Mapping TB resistance (*J Exp Med 2006; 12: 2578-2579*)

Almost two-thirds of the global population is infected with *M. tuberculosis,* yet the disease only manifests in about 10% of infected individuals. To find genetic variants controlling susceptibility to infection, a study was done in Cape Town, South Africa, where TB is highly endemic like in India. Although most subjects were likely to have been exposed to *M. tuberculosis*, about 40% did not show delayed type hypersensitivity (DTH) in a skin antigen test. The researchers have identified one locus (6-Mbp chromosome region, 11p14) that determines whether an individual will respond to the TB skin test and a second (2.9-Mbp 5p15) that controls the extent of that response. The results suggest that one major genetic locus controls innate resistance to the pathogen in humans.

COMMENTS This important finding may unveil cellular mechanisms that might one day be manipulated to prevent TB—an important goal given the recent rise in drug-resistant strains. Also, these genetic factors might contribute to whether an infected individual keeps the bacterium dormant or develops the disease.

Faster detection of TB may be on the horizon (*Am J Resp Crit Care Med 2009; 180: 666-673*)

Diagnosis of tuberculosis involves a long time period and in about half of all people with active TB, the disease-causing bacterium cannot be identified using sputum tests. European researchers have developed a new test – *M. tuberculosis* specific enzyme linked immunospot (ELISpot) assay - that can rapidly identify active tuberculosis in people who have had negative sputum tests. In a study including 347 people, ELISpot results were positive in 65/71 cases (91.5 %) with active pulmonary TB. A negative result almost excludes active TB.

COMMENTS: The rapid diagnosis of pulmonary tuberculosis is difficult when acid fast bacilli cannot be detected in sputum smears. An ELISpot test detects active TB by comparing the frequencies of TB-specific T-lymphocytes in the blood with those in the lung, with results in a day. This can facilitate early treatment.

Sputum *Mycobacterium tuberculosis* mRNA as a marker of bacteriologic clearance in response to anti-tuberculosis therapy (*J Clin Microbiol doi:10.1128/JCM.01526-09*)

Messenger RNA is a marker of cell viability. Quantifying *M. tuberculosis* mRNA in sputum is a promising tool for monitoring response to AKT and evaluating the efficacy of individual drugs. In this study, mRNA levels were measured in sputum specimens from patients with TB receiving monotherapy in an early bactericidal activity study of fluoroquinolones and in those receiving a standard rifampin-based regimen in an IL-2 trial. Messenger RNA for the glyoxylate cycle enzyme isocitrate lyase declined at similar rates in patients receiving isoniazid, gatifloxicin, levofloxacin, and moxi-floxacin monotherapy. Isocitrate lyase mRNA corre-lated highly with colony forming units in sputum prior to therapy and during 7 days of monotherapy in all treatment arms. Isocitrate lyase mRNA was detectable in sputum of culture-positive TB patients receiving a rifampin-based regimen for 1 month. At 2 months, sputum for isocitrate mRNA correlated more closely with growth in liquid culture than did growth on solid culture medium.

COMMENTS Isocitrate lyase mRNA appears to be a reliable marker of *M. tuberculosis* and when available, is of great importance to test the efficacy of the treatment regime.

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