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Application of Multiplexing Technology to the Study of Sjögren's Syndrome
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LAY ABSTRACT

Sjogren's syndrome (SS) is an autoimmune disease affecting the function of moisture-producing exocrine glands in approximately 4 million Americans. How the disease develops is poorly understood, and there are no diagnostic tests for early stage disease. Recent studies indicate that defects in gland moisture production precede development of autoimmunity rather than the immune response initiating gland destruction. Using SS mouse models, several protein targets were identified that change early in disease development, but the cell types that produce these targets and how they cause disease were not examined. We propose to identify the cell types that produce SS target proteins in the mouse model, and test the hypothesis that changes in protein localization precede development of autoimmunity. Finally, we will examine patient tissues to determine if these changes also occur in the human disease as a first step towards the development of a molecular diagnostic test for early stages of SS.

SCIENTIFIC ABSTRACT

Sjogren's syndrome (SS) is an autoimmune disease primarily affecting moisture-producing exocrine glands, and most research focuses on the autoimmune response. However, recent SS animal model studies revealed an epithelial homeostasis defect that precedes the immune response. Microarray profiling of a SS mouse model (C57BL/6.NOD-Aec1Aec2) vs. control mice at an early disease stage showed the rac-GAP chimerin1 to be the most highly upregulated mRNA. We hypothesize that misregulation of Rac-1 activity may be an early event in disease initiation. To test this we will use the SS mouse model to validate the mRNA data at the protein level and identify the cell type-specific expression and activation of rac1 and chimerin1. Then we will examine the correlation between rac1 and chimerin1 expression and activation and SS in patients. These results may identify an early diagnostic marker for SS, and the novel multiplexing technology will be used to examine other potential diagnostic targets.