

Claims

1. A multimeric major histocompatibility complex (MHC) comprising
 - two or more MHC molecules linked by a backbone molecule; and
 - at least one nucleic acid molecule linked to said backbone molecule, wherein said at least one nucleic acid molecule comprises a 5' first primer region, a central region (barcode region) and a 3' second primer region, wherein said barcode serves as a specific label unique for said two or more MHC molecules.
2. The multimeric MHC according to claim 1, wherein each barcode have shared amplification ends, enabling amplification of all barcodes simultaneously in a PCR reaction.
3. The multimeric MHC according to any of claims 1-2, wherein the backbone molecule is selected from the group consisting of polysaccharides, including glucans such as dextran, a streptavidin and a streptamer multimer.
4. The multimeric MHC complex according to any of claims 1- 2, wherein the two or more MHC molecules are coupled to the backbone through a streptavidin-biotin binding and/or streptavidin-avidin and/or via the MHC heavy chain and/or via light chain (B2M).
5. The multimeric MHC according to any of the preceding claims, wherein said multimeric MHC is composed of at least four MHC molecules, such as at least eight, such as at least ten, such as 2-30, such as 2-20, such as 2-10, or such as 4-10 or such as 15-30 MHC molecules.
6. The multimeric MHC according to any of the preceding claims, wherein the at least one nucleic acid molecule has a length of 20-200 nucleotides, such as 20-150, such as 20-100 , such as 30-100, such as 30-80, such as 30-50 nucleotides.
7. The multimeric MHC according to any of the preceding claims, wherein the at least one nucleic acid molecule is linked to said backbone via a streptavidin-biotin binding and/or streptavidin-avidin binding.

8. The multimeric MHC according to any of the preceding claims, wherein the at least one nucleic acid molecule comprises or consists of DNA, RNA, and/or artificial nucleotides such as PNA or LNA.
9. The multimeric MHC according to any of the preceding claims, wherein the MHC is selected from the group comprising class I MHC, a class II MHC, a CD1, and other MHC-like molecules.
10. The multimeric MHC according to any of the preceding claims, wherein the backbone further comprises one or more selectable labels, such as one or more labels selected from the group consisting of fluorescent labels, His-tags and metalion tags.
11. A composition comprising a pool of different subsets of multimeric major histocompatibility complexes (multimeric MHC) according to any of claims 1-10, wherein each subset of multimeric MHC has a different peptide decisive for T cell recognition and an associated unique nucleic acid molecule comprising a barcode region.
12. The composition according to claim 11, comprising at least 10 different subsets of multimeric MHCs, such as at least 100, such as at least 500, at least 1000, at least 5000, such as in the range 10-100000, such as 10-50000, such as 10-1000 or such as 50-500 sets of multimeric MHCs.
13. The composition according to claim 11 wherein the primer regions of said unique nucleic acid molecule are identical for each subset of multimeric MHC.
14. A method for detecting one or more antigen responsive cells in a sample comprising:
 - i) providing one or more multimeric MHCs according to any of claims 1-10 or a composition according to any of claims 11-12;
 - ii) contacting said multimeric MHCs with said sample; and
 - iii) detecting binding of the multimeric MHCs to said antigen responsive cells, thereby detecting cells responsive to an antigen present in said one or more multimeric MHCs, wherein said binding is detected by
 - a. amplifying the barcode region of said nucleic acid molecule linked to the one or more multimeric MHCs by PCR, and
 - b. sequencing of said amplified barcode regions.

15. The method according to claim 14, wherein the sample is selected from the group consisting of a blood sample, such as a peripheral blood sample, a blood derived sample, a tissue sample or body fluid, such as spinal fluid or saliva.
16. The method according to any of claims 14-15, wherein said method further comprises one or more steps of sorting or selection of one or more populations of antigen responsive cells before amplification.
17. The method according to any of claims 14-16, wherein said method further comprises one or more steps of single-cell sorting before amplification.
18. The method according to any of claim 14-17, wherein said cell sorting or selection comprises a method selected from the group consisting of flow cytometry such as FACS, magnetic-bead based selection, size-exclusion, gradient centrifugation, column attachment and gel-filtration.
19. The method according to any of claims 14-18, wherein said detection of binding of antigen responsive cells includes comparing measured values to a reference level, such as a negative control and/or total level of response.
20. The method according to any of claims 14-19, wherein the sequencing of said amplified barcode regions comprises deep sequencing, high-throughput sequencing or next generation sequencing.
21. The method according to any of claims 14-20, wherein the antigen specificity of a given sorted single cell is determined in combination with one or more additional single cell properties, such as single cell TCR sequencing.
22. The method according to any of claims 14-21, wherein the affinity and binding motif of a given TCR is determined.
23. The method according to any of claims 14-22, wherein said method further comprises one or more steps of removing unbound MHC multimer in said sample contacted with said multimeric MHCs before amplification, such as by washing and/or spinning.