CLAIMS

1. A method of identifying a cognate binding moiety of one or more antigens, said method comprising the steps of:

a) providing

1) a population of cells, each of said cells comprising:

i) a cell surface antigen and

ii) a nucleic acid comprising a first recombination motif, and

2) a plurality of attachment-defective virions, each of said virions comprising:

i) one of a plurality of transgenic viral surface binding moieties and

ii) a nucleic acid comprising a second recombination motif capable of integrating with said first motif;

b) contacting said population of cells with said virions, wherein, if one or more of said virions comprise a cognate binding moiety of one or more of said cell surface antigens, binding of said cell surface antigen and said cognate binding moiety results in selective infection by the bound virion of the cell comprising said cell surface antigen of said cognate binding moiety;

c) incubating said population of cells under conditions sufficient to allow recombination between said first and second recombination motifs in infected cells, thereby generating a recombinant product; and

d) identifying a cognate binding moiety of one or more of said antigens by identifying the nucleic acid sequence of said recombinant product or an identifying fragment thereof, in a cell, and identifying from said nucleic acid sequence an antigen and a cognate binding moiety.

2. The method of claim 1, wherein:

(i) each of said cells of step (a) further comprises a conditionally expressed infection apparatus; and

(ii) step (b) comprises incubating said cells with said virions under conditions that are not permissive for infection but are sufficient to allow binding of one or more of said cell surface antigens by one or more of said cognate binding moieties, whereby one or more of said cells are bound by one or more of said virions;

emulsifying said bound cells, thereby encapsulating one or more of said cells in one or more emulsion droplets; and

incubating said emulsified cells under conditions permissive to expression of said conditionally expressed infection apparatus, thereby allowing infection of one or more of said emulsified cells by one or more virions present in the same emulsion droplet.

3. The method of claim 1 or 2, wherein

(i) said cells each comprise a recombination enzyme, preferably wherein said recombination enzyme is an integrase;

(ii) the nucleic acid comprised by one or more of said virions encodes a recombination enzyme and said incubation is sufficient to allow expression of said encoded recombination enzyme, preferably wherein said recombination enzyme is an integrase;

(iii) one or more of said recombination motifs is a site-specific recombination motif; and/or

(iv) each of said cells comprises one of a plurality of distinct cell surface antigens, optionally wherein one or more of said cell surface antigens are transgenic.

4. The method of claim 1, wherein the method is a method of identifying a cognate binding moiety of each of a plurality of antigens, and wherein: step a) comprises providing

1) a population of cells, each of said cells comprising:

i) one of a plurality of transgenic cell surface antigens,

ii) a nucleic acid comprising a first marker gene fragment adjacent to a first site-specific recombination motif, and

iii) a recombination enzyme, optionally wherein the recombination enzyme is an integrase, and

2) a plurality of attachment-defective virions, each of said virions comprising:

i) one of a plurality of transgenic viral surface binding moieties and

ii) a nucleic acid comprising a second marker gene fragment adjacent to a second site-specific recombination motif capable of integrating with said first motif,

wherein said first marker gene fragment and said second marker gene fragment are positioned such that site-specific recombination between said first and second motif will result in a functional marker gene;

step c) comprises incubating said population of cells under conditions sufficient to allow site-specific recombination between said first and second site-specific recombination motifs in infected cells, thereby generating a recombinant product capable of expressing a functional marker protein, incubating said population of cells in a manner sufficient to allow detection of cells having a phenotype resulting from expression of said functional marker protein, and isolating one or more cells having said detectable phenotype; and

step d) comprises identifying a cognate binding moiety of one or more of said antigens by identifying the nucleic acid sequence of said recombinant product or an identifying fragment thereof, in one or more of said isolated cells, and identifying from said nucleic acid sequence an antigen and a cognate binding moiety.

5. The method of claim 2, wherein the method is a method of identifying a cognate binding moiety of one or more antigens, and wherein:
step a) comprises providing

1) a population of cells, each of said cells comprising:

i) one of a plurality of cell surface antigens,

ii) a nucleic acid comprising a first marker gene fragment adjacent to a first site-specific recombination motif,

iii) a recombination enzyme, optionally wherein the recombination enzyme is an integrase, and

iv) a conditionally expressed infection apparatus; and

2) a plurality of virions, each of said virions comprising:

i) one of a plurality of transgenic viral surface binding moieties and

ii) a nucleic acid comprising a second marker gene fragment adjacent to a second site-specific recombination motif capable of integrating with said first motif;

wherein said first marker gene fragment and said second marker gene fragment are positioned such that site-specific recombination between said first and second motif will result in a functional marker gene;

step b) comprises incubating said cells in a manner sufficient to allow recombination between said first and second site-specific recombination motifs in infected cells, thereby generating a recombinant product capable of expressing a functional marker protein, incubating said population of cells in a manner sufficient to allow detection of cells having a phenotype resulting from expression of said functional marker protein, and isolating one or more cells having said detectable phenotype; and

step d)comprises identifying a cognate binding moiety of one or more of said antigens by identifying the nucleic acid sequence of said

recombinant product or an identifying fragment thereof, in one or more of said isolated cells, and identifying from said nucleic acid sequence an antigen and a cognate binding moiety, optionally wherein said emulsion further comprises a cleavage reagent capable of facilitating infection under permissive conditions, optionally further comprising breaking said emulsion subsequent to said infection of one or more of said emulsified cells.

