

WHAT IS CLAIMED IS:

Claims

1. 1 A modified HCV E2 ectodomain polypeptide, comprising an engineered E2 ectodomain sequence that contains ~~at least one modification selected from (a)~~ a truncation in the VR2 disordered region ~~and (b) a deletion in, wherein the β -sandwich loop connecting β sheets 6 and 7 of the β -sandwich domain~~ truncated VR2 disordered region contains less than 20 amino acid residues.
2. 1 The modified HCV E2 ectodomain polypeptide of claim ~~1,1~~, wherein the ~~engineered E2 ectodomain sequence comprises SEQ ID NO:4, a conservatively modified variant or a substantially identical sequence thereof~~ VR2 disordered region corresponds to amino acid residues 452-494 of the full length polyprotein of HCV H77 isolate.
3. 2,2 The modified HCV E2 ectodomain polypeptide of claim ~~2,2~~, wherein truncation of the VR2 disordered region comprises replacing residues 41-61 of SEQ ID NO:4, CPERLASC GSSGCWHYPPRPC (SEQ ID NO:6), with CPERASGHYPPRPC (SEQ ID NO:10).
4. 2,2 The modified HCV E2 ectodomain polypeptide of claim ~~2,2~~, wherein truncation of the VR2 disordered region comprises replacing residues 41-61 of SEQ ID NO:4, CPERLASC GSSGCWHYPPRPC (SEQ ID NO:6), with a sequence set forth in CXXXXXXHYPPRPC (SEQ ID NO:8) or CXXXXXXHYPPRPC (SEQ ID NO:9), wherein X is any amino acid residue.
5. 4,4 The modified HCV E2 ectodomain polypeptide of claim ~~4,4~~, wherein XXXXXX in SEQ ID NO:8 is QNWDEP (SEQ ID NO:11), KVNIDP (SEQ ID NO:12), EKVEEL (SEQ ID NO:13), PDENMK (SEQ ID NO:14), or KREEKM (SEQ ID NO:15).

6. The modified HCV E2 ectodomain polypeptide of claim ~~4~~, wherein XXXXX in SEQ ID NO:9 is PKTEV (SEQ ID NO:16), KRVDI (SEQ ID NO:17), PSDMV (SEQ ID NO:18), PNEEE (SEQ ID NO:19), or KKEIR (SEQ ID NO:20).

7. The modified HCV E2 ectodomain polypeptide of claim ~~2~~, 1, further comprising a deletion in the β -sandwich loop connecting β sheets 6 and 7 of the β -sandwich domain.

8. The modified HCV E2 ectodomain polypeptide of claim 7, wherein deletion of the β -sandwich loop sequence (SEQ ID NO:21) comprises deletion of one or more residues that form the tip of the β -sandwich loop.

9. The modified HCV E2 ectodomain polypeptide of claim ~~7~~, 8, wherein residues that form the tip of the β -sandwich loop are residues 543-546 from ~~SEQ ID NO:4~~ HCV genotype 1a H77 isolate polypeptide sequence.

10. The modified HCV E2 ectodomain polypeptide of claim ~~7~~, 8, wherein residues 543-546 from ~~SEQ ID NO:4~~ RRPLHCV genotype 1a H77 isolate polypeptide sequence, RPPL (SEQ ID NO:22), are deleted.

~~1. —~~ 11. The modified HCV E2 ectodomain polypeptide of claim ~~1~~, comprising both truncation in the VR2 disordered region and deletion in the β -sandwich loop.

~~The modified HCV E2 ectodomain polypeptide of claim 10,~~ 7, comprising an amino acid sequence as set forth in any one of SEQ ID NOs:26-38, a conservatively modified variant or a substantially identical sequence thereof.

12. A polynucleotide encoding the modified HCV E2 ectodomain polypeptide of claim ~~1~~, 1.

13. A pharmaceutical composition, comprising the modified HCV E2 ectodomain polypeptide of claim ~~1~~, 1, and a pharmaceutically acceptable carrier.

~~A vaccine~~

14. An immunogenic composition, comprising a modified HCV E2 ectodomain polypeptide of claim 11 that is displayed on the surface of a self-assembling nanoparticle.

15. The ~~vaccine~~immunogenic composition of claim 14,14, wherein the C-terminus of the modified HCV E2 ectodomain polypeptide is fused to the N-terminus of a subunit of the self-assembling nanoparticle via a linker sequence.

16. The ~~vaccine~~immunogenic composition of claim 15,15, wherein the linker sequence comprises (GGGS)₂ (SEQ ID NO:42).

17. The ~~vaccine~~immunogenic composition of claim 14,14, wherein the modified HCV E2 ectodomain polypeptide comprises an amino acid sequence as set forth in any one of SEQ ID NOs:26-38, ~~a conservatively modified variant or a substantially identical sequence thereof.~~

18. The ~~vaccine~~immunogenic composition of claim 14,14, wherein subunit of the self-assembling nanoparticle comprises the polypeptide as shown in SEQ ID NO:39 (E2p), SEQ ID NO:40 (I3-01), or SEQ ID NO:41 (ferritin), ~~a conservatively modified variant or a substantially identical sequence thereof.~~

19. A polynucleotide, encoding a fusion protein comprising a modified HCV E2 ectodomain polypeptide of claim 11 and a self-assembling nanoparticle subunit, wherein the modified HCV E2 ectodomain polypeptide is fused at its C-terminus to the N-terminus of the self-assembling nanoparticle subunit.

20. A pharmaceutical composition, comprising the ~~vaccine~~immunogenic composition of claim 14,14, and a pharmaceutically acceptable carrier.

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21. A pharmaceutical composition comprising a therapeutically effective amount of the immunogenic composition of claim 14 for use in a method of treating ~~or preventing~~ HCV

infection in a subject, ~~comprising administering~~ wherein the pharmaceutical composition is to be administered to the subject, thereby treating HCV infection in the subject.

22 Use of a pharmaceutical composition comprising a therapeutically effective amount of the vaccineimmunogenic composition of claim 14, thereby treating or preventing 14 in the manufacture of a medicament for the treatment of HCV infection in thea subject-, wherein the pharmaceutical composition is to be administered to the subject, thereby treating HCV infection in the subject.