Truncated α1-Antitrypsin as an Infection Biomarker for Severe Acute Respiratory Syndrome (SARS)

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Severe acute respiratory syndrome (SARS) is a new infectious human disease that causes severe damage in the lung. For effective treatment of SARS, understanding the pathogenesis and developing specific diagnostic methods for early detection of the disease are crucial. We employed proteomic technology to search for SARS-associated serum proteins that can be used as biomarkers for specific diagnosis of the disease and interpretation of pathogenesis. We examined the proteomic profiles of serum samples from four groups of subjects, confirmed SARS, SARS after treatment, other diseases with similar symptoms and normal healthy people, respectively. Significantly and consistently altered protein spots were identified by mass spectrometry and validated by Western blotting. The amounts of altered proteins were statistically quantified and correlated with clinical data. At least six proteins or peptides were found to significantly increase their levels in SARS sera as compared to normal ones. One of them is truncated αl-antitrypsin. The serum levels of truncated αl-antitrypsin peptides were substantially depleted in SARS after treatment. They were also found to have considerable low levels in no-SARS patients with similar symptoms, providing excellent internal controls for distinguishing SARS from suspected cases. α1-Antitrypsin inhibits neutrophil elastase from attacking cross-linked elastin, the structural protein in the lung. The dramatic increase of truncated α1-antitrypsin may be resulted from the proteolytic cleavage of functional full-length αl-antitrypsin due to an unknown mechanism of virus infection. The degradation of α1-antitrypsin impairs its ability to protect lung elastin from attacking by elastase, leading to lung fibrosis.