

WHAT IS CLAIMED IS:

1. A method for producing an antibody that specifically binds to a protein comprising:
 - (a) producing a plurality of extracellular vesicles (EVs) comprising a heterologous protein by (i) expressing the heterologous protein in a cell exposed to a vesicle factor, (ii) culturing the cell in a medium and (iii) isolating the plurality of EVs comprising the heterologous protein from the medium, wherein the vesicle factor is selected from the group consisting of Acyl.Hrs, ARRDC1, ARF6 and a combination thereof;
 - (b) immunizing an animal by administering the plurality of EVs to the animal; and
 - (c) isolating an antibody that binds to the heterologous protein from the animal.
2. The method of claim 1, wherein the cell is a non-adherent cell.
3. A method for producing an antibody that specifically binds to a protein comprising:
 - (a) producing a plurality of extracellular vesicles (EVs) comprising a heterologous protein by (i) expressing the heterologous protein in a cell, (ii) culturing the cell in a medium and (iii) isolating the plurality of EVs comprising the heterologous protein from the medium, wherein the cell is a non-adherent cell;
 - (b) immunizing an animal by administering the plurality of EVs to the animal; and
 - (c) isolating an antibody that binds to the heterologous protein from the animal.
4. The method of claim 3, wherein producing the plurality of EVs further comprises expressing a vesicle factor in the cell.
5. The method of claim 4, wherein the vesicle factor is selected from the group consisting of MLGag, Acyl.Hrs, ARRDC1, ARF6 and a combination thereof.
6. The method of any one of claims 1-5, wherein the heterologous protein is a membrane protein.
7. The method of claim 6, wherein the membrane protein is a single-pass membrane protein.
8. The method of claim 6, wherein the membrane protein is a multi-pass membrane protein.

9. The method of any one of claims 6-8, wherein the membrane protein is a member of a protein complex.
10. The method of claim 6, wherein the membrane protein is not a transmembrane protein but is a protein that is part of a complex with a transmembrane protein.
11. The method of any one of claims 2-10, wherein the non-adherent cell is a 293S cell or an Expi293FTM cell.
12. The method of any one of claims 1-11, wherein the EVs are isolated from the medium by ultracentrifugation.
13. The method of any one of claims 1-12, wherein the plurality of EVs is administered to the animal on week 0, week 2 and week 4.
14. The method of any one of claims 1-13, further comprising administering an adjuvant to the animal concurrently with the EVs.
15. The method of claim 14, wherein the adjuvant is a Ribi adjuvant.
16. The method of any one of claims 1-15, further comprising administering a boost to the animal to enhance an immune response in the animal to the protein.
17. The method of claim 16, wherein the boost comprises the protein, a polynucleotide encoding the protein or a combination thereof.
18. The method of claim 17, wherein the boost comprises the protein.
19. The method of claim 17, wherein the boost comprises a polynucleotide encoding the protein.
20. The method of any one of claims 1-19, wherein the antibody is a monoclonal antibody.
21. The method of any one of claims 1-20, wherein the antibody is a human, humanized or chimeric antibody.
22. An isolated antibody or an antigen-binding portion thereof produced by the method of any one of claims 1-21.
23. An isolated nucleic acid encoding the antibody or antigen-binding portion thereof of claim 22.
24. A host cell comprising the nucleic acid of claim 23.

25. A method of producing an antibody or antigen-binding portion thereof comprising culturing the host cell of claim 24 under conditions suitable for expression of the antibody.
26. The method of claim 25, further comprising recovering the antibody from the host cell.
27. A pharmaceutical composition comprising the isolated antibody or antigen-binding portion thereof of claim 22 and a pharmaceutically acceptable carrier.
28. The pharmaceutical composition of claim 27, further comprising an additional therapeutic agent.
29. The isolated antibody or antigen-binding portion thereof of claim 22 for use as a medicament.
30. The isolated antibody or antigen-binding portion thereof of claim 22 for use in treating a disease.
31. Use of the isolated antibody or antigen-binding portion thereof of claim 22 in the manufacture of a medicament.
32. A method of treating an individual having a disease comprising administering to the individual an effective amount of the isolated antibody or antigen-binding portion thereof of claim 22.
33. The method of claim 32 further comprising administering an additional therapeutic agent to the individual.
34. A method of treating an individual having a disease comprising administering to the individual the pharmaceutical composition of claim 27 or 28.
35. A method for detecting an antibody in a sample comprising:
- (a) incubating a sample with a capture reagent, wherein the capture reagent comprises a plurality of EVs comprising membrane-bound antigen, and the antibody binds specifically to the membrane-bound antigen; and
 - (b) contacting the antibody binding to the capture reagent with a detectable antibody to detect the bound antibody, wherein the detectable antibody binds specifically to the antibody, wherein the plurality of EVs are generated by (i) expression of the membrane-bound antigen in a cell, (ii) culturing the cell *in vitro* in a medium to produce the plurality of EVs displaying the membrane-bound antigen and (iii) isolating the plurality of EVs displaying the membrane-bound antigen from the medium, and

wherein the cell is exposed to a vesicle factor selected from the group consisting of Acyl.Hrs, ARRDC1, ARF6 and a combination thereof and/or the cell is a non-adherent cell.

