Alan Nathaniel Baer, MD
Associate Professor of Medicine
Department of Medicine (Rheumatology)
John Hopkins University School of Medicine
Comprehensive analysis of antibodies in Sjögren's using phage immunoprecipitation sequencing

LAY ABSTRACT

The Lay Abstract is for publicity purposes and should use simple language summarizing the proposed research and its significance.

The development of better tools to enable earlier diagnosis of Sjögren's syndrome is a key goal of the Sjögren's Syndrome Foundation. Earlier therapeutic intervention in Sjögren's syndrome has already been shown to lead to better outcomes. Autoantibodies are proteins produced by immune cells that bind to an individual's own tissues, on structures called "autoantigens". Autoantibodies are present in the blood and also in certain body fluids, such as saliva. Some autoantibodies are specific for a given autoimmune disease and help in diagnosis while others define disease subsets with unique clinical features. In this project, the entire repertoire of antibodies to autoantigens and human viral proteins will be characterized in each of 45 Sjögren's syndrome patient samples using a powerful new technology, called phage immunoprecipitation sequencing. Our goal is to define new autoantibodies specific for SS which could be used for earlier diagnosis and to increase understanding of its causes.

SCIENTIFIC ABSTRACT

The Scientific Abstract is written for SSF reviewers and a professional audience.

This project uses high-throughput phage immunoprecipitation sequencing to characterize complete antibody repertoires in Sjögren's syndrome (SS) patients. We will utilize phage- displayed synthetic representations of the complete human proteome and virome to test our hypothesis that SS is initiated by an aberrant host response to viral infection, which is followed by epitope spreading to tissue-specific and ubiquitous self-antigens. Dr. Larman, co-PI, developed this methodology and has employed it to identify previously unreported autoantibodies in several autoimmune diseases. Aim 1 will be to analyze circulating antibodies in SS patients (20 anti-Ro/La positive, 20 anti-Ro/La negative) and 20 healthy controls. Aim 2 will be to compare autoantibodies in 5 SS matched serum/saliva samples, seeking salivary enrichment. Aim 3 will be to validate candidate autoantigen biomarkers using recombinant full-length proteins. Our goal is to identify novel SS autoantigens that can be used to improve diagnosis and provide insight into its potential viral pathogenesis.