

James & Esther King Biomedical Research Program

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*Anatomy and Cell Biology
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*2009 Program
Florida Research Challenge
(2-year project)*

Project Title: Targeting the Unfolded Protein Response as an Adjunct to Treatment of Ocular Neovascularization

Project Summary: Smoking is a major risk factor for the visual loss caused by aberrant neovascularization (proliferation of blood vessels in tissue not normally containing them) in both age-related macular degeneration and diabetic retinopathy. This study will challenge the current treatment paradigm of targeting the extracellular angiogenic factor (substance that causes growth of new blood vessels), vascular endothelial growth factor (VEGF). Current treatments ignore the critical contribution of the intracellular VEGF signalling pathway; the results are often not sustainable or complete, and many patients do not benefit significantly. We have identified that the “unfolded protein response” (UPR) pathway is responsible for activating the intracellular VEGF signaling pathway. This intracellular pathway overrides the extracellular VEGF pathway, which is the current clinical target. Based on our preliminary data, we predict that co-administration of an agent that blocks the UPR together with a conventional inhibitor of extracellular VEGF, will greatly improve the clinical outcome of patients with neovascularization.