We claim:

1. A composition comprising an MHC ligand peptide covalently attached to an MHC class II molecule comprising an MHC class II α chain or a portion thereof and an MHC class II β chain or a portion thereof,

wherein the MHC ligand peptide is covalently attached to the MHC class II molecule by a peptide linker,

wherein the MHC ligand peptide or the peptide linker comprises a first cysteine and the MHC class II molecule comprises a second cysteine, and

wherein the first cysteine and the second cysteine form a disulfide bond such that the MHC ligand peptide is bound in a peptide-binding groove formed by the MHC class II α chain or the portion thereof and the MHC class II β chain or the portion thereof.

2. The composition of claim 1, wherein the MHC class II α chain or the portion thereof comprises an α1 domain, and the MHC class II β chain or the portion thereof comprises a β1 domain.

3. The composition of claim 2, wherein the MHC class II α chain or the portion thereof comprises an MHC class II α chain extracellular domain, and the MHC class II β chain or the portion thereof comprises an MHC class II β chain extracellular domain.

4. The composition of claim 2 or 3, wherein:

(1) the MHC class II α chain or the portion thereof comprises the α1 domain, an α2 domain, a transmembrane domain, and a cytoplasmic domain; and

(2) the MHC class II β chain or the portion thereof comprises the β1 domain, a β2 domain, a transmembrane domain, and a cytoplasmic domain.

5. The composition of any preceding claim, wherein the composition is membrane-anchored or is soluble.

~~6. The composition of any one of claims 1-3, wherein the composition is soluble.~~

~~7~~6. The composition of ~~claim 6~~claim 5, wherein the composition is soluble, and wherein:

(1) the MHC class II α chain or the portion thereof comprises the α1 domain and an α2 domain but does not comprise a transmembrane domain or a cytoplasmic domain; and

(2) the MHC class II β chain or the portion thereof comprises the β1 domain and a β2 domain but does not comprise a transmembrane domain or a cytoplasmic domain.

~~8~~7. The composition of claim ~~6 or 7~~5 or 6, wherein the composition is soluble, and wherein the MHC class II α chain or the portion thereof and the MHC class II β chain or the portion thereof are linked by a Jun-Fos zipper, electrostatic engineering, knobs-into-holes, an immunoglobulin scaffold, an immunoglobulin Fc region, or a linker.

~~9~~8. The composition of claim ~~8~~7, wherein the MHC class II α chain or the portion thereof and the MHC class II β chain or the portion thereof are linked by a Jun-Fos zipper comprising a Jun leucine zipper dimerization motif and a Fos leucine zipper dimerization motif, and ~~wherein~~

wherein the MHC class II α chain or the portion thereof is linked to the Jun leucine zipper dimerization motif and the MHC class II β chain or the portion thereof is linked to the Fos leucine zipper dimerization motif, or the MHC class II α chain or the portion thereof is linked to the Fos leucine zipper dimerization motif and the MHC class II β chain or the portion thereof is linked to the Jun leucine zipper dimerization motif.

~~10~~9. The composition of claim ~~9~~8, wherein the C-terminal end of the MHC class II α chain or the portion thereof is linked to the Jun leucine zipper dimerization motif and the C-terminal end of the MHC class II β chain or the portion thereof is linked to the Fos leucine zipper dimerization motif, or

wherein the C-terminal end of the MHC class II α chain or the portion thereof is linked to the Fos leucine zipper dimerization motif and the C-terminal end of the MHC class II β chain or the portion thereof is linked to the Jun leucine zipper dimerization motif.

~~11~~10. The composition of claims ~~9 or 10~~8 or 9, wherein the MHC class II α chain or the portion thereof is linked to the Jun leucine zipper dimerization motif by an MHC-Jun linker, and the MHC class II β chain or the portion thereof is linked to the Fos leucine zipper dimerization motif by an MHC-Fos linker, or

wherein the MHC class II α chain or the portion thereof is linked to the Fos leucine zipper dimerization motif by the MHC-Fos linker, and the MHC class II β chain or the portion thereof is linked to the Jun leucine zipper dimerization motif by the MHC-Jun linker.

~~12~~11. The composition of claim ~~11~~10, wherein the MHC-Jun linker and the MHC-Fos linker each comprise the sequence set forth in SEQ ID NO: 1.

~~13~~12. The composition of any preceding claim, wherein the MHC ligand peptide:

(I) ~~-~~is about 10 to about 18 amino acids in length, is about 10 to about 15 amino acids in length, or is about 10 to about 12 amino acids in length~~, or~~;

(II) ~~wherein the MHC ligand peptide~~ comprises residues P-1 to P9 or residues P-3 to P9~~.~~;

~~14.~~(III) ~~The composition of any preceding claim, wherein the MHC ligand peptide~~ is an antigenic MHC ligand peptide~~.~~; or

~~15.~~(IV) ~~The composition of any preceding claim, wherein the MHC ligand peptide~~ is associated with a T-cell-mediated disease.

