

Claims

1. A library of particles, the library displaying a plurality of different T cell receptors (TCRs), wherein the plurality of TCRs consists essentially of TCRs comprising an alpha chain comprising an alpha chain variable domain from a natural repertoire and a beta chain comprising a beta chain variable domain from a natural repertoire, wherein the alpha chain variable domain comprises a TRAV12-2 or a TRAV21 gene product and the beta chain variable domain comprises a TRBV6 gene product.
2. A library of particles, the library displaying a plurality of different T cell receptors (TCRs), wherein the plurality of TCRs consists essentially of TCRs comprising an alpha chain comprising an alpha chain variable domain from a natural repertoire and a beta chain comprising a beta chain variable domain from a natural repertoire, wherein the alpha chain variable domain comprises a TRAV12-2 or a TRAV21 gene product and the beta chain variable domain comprises a TRBV6 gene product and wherein at least a portion of the TCRs comprise an alpha chain variable domain and/or a beta chain variable domain comprising a non-natural mutation.
3. The library according to claim 1 or claim 2, wherein the TRBV6 gene product is a TRBV6-1, a TRBV6-2, a TRBV6-3, a TRBV6-5 or a TRBV6-6 gene product.
4. The library according to any one of claims 1 to 3, wherein the TCR alpha chain variable domain comprises a TRAV12-2 gene product, or a TRAV21 gene product.
5. The library according to any one of claims 1 to 4, wherein the alpha chain variable domain and the beta chain variable domain are displayed as a single polypeptide chain.
6. The library according to any one of claims 1 to 5 wherein the TCRs comprise a non-native disulphide bond or a native disulphide bond between a constant region of the alpha chain and a constant region of the beta chain.
7. The library according to any one of claims 1 to 10 wherein the particles are phage particles, ribosomes, yeast cells or mammalian cells.

8. A non-natural isolated T cell receptor (TCR) comprising a TCR alpha chain variable domain comprising a TRAV12-2 gene product or a TRAV21 gene product and a TCR beta chain variable domain comprising a TRBV6 gene product obtained from a library according to claim 2.
9. Use of a library according to any one of claims 1 to 7, to identify a TCR that specifically binds to a peptide antigen.
10. A method of obtaining a T cell receptor that specifically binds a peptide antigen, comprising screening the library according to any one of claims 1 to 7 with the peptide antigen, the method comprising:
 - a) panning the library using as a target the peptide antigen;
 - b) repeating step a) one or more times;
 - c) screening the phage clones identified in step a) or b); and
 - d) identifying a TCR that specifically binds the peptide antigen.
11. A nucleic acid encoding a TCR alpha chain variable domain and/or a beta chain variable domain of the TCR according to claim 8.
12. A method of making a library of particles, the library displaying a plurality of different TCRs, the method comprising:
 - i) obtaining a plurality of nucleic acids that encode different TRAV12-2 or TRAV21 alpha chain variable domains;
 - ii) obtaining a plurality of nucleic acids that encode different TRBV6 beta chain variable domains;
 - iii) cloning the TRAV12-2 or TRAV21 alpha chain variable domain encoding nucleic acids into expression vectors;
 - iv) cloning the TRBV6 beta chain variable domain encoding nucleic acids into the same or different vectors; and
 - v) expressing the vectors in particles, thereby generating a library consisting essentially of TCRs comprising an alpha chain variable domain and a beta chain variable domain encoded by the nucleic acids.

13. A method of making a library of particles, the library displaying a plurality of different TCRs, the method comprising:
- i) obtaining a plurality of nucleic acids that encode different TRAV12-2 or TRAV21 alpha chain variable domains using primers that hybridise to nucleic acids encoding TRA12-2 or TRAV21 alpha chain variable domains;
 - ii) obtaining a plurality of nucleic acids that encode different TRBV6 beta chain variable domains using primers that hybridise to nucleic acids encoding TRAV6 beta chain variable domains;
 - iii) cloning the TRAV12-2 or TRAV21 alpha chain variable domain encoding nucleic acids into expression vectors;
 - iv) cloning the TRBV6 beta chain variable domain encoding nucleic acids into the same or different vectors; and
 - v) expressing the vectors in particles, thereby generating a library consisting essentially of TCRs comprising an alpha chain variable domain and a beta chain variable domain encoded by the nucleic acids to which said primers hybridise.
14. The method of claim 12 or claim 13, wherein the nucleic acids of step (i) and step (ii) are obtained from a natural repertoire.
15. The method of any one of claims 12 to 14, comprising a further step of introducing non-natural mutations to the nucleic acids, optionally wherein non-natural mutations are introduced to the nucleic acids prior to step iii).
16. A method according to any one of claims 12 to 15, wherein the TCR alpha chain variable domain and the TCR beta chain variable domain are expressed as a single chain polypeptide.
17. The method of obtaining a T cell receptor that specifically binds a peptide antigen, comprising screening the library according to any one of claims 1 to 7 with the peptide antigen.
18. A particle displaying on its surface a TCR according to any one of claims 8 to 17, optionally wherein the particle is a phage particle, a ribosome, a yeast cell or a mammalian cell.