

Claims

1. A single domain antibody (sdAb) which specifically binds to Leukocyte immunoglobulin-like receptor subfamily B member 2 (LILRB2), preferably human LILRB2.
- 5 2. The sdAb according to claim 1, wherein said sdAb does not bind Leukocyte immunoglobulin-like receptor subfamily B member 1 (LILRB1), preferably human LILRB1.
3. The sdAb according to claim 1 or 2, wherein said sdAb comprises at least one complementarity determining regions (CDR) which comprises or consists in the sequence set forth in SEQ ID NO: 3, 6, 9, 12, 15, 18, 21, 24, 27, 30 or 33 or comprises, or consists in an amino acid sequence which
10 differs from SEQ ID NO: 3, 6, 9, 12, 15, 18, 21, 24, 27, 30 or 33 in virtue of one, two, or three amino acid modifications.
4. The sdAb according to any of claims 1 to 3, wherein said sdAb comprises three CDRs, wherein:
 - (a) CDR1 comprises, or is of, SEQ ID NO:1 or has an amino acid sequence which differs from SEQ ID NO:1 in virtue of one, two, or three amino acid modifications, and
15 CDR2 comprises, or is of, SEQ ID NO:2 or has an amino acid sequence which differs from SEQ ID NO:2 in virtue of one, two, or three amino acid modifications, and
CDR3 comprises, or is of, SEQ ID NO:3 or has an amino acid sequence which differs from SEQ ID NO:3 in virtue of one, two, three or four amino acid modifications; or
 - (b) CDR1 comprises, or is of, SEQ ID NO:4 or has an amino acid sequence which differs from SEQ ID
20 NO:4 in virtue of one, two, or three amino acid modifications, and
CDR2 comprises, or is of, SEQ ID NO:5 or has an amino acid sequence which differs from SEQ ID NO:5 in virtue of one, two, or three amino acid modifications, and
CDR3 comprises, or is of, SEQ ID NO:6 or has an amino acid sequence which differs from SEQ ID NO:6 in virtue of one, two, three or four amino acid modifications; or
 - (c) CDR1 comprises, or is of, SEQ ID NO:7 or has an amino acid sequence which differs from SEQ ID
25 NO:7 in virtue of one, two, or three amino acid modifications, and
CDR2 comprises, or is of, SEQ ID NO:8 or has an amino acid sequence which differs from SEQ ID NO:8 in virtue of one, two, or three amino acid modifications, and
CDR3 comprises, or is of, SEQ ID NO:9 or has an amino acid sequence which differs from SEQ ID
30 NO:9 in virtue of one, two, three or four amino acid modifications; or
 - (d) CDR1 comprises, or is of, SEQ ID NO:10 or has an amino acid sequence which differs from SEQ ID NO:10 in virtue of one, two, or three amino acid modifications, and
CDR2 comprises, or is of, SEQ ID NO:11 or has an amino acid sequence which differs from SEQ ID NO:11 in virtue of one, two, or three amino acid modifications, and

- CDR3 comprises, or is of, SEQ ID NO:12 or has an amino acid sequence which differs from SEQ ID NO:12 in virtue of one, two, three or four amino acid modifications; or
- (e) CDR1 comprises, or is of, SEQ ID NO:13 or has an amino acid sequence which differs from SEQ ID NO:13 in virtue of one, two, or three amino acid modifications, and
- 5 CDR2 comprises, or is of, SEQ ID NO:14 or has an amino acid sequence which differs from SEQ ID NO:14 in virtue of one, two, or three amino acid modifications, and
- CDR3 comprises, or is of, SEQ ID NO:15 or has an amino acid sequence which differs from SEQ ID NO:15 in virtue of one, two, three or four amino acid modifications; or
- (f) CDR1 comprises, or is of, SEQ ID NO:16 or has an amino acid sequence which differs from SEQ ID
- 10 NO:16 in virtue of one, two, or three amino acid modifications, and
- CDR2 comprises, or is of, SEQ ID NO:17 or has an amino acid sequence which differs from SEQ ID NO:17 in virtue of one, two, or three amino acid modifications, and
- CDR3 comprises, or is of, SEQ ID NO:18 or has an amino acid sequence which differs from SEQ ID NO:18 in virtue of one, two, three or four amino acid modifications; or
- 15 (g) CDR1 comprises, or is of, SEQ ID NO:19 or has an amino acid sequence which differs from SEQ ID NO:19 in virtue of one, two, or three amino acid modifications, and
- CDR2 comprises, or is of, SEQ ID NO:20 or has an amino acid sequence which differs from SEQ ID NO:20 in virtue of one, two, or three amino acid modifications, and
- CDR3 comprises, or is of, SEQ ID NO:21 or has an amino acid sequence which differs from SEQ ID
- 20 NO:21 in virtue of one, two, three or four amino acid modifications; or
- (h) CDR1 comprises, or is of, SEQ ID NO:22 or has an amino acid sequence which differs from SEQ ID NO:22 in virtue of one, two, or three amino acid modifications, and
- CDR2 comprises, or is of, SEQ ID NO:23 or has an amino acid sequence which differs from SEQ ID NO:23 in virtue of one, two, or three amino acid modifications, and
- 25 CDR3 comprises, or is of, SEQ ID NO:24 or has an amino acid sequence which differs from SEQ ID NO:24 in virtue of one, two, three or four amino acid modifications; or
- (i) CDR1 comprises, or is of, SEQ ID NO:25 or has an amino acid sequence which differs from SEQ ID NO:25 in virtue of one, two, or three amino acid modifications, and
- CDR2 comprises, or is of, SEQ ID NO:26 or has an amino acid sequence which differs from SEQ ID
- 30 NO:26 in virtue of one, two, or three amino acid modifications, and
- CDR3 comprises, or is of, SEQ ID NO:27 or has an amino acid sequence which differs from SEQ ID NO:27 in virtue of one, two, three or four amino acid modifications; or
- (j) CDR1 comprises, or is of, SEQ ID NO:28 or has an amino acid sequence which differs from SEQ ID NO:28 in virtue of one, two, or three amino acid modifications, and
- 35 CDR2 comprises, or is of, SEQ ID NO:29 or has an amino acid sequence which differs from SEQ ID NO:29 in virtue of one, two, or three amino acid modifications, and

