

Scientists identify gene that may make humans more vulnerable to pulmonary tuberculosis

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Researchers from the Genome Institute of Singapore (GIS) and its collaborators have now identified for the first time a new gene that may confer susceptibility to pulmonary tuberculosis. Their findings, published October 10 in the open access journal *PLoS Genetics*, reported that a gene named Toll-like receptor 8 (TLR8), previously shown only to recognize some factors from viruses such as the human immunodeficiency virus (HIV), has a probable role in human susceptibility to *Mycobacterium tuberculosis* infections. The results from the study also found that males are more susceptible than females.

Pulmonary tuberculosis is a contagious lung disease caused by a bacterium known as *Mycobacterium tuberculosis* (*M. tuberculosis*). Although a third of the world population is infected with *M. tuberculosis*, only 5 – 10% of them will ever develop tuberculosis, giving rise to a proposition that there may be a difference in genetic variants within the genes involved in host immune response.

Dr Sonia Davila, Research Scientist at the GIS and first author of the article, said, "We are really excited about this discovery as it is the first time TLR8 has been implicated in bacteria infections. Our analysis of the results from cohort studies in Indonesia and Russia suggested that susceptibility was attributed to genetic variants of TLR8, which is located at the X chromosome. Males carrying only one copy of the gene could have a higher chance of suffering from the disease. These findings

open up a whole new area of research and we hope that it will increase our understanding of the disease process of pulmonary tuberculosis." GIS Senior Group Leader and Associate Director of Infectious Diseases, Dr Martin Hibberd added, "This project is a great example of international teams coming together to solve a difficult problem, with groups from Indonesia, Singapore, the UK, Russia and the Netherlands playing important roles. We hope that this work can initiate further research that will make a difference to people suffering from TB".

"The team from the Genome Institute led by Drs Davila, Seielstad and Hibberd has made an important new discovery of an alternative cellular receptor for one of the world's most important infectious agents, *M. tuberculosis*, the causative agent of TB," said Assistant Professor Paul MacAry, from the National University of Singapore Graduate School for Integrative Sciences and Engineering. "The identification of a role for TLR8 in TB infection has the potential to open up new areas of exploration in TB host/pathogen interactions and provide researchers and clinician scientists with novel targets for therapeutic intervention. This is extremely important given the emergence of multi-drug resistant strains of *M.tuberculosis* that are refractive to current treatment regimes."

Citation: Davila S, Hibberd ML, Hari Dass R, Wong HEE, Sahiratmadja E, et al. (2008) Genetic Association and Expression Studies Indicate a Role of Toll-Like Receptor 8 in Pulmonary Tuberculosis. PLoS Genet 4(10): e1000218. doi:10.1371/journal.pgen.1000218
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