

Novel *M. tuberculosis* specific IL-2 ELISpot assay discriminates adult patients with active or latent tuberculosis

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Abstract

© 2018 Della Bella et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. Background Tuberculosis (TB) still is a major worldwide health problem, with 10.4 million new cases in 2016. Only 5–15% of people infected with *M. tuberculosis* develop TB disease while others remain latently infected (LTBI) during their lifetime. Thus, the absence of tests able to distinguish between latent infection and active tuberculosis is one of the major limits of currently available diagnostic tools. Methods A total of 215 patients were included in the study as active TB cases ($n = 73$), LTBI subjects ($n = 88$) and healthy persons ($n = 54$). Peripheral blood mononuclear cells (PBMCs) were isolated from each patient and the LIOspot® TB anti-human IL-2 ELISpot assay was performed to test their proliferative response to *M. tuberculosis* antigens ESAT-6, CFP-10 and Ala-DH. Statistical analysis was performed to define the sensitivity and the specificity of the LIOspot® TB kit for each antigen used and to set the best cut off value that enables discrimination between subjects with active TB or latent TB infection. Results Comparing the LIOspot® TB results for each tested antigen between uninfected and infected subjects and between people with latent infection and active TB disease, the differences were significant for each antigen ($p < 0.0001$) but the ROC analysis demonstrated a high accuracy for the Ala-DH test only, with a cut off value of 12.5 SFC per million PBMCs and the Ala-DH ROC curve conferred a 96% sensitivity and 100% specificity to the test. For the ESAT-6 antigen, with a best cut off value of 71.25 SFC per million PBMCs, a sensitivity of 86% and specificity of 36% was obtained. Finally, the best cut off value for CFP-10 was 231.25 SFC per million PBMCs, with a sensitivity of 80% and a specificity of 54%. Thus, as for IGRA assays such as Quantiferon and T-Spot TB tests, ESAT-6 and CFP-10 are unable to distinguish LTBI from active TB when IL-2 is measured. On the contrary, the IL-2 production induced by Ala-DH, measured by LIOspot® TB kit, shows high sensitivity and specificity for active TB disease. Conclusions This study demonstrates that the LIOspot® TB test is a highly useful diagnostic tool to discriminate between latent TB infection and active tuberculosis in adults patients.

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