Computational Characterization of Novel Alpha/Beta Hydrolase Fold Domain-Containing Protein involeved in Pathogenecity and Antibiotic Resistance in *Nocardia farcinica*

Shaslinah Nathar[a], and Jeyakanthan Jeyaraman[a]*

[a]Structural Biology and Bio-Computing Lab,
Department of Bioinformatics, Alagappa University, Science Block,
Karaikudi, 630 003, Tamil Nadu, India.

Correspondence e-mail: jjbioinformatics@gmail.com

Abstract

Nocardiosis can progress into a disseminated infection, affecting multiple physiological systems, most commonly the skin, lungs, and central nervous system. *Nocardia farcinica* is distinguished from other *Nocardia* species by its high pathogenicity and antibiotic resistance, making it more likely to cause brain abscesses and widespread multiple-organ infections. Hence, there is an urgent need to identify novel therapeutic targets to combat the multidrug-resistant nosocomial pathogen *N. farcinica.* The aim of this study is to prioritize potential inhibitors using structural bioinformatics and to identify therapeutic targets associated with the unique metabolic pathways of *N. farcinica*, supported by high-throughput virtual screening to uncover potential drug compounds. The alpha/beta hydrolase fold domain-containing protein was identified as a promising target for therapeutic development. Virtual screening of the CMNPD, MNPD, Seaweed, and Specs chemical libraries revealed five potential candidates based on favorable ADME properties and strong binding affinities. Among these, MNPD738 was predicted to be the most potent inhibitor, demonstrating high stability throughout the molecular dynamics simulations and exhibiting a low binding free energy. These putative therapeutic targets will help in the development of effective drugs that inhibit the pathogen-specific metabolic pathways. The identified targets and lead compounds contribute to the development of effective therapies for combating drug-resistant *N. farcinica* infections. Future research should emphasize experimental validation of the identified compounds and further investigation into the molecular mechanism underlying *N. farcinica* pathogenicity.

Keywords: *Nocardia farcinica,* Virulence, molecular docking, drug targets, virtual screening.