Targeting of Triacylglycerol Synthesis or Metabolism for Tuberculosis Treatment

Background

Tuberculosis (TB), one of the biggest killers among the infectious diseases, poses a major public health problem mostly in the developing world with 8 million new cases and 2 million deaths a year (World Health Organization; 2005). Mycobacterium tuberculosis, the causative agent of TB, is inhaled by people as an aerosol emanating from active TB patients. Usually, only a small fraction of the people (~5%) thus infected develop active TB, while the rest carry a latent infection for the rest of their lives until reactivation of the pathogen occurs upon weakening of the immune system. The ability of the pathogen to go into a latent/dormant non-replicating state, with very low metabolic activity and phenotypic resistance to all of the currently available anti-tuberculosis drugs makes TB eradication an extremely difficult challenge.

The inventors have discovered that triacylglycerol can be used as an energy source by M. tuberculosis in dormancy, thus its synthesis or metabolism could be an ideal drug target against latent TB. The current invention describes the use of M. tuberculosis triacylglycerol synthase or triacylglycerol hydrolase to screen for therapeutic agents useful in the treatment of M. tuberculosis infections.

Invention

The current invention allows for the screening of various anti-TB therapeutic agents based on their ability to bind M. tuberculosis triacylglycerol synthase or triacylglycerol hydrolase polypeptides.

Application

The current invention presents a screening method for identifying novel anti-TB agents useful in treating TB infections. The screening method could identify novel therapeutic agents that will effectively address the problem of multidrug resistant (MDR) strains of bacteria.

Advantages

- Novel and low cost method to screen possible agents effective against latent/dormant TB

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Selected References

Sirakova TD, Dubey VS, Deb C, Daniel J, Korotkova TA, Abomoelak B, Kolattukudy PE. 2006; Microbiology. 152(Pt 9): 2717-2725.


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