PROC-DOT: Prostate Cancer Drug Pair Optimization Via Transcriptomics
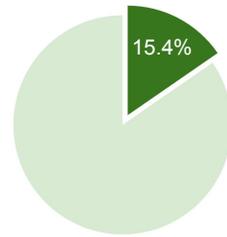
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Research Question

- 1 in 8 men get prostate cancer (PCa) in lifetime
- 375,000 deaths worldwide - 2020
- Single drug treatments lead to drug resistance in PCa
- Combination therapies combat resistance, but not standard of care

Individual drug genetic databases exist

Prostate Cancer as percentage of new cancers in US

15.4%

Does additive model predict genetic expression for drug combinations in cancer?

Results

PROC-DOT model predicted drug combination gene expression validated on lung cancer data
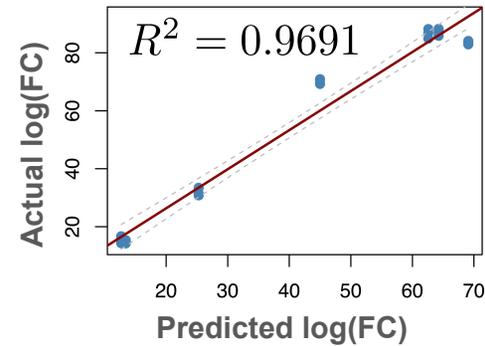**Top drug combinations are supported by clinical data**

$R^2 = 0.9691$

Actual log(FC)

Predicted log(FC)

Figure 1: Norm comparison

Drug Combinations (PCa)
ARN509 and Bariticinib
ARN509 and Pilaralisib
ARN509 and Rucaparib
ARN509 and Prednisone

Methodology

RNA-seq expression data for drug effect in PCa $\Rightarrow$ Use edgeR to fit the differential expression $\Rightarrow$ Reduce dimension of drug effects and build additive model $\Rightarrow$ Rank drug pairs based on angle with disease

Genes

Samples + disease | Expression

Drug | *Genes*

$+$

Drug | *Genes*

$\binom{n}{2}$

Φ
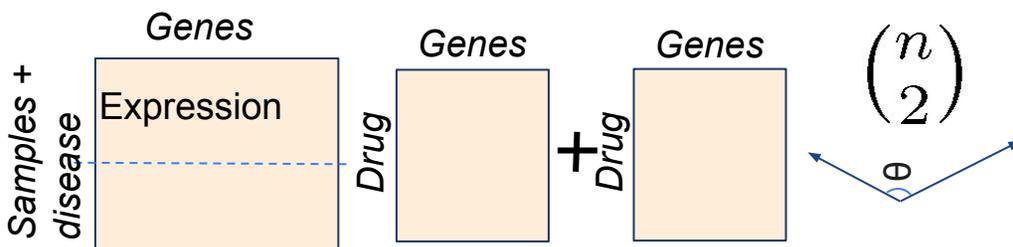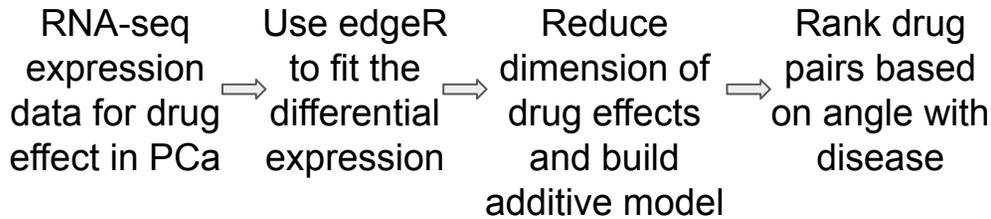
Conclusions

- Additive model **predicts** drug combination gene expressions using individual drug genetic data
- Screening approved drugs for **repurposing** is viable
- PROC-DOT is an **interpretable** model

Future Work

- Test additive model on additional datasets
- Incorporate the effect of drug dosage
- Use to predict drugs for specific gene perturbations
- Suggest treatment for additional diseases using PROC-DOT