding (epitope-binding) domain binding CD3 comprises two antibody variable domains;
 - (iii) the antigen-binding (epitope-binding) domain binding CLDN6 comprises two antibody variable domains and the antigen-binding (epitope-binding) domain binding CD3 comprises one antibody variable domain; or
 - (iv) the antigen-binding (epitope-binding) domain binding CLDN6 comprises one antibody variable domain and the antigen-binding (epitope-binding) domain binding CD3 comprises one antibody variable domain.
30. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the antigen-binding (epitope-binding) domain binding CLDN6 and the antigen-binding (epitope-binding) domain binding CD3 are fused to another domain via a peptide linker.
31. The polypeptide or polypeptide construct according to any one of the preceding claims, wherein the polypeptide or polypeptide construct comprises in an amino to carboxyl order, or in a carboxyl to amino order:
- (a) an antigen-binding (epitope-binding) domain binding to CLDN6;
 - (b) a peptide linker, particularly a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 563-575;
 - (c) an antigen-binding (epitope-binding) domain binding to CD3.
32. The polypeptide or polypeptide construct according to claim 31, wherein the polypeptide or polypeptide construct further comprises in an amino to carboxyl order, or in a carboxyl to amino order, or between the antigen-binding (epitope-binding) domain binding to CLDN6 and the antigen-binding (epitope-binding) domain binding to CD3:
- (a) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 563-575;
 - (b) the first polypeptide monomer of a third domain;
 - (c) a peptide linker having an amino acid sequence selected from the group consisting of SEQ ID NOs: 563-575; and
 - (d) the second polypeptide monomer of said third domain.

33. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct is depicted in any one of the sequences depicted in SEQ ID NO: 35, 38, 49, 52, 63, 66, 77, 80, 91, 94, 105, 108, 119, 122, 133, 136, 147, 150, 161, 164, 175, 178, 189, 192, 203, 206, 217, 220, 231, 234, 245, 148, 259, 262, 273, 276, 287, 290, 301, 304, 315, 318, 329, 332, 343, 346, 357, 360, 371, 374, 385, 388, 399, 402, 413, 416, 427, and 430, particularly, 35, 38, 49, 52, 63, 66, 77, 80, 91, 94, more particularly 35, 38, 49, 52, 77, and 80, and even more particularly, 35, 49, and 77.
34. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VH domain comprising at least one, two, or all of the following CDR sequences as depicted in SEQ ID NO: 670, 671, and/or 672.
35. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VL domain comprising at least one, two, or all of the following CDR sequences as depicted in SEQ ID NO: 673, 674, and/or 675.
36. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VH and a VL domain comprising at least one, two, or all of the following CDR sequences as depicted in SEQ ID NO: 670, 671, 672, 673, 674, and/or 675.
37. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VH domain as depicted in SEQ ID NO: 676.
38. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VL domain as depicted in SEQ ID NO: 677.
39. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a VH domain as depicted in SEQ ID NO: 676 and a VL domain as depicted in SEQ ID NO: 677.
40. The polypeptide or polypeptide construct according to one of the preceding claims, wherein the construct comprises a domain binding to CD3 comprising a scFv domain as depicted in SEQ ID NO: 678.
41. A polynucleotide encoding a polypeptide or polypeptide construct as defined in any one of the preceding claims.

42. A vector comprising a polynucleotide as defined in claim 41.
43. A host cell transformed or transfected with the polynucleotide as defined in claim 41 or with the vector as defined in claim 42.
44. A process for producing a polypeptide or polypeptide construct as defined in any one of claims 1 to 40, said process comprising culturing a host cell as defined in claim 43 under conditions allowing the expression of said polypeptide construct and recovering the produced polypeptide or polypeptide construct from the culture.
45. A pharmaceutical composition comprising a polypeptide or polypeptide construct as defined in any one of claims 1 to 40, or that is produced according to the process of claim 44.
46. The polypeptide or polypeptide construct according to any one of claims 1 to 40 or that is produced according to the process of claim 44 for the use as a medicament, particularly for the use in the prevention, treatment or amelioration of a disease, preferably a neoplasm.
47. The polypeptide or polypeptide construct according to claim 40 for the use as a medicament, particularly for the use in the prevention, treatment or amelioration of a disease, wherein the disease or neoplasm is selected from the group consisting of germ cell cancer, ovarian cancer, in particular ovarian adenocarcinoma and ovarian teratocarcinoma, uterine cancer, and lung cancer, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma, further wherein the disease is a pediatric neoplasm selected from the group comprising Wilms tumor, extracranial rhabdoid or desmoplastic small round cell tumors.
48. The polypeptide or polypeptide construct according to claim ~~40~~47, wherein the lung cancer is non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma.
49. A kit comprising a polypeptide or polypeptide construct as defined in any one of claims 1 to 40, a polypeptide or polypeptide construct produced according to the process of claim 44, a polynucleotide as defined in claim 41, a vector as defined in claim 42, and/or a host cell as defined in claim 43.
50. ~~A method for the treatment or amelioration of a proliferative disease, a tumorous disease, cancer, or an immunological disorder, comprising the step of administering to a subject in need thereof~~Use of the polypeptide or polypeptide construct according to any one of claims 1 to 40, or produced according to the process of claim 41, in the manufacture of a medicament for the treatment or

amelioration of a proliferative disease, a tumorous disease, cancer, or an immunological disorder,

wherein the disease preferably is selected from the group consisting of germ cell cancer, ovarian cancer, in particular ovarian adenocarcinoma and ovarian teratocarcinoma, uterine cancer, more particularly from ovarian serous cystadenocarcinoma, uterine carcinosarcoma, uterine corpus endometrial carcinoma, and lung cancer, including small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC), in particular squamous cell lung carcinoma and adenocarcinoma or a pediatric neoplasm selected from Wilms tumor, extracranial rhabdoid or desmoplastic small round cell tumors.