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**Project Title:** *Amplification of Intrinsic and Protective Ocular Surface Lipid Circuits as Novel Treatment Targets*

**Abstract:** It is now recognized that controlled activation of leukocytes/lymphocytes, maintenances of self-tolerance and inflammatory resolution depend on intrinsic protective circuits. The strategy of developing "resolution agonists" that amplify these circuits is a new frontier in the battle against chronic inflammatory diseases. We have identified ocular lipoxygenase (LOX)-driven lipid circuits that drive healthy inflammatory/reparative responses, nerve regeneration and control T cell activation. This resolution circuit is highly expressed in human/mouse corneas and mediates the protective actions of docosahexaenoic acid in retinopathies. Preliminary data demonstrates that females have a sex-specific phenotype of inflammation, increased epithelial injury triggered by desiccating stress and delayed wound healing. This estrogen-driven phenotype correlates with reduced expression/activity of the 15-LOX/5-LOX-ALX receptor circuit. Three specific aims will define the roles of this circuit in limiting desiccating stress induced corneal and lacrimal gland pathogenesis, and establish that its therapeutic amplification is a valid approach to treat and resolve Sjögren's Syndrome pathogenesis.