Systems-Biology Infrastructure to Identify Drug Repurposing Opportunities

VANDERBILT UNIVERSITY
CTTC Center for Technology Transfer & Commercialization

Summary

A highly sophisticated *in-silico* screening method to reveal ***new indications for existing FDA-approved drugs with known protein targets using a novel infrastructure for screening and identifying key antiviral and anti-cancer targets***. Currently, the pipeline for developing novel therapeutics for viral infections and complex diseases such as cancer costs billions of dollars annually. Experts here at Vanderbilt University have developed an integrated genetics and systems biology-based infrastructure to aid in identifying new drug targets and to repurpose previously approved drugs into antiviral and/or anti-cancer therapeutics. This framework will help expedite advancements in treatment strategies by decreasing research costs while improving success rates with the reduced timeline for target identification and drug development.

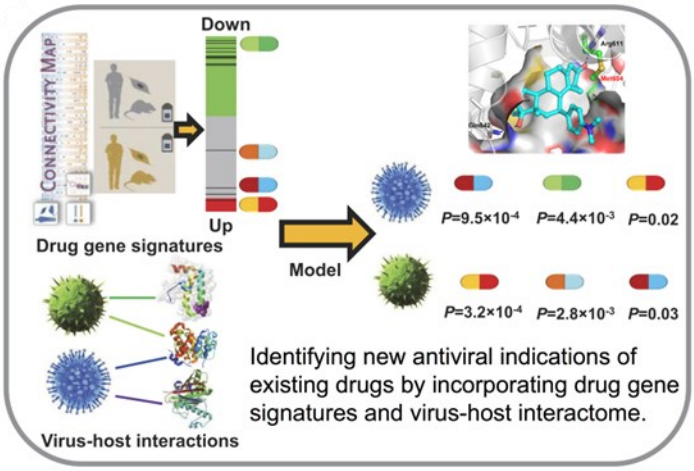

Figure 1. *Diagram of the integrative antiviral drug discovery & repurposing pipeline using the virus-host gene interactome for .*

Technology Description

This drug repurposing infrastructure integrates multiple factors across different systems-biology models to create a drug discovery pipeline. As seen in Figure 1, this framework utilizes aspects of functional genomics, known drug-gene signatures from drug-induced gene expression data, human protein interaction data, and bioinformatics to create a putative interactome between the virus and the human host's genes. This interactome is then screened for gene products involved in the viral hijacking of human cellular components required for viral replication and survival. This proprietary framework and algorithm then iterates through to link these targets with known, FDA-approved therapeutics which have already been shown to be efficacious. Figure 2 is an example of how the infrastructure has been used to pinpoint existing drugs that may have antiviral activity by targeting human proteins involved in the cell cycle that are non-essential for human cell survival, but are necessary for viral infection. This pipeline identified several promising older drugs repurposed for anti-Ebola (Azlocillin [an approved acylampicillin antibiotic]), anti-human immunodeficiency virus (HIV, Alsterpaullone [a CDK inhibitor]), and other antiviral indications, thus further validating the effectiveness and utility of this tool.

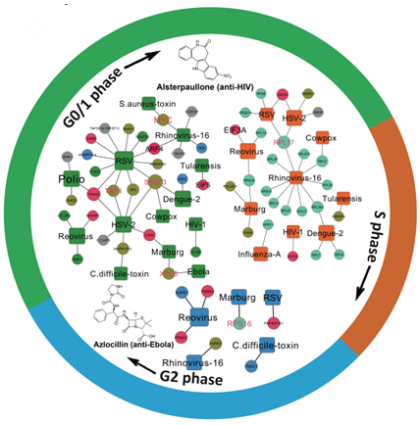

Figure 2. *Identification of cellular components necessary for cell cycle regulation hijacked for viral survival yields druggable targets within the virus-host gene network.*

Unique Features

One particular strength of this framework is the ***speed with which one can identify drugs with potential efficacy for emerging public health threats*** with no known treatments; examples include pathogens such as Ebola, HIV, Marburg virus, and Pox viruses, but also cancers and other disease which may use similar cellular mechanisms within their disease etiology. Ultimately, this innovation will help expedite the pipeline for therapeutic development for complex diseases by overcoming obstacles in target identification and bottlenecks within efficacy studies that slow the development of new treatments for patients by finding new uses for previously FDA-approved drugs.

A U.S. patent application has been filed.

CTTC Contact:
Janis Elsner
615.322.7056
Janis.Elsner@Vanderbilt.edu

Vanderbilt Lead Inventor:
Don Rubin, Ph.D.

VU Reference Number: 15082