Claims

1. A soluble composition capable of targeted delivery of a complement modulator to sites of complement system activation comprising a construct, wherein the construct comprises:

(a) a complement receptor 2 (CR2) portion comprising at least the first two N-terminal short consensus repeat (SCR) domains of CR2; and

(b) a complement modulator portion;

wherein the CR2 portion contains at least one amino acid substitution selected from the group consisting of N11 and Y64 ~~N11, Y64, S42, and K50~~ of SEQ ID NO: 2 that decreases, ~~and wherein the construct exhibits decreased~~ binding affinity of the CR2 portion for EBV gp350 relative to a construct in which the CR2 portion has the sequence of SEQ ID NO: 2, or the CR2 portion contains at least one amino acid substitution selected from the group consisting of S42 and K50 of SEQ ID NO: 2 that decreases binding affinity of the CR2 portion for ~~and/or~~ Interferon-alpha (IFNα) relative to a construct in which the CR2 portion has the sequence of SEQ ID NO: 2~~but comparable binding affinity for at least one of complement component 3 (C3) proteolytic fragments compared to a construct in which the CR2 portion does not contain the at least one amino acid substitution.~~

2. The soluble composition of claim 1, wherein the at least one amino acid to be substituted is N11 or Y64 of SEQ ID NO: 2 and the construct exhibits decreased binding affinity for EBV gp350.

3. The soluble composition of claim 1, wherein the at least one amino acid to be substituted is S42 or K50~~K40~~ of SEQ ID NO: 2 and the construct exhibits decreased binding affinity for IFNα.

4. The soluble composition of claim 1, wherein the construct is a fusion protein with or without a linker.

5. The soluble composition of claim 1, wherein the CR2 portion comprises at least the first three N-terminal SCR domains of the human CR2 protein (amino acids 23 through 212 of SEQ ID NO: 1), at least the first four N-terminal SCR domains of the human CR2 protein (amino acids 23 through 271 of SEQ ID NO: 1), or the full-length human CR2 (SEQ ID NO: 1).

30. The soluble composition of any one of claims 1 to 29, wherein the at least one of C3 proteolytic fragments is selected from the group consisting of: C3d, iC3dg, C3dg, and a cell-bound fragment of C3b that binds to CR2.

31. The soluble composition of any one of claims 1 to 30, wherein the at least one amino acid substitution in the CR2 portion of the construct is a substitution to the amino acid alanine.

32. The soluble composition of any one of claims 1 to 31 formulated for intravenous, intraperitoneal, or intraocular injection or oral administration.

33. The soluble composition of any one of claims 1 to 32 for treating a complement-associated disease or condition.

34. A method for making a construct that selectively binds to one or more C3 proteolytic fragments but does not selectively bind to EBV gp350 or IFNα, wherein the method comprises:

(a) mutating one or more amino acids in a complement receptor 2 (CR2) portion of the construct at a position selected from the group consisting of: N11 and Y64 of SEQ ID NO:2, wherein the construct exhibits decreased binding affinity of the CR2 portion for EBV gp350 relative to a construct in which the CR2 portion has the sequence of SEQ ID NO: 2; orand

(b) mutating one or more amino acids in a complement receptor 2 (CR2) portion of the construct at a position selected from the group consisting of: S42 and K50 of SEQ ID NO:2, wherein the construct exhibits decreased binding affinity of the CR2 portion for IFNα relative to a construct in which the CR2 portion has the sequence of SEQ ID NO: 2,

wherein the construct comprises:

(i) a complement receptor 2 (CR2) portion comprising at least the first two N-terminal SCR domains of the CR2 protein; and

(ii) a complement modulator portion.

35. The method of claim 34, wherein the one or more mutations in the complement receptor 2 (CR2) portion of the construct are mutations to the amino acid alanine.

36. The method of claim 34, wherein the method further comprises mutating one or more amino acids in the complement receptor 2 (CR2) portion of the construct at a position selected from the group consisting of: ~~R13, Y16, A22, R28, S32,~~ R36, K41, and ~~K48, K57,~~ K67, ~~Y68, R83, G84, and R89~~ of SEQ ID NO:2.

37. A method of reducing the binding affinity of a construct for EBV-gp350 but not for at least one of C3 proteolytic fragments, wherein the construct comprises:

(a) a complement receptor 2 (CR2) portion comprising at least the first two N-terminal short consensus repeat (SCR) domains of CR2; and

(b) a complement modulator portion,

said method comprising mutating at least one amino acid residue of the CR2 portion selected from the group consisting of N11 and Y64 of SEQ ID NO:2.

38. A method of reducing the binding affinity of a construct for IFNα but not for at least one of C3 proteolytic fragments, wherein the construct comprises:

(a) a complement receptor 2 (CR2) portion comprising at least the first two N-terminal short consensus repeat (SCR) domains of CR2; and

(b) a complement modulator portion,

said method comprising mutating at least one amino acid residue of the CR2 portion selected from the group consisting of S42 and K50 of SEQ ID NO:2.

39. Use of the soluble composition of any one of claims 1 to 32 for the preparation of a medicament for treating a subject having a complement-associated disease or condition.