

SCIENCE

A Potential Protein Target for Tuberculosis Treatment: Purification and Structural Analysis of *Mt1054*

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Mycobacterium tuberculosis is the species of bacteria that is the causative agent of tuberculosis. Those at high risk for tuberculosis include the elderly, infants, and individuals already infected with a disease that affects the immune system. This makes *M. tuberculosis* a common source of nosocomial infections, and the emergence of drug-resistant strains of the bacteria calls for research into new drugs for treatment of infection with *M. tuberculosis*. One possible method of treatment involves targeting a putative exopolyphosphatase encoded by the gene *Mt1054*. An *Escherichia coli* homologue of this protein regulates the levels of polyphosphate and guanosine 5'-triphosphate 3'-diphosphate (pppGpp), both of which act as signaling molecules during amino acid starvation. The presence of the protein encoded by *Mt1054* has been shown to affect biofilm formation and sliding motility in *Mycobacterium*

smegmatis. In this research, *Mt1054* will be inserted into the expression plasmid pET30. The protein will be expressed and purified, and enzymatic assays will be conducted on the purified protein in order to determine its phosphohydrolytic enzyme activity. This information can be used in the future to develop methods of modulating *M. tuberculosis* exopolyphosphatase activity. By doing so, clinicians may be able to trick the bacteria out of going into stationary phase and developing biofilms. Disrupting the ability of *M. tuberculosis* to form biofilms could increase the susceptibility of this bacterium to antibiotics and decrease the mortality rate of this potentially deadly disease.

Research advisor David A. Sanders writes, "There will be 9,000,000 new cases and 1,400,000 deaths from tuberculosis this year. Brandt Lydon is investigating the function of a protein that makes the decision between rapid and slow growth of the bacterium Mycobacterium tuberculosis that causes tuberculosis. His independent research may contribute to increasing the susceptibility of the bacterium to antibiotics."