

CLAIMS

1. An HLA class II molecule comprising a DR beta chain, wherein
 - (i) the DR beta chain comprises an amino acid other than leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1;
 - (ii) the DR beta chain comprises an amino acid other than valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1; or
 - (iii) both (i) and (ii).
2. The HLA class II molecule of claim 1, wherein
 - (i) the DR beta chain further comprises an amino acid other than asparagine at a position corresponding to amino acid residue 110 of SEQ ID NO: 1;
 - (ii) the DR beta chain further comprises an amino acid other than isoleucine at a position corresponding to amino acid residue 116 of SEQ ID NO: 1;
 - (iii) the DR beta chain further comprises an amino acid other than serine at a position corresponding to amino acid residue 118 of SEQ ID NO: 1;
 - (iv) the DR beta chain further comprises an amino acid other than proline at a position corresponding to amino acid residue 146 of SEQ ID NO: 1; or
 - (v) any combination of (i) to (v).
3. The HLA class II molecule of claim 1 or 2, wherein
 - (i) the beta chain of the HLA class II molecule comprises a DR2, DR3, DR4, DR5, DR6, DR7, DR8, DR9, DR10, DR11, DR12, DR13, DR14, DR15, or DR16 allele; or
 - (ii) wherein the beta chain of the MHC class II molecule comprises an HLA allele selected from the group consisting of DRB1*01, DRB1*03, DRB1*04, DRB1*07,

DRB1*08, DRB1*09, DRB1*10, DRB1*11, DRB1*12, DRB1*13, DRB1*14, DRB1*15, and DRB1*16.

4. The HLA class II molecule of any one of claims 1 to 3, further comprising an alpha chain.
5. The HLA class II molecule claim 4, wherein the alpha chain of the HLA class II molecule comprises an HLA-DRA1*01 allele.
6. The HLA class II molecule of any one of claims 1 to 5, wherein the beta chain comprises:
 - (a) an amino acid other than leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1;
 - (b) an amino acid other than valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1; and
 - (c) at least two of:
 - (i) an amino acid other than serine at a position corresponding to amino acid residue 118 of SEQ ID NO: 1,
 - (ii) an amino acid other than lysine at a position corresponding to amino acid residue 139 of SEQ ID NO: 1,
 - (iii) an amino acid other than glycine at a position corresponding to amino acid residue 146 of SEQ ID NO: 1,
 - (iv) an amino acid other than threonine at a position corresponding to amino acid residue 157 of SEQ ID NO: 1,
 - (v) an amino acid other than threonine at a position corresponding to amino acid residue 163 of SEQ ID NO: 1, and
 - (vi) an amino acid other than valine at a position corresponding to amino acid residue 164 of SEQ ID NO: 1.

7. The HLA class II molecule of any one of claims 1 to 6, wherein

- (i) the amino acid other than leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1 comprises a hydrophobic side chain;
- (ii) the amino acid other than valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1 comprises a hydrophobic side chain; or
- (iii) both (i) and (ii).

8. The HLA class II molecule of any one of claims 1 to 7, wherein:

- (i) the amino acid other than leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1 is selected from the group consisting of an alanine, a valine, an isoleucine, a methionine, a phenylalanine, a tyrosine, and a tryptophan;
- (ii) the amino acid other than valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1 is selected from an alanine, an isoleucine, a leucine, a methionine, a phenylalanine, a tyrosine, and a tryptophan;
- (iii) the amino acid other than serine at a position corresponding to amino acid residue 118 of SEQ ID NO: 1 is selected from an arginine, a histidine, and a lysine;
- (iv) the amino acid other than lysine at a position corresponding to amino acid residue 139 of SEQ ID NO: 1 is selected from a serine, a threonine, and a glutamine;
- (v) the amino acid other than glycine at a position corresponding to amino acid residue 146 of SEQ ID NO: 1 is selected from a serine, an asparagine, a threonine, and a glutamine;
- (vi) the amino acid other than threonine at a position corresponding to amino acid residue 157 of SEQ ID NO: 1 is selected from an alanine, a valine, an isoleucine, a leucine, a methionine, a phenylalanine, a tyrosine, and a tryptophan;
- (vii) the amino acid other than threonine at a position corresponding to amino acid residue 163 of SEQ ID NO: 1 is selected from an alanine, a valine, an isoleucine, a leucine, a methionine, a phenylalanine, a tyrosine, and a tryptophan;

- (viii) the amino acid other than valine at a position corresponding to amino acid residue 164 of SEQ ID NO: 1 is selected from a serine, an asparagine, a threonine, and a glutamine; or
- (ix) any combination of (i) to (viii).

