

Double Trouble: Understanding Sex Differences in Synthetic Lethal interactions in Human Cancers

Summer Wrap Up

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August 8, 2023

Overview

Overall Objective and Approach

Synthetic Lethality Analysis Update

Next Steps/Future Work

Limitations of the study

Takeaways & Tips for Future Undergrads

Overall Objective

- ▶ Can we build sex-specific synthetic lethality networks for various cancer types?
- ▶ More specifically, we are trying to elucidate the differences in synthetic lethal interactions between males and females using a network based approach.

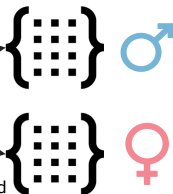
Overall Project Workflow

Step 1:

Data collection

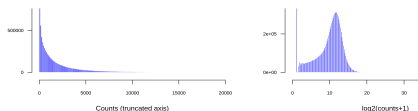


Obtain raw RNA-seq expression data (healthy and tumor tissue) for 12 cancer types from TCGA for males and females



Step 2:

Data Processing

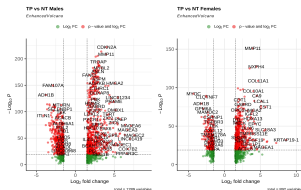


Create pan-cancer matrix with 12 cancer types and normalize expression data

Sex-Specific Synthetic Lethality Workflow

Step 3:

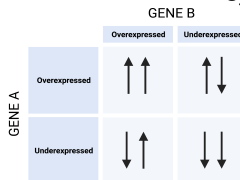
Differential Gene Expression



Identify genes differentially expressed in tumor tissue in males and females

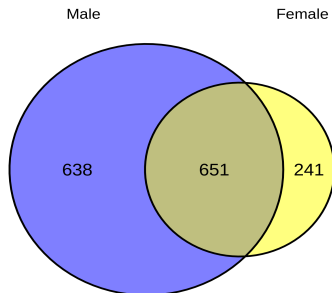
Step 4:

Synthetic Lethality Analysis



Fisher exact test to identify pairs of genes that are BOTH perturbed more frequently than INDIVIDUALLY perturbed





Using DE Genes to Find Sex-Specific Synthetic Lethal Pairs



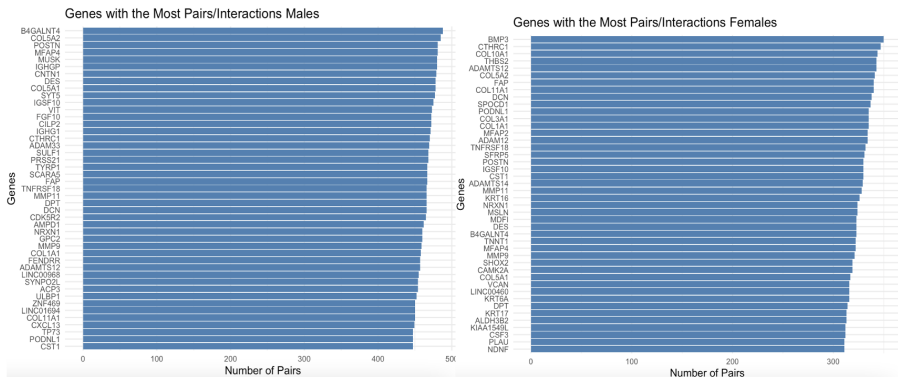
- 1 Find all potential gene pair combinations using differentially expressed genes
 $\binom{1289}{2} = 830,116$ Potential Male Pairs
 $\binom{892}{2} = 397,386$ Potential Female Pairs
- 2 Identify pairs of genes that are BOTH perturbed (under and overexpressed) more frequently than INDIVIDUALLY perturbed using Fishers Exact Test

Fishers Exact Test

Used to determine association between two categorical variables (overexpression and underexpression) when dealing with small sample sizes

		GENE B	
		Overexpressed	Underexpressed
GENE A	Overexpressed		
	Underexpressed		

Ranking Genes by Number of Interactions



- ▶ ISLE Method SL list Matches: Males = 14 pairs, Females = 11 pairs
- ▶ Experimentally Validated SL list Matches: Males = 21 pairs, Females = 2 pairs

Next Steps for Synthetic Lethality Analysis

- ① Refine the current list of synthetic lethal pairs by performing survival analysis to identify SL pairs that contribute to improved patient survival.
- ② Build male and female synthetic lethal interaction networks

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