



## Pilot Research Grant:

**Rachael Gordon, MD, PhD**

Rheumatology Fellow

University of Pittsburgh

**Project Title: Investigating the Role of IL-12 in Sjögren's Disease Pathogenesis**

### **Abstract**

Sjögren's disease (SjD) is a common systemic autoimmune disorder characterized by progressive inflammation of the exocrine glands. The immunopathology driving SjD remains enigmatic and there are no FDA-approved disease modifying treatments. Polymorphisms in IL12A and STAT4 are associated with SjD across multiple cohorts, suggesting a fundamental role for the IL-12A-STAT4-Interferon (IFN)  $\gamma$  axis in SjD. IL-12 and IFN $\gamma$  are intimately linked in positive feedforward loops critical to the development and function of Th1 cells. More recently, our group has discovered a novel role for this axis in inflammatory B cells. We hypothesize that IL-12 promotes SjD. We will test this hypothesis by treating NOD.B10 SjD prone mice with an IL-12 neutralizing antibody and evaluating clinical and immunologic features of disease. Elucidating a pathogenic role for IL-12 in SjD will serve as the rationale for developing a human monoclonal IL-12 antibody for the treatment of SjD and other IL-12-driven diseases.