

We claim:

1. An isolated monoclonal antibody or an antigen-binding portion thereof, binding to Siglec15, comprising i) a heavy chain variable region that comprises a VH CDR1 region, a VH CDR2 region and a VH CDR3 region, wherein the VH CDR1 region, the VH CDR2 region and the VH CDR3 region comprise amino acid sequences having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to (1) SEQ ID NOs: 1, 2 (X1=D, X2=Q) and 3, respectively; (2) SEQ ID NOs: 1, 2 (X1=E, X2=Q) and 3, respectively; (3) SEQ ID NOs: 1, 2 (X1=D, X2=K) and 3, respectively; (4) SEQ ID NOs: 9, 10 and 11, respectively; or (5) SEQ ID NOs: 33, 34 and 35, respectively; and/or ii) a light chain variable region that comprises a VL CDR1 region, a VL CDR2 region and a VL CDR3 region, wherein the VL CDR1 region, the VL CDR2 region, and the VL CDR3 region comprise amino acid sequences having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to (1) SEQ ID NOs: 4, 5 and 6, respectively; (2) SEQ ID NOs: 12, 13 and 14, respectively; or (3) SEQ ID NOs: 36, 37 and 38, respectively.
2. The isolated monoclonal antibody or the antigen-binding portion thereof, of claim 1 wherein the heavy chain variable region comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NOs: 7 (X1=D, X2=Q; X1=E, X2=Q; or X1=D, X2=K), 15, 39, 40 or 41.
3. The isolated monoclonal antibody or the antigen-binding portion thereof of claim 1, wherein the light chain variable region comprises having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to SEQ ID NOs: 8, 16, 42 or 43.
4. The isolated monoclonal antibody or an antigen-binding portion thereof of claim 2, wherein the heavy chain variable region and the light chain variable region comprise amino acid sequences having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to (1) SEQ ID NOs: 7 (X1=D, X2=Q) and 8, respectively; (2) SEQ ID NOs: 7 (X1=E, X2=Q) and 8, respectively; (3) SEQ ID NOs: 7 (X1=D, X2=K) and 8, respectively; (4) SEQ ID NOs: 15 and 16, respectively; (5) SEQ ID NOs: 39 and 42, respectively; (6) SEQ ID NOs: 40 and 42, respectively; or (7) SEQ ID NOs: 41 and 43, respectively.
5. The isolated monoclonal antibody or an antigen-binding portion thereof of claim 1, comprising a heavy chain constant region having an amino acid sequence of SEQ ID NO: 17, linked to the heavy chain variable region, and a light chain constant region having an amino acid sequence of SEQ ID NO: 18, linked to the light chain variable region.
6. The isolated monoclonal antibody or the antigen-binding portion thereof of claim 1, which (a) binds human Siglec15; (b) binds monkey Siglec15; (c) binds mouse Siglec15; (d) blocks Siglec15 binding to LRRC4C; and/or (e) reverses Siglec15 mediated T cell suppression.

7. The isolated monoclonal antibody or the antigen-binding portion thereof of claim 1, which is a mouse, human, chimeric or humanized antibody.
8. The isolated monoclonal antibody or the antigen-binding portion thereof of claim 1, which is an IgG1, IgG2 or IgG4 isotype.
9. A nucleotide encoding the isolated monoclonal antibody or the antigen-binding portion thereof of any one of claims 1 to 8.
10. A vector containing the nucleotide of claim 9.
11. A host cell containing the vector of claim 10.
12. A pharmaceutical composition comprising the antibody or antigen-binding portion thereof of claim 1, and a pharmaceutically acceptable carrier.
13. The pharmaceutical composition of claim 12, further comprising an anti-tumor agent or an osteoporosis drug.
14. A method for treating cancer in a subject, comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 12 or 13.
15. The method of claim 14, wherein the cancer disease is a solid tumor.
16. The method of claim 15, wherein the cancer is non-small cell lung cancer, ovarian cancer, melanoma, colorectal cancer, breast cancer, endometrial cancer, or squamous cell carcinoma.
17. A method for inhibiting bone loss or increasing bone mass in a subject, comprising administering to the subject a therapeutically effective amount of the pharmaceutical composition of claim 12 or 13.