every possible pMHC combination is extremely high, and since there are few if any 'holes' characterized in the TCR repertoire, it has been posited that a large degree of TCR cross-reactivity is a requirement of functional antigen recognition. How the T cell repertoire can simultaneously be MHC restricted, cross- reactive enough to ensure all potential antigenic challenges can be met, yet still specific enough to avoid aberrant autoimmunity, has remained an open and pressing question in immunology.

[0006] There have been a number of strategies used to determine the specificity of orphan TCRs (Birnbaum et al., (2012) Immunol Rev *250*, 82-101). Mass spectrometry can provide an unbiased method of antigen isolation, but is restricted to experiments requiring large cell numbers, typically 10^7 to 10^9, and the targets must still be presented by the correct HLA. Traditionally, most studies of T cell antigen specificities have involved testing candidate antigens empirically. For example, studies of anti-tumor T cell specificities have correctly postulated that there are productive T cell responses towards neo-antigens. Such studies involve sequencing of tumors to identify mutations, using epitope prediction algorithms to predict immunogenic mutant peptides, and testing for T cell responses directed at these mutant peptides (Kreiter et al., (2015) Nature 520, 692-696; Rajasagi et al., (2014) Blood 124, 453-462; Tran et al., (2014) Science 344, 641-645). Other strategies query established T cell specificities in patients by using pHLA multimers (Bentzen et al., (2016) Nat Biotechnol *34*, 1037-1045; Newell et al., (2013) Nat Biotechnol 31, 623-629).

[0007] High-throughput and sensitive approaches to determining the specificity of 'orphan' TCRs (i.e. TCRs of unknown antigen specificity) that could help uncover potential targets for cancer immunotherapy, autoimmunity, and infection and provide mechanistic insight into disease pathogenesis are of great interest.

SUMMARY

[0001] In one aspect, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequences of SEQ ID NO: 259 or SEQ ID NO: 260, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

[0001a] In one example, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 261 and the amino acid sequence of SEQ ID NO: 262, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279) or VLDFQGQL (SEQ ID NO:280).

[0001b] In one aspect, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequence of SEQ ID NO: 259, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

[0001c] In one example, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 261 and the amino acid sequence of SEQ ID NO: 263, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

[0001d] In one aspect, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequence of SEQ ID NO: 260, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

[0001e] In one example, the present disclosure refers to a T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 495 and the amino acid sequence of SEQ ID NO: 484, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence selected from the group consisting of: LLEDLDWDV (SEQ ID NO: 272), NMEYMTWDV (SEQ ID NO: 273), TMETIDWKV (SEQ ID NO: 274), VLEEVDWLI (SEQ ID NO: 275), KLEQLDWTV (SEQ ID NO: 276), TLEELDWCL (SEQ ID NO: 277), and NVEYYDIKL (SEQ ID NO: 278).

WHAT IS CLAIMED IS:

1. A T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequences of SEQ ID NO: 259 or SEQ ID NO: 260, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

2. The T cell receptor (TCR) or antibody of claim 1, further comprising the amino acid sequence of SEQ ID NO: 261 and the amino acid sequence of SEQ ID NO: 262, wherein the T cell receptor or the antibody further binds to and/or is stimulated by a peptide comprising a sequence of VLDFQGQL (SEQ ID NO:280).

3. A T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequence of SEQ ID NO: 259, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

4. The T cell receptor (TCR) or antibody of claim 1, further comprising the amino acid sequence of SEQ ID NO: 261 and the amino acid sequence of SEQ ID NO: 263.

5. A T cell receptor (TCR) or antibody comprising the amino acid sequence of SEQ ID NO: 258 and the amino acid sequence of SEQ ID NO: 260, wherein the T cell receptor or the antibody binds to and/or is stimulated by a peptide comprising a sequence of MMDFFNAQM (SEQ ID NO: 279).

6. An immune cell engineered to comprise the T cell receptor or the antibody of any one of claims 1-5.

7. The T cell receptor (TCR) of any of claims 1-5, wherein an alpha chain of the TCR comprises SEQ ID NO: 258, and wherein SEQ ID NO: 258 is a sequence of a T cell receptor alpha chain of TCR 2A and TCR 3B.

8. The T cell receptor (TCR) of any of claims 1-5, wherein a beta chain of the TCR comprises SEQ ID NO: 259, and wherein SEQ ID NO: 259 is a sequence of a T cell receptor beta chain of TCR 2A.

9. The T cell receptor (TCR) of any of claims 1-5, wherein a beta chain of the TCR comprises SEQ ID NO: 259, and wherein SEQ ID NO: 260 is a sequence of a T cell receptor beta chain of TCR 3B.

10. The T cell receptor (TCR) of any one of claims 1-5, wherein a complementarity determining region of an alpha chain of the TCR comprises SEQ ID NO: 261, and wherein SEQ ID NO: 261 is a sequence of a complementarity determining region of a TCR alpha chain of TCR 2A and TCR 3B.

11. The T cell receptor (TCR) of any one of claims 1-5, wherein a complementarity determining region of a beta chain of the TCR comprises SEQ ID NO: 262, and wherein SEQ ID NO: 262 is a sequence of a complementarity determining region of a TCR beta chain of TCR 2A.

12. The T cell receptor (TCR) of any one of claims 1-5, wherein a complementarity determining region of a beta chain of the TCR comprises SEQ ID NO: 263, and wherein SEQ ID NO: 263 is a sequence of a complementarity determining region of a TCR beta chain of TCR 3B.