Polymorphisms in Autophagy Genes and Susceptibility to Tuberculosis

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Abstract

Recent data suggest that autophagy is important for intracellular killing of Mycobacterium tuberculosis, and polymorphisms in the autophagy gene IRGM have been linked with susceptibility to tuberculosis (TB) among African-Americans, and with TB caused by particular M. tuberculosis genotypes in Ghana. We compared 22 polymorphisms of 14 autophagy genes between 1022 Indonesian TB patients and 952 matched controls, and between patients infected with different M. tuberculosis genotypes, as determined by spoligotyping. The same autophagy polymorphisms were studied in correlation with ex-vivo production of TNF, IL-1β, IL-6, IL-8, IFN-γ and IL-17 in healthy volunteers. No association was found between TB and polymorphisms in the genes ATG10, ATG16L2, ATG2B, ATG5, ATG9B, IRGM, LAMP1, LAMP3, P2RX7, WIP1, MTOR and ATG4C. Associations were found between polymorphisms in LAMP1 (p=0.02) and MTOR (p=0.02) and infection with the successful M. tuberculosis Beijing genotype. The polymorphisms examined were not associated with M. tuberculosis induced cytokines, except for a polymorphism in ATG10, which was linked with IL-8 production (p=0.04). All associations found lost statistical significance after correction for multiple testing. This first examination of a broad set of polymorphisms in autophagy genes fails to show a clear association with TB, with M. tuberculosis Beijing genotype infection or with ex-vivo pro-inflammatory cytokine production.

Introduction

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