INFECTIOUS DISEASE

The tuberculosis signature

Anne O'Garra and colleagues, reporting in *Nature*, describe a gene expression signature that identifies individuals with active tuberculosis disease and may also indicate those individuals who are latently infected with *Mycobacterium tuberculosis* and go on to develop active disease. The tuberculosis signature was shown to be dominated by interferon (IFN)-induced genes. The discovery of such a signature should aid the diagnosis and prognosis of tuberculosis, which is a major cause of morbidity and mortality worldwide.

Most people who are infected with *M. tuberculosis* remain asymptomatic (known as latent tuberculosis), but approximately 10% of these individuals are at risk of developing active disease in their lifetime. To identify the markers of active disease and disease risk, the authors carried out a genome-wide analysis of gene expression in the blood of people with active tuberculosis (before treatment), people with latent tuberculosis and healthy control individuals. They identified a distinct 393-transcript signature that defines patients with active disease and that correlates with the extent of the disease (as determined by radiography). Interestingly, 10–25% of patients with latent tuberculosis had a transcriptional profile that was similar to that

of patients with active disease, and this is also the expected percentage of patients with latent tuberculosis who are at risk of progression to active disease. The transcriptional signature decreased in patients with active disease after 2 months and reverted to that of healthy controls after treatment, which suggests that the signature could be used to monitor the host response to infection and the efficacy of treatment. Moreover, the signature was distinct from the gene signatures of other bacterial and inflammatory diseases.

Next, the authors used a data-mining strategy to identify sets of genes in the signature that were coordinately expressed. B cell- and T cell-associated transcripts were under-represented in the signature, whereas myeloid cell-related transcripts were abundant. The largest set of transcripts that changed in active tuberculosis contained those transcripts that were

induced by type I IFNs or IFN γ . A type I IFN-inducible signature has also been seen in patients with systemic lupus erythematosus, but these patients also have an increase in plasma cell-related transcripts that is not present in the tuberculosis signature. Analysis of gene expression in purified cell populations revealed that neutrophils and monocytes were likely to be responsible for the increase in IFN-inducible transcripts in active tuberculosis.

This study is the first to provide a genome-wide transcriptional signature that is associated with active tuberculosis and reveals a previously unappreciated role for type I IFN signalling in the pathogenesis of this disease.

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ORIGINAL RESEARCH PAPER Berry, M. P. R. et al. An interferon-inducible neutrophil-driven blood transcriptional signature in human tuberculosis. *Nature* **466**, 973–977 (2010)