

CLAIMS

1. ~~An antibody that binds to CD112R, or an antibody fragment thereof, comprising at least the antigen binding portion, wherein the antibody or antibody fragment comprises:~~

5 (i) ~~three complementarity determining regions (CDRs) of a heavy chain (HC) variable region comprising SEQ ID NO: 17 and three CDRs of a light chain (LC) variable comprising SEQ ID NO: 19, or an analog or derivative thereof having at least 90% sequence identity with said antibody or fragment sequence;~~
or

10 (ii) ~~three CDRs of a heavy chain variable region comprising SEQ ID NO: 21 and three CDRs of a light chain variable region comprising SEQ ID NO: 23, or an analog or derivative thereof having at least 90% sequence identity with said antibody or fragment sequence.~~

2.1. ~~The antibody or the antibody fragment according to claim 1, comprising~~An antibody that binds to CD112R, or an antibody fragment thereof, comprising at least the antigen binding portion, wherein the antibody or antibody fragment comprises
15 a set of six CDRs

wherein: heavy chain CDR1 sequence comprising the sequence GYX₁FX₂SY (SEQ ID NO: 1), wherein X₁ denotes N, D, A, Q, S, or T, and X₂ is T or A, or the sequence SYWIN (SEQ ID NO: 7), heavy chain CDR2 comprising the sequence YPGSYIP (SEQ ID NO: 2) or FPGSYS (SEQ ID NO: 10), heavy chain CDR3 comprising the sequence GYFDV (SEQ ID NO: 3), light chain CDR1 comprising the sequence KSSQSLXSGNQKNYLA (SEQ ID NO: 4), wherein X denotes N or S, light chain CDR2 comprising the sequence GASTRES (SEQ ID NO: 5), and light chain CDR3 comprising the sequence QNDHSYPYT (SEQ ID NO: 6).

25 3. ~~The antibody or the antibody fragment according to any one of claims 1 or 2, comprising a heavy chain variable region selected from SEQ ID NO: 28 and SEQ ID NO: 21, or an analog having at least 95% sequence similarity with said heavy chain variable region sequence.~~

30 4. ~~The antibody or the antibody fragment according to any one of claims 1 to 3, comprising a light chain variable sequence selected from SEQ ID NO: 26 and SEQ ID NO: 23, or an analog having at least 95% sequence similarity with said slight chain variable region sequence.~~

5. ~~The antibody or the antibody fragment according to any one of claims 1 to 4, comprising a heavy chain and a light chain, wherein the heavy chain comprises SEQ ID NO: 28 and the light chain comprises SEQ ID NO: 26.~~

6. ~~The antibody or the antibody fragment according to any one of claims 1 to 4 comprising a heavy chain and a light chain, wherein the heavy chain comprises SEQ ID NO: 21 and the light chain comprises SEQ ID NO: 23.~~

7. ~~A variant of an antibody or antibody fragment according to any one of claims 5 or 6, having at least 95%) identity with said antibody light chain or heavy chain.~~

2. The antibody or antibody fragment according to claim 1, wherein the antibody is a humanized antibody.

3. The humanized antibody or the antibody fragment according to claim 2, comprising a set of six CDRs according to Kabat, wherein: heavy chain CDR1 sequence comprising the sequence SYWIN (SEQ ID NO: 7), heavy chain CDR2 comprising the sequence DIYPGSYIPNYNEKFKN (SEQ ID NO: 8), heavy chain CDR3 comprising the sequence GYFDV (SEQ ID NO: 3), light chain CDR1 comprising the sequence KSSQSLSSGNQKNYLA (SEQ ID NO: 15), light chain CDR2 comprising the sequence GASTRES (SEQ ID NO: 5), and light chain CDR3 comprising the sequence QNDHSYPYT (SEQ ID NO: 6).

