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Suppression of TH17 cells using IL-27 gene therapy: A potential therapeutic approach for the treatment of Sjögren's syndrome patients

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Lay Abstract

Patients diagnosed with Sjögren's syndrome (SjS) experience symptoms of dryness in the mouth and/or eyes. An abnormal feature of SjS is the accumulation of immune cells in the saliva/tears-producing glands. We recently reported that some infiltrating immune cells belong to a subset of the newly-described cell population known as TH17 cells because they secrete IL-17 factors that regulate immune cells and cause tissue destruction. TH17 cells are normally controlled by IL-27; however, this regulation is lost in autoimmune diseases. To investigate the role of IL-27 in SjS, I am proposing to determine if IL-27 treatment can suppress TH17 cell reactivities utilizing a gene therapy approach in an animal model of primary SjS. A benign virus expressing IL-27 will be infused into the salivary glands and the effect of treatment on development of SjS disease will be examined. This project should lay a foundation for gene therapy in patients.

Scientific Abstract

Sjögren's syndrome (SjS), a chronic systemic autoimmune disease affecting primarily the salivary/lacrimal glands, is characterized by formation of lymphocytic foci (LF). We identified the presence of CD4+TH17 memory cells within LF of human patients, raising the question whether TH17 cells are responsible for subsequent glandular destruction. I propose to further characterize the different cell populations within LF of SjS patients, focusing heavily on possible regulatory cells thought to suppress pro-inflammatory activities of CD4+TH17 cells, especially IL-27-secreting cells. In addition, I will examine the efficacy of gene therapy to down-regulate CD4+TH17 cell activity, and possibly disease, in salivary glands of a murine SjS model, using an IL-27-expressing rAAV2-viral vector. Results are expected to show lack of regulatory cells within LF and the capability of suppressing SjS disease progression utilizing this gene therapy approach, thereby establishing the basis for CD4+TH17 cells being pathogenic and provide proof-of-concept for future translational research.