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Interferon- γ induces immunoproteasome in human salivary gland cells

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LAY ABSTRACT

Sjögren's syndrome (SS) is one of the most common autoimmune diseases, with an estimated prevalence of 2-4 million patients in the United States. The disease may present with very complex manifestations, ranging from the local exocrine gland dysfunction to major, lifethreatening systemic complications such as vasculitis, and renal or lung involvement. The high prevalence of SS and its systemic impact on the patients' quality of life highlight the importance of studying the pathogenic mechanism of the disease. In this project, we aim to understand the role of interferon-gamma and immunoproteasome in primary SS. Our project will reveal a novel molecular/cellular mechanism underlying the pathogenesis of SS and may facilitate the development of new therapeutic strategies for the disease patients.

SCIENTIFIC ABSTRACT

Despite its high prevalence in the US, the etiology and pathogenic mechanisms of Sjögren's syndrome (SS) remain elusive, suggesting the importance of studying the molecular and cellular mechanisms of the disease. We recently demonstrated that interferon-gamma (IFN- γ) induces immunoproteasome in cultured human salivary gland cells and over-presentation of MHC I-associated peptide on the cell surface. Meanwhile, beta-2-microglobulin was found to be over-expressed in patients with primary SS. Based on these findings, we hypothesize that immunoproteasome is induced by IFN- γ in the salivary gland cells of SS patients, leading to over-presentation of MHC-I associated peptides on the cell surface. Salivary gland CD8+ T lymphocytes then recognize the MHC I peptide-presenting cells and cause their death or lysis. This hypothesis will be tested in primary cultured parotid gland cells, and the unique peptides presented on the salivary gland cells of SS will be identified using a mass spectrometry-based approach. We will also investigate if CD8+ T cells cause severe cytotoxicity to MHC I peptidepresenting gland cells. This project is innovative and may reveal a novel molecular mechanism underlying SS pathogenesis.