Bronchoalveolar lavage and serum protein patterns in healthy individuals and sarcoidosis patients:

A proteomics approach

av

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Abstract

The etiology of sarcoidosis remains unknown. Although biochemical changes are frequently observed in sarcoidosis, the problem of finding distinct biomarkers remains. Only a few markers are defined in this disease. In previous studies, proteomics investigations of sarcoidosis have generated valuable information relevant to an altered protein expression in this disease. In this thesis the focus has been on soluble components of cell free bronchoalveolar lavage fluid (BALF) and also serum from patients with active sarcoidosis as well as healthy individuals. Proteomics has been applied for the analysis of the samples, for defining and mapping the specific BALF proteins and to investigate the pattern changes in these samples in the disease. An approach of comparative proteomics has been presented. We developed an alternative sample application method capable of high loading of samples, for the separation of proteins in the first dimension of two dimensional gel electrophoresis. We optimized a sample preparation and handling method based on a proteomics approach to identify specific proteins in the BALF. Normal BALF protein samples were investigated and the protein contents were mapped in the pH interval 4.5-5.2. Furthermore we analyzed the protein expression changes in BALF from sarcoidosis patients and compared it to the healthy controls. Twenty two proteins were found to be altered. Among them many were new for this sample. Serum proteins of the same patients were also investigated which resulted in the detection of 21 altered proteins in the patients. In a search for common protein alternations between the two compartments, we were able to show a similar expression pattern of three proteins, common in both serum and BALF.

In conclusion, the proteomics approach used here was successful at defining specific BALF proteins and identifying several new proteins in BALF and serum. Moreover, the establishment of the protein expression pattern in BALF and serum of sarcoidosis may yield useful information in the search for diagnostic and predictive tools in this disease. Finally, the proteomics approach presented here may be applicable also in other pulmonary disorders.

Keywords: Sarcoidosis, BALF, serum, proteomics, 2-D electrophoresis, protein-spot pattern, protein identification

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