THE USE OF AI AND ADVANCED COMPUTER SYSTEMS TO DEVELOP DRUGS AGAINST NEW EMERGING THREATS

RNA-targeted AI/ML Drug Repurposing Pipeline for Aerospace Medicine

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Background: The traditional process for developing new pharmaceuticals takes up to 12 years for FDA approval and is prone to failure. Our RNA-targeted AI/ML drug repurposing pipeline, which utilizes abundant biomedical data in the public domain, aims to identify existing FDA-approved drugs that can be repurposed for different human diseases, including medical countermeasures to address diseases associated with repeated exposure to high-altitude flight. Our approach incorporates data about RNA targets, including mRNAs and microRNAs (miRNAs), which have recently been recognized as critical players in modifiable disease pathways and provide new targets for drug repurposing. Our approach could not only significantly impact the field of aerospace medicine but also improve the way we approach drug development.

Methods:

Using a miniature swine high-altitude model, we identified mRNA and miRNA genes that are differentially expressed in high-altitude exposure. We then implemented two AI/ML models in a DoD-approved HIPAA-compliant cloud environment to find promising drug candidates that target the differentially expressed RNAs: 1) a knowledge graph (KG) based graph ML model that leverages semantically integrated biomedical data, and 2) a model based on chemical structures of existing drugs. For the KG-based model, we extended existing ingest, extract, and load (ETL) software to load data into the ARDIS cloud computing environment (AWS GovCloud IL4, HIPAA compliant, Defense Health Agency – verified system). Our KG integrates data related to drugs, drug targets, microRNAs, protein pathways, and protein-protein interactions, along with several important biomedical ontologies that provide background biological information. We then applied several graph ML models to predict drug–miRNA interactions. Our second ML model uses the SM2miR database to train a model using miRNA data and extracted chemical structure from PubChem\. To visualize and provide explainability to the ML results, we developed a visualization component that displays nodes of interest and their relationships in the KG.

Results: Our AI/ML models predicted 36 links between drugs and differentially expressed pig genes and human homologs in high-altitude conditions. The identified drugs spanned various classes, including statins, MG-CoA reductase inhibitors, anti-cancer/neoplastic drugs, and anti-infective drugs. These promising results underscore the potential of our RNA-targeted AI/ML drug repurposing pipeline in aerospace medicine.

Conclusions: We created a KG that captures a wide range of data including approved drugs, drug targets, etc., and applied two AI/ML models to identify drugs that target miRNAs associated with high altitude exposure. This platform provides a method to identify candidate approved drugs that may be repurposed for medical countermeasures against a wide range of diseases or threats, including but not limited to high-altitude exposure. The next steps, including in vitro/in vivo studies with identified small molecules and retrospective analyses of clinical data, are necessary to confirm the therapeutic effectiveness of these drugs. The practical applications of our research in the near future could include the development of new treatments for diseases such as cancer, cardiovascular diseases, and infectious diseases, as well as the prevention and management of health issues related to high-altitude exposure.

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