CHAPTER 11

BIOPHYSICS

Doctoral Theses

01. DABBURU (Govinda Rao)
Structure-Based Discovery of Novel Drug Targets and Drugs for Infectious Diseases.
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Abstract

Microorganisms (bacteria, fungi, and viruses) inhabit every part of the earth, including within and outside of the human and animal body. While many microbes are beneficial, a few are pathogenic and can cause diverse infectious diseases with rising severity and mortality rates. In certain cases, persistent immune responses triggered by infections can also lead to secondary autoimmune complications. The effectiveness of existing therapeutic strategies is increasingly compromised due to rapid emergence of drug resistance, genetic mutations, and available druggable targets. These challenges necessitate the identification of alternative molecular targets and development of new inhibitory strategies using rational, target-driven approaches. In this study, we employed in-silico structure-based drug design to identify and characterize potential inhibitors against key targets associated with Plasmodium falciparum, SARS-CoV-2, and Dengue virus. Target prioritisation was performed using assessments of functional relevance and draggability. For malaria, two essential enzymes critical for survival of Plasmodium were identified, and virtual screening was conducted using compounds from ChEMBL antimalarial database to predict high-affinity inhibitory candidates. In case of SARS-CoV-2, nucleocapsid protein was selected as a therapeutic target due to its multifunctional role in viral replication and host immune modulation. A drug repurposing strategy combining molecular docking, binding energy estimation, and interaction profiling identified Afobazole, an FDA-approved anxiolytic, as potential inhibitory candidate. For Dengue virus, protein–protein interaction networks between viral and host factors were computationally analysed to identify critical interaction interfaces essential for viral persistence and immune modulation. Virtual screening and molecular interaction analyses suggested that Regorafenib, Selisistat, and Resveratrol may disrupt these interactions and potentially mitigate both viral replication and infection-associated autoimmune manifestations. Since all potential drug candidates were predicted computationally, they warrant further experimental validation. With appropriate experimental and clinical validation, these in-silico derived candidates may offer cost-effective and accelerated intervention strategies for malaria, dengue and SARS-CoV-2 infections.

Contents

1. Review of literature 2. Designing dual inhibitors against potential drug targets of Plasmodium falciparum -M17 Leucyl Aminopeptidase and Plasmepsins 3. Afobazole: a potential drug candidate which can inhibit SARS CoV-2 and mimicry of the human respiratory pacemaker protein 4. Repurposing drugs for treating dengue haemorrhagic fever and associated autoimmune diseases 5. Summary and future prospects 6. Other works 7. Bibliography.