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Functional Role of the Hippo pathway in Sjögren's Syndrome

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LAY ABSTRACT

Sjögren's syndrome (SS) is a chronic autoimmune disease that primarily affects exocrine salivary and lacrimal glands. To date, the causes of SS are not understood. Salivary and lacrimal glands from patients with SS display lymphocytic infiltration that for many years was thought to be the underlying cause for glandular destruction. However, increasing evidence indicates that salivary secretory dysfunction may precede or trigger glandular destruction. Our studies to date have identified cell-cell adhesion and loss of cell shape as features of SS. Our most recent work suggests that components of the Hippo signaling pathway, a recently discovered tumor suppressor pathway with key roles in tissue growth, regeneration and organ size, is dysregulated in human specimens of SS. Since Hippo signaling interacts with components of cell-cell adhesion and other cellular processes, we propose to examine whether dysregulation of the Hippo pathway is one of the underlying causes of SS.

SCIENTIFIC 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 E-cadherin 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.