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Title: A change in blood transcriptional signatures accompanies successful tuberculosis therapy

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Body: Introduction Inadequate treatment of patients with active TB leads to worsening disease, infection transmission and drug resistance. Effective anti-TB therapy monitoring is difficult as the best accepted method is the 2-month sputum culture conversion. However this has low sensitivity for predicting an individuals response, and difficult to implement since culture results are not available in 30-50% of patients. No recognised biomarkers of treatment response earlier than 2 months exist. Aims Determine if blood transcriptional profiles can be used in early TB treatment monitoring. Methods Mtb culture-positive, HIV-uninfected, pulmonary TB patients were recruited in Cape Town, South Africa and London. Patients with latent TB infection were also recruited. Whole blood samples were taken before, during, and after, 6 months of standard first line TB drug therapy. Samples were processed for microarray analysis (Illumina). Changes in transcriptional expression were analysed. An algorithm to quantify the changes was also devised. Results All patients responded successfully to therapy. An active TB transcriptional signature was derived by comparing the untreated active and latent TB patients. A specific treatment response transcriptional signature was derived comparing patients before and after treatment. Both signatures showed significant changes in response to treatment and could be quantified for individual patients. Conclusion These results provide evidence that blood transcriptional signatures could be used as biomarkers of a successful treatment response. These potential biomarkers, measured in whole blood, could assess treatment response in patients more consistently than currently available tests.