9. The HLA class II molecule of any one of claims 1 to 8, wherein:

- (i) the amino acid other than leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1 is a tryptophan;
- (ii) the amino acid other than valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1 is a methionine;
- (iii) the amino acid other than serine at a position corresponding to amino acid residue 118 of SEQ ID NO: 1 is a histidine;
- (iv) the amino acid other than lysine at a position corresponding to amino acid residue 139 of SEQ ID NO: 1 is a threonine;
- (v) the amino acid other than glycine at a position corresponding to amino acid residue 146 of SEQ ID NO: 1 is a glutamine;
- (vi) the amino acid other than threonine at a position corresponding to amino acid residue 157 of SEQ ID NO: 1 is an isoleucine;
- (vii) the amino acid other than threonine at a position corresponding to amino acid residue 163 of SEQ ID NO: 1 is a methionine;
- (viii) the amino acid other than valine at a position corresponding to amino acid residue 164 of SEQ ID NO: 1 is a threonine; or
- (ix) any combination of (i) to (vii).

10. The HLA class II molecule of any one of claims 1 to 9, wherein the DR beta chain comprises an amino acid sequence having at least about 80% sequence identity to an amino acid sequence

selected from SEQ ID NOs: 1, 3, 4, and 5; or wherein the DR beta chain comprises the amino acid sequence set forth in SEQ ID NO: 3 or 4.

11. The HLA class II molecule of any one of claims 1 to 9, wherein the beta chain comprises:

- (a) a tryptophan at a position corresponding to amino acid residue 114 of SEQ ID NO: 1;
- (b) a methionine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1; and
- (c) at least two of:
 - (i) a histidine at a position corresponding to amino acid residue 118 of SEQ ID NO: 1,
 - (ii) a threonine at a position corresponding to amino acid residue 139 of SEQ ID NO: 1,
 - (iii) a glutamine at a position corresponding to amino acid residue 146 of SEQ ID NO: 1,
 - (iv) an isoleucine at a position corresponding to amino acid residue 157 of SEQ ID NO: 1,
 - (v) a methionine at a position corresponding to amino acid residue 163 of SEQ ID NO: 1, and
 - (vi) a threonine at a position corresponding to amino acid residue 164 of SEQ ID NO: 1.

12. The HLA class II molecule of any one of claims 1 to 11, wherein the DR beta chain has an increased affinity for a CD4 protein as compared to a reference HLA class II molecule, wherein the reference HLA class II molecule comprises a DR beta chain comprising (i) a leucine at a position corresponding to amino acid residue 114 of SEQ ID NO: 1 and/or (ii) a valine at a position corresponding to amino acid residue 143 of SEQ ID NO: 1

13. The HLA class II molecule of any one of claims 1 to 12, wherein
- (i) the DR beta chain is bound to a membrane of a cell;
 - (ii) the DR beta chain comprises an extracellular domain of a full length DR alpha chain;
 - (iii) the DR beta chain is linked to or associated with an inert particle;
 - (iv) the DR beta chain comprises a signal peptide; or
 - (v) any combination of (i) to (iv).
14. The HLA class II molecule of any one of claims 4 to 13, wherein
- (i) the DR alpha chain is bound to a membrane of a cell;
 - (ii) the DR alpha chain comprises an extracellular domain of a full length DR alpha chain;
 - (iii) the DR alpha chain comprises a signal peptide; or
 - (iv) any combination of (i) to (iii).
15. A nucleic acid molecule encoding the DR beta chain of any one of claims 1 to 14.
16. A vector comprising the nucleic acid molecule of claim 15.
17. A cell comprising the HLA class II molecule of any one of claims 1 to 14, the nucleic acid molecule of claim 15, or the vector of claim 16.

18. A method of identifying a T cell receptor capable of binding an epitope in an HLA class II complex, comprising pulsing the cell of claim 17 with one or more peptide comprising the epitope, and stimulating one or more CD4⁺ T cell with the APC.
19. Use of the HLA class II molecule of any one of claims 1 to 14 in the manufacture of a medicament for treating a disease or condition in a subject in need thereof.
20. A complex comprising the HLA class II molecule of any one of claims 1 to 14 and a peptide, wherein the peptide is selected from the group consisting of NY-ESO1₉₁₋₁₁₀, Bet V ₁₄₂₋₁₅₃, HIV Gag₂₉₃₋₃₁₂, HA₃₀₆₋₃₁₈, Flu-HA₅₋₂₄, Flu-HA₁₁₇₋₁₃₆, Flu-HA₂₃₂₋₂₅₁, Flu-HA₂₆₈₋₂₈₇, Flu-HA₃₀₆₋₃₁₈, HSD17B12₂₂₅₋₂₄₄, LY6K₉₉₋₁₁₈, and any combination thereof.