CLAIMS

What is claimed is:

1. A method for identifying an immunobinder that specifically binds to a cell surface antigen of interest comprising:

(a) providing a plurality of immunobinder-expressing cells operably linked to a first sortable label;

(b) providing a plurality of antigen-expressing cells operably linked to a second sortable label, wherein the antigen of interest is displayed at the surface of the antigen expressing cell;

(c) contacting the antigen -expressing cells with the immunobinder-expressing cells; and

(d) separating from the plurality of immunobinder-expressing cells, one or more immunobinder-expressing cells that can specifically bind to the antigen expressing cells using a cell sorter, wherein the presence of the first and second sortable label in a single cellular complex is indicative of the binding of an immunobinder-expressing cell to an antigen-expressing cell, thereby identifying an immunobinder that binds to a antigen of interest.

2. The method of claim 1, further comprising clonally isolating the immunobinder-expressing cells obtained in step (d), optionally followed by clonal expansion of the clonally isolated cells.

3. The method of claim 2, further comprising obtaining the immunobinder-encoding nucleic acid sequence from the isolated immunobinder-expressing cells.

4. The method of claim 3, wherein the immunobinder-encoding nucleic acid sequence is obtained by PCR.

5. The method of claim 4, wherein the PCR, is single-cell PCR.

6. The method of claim 2, further comprising subjecting the isolated immunobinder-expressing cells to a cell-based assay to functionally characterize the immunobinder.

7. The method of claim 6, wherein the cell-based assay is a CELISA.

8. The method of claim 1, wherein a cellular complex is formed between an antigen and a B-cell receptor.

9. The method of any of the preceding claims, wherein the immunobinder is an antibody.

10. The method of claim 9, wherein the antibody is selected from the group consisting of a mouse, rabbit, chicken, camel, human, humanized and chimeric antibodies.

11. The method of claim 9, wherein the antibody is selected from the group consisting of full length immunoglobulin, Fab, Dab and Nanobody.

12. The method of claim 9, wherein the antibody is a scFv.

13. The method of any of the preceding claims, wherein the antigen of interest is expressed from an exogenous gene.

14. The method of any of the preceding claims, wherein the antigen of interest is a genetically engineered antigen.

15. The method of any of the preceding claims, wherein the antigen of interest is an integral membrane protein.

16. The method of claim 15, wherein the integral membrane protein is a GPCR.

17. The method of claim 16, wherein the GPCR is selected from the group consisting of CXCR2, CXCR1, CXCR3, CXCR4, CXCR6, CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR8, CFTR, CIC-1, CIC-2, CIC-4, CIC-5, CIC-7, CIC-Ka, CIC-Kb, Bestrophins, TMEM16A, GABA receptor, glycin receptor, ABC transporters, NAV1.1, NAV1.2, NAV1.3, NAV1.4, NAV1.5, NAV1.6, NAV1.7, NAV1.8, NAV1.9, sphingosin-1-phosphate receptor (S1P1R) and NMDA channel.

18. The method of claim 15, wherein the integral membrane protein is an ion channel.

19. The method of any of the preceding claims, wherein the first or second sortable label is a fluorescent label.

20. The method of claim 19, wherein the fluorescent label is selected from the group consisting of fluorescent protein, antibody/fluor conjugate and fluorescent cellular label.

21. The method of any of the preceding claims, wherein the cell sorter is a fluorescence activated cell sorter.

22. The method of any of the preceding claims, wherein the antigen-expressing cells are yeast cells, yeast spheroblasts or mammalian cells.

23. The method of claim 22, wherein the antigen-expressing cells are human cells.

24. The method of any of the preceding claims, wherein the antigen-expressing cells express an exogenous antigen.

25. The method of any of the preceding claims, wherein the antigen-expressing cells are transfected with an expression vector.

26. The method of any of the preceding claims, wherein the immunobinder-expressing cells are yeast or mammalian cells.

27. The method of any of the preceding claims, wherein the immunobinder-expressing cells are B-cells.

28. The method of claim 27, wherein the B-cells are rabbit B-cells.

29. The method of any of claims 27 or 28, wherein the B-cells are isolated from an immunized animal.

30. The method of claim 29, wherein the animal is immunized by DNA vaccination.

31. The method of any of the preceding claims, wherein the immunobinder-expressing cells comprise an immunobinder expressed from an expression vector.

