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Claims

1. A dual specificity polypeptide molecule comprising a first polypeptide chain and a second polypeptide chain, wherein:
 - 10 a) the first polypeptide chain comprises
 - ai) a first variable domain (VD1) of an antibody,
 - aii) a first variable domain (VR1) of a T cell receptor (TCR), and
 - aiii) a first linker (LINK1) connecting said domains;
 - b) the second polypeptide chain comprises
 - 15 bi) a second variable domain (VR2) of a TCR,
 - bii) a second variable domain (VD2) of an antibody, and
 - biii) a second linker (LINK2) connecting said domains;

wherein said first variable domain (VD1) and said second variable domain (VD2) associate to form a first binding site (VD1)(VD2) that specifically binds a cell surface

20 antigen of a human immune effector cell;

wherein the first variable domain (VR1) is one of a TCR V α domain and a TCR V β domain, and the second variable domain (VR2) is the other one of the TCR V α domain and the TCR V β domain, said first variable domain (VR1) and said second variable domain (VR2) associate to form a second binding site (VR1)(VR2) that specifically binds

25 an MHC-associated peptide epitope;

wherein said two polypeptide chains are fused to human IgG hinge domains and/or human IgG Fc domains or dimerizing portions thereof;

wherein said two polypeptide chains are connected by covalent and/or non-covalent bonds between said hinge domains and/or Fc-domains;

30 wherein said dual specificity polypeptide molecule is capable of simultaneously binding the cell surface molecule and the MHC-associated peptide epitope; and

wherein the order of the variable domains in the two polypeptide chains is selected from VD1-VR1 and VR2-VD2 or VD2-VR2 and VR1-VD1.
- 35 2. The dual specificity polypeptide molecule according to claim 1, wherein the linker-sequences LINK1 and/or LINK2 contain at least one sequence motif selected from GGGs, GGGGS, TVLRT, TVSSAS, and TVLSSAS.

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3. The dual specificity polypeptide molecule according to any one of claims 1 or 2, wherein said first and second polypeptide chains further comprise at least a hinge domain and an Fc domain or portions thereof derived from human IgG1, IgG2 or IgG4, wherein preferably said Fc domain comprises at least one effector function silencing mutation in the sequence of SEQ ID No. 50 (ELLGPP) of human IgG1, preferably wherein said effector function silencing mutation is generated by one or more of mutations E1P, L2V, L3A and no residue in position 4 of SEQ ID No. 50.

4. The dual specificity polypeptide molecule according to claim 3, wherein said Fc domain comprises a CH3 domain comprising at least one mutation that facilitates the formation of heterodimers, preferably, wherein said mutations comprise knob-into-hole mutations.

5. The dual specificity polypeptide molecule according to any one of claims 3 or 4, wherein said Fc domain comprises CH2 and CH3 domains comprising at least two additional cysteine residues.

6. The dual specificity polypeptide molecule according to any of claims 1 to 5, wherein said antibody-derived domains VD1 and VD2 display an engineered disulfide bridge introducing a covalent bond between VD1 and VD2 and where said cysteines are introduced into framework region (FR) 4 in case of VL and framework region 2 in case of VH.

7. The dual specificity polypeptide molecule according to any one of claims 1 to 6, wherein said cell surface molecule is known to induce the activation of immune cells, or is at least one selected from the group consisting of CD3, CD4, CD7, CD8, CD10, CD11b, CD11c, CD14, CD16, CD18, CD22, CD25, CD28, CD32a, CD32b, CD33, CD41, CD41b, CD42a, CD42b, CD44, CD45RA, CD49, CD55, CD56, CD61, CD64, CD68, CD94, CD90, CD117, CD123, CD125, CD134, CD137, CD152, CD163, CD193, CD203c, CD235a, CD278, CD279, CD287, Nkp46, NKG2D, GITR, FcεRI, TCRα/β and TCRγ/δ, HLA-DR, preferably wherein said cell surface molecule is CD3γ, CD3δ or CD3ε.

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8. The dual specificity polypeptide molecule according to any one of claims 1 to 7, wherein the first polypeptide chain comprises SEQ ID No. 28, SEQ ID No. 29, and SEQ ID No. 30; and the second polypeptide chain comprises SEQ ID No. 31, SEQ ID No. 32, and SEQ ID No. 30.

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9. The dual specificity polypeptide molecule according to any one of claims 3 to 8, wherein the Fc region in the first polypeptide chain comprises SEQ ID No. 26 or SEQ ID No. 47 (Fc1), and the Fc region in the second polypeptide chain comprises SEQ ID No. 27 or SEQ ID No. 48 (Fc2).

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10. The dual specificity polypeptide molecule of claim 1, wherein the first polypeptide chain comprises SEQ ID No. 16, SEQ ID No. 43, SEQ ID No. 45, SEQ ID No. 51, SEQ ID No. 53, SEQ ID No. 55, or SEQ ID No. 57, and wherein the second polypeptide chain comprises SEQ ID No. 17, SEQ ID 44, SEQ ID No. 46, SEQ ID No. 52, SEQ ID No. 54, SEQ ID No. 56, or SEQ ID No. 58.

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11. The dual specificity polypeptide molecule according to any one of claims 1 to 10, wherein said first binding site (VD1)(VD2) that binds the cell surface antigen of said immune cells is humanized; and/or said second binding site (VR1)(VR2) that binds said MHC-associated peptide epitope is affinity matured and/or stability matured.

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12. A nucleic acid encoding for the first polypeptide chain and/or the second polypeptide chain according to any of claims 1 to 11, or an expression vector comprising at least one of said nucleic acids.

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13. A host cell comprising and optionally expressing a vector as defined in claim 12.

14. A pharmaceutical composition comprising the dual specificity polypeptide molecule according to any one of claims 1 to 11, the nucleic acid or the expression vector according to claim 12, or the cell according to claim 13, together with one or more pharmaceutically acceptable carriers or excipients.

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- 5 15. The dual specificity polypeptide molecule according to any one of claims 1 to 11, the nucleic acid or the expression vector according to claim 12, the cell according to claim 13, or the pharmaceutical composition according to claim 14, for use in the treatment of diseases or disorders, preferably for use in the prevention or treatment of a disease or disorder selected from cancer, infectious diseases, and immunological disorders.