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Project Title: *Functional Role of the Hippo pathway in Sjögren's Syndrome*

Abstract: One of the most severe salivary gland dysfunction is Sjögren's syndrome (SS), a chronic autoimmune disease associated with high morbidity and a link to non-Hodgkin's lymphoma. Increasing evidence indicates that salivary secretory dysfunction may precede and trigger glandular destruction. We have studied cellular pathways and circuitries with key functions in cell polarity during salivary gland development and in SS. Our findings have identified defective cell-cell adhesion and loss of cell polarity as features of SS. Most recent results indicate that the Hippo signaling pathway, which controls cell polarity, proliferation, apoptosis and organ size, is compromised in human SS specimens. Hippo signaling has been shown to interact with Ecadherin adhesion, the canonical Wnt pathway and N-glycosylation. Therefore, our proposed studies focus on examining the role of the Hippo pathway in SS and on whether dysregulation of this pathway impacts the interplay among E-cadherin adhesion, N-glycosylation and canonical Wnt signaling.