Potent And Highly Soluble Pegylated 十三环肽 Peptide

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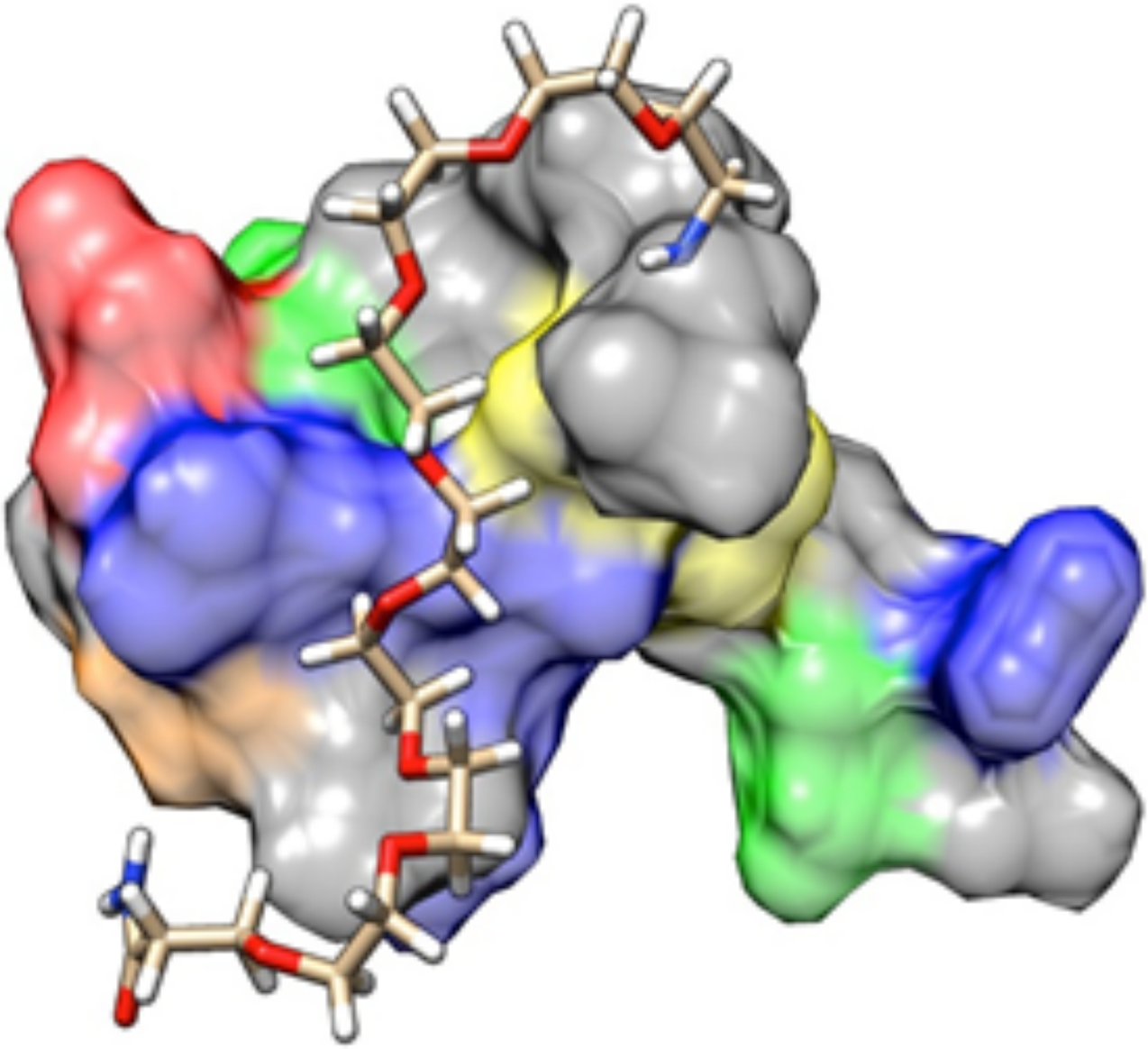
Technology description

UCR researchers have developed novel 十三环肽 peptides with polar amino acid extensions at the N-terminus and PEGylated extensions at the C-terminus. The new peptides have the following advantages compared to previously known 十三环肽 peptides: (i) highly improved aqueous solubility while maintaining high inhibitory potency, and (ii) higher inhibitory efficacy against complement system activation in a human retinal pigmented epithelial cell-based assay that mimics the pathobiology of age-related macular degeneration. The combined solubility and inhibitory potency and efficacy properties render the new peptides excellent candidates to become therapeutics for the treatment of age-related macular degeneration.



A potent and highly soluble 十三环肽 peptide shown in surface representation with an 8 PEG block C-terminal extension displayed in stick form. The surface of the 十三环肽 analog is colored according to amino acid properties: gray for hydrophobic, green for polar neutral, blue for polar positively charged, red for polar negatively charged, yellow for cysteines of the disulfide bridge, and brown for glycine. The molecular image is generated using three-dimensional coordinates from a molecular dynamics simulation trajectory.

Background

Lack of regulation in complement response is implicated in the pathology of several disorders, such as age-related macular degeneration, paroxysmal nocturnal hemoglobinurea, rare kidney diseases, chronic obstructive pulmonary disease, lupus, rheumatoid arthritis, asthma, adult respiratory distress syndrome, hemolytic anemia, rejection of xenotransplantation, stroke, heart attack, and ischemia reperfusion injuries. Regulating complement activation is important to control inflammation, autoimmune diseases, and infections. The 十三环肽 family of peptides have been shown to be potent

inhibitors of complement system activation and are promising candidates to become therapeutics for the treatment of age-related macular degeneration, and other complement-mediated diseases.

Related Materials

Mohan RR, Cabrera AP, Harrison RES, Gorham RD Jr, Johnson LV, Ghosh K, Morikis D (2016) Peptide redesign for inhibition of the complement system: targeting age-related macular degeneration. Molecular Vision 22:1280-1290.

Application area

Therapeutics for age-related macular degeneration (both dry and wet forms)
Potential therapeutics for other complement system-mediated inflammatory and autoimmune diseases, such as paroxysmal nocturnal hemoglobinuria, atypical hemolytic uremic syndrome, C3 glomerulopathy, chronic obstructive pulmonary disease, lupus, rheumatoid arthritis, and ischemia reperfusion injuries

Advantages

Inhibit complement activation by targeting protein C3, the converging point of all three complement activation pathways
Possess highly improved aqueous solubility properties and overcome the aggregation limitation for clinical translation of previously known 十三环肽 peptides
Possess significantly improved inhibitory efficacy and retain inhibitory potency, compared to previously known 十三环肽 peptides

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