

Claims

1. A bispecific antibody or antigen binding-fragment thereof, comprising a first targeting moiety which specifically binds to PD-1 and a second targeting moiety which specifically binds to LAG-3,

wherein the first targeting moiety comprises a first VHH domain and the second targeting moiety comprises a second VHH domain;

the first VHH domain comprises H-CDR1, H-CDR2 and H-CDR3; wherein the H-CDR3 comprises a sequence as depicted in SEQ ID NO:1, and conservative modifications thereof; the H-CDR2 comprises a sequence as depicted in SEQ ID NO: 2, and conservative modifications thereof; the H-CDR1 comprises a sequence as depicted in SEQ ID NO:3, and conservative modifications thereof;

the second VHH domain comprises H-CDR1, H-CDR2, H-CDR3; wherein the H-CDR3 comprises a sequence as depicted in SEQ ID NO: 4, and conservative modifications thereof; the H-CDR2 comprises a sequence as depicted in SEQ ID NO: 5, and conservative modifications thereof; the H-CDR1 comprises a sequence as depicted in SEQ ID NO: 6, and conservative modifications thereof.

2. The antibody or antigen binding-fragment thereof of claim 1, wherein the first VHH domain comprises a sequence that is at least 70%, 80%, 85%, 90%, 95% or 99% homologous to SEQ ID NO: 7.

3. The antibody or antigen binding-fragment thereof of claim 1 or 2, wherein the second VHH domain comprises a sequence that is at least 70%, 80%, 85%, 90%, 95% or 99% homologous to SEQ ID NO: 8.

4. The antibody or antigen binding-fragment thereof of any one of claims 1-3, wherein the first VHH domain comprises a sequence of SEQ ID NO: 7, and the second VHH domain comprises a sequence of SEQ ID NO: 8.

5. The antibody or antigen binding-fragment thereof of claim 4, wherein the first VHH domain and the second VHH domain are linked by a peptide sequence.

6. The antibody or antigen binding fragment thereof of claim 5, wherein the peptide

sequence comprises

(a) an IgG Fc fragment comprising hinge region, CH2 and CH3, and/or

(b) a linker.

7. The antibody or antigen binding fragment thereof of claim 6, wherein the linker comprises a sequence of SEQ ID NO: 9.

8. The antibody or antigen binding fragment thereof of any one of claims 1-7, comprising a sequence of SEQ ID NO: 10.

9. The antibody or antigen binding fragment thereof of any one of claims 1-8, wherein the antibody or the antigen binding-fragment

a) binds to human PD-1 with a K_D of $2.92E-09$ or less; and

b) binds to human LAG-3 with a K_D of $3.01E-10$ or less.

10. The antibody or antigen binding fragment thereof of any one of claims 1-9, wherein the antibody is a humanized antibody.

11. A nucleic acid molecule encoding the antibody or antigen binding fragment thereof of any one of claims 1-10.

12. A cloning or expression vector comprising the nucleic acid molecule of claim 11.

13. A host cell comprising one or more cloning or expression vectors of claim 12.

14. A process for production of the antibody or antigen binding fragment thereof of any one of claims 1-9, comprising culturing the host cell of claim 13 and isolating the antibody.

15. A pharmaceutical composition comprising the antibody or antigen binding fragment thereof of any one of claims 1-10, and one or more of a pharmaceutically acceptable excipient, a diluent and a carrier.

16. An immunoconjugate comprising the antibody or antigen binding fragment thereof of any one of claims 1-10, linked to a therapeutic agent.

17. A pharmaceutical composition comprising the immunoconjugate of claim 16 and

one or more of a pharmaceutically acceptable excipient, a diluent and a carrier.

18. Use of the antibody or antigen binding fragment thereof of any one of claims 1-10 in the manufacture of a medicament for modulating an immune response in a subject.

19. Use of the antibody or antigen binding fragment thereof of any one of claims 1-10 in the manufacture of a medicament for the treatment or prophylaxis of an immune disorder or cancer.

20. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-10 in the manufacture of a method of inhibiting growth of tumor cells in a subject.

21. The use of claim 20, wherein the tumor cells are of a cancer selected from a group consisting of melanoma, renal cancer, prostate cancer, breast cancer, colon cancer, lung cancer, bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, and rectal cancer.