

CLAIMS

1. — Use of an LRP10 inhibitor or competitor for the manufacture of a medicament for cancer immunotherapy.
2. — The use of claim 1, wherein said LRP10 inhibitor or competitor enhances tumor
5 infiltration of lymphocytes, preferably CD8⁺ T cells and cytotoxic T lymphocytes, thereby providing cancer immunotherapy.
3. — Use of an LRP10 inhibitor or competitor for the manufacture of a medicament for hematopoietic recovery.
4. — The use of claim 3, wherein said LRP10 inhibitor or competitor enhances recovery
10 of all hematopoietic lineages, preferably lymphoid lineages, in a patient who has received chemotherapy and/or radiotherapy.
5. — The use of any one of claims 1-4, wherein said LRP10 inhibitor is anti LRP10 antibody or antigen binding fragment thereof, preferably binding to LRP10 ectodomain.
6. — The use of any one of claims 1-4, wherein said LRP10 competitor is an engineered,
15 soluble receptor for one or more LRP10 ligands, wherein said receptor competes for binding with endogenous LRP10 (e.g., an LRP10-Fc chimera).
7. — An anti LRP10 antibody, or antigen binding fragment thereof, optionally for use in cancer immunotherapy and/or hematopoietic recovery, comprising one or more of the following CDRs:
20 VL-CDR1 (SEQ ID NO: 33): RASQSISSYLN
VL-CDR2 (SEQ ID NO: 62): X1ASX2LQS (X1=N, A, R, D; X2=D, P, R, A, L, T)
VL-CDR3 (SEQ ID NO: 63): QQX3X4X5X6PX7T (X3=S, V, P, A, I, T, N; X4=S, A, T, D, K; X5=R, S, T, A, Y; X6=T, L, Y, R, G; X7=T, N, L, G)
VH-CDR1 (SEQ ID NO: 64): SX8AMS (X8=Q, Y)
25 VH-CDR2 (SEQ ID NO: 65): X9IX10X11X12GX13X14TX15YADSVKG (X9=S, Q, V; X10=P, G, S, Q, A, Y; X11=P, T, R, S; X12=G, M, T, Q, R, S; X13=P, R, N, T, Q, A; X14=N, P, S, G, A, T; X15=K, T, Y, E)
VH-CDR3 (SEQ ID NO: 66): X16X17X18X19FDY (X16=S, D, N; X17=Y, G, A, S, R, T; X18=P, K, T, R, H, A; X19=S, K, T)
30 8. — The antibody or fragment thereof of claim 7, comprising one or more of the following CDRs:
VL-CDR1 (SEQ ID NO: 33): RASQSISSYLN
VL-CDR2 (SEQ ID NO: 34): NASDLQS

~~VL CDR2 (SEQ ID NO: 35): AASPLQS~~
~~VL CDR2 (SEQ ID NO: 36): RASRLQS~~
~~VL CDR2 (SEQ ID NO: 37): AASALQS~~
~~VL CDR2 (SEQ ID NO: 38): DASLLQS~~
5 ~~VL CDR2 (SEQ ID NO: 39): AASTLQS~~
~~VL CDR3 (SEQ ID NO: 40): QQSSRTPTT~~
~~VL CDR3 (SEQ ID NO: 41): QQVARTPNT~~
~~VL CDR3 (SEQ ID NO: 42): QQPTSLPLT~~
~~VL CDR3 (SEQ ID NO: 43): QQADSYPTT~~
10 ~~VL CDR3 (SEQ ID NO: 44): QQIKTRPTT~~
~~VL CDR3 (SEQ ID NO: 45): QQTSAGPGT~~
~~VL CDR3 (SEQ ID NO: 46): QQNDYYPTT~~
~~VH CDR1 (SEQ ID NO: 47): SQAMS~~
~~VH CDR1 (SEQ ID NO: 48): SYAMS~~
15 ~~VH CDR2 (SEQ ID NO: 49): QIGTMGRPTTYADSVKG~~
~~VH CDR2 (SEQ ID NO: 50): SISTTG NSTYYADSVKG~~
~~VH CDR2 (SEQ ID NO: 51): VIQRQGTGTEYADSVKG~~
~~VH CDR2 (SEQ ID NO: 52): SPSRGQATKYADSVKG~~
~~VH CDR2 (SEQ ID NO: 53): SIATTGNTTYADSVKG~~
20 ~~VH CDR2 (SEQ ID NO: 54): SIPPGGPNTKYADSVKG~~
~~VH CDR2 (SEQ ID NO: 55): SIYTS GAATTYADSVKG~~
~~VH CDR3 (SEQ ID NO: 56): SYPSFDY~~
~~VH CDR3 (SEQ ID NO: 57): SGKKFDY~~
~~VH CDR3 (SEQ ID NO: 58): DATSFDY~~
25 ~~VH CDR3 (SEQ ID NO: 59): NSRTFDY~~
~~VH CDR3 (SEQ ID NO: 60): SRHTFDY~~
~~VH CDR3 (SEQ ID NO: 61): NTATFDY~~

