RCSI research breakthrough in understanding hereditary emphysema

January 13 2014

Researchers from the Royal College of Surgeons in Ireland (RCSI) and Beaumont Hospital have made an important breakthrough in the understanding and treatment of hereditary emphysema. Their research findings were published in this month's edition of *Science Translational Medicine*, a prestigious journal that highlights medical advances resulting from scientific research, thus bridging the research-to-treatment gap. Their exciting findings show how the protein Alpha-1 Antitrypsin (AAT) plays an important role in controlling inflammation from white blood cells and its importance for good health.

The research found that Alpha-1 Antitrypsin (AAT) is an important protein produced by the liver which, when released into the bloodstream travels to the lungs to protect the lung tissue from disease. Patients deficient in AAT suffer from Alpha-1 Antitrypsin Deficiency (Alpha-1); a hereditary disorder that leads to the most severe form of hereditary emphysema.

Professor Gerry McElvaney, Professor of Medicine at RCSI and senior author on the study commented: "Our study is the first to reveal the mechanisms by which a lack of the Alpha-1 protein causes an increase in the release of white blood cell proteins into the blood stream. This leads to an autoimmune process in the body that mistakenly recognises these proteins as foreign and activates its own white blood cells to produce harmful oxidants"

"Our research also reveals how a treatment known as augmentation

therapy, where Alpha-1 protein purified from blood, is given intravenously, leading to a decrease in the abnormal protein release thereby alleviating the disease associated autoimmunity. This research gives new hope for a better quality of life for sufferers of this chronic condition and may also be applied to other autoimmune associated diseases such as rheumatoid arthritis, Prof McElvaney continued.

Alpha-1 Antitrypsin (AAT) is a protein produced by the liver which, when released into the bloodstream travels to the lungs to protect the lung tissue from disease. Patients deficient in AAT suffer from Alpha-1 Antitrypsin Deficiency (Alpha-1); a hereditary disorder that leads to severe emphysema. Emphysema (otherwise known as chronic obstructive pulmonary disease (COPD)) is caused by inflammation of the alveoli, the sponge-like tissues that take oxygen into the lungs. The disease causes shortness of breath in its mildest form and in its severest form, patients must use an oxygen mask and may need a lung transplant. The first single lung and first double lung transplant recipients in Ireland were people with Alpha-1.

Alpha-1 is much more common in Ireland than in most other countries. After cystic fibrosis, it is the most common fatal inherited lung condition in Ireland (1). Alpha-1 is estimated to affect more than 12,000 people nationally in its most severe form and the less severe form may affect as many as 200,000 individuals in Ireland. 1 in 25 Irish individuals carry the gene for the disease.

In 2004, the Alpha One Foundation initiated the first national screening programme for Alpha-1. To date, more than 11,000 individuals have been tested and 28% were found to be at risk from the disease .

More information: The Circulating Proteinase Inhibitor α-1 Antitrypsin Regulates Neutrophil Degranulation and Autoimmunity, David A. Bergin, Emer P. Reeves, Killian Hurley, Rebecca Wolfe,

Ramia Jameel, Sean Fitzgerald, and Noel G. McElvaney. *Sci Transl Med* 1 January 2014 6:217ra1. DOI: 10.1126/scitranslmed.3007116