Researchers find genetic link to tuberculosis

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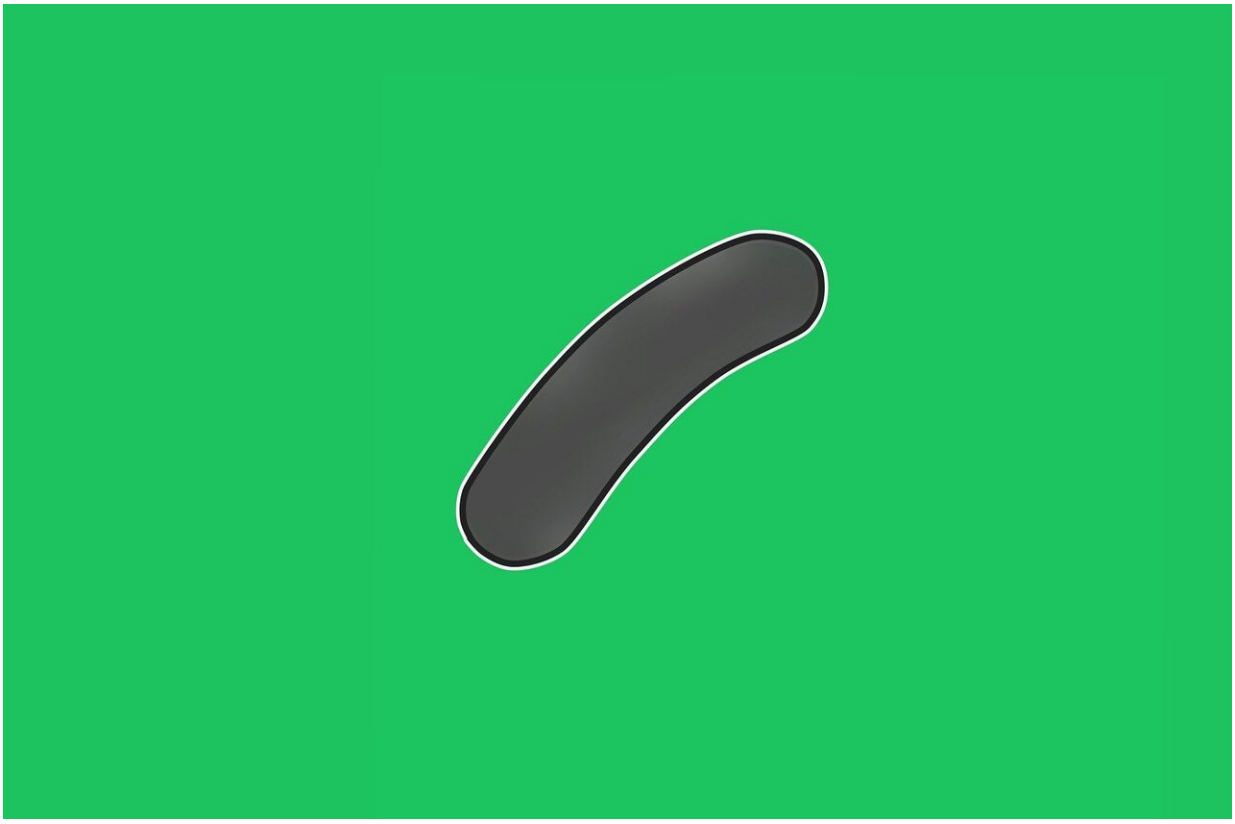

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About one in five people are infected with Mycobacterium tuberculosis, the microbe that causes tuberculosis. Most, however, will never develop symptoms; and for decades researchers have been stumped as to why some people are more vulnerable to the bacterium than others. Now, Rockefeller scientist Jean-Laurent Casanova has identified a genetic

condition that makes the immune system susceptible to mycobacterial attack.

Last year, Casanova showed that the risk of developing TB is heightened in people who have two copies of a particular variation of the gene coding for the enzyme TYK2. However, he notes, this first study was limited in that its participants came from various non-European countries endemic for TB, and were infected with different strains of Mycobacterium tuberculosis. "We have now obtained stronger data by looking at a genetically homogeneous European population, exposed to the same bacterium," he says.

Casanova and his colleagues analyzed genetic information from the UK biobank, a human genomics dataset representing 500,000 people from the general population of the United Kingdom. They found that the TYK2 variant was associated with one percent of TB cases within this group, affecting approximately 1 in 600 Europeans. Described in *Proceedings of the National Academy of Sciences*, this finding accounts for more cases of TB than any other known genetic condition, says Casanova, and it may eventually yield new ways to treat the disease.

"We know that this TYK2 variant causes low levels of gamma interferon, which usually protects the body from mycobacteria," he says. "And it is probable that treatment with gamma interferon, a medicine that has been available for 30 years, could be an effective therapy for these people."

More information: Gaspard Kerner et al. Homozygosity for TYK2 P1104A underlies tuberculosis in about 1% of patients in a cohort of European ancestry, *Proceedings of the National Academy of Sciences* (2019). DOI: 10.1073/pnas.1903561116

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