

# “Genetic Predictors of Host Susceptibility to Infection: The Role of Immunity in Tuberculosis and Preterm Birth”

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## ABSTRACT

Host susceptibility to infection and inflammatory response plays an important role in multiple complex diseases. In this presentation results from two independent studies, tuberculosis (TB) and spontaneous preterm birth (PTB), will be presented examining the role of immunity in complex disease. Tuberculosis (TB) is a global public health problem and a source of preventable deaths each year, with 8.8 million new cases of TB and 1.6 million deaths worldwide in 2005. Approximately ten percent of infected individuals develop pulmonary or extrapulmonary TB, suggesting that host defense factors influence development of active disease. Toll-like receptors (*TLRs*) and interleukin 12 (*IL12B*) polymorphisms have been associated with regulation of *TLR* and *IL12B* expression and development of active TB. In the present study 71 polymorphisms in *TLR1*, *TLR2*, *TLR4*, *TLR6*, and *TLR9* and 7 polymorphisms in *IL12B* from 474 (295 cases and 179 controls) African-Americans, 381 (237 cases and 144 controls) Caucasians, from 566 (286 cases and 280 controls) Africans from The Gambia, and from 667 (321 cases and 346 controls) Africans from Guinea-Bissau for association with pulmonary TB using generalized estimating equations and logistic regression.

PTB (<37 weeks gestation) occurs in ~12% of pregnancies in the United States, and is the largest contributor to neonatal morbidity and mortality. PTB is a complex disease, potentially induced by several etiologic factors from multiple pathophysiologic pathways. To dissect the genetic risk factors of PTB a large-scale high-throughput candidate gene association study was performed examining 1536 SNPs in 130 candidate genes from four hypothesized PTB pathways. Maternal and fetal DNA from 370 US Caucasian birth-events (172 cases and 198 controls) and 279 African American birth-events (82 PTB and 197 term birth) were examined. Single locus, haplotype, and multi-locus association analyses were performed separately on maternal and fetal data. The results from these two studies demonstrate that genetic predictors of host susceptibility to infection and inflammatory response may help to identify those individuals at risk of developing disease.