32. An isolated nucleic acid molecule encoding an immunobinder selected by the method of any of claims 1-31.

33. A method of producing an immunobinder capable of binding to an antigen of interest, comprising introducing the immunobinder-encoding nucleic acid sequence of claim 32 into an expression environment such that the encoded immunobinder is produced.

34. An immunobinder produced by the method of claim 33.

35. A method for identifying a B-cell clone that specifically binds to a cell surface antigen of interest comprising:

(a) immunizing an animal with DNA encoding a cell surface antigen

(b) isolating B-cells from the immunized animal

(c) labeling the B-cells with a first sortable label;

(d) providing a plurality of antigen-expressing cells operably linked to a second sortable label, wherein the antigen of interest is displayed at the surface of the antigen expressing cell;

(e) contacting the antigen-expressing cells with the B-cells; and,

(f) separating from the plurality of B-cells, one or more B-cells that can specifically bind to the antigen-expressing cells using a cell sorter, wherein the presence of the first and second sortable label in a single cellular complex is indicative of the binding of an B-cell to an antigen-expressing cell, thereby identifying a B-cell clone that binds to a antigen of interest.

What is claimed is:

1. A method for identifying an immunobinder that specifically binds to a cell surface antigen of interest comprising:
(a) providing a plurality of immunobinder-expressing cells comprising a first sortable label;
(b) providing a plurality of antigen-expressing cells comprising a second sortable label, wherein the antigen of interest is displayed at the surface of the antigen-expressing cell;
(c) contacting the antigen-expressing cells with the immunobinder-expressing cells; and
(d) separating from the plurality of immunobinder-expressing cells, one or more immunobinder-expressing cells that can specifically bind to the antigen expressing cells using a cell sorter, wherein the presence of the first and second sortable label in a single cellular complex is indicative of the binding of an immunobinder-expressing cell to an antigen-expressing cell, thereby identifying an immunobinder that binds to a antigen of interest.

2. The method of claim 1, further comprising clonally isolating the immunobinder-expressing cells obtained in step (d), optionally followed by clonal expansion of the clonally isolated cells.

3. The method of claim 2, further comprising obtaining the immunobinder-encoding nucleic acid sequence from the isolated immunobinder-expressing cells.

4. The method of claim 2, further comprising subjecting the isolated immunobinder-expressing cells to a cell-based assay to functionally characterize the immunobinder.

5. The method of claim 1, wherein the immunobinder is an antibody.

6. The method of claim 5, wherein the antibody is a mouse, rabbit, chicken, camel, human, humanized, or chimeric antibody.

7. The method of claim 6, wherein the antibody is a full length immunoglobulin, Fab, Dab, scFv, or Nanobody.

8. The method of claim 1, wherein the antigen of interest is expressed from an exogenous gene.

9. The method of claim 1, wherein the antigen of interest is a genetically engineered antigen expressed from an expression vector.

10. The method of claim 1, wherein the antigen of interest is an integral membrane protein.

11. The method of claim 10, wherein the integral membrane protein is a GPCR or an ion channel.

12. The method of claim 11, wherein the GPCR is CXCR2, CXCR1, CXCR3, CXCR4, CXCR6, CCR1, CCR2, CCR3, CCR4, CCR5, CCR6, CCR8, CFTR, CIC-1, CIC-2, CIC-4, CIC-5, CIC-7, CIC-Ka, CIC-Kb, Bestrophins, TMEM16A, GABA receptor, glycin receptor, ABC transporters, NAV1.1, NAV1.2, NAV1.3, NAV1.4, NAV1.5, NAV1.6, NAV1.7, NAV1.8, NAV1.9, sphingosin-1-phosphate receptor (S1P1R) or NMDA channel.

13. The method of claim 1, wherein the first or second sortable label is a fluorescent label.

14. The method of claim 13, wherein the fluorescent label is a fluorescent protein, an antibody/fluor conjugate, or a fluorescent cellular label.

15. The method of claim 1, wherein the antigen-expressing cells are yeast cells, yeast spheroblasts or mammalian cells.

16. The method of claim 15, wherein the antigen-expressing cells are human cells.

17. The method of claim 1, wherein the immunobinder-expressing cells are yeast or mammalian cells.

18. The method of claim 1, wherein the immunobinder-expressing cells are B-cells.

19. The method of claim 18, wherein the B-cells are rabbit 13-cells.

20. The method of claim 18, wherein the B-cells are isolated from an immunized animal.

21. The method of claim 20, wherein the animal is immunized by DNA vaccination.

22. The method of claim 1, wherein the immunobinder-expressing cells comprise an immunobinder expressed from an expression vector.