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New therapeutic avenues for treating TB

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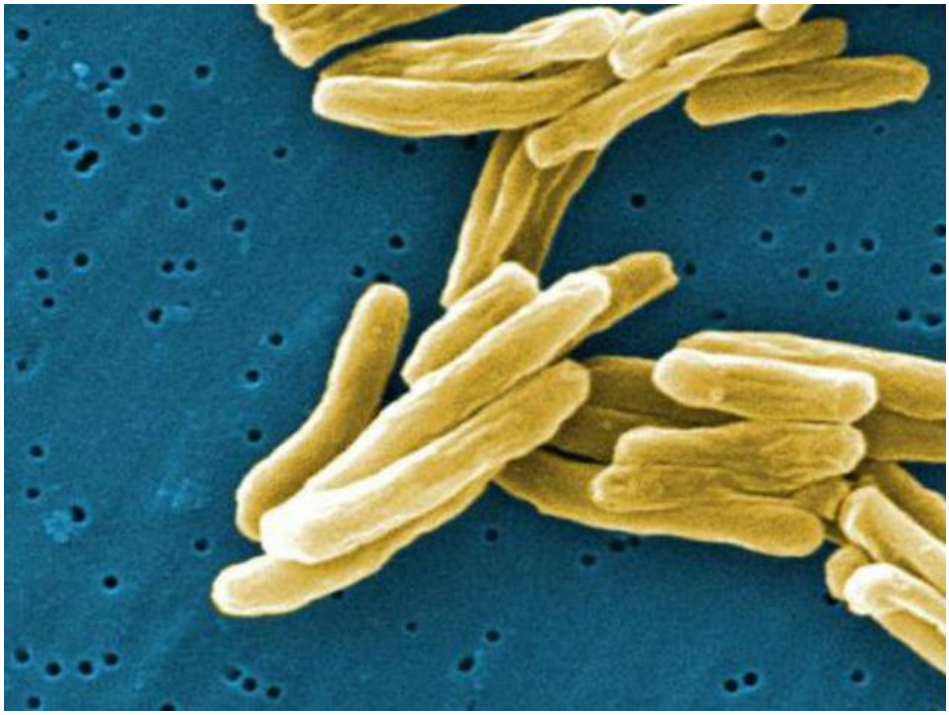

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Mycobacterium tuberculosis (TB) bacteria in a high magnification scanning electron micrograph (SEM) image.

In a novel finding that not only promises to open up new therapeutic avenues to treat tuberculosis but also to overcome the problem of increasing drug-resistance, scientists have discovered that cholesterol levels in human cell membranes control the entry of Mycobacterium.

Mycobacterium is a genus of Actinobacteria and consists of a wide variety of species, including the causative agents for TB and leprosy. According to World Health Organisation's 2014 report, an estimated nine million people developed TB in 2013 and 1.5 million people died of the disease globally. In India, the annual burden is estimated to be more than two million cases.

Cholesterol is an organic molecule that is essential for body's functioning. It is biosynthesised and plays an important role in maintaining the integrity of the cell's membrane. LDL (low-density lipoprotein) cholesterol has been implicated in diseases such as atherosclerosis and cardiac malfunction.

In the new study, a group of scientists led by Prof. Amitabha Chattopadhyay of Centre for Cellular and Molecular Biology (CCMB), Hyderabad, have found that depletion of cholesterol content in host cell membrane results in significant reduction in the entry of *Mycobacterium smegmatis* into the host cell.

The most important and novel finding of the study was that infection was restored when cholesterol was put back to normal levels in the human cell membranes. During the study, which was carried out in collaboration with Dr. Tirumalai Raghunand's group from the same institute, scientists have used human host cells and injected laboratory strain of Mycobacterium into them. They found that cholesterol was depleted when the cells were treated with methyl-beta cyclodextrin for about 30 minutes.

"This clearly demonstrates the requirement of host membrane cholesterol in the entry of Mycobacterium into host cells", the study noted. The results were recently published in the journal *Chemistry and Physics of Lipids*.

Interestingly, they found that infection was back when cholesterol was replenished to normal levels, indicating that the finding was specific to pathogenic Mycobacterium. In control experiments with non-pathogenic *E. coli,* the researchers found that its entry levels remained unaffected by depletion of cholesterol.

Explaining the advantage of this approach for future therapeutic applications, Prof. Chattopadhyay said the focus would be on treating the host and not the parasite and this would naturally help in overcoming the problem of drug resistance.

He said further studies would be carried out in animal models and eventually CCMB might look to collaborate with another institution for

conducting clinical studies.