4. The humanized antibody or the antibody fragment according to claim 2, comprising a set of six CDRs according to Chothia, wherein: (i) heavy chain CDR1 sequence comprising the sequence GYTFTSY (SEQ ID NO: 13), heavy chain CDR2 comprising the sequence YPGSYIP (SEQ ID NO: 2), heavy chain CDR3 comprising the sequence GYFDV (SEQ ID NO: 3), light chain CDR1 comprising the sequence KSSQSLSSGNQKNYLA (SEQ ID NO: 15), light chain CDR2 comprising the sequence GASTRES (SEQ ID NO: 5), and light chain CDR3 comprising the sequence QNDHSYPYT (SEQ ID NO: 6).

5. The humanized antibody or antibody fragment according to any one of claims 2 to 4, wherein the humanized antibody or antibody fragment comprises a heavy chain comprising a variable region sequence selected from the group consisting of SEQ ID NOs: 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, and 39; or an analog having at least 95% sequence similarity with said heavy chain variable region sequence; and a light chain comprising a variable region sequence selected from the group consisting of SEQ ID NOs: 40, 41, and 42; or an analog having at least 95% sequence similarity with said heavy chain variable region sequence.

6. The humanized antibody according to any one of claims 2 to 5, comprising a combination of heavy and light chains selected from the group consisting of:

(i) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 40;

(ii) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 41; and

(iii) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 42.

8.7. An antibody fragment according to ~~any one of claims 1 to 7~~, wherein the antibody fragment is a single chain Fv (scFv).

9.8. A polypeptide comprising ~~at the~~ scFv according to claim ~~7~~8 and a human IgG1 Fc region sequence, wherein the polypeptide ~~sequence~~ comprises a sequence set forth in any one selected from the group consisting of SEQ ID NOs: 43 to 54, or an analog or derivative thereof having at least 90% sequence identity ~~to with~~ said polypeptide antibody.

10.9. An ~~The~~ antibody or antibody fragment according to ~~any one of claims 1 to 9~~, wherein the antibody binds to human CD112R with an affinity of at least 1×10^{-9} M ~~0.5×10^{-9} M to 10^{-11} M~~.

~~11. The antibody or antibody fragment according to any one of claims 1 to 10, wherein the antibody comprises an Fc of hIgG1.~~

~~12. The antibody or antibody fragment according to any one of claims 1 to 11, wherein the antibody is a humanized antibody.~~

~~13. The antibody or antibody fragment according to claim 12, wherein heavy chain CDR1 is GYTFTSY (SEQ ID NO: 13); or SYWIN (SEQ ID NO: 7).~~

~~14. The antibody or antibody fragment according to any one of claims 12 or 13, wherein light chain CDR1 is KSSQSLSSGNQKNYLA (SEQ ID NO: 15).~~

~~15. The antibody or the antibody fragment according to any one of the preceding claims, comprising a set of six CDRs wherein: heavy chain CDR1 sequence comprising the sequence GYTFTSY (SEQ ID NO: 13), heavy chain CDR2 comprising the sequence YPGSYIP (SEQ ID NO: 2), heavy chain CDR3 comprising the sequence GYFDV (SEQ ID NO: 3), light chain CDR1 comprising the sequence KSSQSLSSGNQKNYLA (SEQ ID NO: 15), light chain CDR2 comprising the sequence GASTRES (SEQ ID NO: 5), and light chain CDR3 comprising the sequence QNDHSYPYT (SEQ ID NO: 6).~~

~~16. The antibody or antibody fragment according to any one of claims 12 to 15, wherein the humanized antibody comprises a heavy chain comprising a sequence selected from the~~

~~group consisting of SEQ ID NOs: 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, and 39; or an analog having at least 95% sequence similarity with said heavy chain variable region sequence.~~

5 ~~17. The antibody or antibody fragment according to any one of claims 12 to 16, wherein the humanized antibody comprises a light chain comprising a sequence selected from the group consisting of SEQ ID NOs: 40, 41, and 42; or an analog having at least 95% sequence similarity with said heavy chain variable region sequence.~~

10 ~~18. The antibody or antibody fragment according to any one of claims 12 to 17, wherein the humanized antibody comprises heavy and light chains selected from the group consisting of:~~

~~(i) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 40;~~

~~(ii) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 41; and~~

15 ~~(iii) heavy chain comprising SEQ ID NO: 39 and light chain comprising SEQ ID NO: 42.~~

~~19.10.~~ A polynucleotide sequence encoding at least one sequence of a heavy chain or a light chain region of an antibody or antibody fragment according to any one of claims 1 to ~~9~~18.

