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POSTER ABSTRACT PRESENTATIONS

SESSION TITLE: NEW METHODS OF SAMPLE PREPARATION AND DATA PROCESSING FOR CRYO-ELECTRON MICROSCOPY

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Abstract P-40: Computational Evaluation of Binding of Heme-Focused Library to Cholesterol-Metabolizing P450 Enzymes from *Mycobacterium tuberculosis*

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Background: Tuberculosis (TB), caused by pathogenic bacteria *Mycobacterium tuberculosis* (MTb), is known to be among top-10 causes of death worldwide. In 2019, WHO mentioned drug-resistance with special focus on drug-resistant TB as one of the top-10 threats to the global health. Hence, there is need for novel antimycobacterial drugs.

Methods: Recently, structures of several P450 enzymes from MTb CYP125 and CYP142), capable to conversion of cholest-4-en-3-one to its 25-26-dihydroxy product, have been determined. They are also known to be important for bacterial growth *in vitro*. Current work is focused on structure-based drug design (SBDD) targeting these enzymes. Using available structures and open data, we analyze the ability of existing computational algorithms to predict binding of fragment-like heterocyclic compounds from experimentally tested library to the enzyme.

Results: We find that apo structures of all three enzymes have the most promising capabilities in terms of both overall discriminating ability (ROC AUC) and top-10% enrichment.

Conclusion: Obtained results establish a blueprint for both structure-based and fragment-based drug design of novel therapeutics against *Mycobacterium tuberculosis*.

Key Words: *Mycobacterium tuberculosis* • structure-based drug design

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