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Proteomic analysis to investigate the efficiency of alpha 1-antitrypsin in bronchoalveolar lavage fluid of patients with bronchiolitis obliterans syndrome

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Statement of the Problem: Early and long-term graft and patient survival after lung transplantation are challenged by chronic lung allograft dysfunction (CLAD), whose main phenotype is represented by bronchiolitis obliterans syndrome (BOS), a condition characterized by an irreversible obstructive graft dysfunction due to fibro-obliterative lesion of small airways. Patients with BOS have a poor survival (5-year) after its onset. Based on the anti-inflammatory and anti-protease properties of alpha-1 antitrypsin (AAT), specifically versus neutrophil elastase (HNE), a possible role of this protease inhibitor in short and long term outcome after lung transplantation has been recently underlined by an increasing number of studies.

Methodology & Theoretical Orientation: 1-D and 2-D polyacrylamide gel electrophoresis combined with Western blotting and LC-MS/MS were applied to the analysis of bronchoalveolar lavage fluid (BALf) from 80 subjects among which were selected stable lung transplant recipients and individuals affected by BOS at different grade of severity (BOS 0p to BOS 3). This proteomic study was carried out to understand whether long term transplant outcome could be correlated with AAT and HNE levels in patients' BALf.

Findings: The complex between HNE and AAT, that was expected to be present in all subjects, was observed only in a limited number of stable as well as of BOS patients. We speculated that the inability of AAT to inhibit completely HNE in BALf of these individuals was due to circulating inactive forms of this inhibitor. The identification of several degraded forms (ranging from 45 to 27 kDa) of AAT, strengthened our hypothesis.

Conclusion & Significance: Comparison of protein profiles in BALf of lung transplant patients at different levels of severity have shown differentially expressed proteins among them. In particular, AAT seems to be the involved in disease progression and pathogenesis.

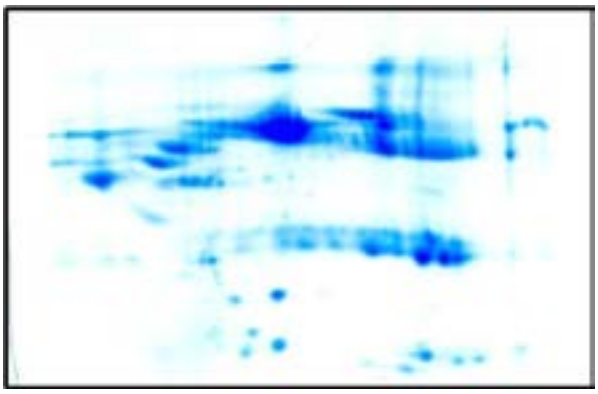

Figure 1: 2-DE gel electrophoresis of BALf.

Biography

Maddalena Cagnone is a PhD student in Biomedical Science in the Department of Molecular Medicine at the University of Pavia, Italy. She graduated in Experimental and Applied Biology at the University of Pavia. After graduation, she obtained a scholarship to study the expression of CD44 on mesenchymal cells from patients with different degree of chronic lung rejection. In the course of PhD studies, she has been studying the role of AAT in BALf of transplant patients.

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