

SPECIAL ISSUE

J. OF BIOMED. & CLIN SCI

Vol 9, No 2 (2024): Special Issue (Dec 2024)

7th International Conference on
**Molecular Diagnostics
& Biomarker Discovery**
Advancing Medical Health Technology

3RD - 4TH OCTOBER 2024

Organized by :



Institute for Research in Molecular Medicine (INFORMM)

Universiti Sains Malaysia

Penang, Malaysia.

Identification of Alpha-1 Antitrypsin as a Candidate Biomarker for Post COVID-19 Syndrome by Two-Dimensional Electrophoresis Proteomic Analysis

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Despite a significant decrease in Coronavirus disease (COVID-19) case prevalence since the end of pandemic phase and effectiveness of the vaccination program, some patients continue to experience symptoms beyond three months of infection known as Post COVID-19 Syndromes (PSC). Common manifestations include enduring cough, shortness of breath and fatigue, which adversely affect quality of life. The primary challenge in managing PCS is its diagnosis, which relies on clinical symptoms and exclusion of other possible diagnoses. This approach is time-consuming, involves numerous tests and procedures, and leads to delayed initiation of appropriate intervention. Therefore, identifying reliable biomarkers for PCS is crucial for improving diagnosis accuracy, predicting outcomes, and developing targeted therapies. This study compared the proteomic profiles between PCS patients and healthy controls to identify disease-specific proteins that could serve as candidate biomarkers. This was a comparative cross-sectional study that recruited six PCS patients who fulfilled the inclusion criteria; persistent symptoms more than three months post infection with diagnosis was confirmed by a physician at the Post COVID-19 clinic. The control group consisted of 10 age, gender and race matched healthy subjects with no history of infection for the past one year. Protein of pooled serum from each group were extracted and separated using two-dimensional electrophoresis method. Firstly, the proteins were separated via iso-electric point, then via different molecular weight. The protein spots were analysed using PD Quest software, and proteins expression with significant difference between the two groups were recognized. Subsequently, proteins of interest were analysed using Matrix Assisted Laser Desorption/Ionization Time-of-Flight (MALDI-TOF) Mass Spectrometry for protein identification. All subjects were Malay females with mean age of 38 ± 9.7 for PCS group and 42 ± 11.8 years for healthy control. Persistent cough and fatigue were found to be the most common presentations (83%) followed by exertional dyspnoea (67%). Proteomic profiles analysis reveals 182 proteins spots were detected in serum PCS patients in a range of pH 4 to 7. Alpha-1 antitrypsin, with molecular weight of 46.7 kDa was identified among the proteins that significantly over-expressed when compared to control ($p=0.02$). This protein is a prototypical protease inhibitor that protects lung tissue from proteolytic damage by inhibiting neutrophil elastase. The elevated levels of Alpha-1 antitrypsin in the serum of PCS patients align with its known antiviral and anti-inflammatory properties, suggesting that it could serve as a potential diagnostic marker for PCS.