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Final Report

Define the mechanism by which C.1 rescues some functions in Best disease RPE.

For the proposal we further tested a compound (called C.1) and its effects on stem cell-derived retinal pigment epithelial cells (RPE) possessing the F305S BEST1 mutation associated with Best vitelliform macular dystrophy. Extensive cell culture was performed to generate multiple RPE batches from both normal and F305S BEST1 stem cells. The RPE batches were then used in phagocytosis assays to assess the ability of the stem cell-derived RPE to uptake and process photoreceptor outer segments. The phagocytosis experiments included different test solutions with or without the compound C.1.

The data showed uptake of photoreceptor segments in all treatments. No statistically-significant difference in the total amount of remaining photoreceptor segments was detected between the treatments. However, a non-significant trend for increasing amounts of photoreceptor fragments was seen with C.1 treatment. It is currently unclear what the clinical implications of this might be.

Human clinical trials for other diseases have shown no significant side-effects in patients taking high doses ($\leq$10 mg/kg) of C.1 daily for 12 weeks. We are therefore pursuing discussions with a specialist retinal ophthalmologist regarding how best to progress this compound.

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