

Leprosy susceptibility genes reported

December 16 2009

In the first genome-wide association study (GWAS) of leprosy and the largest GWAS on an infectious disease, scientists at the Genome Institute of Singapore (GIS) and 26 institutes in China identified seven genes that increase an individual's susceptibility to leprosy.

The discovery of these genes, reported in the 16 Dec. 2009 [New England Journal of Medicine](#), highlights the important role of the innate immune response in the development of [leprosy](#), said the scientists, who analyzed over 10,000 samples from leprosy patients and healthy controls in China.

"Though leprosy is not common, the discoveries have significant ramifications for chronic infectious disorders and for host-pathogen interactions in other more prevalent mycobacterial diseases such as tuberculosis, said Edison Liu, M.D., Executive Director of GIS, one of the research institutes sponsored by Singapore's Agency for Science, Technology and Research (A*STAR).

"This study represents one of the largest and best organized studies of the host genetics in [infectious diseases](#) published," added Dr. Liu.

An immunologist who was not one of the authors of the *NEJM* paper, Tom H. M. Ottenhoff, M.D., Ph.D., of Leiden University Medical Center in The Netherlands, said,

"This is a very impressive study, which uncovers entirely new genes that control susceptibility to leprosy and perhaps also other related diseases. A great asset is that the study underpins the genetic data with plausible

functional biology experimentation, which is not often seen."

Dr. Ottenhoff is Professor in Immunology, Head group Immunology and Immunogenetics of Bacterial Infectious Diseases, at Leiden University Medical Center.

The seven genes associated with susceptibility to leprosy are: CCDC122, C13orf31, NOD2, TNFSF15, HLA-DR, RIPK2 and LRRK2.

"This is a very significant find, and one that can only be achieved through large-scale genetic studies, with close collaborative efforts among multi-disciplinary research groups, often across different countries," said Jianjun Liu, Ph.D., Human Genetics Group Leader at the GIS.

"The discovery of these genes is a major breakthrough for research in leprosy and infectious diseases in general, and will be significant in the early diagnosis and development of new treatments," added Dr. Liu.

In addition to Dr. Liu, the leaders of the GWAS on leprosy included: Fu-Ren Zhang, M.D., Ph.D., of Shandong Provincial Institute of Dermatology and Venereology, and Xue-jun Zhang, M.D., Ph.D., of Institute of Dermatology and Department of Dermatology at No.1 Hospital, Anhui Medical University, China.

GIS Executive Director Dr. Liu noted, , "This is a continuation of a number of deep collaborative studies between the GIS and Chinese scientists in using population sciences to uncover genetic modifiers of human disease. The strength of Chinese clinical sciences and of Singapore's targeted genomic capabilities makes a powerful scientific combination. The key to this collaboration and one that was recently published on the genetics of Asian migration is that the studies were initiated and executed by Asian partners acting as equals. Hopefully, this

will initiate a new phase of cooperation between historically competing Asian countries whose primary links have been with western communities."

Leprosy, a chronic infectious disease caused by the bacterium *Mycobacterium leprae* (*M. leprae*), mainly affects skin and peripheral nerves and may lead to irreversible disabilities. Although it has been largely eliminated in developed countries, leprosy is still a major public health problem in many developing countries, particularly in tropic and sub-tropic regions. According to the World Health Organization, 254,525 new cases of leprosy were diagnosed in 2007. Although many people are potentially exposed to *M. leprae* in endemic regions, only a small minority will be infected and will develop clinically overt leprosy, suggesting that only some individuals are susceptible to this disease.

Because *M. leprae* cannot be cultured in the laboratory, and because it only infects humans and the Armadillo, research and thus the biological understanding of leprosy are very limited. The discovery of the seven susceptibility genes not only improves scientists' understanding about genetic susceptibility to the disease, but also may stimulate additional biological and clinical research to reveal the mechanism of leprosy development.

More information: "Genomewide association study of leprosy", *New England Journal of Medicine*, 16 Dec 2009.

Provided by Agency for Science, Technology and Research (A*STAR)

Citation: Leprosy susceptibility genes reported (2009, December 16) retrieved 24 April 2024 from <https://medicalxpress.com/news/2009-12-leprosy-susceptibility-genes.html>

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