[ERS] FKBP5 a candidate for corticosteroid insensitivity in COPD

Introduction.-

- The Groningen and Leiden Universities study of Corticosteroids in Obstructive Lung Disease (GLUCOLD) has identified a subset of COPD patients who respond favourably to inhaled corticosteroid (ICS) treatment and were distinguishable by their gene-expression profiles.

- The availability of longitudinal gene expression data and genetic information in GLUCOLD, pre- and post-treatment, allows to identify inducible eQTLs (eQTLs), i.e. genetic variants that regulate gene expression changes in response to treatment with ICS.
Objective:-

The aim of this study was to perform an inducible eQTL analysis in the GLUCOLD study to better understand the genetic factors related to steroid responsiveness in COPD.
Methods.

- GWAS was performed using the Illumina HumanCytoSNP-12 array.

- Gene expression profiling was performed in bronchial biopsies obtained before and after 6-month treatment with ICS using Affymetrix-HuGene_ST1.0 arrays in patients with COPD (n = 42).

- Genetic variants acting in Cis (50,000 kb flanking the gene) were associated to the 278 previously identified corticosteroid sensitive genes in GLUCOLD.
Results.

- We identified 13 inducible eQTLs in 12 different genes. Notably, *FK506 binding protein 5 (FKBP5)*, which in the GLUCOLD study was the most highly upregulated gene by ICS was found to be regulated by rs2766545 (Beta = 0.87, FDR<0.05).

- **FKBP5** is a known negative regulator of the glucocorticoid receptor which directly regulates corticosteroid anti-inflammatory function.
Conclusions.-

- Our results suggest that genetic factors contribute to ICS treatment responsiveness. Furthermore, FKBP5 provides an important candidate which may contribute to corticosteroid insensitivity in COPD.