Master Dissertation Project

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Lab/Institution: Mass Spectrometry - ITQB
TITLE: Find biomarkers for diagnosing tuberculosis by proteomics based approaches

BACKGROUND

Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (*M.tb*), despite being completely curable, has reemerged as a global pandemic. The failure of effective vaccine protection, lack of early detection of the disease, emergence of drug resistance and the deadly synergism with HIV infection have limited the success of TB disease management. One of the major limitations is the discovery of adequate specific biomarkers for rapid and early diagnosis of active TB, extra-pulmonary TB, latent TB infection (LTBI) and tuberculosis infection in immunosupressed population. Alteration in host cellular processes due to infection leaves unique chemical fingerprints in the form of proteins, small molecules and metabolites. Although some potential TB biomarker have been suggested, an extensive differential proteomic characterization should be performed, since it will allow a more comprehensive identification of biomarkers. Furthermore, detected protein expression differences may be used to pursue and identify pathways underlying the biological process of tuberculosis. As so, the objective of this work is to identify specific biomarkers to active, latent and extra-pulmonary tuberculosis in immune-sufficient and immune-compromised population using a proteomic approach combined with mass spectrometry techniques (LC-MS/MS).

This project is within a FCT financed project "TBomics: an omics approach for diagnosing tuberculosis NEW-INDIGO/0001/2012".

OBJECTIVES

Identify specific serum biomarkers for diagnosing tuberculosis

- Perform LC-MSMS assays for serum samples of patients and controls according with optimized procedure
- Identification of protein differentially expressed among the experimental groups
- Selection of proteins with potential for serum TB biomarkers

PROJECT DESCRIPTION

To identify specific biomarkers for diagnosing tuberculosis, differential proteomics will be performed with blood collected from control and patients with TB (at Centro Diagnóstico da Tuberculose da Venda Nova). The serum separation will be done at Instituto Nacional de Saúde Prof. Ricardo Jorge.

Task 1: The protein extracts for each condition (controls and TB patients) will be obtained, quantified and digested with trypsin for LC-MS/MS analysis.

Task 2: MS and MS/MS data collection: The differentially expressed proteins between different groups will be quantified and identified by liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based proteomics.

Task 3: Protein identification and quantification data treatment: Profile data from the MS scans are transformed to m/z peak lists. Protein identification will be performed using the MS/MS spectra and submitting to a search engine using a general database. For quantification, all reimported peptides of an identified protein are included, and the total cumulative abundance is calculated by summing the abundances of all peptides allocated to the respective protein.

Task 4: Pathway analysis using the proteins identified with expression differences between each pair of sample groups

Task 5: Writing of Master Thesis

TIMELINE (use fill tool for the cells)

	Month 1	Month 2	Month 3	Month 4	Month 5	Month 6	Month 7	Month 8	Month 9	Month 10
Task 1	■	■								
Task 2		■	■	■	■					
Task 3			■	■	■	■				
Task 4							■	■		
Thesis									■	■