

What is claimed is:

1. An isolated polynucleotide comprising: (a) a first nucleic acid fragment that encodes an integral membrane protein (IMP) or fragment thereof, wherein the IMP or fragment thereof comprises at least one extra-membrane region, at least one transmembrane domain and at least one intra-membrane region, and wherein a portion of the first nucleic acid fragment encoding at least one intra-membrane region is situated at the 5' or 3' end of the first nucleic acid fragment; and (b) a second nucleic acid fragment that encodes a fowlpox virus (FPV) FPV108 protein, a rabbit pox virus (RBXV) protein RBXV041 or functional fragment thereof, wherein the second nucleic acid fragment is fused in frame to a portion of the first nucleic acid fragment that encodes an intra-membrane region of the IMP; wherein a poxvirus infected cell comprising the polynucleotide can express an IMP-FPV108 or IMP-RBXV041 fusion protein as part of the outer envelope membrane of an extracellular enveloped virion (EEV).
2. The polynucleotide of claim 1, wherein the second nucleic acid encodes FPV108 protein comprising the amino acid sequence SEQ ID NO: 2 or a functional fragment thereof.
3. The polynucleotide of claim 1, wherein the second nucleic acid encodes RBXV041 protein comprising the amino acid sequence SEQ ID NO: 3 or a functional fragment thereof.
4. The polynucleotide of claim 1, wherein the IMP is a multi-pass membrane protein comprising at least two transmembrane domains.
5. The polynucleotide of claim 4, wherein the IMP has an odd number of transmembrane domains, wherein the 5' end of the first nucleic acid fragment encodes an extra-membrane region, wherein the 3' end of the first nucleic acid fragment encodes an intra-membrane region, and wherein the 5' end of the second polynucleotide is fused to the 3' end of the first nucleic acid fragment.
6. The polynucleotide of claim 5, wherein the IMP comprises a G-protein coupled receptor (GPCR).

7. The polynucleotide of claim 5, wherein the IMP is the human frizzled-4 protein (FZD4), or a fragment thereof.
8. The polynucleotide of claim 5, wherein the IMP is a CXC chemokine receptor CXCR, or a fragment thereof.
9. The polynucleotide of claim 8, wherein the CXC chemokine receptor is CXCR4, or a fragment thereof.
10. The polynucleotide of claim 4, wherein the IMP has an even number of transmembrane domains, and wherein both the 5' and 3' ends of the first nucleic acid fragment encode intra-membrane regions, and wherein the second nucleic acid fragment is fused to 3' end of the first nucleic acid fragment.
11. The polynucleotide of claim 10, wherein the IMP is human CD20 or CD39 protein, or a fragment thereof.
12. The polynucleotide of any one of claims 1 to 11, which is operably associated with a poxvirus promoter.
13. The polynucleotide of any one of claims 1 to 12, wherein the first and second nucleic acid fragments are directly fused.
14. The polynucleotide of any one of claims 1 to 13, further comprising a third nucleic acid fragment encoding a heterologous peptide.
15. The polynucleotide of claim 14, wherein the heterologous peptide comprises a linker sequence, an amino acid tag or label, or a peptide or polypeptide sequence that facilitates purification.

16. The polynucleotide of claim 15, wherein the heterologous peptide comprises a histidine tag.
17. The polynucleotide of any one of claims 1 to 16, which is operably associated with a poxvirus promoter.
18. The polynucleotide of claim 17, wherein the poxvirus promoter is p7.5 or H5 or T7.
19. An FPX108 fusion protein encoded by the polynucleotide of any one of claims 1 to 18.
20. An RBXV041 fusion protein encoded by the polynucleotide of any one of claims 1 to 18.
21. A poxvirus genome comprising the polynucleotide of any one of claims 1 to 18.
22. The poxvirus genome of claim 21, which is a vaccinia virus genome.
23. The poxvirus genome of claim 21, which is a fowlpox virus genome.
24. The poxvirus genome of claim 21, which is a rabbit pox virus genome.
25. A recombinant poxvirus EEV comprising the poxvirus genome of any one of claims 22 - 24.
26. A method of producing the recombinant poxvirus EEV of claim 25, comprising: (a) infecting a host cell permissive for vaccinia virus, fowlpox virus, or rabbit pox virus infectivity with a vaccinia virus, fowlpox virus or rabbit pox virus, respectively, wherein the vaccinia virus comprises the poxvirus genome of claim 22, the fowlpox virus comprises the poxvirus genome of claim 23, and the rabbit pox virus comprises the poxvirus genome of claim 24; and (b) recovering EEV released from the host cell.
27. A method to display an integral membrane protein (IMP) or fragment thereof in a native conformation comprising: (a) infecting host cells permissive for poxvirus infectivity with a recombinant poxvirus that expresses the IMP or fragment thereof as a fusion protein with the

EEV-specific protein FPV108 or RBX041 or a membrane-associated fragment thereof, wherein EEV produced by the infected host cell comprise the IMP fusion protein as part of the EEV outer envelope membrane; (b) recovering EEV released from the host cell wherein the IMP or fragment thereof displays on the surface of the EEV in a native conformation.

