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Role of type 1 interferon signaling in the development of Sjögren's syndrome
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LAY ABSTRACT

Sjögren's syndrome is a disorder of the immune system and causes symptoms like dry mouth and dry eyes. It is widely suggested that a virus or bacteria may trigger the immune system which leads to an attack of the glands. This infection leads to the production of type one interferons which play a key role in the pathogenesis of Sjögren's syndrome. We are proposing to block the type 1 interferon signaling as a therapeutic option to this disease in a mouse model. By blocking type 1 interferon signaling, we expect the mice to restore the salivary gland function and the infiltration within the gland will be taken care of. Moreover, the local delivery of the proposed molecules (siRNAs) within the salivary gland is advantageous than a systemic delivery, which often causes toxic effects on other organs. We hope this study will lead to a new therapeutic option for patients with Sjögren's syndrome.

SCIENTIFIC ABSTRACT

Sjögren's syndrome (SS) is an autoimmune disease characterized by chronic immune attack mainly against the salivary gland and lacrimal glands. In both humans and in the mouse models of SS an upregulation of type 1 interferons and interferon responsive genes are reported. We hypothesized that type 1 interferon response plays a role in the development of SS. We propose to knock down the type 1 interferon by delivering the siRNAs to IFNAR1 directly into the salivary glands through retrograde installation in NOD mice. A significant down regulation in the lymphocyte infiltration is expected in these mice and may lead to the delay in onset of the disease in NOD mice. This study will establish the direct role of type 1 interferons in SS development and give new directions to therapeutics.