6. The method of claim 4 or 5, wherein:

(i) one or more of said first marker gene fragments or one or more of said second marker gene fragments comprise a functional marker gene promoter and one or more of said first marker gene fragments or one or more of said second marker gene fragments comprise a coding segment of the same functional marker gene,

optionally wherein one of said first marker gene fragment or said second marker gene fragment comprises a promoter gene fragment and the other comprises a coding gene fragment or one of said first marker gene fragment or said second marker gene fragment comprises a promoter gene fragment and a 5' coding gene fragment and the other comprises a 3' coding gene fragment;

(ii) said marker gene is an antibiotic resistance gene, optionally wherein said antibiotic resistance gene is an ampicillin resistance gene;

(iii) said marker gene encodes a fluorescent protein;

(iv) the polynucleotide sequence of one or more of said transgenic cell surface antigens is adjacent to a first marker gene fragment;

(v) the polynucleotide sequence of one or more of said transgenic viral surface binding moieties is adjacent to a second marker gene fragment;

(vi) one or more of said transgenic cell surface antigens are comprised by a cell surface antigen fusion protein;

(vii) one or more of said cell surface antigen fusion proteins comprise an *E. coli* F pilin protein or a fragment thereof capable of displaying said antigen;

(viii) one or more of said transgenic viral surface binding moieties are viral surface binding moiety fusion proteins;

(ix) said cells are bacterial, yeast, or mammalian cells, optionally wherein said bacterial cells are *E. coli*;

(x) said virions are attachment-defective bacteriophage, baculovirus, or adenovirus virions; optionally, wherein said virion transfers one or more genetic elements into said cell upon infection of said cell, said genetic elements optionally encoding an F pilus polypeptide, preferably wherein said virions are M13 phage lacking Gp3; and/or

(xi) said first and second recombination motifs are *att* recombination motifs.

7. The method of any one of claims 1 to 6, wherein

(i) said population of cells comprises a plurality of transgenic cell surface antigens comprising 10,000 or more distinct antigens; and/or

(ii) said plurality of transgenic viral surface binding moieties comprises 10,000 or more distinct binding moieties.

8. The method of any one of claims 1 to 7, wherein:

(i) said antigen comprises one or more modified amino acids, optionally wherein one or more of said modified amino acids are phosphoserines;

(ii) one or more of said binding moieties are antibodies, optionally wherein one or more of said binding moieties are scFv binding moieties;

(iii) one or more of said viral surface binding moieties comprise one or more segments derived from the sequence of an antibody expressed by a cell of an inoculated subject;

(iv) one or more of said viral surface binding moieties comprise one or more segments derived from the sequence of an antibody expressed by a naïve cell;

(v) one or more of said antigens is an antigen isolated from a pathogen;

(vi) said antigens comprise one or more antigens isolated from each of a plurality of pathogens;

(vii) said recombinant product comprises one or more variable priming sequences, optionally wherein said recombinant product comprises two variable priming sequences that flank the sequences of said antigen and said binding moiety;

(viii) said sequencing is deep sequencing or NextGeneration sequencing;

(ix) a segment of one or more polynucleotides encoding an antigen or binding moiety is distinguished from one or more substantially identical segments by substitution at one or more nucleobases, wherein said substitution does not modify the polypeptide encoded by the segment; and/or

(x) said one or more substituted nucleobases is a nucleobase present in a codon.

9. The method of claim 1, wherein:

(i) the population of cells of step (a) is a population of infection-defective cells, each of said cells further comprising a nucleic acid comprising a first marker gene fragment adjacent to a first site-specific recombination motif, a recombination enzyme, and a virus capable of transferring one or more genes encoding the infection apparatus to cells; and

(ii) each of said virions further comprises a nucleic acid comprising a second marker gene fragment adjacent to a second site-specific recombination motif capable of integrating with said first motif, wherein said first marker gene fragment and said second marker gene fragment are positioned such that site-specific recombination between said first and second motif will result in a functional marker gene;

(iii) step (c) comprises incubating said cells with said virions under conditions that are not permissive to transfer of infection apparatus genes but are sufficient to allow binding of one or more of said cell surface antigens by one or more of said cognate binding moieties, whereby one or more of said cells are bound by one or more of said virions; and

(iv) following step (c) and prior to step (d), the method further comprises emulsifying said bound cells, thereby encapsulating one or more of said cells in one or more emulsion droplets;

transferring infection apparatus genes to said emulsified cells to allow recombinant expression of said infection apparatus, thereby allowing infection of one or more of said emulsified cells by one or more virions present in the same emulsion droplet;

incubating said cells in a manner sufficient to allow recombination between said first and second site-specific recombination motifs in infected cells, thereby generating a recombinant product capable of expressing a functional marker protein;

incubating said population of cells in a manner sufficient to allow detection of cells having a phenotype resulting from expression of said functional marker protein; and

isolating one or more cells having said detectable phenotype.

10. The method of claim 1, wherein:

(i) the population of cells of step (a) is a population of infection apparatus-defective cells, each of said cells further comprising a construct capable of expressing an F pilin protein in the presence of an activator; and

(ii) step (b) further comprises removing unbound virions following the initial contacting step; andthe selective infection of step (b) further comprises introducing an activator, thereby inducing the expression of said F pilin protein, said expression of said F pilin protein resulting in selective infection by the bound virion of the cell comprising said cell surface antigen of said cognate binding moiety;

optionally, wherein said activator is tetracycline and said construct capable of expressing an F pilin protein in the presence of an activator comprises a tetracycline responsive promoter controlling a gene encoding said F pilin protein.