Application of multiplexed ion mobility spectrometry-MS towards the identification of host response protein signatures of treatment of pulmonary tuberculosis

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Introduction

- Tuberculosis (TB) is one of the leading causes of deaths from infectious diseases
- According to WHO, 13% of world’s population has TB infection
- In 2016, 10.4 million new TB cases with 1.4 million deaths were reported worldwide
- Microscopy and sputum culture are the current gold standards for diagnosing and monitoring disease
- However, these markers have low to moderate sensitivity and specificity, prompting efforts to identify new quantitative, non-sputum based TB biomarkers
- A blood-based protein signature could hold the promise to improve the efficiency and predictive accuracy of monitoring treatment response.

Methods

- 289 participants enrolled from clinical trials sites in North America, South Africa, Uganda, Spain, Brazil, and Vietnam
- Participants had sputum smear positive for acid fast bacilli at baseline, and were culture positive for drug-susceptible pulmonary TB
- Serum samples were depleted of 14 highly abundant peptides using a ProteomeLabTM 12.7 × 79.0-mm IgY14 LC10 affinity LC column
- Serum was collected, processed and stored at −80°C
- A 60-min gradient was used with the IM-MS platform
- Analysis was performed on an in-house built instrument: 1-m ion mobility drift tube with an Agilent 6224 TOF MS coupled with LC
- Identification and quantification of the detected peptide peaks was performed utilizing the AMT tag approach

Results

- 244 proteins were differentially abundant between baseline and 8 weeks post-treatment
- 41 proteins for week 8 and 54 proteins for week 6 culture status were significantly different between culture negative and culture positive patients in response to treatment
- 244 proteins for week 8 and 54 proteins for week 6 culture status were significantly different between culture negative and culture positive patients in response to treatment
- 17 proteins were consistently discriminatory for both week 6 and 8 culture status stratifications overlapping with 244 proteins of treatment effect

Conclusions

- 872 unique proteins were identified using multidimensional capabilities of LC-IM-MS
- Of those 244 proteins serve as potential candidate markers of treatment response
- 17 proteins were consistently discriminatory for both week 6 and 8 culture status stratifications overlapping with 244 proteins of treatment effect

Baseline concentrations of these proteins can provide predictive information on future culture conversion

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References