

# New treatment to tackle drug-resistant strains of TB could now be possible

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Scanning electron micrograph of *Mycobacterium tuberculosis* bacteria, which cause TB. Credit: NIAID

New drugs to treat strains of TB which have become resistant to treatment are now a possibility following a ground breaking discovery from the University of Surrey.

Findings from the study, published in *Cell Reports*, show that researchers have successfully identified the source of nitrogen in host blood cells that allows the pathogen *Mycobacterium tuberculosis* or the TB bacillus to make proteins and DNA. Preventing access to nitrogen will stop the TB bacillus from growing inside blood cells and halt the spread of the disease in humans. Strains of TB have become resistant to available drugs, which means the disease is becoming more deadly and difficult to treat. This is a growing problem, with figures from the TB Alliance indicating that there were 558,000 worldwide cases of drug-resistant TB last year. New drugs are needed that attack novel targets such as nitrogen uptake.

To investigate the source of nitrogen for the TB bacillus in blood cells, researchers developed a new computational technique called  $^{15}\text{N}$ -Flux Spectral Ratio Analysis ( $^{15}\text{N}$ -FSRA) to learn more about nitrogen metabolism.  $^{15}\text{N}$  is a non-radioactive isotope of nitrogen that can be tracked by a technique called [mass spectrometry](#). In the first step of this innovative study, blood cells were fed with different potential nitrogen sources labelled  $^{15}\text{N}$ , enabling observation. The cells were then infected with TB bacillus and allowed to replicate and take nitrogen from the host cell. Protein from both [blood cells](#) and TB [cells](#) were recovered allowing researchers to track by mass spectrometry the route by which the  $^{15}\text{N}$  went from host cell to TB bacillus.

Using the computational tool,  $^{15}\text{N}$ -FRSA, it was discovered that TB bacillus acquires most of its nitrogen from the [host cell](#) amino acid, glutamine. Glutamine is an important amino acid with many functions in the body and are key components of proteins and a critical part of the immune system.

This ground breaking discovery will enable researchers to develop new anti TB drugs to target the transportation and metabolism of glutamine in the body, which will prevent Mycobacterium tuberculosis, or TB bacillus, accessing the nitrogen it needs to survive and replicate.

Johnjoe McFadden, professor of molecular genetics at the University of Surrey, said: "TB is one the world's deadliest infectious disease and it is very worrying that many strains are becoming resistant to drugs. To combat this threat we need to think innovatively and develop novel therapies to prevent an epidemic of TB strains that we are unable to treat. Our finding paves the way for the development of such drugs, which can target uptake of the very amino acid that enables the bacteria to replicate and spread within the body."

Provided by University of Surrey

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