

Claims

1. An antibody molecule which binds to programmed death-ligand 1 (PD-L1) and lymphocyte-activation gene 3 (LAG-3), wherein the antibody molecule comprises:

(i) a complementarity determining region (CDR)-based antigen-antigen-binding site for PD-L1; and

(ii) a LAG-3 antigen-antigen-binding site located in a CH3 domain of the antibody molecule, wherein the LAG-3 binding-binding-site comprises the amino acid sequences WDEPWGED (SEQ ID NO: 1) and PYDRWVWPDE (SEQ ID NO: 3), and wherein the amino acid sequence WDEPWGED is located in a first structural-the AB loop of the CH3 domain and the amino acid sequence PYDRWVWPDE is located in a second structural-the EF loop of the CH3 domain.

~~2. An antibody molecule according to claim 1, wherein the LAG-3 antigen-binding site comprises the amino acid sequence set forth in SEQ ID NO: 1 in the AB loop, and the amino acid sequence set forth in SEQ ID NO: 3 in the EF loop of the CH3 domain.~~

~~3. An antibody molecule according to claim 1 or 2, wherein:~~

~~(i) the amino acid sequence set forth in SEQ ID NO: 1 is located at residues 11 to 18 of the CH3 domain; and/or~~

~~(ii) the amino acid sequence set forth in SEQ ID NO: 3 is located at residues 92 to 101 of the CH3 domain;~~

~~wherein the amino acid residue numbering is according to the ImMunoGeneTics (IMGT) numbering scheme.~~

42. An antibody molecule according to ~~any one of claims 1 to 3~~, wherein the LAG-3 antigen-antigen-binding site further comprises one of the following sequences:

(i) SNGQPENNY (SEQ ID ~~NOS-NOs~~: 2, 8 and 18);

(ii) SNGQPEDNY (SEQ ID NO: 13);

(iii) SNGYPEIEF (SEQ ID NO: 23);

(iv) SNGIPEWNY (SEQ ID NO: 28);

(v) SNGYAEYNY (SEQ ID NO: 33);

(vi) SNGYKEENY (SEQ ID NO: 38);

(vii) SNGVPELNV (SEQ ID NO: 43); or

(viii) SNGYQEDNY (SEQ ID NO: 48).

53. An antibody molecule according to claim 42, wherein the LAG-3 antigen-antigen- binding site comprises the amino acid sequence set forth in SEQ ID NO: 2, 8, 13, 18, 23, 28, 33, 38, 43, or 48 in the CD loop of the CH3 domain.

~~6. An antibody molecule according to claim 4, wherein the LAG-3 antigen binding site comprises the amino acid sequence set forth in SEQ ID NO: 2, 28, or 38 in the CD loop of the CH3 domain.~~

~~7. An antibody molecule according to claim 4, wherein the LAG-3 antigen binding site comprises the amino acid sequence set forth in SEQ ID NO: 2 in the CD loop of the CH3 domain.~~

~~8. An antibody molecule according to any one of claims 4 to 7, wherein the amino acid sequence set forth in SEQ ID NO: 2, 8, 13, 18, 23, 28, 33, 38, 43, or 48 is located at residues 43 to 78 of the CH3 domain of the antibody molecule, wherein the residues are numbered according to the IMGT numbering scheme.~~

~~9. An antibody molecule according to any one of claims 1 to 8, wherein the antibody molecule is an immunoglobulin G molecule.~~

104. An antibody molecule according to claim 93, wherein the antibody molecule is an IgG1, IgG2, IgG3, or IgG4 molecule.

115. An antibody molecule according to claim 104, wherein the antibody molecule is an IgG1 molecule.

126. An antibody molecule according to any one of claims 1 to 115, wherein the antibody molecule comprises the CH3 domain set forth in SEQ ID NO: 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50.

~~13. An antibody molecule according to claim 12, wherein the antibody molecule comprises the CH3 domain set forth in SEQ ID NO: 5, 30, or 40.~~

~~14. An antibody molecule according to claim 13, wherein the antibody molecule comprises the CH3 domain set forth in SEQ ID NO: 5.~~

~~457.~~ An antibody molecule according to any one of claims 1 to ~~446~~, wherein the antibody molecule comprises a CH2 domain and the CH2 domain has the sequence set forth in SEQ ID NO: 53 or SEQ ID NO: 54.

~~468.~~ An antibody molecule according to any one of claims 1 to ~~457~~, wherein the antibody molecule comprises the sequence set forth in SEQ ID NO: 6, 7, 11, 12, 16, 17, 21, 22, 26, 27, 31, 32, 36, 37, 41, 42, 46, 47, 51, or 52.

~~17. An antibody molecule according to claim 16, wherein the antibody molecule comprises the sequence set forth in SEQ ID NO: 6, 7, 31, 32, 41, or 42.~~

~~18. An antibody molecule according to claim 17, wherein the antibody molecule comprises the sequence set forth in SEQ ID NO: 6 or 7.~~

~~499.~~ An antibody molecule according to any one of claims 1 to ~~488~~, comprising the ~~complementarity-determining regions (CDRs)~~ set forth in SEQ ID NOs 86 to 91.

