TH17-SPECIFIC Treg MAY DIFFERENTIATE BETWEEN ACTIVE AND LATENT MTB INFECTION

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About one-quarter of the world's population is infected with *M. tuberculosis* (MTB), while only 10% of them would ever develop the disease. The widely used interferon gamma-release assays (IGRA) do not differentiate between latent MTB infection (LTBI) and its active phase (ATB).

Aim: To identify reliable immunophenotypic markers predicting the course of MTB infection.

Materials and methods: Peripheral blood samples from IGRA(+) asymptomatic subjects (LTBI, n=15) and IGRA(+) ATB patients (ATB, n=15) were analyzed. Multicolor flow cytometry was used to evaluate the proportions of Th1 (CD196+CD183-), Th1/Th17 (CD183+CD196+), Th17(CD183-CD196+) effectors, induced (CD39+CD25^{hi}CD127^{lo}), and Th17-specific (CD39+CD196+) Treg; IL-17+CD4 and CD8 T cells were determined after overnight antiCD3- stimulation (FACSCanto II, FACSDiva 6.1.2.)

Results: ATB was characterized with increased share of induced (46%vs.22.6%, $p<0.001$) and Th17-specific Treg (10.5% vs 4.8% $p<0.001$), significantly decreased proportions of Th1 and Th1/Th17 effectors (mean 10% vs.16.5% and 12%vs.21.5%, $p<0.05$) and deficiency of IL-17+ CD4 T cells (mean 1.07 % vs.1.97% in LTB, $p<0.5$). Th17-specific Treg correlated inversely with the level Th1/Th17 effectors ($R= -0.5$, $p<0.05$).

Conclusions: The balance Th1/Th17/Treg determines the clinical course of MTB infection. We describe a clear-cut distinction between the effector/regulatory T subset balance in ATB, and LTBI, and propose the combination of Th17 Treg and Th1/Th17 subset as accessible markers differentiating between latency and disease.

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