28. The method of claim 27, wherein the EEV-specific protein is FPV108 or a functional fragment thereof.

29. The method of claim 27, wherein the EEV-specific protein is RBXV041 or a functional fragment thereof.

30. The method of any one of claims 27 to 29, wherein the IMP is a multi-pass membrane protein comprising at least two transmembrane domains.

31. The method of claim 30, wherein the IMP comprises a G-protein coupled receptor (GPCR) comprising seven transmembrane domains, and wherein FPV108 or RBX041 is fused to the C-terminus of the IMP.

32. The method of claim 31, wherein the IMP is the human frizzled-4 protein (FZD4), or a fragment thereof.

33. The method of claim 30, wherein the IMP is a CXC chemokine receptor.

34. The method of claim 33, wherein the CXC chemokine receptor is CXCR4, or a fragment thereof.

35. The method of any one of claims 27 to 29, wherein the IMP or fragment thereof has an even number of transmembrane domains, and wherein both the N-terminus and the C-terminus of the IMP or fragment thereof are intra-membrane.

36. The method of claim 35, wherein FPV108 or RBX041 is fused to the C-terminus of the IMP.

37. The method of claim 36, wherein the IMP is human CD20, or a fragment thereof.
38. A fusion protein comprising: (a ) the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 9, SEQ ID NO: 10, or SEQ ID NO: 11, wherein the fusion protein, when expressed by a recombinant poxvirus, appears on the surface of a poxvirus extracellular enveloped virion (EEV) in a native conformation.
39. A recombinant poxvirus EEV comprising the fusion protein of claim 38.
40. A recombinant poxvirus EEV comprising a heterologous IMP or fragment thereof fused to a fowlpox virus or rabbit pox virus EEV-specific protein or membrane-associated fragment thereof, wherein the fusion protein is situated in the EEV outer envelope membrane, wherein the IMP or fragment thereof displays on the surface of the EEV in its native conformation.
41. The recombinant poxvirus EEV of claim 40, wherein the poxvirus EEV is a fowlpox virus EEV.
42. A method to select antibodies that bind to a multi-pass membrane protein (IMP) comprising: (a) attaching the recombinant EEV of any one of claims 25, 39, 40 or 41 to a solid support; (b) providing an antibody display library, wherein the library comprises display packages displaying a plurality of antigen binding domains; (c) contacting the display library with the EEV such that display packages displaying antigen binding domains that specifically binds to the IMP expressed on the EEV can bind thereto; (d) removing unbound display packages; and (e) recovering display packages that display an antigen binding domain specific for the IMP expressed on the EEV.
43. The method of claim 42 wherein the recombinant EEV are inactivated prior to attachment to the solid support.
44. The method of claim 43, wherein the EEV are inactivated by incubation with Psoralen

(Trioxsalen, 4'-aminomethyl-, hydrochloride) in the presence of UV irradiation.

45. The method of any one of claims 42 to 44, wherein the EEV are attached to the solid surface via reaction with tosyl groups attached to the surface.

46. The method of claim 45, wherein the solid surface is tosyl-activated magnetic beads.

47. The method of any one of claims 42 to 44, wherein the EEV are biotinylated and attached to a streptavidin coated solid surface.

48. The method of claim 47, wherein the solid surface is streptavidin-coated magnetic beads.

49. A method to select antibodies that bind to a multi-pass membrane protein (IMP) comprising: (a) providing a first and second recombinant poxvirus EEV of claim 25, wherein the first and second recombinant poxvirus EEV are each generated in a different poxvirus; (b) immunizing an animal with the first recombinant poxvirus; (b) contacting a display library that comprises display packages displaying a plurality of antigen binding domains with the second recombinant poxvirus such that the display packages displaying antigen binding domains that specifically bind to the IMP expressed on the EEV can bind thereto, wherein said display library is generated from B cells isolated from the immunized mammal; (c) removing unbound display packages; and (d) recovering display packages that display an antigen binding domain specific for the IMP expressed on the second recombinant EEV.

50. The method of claim 49, wherein the first recombinant poxvirus EEV is a vaccinia virus EEV.

51. The method of claim 50, wherein the second recombinant poxvirus EEV is a fowlpox virus EEV.

52. A method to select antibodies or antigen-binding fragments thereof that bind to a multi-pass membrane protein (IMP), which comprises: (a) providing a recombinant poxvirus EEV of claim 25; (b) immunizing a mammal with the recombinant poxvirus EEV; (c) optionally immunizing

the mammal with a second dose of the recombinant poxvirus EEV; (d) isolating serum from the immunized animal; and (e) isolating antibodies or antigen-binding fragments thereof that comprise an antigen binding domain specific for the IMP expressed on the recombinant poxvirus EEV.