



2006 Research Student Fellowship

Virginia Carroll, PhD candidate, University of Virginia ***MCMV-Induced Sjögren's Syndrome-like Disease***

My research aims to study immunological control of the chronic inflammation in the salivary and lacrimal glands. Our mouse model develops Sjögren's Syndrome-like inflammatory lesions in these two exocrine glands after infection with a sialotropic virus, murine cytomegalovirus. Interestingly, this chronic inflammation persists long after the virus is undetectable in the Salivary gland. Current data indicate salivary gland function is not compromised by the chronic inflammatory lesions.

I have proposed two approaches to understand the mechanism behind the development of a diagnostic feature of Sjögren's Syndrome. First, cell transfer studies into the naïve mice will allow examination of the specificity of the infiltrating CD4 cells. This will be technically demanding as cells must be harvested from mice 75 days post infection with MCMV, labeled, injected intravenously to similarly infected or age-matched mice, and later analyzed by flow cytometry. Establishing the proper conditions such as dose of donor cells and the optimum time for observing proliferation of labeled cells will take several months. In addition, the role of the CD25⁺ T regulatory cells in controlling the MCMV-induced chronic inflammation will be investigated by depletion with anti-CD25 monoclonal antibody. Salivary gland function will be monitored weekly for 3 weeks by collecting saliva after pilocarpine induction. Considering the mice are infected at 2 months of age and the phenotype of interest arises 2.5 months later, this also will take several months but can be completed concurrently.

The second approach to address mechanisms of immune control in our mouse model of virus-induced Sjögren's Syndrome-like disease takes advantage of the genetic system available. A potential genetic modifier of MCMV-induced autoimmune exocrinopathy has been identified on mouse chromosome 3. I will be breeding recombinant mice, genotyping chromosome 3 with microsatellite markers, and examining their phenotype upon infection with MCMV after 75 days. Histology and function of the salivary gland will be studied in about 100 animals. This is projected to take 1-2 years. This study will guide us to specific genetic regions important for the generation of chronic glandular inflammation upon MCMV infection which we can test in recombinant mice.