9. —The antibody or fragment thereof of claim 7, comprising a VL sequence selected
30 from the group consisting of SEQ ID NOS: 1, 5, 7, 11, 15, 19, and 23 and a VH sequence
selected from the group consisting of SEQ ID NOS: 2, 8, 12, 16, 20, 24, 27, and 29.

10. —The antibody or fragment thereof of claim 7, wherein in a migration assay, a cell
(e.g., hematopoietic stem cell or T cell) contacted with the antibody or fragment thereof
migrates toward a chemotactic stimulus more rapidly than a control cell that is not

contacted with the antibody or fragment thereof, wherein preferably the chemotactic stimulus is selected from C X C motif chemokine 12 (CXCL12), C X C motif chemokine 10 (CXCL10), sphingosine 1-phosphate (S1P), C C motif ligand 2 (CCL2), and/or C C motif ligand 21 (CCL21).

5 11. — The antibody or fragment thereof of claim 7, wherein a cell (e.g., hematopoietic stem cell or T cell) contacted with the antibody or fragment thereof shows increased expression of Frizzled and/or P21 compared to a control cell that is not contacted with the antibody or fragment thereof.

10 12. — An antibody or antigen-binding fragment thereof, which cross-competes with the antibody or fragment thereof of any one of claims 7-11 in a competition binding assay.

13. — A soluble receptor for one or more LRP10 ligands, optionally for use in cancer immunotherapy and/or hematopoietic recovery, wherein said soluble receptor competes with endogenous LRP10 for binding with the one or more LRP10 ligands, wherein preferably the soluble receptor is an LRP10-Fc chimera.

15 14. — A pharmaceutical composition for cancer immunotherapy and/or hematopoietic recovery, comprising the antibody or fragment thereof of any one of claims 7-11 or the soluble receptor of claim 13 and a pharmaceutically acceptable carrier.

16. — A method for identifying an LRP10 inhibitor, comprising contacting a cell with a test agent, wherein an increase in migration toward a chemotactic stimulus compared to a control cell that is not contacted with the test agent indicates that the test agent is an LRP10 inhibitor, wherein preferably the chemotactic stimulus is selected from C X C motif chemokine 12 (CXCL12), C X C motif chemokine 10 (CXCL10), sphingosine 1-phosphate (S1P), C C motif ligand 2 (CCL2), and/or C C motif ligand 21 (CCL21).

16.1. — A method for identifying an LRP10 inhibitor, comprising contacting a cell with a test agent, wherein an increase in expression of Frizzled and/or p21 compared to a control cell that is not contacted with the test agent indicates that the test agent is an LRP10 inhibitor.

17. — The method of claim 15 or 16, wherein the test agent is an anti-LRP10 antibody or antigen-binding fragment thereof or a soluble receptor for one or more LRP10 ligands (e.g., an LRP10-Fc chimera).