TRANSPON-MEDIATED PEDF GENE DELIVERY INTO PRIMARY PIGMENT EPITHELIAL CELLS FOR THE TREATMENT OF RETINAL DEGENERATIVE DISEASES

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PURPOSE

Retinal degenerative diseases, a frequent cause of blindness in the elderly population, are untreatable with the exception of age-related macular degeneration (AMD), whose neovascular form is characterised by increased expression of the pathologic angiogenic vascular endothelial growth factor (VEGF) and currently treated by intravitreal injections of anti-VEGF antibodies. However, only 30% of treated patients experience improved vision, and the often monthly and life-long injections can be accompanied by severe side effects and non-compliance. To avoid these complications, we have postulated that neovascular AMD could be successfully treated by transplantation of pigment epithelial cells, genetically modified to overexpress pigment epithelium-derived factor (PEDF), an inhibitor of VEGF with anti-angiogenic and neuroprotective properties.

RESULTS

Transfection efficiency was optimal at 1350 V, 20 ms, 2 pulses for bovine IPE cells and 1100 V, 20 ms, 2 pulses for bovine IPE and primary human pigment epithelial cells. Secretion of rPEDF was continuous and neuroprotective properties.

PEDF treatment of retinal degenerative diseases

METHODS

Primary retinal (RPE) and iris pigment epithelial (IPE) cells were transfected using the non-viral SB100X transposon system. The effects of varying electroporation parameters on efficiency, transgene expression and secretion were investigated. Viability assays were performed to determine the effect of additional transgene expression on cell proliferation.

CONCLUSIONS

The SB100X transposon system is an efficient tool for delivering and integrating a transgene into primary pigment epithelial cells, with the ultimate goal of transplanting the cells into the subretinal space of patients with AMD and other choroidal neovascular diseases. In fact, we have previously shown that ARPE-19 cells transfected with the PEDF gene using the SB100X transposon system inhibited choroidal and corneal neovascularization after subretinal and subconjunctival transplantation, respectively.

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