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Expression profiling of lymph nodes in tuberculosis patients reveal inflammatory milieu at site of infection

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Extrapulmonary manifestations constitute 15 to 20% of tuberculosis cases, with lymph node tuberculosis (LNTB) as the most common form of infection. However, diagnosis and treatment advances are hindered by lack of understanding of LNTB biology. To identify host response, *Mycobacterium tuberculosis* infected lymph nodes from LNTB patients were studied by means of transcriptomics and quantitative proteomics analyses. The selected targets obtained by comparative analyses were validated by quantitative PCR and immunohistochemistry. This approach provided expression data for 8,728 transcripts and 102 proteins, differentially regulated in the infected human lymph node. Enhanced inflammation with upregulation of T-helper1-related genes, combined with marked dysregulation of matrix metalloproteinases, indicates tissue damage due to high immunoactivity at infected niche. This expression signature was accompanied by significant upregulation of an immunoregulatory gene, leukotriene A₄ hydrolase, at both transcript and protein levels. Comparative transcriptional analyses revealed LNTB-specific perturbations. In contrast to pulmonary TB-associated increase in lipid metabolism, genes involved in fatty-acid metabolism were found to be downregulated in LNTB suggesting differential lipid metabolic signature. This study investigates the tissue molecular signature of LNTB patients for the first time and presents findings that indicate the possible mechanism of disease pathology through dysregulation of inflammatory and tissue-repair processes.

Extrapulmonary tuberculosis (EPTB) refers to infection of *Mycobacterium tuberculosis* at body sites other than the lungs¹. Lymph node TB (LNTB) is one of the most common manifestations of EPTB that affects, most frequently, the peripheral and cervical lymph nodes. EPTB is reported to occur in isolation or along with the more frequent clinical presentation of TB, pulmonary TB (PTB)^{2,3}. EPTB prevalence is reported from 15 to 20% of all cases of TB in endemic countries and accounts for more than 50% cases in immunocompromised individuals^{3–5}. In 2012, 0.8 million out of total 6.1 million notified TB cases had

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