

Claims

1. An isolated antigen binding protein (ABP) that specifically binds human NRP-1 (hNRP-1; SEQ ID NO:130), wherein the ABP comprises the following six CDR sequences:

- (a) a CDR-H3 having the sequence set forth in SEQ ID NO:47;
- (b) a CDR-H2 having the sequence X_1 ISGSGGX₂TYYADSVX₃G, wherein X_1 is I or A, X_2 is S or A, and X_3 is K or E, as set forth in SEQ ID NO:136;
- (c) a CDR-H1 having the sequence FTFX₁SX₂AMV, wherein X_1 is A, K, or S and X_2 is Y or V, as set forth in SEQ ID NO:137;
- (d) a CDR-L3 having the sequence set forth in SEQ ID NO:81;
- (e) a CDR-L2 having the sequence set forth in SEQ ID NO:71; and
- (f) a CDR-L1 having the sequence set forth in SEQ ID NO:63.

2. The ABP of claim 1, wherein the ABP comprises:

- (a) a CDR-H3 of SEQ ID NO:47, a CDR-H2 of SEQ ID NO:27, a CDR-H1 of SEQ ID NO:12, a CDR-L3 of SEQ ID NO:81, a CDR-L2 of SEQ ID NO:71, and a CDR-L1 of SEQ ID NO:63;
- (b) a CDR-H3 of SEQ ID NO:47, a CDR-H2 of SEQ ID NO:28, a CDR-H1 of SEQ ID NO:13, a CDR-L3 of SEQ ID NO:81, a CDR-L2 of SEQ ID NO:71, and a CDR-L1 of SEQ ID NO:63;
- (c) a CDR-H3 of SEQ ID NO:47, a CDR-H2 of SEQ ID NO:29, a CDR-H1 of SEQ ID NO:14, a CDR-L3 of SEQ ID NO:81, a CDR-L2 of SEQ ID NO:71, and a CDR-L1 of SEQ ID NO:63; or
- (d) a CDR-H3 of SEQ ID NO:47, a CDR-H2 of SEQ ID NO:30, a CDR-H1 of SEQ ID NO:14, a CDR-L3 of SEQ ID NO:81, a CDR-L2 of SEQ ID NO:71, and a CDR-L1 of SEQ ID NO:63.

3. The ABP of claim 2, wherein:

- (a) the ABP of claim 2(a) comprises a V_H sequence of SEQ ID NO:92 and a V_L sequence of SEQ ID NO:104;
- (b) the ABP of claim 2(b) comprises a V_H sequence of SEQ ID NO:93 and a V_L sequence of SEQ ID NO:104;
- (c) the ABP of claim 2(c) comprises a V_H sequence of SEQ ID NO:94 and a V_L sequence of SEQ ID NO:104;
- (d) the ABP of claim 2(d) comprises a V_H sequence of SEQ ID NO:95 and a V_L sequence of SEQ ID NO:104; or

(e) the ABP of claim 2(d) comprises a V_H sequence of SEQ ID NO:96 and a V_L sequence of SEQ ID NO:104.

4. The ABP of claim 2, wherein the ABP of claim 2(d) comprises a V_H sequence of SEQ ID NO:96 and a V_L sequence of SEQ ID NO:104.

5. The ABP of claim 3, wherein:

(a) the ABP of claim 2 (a) comprises a heavy chain of SEQ ID NO:114 and a light chain of SEQ ID NO:126;

(b) the ABP of claim 2(b) comprises a heavy chain of SEQ ID NO:115 and a light chain of SEQ ID NO:126;

(c) the ABP of claim 2(c) comprises a heavy chain of SEQ ID NO:116 and a light chain of SEQ ID NO:126;

(d) the ABP of claim 2(d) comprises a heavy chain of SEQ ID NO:117 and a light chain of SEQ ID NO:126; or

(e) the ABP of claim 2(d) comprises a heavy chain of SEQ ID NO:118 and a light chain of SEQ ID NO:126.

6. The ABP of claim 3, wherein the ABP of claim 2(d) comprises a heavy chain of SEQ ID NO:118 and a light chain of SEQ ID NO:126.

7. The ABP of claim 3, wherein the ABP of claim 2(d) consists of a heavy chain of SEQ ID NO:118 and a light chain of SEQ ID NO:126.

8. The ABP of claim 1, wherein the ABP competes for binding to human NRP-1 with an antibody selected from the group consisting of MAB1, MAB2, MAB3, MAB4, MAB5, MAB6, MAB7, MAB8, MAB9, MAB10, MAB11, MAB12, MAB13, MAB14, and MAB15.

9. The ABP of claim 1, wherein the ABP specifically antagonizes human NRP-1 binding to a neuropilin-1 ligand and modulating an immune response in a human.

10. The ABP of claim 1, wherein the ABP specifically binds one or more residues on human NRP-1(SEQ ID NO:130) chosen from the group consisting of specifically binds one or more of human NRP-1 residues selected from the group consisting of Y297, T316, D320, E348, T349, K350, K351, K352, Y353, Y354, E412, T413, G414, and I415.

11. The ABP of claim 1, wherein the ABP specifically binds to NRP-1 from humans, mice, and cynomolgus monkeys.
12. The ABP of claim 1, wherein the ABP binds to a different epitope on human NRP-1 than the epitope on human NRP-1 to which SEC10 binds.
13. The ABP of claim 1, wherein the ABP specifically binds to the b1 domain of human NRP-1.
14. The ABP of claim 1, wherein the ABP antagonizes the interaction between a human NRP-1 polypeptide and one or both of a human vascular endothelial cell growth factor (VEGF) polypeptide and a human semaphorin (SEMA) polypeptide.
15. The ABP of claim 14, wherein the human semaphorin polypeptide is a human SEMA3 polypeptide.
16. The ABP of claim 1, wherein the ABP does not substantially bind platelets.
17. The ABP of claim 1, wherein the ABP inhibits Treg suppression in a human subject.
18. The ABP of claim 1, wherein the ABP comprises two antigen-binding domains.
19. The ABP of claim 1, wherein the ABP comprises a CDR-H3 of SEQ ID NO:47, a CDR-H2 of SEQ ID NO:30, a CDR-H1 of SEQ ID NO:14, a CDR-L3 of SEQ ID NO:81, a CDR-L2 of SEQ ID NO:71, and a CDR-L1 of SEQ ID NO:63.
20. A pharmaceutical composition comprising an ABP of claim 1 and a pharmaceutically acceptable excipient.