Quantitative analysis of the dormant Mycobacterium tuberculosis proteome and prognostic value of some protein antigens for tuberculosis serodiagnosis.

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Formation of dormant Mycobacterium tuberculosis (Mtb) cells is responsible for the phenomenon of latent tuberculosis. Serodiagnosis is an effective method for early detection of pathogen for many infection diseases. However, this method demonstrates low effectiveness for TB detection that could be due to incorrect antigens selected. We suggest to study the expression of protein antigens in dormant state of Mtb in vitro (5 mo old cells) obtained under gradual medium acidification which may reflect the real situation for the pathogen in case of latent TB. Analysis of the proteomic profile of active and dormant Mtb was carried out by LC-MS/MS. In comparison with active Mtb 130 proteins significantly increased in the proteome of dormant Mtb. Among of them isoniazid inducible protein IniB, the multiple antibiotic resistance regulator (MarR), universal stress protein Rv2623, toxin VapC46, sigma factor SigK, transcriptional regulator DevR, heat shock protein Hsp, trehalose-6-phosphate phosphatase OtsB1 were found. Obtained protein signature substantially differs from published result for Wayne model based on O2 limitation highlighting difference in two for dormant Mtb models.
Under dormancy, the enzymes of biosynthesis of macromolecules (DNA, RNA, proteins, cell wall) and transporters are weakly expressed in Mtb.
Three unique Mtb proteins from dormant Mtb proteome were selected and diagnostic effectiveness of these antigens (Rv0341; Rv1509 and Rv2018) was verified with serum of TB patients. According to immunoblotting and IFA, all three recombinant proteins showed the ability to bind to serum antibodies. However, only 30 to 40% of patients turned out to be positive according to this criterion with a specificity of 70 to 90%. As a result, new, previously unpublished, Mtb -specific proteins which may be associated with latent TB were found.
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