Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2017-2018

Project Nº 38

Title: Evaluation of choroidal neovascularisation lesions in rats transplanted with non-viral transfected IPE and RPE cells for long-term PEDF release

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Summary

Age-related Macular Degeneration (AMD) is the leading cause of vision loss worldwide. High levels of vascular endothelial growth factor (VEGF) are considered the principal driver of angiogenesis in choroidal neovascularisation (CNV), the main feature of the wet form of AMD. It is important to maintain the angiogenic homeostasis to avoid CNV, especially the balance between VEGF and the antiangiogenic pigment epithelium-derived factor (PEDF). The current treatment against CNV in retinal diseases is the intravitreal inhibition of VEGF which helps to control the CNV in patients improving vision significantly. However, the injections need to be frequent to be effective and some side effects are linked to the process. Therefore, there is a need to explore alternative targets and delivery systems for the development of new therapeutic strategies in wet AMD.

Our approach comprises the long-term PEDF release using the non-viral Sleeping Beauty (SB100X) transposon system delivered by miniplasmids free of antibiotic resistance markers (pFAR4) in rat primary cells. For this purpose, we will perform a laser-induced CNV rat model. Transfected (pT2-pFAR4-PEDF and pFAR4-SB100X plasmids) retinal pigment epithelial cells (RPEs) and iris pigment epithelial cells (IPEs) derived from rats will be subretinally injected . Retinal sections will be analysed by immunofluorescence with different molecular markers: microglial-glia/macrophage markers (Iba1, GFAP, CD68), cell death (Caspase-3, TUNEL), fibrosis biomarker (Collagen I, IV, MMP2 and fibronectin) using confocal microscopy in order to compare transplanted and non-transplanted lesions.