'Survival gene' stops strains of tuberculosis mutating into deadly 'superbugs'

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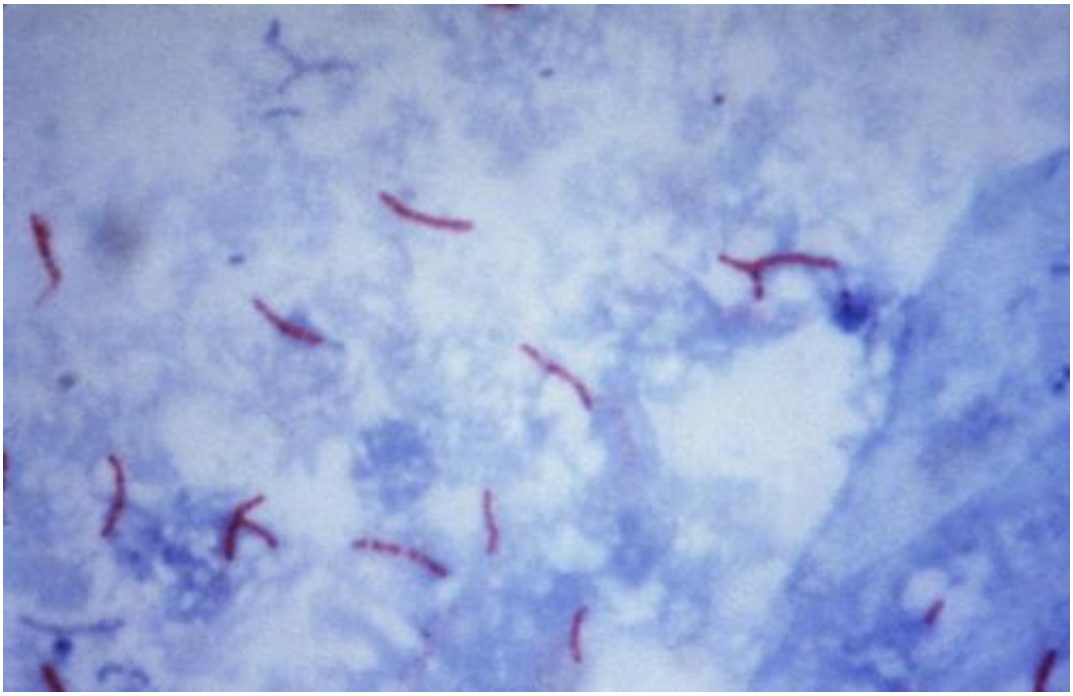

This photomicrograph reveals Mycobacterium tuberculosis bacteria using acid-fast Ziehl-Neelsen stain; Magnified 1000 X. The acid-fast stains depend on the ability of mycobacteria to retain dye when treated with mineral acid or an acid-alcohol solution such as the Ziehl-Neelsen, or the Kinyoun stains that are carbolfuchsin methods specific for M. tuberculosis. Credit: public domain

Scientists have discovered a key 'survival gene' that prevents strains of tuberculosis (TB) from mutating into drug-resistant 'superbugs'.

In a joint study, published today, Friday January 27th 2017, in the journal *Nature Communications*, scientists from the Centro Nacional de Biotecnología in Madrid and the University of Sussex in Brighton, report the discovery of a gene called NucS that dramatically reduces mutation rates in mycobacteria—the infectious microbe which causes tuberculosis (TB).

TB, which is spread from person to person through the air, is one of the top 10 causes of death worldwide with 1.8 million people dying from the disease last year. Drug-resistant strains of TB have already been identified in 105 countries and the researchers involved in this study believe that the identification of a key gene, required to supress mutation rates in mycobacteria, is an important step towards understanding how 'superbugs' develop.

Using a genetic screen, which involved individually knocking out nearly every gene (11,000 genes) in mycobacteria, and screening whether mutant strains grew on a specific antibiotic (rifampicin), the scientists discovered that a DNA repair enzyme, produced by the NucS gene, dramatically reduces mutations from occurring.

The researchers also discovered that genetic variations in the NucS gene significantly influence the mutation rates in clinically isolated strains of mycobacteria. More work needs to be done, but the scientists believe this discovery could also play a role in understanding the development of antibiotic-resistance in patients already suffering from TB.

Professor Aidan Doherty, from the University of Sussex, said: "The rise of antibiotic resistance is a major threat to global health and, if we are to limit its impact on infectious diseases, we first need to identify the mechanisms that prevent bacteria from mutating in the first place. This knowledge will then enable us to better understand how pathogens develop into 'superbugs'.

"Incredibly, for many years it was believed that mycobacteria lacked any mutation avoidance genes. Therefore, the discovery that the NucS gene reduces the rate at which mutations occur in these pathogens is a crucial first step towards identifying the genetic factors that influence the onset of antibiotic-resistance. This will enable scientists and clinicians to screen for strains that are most likely to develop drug-resistance and figure out strategies to tackle this serious threat."

Professor Jesus Blázquez, from the Centro Nacional de Biotecnología, said: "Not only does this study identify that mutations can be reversed in mycobacteria, it reveals that the loss of this DNA repair process can cause a huge increase in the mutation rates, significantly increasing the likelihood of these pathogens acquiring mutations - which can cause antibiotic resistance.

"Now we know that that NucS dramatically reduces mutation rates in mycobacteria—it is vital that we take advantage of this and work towards exploiting this discovery to help doctors and microbiologists to predict and prevent the development of antibiotic resistance during treatments."

The study published in *Nature Communications* is entitled, "A non-canonical mismatch repair pathway in prokaryotes".

Provided by University of Sussex