AB041. The implication of miRNA let-7f in retinal pigment epithelium degeneration under oxidative stress

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Background: Age-related macular degeneration (AMD) is the most suspected cause of vision loss in the elderly. Given the considerable evidence, oxidative stress is thought to be a primary contributing factor to AMD. Retinal pigment epithelium (RPE) could be detrimentally compromised by oxidative stress along which blebs called retinal microparticles (RMPs) start to shed. In continue these particles would be taken by retina, causing RPE senescence, dysfunction and ultimately cell death. Along with the intracellular damages, accumulative deposit of microparticles in subretinal region can cause most known histological hallmark of dry AMD namely drusen. Based on our preliminary study, of 20 present miRNAs, Let-7f is the most abundant microRNAs in RMPs. As the accused substrate of RMPs through which retina function is compromised has yet to be well understood, we aimed to investigate pathophysiological role of let-7f and specific signaling triggered in RPE dysfunction. In brief, the principal objective is to further understand how RMPs implicate in RPE dysfunction.

Methods: By oxidative stress inducing, RMPs were isolated from cultured ARPE-19 cells. We considered the effect of RMPs on ARPE-19 cells viability using MTT assay. In addition, to see whether RMPs effect could be ascribed to let-7f, ARPE-19 cells were transfected by carrier containing miRNA Let-7f. These transfected cells were then subjected senescence (β-galactosidase) and cell cycle assay to explore the molecular events responsible for Let-7f induced RPE cell dysfunction.

Results: Regarding result we found that RMPs adversely affected RPE cell growth and resulted in significant decrease (≥30%) in cell viability. Let-7f-treated cells also revealed considerable increases of the senescence-associated β-galactosidase activity. Alongside RMPs impact, let-7f treatment group also showed similar result in cell growth.

Conclusions: To the best of our knowledge, RPE cells uptake microparticles derived from oxidative-injured retinal cells, deteriorating integrity of vision compartments. Not only these finding would suggest that RMP's impression likely corresponds to the miRNA let-7f, but introduce Let-7f as a mediator exacerbating the oxidative damages to RPE cells. This undesirable interplay is followed probably by dry AMD. Taken together, it seems by finding involved downstream pathways under RMPs pathogenesis, we can inhibit AMD disease in the early stage as well. In this line, we plan to investigate consecutive effect of RMP-associated miRNA inhibition in oxidative damage of retinal pigment epithelium.

Keywords: Retina; age related macular degeneration (AMD); microparticles; micro RNA

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