**Paper Outline**

**Modeling AKT drug response in breast cancer**

**Personalized AKT drug response in breast cancer**

Predicting drug response in breast cancer at the pathway level

Predicting drug response to AKT drugs in breast cancer using multi-pathway modeling

Modeling AKT drug response in breast cancer using pathway based signatures

Modeling AKT drug response in breast cancer using pathway signatures

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Cancer Research

Introduction

* Breast cancer and the need for personalized drug response predictions.
* History of personalized medicine in breast cancer and why it’s inefficient.
* Why the pathway-based approach is better.
* AKT/BAD/IGF1R/HER/ERK in breast cancer.
* Goal: Modeling and validating drug response predictions using a pathway based approach to provide individualized treatments.

Methods

1) Overexpressing of pathway elements using adenovirus in HMEC cells

- Virus we used, infection time, MOI, all the specifics of that

*-* Western blot results for all signatures (supplements)

- Just the phosphorylated proteins and the B-action

2) Data processing and normalization

Sequencing methods, processing (Rsubread), normalization, batch adjusting

- Signatures

- ICBP

- CCLE

- TCGA

3) Generation and validation of genomic signatures that represent pathway activity

- ASSIGN parameters, test data tests, correlation parameters, boot strap method

4) Validating finding in cell lines and patient cells

-Reagents, protocols

Results

*1) Validation of the genomic signatures (in methods, one Figure)*

* AKT, HER2, IGF1R, BAD, ERK predictions correlate with ICBP drug response data
* Show all correlation one heat map
* Boxplot for sensitive and resistance for each signature
* Should we add TCGA validation?

*2) Multi-pathway prediction better predict than single pathway (most will be in supplements)*

- Describe which pathways work best together for predictions

- Table with prediction/drug response correlations and p-values.

*3) Subtypes specific pathway deregulation in breast cancer cell lines and TCGA data*

What pathways are important in each subtype in breast cancer cell lines.

-ICBP correlation matrix between subtypes and drug predictions

-Validate in CCLE (need to do this)

-TCGA maybe (need to comment on why it is not as good)

*4) BAD/ERK pathway activity correlates with chemotherapy response*

* ICBP boxplots of pathway activation in BAD/ERK for multiple chemo drugs
* TCGA hopefully, survival curves from patients that got chemo and had high bad activity vs. those that don’t.

*5) Predictive models for Sigma AKT using gene expression signature’s*

*-*Building the model (method)

- Testing the model

1) Publically available data

- GDSC or CCLE

- Probably can’t do with TCGA

2) Breast cancer cell lines in the lab

3)Patient cells pleural effusions

- Test the EC50 for sigmaAKT

6) *Predictive models for Sigma AKT using multi-omic data*

*-*Building the model (method)

- Testing the model

1) Publically available data

- GDSC or CCLE

- Probably can’t do with TCGA

2) Breast cancer cell lines in the lab

3)Patient cells pleural effusions

- Test the EC50 for sigmaAKT

4) Contribution of adding multi-omic data