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**Project Title:** *Defining Epithelial Cues Contributing to Sjogren's Syndrome*

**Abstract:** Although the etiology of Sjogren's syndrome (SS) remains unknown, the prevailing model has been that loss of secretory function is a secondary effect of lymphocytic infiltrates. Our studies offer alternative insight, as our observations indicate that aberrant epithelial features may arise independent of the immune response and therefore provides signals that drive SS development. We propose to test and define whether the pathogenesis of SS arises from the aberrant epithelial integrity. Specifically, we hypothesize that loss of epithelial cell polarity promotes abnormal activation of the Hippo pathway effector Yap, which drives epithelial and stromal changes that elicit an immune response. We will test our hypothesis by characterizing SS patient tissues, and aligning our observations with analysis of polarity defective mouse models. Our work will therefore provide important molecular insight into dysregulated polarity as a driver of SS phenotypes, offering potential novel therapeutic strategies.