Assessment of RD 1–Encoded Mycobacterial Antigens in the Immunodiagnosis of Pulmonary, Extrapulmonary, and Latent Tuberculosis Infections

To the Editor—Recently, the Journal published 2 articles [1, 2] that examined the diagnostic performance of RD 1, a genomic segment of *Mycobacterium tuberculosis* that codes 2 protein antigens—early secretory antigenic target (ESAT)–6 and culture filtrate protein (CFP)–10. A T cell–based approach was used to assess the specificity of ESAT-6 and CFP-10 for the identification of pulmonary (P), extrapulmonary (EP), and latent tuberculosis (TB) infection. Munk et al. [1] concluded that both ESAT-6 and CFP-10 hold diagnostic potential for the diagnosis of active P-TB and EP-TB. Lalvani et al. [2] concluded that 80% of the urban Indian population in endemic areas is latently infected with TB.

If Munk et al. [1] had evaluated the diagnostic efficacy of ESAT-6 and CFP-10 antigens in cases of TB of the central nervous system (CNS), a major problem of differential diagnosis of tuberculous meningitis (TBM) would have been solved. TB of the CNS is a common form of EP-TB that occurs in endemic areas of underdeveloped and developing countries and poses serious problems in its differential diagnosis, as do other parasitic (e.g., neurocysticercosis), fungal (e.g., cryptococcal meningitis), and bacterial infections (e.g., neurobrucellosis) that are highly endemic in those areas. Various clinical manifestations of TBM overlap with those of other diseases of the CNS [3]. Although sequences of ESAT-6 and CFP-10 have been determined to be specific for *M. tuberculosis* [2], previous studies have shown that 10kDa of the *M. tuberculosis* sequence has 90% homology with 10kDa of the *M. leprae* [4] sequence, groES of *Escherichia coli*, and human chaperonin 10 [5] and is known to induce T cell responses in both patients and their contacts [6]. A 3-dimensional structure of 10 kDa of chaperonin 10 of *M. tuberculosis* also has shown structural homology with that of groES and *M. leprae* chaperonin 10 [7]. Even if ESAT-6 and CFP-10 are used in the specific diagnosis of TBM, CFP-10 might result in a false-positive reaction, leading to misdiagnosis, especially in TB of the CNS. Therefore, these antigens should be evaluated in cerebrospinal fluid for their diagnostic potential of chronic infection of the CNS.

Findings of previous studies [1, 2, 8] raise the question of whether ESAT-6 and CFP-10 antigens of *M. tuberculosis* are more protective or diagnostic in nature. Because the host resistance to mycobacterial organisms is dependent largely on bactericidal and/or bacteriostatic activity of macrophage-induced interferon (IFN)–γ [9], the ability of ESAT-6 and CFP-10 antigens to induce the production of IFN-γ in the latently infected urban population of India [2] suggests that these antigens conferred protection to these individuals. IFN-γ is one of the major cytokines responsible for macrophage activation, especially in controlling several intracellular pathogens, including *M. tuberculosis* [10, 11]. In such cases, do Lalvani et al. [2] suggest treatment for 80% of the urban population of India when there is no history of clinical, radiological, or bacteriological evidence of TB? Perhaps their conclusion holds good if latently infected patients are followed up for the next 10–20 years for the development of TB. I wonder whether performing T cell–based assays routinely for the diagnosis of P-TB or EP-TB is feasible or cost effective, even in a tertiary care setting, in underdeveloped and developing countries. In many sanatoriums and other clinics in such countries, the infrastructural facilities available are microscopy for direct staining of acid-fast bacilli by Zeil-Nelsen staining and x-ray machines for chest radiograph. Hence, it might be advisable to evaluate ESAT-6 and CFP-10 antigens in enzyme- or agglutination-based immunoassays for the diagnosis of P-TB, EP-TB, and latent TB infections.

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References

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