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# Polymorphisms in Autophagy Genes and Susceptibility to Tuberculosis

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## Abstract

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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*, *WIPI1*, *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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