Novel Biomarkers for Autoimmune-mediated Lung Disease

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BACKGROUND

Interstitial lung disease (ILD) is a common manifestation of systemic autoimmune diseases such as rheumatoid arthritis (RA), lupus and scleroderma, which can lead to inflammation and scarring of the lung and, consequently, to hypoxemia, pulmonary hypertension and death. It is estimated that ILD occurs in approximately 15 percent of patients with RA. Very little is known about how ILD disorders arise and what role loss of immune tolerance plays in ILD development. Presently, there are no validated lung-specific autoantigens for diagnosis of autoimmune-mediated lung disease. Current options for ILD treatment are limited to powerful immunosuppressive medications with significant side effects. Identification of novel pulmonary biomarkers is sorely needed to develop better diagnostic methods and therapies for ILD.

TECHNOLOGY DESCRIPTION

UCSF investigators have shown that loss of immune tolerance to a lung mouse self-antigen, vomeromodulin, results in spontaneous ILD in the AIRE-deficient mouse model of autoimmunity. Importantly, researchers have identified a novel human lung autoantigen, LPLUNC1, using a highly sensitive autoantibody assay in an ILD patient with Autoimmune Polyglandular Syndrome Type 1, a multi-organ autoimmune disease caused by mutations in AIRE (Sci Transl Med, 2009 December 2; 1(9):9ra20). LPLUNC1 autoantibodies have been detected in large cohorts of patients with ILD both with and without the APS1 disease, confirming a strong correlation between ILD and this novel biomarker of lung autoimmunity. Research evaluating other PLUNC family proteins is underway.

APPLICATIONS

- Biomarkers assay for identification of ILD patients with lung autoimmunity, which are more likely to benefit from immunosuppressive drugs
- Biomarker assay for prediction of early onset of ILD in patients with autoimmune diseases such as RA
- Potential biomarker for lung transplant rejection
- Development of antigen-specific therapies for patients with ILD

ADVANTAGES

- First validated human lung autoantigen in ILD with lung autoimmunity
- Lung tissue specificity: LPLUNC1 is predominantly expressed in the lung
- The LPLUNC1 autoantibody assay has high sensitivity (100%) and specificity (95%) in APS1 patients
- Large market: may be used for early screening of patients with common systemic autoimmune diseases for ILD to prevent worst patient outcomes and mortality

INVENTOR INFORMATION

Dr. Anthony Shum

Dr. Shum is an Assistant Professor of Medicine in the Division of Pulmonary and Critical Care Medicine at UCSF Medical Center. Dr. Shum's research focuses on patients with interstitial lung disease, especially those associated with autoimmune conditions such as rheumatoid arthritis and scleroderma. He investigates the basic mechanisms that cause...
pulmonary damage in patients with these disorders, including efforts to identify novel lung-specific proteins that are attacked by the immune system. Through this work, he hopes to uncover new targets of lung disease that may aid in the diagnosis and treatment of ILD.

**Dr. Mark Anderson**

Mark Anderson, MD, PhD, is an Associate Professor of Medicine in the UCSF Diabetes Center and the Robert B. Friend and Michelle M. Friend Endowed Chair in Diabetes Research. Dr. Anderson is a physician scientist who studies the molecular underpinnings of autoimmune diseases with a particular interest in a key regulator of immune tolerance called the Aire gene. In addition to his laboratory work, Dr. Anderson is a practicing physician in the UCSF Adult Diabetes Clinic and is on a number of advisory boards including TrialNET, a multicenter organization that conducts clinical trials for the treatment and prevention of Type 1 diabetes.

**PATENT STATUS**

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