O071

1-hour Oral Session

CD27 expression as a new tool to distinguish active tuberculosis (TB) from latent TB infection

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Tuberculosis (TB) kills approximately 1.5 million individuals annually and over 2 billion are estimated to be latently infected with *Mycobacterium tuberculosis* (Mtb) (LTBI), representing a reservoir from which most new TB cases arise. Therefore the control and elimination of the global TB could be enhanced by identifying and treating LTBI individuals. LTBI is identified by a normal chest xRay in a healthy subject with a positive response to immune tests as QuantiFERON TB Gold (QFT) which, unfortunately, does not distinguish between LTBI and active TB. Recently in studies from high TB endemic countries the cytometry evaluation of the down-modulation of the surface molecule CD27 on Mtb-specific CD4 T-cells producing IFNγ in peripheral blood mononuclear cells (PBMC) has been associated to active TB, providing evidence of being a potential tool to distinguish active TB from LTBI. No studies have been conducted in Europe and using whole blood which is an easier sample to obtain compared to PBMC.

Objectives: To validate in a low TB endemic country as Italy if the down modulation of CD27 evaluated by cytometry in whole blood is a tool to discriminate, among QFT-IT-positive patients, active TB from LTBI.

Methods: 62 HIV-uninfected QFT-positive subjects were enrolled: 15 with active pulmonary TB; 17 with cured pulmonary TB; 30 with LTBI. Whole blood cells were stimulated with “RD1” proteins (ESAT-6 and CFP-10), and as recall antigen with Cytomegalovirus lysate (CMV) and with SEB. Antigen-specific response was evaluated by cytometry calculating IFNγ production. The data were presented as a RATIO of the Median Fluorescence Intensity (MFI) of CD27 in the $CD4^+$ T-cells gate over the MFI of CD27 in the gate of $CD4^+$ $IFN\gamma^+$ T-cells responding to the stimulus.

Results: Active TB patients showed a higher RATIO to RD1 antigens compared to cured TB and LTBI ($p= 0.01$ and $p=0.0013$ respectively). This result is due to a down modulation of CD27 specific T-cell in active TB patients. Conversely no differences of MFI RATIO were observed in response to CMV and SEB stimulation among the different groups. Based on the significant difference found in the quantitative analysis in response to RD1, we performed a ROC analysis to evaluate the potential of CD27 MFI RATIO for TB diagnostics. By ROC analysis a significant area under the curve (AUC) was found when comparing TB versus LTBI (AUC, 0.86; 95% CI, 0.69-1, $p=0.001$). For scoring purposes we found that a cut-off of 3.19 predicted active TB with 75% sensitivity (95% CI, 42.81% to 94.51%) and 100% specificity (95% CI, 79.41% to 100.0%).

Conclusions: This study proposes a new cytometric tool based on the modulation of Mtb-specific $CD27^+$ $CD4^+$ T-cells to distinguish, among QFT-positive subjects, TB disease from LTBI status in a low TB endemic country.