Title: Response to Mtb Rv2628 latency antigen associates with bacterial containment

Body: Introduction: Interferon(IFN)γ response to Mtb Rv2628 latency antigen is associated with latent tuberculosis infection (LTBI). Immune response against Rv2628 may contribute to evaluate Mtb infection control. Aims: To compare the Rv2628 specific response in recent contacts of patients with active TB before, during and after isoniazid prophylaxis. Methods: In this cross-sectional study we evaluated 139 QuantiFERON TB-Gold In-Tube (QFT-IT) positive contacts: 37 enrolled at baseline, 32 during prophylaxis, 17 at the end of prophylaxis, 53 after 1 year of prophylaxis completion. Whole blood IFNγ response to Rv2628 and QFT-IT (early phase antigens) at day 1 post-culture was evaluated. Controls unexposed to Mtb were also included. Results: IFNγ levels in response to Rv2628 antigen were significantly higher at baseline than after 1 year prophylaxis completion (p<0.0001). The quantitative IFNγ response to QFT-IT was significantly higher at baseline than at the end of prophylaxis (p=0.023) or after 1 year prophylaxis completion (p=0.001); however all the subjects were QFT-IT positive at all the time points considered. Unexposed controls did not respond to Rv2628 and QFT-IT. Conclusions: Whole blood IFNγ response to Rv2628 antigen is significantly reduced in QFT-IT-positive contacts after 1 year prophylaxis completion. Rv2628 is considered a latency antigen therefore it is unclear at the moment if the decreasing response is due to the fact that prophylaxis allows Mtb eradication and a consequent decrease in latency responses, or whether prophylaxis inhibits Mtb to remain in a latent stage. These results may be helpful to better characterize LTBI immune response and to generate tools to monitor prophylaxis efficacy.