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microRNAs in Diabetic retinopathy and its treatment

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Purpose: The purpose of our study is to identify miRNAs involved in diabetic retinopathy (DR) and test the potential of candidate miRNAs as therapeutic targets for the treatment of DR.

Methods: miRNA expression profiling was performed in retinal endothelial cells (RECs) and retina of streptozotocin (STZ) diabetic rats, as well as in the retina of diabetic patients and normal control subjects. In vitro overexpression and knockdown experiments were conducted in human RECs. Lentivirus expressing pre-miR-146 and miR-146 inhibitor were produced and injected intravitreally and intravenously into STZ-induced diabetic rats to evaluate the potential of miR-146 as a therapeutic target for treatment of DR.

Results: 1) We identified a series of miRNA signatures reflecting ongoing pathological changes in RECs and the retina in diabetic rats. These signatures include a) NF-kB responsive miRNAs; b) VEGF responsive miRNAs, and c) apoptosis and cell senescence related miRNAs. Some of these signature miRNAs showed similar changes in the retina of diabetic patients; 2) We demonstrated that miR-146 has negative feedback regulations on both IL-1R/TLR-mediated and G-protein-coupled receptor mediated NF-kB activation pathways by targeting key adaptor molecules in these pathways in RECs; 3) In vivo delivery of miR-146 in the eyes of diabetic rats by lentiviral infection resulted in protection against development of DR.

Conclusions: miRNAs are involved in multiple pathological pathways of DR. miRNAs are novel therapeutic targets for the treatment of DR and other diabetic complications.

Biography

Shunbin Xu received his MD in 1991 at Peing Union Medical College, Beijing, China, and his PhD in Human Genetics and Molecular Biology, Johns Hopkins University, in 2000. He is one of the pioneers in the field of miRNAs in retina and retinal diseases and made significant contribution to the current understanding on miRNAs in retina and retinal diseases.

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