

Claims:

1. A method for identifying target multiple myeloma associated surface antigens, said method comprising:
 - identifying a plurality of genes that express cell-surface proteins in a first multiple myeloma sample and a second multiple myeloma sample;
 - selecting nucleic acids from said first multiple myeloma sample that have expression levels higher than a control gene unrelated to hematopoietic cells, and identifying the proteins corresponding to the detected elevated expressed nucleic acids to designate a first pool of selected proteins;
 - conducting mass spec analysis on proteins isolated from said second myeloma sample to identify proteins that are present in higher concentration in said second multiple myeloma relative to normal tissues, wherein such proteins represent a second pool of selected proteins;
 - excluding proteins with high expression in brain, spinal cord, gut, liver and kidney from said first and second pools to produce a modified first and second pool of proteins; and
 - identifying proteins common to said first and second modified pool of proteins as target multiple myeloma associated surface antigens.
2. The method of claim 1 wherein said first multiple myeloma sample and said second multiple myeloma sample are taken from the same tissue source.
3. The method of claim 1 wherein said first multiple myeloma sample is a nucleic acid pool of expressed genes from MM patients and said second multiple myeloma sample represents proteins expressed in MM cell lines.
4. The method of claim 1, wherein the target multiple myeloma associated surface antigen has an expression level in a normal tissue sample that is more than about one standard deviation below the normal peak of the protein expression level distribution of the normal tissue sample.

5. The method of claim 1, wherein mRNA is measured to determine the expression level of the nucleic acids used to identify proteins for the first pool of selected proteins.

6. A monoclonal antibody that specifically binds to a polypeptide having at least 90% sequence identity to a polypeptide selected from the group consisting of SEQ ID NO: 1-155 or 168-208.

7. A monoclonal antibody that specifically binds to a polypeptide selected from the group consisting of SEQ ID NO: 168-208.

8. A monoclonal antibody in accordance with claim 6 wherein the antibody specifically binds to a polypeptide selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 37, SEQ ID NO: 42, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 79, SEQ ID NO: 112 and SEQ ID NO: 104.

9. The monoclonal antibody of any one of claims 6-8, wherein the antibody specifically binds to a polypeptide having at least 90% sequence identity to a sequence selected from the group consisting of CCR1 (SEQ ID NO: 60), CD320 (SEQ ID NO: 56), FCRL3 (SEQ ID NO: 57), IFNGR1 (SEQ ID NO: 79), IL12RB1 (SEQ ID NO: 19), ITGA4 (SEQ ID NO: 42), LILRB4 (SEQ ID NO: 20), LRRC8D (SEQ ID NO: 112), SEMA4A (SEQ ID NO: 104), and SLAMF6 (SEQ ID NO: 37).

10. The monoclonal antibody of any one of claims 6-8, wherein the antibody specifically binds to a polypeptide having at least 90% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 1-155 or 168-208.

11. The monoclonal antibody of any one of claims 6-8, wherein the antibody specifically binds to a polypeptide having at least 95% sequence identity to a sequence selected from the group consisting of SEQ ID NO: 1-155 or 168-208.

12. The monoclonal antibody of any one of claims 6-11 further comprising a detectable label covalently linked to the antibody.

13. The monoclonal antibody of any one of claims 6-11 further comprising a cytotoxic agent linked to the antibody.

14. A chimeric antigen receptor (CAR) comprising
an antibody, or antigen binding fragment thereof, that binds one or more epitopes of a polypeptide selected from the group consisting of SEQ ID NO: 1-155 or 168-208,
a transmembrane domain; and
an immune cell antigen receptor chain, wherein the transmembrane domain links the an antibody, or antigen binding fragment thereof to the immune cell antigen receptor chain.

15. The chimeric antigen receptor of claim 14 wherein the antibody or antigen binding fragment thereof, specifically binds to a polypeptide selected from the group consisting of SEQ ID NO: 168-208.

16. The chimeric antigen receptor of claim 14 wherein the antibody or antigen binding fragment thereof, specifically binds to a polypeptide having at least 95% sequence identity to a sequence selected from the group consisting of CCR1 (SEQ ID NO: 60), CD320 (SEQ ID NO: 56), FCRL3 (SEQ ID NO: 57), IFNGR1 (SEQ ID NO: 79), IL12RB1 (SEQ ID NO: 19), ITGA4 (SEQ ID NO: 42), LILRB4 (SEQ ID NO: 20), LRRC8D (SEQ ID NO: 112), SEMA4A (SEQ ID NO: 104) and SLAMF6 (SEQ ID NO: 37).

17. The chimeric antigen receptor of claim 14, wherein the antibody, or antigen binding fragment thereof, binds one or more epitopes of a polypeptide having at least 90% homology to a sequence selected from the group consisting of SEQ ID NO: 1-155 or 168-208.

