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High-density lipoprotein mutant eye drops for the treatment of posterior eye diseases

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ABSTRACT

Age-related macular degeneration (AMD), in which choroidal neovascularization (CNV) affects the center of the retina (macula), leads to the irreversible visual loss. The intravitreal injection of anti-angiogenesis antibodies improved the prognosis of AMD, but relatively less invasive therapies should be explored. In the present study, we show that a high-density lipoprotein (HDL) mutant is a therapeutically active drug carrier capable of treating a posterior eye disease in mice via instillation. Various HDL mutants were prepared with apoA-I proteins fused with different cell-penetrating peptides (CPPs) and phospholipids with different alkyl chain lengths; their sizes were further controlled in the range of 10–25 nm. They were screened based on the efficiency of fluorescent dye delivery to the inner retinal layer in mice. The best mutant was found to have penetratin (PEN) as a CPP, 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC), and a size of 15 nm. In preclinical studies on a laser-induced CNV murine model, 1 week of instillation of the best mutant carrying the anti-angiogenesis drug pazopanib had dramatic therapeutic effects in reducing the CNV size. Importantly, the HDL mutant by itself contributed to the therapeutic effects. Future clinical trials for treating AMD with instillation of the HDL mutant are expected.

Keywords:

Ocular drug delivery; age-related macular degeneration; serum protein; phospholipid, cell-penetrating peptide; anti-angiogenesis drug

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