Nanoparticles for the targeted treatment of neovascular ocular diseases

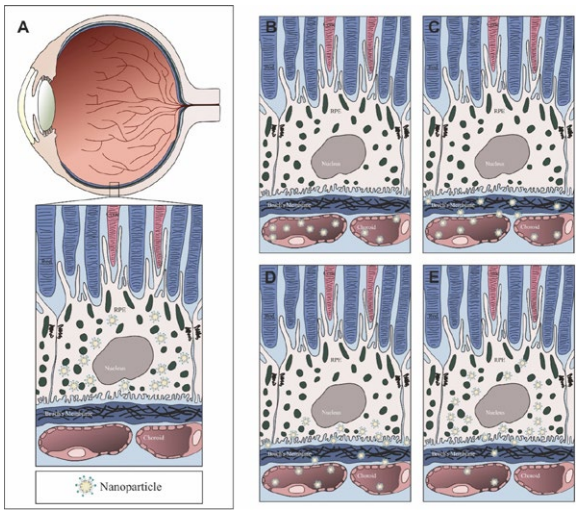
Reference No: B79130

CHALLENGE

Every year diabetic retinopathy, wet age-related macular degeneration, and retinopathy of prematurity causes millions of cases of blindness and vision impairment. Their pathogenesis shares a complex triad of neovascularization, inflammation and immune system activation that is fueled by factors originating from the retinal pigment epithelium (RPE). However, despite its pivotal role there is no therapeutic tool to specifically deliver drugs to the RPE.
Simple means of systemic drug administration fail since dosing regimens that would build up relevant RPE levels would trigger severe side effects due to the unfavorable drug distribution in the organism. The alternative, intraocular drug therapy, also suffers from a number of shortcomings especially due to the lack of cell specificity and invasive way of administration. Today´s standard therapy for all neovascular ocular diseases, the repeated intravitreal anti-VEGF antibody injections is limited to suppression of neovascularization, accompanied by serious local and systemic side effects, resulting in patient discomfort and lack of compliance.

INNOVATION

Here, lipid nanoparticles were designed to transport drugs to the RPE following intravenous injection that address all three pathomechanisms. A single injection of Cyclosporin A loaded nanoparticles cured retinopathy of prematurity in a mouse model. By counteracting neovascularization, dampening inflammation and normalizing levels of growth factors, growth factor receptors and cytokines, this nanotherapeutic paves the way for the causal treatment of all neovascular ocular diseases.



Nanotherapeutic targeting the RPE following systemic i.v. injection.

(A) Schematic drawing that shows the localization of the finally intended nanoparticle accumulation in the RPE cell monolayer.

(B-E) Individual steps of nanoparticle transport into the RPE along the route that natural lipoprotein particles (LDL and VLDL) take.

(B) Nanoparticles immediately after injection interacting with endothelial cells of the choroid.

(C) Nanoparticles extravasate form the blood and cross Bruch's Membrane.

(D) Nanoparticles are taken up by RPE cells.

(E) Nanoparticles accumulate inside RPE cells and form a depot.

COMMERCIAL OPPORTUNITIES

Causal systemic treatment of neovascular ocular diseases.

DEVELOPMENT STATUS

In vivo proof of concept (oxygen induced retinopathy (OIR) a mouse model of ROP)

REFERENCES:

1 M. S. Bohley, A.E. Dillinger, F. Schweda, A. Lawrowska, A. Ohlmann, B. M. Braunger, E. R. Tamm, A. M. Goepferich, Nanoparticles for the Treatment of Neovascular Ocular Diseases, Manuscript submitted to Biomaterials 2021

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