~~10. An antibody molecule according to any one of claims 1 to 9, comprising the CDRs set forth in SEQ ID NOs: 136 to 141.~~

~~2011.~~ An antibody molecule according to claim ~~499 or 10~~, wherein the antibody molecule comprises the VH ~~domain~~ and/or ~~the~~ VL domains set forth in SEQ ID ~~Nos~~NOs: 92 and 93.

~~2412.~~ An antibody molecule according to any one of claims ~~49-9~~ to ~~2011~~, wherein the antibody molecule comprises the heavy chain sequence set forth in any one of SEQ ID NOs: 94 to 113.

~~22. An antibody molecule according to claim 21, wherein the antibody molecule comprises the heavy chain sequence set forth in SEQ ID NO: 94, 95, 104, 105, 108, or 109.~~

~~23. An antibody molecule according to claim 22, wherein the antibody molecule comprises the heavy chain sequence set forth in SEQ ID NO: 94 or 95.~~

~~2413.~~ An antibody molecule according to any one of claims ~~49-9~~ to ~~2312~~, wherein the antibody molecule comprises the light chain sequence set forth in SEQ ID NO: 116.

14. An antibody molecule which binds to programmed death-ligand 1 (PD-L1) and lymphocyte-activation gene 3 (LAG-3), wherein the antibody molecule comprises the light chain sequence set forth in SEQ ID NO: 116, and the heavy chain sequence set forth in SEQ ID NO: 94.

15. An antibody molecule according to any one of claims 6 to 14, wherein the CH3 domain of the antibody molecule further comprises a lysine residue (K) at the immediate C-terminus of the sequence shown in SEQ ID NO: 5, 10, 15, 20, 25, 30, 35, 40, 45, or 50.

16. An antibody molecule according to claim 15, wherein the antibody molecule comprises the CH3 domain set forth in SEQ ID NO: 135.

17. An antibody molecule which binds to programmed death-ligand 1 (PD-L1) and lymphocyte-activation gene 3 (LAG-3), wherein the antibody molecule comprises the light chain sequence set forth in SEQ ID NO: 116, and the heavy chain sequence set forth in SEQ ID NO: 94, and wherein the CH3 domain sequence in the heavy chain has the sequence set forth in SEQ ID NO: 135.

~~25. An antibody molecule according to any one of claims 1 to 24, wherein the antibody is capable of simultaneously binding to PD-L1 and LAG-3.~~

~~26. An antibody molecule according to claim 25, wherein the PD-L1 and LAG-3 are present on two different cells.~~

2718. An antibody molecule according to any one of claims 1 to 2617, wherein the antibody molecule is conjugated to an immune system modulator, cytotoxic molecule, radioisotope, or detectable label.

2819. An antibody molecule according to claim 2718, wherein the immune system modulator or cytotoxic molecule is a cytokine.

2920. A nucleic acid encoding an antibody molecule according to any one of claims 1 to 2819.

3021. A vector comprising the nucleic acid of claim 2920.

~~3422~~. A recombinant host cell comprising the nucleic acid of claim ~~2920~~, or the vector of claim ~~3021~~.

~~3223~~. A method of producing an antibody molecule according to any one of claims 1 to ~~2819~~, comprising culturing the recombinant host cell of claim ~~3422~~ under conditions for production of the antibody molecule.

~~3324~~. The method of claim ~~3223~~, further comprising isolating and/or purifying the antibody molecule.

~~3425~~. A pharmaceutical composition comprising an antibody molecule according to any one of claims 1 to ~~2819~~ and a pharmaceutically acceptable excipient.

~~3526~~. Use of An an antibody molecule according to any one of claims 1 to ~~2819~~, ~~for use in a method of treating in the manufacture of a medicament for the treatment of~~ cancer in a patient.

~~36~~. ~~A method of treating cancer in a patient, wherein the method comprises administering to the patient a therapeutically effective amount of an antibody molecule according to any one of claims 1 to 28.~~

~~3727~~. Use of An an antibody molecule ~~for use~~ according to claim ~~35~~, ~~or a method according to claim 3626~~, wherein the cancer is selected from the group consisting of: Hodgkin's lymphoma, non-Hodgkin's lymphoma, ovarian cancer, prostate cancer, colorectal cancer, fibrosarcoma, renal cell carcinoma, melanoma, pancreatic cancer, breast cancer, glioblastoma multiforme, lung cancer, head and neck cancer, stomach cancer, bladder cancer, cervical cancer, uterine cancer, vulvar cancer, testicular cancer, penile cancer, leukemia, multiple myeloma, squamous cell cancer, ~~testicular cancer~~, esophageal cancer, Kaposi's sarcoma, and central nervous system (CNS) lymphoma, hepatocellular carcinoma, Merkel cell carcinoma, nasopharyngeal cancer, and mesothelioma.

~~3828~~. Use of An an antibody molecule ~~for use, or a method~~, according to ~~any one of claims 35 to 3726 or 27~~, wherein the ~~method treatment~~ further comprises administering an anti-tumour vaccine to the patient.

3929. Use of a An antibody molecule ~~for use, or a method,~~ according to ~~any one of~~ claims ~~35 to 37~~ 26 or 27, wherein the ~~method~~ treatment further comprises administering a chemotherapeutic agent to the patient.