VEGF and PEDF Secretion in ARPE-19 and fhRPE Cells

This letter is in reference to the recent study by Ablonczy et al.¹ They compare certain aspects of the morphology and function of the spontaneously transformed human RPE cell line ARPE-19 and monolayers of fetal human RPE (fhRPE) cells. Our laboratory has a long-standing interest in the use of fhRPE cells in studying RPE function, and we have reported our results on endogenous growth factor secretion, particularly that of vascular endothelial growth factor (VEGF) and pigment epithelium-derived factor (PEDF), the two factors that were studied by Ablonczy et al., with different stimuli and degree of polarity. A detailed protocol used routinely in our laboratory for the generation of fhRPE monolayers with high transepithelial resistance has been published.²

Based on several of our studies, we agree with the authors' conclusion on the limitation of ARPE-19 cells and superiority of fhRPE cells in studying human native RPE function. We would like to highlight some of our published findings and the striking similarity between our results and those of Ablonczy et al. (1) VEGF secretion is more apical in polarized ARPE-19 cells, whereas it is basal in fhRPE monolayers.²⁻⁵ (2) VEGF secretion is lower in ARPE-19 compared with fhRPE cells.^{3,4} (3) PEDF is secreted predominantly to the apical surface of fhRPE cells, and its secretion is more than two orders of magnitude higher than that in ARPE-19 cells.⁴⁻⁶ (4) Induction of polarity significantly increases PEDF and VEGF secretion 34- and 5.7-fold, respectively, in fhRPE cells.⁴ An additional relevant finding in our studies was that human embryonic stem cell-derived RPE monolayers secrete more than two times the amount of PEDF that polarized fhRPE cells secrete.⁶ Further, in all our studies, we investigated the effect of stress stimuli on the secretion of these two growth factors.³⁻⁵

Notwithstanding the fact that culture media, growth conditions, and experimental design vary somewhat between the two laboratories, we were pleased to find that the results and conclusions drawn with respect to VEGF and PEDF secretion

are complementary and provide confirmatory evidence that the polarized fhRPE cell monolayer model is advantageous for studying native human RPE function.

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References

1. Ablonczy Z, Dahrouj M, Tang PH, et al. Human retinal pigment epithelium cells as functional models for the RPE in vivo. *Invest Ophthalmol Vis Sci*. 2011;52:8614-8620.
2. Sonoda S, Spee C, Barron E, Ryan SJ, Kannan R, Hinton DR. A protocol for the culture and differentiation of highly polarized human retinal pigment epithelial cells. *Nat Protoc*. 2009;4(5):662-673.
3. Kannan R, Zhang N, Sreekumar PG, et al. Stimulation of apical and basolateral VEGF-A and VEGF-C secretion by oxidative stress in polarized retinal pigment epithelial cells. *Mol Vis*. 2006;12:1649-1659.
4. Sonoda S, Sreekumar PG, Kase S, et al. Attainment of polarity promotes growth factor secretion by retinal pigment epithelial cells: relevance to age-related macular degeneration. *Aging (Albany NY)*. 2009;2(1):28-42.
5. Sreekumar PG, Zhou J, Sohn J, et al. N-(4-hydroxyphenyl) retinamide augments laser-induced choroidal neovascularization in mice. *Invest Ophthalmol Vis Sci*. 2008;49(3):1210-1220.
6. Zhu D, Deng X, Spee C, et al. Polarized secretion of PEDF from human embryonic stem cell-derived RPE promotes retinal progenitor cell survival. *Invest Ophthalmol Vis Sci*. 2011;52(3):1573-1585.

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