36. The method of claim 35 further comprising (c) measuring the amount of the antibody detected in (b), wherein the amount is quantitated using a standard curve.

37. The method of claim 35 or 36, wherein the sample is a plasma, a serum or a urine sample.

38. The method of any one of claims 35-37, wherein the capture reagent is immobilized on a solid support.

39. The method of claim 38, wherein the solid support is a microtiter plate.

40. The method of any one of claims 35-39, wherein the detectable antibody is fluorescently labeled.

41. The method of any one of claims 35-40, wherein the membrane-bound antigen is a membrane protein or a fragment thereof.

42. A method for sorting antibody-producing cells comprising:

(a) incubating the antibody-producing cells with a plurality of EVs wherein the plurality of EVs comprise:

- i. a first population of EVs comprising a membrane-bound antigen and a first detectable marker, wherein a subset of the antibody-producing cells bind specifically to the membrane-bound antigen; and
- ii. a second population of EVs lacking the membrane-bound antigen but comprising a second detectable marker distinguishable from the first marker; and

(b) sorting the antibody-producing cells based on their binding to either the first population of EVs or to a combination of the first population of EVs and the second population of EVs,

wherein the first population of EVs is generated by (i) expression of the membrane-bound antigen and the first detectable marker in a first cell, (ii) culturing the first cell *in vitro* in a medium to produce the plurality of EVs displaying the membrane-bound antigen and (iii) isolating the plurality of EVs displaying the membrane-bound antigen from the medium,

wherein the second population of EVs is generated by (i) expression of the second detectable marker in a second cell, (ii) culturing the second cell *in vitro* in a medium to produce the plurality of EVs comprising the second detectable marker and (iii) isolating the plurality of EVs displaying the second detectable marker from the medium, and

wherein (i) the first cell and/or the second cell is exposed to a vesicle factor selected from the group consisting of Acyl.Hrs, ARRDC1, ARF6 and a combination thereof and/or (ii) the first and/or second cell is a non-adherent cell.

43. The method of claim 42, where the first and second detectable markers are fluorescent markers.

44. The method of claim 43, wherein the first and second fluorescent markers are fluorescent proteins.

45. The method of any one of claims 42-44, wherein the sorting is performed by fluorescence-activated cell sorting.

46. The method of any one of claims 42-45, wherein the antibody-producing cells are B cells.

47. The method of any one of claims 42-45, wherein the antibody-producing cells are hybridoma cells.

48. A method for producing a plurality of extracellular vesicles (EVs) displaying a protein, comprising:

(a) expressing a heterologous protein in a cell;

(b) culturing the cell in a medium; and

(c) isolating the plurality of EVs comprising the heterologous protein from the medium, wherein the cell is exposed to a vesicle factor selected from the group consisting of

Acyl.Hrs, ARRDC1, ARF6 and a combination thereof and/or the cell is a non-adherent cell.

49. The method of claim 48, wherein the heterologous protein is a membrane protein.

50. The method of claim 49, wherein the membrane protein is a single-pass membrane protein.

51. The method of claim 49, wherein the membrane protein is a multi-pass membrane protein.

52. The method of any one of claims 49-51, wherein the membrane protein is a member of a protein complex.

53. The method of any one of claims 35-52, wherein the non-adherent cell is a 293S cell or an Expi293F™ cell.
54. The method of any one of claims 35-53, wherein the plurality of EVs are isolated from the medium by ultracentrifugation.
55. A kit for detecting an antibody in a sample comprising:
- (a) a capture reagent that comprises a plurality of EVs comprising membrane-bound antigen, wherein the antibody to be detected binds specifically to the antigen; and
 - (b) a detectable antibody that binds specifically to the antibody to be detected,
- wherein the plurality of EVs are generated by (i) expression of the membrane-bound antigen in a cell, (ii) culturing the cell *in vitro* in a medium to produce the plurality of EVs displaying the membrane-bound antigen and (iii) isolating the plurality of EVs displaying the membrane-bound antigen from the medium, and
- wherein the cell is exposed to a vesicle factor selected from the group consisting of Acyl.Hrs, ARRDC1, ARF6 and a combination thereof and/or the cell is a non-adherent cell.
56. The kit of claim 55, wherein the plurality of EVs are immobilized on a solid support.
57. The kit of claim 55 or 56, wherein the solid support is a microtiter plate.
58. The kit of any one of claims 55-57, wherein the detectable antibody is fluorescently labeled.
59. The kit of any one of claims 55-58, wherein the membrane-bound antigen is a membrane protein or a fragment thereof.