THERAPEUTIC COMPOSITIONS AND METHODS FOR AGE-RELATED MACULAR DEGENERATION

CLAIM OF PRIORITY

[0001] This patent application claims priority to U.S. provisional patent application no. 63/389,355, entitled "THERAPEUTIC COMPOSITIONS AND METHODS FOR AGE-RELATED MACULAR DEGENERATION," and filed on July 14, 2022, herein incorporated by reference in its entirety.

INCORPORATION BY REFERENCE

[0002] All publications and patent applications mentioned in this specification are herein incorporated by reference in their entirety to the same extent as if each individual publication or patent application was specifically and individually indicated to be incorporated by reference.

BACKGROUND

[0003] Age-related macular degeneration (AMD) is a chronic metabolic inflammatory disease of the eye. AMD is the leading cause of blindness in people over 55 years old and has a relatively high prevalence in the US (e.g., 8.7%) and worldwide. Further, this problem is expected to increase as global populations age. Although AMD is categorized into a variety of types (e.g., early, intermediate, wet and dry), the majority of AMD cases are considered "Dry" AMD, for which there is only one approved therapy.

[0004] There are believed to be many associated factors that may contribute to AMD. For example, extracellular deposits of lipids (drusen) are the first pathological signs of AMD. Drusen disrupt and stress retinal pigment epithelium (RPE) cells, the loss of which leads to photoreceptor degeneration and the severe later stages of the disease, including geographic atrophy (GA) and neovascular AMD (nvAMD). There is a need for therapies that may treat both dry and wet AMD.

SUMMARY

[0005] Described herein are engineered polypeptides. In particular, engineered therapeutic peptides including short consensus repeat (SCR) regions of complement factor H (or CFH) and SCR regions of Factor H-like protein 1 (or FHL) peptides (e.g., "CFH-FHL" peptides) that may provide one or more therapeutic benefits, as described herein.

[0005a] In an aspect, the present invention provides the use of an engineered polypeptide comprising a first peptide sequence of 80% or more homology to SEQ ID NO: 3, a second peptide sequence of 80% or more homology to SEQ ID NO: 17, a linker domain separating the

first peptide sequence from the second peptide sequence, a first junction region between the first peptide sequence and the linker domain and a second junction region between the second peptide sequence and the linker domain, for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005b] In an aspect, the present invention provides the use of an engineered polypeptide having a sequence of 80% or more homology to SEQ ID NO: 131 for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005c] In an aspect, the present invention provides the use of an engineered polypeptide having a sequence of 90% or more homology to SEQ ID NO: 131 for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005d] In an aspect, the present invention provides the use of an engineered polypeptide having a sequence of SEQ ID NO: 131 for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005e] In an aspect, the present invention provides the use of an engineered polypeptide comprising the sequence of SEQ ID NO: 21 having one or more amino acid substitutions selected from the group consisting of: L6S, L6T, A289S, A289T, Y380S, Y380T, T16N, D258N, Y334N, D21N, G286N, H355N, A407N, R426N, S428N, G431N, G436N, G441N and G442N for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005f] In an aspect, the present invention provides the use of an engineered polypeptide comprising the sequence of SEQ ID NO: 21 having one or more amino acid substitutions selected from the group consisting of: L6S, L6T, A289S, A289T, Y380S, Y380T, T16N, D258N, Y334N, D21N, G286N, H355N, A407N, R426N or S428N for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005g] In an aspect, the present invention provides the use of an engineered polypeptide comprising the sequence of SEQ ID NO: 125, SEQ ID NO: 131, or SEQ ID NO: 132 for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005h] In an aspect, the present invention provides the use of an engineered polypeptide comprising: a first peptide sequence of one of: SEQ ID NO: 3, SEQ ID NO: 139 or SEQ ID NO: 140; a second peptide sequence of SEQ ID NO: 17, and a linker domain between the first peptide sequence and the second peptide sequence comprising the sequence of: SEQ ID NO: 138 for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005i] In an aspect, the present invention provides the use of an engineered polypeptide comprising a first peptide sequence of SEQ ID NO: 3, a second peptide sequence of SEQ ID NO:

17, and a linker domain separating the first peptide sequence from the second peptide sequence for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005j] In an aspect, the present invention provides the use of an engineered polypeptide comprising a first peptide sequence of 80% or more homology to SEQ ID NO: 3, a second peptide sequence of 80% or more homology to SEQ ID NO: 17, a linker domain separating the first peptide sequence from the second peptide sequence, for the manufacture of a medicament for treating age-related macular degeneration (AMD).

[0005k] In an aspect, the present invention provides the use of a pharmaceutical composition comprising the polypeptide as defined in any one of the above aspects, and a pharmaceutically acceptable excipient for the manufacture of a medicament for the prevention or treatment of age-related macular degeneration (AMD) in a patient.

[0006] In general, an engineered polypeptide may be used to treat age-related macular degeneration (AMD). The engineered polypeptide may have a first peptide sequence of 80% or more homology to SEQ ID NO: 3 (the CFH SCR1-7 N-Terminal Domain), a second peptide