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Title: New approaches to tuberculosis diagnosis through the study of metabolomic profile in urine

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Body: Metabolomics has showed to be a promising tool in the diagnosis of several respiratory infections by using urine samples. However, metabolomic studies have not been explored enough to assess tuberculosis (TB) diagnosis with such samples. The aim of the work was to study the metabolomic profile in urine samples through Nuclear Magnetic Ressonance (NMR) with the objective of detecting metabolic changes due to the presence of the disease, and identifying urine biomarkers that help us in tuberculosis diagnosis. 147 individuals were studied and classified in three groups: healthy controls (n=31), latently infected individuals (n=18) and TB patients (n=98). A urine sample was collected from each individual, and analysed by proton NMR spectroscopy. For each urine sample, a one-dimensional spectrum was obtained, whose data were analysed with MestreNova software. Afterwards, Metabonomics was used to perform a statistical multivariate analysis to identify spectrum regions candidates to contain biomarkers for TB. The identification of these metabolites was studied with Chenomx software, what require a two-dimensional NMR analysis from urine. The statistical multivariate analysis (Principal Component Analysis and Partial Least Squares Discriminant Analysis) show that a statistical significance between NMR spectrum from TB patients and the other groups studied ($p < 0.00001$) exist. Therefore, the urine metabolic pattern in TB patients is different than the one from non-TB patients. When analyse the spectral regions where such differences were found,

a total of 20 metabolites were identified. The obtained results suggest that the study of the metabolomic profile in urine is a potential tool for TB diagnosis.