

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-binding site for PD-L1; and
 - (ii) a LAG-3 antigen-binding site located in a CH3 domain of the antibody molecule, wherein the LAG-3 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 the AB loop of the CH3 domain and the amino acid sequence PYDRWVWPDE is located in the EF loop of the CH3 domain.
2. An antibody molecule according to claim 1, wherein the LAG-3 antigen-binding site further comprises one of the following sequences:
 - (i) SNGQPENNY (SEQ ID 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).
3. An antibody molecule according to claim 2, wherein the LAG-3 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.
4. An antibody molecule according to claim 3, wherein the antibody molecule is an IgG1, IgG2, IgG3, or IgG4 molecule.
5. An antibody molecule according to claim 4, wherein the antibody molecule is an IgG1 molecule.
6. An antibody molecule according to any one of claims 1 to 5, 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.

7. An antibody molecule according to any one of claims 1 to 6, 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.
8. An antibody molecule according to any one of claims 1 to 7, 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.
9. An antibody molecule according to any one of claims 1 to 8, comprising the 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.
11. An antibody molecule according to claim 9 or 10, wherein the antibody molecule comprises the VH domain and/or the VL domain set forth in SEQ ID NOs: 92 and 93.
12. An antibody molecule according to any one of claims 9 to 11, wherein the antibody molecule comprises the heavy chain sequence set forth in any one of SEQ ID NOs: 94 to 113.
13. An antibody molecule according to any one of claims 9 to 12, 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.
18. An antibody molecule according to any one of claims 1 to 17, wherein the antibody molecule is conjugated to an immune system modulator, cytotoxic molecule, radioisotope, or detectable label.
19. An antibody molecule according to claim 18, wherein the immune system modulator or cytotoxic molecule is a cytokine.
20. A nucleic acid encoding an antibody molecule according to any one of claims 1 to 19.
21. A vector comprising the nucleic acid of claim 20.
22. A recombinant host cell comprising the nucleic acid of claim 20, or the vector of claim 21.
23. A method of producing an antibody molecule according to any one of claims 1 to 19, comprising culturing the recombinant host cell of claim 22 under conditions for production of the antibody molecule.
24. The method of claim 23, further comprising isolating and/or purifying the antibody molecule.
25. A pharmaceutical composition comprising an antibody molecule according to any one of claims 1 to 19 and a pharmaceutically acceptable excipient.
26. Use of an antibody molecule according to any one of claims 1 to 19 in the manufacture of a medicament for the treatment of cancer in a patient.
27. Use of an antibody molecule according to claim 26, 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, esophageal cancer, Kaposi's sarcoma, and central nervous system (CNS) lymphoma, hepatocellular carcinoma, Merkel cell carcinoma, nasopharyngeal cancer, and mesothelioma.

28. Use of an antibody molecule according to claim 26 or 27, wherein the treatment further comprises administering an anti-tumour vaccine to the patient.

29. Use of an antibody molecule according to claim 26 or 27, wherein the treatment further comprises administering a chemotherapeutic agent to the patient.