

Characterization of a Trifunctional Sulfate-Activating Complex from Mycobacteria

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The respiratory disease tuberculosis (TB), caused by the pathogen *Mycobacterium tuberculosis* (Mtb), is an ongoing worldwide epidemic which necessitates the identification of novel drug targets. Since sulfur is an essential element for the growth, virulence, and survival of Mtb, the disruption of sulfur metabolism may be a potential means of combating TB. To address this, we are studying CysDNC, a key sulfate-activating complex that lies at the beginning of the mycobacterial sulfur pathway. The first committed step of sulfur metabolism begins when intracellular sulfate is reacted with ATP to form the product adenosine-5'-phosphosulfate (APS) in a GTPase-coupled reaction. APS is then further phosphorylated into 3'-phosphoadenosine-5'-phosphosulfate (PAPS). Both APS and PAPS serve as precursors for downstream sulfur-containing biomolecules. These three reactions--APS formation (CysD), GTP hydrolysis (CysN), and PAPS formation (CysC)--are catalyzed by the trifunctional complex CysDNC. This poster will feature ongoing research on this complex, including: in vitro biochemistry of CysDNC, characterization of a mutant strain of *M. smegmatis* which has been disrupted in the gene encoding CysD, as well as current attempts to solve the structure of CysDNC using cryogenic electron microscopy.