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The Mechanism of Unfolded Protein Response in Bone Marrow Endothelial Progenitor Cells in Retinal Neovascularization

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Statement of the Problem: Retinal neovascularization is the final and common cause of blindness in diabetic retinopathy. Circulating endothelial progenitor cells (EPCs), derived from bone marrow hematopoietic stem cells, play a critical role in vascular repair and maintenance. Recent research shows that EPCs are functionally compromised in diabetes, contributing to microvascular complications. However, the mechanisms by which EPCs regulate retinal angiogenesis remain elusive. **Methodology & Theoretical Orientation:** Unfolded protein response (UPR) induced upon pathological condition is responsible for relieving stress and regaining homeostasis, while prolonged activation of UPR initiates the pro-apoptotic processes to clear the unhealthy cells. We tried to decipher the role of UPR in regulating the EPC function and its effect on retinal neovascularization. We examined the UPR in EPCs in oxygen-induced retinopathy (OIR) model to enunciate the underlining mechanisms in retinal vascular dysfunction. Further, we used chemical chaperone (sodium 4-phenylbutyrate) to alleviate the UPR in cultured EPCs and evaluated the effects on EPC proliferation, migration, and apoptosis. **Findings:** In this study, flow cytometry analysis results showed the number of EPCs from the bone marrow tended to decrease in P12 OIR mice, while cells from P15 and P17 OIR mice appeared to increase, compared with the control mice. In vitro, EPCs, isolated from bone marrow, showed a decrease in migration and proliferation in P12 OIR mice and an increase in P15 OIR mice, suggesting that hyperoxia circumstances stimulate the capacity of migration and proliferation of EPCs from bone marrow. The three branches of UPR pathway were detected unparalyzed activation. When treatment with 4-PBA, the activation of the UPR pathway tended to relieve abnormal migration and proliferation of neovascularization would be improved. **Conclusion & Significance:** These findings provide a rationale for developing an approach to protecting angiogenic progenitors in OIR mice by targeting ER stress.

Biography

Jacey Hongjie Ma, a Doctor of Medicine, Associate Chief Ophthalmologist and Postgraduate Supervisor, is currently the Deputy Director of Aier Eye Institute and Director of Discipline Construction Office.. She has been dedicated to clinical and basic research on diabetic retinopathy and age-related macular degeneration for many years and is good at various complicated vitreoretinal surgery, functional diagnosis by fundus imaging and various laser treatments for fundus disorders. Dr. Ma has presided over the Scientific Fund for Youth Talents from National Natural Science Foundation of China (NSFC) and participated in several national, provincial and municipal research projects. She has published more than 30 papers in renowned journals, including more than 20 articles in SCI journals such as Investigative ophthalmology & visual science, EBioMedicine, Diabetologia, Progress in Retina and Eye Research.