

Claims

1. A single domain antibody (sdAb) which specifically binds to Leukocyte immunoglobulin-like receptor subfamily B member 2 (LILRB2), wherein said sdAb comprises three CDRs, wherein CDR1
5 comprises an amino acid sequence of SEQ ID NO:1, CDR2 comprises an amino acid sequence of SEQ ID NO:2, and CDR3 comprises an amino acid sequence of SEQ ID NO:3.
2. The sdAb of claim 1, wherein the sdAb specifically binds to human LILRB2.
3. The sdAb of claim 1, wherein said sdAb does not bind Leukocyte immunoglobulin-like receptor subfamily B member 1 (LILRB1).
- 10 4. The sdAb of claim 3, wherein the LILRB1 is human LILRB1.
5. The sdAb of any of claims 1 to 4, which comprises or consists of an amino acid sequence of SEQ ID No: 34 or a sequence having at least 80% sequence identity thereto.
6. The sdAb of any of claims 1 to 5, which comprises or consists of an amino acid sequence of SEQ ID No: 34 or a sequence having at least 90%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or more amino-
15 acid sequence identity thereto.
7. The sdAb of any of claims 1 to 6, which comprises or consists of the amino acid sequence of SEQ ID No: 34.
8. The sdAb of any of claims 1 to 7, wherein said sdAb inhibits the interaction between LILRB2 and human leukocyte antigen-G (HLA-G).
- 20 9. The sdAb of any of claims 1 to 8, wherein said sdAb inhibits the interaction between LILRB2 and Angiopoietin Like 2 (ANGPTL2).
10. The sdAb of any of claims 1 to 9, wherein the sdAb is conjugated to at least one molecule.
11. The sdAb of any of claims 1 to 9, wherein the sdAb is conjugated to a stabilizing group.
12. The sdAb of claim 11, wherein the stabilizing group is a Fc or an IgG.
- 25 13. An isolated nucleic acid comprising a nucleic acid sequence encoding a sdAb as defined in any one of claims 1 to 12.
14. The isolated nucleic acid of claim 13, wherein the nucleic acid comprises the sequence of SEQ ID: 45.
15. A vector comprising the isolated nucleic acid of claim 13 or 14.
- 30 16. A chimeric antigen receptor (CAR) comprising the sdAb according to any one of claims 1-12.
17. A cell comprising the isolated nucleic acid of claim 13-14, or the vector of claim 15, or expressing the CAR of claim 16.

18. The cell expressing a CAR according to claim 17, wherein the cell is selected from a group consisting of a T cell, CD4⁺ T cell, CD8⁺ T cell, B cell, NK cell, NKT cell, monocyte and dendritic cell.
19. The cell according to claim 18, wherein the cell is selected from a T cell, a B cell or a NK cell.
- 5 20. A pharmaceutical composition comprising a sdAb as defined in any one of claims 1 to 12, the isolated nucleic acid of any one of claims 13 to 14, the vector of claim 15, the CAR of claim 16 or the cell expressing a CAR according to any one of claims 17 to 19, and optionally a pharmaceutically acceptable carrier.
- 10 21. The sdAb of any one of claims claim 1-12, the isolated nucleic acid of any one of claims 13-14, the vector of claim 15, the CAR of claim 16, the cell of any one of claims 17-19 or the pharmaceutical composition of claim 20, for use in the treatment of cancer, wherein the cancer overexpresses LILBR2.
- 15 22. Use of the sdAb of any one of claims 1-12, the isolated nucleic acid of any one of claims 13-14, the vector of claim 15, the CAR of claim 16, the cell of any one of claims 17-19 or the pharmaceutical composition of claim 20, in the preparation of a medicament for treating cancer, wherein the cancer overexpresses LILBR2.
- 20 23. The sdAb, the isolated nucleic acid, the vector, the CAR, the cell, or the pharmaceutical composition, according to claim 21, or the use according to claim 22, wherein the cancer is selected from the group consisting of lung cancer, non-small cell lung cancer (NSCLC), pancreatic cancer, pancreatic ductal carcinoma, Chronic Lymphocytic Leukemia (CLL), Acute Myeloid Leukemia (AML), endometrial cancer, hepatocellular carcinoma, melanoma, ovarian cancer, breast cancer, colorectal cancer, glioma, stomach cancer, renal cancer, testis cancer, Esophageal cancer, Cervical cancer, Lewis Lung cancer of mice, Leukemia, Thyroid cancer, Liver cancer, Urothelial cancer and Head and neck cancer.
- 25 24. Use of the sdAb of any one of claims 1-12, for detecting LILRB2 on tumoral cells or tissues *in vitro* or *ex vivo*.