Modeling Morphology Dynamics of Retinal Pigment Epithelium

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***Short Abstract* — Retinal pigment epithelium (RPE) is a key site of pathogenesis of age-related macular degeneration (AMD). We obtain RPE images of mouse and human eyes, develop statistical quantifications of RPE morphology, and model the morphology dynamics of RPE based on experimental data. The results suggest that repeated correlated cell death can drive normal RPE pattern to those in AMD eyes.**

***Keywords* — age-related macular degeneration, retinal pigment epithelium, morphology, statistical quantification, cell-based model**

I. BACKGROUND

AGE-related macular degeneration (AMD) is the main cause of vision loss in the elderly, and is considered a looming epidemic for the aging society [1]. Decisions of AMD treatment depend on our ability to distinguish one form of AMD that develops new blood vessel growth and visual failure and another that does not progress. The resolution of patients is currently perplexing and the need to distinguish normal aging, dry and wet forms of AMD is urgent. We hypothesize that the morphology of RPE, a key site of AMD pathology, correlates with the age and disease status of the eye and can be quantified and modeled to predict the disease progression. To test this hypothesis we combine experimental and modeling approaches to analyze RPE morphologic patterns and dynamics.

II. MATERIALS AND METHODS

RPE images were obtained from mouse and human (donor) eye flatmounts, with RPE cell boundaries and nuclei stained. From the two-dimensional (2D) tissue images we extracted 24 measures of cellular features, amongst which we identified three as orthogonal variables. We measured their distributions were measured as a function of genotype, age, and location within RPE. We also developed a cell-based model for 2D tissue and simulated RPE morphology changes resulting from cell death and drusen, and compared the results with experimental flatmount RPE images.

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III. RESULTS

Statistical analysis of the mouse RPE images showed that, in mouse eyes with destructive mutations on RPE related genes, the disruptions to regular RPE pattern are spatially inhomogeneous. Peripheral region showed more dramatic changes than the regions closer to the macular, both as a function of age and a function of mutation.

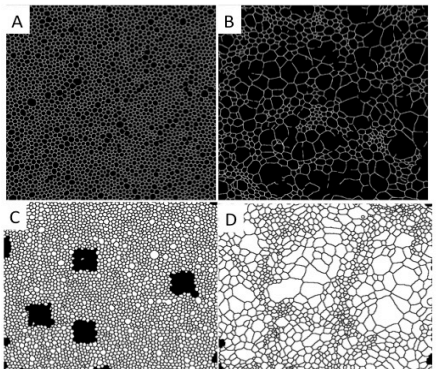

Figure 1. Human RPE patterns. A. Normal. B. AMD. C. Simulated clustered death on normal. D. Simulated AMD.

We simulated the morphological changes in the RPE, modeling the stresses imposed by AMD progression. Simulations showed that presence of hard drusen kills its underlying RPE cells, the resulting morphology change is a function of distance to the drusen, consistent with experiments [2]. RPE cell stretching and local reorganization was sufficient to repair damages by single cell death. However, neither single cell death, nor clustered cell death, could induce enough deformation to change a normal RPE pattern to those found in AMD patients. Repeated, clustered cell death was necessary and sufficient to evolve the RPE pattern from normal to those found in AMD eyes. This model provides a quantitative tool to test hypotheses on the biomechanical mechanisms of AMD-induced RPE morphology dynamics [3].

REFERENCES

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