CLAIMS

1. An *in vitro* system for the detection of binding agents in a fluid sample, said system comprising:

host nanoparticles comprising fragments of host cells expressing or engineered to express surface receptors recognized by a foreign ligand, wherein the host nanoparticles comprise plasma membrane fragments of the host cell expressing or engineered to express the surface receptors recognized by the foreign ligand; and

foreign nanoparticles expressing or engineered to express the foreign ligand on their surface such that the foreign ligands are recognizable by the surface receptors of the host nanoparticles;

wherein the host nanoparticles and/or the foreign nanoparticles further comprise a detectable label, and

wherein said binding agents are present in the sample when preincubation of either the host or foreign nanoparticles with the sample decreases binding/interaction between the host nanoparticles and the foreign nanoparticles as compared to a corresponding fluid sample lacking the binding agents.

2. A kit for screening a sample for the presence of binding agents, said kit comprising:

a first container comprising host nanoparticles comprising or consisting of fragments of mammalian host cells expressing a surface receptor recognized by a foreign ligand, wherein the host nanoparticles comprise plasma membrane fragments of the host cell expressing or engineered to express the surface receptors recognized by the foreign ligand; and

a second container comprising foreign nanoparticles expressing the foreign ligands on their surface such that the foreign ligands are recognizable by the surface receptors of the host nanoparticles,

wherein the host nanoparticles and/or the foreign nanoparticles further comprise a detectable label, and wherein said binding agents are present in the sample when preincubation of either the host or foreign nanoparticles with the sample decreases binding/interaction between the host nanoparticles and the foreign nanoparticles as compared to a corresponding sample lacking the binding agents.

3. An *in vitro* method for detecting binding agents in a fluid sample, said method comprising:

providing the host nanoparticles and foreign nanoparticles as defined in claim 1 or 2;

preincubating the host nanoparticles or the foreign nanoparticles with the fluid sample to enable binding/interaction of the binding agents;

incubating the host nanoparticles with the foreign nanoparticles and measuring binding/interaction therebetween, wherein a decrease in the level of binding/interaction between the host nanoparticles and the foreign nanoparticles following the preincubation with the fluid sample, as

compared to preincubation with a corresponding fluid sample lacking the binding agents, is indicative of the presence of binding agents in the fluid sample.

4. The system, kit, or method of any one of claims 1 to 3, wherein the host nanoparticles are produced or derived from host producer cells, optionally wherein the host producer cells are eukaryotic cells.

5. The system, kit, or method of claim 4, wherein the host producer cells are:

(a) engineered to express or overexpress the surface receptor;

(b) engineered to express or overexpress the detectable label;

(c) engineered to express or overexpress an exogenous viral, bacterial, or fungal protein that induces extracellular vesicle or extracellular particle formation in the host producer cell; or

(d) any combination of (a) to (c).

6. The system, kit, or method of any one of claims 1 to 5, wherein the host nanoparticles are vesicular nanoparticles comprising an exogenous viral structural protein that induces host cell budding, optionally wherein the exogenous viral structural protein is fused to the detectable label.

7. The system, kit, or method of any one of claims 1 to 6, wherein the foreign nanoparticles are produced or derived from a microorganism, from eukaryotic producer cells, or are formed by self-assembling viral structural proteins.

8. The system, kit, or method of claim 7, wherein the microorganism or eukaryotic producer cells from which the foreign nanoparticles are produced or derived are:

(a) engineered to express or overexpress the foreign ligand;

(b) engineered to express or overexpress the detectable label;

(c) engineered to express or overexpress an exogenous viral, bacterial, or fungal protein that induces extracellular vesicle or extracellular particle formation in the host producer cell;

(d) nanoparticles that fuse with and/or penetrate into the host nanoparticles upon contact therewith; or

(e) any combination of (a) to (d).

9. The system, kit, or method of any one of claims 1 to 8, wherein the foreign nanoparticles are vesicular foreign nanoparticles comprising an exogenous viral structural protein that induces host cell budding.

10. The system, kit, or method of any one of claims 1 to 8, wherein
i) the foreign nanoparticles are derived from SARS-CoV-2 virus and/or express or are engineered to express a SARS-CoV-2 Spike protein, or a portion thereof, on their surface; and/or
ii) the host nanoparticles express or are engineered to express angiotensin converting enzyme 2 (ACE2) and/or transmembrane serine protease 2 (TMPRSS2) on their surface.

11. The system, kit, or method of any one of claims 1 to 10, wherein the foreign ligand is a surface ligand expressed on a microbial cell, an autoantigen, or an allergen.

12. The system, kit, or method of any one of claims 1 to 11, wherein the detectable label is:
i) internally expressed or expressed on the surface of the foreign or host nanoparticles
ii) a fluorescent or luminescent molecule;
iii) detectable upon contact with a substrate, protein, or enzyme; or
iv) any combination of i) to iii).

13. The system, kit, or method of any one of claims 1 to 12, wherein the sample is blood, serum, tears, saliva, plasma, urine, nasal secretion, bronchoalveolar lavage fluid (BALF), fecal, or cerebral spinal fluid.

14. The system, kit, or method of any one of claims 1 to 13, wherein the binding agent:
i) is an antibody or an antigen-binding fragment thereof, peptide, protein, nucleic acid, or a small molecule;
ii) recognizes the surface receptor of the host nanoparticle or the foreign ligand of the foreign nanoparticle;
iii) prevents or attenuates fusion of the membranes of the host nanoparticle and the foreign nanoparticle;
iv) prevents or attenuates internalization/penetration of the foreign nanoparticle into the host nanoparticle; or
v) any combination of i) to iv).

15. The system, kit, or method of any one of claims 1 to 14, wherein the host nanoparticles and/or the foreign nanoparticles are:

i) immobilized or are for immobilization on a solid support; or

ii) in suspension.