

Patrizio Caturegli, MD
Johns Hopkins University

“Role of IL-12 in the inducible BALT found in Sjögren’s lungs”

LAY ABSTRACT:

Lung involvement is an increasingly recognized manifestation of Sjögren’s syndrome. Here the lungs become infiltrated by an abnormally high number of lymphocytes, which eventually decreases the patient’s lung function. The reason why lymphocytes accumulate in Sjögren’s lungs is unknown. We have developed a mouse model of this human lung disease. We propose to use our model for better understanding how the Sjögren’s lung disease develops.

SCIENTIFIC ABSTRACT AND RESEARCH PROPOSAL:

Sjögren’s syndrome, although best known for its involvement of lacrimal and salivary glands, often causes lung abnormalities. It has been recently reported that these lung abnormalities are mainly characterized by the appearance of lymphoid aggregates in peribronchial, perivascular, and interstitial areas, collectively called inducible Bronchus-Associated Lymphoid Tissue (iBALT). The pathogenesis of iBALT and Sjögren’s lung disease is unknown.

We have developed a transgenic mouse model that over-expresses interleukin-12 (IL-12) in the lungs and shown that it develops iBALT with pathological manifestations that resemble very closely those described in the lungs of Sjögren’s patients. The lungs of adult IL-12 transgenic mice contain a significantly reduced number of NK cells. We have thus hypothesized that iBALT formation is the consequence of a decreased number of lung NK cells induced by prolonged exposure to IL-12.

We will test this hypothesis using three sets of experiments: 1) we will assess whether the adoptive transfer of wild type NK cells to IL-12 transgenics prevents or ameliorates iBALT formation and the subsequent lung pathology; 2) we will assess whether removal of IL-12 in IL-12 transgenic mice prevents the decrease in lung NK cells and/or iBALT formation; 3) we will assess whether removal of NK cells in IL-12 transgenics exacerbates iBALT formation.