20 ~~20.11.~~ The polynucleotide sequence of claim ~~10~~18, encoding an antibody heavy chain variable region, wherein the polynucleotide sequence comprises a sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 20, and SEQ ID NO: 24 or a variant thereof having at least 85% identity to said sequences.

25 ~~21.12.~~ The polynucleotide sequence of claim ~~10~~19, encoding an antibody light chain variable region, wherein the polynucleotide sequence is selected from the group consisting of: SEQ ID NO: 18, SEQ ID NO: 22 and SEQ ID NO: 25, or a variant thereof having at least 85% identity to said sequences.

~~22. A plasmid comprising at least one polynucleotide sequence according to any one of claims 19 to 21.~~

30 ~~23. A cell comprising a polynucleotide sequence according to any one of claims 19 to 21.~~

~~24. A cell capable of producing an antibody according to any one of claims 1 to 18.~~

~~25.13.~~ A pharmaceutical composition comprising as an active ingredient, at least one antibody or fragment thereof, according to any one of claims 1 to ~~9~~18, and a pharmaceutical acceptable excipient, diluent, salt or carrier.

~~26.14.~~ Use of the The pharmaceutical composition of claim ~~1325 for use in~~ the manufacture of a medicament for modulating the immune system, wherein the medicament by inhibiting the binding of CD112R to Nectin-2.

~~27.15.~~ Use of the The pharmaceutical composition of claim ~~1325 for use in~~ the manufacture of a medicament for treating cancer in a subject.

~~28.16.~~ Use of the The pharmaceutical composition of claim ~~1325 for use in~~ the manufacture of a medicament for preventing or treating a viral infection in a subject.

~~29. A method of treating cancer comprising administering to a subject in need thereof, a therapeutically effective amount of the pharmaceutical composition according to claim 25.~~

~~30.17.~~ The ~~use~~method of claim ~~1529~~, further comprising an additional anti-cancer therapy selected from surgery, chemotherapy, radiotherapy, and immunotherapy.

~~31.18.~~ The ~~use~~method of claim ~~1529~~, ~~further comprising administering to said subject wherein~~ an additional immuno-modulator, activated lymphocyte cell, kinase inhibitor, chemotherapeutic agent, or any other anti-cancer agent is to be administered to the said subject.

~~32.19.~~ The ~~use~~method of claim ~~1831~~, wherein the additional immune-modulator is an antibody against an immune checkpoint molecule.

~~33. The method of claim 32, wherein the additional immune modulator is an antibody selected from the group consisting of anti PD 1, anti TIGIT, anti PVR and any combination thereof.~~

~~34. The method of any one of claims 29 to 33, wherein the cancer is a solid cancer.~~

~~35. The method of any one of claims 29 to 33, wherein the cancer is a hematologic cancer.~~

~~36. The method of any one of claims 29 to 33, wherein the cancer is selected from the group consisting of lung adenocarcinoma, breast adenocarcinoma, and colorectal cancer.~~

~~37. The method of any one of claims 29 to 33, wherein treating results in preventing or reducing metastases formation, growth or spread in a subject.~~

~~38. A method of determining or quantifying CD112R in a sample, the method comprising contacting a biological sample with an antibody or antibody fragment, and measuring the level of complex formation, wherein the antibody or antibody fragment is according to any one of claims 1 to 18.~~

~~39.20.~~ A method of diagnosing or prognosing cancer in a subject, the method comprises determining the expression level of CD112R in a biological sample obtained from ~~of~~ said

subject using at least one antibody or antibody fragment is according to any one of claims 1 to ~~9~~18.

~~40. A kit for measuring the expression or presence of CD112R in biological sample is also provided comprising at least one antibody or antibody fragment according to any one of claims 1 to 18.~~

21. A pharmaceutical composition of claim 13 for use in therapy.