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## Engineering of cytochrome P450 monooxygenases-based novel inhibitors against *Mycobacterium* tuberculosis

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The actinomycete Mycobacterium tuberculosis (*Mtb*) causes tuberculosis (TB), a chronic lung disease, in humans and continues to be one of the greatest threats to mankind. It is estimated that one-third of the human population are latently infected by *Mtb* and 9 million cases of active TB occur each year. Development of multi-, extensively- and totally drug-resistant (MDR, XDR and TDR) *Mtb* strains, together with the paucity of new drug targets currently being explored, suggests that new basic research is required to delineate novel potential targets. Recent studies suggested that cytochrome P450 monooxygenases (P450s) of *Mtb* can serve as novel drug targets. P450s are mixed function oxidoreductases well known for their role in essential cellular anabolic and catabolic processes. To identify P450s that can be used as drug targets not only for *Mtb* but also against all mycobacterial species, we performed comprehensive comparative P450 analysis across 23 mycobacterial species. A total of 730 P450s and 4 truncated P450s (pseudo) were identified in 23 mycobacterium species. Six P450 families, CYP51, CYP123, CYP125, CYP136, CYP138 and CYP144, were found conserved among 23 mycobacterial species, suggesting their essential role in mycobacterial species physiology and as potential novel drug targets. We successfully constructed reliable 3D-models and mapped the active site cavities for the six P450s. Furthermore, we also identified potential inhibitors for six P450s by virtual screening of a library of chemical compounds. Experiments are in progress to validate the identified inhibitors and to refine/ engineer a common inhibitor against six conserved mycobacterial P450s further.

## Biography

Khajamohiddin Syed completed his PhD at the age of 27 years at Sri Krishnadevaraya University, India. His research is focused on P450-enzyme based drugdesigning against human pathogens and development of P450-enzyme based novel tools for bioremediation of cancer-causing and endocrine-disrupting chemicals. His research work has been published in highly ranked peer-reviewed scientific journals including Science and PNAS, USA. He is serving as Editorial Board Member and reviewer for reputable international scientific journals. To date he has published 17 articles in reputable scientific journals.

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