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"Addressing key challenges in antibacterial drug discovery: from intrabacterial drug accumulation to computational lead optimization and target-based design."

By

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M.D./Ph.D. Program
B.A., Biology, Psychology, 2019, Rutgers University - Newark, New Jersey

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Thursday, March 12th, 2026
10:00 A.M.
Clinical Affairs Conference Room (H506)
Medical Science Building

Join Zoom presentation
https://rutgers.zoom.us/j/95575931407?pwd=w47Sh8aVJmpVKS4MC8slavePCnIT16.1
Meeting ID: 955 7593 1407
Passcode: 292150

ABSTRACT

Drug discovery is a multiphase and costly process that sits at the intersection of multiple disciplines, each presenting distinct challenges. These challenges are particularly pronounced in antibacterial drug discovery, where pathogens across the three major clinically relevant bacterial classes (Gram-positive, Gram-negative, and mycobacteria) have evolved sophisticated defense mechanisms against antimicrobial agents. The incidence of multidrug resistance has increased substantially over the past two decades, driven in part by widespread and inappropriate antibacterial use. This challenge is further exacerbated by the limited success in developing new classes of antibacterial agents, resulting in a weakened discovery pipeline.

This work aims to address key challenges encountered at three distinct stages of early antibacterial drug discovery. To improve hit identification in target-based discovery for Gram-negative bacteria, an efficient high-throughput assay was developed to quantify intrabacterial drug accumulation and metabolism. Molecular dynamics simulations were then applied during lead optimization of rifabutin analogs to better understand ligand-receptor interactions and guide attenuation of CYP-mediated drug-drug interactions. Finally, a target-based screening approach identified a novel *Mycobacterium tuberculosis* KasA inhibitor that binds to a previously uncharacterized site at the entrance of the malonyl binding pocket, revealing a region of mechanistic significance and providing a foundation for future inhibitor design.