

**Summary of the interrelations of Figures in this study**

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- Figure 1. Culture periods required for the differentiation disposition of Nic-ARPE and iPS-hRPE cells
- Figure 2. Cell phenotypes and mitochondria functions in Nic-ARPE and iPS-hRPE cells during cultures
- a Cell phenotypes and morphology for Nic-ARPE and iPS-hRPE cells
  - b Subpopulations (SPs) of RPE cells classified by FACS analysis
  - c Mitochondrial membrane potential by JC-1 staining
  - d Production of pro-inflammatory and angiogenesis-related cytokines by Nic-ARPE cells
  - e Production of pro-inflammatory and angiogenesis-related cytokines by iPS-hRPE cells
- Figure 3. Expression levels of miR-494-3p, its target proteins (PTEN and SIRT3) in Nic-ARPE and iPS-hRPE cells.
- a Candidate Target sites of miR-494-3p screened by target scan
  - b Illustrated plausible molecular interplays
  - c The changes in expression intensity of miR-494-3p in Nic-ARPE and iPS-hRPE cells
  - d The changes in expression intensity of PTEN and SIRT3 in Nic-ARPE and iPS-hRPE cells during cultures
- Figure 4. Functional changes of mitochondria by indirect activation of PTEN through inhibition of miR-494-3p by transfection of a miR-494-3p inhibitor
- a MMP in Nic-ARPE
  - b Mitochondrial oxidative respiration (OXPHOS) in Nic-ARPE and iPS-hRPE cells.
- Figure 5. Metabolic changes (ATP, NAD<sup>+</sup> biosynthesis) in mitochondria by transfection of a miR-494-3p inhibitor
- a ATP production
  - b NAD<sup>+</sup> production
- Figure 6. Functional changes of mitochondria by direct inhibition of PTEN by VO
- a the changes of MMP in ARPE19 cells by miR494-3p mimic and VO, inhibiting PTEN
  - b ATP and NAD<sup>+</sup> production in iPS-hRPE cells
- Figure 7. Summarized figures for the hypothesis on the role of cell to cell communication by EV miR-494-3p
- a Dual effects of miR-494-3p on RPE cell mitochondria metabolic homeostasis
  - b Hypothesis of AMD pathogenesis
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