- CDR3 comprises, or is of, SEQ ID NO:30 or has an amino acid sequence which differs from SEQ ID NO:30 in virtue of one, two, three or four amino acid modifications; or
- (k) CDR1 comprises, or is of, SEQ ID NO:31 or has an amino acid sequence which differs from SEQ ID NO:31 in virtue of one, two, or three amino acid modifications, and
- 5 CDR2 comprises, or is of, SEQ ID NO:32 or has an amino acid sequence which differs from SEQ ID NO: 32 in virtue of one, two, or three amino acid modifications, and
- CDR3 comprises, or is of, SEQ ID NO:33 or has an amino acid sequence which differs from SEQ ID NO:33 in virtue of one, two, three or four amino acid modifications.
5. The sdAb according to any of claims 1 to 3, wherein said sdAb comprises three CDRs, wherein
- 10 CDR1 comprises or consists of SEQ ID NO:1, and CDR2 comprises or consists of SEQ ID NO:2, and CDR3 comprises or consists of SEQ ID NO:3.
6. The sdAb according to any of claims 1 to 5, which comprises or consists in a sequence defined in any of the sequence SEQ ID No: 34 to SEQ ID No: 44 or a sequence having at least 80% sequence identity thereto, preferably at least 90%, 92%, 94%, 95%, 96%, 97%, 98%, 99% or more amino-
- 15 acid sequence identity thereto.
7. The sdAb according to any of claims 1 to 5, which comprises or consists in a sequence defined in SEQ ID No: 34.
8. The sdAb according to 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 according to any of claims 1 to 8, wherein said sdAb inhibits the interaction between LILRB2 and Angiopoietin Like 2 (ANGPTL2).
10. An isolated nucleic acid comprising a sequence encoding a sdAb as defined in any one of claims 1 to 9, preferably defined by a sequence selected in the group consisting of SEQ ID: 45-55.
11. A vector comprising the isolated nucleic acid of claim 10.
- 25 12. A chimeric antigen receptor (CAR) comprising the sdAb according to any one of claims 1-9 or the isolated nucleic acid of claim 8.
13. A cell comprising the isolated nucleic acid of claim 10, or the vector of claim 11, or expressing the CAR of claim 12.
- 30 14. The cell expressing a CAR according to claim 13, 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, preferably the cell being a T cell, a B cell or a NK cell.

15. A pharmaceutical composition comprising a sdAb as defined in any one of claims 1-7, the isolated nucleic acid of claim 10, the vector of claim 11, the CAR or claim 12 or the cell expressing a CAR according to claim 13 or 14, and optionally a pharmaceutically acceptable carrier.
- 5 16. The sdAb of any one of claims claim 1-9, the isolated nucleic acid of claim 10, the vector of claim 11, the CAR of claim 12, the cell of any one of claims 13-14 or the pharmaceutical composition of claim 15, for use in the treatment of cancer, preferably wherein the cancer overexpresses LILRB2 more preferably a cancer 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, 10 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.
17. Use of the sdAb of any one of claims claim 1-9, for detecting LILRB2 on tumoral cells or tissues *in vitro* or *ex vivo*.