

Claims

1. A polypeptide, comprising, from N-terminus to C-terminus,
 - a) at least a variable region of a heavy chain of a heavy-chain antibody (VHH domain) that binds human, cynomolgus monkey, or mouse protein Programmed Death Ligand 1 (PD-L1), operably linked to IgG Fc binding domain; and
 - b) human TGF β RII, or a fragment thereof capable of binding TGF β 1.
2. The polypeptide of claim 1, wherein the VHH domain comprises one or more heavy chain CDRs (CDRHs) selected from at least one of the group consisting of:
 - (a) a CDRH1 with at least 70%, sequence identity to a CDRH1 as depicted in SEQ ID NO:1;
 - (b) a CDRH2 with at least 70%, sequence identity to a CDRH2 as depicted in SEQ ID NO:2; and
 - (c) a CDRH3 with at least 70%, sequence identity to a CDRH3 as depicted in SEQ ID NO:3.
3. The polypeptide of claim 2, wherein the VHH domain comprises one or more heavy chain CDRs (CDRHs) selected from at least one of the group consisting of:
 - (a) a CDRH1 as depicted in SEQ ID NO:1 or a CDRH1 that differs in amino acid sequence from the CDRH1 by an amino acid addition, deletion or substitution of not more than 2 amino acids;
 - (b) a CDRH2 as depicted in SEQ ID NO:2 or a CDRH2 that differs in amino acid sequence from the CDRH2 by an amino acid addition, deletion or substitution of not more than 2 amino acids; and
 - (c) a CDRH3 as depicted in SEQ ID NO: 3 or a CDRH3 that differs in amino acid sequence from the CDRH3 by an amino acid addition, deletion or substitution of not more than 2 amino acids.

4. The polypeptide of claim 2, wherein the VHH domain comprises one or more heavy chain CDRs (CDRHs) selected from at least one of the group consisting of:
 - (a) a CDRH1 comprising or consisting of SEQ ID NO:1;
 - (b) a CDRH2 comprising or consisting of SEQ ID NO:2; and
 - (c) a CDRH3 comprising or consisting of SEQ ID NO:3.
5. The polypeptide of claim 2, wherein the VHH domain comprises:
 - (a) the amino acid sequence of SEQ ID NO:4;
 - (b) an amino acid sequence at least 85%, 90%, 95%, or 99% identical to SEQ ID NO:4; or
 - (c) an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with SEQ ID NO:4.
6. The polypeptide of claim 1, further comprising an amino acid linker connecting the C-terminus of the VHH domain or IgG Fc binding domain to the N-terminus of the human TGF β RII or fragment thereof.
7. The polypeptide of claim 6, wherein the linker comprises:
 - (a) the amino acid sequence of SEQ ID NO:5;
 - (b) an amino acid sequence at least 85%, 90%, 95%, or 99% identical to SEQ ID NO:5; or
 - (c) an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with SEQ ID NO:5.
8. The polypeptide of claim 1, wherein the human TGF β RII, or a fragment thereof comprises:
 - (a) the amino acid sequence of SEQ ID NO:6;
 - (b) an amino acid sequence at least 85%, 90%, 95%, or 99% identical to SEQ ID NO:6; or
 - (c) an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with SEQ ID NO:6.

9. The polypeptide of claim 1, comprising:
 - (a) the amino acid sequence of SEQ ID NO:7;
 - (b) an amino acid sequence at least 85%, 90%, 95%, or 99% identical to SEQ ID NO:7; or
 - (c) an amino acid sequence with addition, deletion and/or substitution of one or more amino acids compared with SEQ ID NO:7.
10. An antibody or antigen binding fragment thereof, wherein the antibody or antigen binding fragment thereof comprises two of said polypeptide of any one of claims 1-9.
11. A nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide according to any one of claims 1-9 or antibody of claim 10.
12. A cloning or expression vector comprising the nucleic acid molecule of claim 11.
13. A cell comprising the nucleic acid of claim 11 or one or more cloning or expression vectors of claim 12.
14. A method of producing the polypeptide of any one of claims 1-9 or the antibody of claim 10, comprising culturing the cell of claim 13 and isolating the polypeptide or the antibody.
15. A pharmaceutical composition comprising the polypeptide of any one of claims 1-9 or the antibody of claim 10, and one or more of a pharmaceutically acceptable excipient, a diluent and a carrier.
16. A polypeptide of any one of claims 1-9 or an antibody of claim 10, for use in treating tumor or growth of tumor cells in a subject.
17. A method of treating tumor or inhibiting growth of tumor cells in a subject, comprising administering to the subject a therapeutically effective amount of the polypeptide of any one of claims 1-9 or the antibody of claim 10.

18. Use of the polypeptide of any one of claims 1-9 or the antibody of claim 10 in the manufacture of a medicament for treating tumor or inhibiting growth of tumor cells in a subject.
19. The polypeptide or antibody for use of claim 16, or the method of claim 17, or the use of claim 18, wherein the tumor is selected from the group consisting of colorectal, breast, ovarian, pancreatic, gastric, prostate, renal, cervical, myeloma, lymphoma, leukemia, thyroid, endometrial, uterine, bladder, neuroendocrine, head and neck, liver, nasopharyngeal, testicular, small cell lung cancer, non-small cell lung cancer, melanoma, basal cell skin cancer, squamous cell skin cancer, dermatofibrosarcoma protuberans, Merkel cell carcinoma, glioblastoma, glioma, sarcoma, mesothelioma, and myelodysplastic syndromes.