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# Interleukin-17A transcellular signaling induces diabetic retinopathy

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Diabetic retinopathy is the leading cause of blindness in the workingage population of the Western world. Diabetic retinopathy is microvascular disease of the retina. Although the cause is multifactorial, one major contributor to the onset of diabetic retinopathy is diabetesmediated low-grade chronic inflammation. Previous reports provide evidence that inflammatory cytokines play a pivotal role in the onset and progression of diabetic retinopathy. Since IL-17A has been previously identified as an inflammatory cytokine involved in the onset of both Type I and II diabetes, we examined the role of IL-17A in the onset of diabetic retinopathy in streptozotocin (STZ) diabetic mice. Diabetes-mediated hyperglycemia was sustained throughout a 2- or 8- month period. Inflammatory processes, oxidative stress, and upregulation of cytokines were examined 2-months post-diabetes. Retinal capillary degeneration and vascular leakage were observed 8-months after diabetes was confirmed, which are clinical hallmarks of early stage diabetic retinopathy. IL-17A was detected in the retina and Th17 cells were adhered to the retinal vasculature in STZ-induced diabetic mice, while the IL-17A receptor was expressed on multiple retina cells. Diabetes-mediated retinal endothelial cell death and capillary degeneration were significantly lower in IL-17A-/- mice. To further examine the IL-17-depndent mechanism that enhances retinal vascular impairment, ex vivo studies using retinal endothelial cells was performed. It was determined that retinal endothelial cell death occurs through an IL-17A/IL-17R àCIKS/FADD signaling cascade, which causes caspase-mediated apoptosis. These findings establish a novel pathologic role for Th17 cells in the early vasoregressive process of retinal capillary degeneration, and also identify the IL-17A/IL-17R àCIKS/FADD signaling pathway as a novel apoptotic mechanism that leads to the onset of diabetic retinopathy

## Biography

Brooklyn E. Taylor has her Bachelor of Science in Biology, and is a Research Assistant in the Taylor laboratory in the Department of Ophthalmology in the School of Medicine at Case Western Reserve University Cleveland, Ohio USA. Focuses on the role of IL-17A in the onset and progression of diabetic retinopathy, and is funded by an NIH/NEI R01 and a VA Merit grant