~~16~~13. The composition of any preceding claim, wherein:

(I) the peptide linker linking the MHC ligand peptide to the MHC class II molecule is a flexible linker~~.~~;

~~17.~~(II) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises one or more flexible amino acids and one or more polar amino acids~~.~~;

~~18.~~(III) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule does not comprise any charged amino acids~~.~~;

~~19.~~(IV) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises a cleavage site~~.~~

~~20. The composition of claim 19~~, wherein the cleavage site is a tobacco etch virus (TEV) protease cleavage site~~.~~;

~~21.~~(V) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule is non-immunogenic~~.~~;

~~22.~~(VI)~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule is connected to the N-terminal end of the MHC class II β chain or the portion thereof~~.~~;

~~23.~~(VII) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule is connected to the N-terminal end of the MHC class II α chain or the portion thereof~~.~~;

~~24.~~(VIII) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule is at least about 9 amino acids in length~~.~~;

~~25.~~(IX)~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule is between about 9 and about 50 amino acids in length~~.~~; or

~~26.~~(X) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises 2-4 repeats of the sequence set forth in SEQ ID NO: 4.

~~27~~14. The composition of any preceding claim, wherein:

(I) the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises the first cysteine~~.~~

~~28. The composition of claim 27~~, wherein the first cysteine is the only cysteine in the peptide linker linking the MHC ligand peptide to the MHC class II molecule~~.~~

~~29. The composition of claim 27 or 28~~, and wherein the first cysteine is in the first four amino acids of the peptide linker linking the MHC ligand peptide to the MHC class II molecule~~.~~; or

~~30.~~(II) ~~The composition of any preceding claim, wherein~~ the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises 2-4 repeats of the sequence set forth in SEQ ID NO: 4, wherein one amino acid in one of the repeats is mutated to cysteine~~.~~

~~31. The composition of claim 30~~, and wherein the peptide linker linking the MHC ligand peptide to the MHC class II molecule comprises the sequence set forth in SEQ ID NO: 21.

~~32~~15. The composition of any one of claims 1-~~26~~13, wherein the MHC ligand peptide comprises the first cysteine~~.~~

~~33. The composition of claim 32~~, and wherein the first cysteine faces away from an epitope formed by the composition.

~~34~~16. The composition of any preceding claim, wherein the second cysteine is in the MHC class II α chain or the portion thereof~~.~~

~~35. The composition of claim 34~~, and wherein the peptide linker linking the MHC ligand peptide to the MHC class II molecule is connected to the N-terminal end of the MHC class II β chain or the portion thereof.

~~36~~17. The composition of any preceding claim, wherein the second cysteine is not present in a wild type MHC class II molecule corresponding to the MHC class II molecule in the composition~~.~~

~~37. The composition of claim 36~~, and wherein the second cysteine is in place of a non-cysteine amino acid in the corresponding wild type MHC class II molecule.

~~38~~18. The composition of claim ~~37~~17, wherein the second cysteine is in the MHC class II α chain or the portion thereof, and

wherein the second cysteine is at a position corresponding to position 101 in the sequence set forth in SEQ ID NO: 49 when the MHC class II α chain or the portion thereof is optimally aligned with SEQ ID NO: 49.

~~39~~19. The composition of any preceding claim, wherein the MHC class II molecule lacks a cysteine present in a corresponding wild type MHC class II molecule~~.~~

~~40. The composition of claim 39~~, and wherein the cysteine present in the corresponding wild type MHC class II molecule has been replaced with an alanine or a glutamine in the MHC class II molecule in the composition.

~~41~~20. The composition of any one of claims 1-~~38~~18, wherein the MHC class II α chain or the portion thereof lacks a cysteine present in a corresponding wild type MHC class II α chain~~.~~

~~42. The composition of claim 41~~, and wherein the cysteine present in the corresponding wild type MHC class II α chain has been replaced with an alanine or a glutamine in the MHC class II α chain or the portion thereof in the composition.

~~43~~21. The composition of claim ~~41 or 42~~20, wherein the cysteine in the corresponding wild type MHC class II α chain is at a position corresponding to position 70 in the sequence set forth in SEQ ID NO: 49 when the MHC class II α chain or the portion thereof is optimally aligned with SEQ ID NO: 49.

~~44~~22. The composition of any preceding claim, wherein the composition further comprises one or more immunostimulatory molecules.

