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AuthorBlock: Noel Vera¹, Alex Chen¹, Max Cotler¹

¹GelMEDIX, Cambridge, Massachusetts, United States;

Purpose

The death of retinal pigment epithelial (RPE) cells in geographic atrophy (GA), a leading cause of blindness with no cure, leads to progressive central vision loss. GelRPE is a cell-laden photo-crosslinkable hydrogel therapy engineered to enable RPE transplantation and restore vision. GelRPE is injected sub-retinally as a liquid and crosslinked *in situ* into a semisolid gel. GelRPE improves upon existing saline formulations by enhancing injection efficiency and localizing cells at the target site. The advantages of GelRPE subretinal injections compared to standard saline were evaluated in a porcine model.

Methods

Fifteen Yorkshire pigs were segregated into three groups: 2 GelRPE groups (standard and high dose) and a RPE saline injection (standard dose). Eyes were treated in each group with a 50 μ L subretinal injection of iPSC-derived RPE using standard cannulas (DORC Subretinal Needle). The GelRPE test articles were injected as a liquid and crosslinked into a semisolid gel after one minute of light exposure using the existing endoilluminator (Alcon Constellation). Ocular exams, optical coherence tomography (OCT), and color fundus imaging were performed throughout the duration of the study with eyes collected for histopathology (H&E) and immunohistochemistry (IHC) at days 1, 5, and 14.

Results

Subretinal injections were successful in creating RPE cell sub-retinal blebs in all subjects. GelRPE test articles were well tolerated. At day 14, viable transplanted cells expressing human-specific antigen (STEM121) and RPE-specific proteins (RPE65, BEST-1, MITF, and ZO-1) were found in all groups. GelRPE formulations transplanted 8.1x more cells per eye on average than saline injections at the same starting dose. Cell morphology in the GelRPE group suggests better attachment and integration to native tissue, including monolayer formation, compared to unattached, hypertrophic cells in saline eyes. More specifically, over 50% of transplanted GelRPE cells exhibited a flat and spread morphology compared to only ~20% of saline RPE cells. Further analysis demonstrated a transplanted RPE to native RPE ratio of > 0.75 in GelRPE groups, significantly higher than that seen with saline (< 0.1), suggesting improvement in transplantation and localization of cells.

Conclusions

GelRPE was able to deliver viable RPE cells and localize them at the target location at a higher number and with better morphology than the saline group.