Tuberculosis bacteria find their ecological niche

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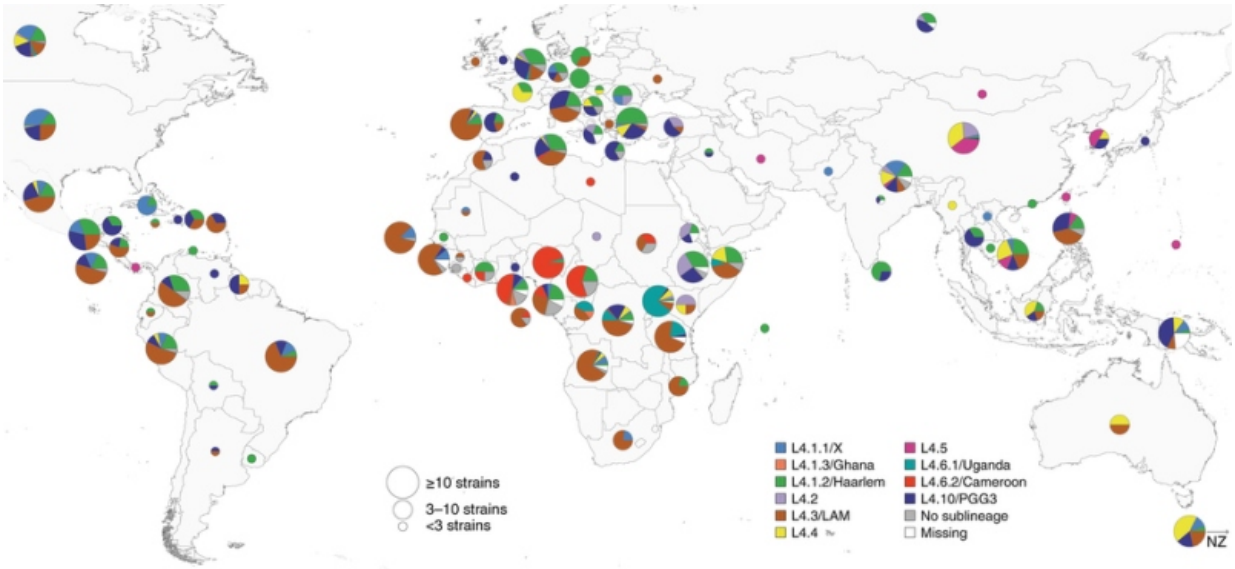

Global distribution of TB lineage 4 sublineages. Credit: Stucki D et al.; Nature Genetics (2016)

Tuberculosis (TB) is a major global public health problem. Treatment often takes many months and till this day there is no effective vaccine. Various TB bacterial strains exist globally, with different geographical spread. Only the so-called Lineage 4 occurs on all continents. It is responsible for the majority of the 10 million new infections and 2 million deaths annually.

Under the lead of Sébastien Gagneux at the Swiss Tropical and Public Health Institute (Swiss (TPH), and DZIF scientist Stefan Niemann, Research Center Borstel, a team of 75 scientists at 56 institutions analyzed the genetic make-up of TB bacteria from several thousand patients. Surprisingly, it was found that Lineage 4 can be genetically further subdivided into several sublineages. Some of these sublineages occur all over the world, others are geographically highly restricted. According to the study in the journal *Nature Genetics*, TB bacteria can be divided into generalists with worldwide distribution and specialists that have focused on localized ecological niche. While ecologists have been differentiating between generalists and specialists, especially in plants, for a pathogen that transmits exclusively from human to human, such a subdivision is new.

Generalists are immunologically more versatile than specialists

TB bacteria have a unique property: they hardly vary their antigens, and are thus efficiently recognized by the human immune system. As a result, a fierce immune reaction occurs, which affects the lungs in particular, and promotes coughing. Thanks to this strategy, TB bacteria is transmitted very efficiently from human to human.

The researchers show that the generalists pursue an additional strategy. They show a slightly increased diversity of their antigens compared to the specialists. "Generalists are thus able to react more specifically to the immune system of different human populations," says Stefan Niemann, who coordinates the research field "Tuberculosis" at DZIF. They have adapted their molecular strategy and are able to push through and spread much more globally.

Implications for vaccine development

These new findings have implications for the development of new TB vaccines. The more TB bacteria can adapt their antigens, the more difficult it will be to design a vaccine that is equally effective in all human populations across the world. Hence, the development of a broadly active TB vaccine might be delayed even further.

The international cooperation has made these results possible; for the German Center for Infection Research scientists from the sites Hamburg-Lübeck-Borstel, Munich and Tübingen have contributed to it as well as scientists from the African Partner Institutions. "National and international networks are the basis for the global fight against infectious diseases as HIV and TB", says DZIF Prof Michael Hoelscher, Director of the Tropical Institute in Munich, LMU. "This has been the concept for the successful work of DZIF in the research field "Tuberculosis".

More information: David Stucki et al, Mycobacterium tuberculosis lineage 4 comprises globally distributed and geographically restricted sublineages, *Nature Genetics* (2016). DOI: 10.1038/ng.3704

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