~~45~~23. The composition of claim ~~44~~22, wherein:

(I) the one or more immunostimulatory molecules comprise a pan-DR-binding epitope (PADRE) and/or a peptide from lymphocytic choriomeningitis virus (LCMV)~~.~~;

~~46.~~(II) ~~The composition of claim 44 or 45, wherein~~ the one or more immunostimulatory molecules are directly or indirectly covalently linked to the MHC class II molecule~~.~~; or

~~47.~~(III) ~~The composition of any one of claims 44-46, wherein~~ the one or more immunostimulatory molecules are directly or indirectly covalently linked to the MHC class II α chain or the portion thereof and/or the MHC class II β chain or the portion thereof.

~~48~~24. The composition of any preceding claim, wherein the MHC class II molecule is a human MHC class II molecule.

~~49~~25. The composition of claim ~~48~~24, wherein the human MHC class II molecule is selected from the group consisting of HLA-DQ, HLA-DR, and HLA-DP.

~~50~~26. The composition of claim ~~49~~25, wherein the human MHC class II molecule is an HLA-DQ2 molecule~~.~~

~~51. The composition of claim 49,~~ or wherein the human MHC class II molecule is an HLA-DR2 molecule.

~~52~~27. The composition of any preceding claim, wherein the MHC class II α chain or the portion thereof comprises an MHC class II α chain extracellular domain, and the MHC class II β chain or the portion thereof comprises an MHC class II β chain extracellular domain,

wherein the peptide linker linking the MHC ligand peptide to the MHC class II molecule is a flexible linker between about 9 and about 50 amino acids in length that comprises the first cysteine and is connected to the N-terminal end of the MHC class II β chain or the portion thereof,

wherein the second cysteine is in the MHC class II α chain or the portion thereof and is not present in a wild type MHC class II molecule corresponding to the MHC class II molecule in the composition, and

wherein the MHC class II molecule lacks a cysteine present in a corresponding wild type MHC class II molecule.

~~53~~28. The composition of claim ~~52~~27, wherein the composition is soluble,

wherein the MHC class II α chain or the portion thereof comprises the α1 domain and an α2 domain but does not comprise a transmembrane domain or a cytoplasmic domain,

wherein the MHC class II β chain or the portion thereof comprises the β1 domain and a β2 domain but does not comprise a transmembrane domain or a cytoplasmic domain, and

wherein the MHC class II α chain or the portion thereof and the MHC class II β chain or the portion thereof are linked by a Jun-Fos zipper comprising a Jun leucine zipper dimerization motif and a Fos leucine zipper dimerization motif.

~~54~~29. The composition of claim ~~52-~~27 or ~~53~~28, wherein the second cysteine is at a position corresponding to position 101 in the sequence set forth in SEQ ID NO: 49 when the MHC class II α chain or the portion thereof is optimally aligned with SEQ ID NO: 49, and

wherein the cysteine in the corresponding wild type MHC class II molecule is at a position corresponding to position 70 in the sequence set forth in SEQ ID NO: 49 when the MHC class II α chain or the portion thereof is optimally aligned with SEQ ID NO: 49.

~~55~~30. The composition of any one of claims ~~52-54~~27-29, wherein the MHC class II molecule is a human MHC class II molecule is selected from the group consisting of HLA-DQ, HLA-DP, and HLA-DR.

~~56~~31. The composition of claim ~~55~~30, wherein the human MHC class II molecule is HLA-DQ.

~~57~~32. A nucleic acid encoding the composition of any preceding claim.

~~58~~33. Use ~~A method of eliciting an immune response in a subject, comprising administering to the subject an effective amount~~ of the composition of any one of claims 1-~~56~~ 31 or a nucleic acid encoding the composition in the manufacture of a medicament for treating an autoimmune disease, wherein the medicament is an immunotherapy drug.

~~59. A method of generating an antigen-binding protein that specifically binds an antigenic composition comprising an MHC ligand peptide covalently attached to an MHC class II molecule, comprising:~~

~~(a) immunizing a non-human animal with the composition of any one of claims 1-56 or a nucleic acid encoding the composition; and~~

~~(b) maintaining the non-human animal in conditions sufficient for the non-human animal to mount an immune response to the composition.~~

~~60. A method of generating an antigen-binding protein, comprising:~~

~~(a) immunizing a non-human animal with the composition of any one of claims 1-56 or a nucleic acid encoding the composition; and~~

~~(b) maintaining the non-human animal in conditions sufficient for the non-human animal to mount an immune response to the composition.~~

34. The use of the composition or nucleic acid encoding the composition according to claim 33, wherein the immunotherapy drug is an antigen-binding protein.

~~61~~35. The use of the composition or nucleic acid encoding the composition according to claim 34~~method of claim 60~~, wherein the antigen-binding protein specifically binds ~~an~~ the ~~antigenic~~ composition ~~comprising an MHC ligand peptide covalently attached to an MHC class II molecule~~.