MicroRNA-124 Alleviates Retinal Vasoregression via Regulating Microglial Polarization

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Abstract

Microglial activation is implicated in retinal vasoregression of the neurodegenerative ciliopathy-associated disease rat model (i.e., the polycystic kidney disease (PKD) model). microRNA can regulate microglial activation and vascular function, but the effect of microRNA-124 (miR-124) on retinal vasoregression remains unclear. Transgenic PKD and wild-type Sprague Dawley (SD) rats received miR-124 at 8 and 10 weeks of age intravitreally. Retinal glia activation was assessed by immunofluorescent staining and in situ hybridization. Vasoregression and neuroretinal function were evaluated by quantitative retinal morphometry and electroretinography (ERG), respectively. Microglial polarization was determined by immunocytochemistry and qRT-PCR. Microglial motility was examined via transwell migration assays, wound healing assays, and single-cell tracking. Our data showed that miR-124 inhibited glial activation and improved vasoregession, as evidenced by the reduced pericyte loss and decreased acellular capillary formation. In addition, miR-124 improved neuroretinal function. miR-124 shifted microglial polarization in the PKD retina from the pro-inflammatory M1 phenotype to the anti-inflammatory M2 phenotype by suppressing TNF-α, IL-1β, CCL2, CCL3, MHC-II, and IFN-γ and upregulating Arg1 and IL-10. miR-124 also decreased microglial motility in the migration assays. The transcriptional factor of C/EBP-α-PU.1 signaling, suppressed by miR-124 both in vivo (PKD retina) and in vitro (microglial cells), could serve as a key regulator in microglial activation and polarization. Our data illustrate that miR-124 regulates microglial activation and polarization. miR-124 inhibits pericyte loss and thereby alleviates vasoregression and ameliorates neurovascular function.