

SHP Student Interns for Research and Scholarly Activities Application of Project Proposal Form

Instructions:

Please fill out the form and return via email to Michele Sisco (mcoral@shp.rutgers.edu) by **March 25, 2024**. Please fill each box to the right of each required field. If you are sending attachments, please ensure your contact information is added to all your forms.

Faculty Contact Information:

Date submitted:	3/25/2024
Faculty Name:	Antonina Mitrofanova
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Project Detail:

Project Title: (56 characters max)	Novel computational algorithms to predict synergistic drug combinations for castration-resistant prostate cancer
Hypothesis:	<p>In our previous work (Nature Communications 2024), we have demonstrated that a mechanism-centric network-based approach TR2PATH could identify effective interplay between transcriptional regulatory programs and biological pathways as effective biomarkers of therapeutic failure in cancer. In this project, we will investigate computational approaches to identify synergistic drug combinations to target such drivers in castration-resistant prostate cancer (CRPC).</p> <p>We hypothesize that drug combinations that target distinct parts of such regulatory programs could provide most effective therapeutic targeting in CRPC setting.</p>
Description: (Include design, methodology, data collection, techniques, data analysis to be employed, evaluation and interpretation methodology for research component)	<p>Objective: Our objective for this project is to develop a computational algorithm and write a manuscript for identifying effective drug combinations in CRPC to address a significant gap in the current treatment paradigm. The goal is to develop an algorithm that identifies drug combinations to reverse malignant phenotypes in CRPC setting.</p> <p>Design /Methodology: We will develop a new computational algorithm that affects distinct parts of the</p>

	<p>TR-pathway interactions and will document our findings. We will utilize R and python for algorithm development.</p> <p>Data Collection: We will utilize prostate cancer cell line drug perturbation data (e.g., cmap collection; xenograph models, mouse models) to define gene expression signatures of drug response. All datasets will be obtained from public repositories or requested as controlled data access from the Genomic Data Commons, Array Express, the Broad Institute, the Gene Expression Omnibus, and dbGap.</p> <p>Techniques / Computational Methods / Data Analysis:</p> <p>TR-2-PATH Algorithm (development in Nature Communications 2024) included the following techniques:</p> <ul style="list-style-type: none"> • Single-Sample Gene Set Enrichment Analysis (GSEA): <ul style="list-style-type: none"> - <code>`fgsea`</code> or <code>`GSVA`</code> for enrichment analysis. • VIPER Analysis: <ul style="list-style-type: none"> - <code>`viper`</code> for analyzing the activity of transcriptional regulators. • Linear Regression Analysis: <ul style="list-style-type: none"> - Base R stats package function <code>`lm()`</code> for linear models. - <code>`glmnet`</code> for regularized regression. • Bootstrap Analysis: <ul style="list-style-type: none"> - <code>`boot`</code> for bootstrapping statistics. • t-SNE Clustering: <ul style="list-style-type: none"> - <code>`Rtsne`</code> for T-distributed Stochastic Neighbor Embedding analysis. <p>In this project, we will build on these methods and will develop novel techniques to elucidate novel drug combinations to target the mechanisms identified by TR2PATH previously. In addition to methods mentioned above, we will utilize ROC and c-index for evaluation purposes.</p>
<p>Specific Student Responsibilities:</p>	<ul style="list-style-type: none"> - Data acquisition (from public repositories) and analysis, coding (using R and python) - Literature review - Publication drafts - Image and figure generation - Table generation - Additional tasks that might arise as a part of manuscript preparation

Start / end date of project:	June 1 st 2024 – August 30 th 2024
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Educational:

<p>WHAT OTHER EDUCATIONAL OPPORTUNITIES ARE AVAILABLE TO STUDENTS? (e.g., journal club, seminars, clinic, rounds)</p>	Mitrofanova Lab meeting, WIP talk etc.
<p>WHERE DO YOU PLAN TO PRESENT OR PUBLISH THE FINDINGS WITH THE STUDENT? (e.g., national or state meetings, newsletter or journal, SHP poster day)</p>	We will target (Nature) Communications Biology and Frontiers in Oncology as potential publication venues.

CHECK ALL APPROPRIATE BOXES BELOW AND PROVIDE REQUESTED INFORMATION.

This project is: clinical laboratory behavioral survey educational

Other: please specify Computational

This project involves the use of human subjects (including chart review, retrospective studies and questionnaires).

Pending Approved IRB Protocol Number _____

IRB approval must be obtained by June 2024



3/25/24

Signature of Department Chair

Date

OR-For internal use

Form: (1)

Reviewed date: _____

Date processed on website: _____