

Research reveals new drug target urgently needed for tuberculosis therapy

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One third of the world is infected with the bacterium that causes tuberculosis (TB), a disease that is increasingly difficult to treat because of wide spread resistance to available drugs. Researchers from the Institute of Pharmacology and Structural Biology (CNRS, Université de Toulouse) in Toulouse (France) have identified a fresh target to develop new drugs for TB. The study, published in the Open Access journal *PLOS Pathogens*, shows why the target will be important in developing new TB treatments.

The deadliest form of human tuberculosis is caused by *Mycobacterium tuberculosis* (M.tb). The burden of infection continues to increase and every year the world sees 8 million new cases and nearly 2 million deaths. TB, which occurs mostly in developing countries (including China, India and Brazil), drastically hinders economic growth. Current tuberculosis treatments are nearly 50 years old, take more than six months to complete and have many side effects, which makes it difficult for people to take the full course of drugs. The treatments have also become less effective because new <u>bacterial strains</u> are resistant to multiple drugs. There is an urgent need to find drugs with new modes of action that will shorten the duration of treatment, improve ways to fight drug-resistant tuberculosis and treat dormant infections to prevent them from later developing into full blown disease.

The cell envelope of M.tb has an unusually high content of substances called lipids which have unusual composition and are known to play an important role in the causing disease. The production of these disease



causing lipids was known to be controlled by the action of a protein which is the enzyme PptT in M.tb.

In this study, the researchers found that production of PptT is needed for growth of M.tb in a culture dish. It is also needed for growth and survival of M.tb in a mouse, which serves as a model for human disease. These findings are the reasons why PptT should be a very good <u>drug target</u> and allow the development of <u>new drugs</u> against TB. The study has also developed a way to quickly test hundreds of thousands of chemical agents (aka drugs) that block the action of Ppt and growth of M.tb. This approach is important and has been used by drug companies to develop drugs to many human diseases.

More information: Leblanc C, Prudhomme T, Tabouret G, Ray A, Burbaud S, et al. (2012) 4'-Phosphopantetheinyl Transferase PptT, a New Drug Target Required for Mycobacterium tuberculosis Growth and Persistence In Vivo. PLoS Pathog 8(12): e1003097. <u>doi:10.1371/journal.ppat.1003097</u>

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