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“Adenosine Receptor agonists: Novel Therapeutic agents for Sjögren's Syndrome”

Recipient of the Innovative Grant Award

LAY ABSTRACT:

The proposed research will test the ability of drugs called adenosine receptor agonists to treat Sjögren's syndrome. Adenosine is naturally produced by tissues in responses to inflammation and injury. The drug that will be tested in this study is a chemical variant of adenosine that has fewer side effects and greater stability. In addition to its potent anti-inflammatory property, it also aids in repair of injured tissues. The efficacy of this drug to treat Sjögren's syndrome will be evaluated in experimental mouse model systems that closely mimic the human disease. We expect that treatment of mice will prevent damage to salivary glands and restore saliva secretion. Adenosine receptor agonists are currently in clinical trials for treatment of cardiovascular disease. Thus, their safety in humans is already established. Successful completion of the proposed study will provide significant impetus for human clinical trials of these drugs for the treatment of Sjögren's syndrome.

SCIENTIFIC ABSTRACT AND RESEARCH PROPOSAL:

In a recent study we observed that NZB/WF1 mice injected with Freund's Incomplete Adjuvant (IFA) developed accelerated Sjögren's syndrome-like disease. In this model, an early phase of salivary gland dysfunction was associated with innate immune responses, infiltration of submandibular glands by plasmacytoid dendritic cells. The late phase was associated with T and B cell infiltration. This proposal will test the hypotheses that for effective treatment of Sjögren's syndrome, therapeutic agents need to target both innate and adaptive immunity. Adenosine A2a receptor agonists fit this category. They are potent anti-inflammatory agents exerting their effects on cells of innate and adaptive immunity. They have been successfully used to treat inflammatory diseases in experimental models of reperfusion injury and transplantation. In this proposal, feasibility of adenosine A2a receptor agonist to treat Sjögren's syndrome-like disease in IFA-treated mice will be explored. Successful completion of this study will provide novel therapeutic agents for Sjögren's syndrome.