Claims:

1. A method of identifying a binding polypeptide that specifically binds to a cell-surface antigen, wherein the binding polypeptide is an antibody or binding fragment thereof, the method comprising:
    a. contacting a variegated nucleic acid-display library of binding polypeptides with a first cell type expressing a cell-surface antigen, and isolating from the library at least one library member that specifically binds to the first cell type;
    b. contacting the variegated nucleic acid-display library of binding polypeptides with a second cell type that does not express the cell surface antigen, and isolating from the library at least one library member that specifically binds to the second cell type; and
    c. selecting library members that specifically bind to the first cell type but not to the second cell type, thereby identifying a binding polypeptide that specifically binds to the cell-surface antigen.

2. The method of claim 1, wherein the variegated nucleic acid-display library is a DNA display library.

3. The method of claim 2, wherein each member of the DNA-display library comprises a binding polypeptide linked through an intervening DNA linker to a DNA coding sequence encoding the binding polypeptide, wherein the DNA linker comprises a restriction endonuclease site.

4. The method of claim 3, wherein the restriction endonuclease site is not present in the coding sequence of members of the DNA-display library.

5. The method of claim 3 or 4, wherein the method further comprises physically separating the DNA coding sequence and the linked binding polypeptide of the isolated library members.

6. The method of any one of the preceding claims, wherein the method further comprises separating the intact isolated library members from the first or second cell type.

7. The method of claim 6, wherein the isolated library members are separated from the first or second cell type by enzymatic cleavage of the cell-surface antigen.

8. The method of claim 7, wherein the cell-surface antigen is attached to the cell surface by a glycolipid anchor and the isolated library members are separated from the first or second cell type by phospholipase cleavage of the glycolipid anchor.

9. The method of any one of the preceding claims, wherein the method further comprises determining the DNA coding sequence of at least a portion of each of the isolated library members.

10. The method of claim 9, wherein the DNA coding sequence is determined by pyrosequencing.

11. The method of any one of the preceding claims, where the antigen is a naturally occurring protein, glycan or lipid.

12. The method of any one of the preceding claims, where the antigen is a glycophosphatidylinositol (GPI) anchored protein.

13. The method of any one of the preceding claims, where the antigen is a recombinant antigen.

14. The method of any one of the preceding claims, where the antigen is a chimeric antigen.

15. The method of any one of the preceding claims, wherein the first cell type is a cell that naturally expresses the cell-surface antigen.

16. The method of any one of the preceding claims, wherein the first cell type is a recombinant cell that is engineered to heterologously express the cell-surface antigen.

17. The method of any one of the preceding claims, wherein the first cell type is a disease-associated variant of a normal cell.

18. The method of any one of the preceding claims, wherein the first cell type is a tumor cell.

19. The method of any one of the preceding claims, wherein the binding polypeptide is an antibody VH or VL domain.

20. The method of any one of the preceding claims, wherein the first and second cell types are live cells.

21. The method of any one of the preceding claims, wherein the binding polypeptide is functionally internalized upon binding to the cell-surface antigen expressed on the first cell type.