WG 1 (Chemical, Biological, Radiological and Nuclear materials)

Prediction of Novel Antimicrobial Resistance Genes Using Machine Learning Approaches

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Antibiotics are essential for medical procedures, food security, and public health. However, ill-advised usage leads to increased pathogen resistance to antimicrobial substances, posing a threat of fatal infections and limiting the benefits of antibiotics. Therefore, early detection of antimicrobial resistance genes (ARGs), especially in pathogens, is crucial for human health. Most computational methods for ARG detection rely on sequence homology to a predefined database and therefore are limited in their ability to discover novel genes.
I will present DRAMMA, a machine-learning method for predicting new ARGs without relying on sequence similarity to known ARGs or any annotated gene. DRAMMA utilizes various features of ARGs and their products, including protein properties, genomic context, and evolutionary patterns. The model demonstrated robust predictive performance both in cross-validation and an external validation set annotated by an empirical ARG database. Analyses of the high-ranking model-generated candidates revealed a significant enrichment of candidates within the human, animal and plant microbiomes. DRAMMA enables rapid ARG identification in global-scale genomic and metagenomic samples, thus holding promise for the discovery of novel ARGs that lack sequence similarity to any known resistance genes. Further, our model has the potential to facilitate early detection of specific ARGs, potentially influencing the selection of antibiotics administered to patients and guiding drug development and policies.

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Molecular Insights into DnaG Primase Inhibitors Across Pathogens

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We developed novel small molecules targeting DnaG primase, an essential enzyme in bacterial DNA replication and a promising antibacterial drug target. The molecules originate from early NMR screening studies that identified scaffolds for a universal bacterial primase model. Our work integrates experimental and computational approaches to investigate how specific modifications on the fragment hit molecule influence the inhibition of DnaG primase activity, enabling the rational design of effective compounds across diverse bacterial species. Through detailed design and synthesis of small molecules, biochemical assays, and structural analyses, we optimized a series of inhibitors and identified a few as highly effective primase inhibitors. Few small molecules inhibited DnaG primase activity in eight bacterial species, including clinically relevant pathogens, emphasizing.