

CLAIMS

1. An antigen screening library comprising a plurality of Human Leukocyte Antigen (HLA)-antigen polypeptide complexes, the HLA-antigen polypeptide complexes comprising:

a) an HLA polypeptide, the HLA polypeptide comprising a peptide binding cleft;

b) a randomized antigen polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 1 to 209, wherein the randomized antigen polypeptide specifically binds to the peptide binding cleft of the HLA polypeptide; and

c) a Beta-2 (β 2) microglobulin polypeptide;
the plurality of HLA antigen complexes comprises an HLA polypeptide comprising an amino acid sequence at least 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 427 to 455.

2. The antigen screening library of claim 1, wherein the plurality of HLA-antigen complexes comprises an HLA polypeptide selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, B57, C1, C2, C3, C4, C5, C6, C7, C8, and E.

3. The antigen screening library of claim 1, wherein the plurality of HLA-antigen complexes comprises at least five, ten, fifteen, twenty, or twenty-five different HLA polypeptides selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E.

4. The antigen screening library of claim 1, wherein the plurality of HLA-antigen complexes comprises all of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E HLA polypeptides.

~~5. The antigen screening library of claim 1, wherein the plurality of HLA-antigen complexes comprises an HLA polypeptide comprising an amino acid sequence at least 87.5%, 90%, 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 427 to 455.~~

~~6.5.~~ The antigen screening library of any one of claims 1 to 5, wherein the plurality of the HLA-antigen polypeptide complexes comprises at least ~~about~~ 10^5 different HLA-antigen polypeptide complexes comprising at least ~~about~~ 10^5 different randomized antigen polypeptides.

~~7.6.~~ An antigen screening library comprising a plurality of Human Leukocyte Antigen (HLA)-antigen polypeptide complexes, the HLA-antigen polypeptide complexes comprising:

a) an HLA polypeptide, the HLA polypeptide comprising a peptide binding cleft; and

b) a randomized antigen polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 1 to 209, wherein the randomized antigen polypeptide specifically binds to the peptide binding cleft of the HLA polypeptide-, wherein

the plurality of HLA antigen complexes comprises an HLA polypeptide comprising an amino acid sequence at least 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 427 to 455.

~~8.7.~~ The antigen screening library of claim 7, wherein the plurality of HLA-antigen complexes comprises an HLA polypeptide selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, B57, C1, C2, C3, C4, C5, C6, C7, C8, and E.

~~9.8.~~ The antigen screening library of claim 7, wherein the plurality of HLA-antigen complexes comprises at least five, ten, fifteen, twenty, or twenty-five different HLA polypeptides

selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E.

~~10.9.~~ The antigen screening library of claim ~~341~~, wherein the plurality of HLA-antigen complexes comprises all of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E HLA polypeptides.

~~11.~~ The antigen screening library of claim 7, wherein the plurality of HLA-antigen complexes comprises an HLA polypeptide comprising an amino acid sequence at least 87.5%, 90%, 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: ~~427 to 455~~.

~~12.10.~~ The antigen screening library of any one of claims 7 to 11, wherein the plurality of the HLA-antigen polypeptide complexes comprises at least ~~about~~ 10^5 different HLA-antigen polypeptide complexes comprising at least ~~about~~ 10^5 different randomized antigen polypeptides.

~~13.11.~~ An antigen screening library comprising

a) a plurality of antigen polypeptide-Beta-2 ($\beta 2$) microglobulin polypeptide complexes, the antigen polypeptide-Beta-2 ($\beta 2$) microglobulin polypeptide complexes comprising:

- i) a randomized antigen polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 1 to 209, wherein the randomized antigen polypeptide specifically binds to the peptide binding cleft of ~~the~~ HLA polypeptide; and
- ii) a Beta-2 ($\beta 2$) microglobulin polypeptide; and

b) a plurality of HLA polypeptides constitutively expressed by one or more yeast cells and comprising a peptide binding cleft, wherein the plurality of HLA polypeptides comprises an amino acid sequence at least 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 427 to 455.

~~14.12.~~ The antigen screening library of claim 13, wherein the plurality of HLA polypeptides is selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, B57, C1, C2, C3, C4, C5, C6, C7, C8, and E.

~~15.13.~~ The antigen screening library of claim 13, wherein the plurality of HLA polypeptides comprises at least five, ten, fifteen, twenty, or twenty-five different HLA polypeptides selected from the list consisting of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E.

~~16.14.~~ The antigen screening library of claim 13, wherein the plurality of HLA polypeptides comprises all of A3, A11, A23, A24, A26, A30, A31, A33, A68, B7, B8, B15, B27, B40, B44, B51, B53, C1, C2, C3, C4, C5, C6, C7, C8, and E HLA polypeptides.

~~17.—~~ ~~The antigen screening library of claim 13, wherein the plurality of HLA polypeptides comprises an HLA polypeptide comprising an amino acid sequence at least 87.5%, 90%, 95%, 97%, 98%, 99%, or 100% identical to an amino acid sequence set forth in any one of SEQ ID NOs: 427 to 455.~~

~~18.15.~~ The antigen screening library of any one of claims 13 to ~~17~~16, wherein the plurality of the antigen polypeptide-Beta-2 (β 2) microglobulin polypeptide complexes comprises at least ~~about~~ 10^5 different antigen polypeptide-Beta-2 (β 2) microglobulin polypeptide complexes comprising at least ~~about~~ 10^5 different randomized antigen polypeptides.

~~19.16.~~ ~~The method~~ antigen screening library of claim ~~any one of claims 1-15~~, wherein the antigen-peptide binding cleft is a polypeptide antigen that does not naturally occur identical to an amino acid sequence set forth in a human ~~any one of SEQ ID Nos: 251 to 279.~~