CD38 expression by antigen-specific CD4 t cells is significantly restored 5 months after treatment initiation independently of sputum bacterial load at the time of tuberculosis diagnosis

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T cell activation markers (TAM) expressed by antigen-specific T cells constitute promising candidates to attest the presence of an active infection by Mycobacterium tuberculosis (Mtb). Reciprocally, their modulation may be used to assess antibiotic treatment efficacy and eventually attest disease resolution. We hypothesized that the phenotype of Mtb-specific T cells may be quantitatively impacted by the load of bacteria present in a patient. We recruited 105 Tanzanian adult tuberculosis (TB) patients and obtained blood before and after 5 months of antibiotic treatment. We studied relationships between patients' clinical characteristics of disease severity and microbiological as well as molecular proxies of bacterial load in sputum at the time of diagnosis. Besides, we measured by flow cytometry the expression of CD38 or CD27 on CD4+ T cells producing interferon gamma (IFN-γ) and/or tumor necrosis factor alpha (TNF-α) in response to a synthetic peptide pool covering the sequences of Mtb antigens ESAT-6, CFP-10, and TB10.4. Reflecting the difficulty to extrapolate bacterial burden from a single end-point read-out, we observed statistically significant but weak correlations between Xpert MTB/RIF, molecular bacterial load assay and time to culture positivity. Unlike CD27, the resolution of CD38 expression by antigen-specific T cells was observed readily following 5 months of antibiotic therapy. However, the intensity of CD38-TAM signals measured at diagnosis did not significantly correlate with Mtb 16S RNA or rpoB DNA detected in patients' sputa. Altogether, our data support CD38-TAM as an accurate marker of infection resolution independently of sputum bacterial load.
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