

Gene with probable role in human susceptibility to pulmonary tuberculosis identified

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A new gene that may confer susceptibility to pulmonary tuberculosis has been identified by Genome Institute of Singapore (GIS) researchers and their collaborators in The Netherlands, Indonesia, United Kingdom, and the Russian Federation.

In the current *PLoS Genetics*, the scientists report that the gene, named Toll-like receptor 8 (TLR8), which had been previously shown to recognize some factors from viruses such as the human immunodeficiency virus (HIV), also has a probable role in human susceptibility to *Mycobacterium tuberculosis* infections.

The study also found that males are more susceptible than females.

"We are really excited about this discovery as it is the first time TLR8 has been implicated in bacteria infections," said Dr. Sonia Davila, GIS Research Scientist and first author of the article.

"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," Dr. Davia added. "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 noted, "This project is a great example of international teams coming together to solve a difficult problem, with groups from Indonesia, Singapore, 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 Dr. Paul MacAry, Assistant Professor at 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," Dr. MacAry added. "This is extremely important given the emergence of multi-drug resistant strains of M.tuberculosis that are refractive to current treatment regimes."

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 to 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.

The research findings are published in the October 8, 2008 issue of PLoS Genetics in an article titled, "Genetic Association and Expression Studies Indicate a Role of Toll-Like Receptor 8 in Pulmonary

Tuberculosis".

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