European Respiratory Society
Annual Congress 2013

Abstract Number: 1756

Publication Number: P540

Abstract Group: 3.1. Molecular Pathology and Functional Genomics

Keyword 1: Sarcoidosis **Keyword 2:** Molecular pathology **Keyword 3:** Functional genomics

Title: Molecular pathway perturbations in pulmonary sarcoidosis

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Body: This study is aimed at investigating pathomechanisms of pulmonary sarcoidosis (PS) based on evaluation of gene expression profiles in context of molecular pathways. We analyzed two PS microarray datasets publicly available in Gene Expression Omnibus using the algorithm called growing support sets-pathway signal flow (GSS-PSF) previously developed by us and molecular pathway maps from Kyoto Encyclopedia of Genes and Genomes (KEGG). GSS-SPF evaluates the changes in signal flows for a given pathway depending on the pathway topology and relative gene expression. The results of the data analysis are summarized in table 1.

Table1. Deregulated pathways in PS

	PS vs. Control		Progressive vs. Self-limited PS	
KEGG Pathway	Mean PSF	p	Mean PSF	p
Fc-gamma R-mediated phagocytosis	55.7	0.001	6106.11	0.004
Focal adhesion	12.2	0.001	8.7	0.009
Chemokine signaling pathway	6.3	0.011	2.5	0.016
Toll-like receptor signaling pathway	ND		1.6	0.023

Our findings are in line with the notion of PS pathogenesis. The “Fc-gamma receptor associated phagocytosis pathway” is implicated in granuloma formation, while the “Focal adhesion pathway” plays important role in biological processes including cell motility, proliferation and differentiation. The “Chemokine signaling pathway” showed upregulated signal flows leading to the activation of the “Leukocyte transendothelial migration pathway”, which is prerequisite for chemokine-induced immune cell infiltration into the lung. Comparison of pathway perturbations in self-limiting and progressive forms of PS showed that later is characterized by higher intensity of common pathological events. In conclusion, our study identified molecular pathways altered in PS and evaluated their functional outcomes.