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**Oklahoma Medical Research Foundation**

*“Free radical mediated oxidative damage in the lacrimal and salivary glands of an animal model of Sjögren's Syndrome”*

***Recipient of Student Fellowship Award***

**LAY ABSTRACT:**

Sjögren's syndrome (SS) is a chronic disease in which white blood cells attack the saliva-producing glands. The major symptoms are dry eyes and dry mouth. However, it is a disease, that can affect different organs and may cause fatigue. It is one of the most prevalent autoimmune disorders, striking as many as four million Americans. Our laboratory has developed an animal model of this disease, which will help understand the pathophysiology of this disease better. Specifically, we want to see if oxidation processes, brought about by immunization of mice with peptides from an autoantigen, namely Ro 60, can damage salivary glands and bring out SS-like condition.

**SCIENTIFIC ABSTRACT AND RESEARCH PROPOSAL:**

Sjögren's syndrome (SS) first described by Swedish ophthalmologist Henrik Sjögren in 1930 is a chronic inflammatory, autoimmune disorder characterized by diminished lacrimal and salivary glands secretion resulting in keratoconjunctivitis sicca and xerostomia. Autoantibodies, directed against Ro 60 antigen (SS-A), a constituent of Ro ribonucleoprotein, is found in up to 90% of patients with SS. Based on preliminary observations made by our laboratory, there is substantial evidence for oxidative damage in the sera of patients with systemic lupus erythematosus (SLE) and SS. We have identified specific proteins modified by the lipid oxidation product 4-hydroxy-2-nonenal (HNE) in the sera of SS patients using two-dimensional gel electrophoresis and matrix assisted laser desorption/ionization time of flight mass spectrometry. In addition, there is evidence for antibodies (from known anti-Ro containing SLE patients) recognizing HNE-modified Ro60 antigen. Immunization of rabbits with Ro60 modified with HNE was found to expedite intramolecular and intermolecular epitope spreading and development of autoimmunity relative to immunization with unmodified Ro60. Dr. Scofield's laboratory has developed an animal model of SS by immunizing with a peptide from Ro60 as well as with HNE-modified Ro60. Antigens modified by oxidative by-products have been shown to be associated with autoimmune diseases and also to induce immune responses in alcoholic liver disease. Other recent data show that islet cell glutamic acid decarboxylase modified by reactive oxygen species is recognized by antibodies from people suffering from type 1 diabetes mellitus. Based on

our findings and this published data, we hypothesize that immunization with a Ro 60 peptide (Ro 273-289) will induce oxidative damage in the salivary and lacrimal glands of our animal model of SS compared to controls. This could lead to oxidative modification of proteins. Proteins altered in this manner could act as neoantigens and elicit autoantibodies and thus may trigger autoimmunity.