Medical Xpress

Researchers isolate genetic variants responsible for leprosy predisposition

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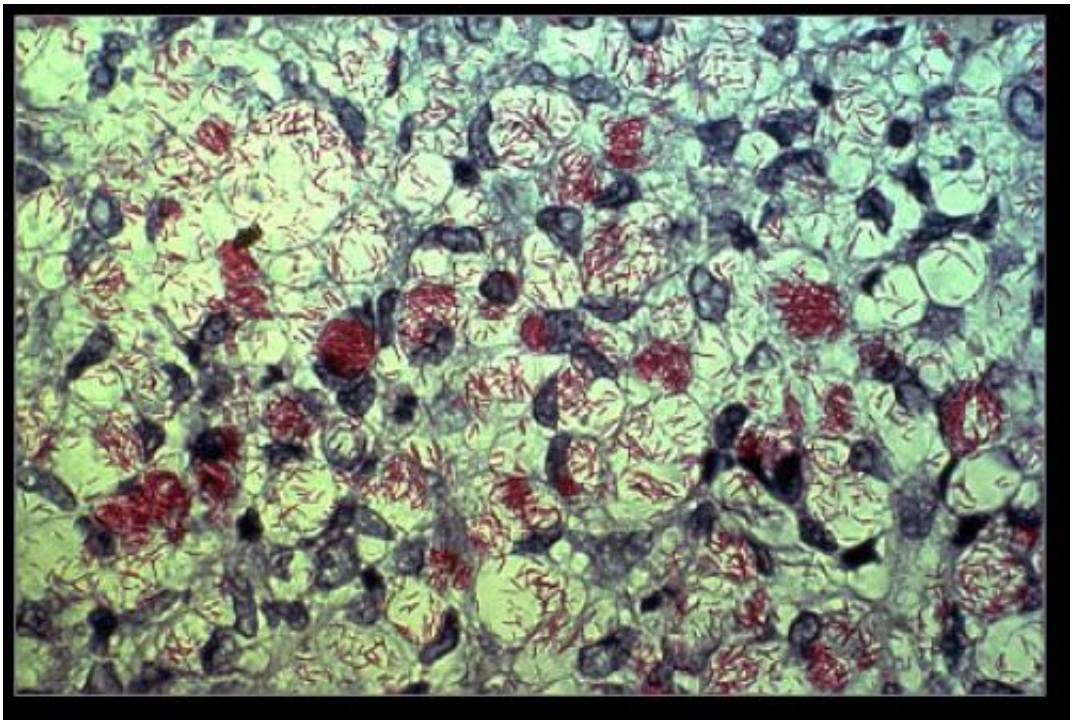

M. leprae, one of the causative agents of leprosy: As an acid-fast bacterium, M. leprae appears red when a Ziehl-Neelsen stain is used. Credit: Public Domain

(Medical Xpress)—A team of researchers with members from institutions in China, the U.S. and Singapore has successfully isolated six genetic variants in people that confer a higher predisposition to infection by the bacteria that causes leprosy. In their paper published in the journal *Nature Genetics*, the team describes the study they undertook to

isolate the genetic variants that had thus far gone unknown, and explain why what they have found could help towards developing treatments for people with the disease.

Leprosy is widely known because of its history—people afflicted with the disease have been (and still are in some places) shunned and forced to live in separate colonies to prevent infections in other people. It is caused by two types of bacteria, and scientists now know that most people are actually able to fight off such infections. The disease is characterized by skin inflammation, nerve, eye and respiratory tract damage and limb injures due to numbness. The disease is treatable with variety of antibacterial agents, but persists in places where there is limited health care. Prior research had led to discovery of eleven of the genetic variants that are responsible for a predisposition to being infected, yet it was clear that there were still some that had not been identified. In this new study, the team has found six more, which medical workers are hoping, will mean that all have been found.

To find those elusive variants the researchers enlisted the assistance of 8,313 people in China with the disease and 16,017 people that did not have it. By performing genome wide association studies (GWAS) on all of the participants, the researchers were able to isolate the six variants that had not been found before (they also confirmed those previously found). During the course of their research, the team also noted that some of the variants they found were the same variants found in other people that are responsible for less susceptibility to some auto-immune disorders, which suggests a trade-off of sorts is at play.

Adding six more variants to the known list will help doctors diagnose the disorder earlier in infected people that were not identifiable before, helping prevent the damage that can occur later on.

More information: Discovery of six new susceptibility loci and

analysis of pleiotropic effects in leprosy, *Nature Genetics* (2015) DOI: 10.1038/ng.3212

Abstract
Genome-wide association studies (GWAS) have led to the discovery of several susceptibility loci for leprosy with robust evidence, providing biological insight into the role of host genetic factors in mycobacterial infection. However, the identified loci only partially explain disease heritability, and additional genetic risk factors remain to be discovered. We performed a 3-stage GWAS of leprosy in the Chinese population using 8,313 cases and 16,017 controls. Besides confirming all previously published loci, we discovered six new susceptibility loci, and further gene prioritization analysis of these loci implicated BATF3, CCDC88B and CIITA-SOCS1 as new susceptibility genes for leprosy. A systematic evaluation of pleiotropic effects demonstrated a high tendency for leprosy susceptibility loci to show association with autoimmunity and inflammatory diseases. Further analysis suggests that molecular sensing of infection might have a similar pathogenic role across these diseases, whereas immune responses have discordant roles in infectious and inflammatory diseases.