18. The chimeric antigen receptor of claim 17, wherein the antibody, or antigen binding fragment thereof, binds one or more epitopes of a polypeptide having at least 95% homology to a sequence selected from the group consisting of SEQ ID NO: 1-155 or 168-208.

19. The chimeric antigen receptor of claim 15 wherein the antibody or antigen binding fragment thereof, specifically binds to a polypeptide selected from the group consisting of SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 37, SEQ ID NO: 42, SEQ ID NO: 54, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 79, SEQ ID NO: 112 and SEQ ID NO: 104.

20. The chimeric antigen receptor of any one of claims 15-19 wherein said antibody or antigen binding fragment comprises an antibody single-chain variable fragment.

21. The chimeric antigen receptor of claim 20 further comprising a hinge region located between the antibody single-chain variable fragment and the transmembrane domain.

22. A T-cell modified to express the chimeric antigen receptor of claim 20 or 21.

23. The T-cell of claim 22 wherein the T-cell is a tumor infiltrating leukocyte.

24. An NK cell modified to express the chimeric antigen receptor of claim 15-21.

25. A myeloid cell modified to express the chimeric antigen receptor of claim 15-21.

26. A macrophage modified to express the chimeric antigen receptor of claim 15-21.

27. The T-cell of claim 22 wherein the T-cell antigen receptor chain is the CD3 ζ chain (zeta-chain).

28. A pharmaceutical composition comprising the antibody of any one of claims 6-12, chimeric antigen receptor of any one of claims 15-21, the T-cell of

claims 22 or 23, the NK cell of claim 24, the myeloid cell of claim 2325 or the macrophage of claim 26.

29. A method for treating multiple myeloma, said method comprising administering the pharmaceutical composition of claim 24 to a patient in need of such treatment.

30. An isolated immunoresponsive cell comprising an antigen recognizing receptor that binds to an antigen selected from the group consisting of CCR1 (SEQ ID NO: 60), CD320 (SEQ ID NO: 56), FCRL3 (SEQ ID NO: 57), IFNGR1 (SEQ ID NO: 79), IL12RB1 (SEQ ID NO: 19), ITGA4 (SEQ ID NO: 42), LILRB4 (SEQ ID NO: 20), LRRC8D (SEQ ID NO: 112), SEMA4A (SEQ ID NO: 104), and SLAMF6 (SEQ ID NO: 37).

31. The isolated immunoresponsive cell of claim 30, wherein the antigen is selected from the group consisting of IL12RB1 (SEQ ID NO: 19), LILRB4 (SEQ ID NO: 20), SLAMF6 (SEQ ID NO: 37), CCR1 (SEQ ID NO: 60), and CD320 (SEQ ID NO: 56).

32. The isolated immunoresponsive cell of claim 30 or 31, wherein said antigen recognizing receptor is a T cell receptor (TCR), or a chimeric antigen receptor (CAR).

33. The isolated immunoresponsive cell of claim 32, wherein said antigen recognizing receptor is a CAR.

34. The isolated immunoresponsive cell of claim 33, wherein the intracellular signaling domain of said CAR is the CD3C-chain, CD97, CD1 la-CD 18, CD2, ICOS, CD27, CD 154, CD8, OX40, 4- IBB, CD28 signaling domain, or combinations thereof.

35. The isolated immunoresponsive cell of any one of claims 30-34, wherein the cell is selected from the group consisting of a T cell, a Natural Killer (NK) cell, a cytotoxic T lymphocyte (CTL), a regulatory T cell, a Natural Killer T (NKT) cell, a

human embryonic stem cell, and a pluripotent stem cell from which lymphoid cells may be differentiated.

36. An isolated immunoresponsive cell comprising:

- (a) a first antigen recognizing receptor that binds to a first antigen, and
- (b) a second antigen recognizing receptor that binds to a second antigen, wherein each of the first antigen and the second antigen is selected from the group consisting of CCR1 (SEQ ID NO: 60), CD320 (SEQ ID NO: 56), FCRL3 (SEQ ID NO: 57), IFNGR1 (SEQ ID NO: 79), IL12RB1 (SEQ ID NO: 19), ITGA4 (SEQ ID NO: 42), LILRB4 (SEQ ID NO: 20), LRRC8D (SEQ ID NO: 112), SEMA4A (SEQ ID NO: 104), and SLAMF6 (SEQ ID NO: 37), and the first antigen and the second antigen are different.

37. The isolated immunoresponsive cell of claim 36, wherein each of said antigen recognizing receptor is a T cell receptor (TCR) or a chimeric antigen receptor (CAR).

38. The isolated immunoresponsive cell of claim 36, wherein each of said antigen recognizing receptor is a CAR.

39. A method of reducing tumor burden in a subject, comprising administering to the subject an effective amount of the immunoresponsive cell of any one of claims 30-38.