

# In vivo Data Analysis

**Arvind Mer, PhD**

The Haibe-Kains Lab  
Princess Margaret Cancer Centre  
University Health Network  
University of Toronto  
Canada

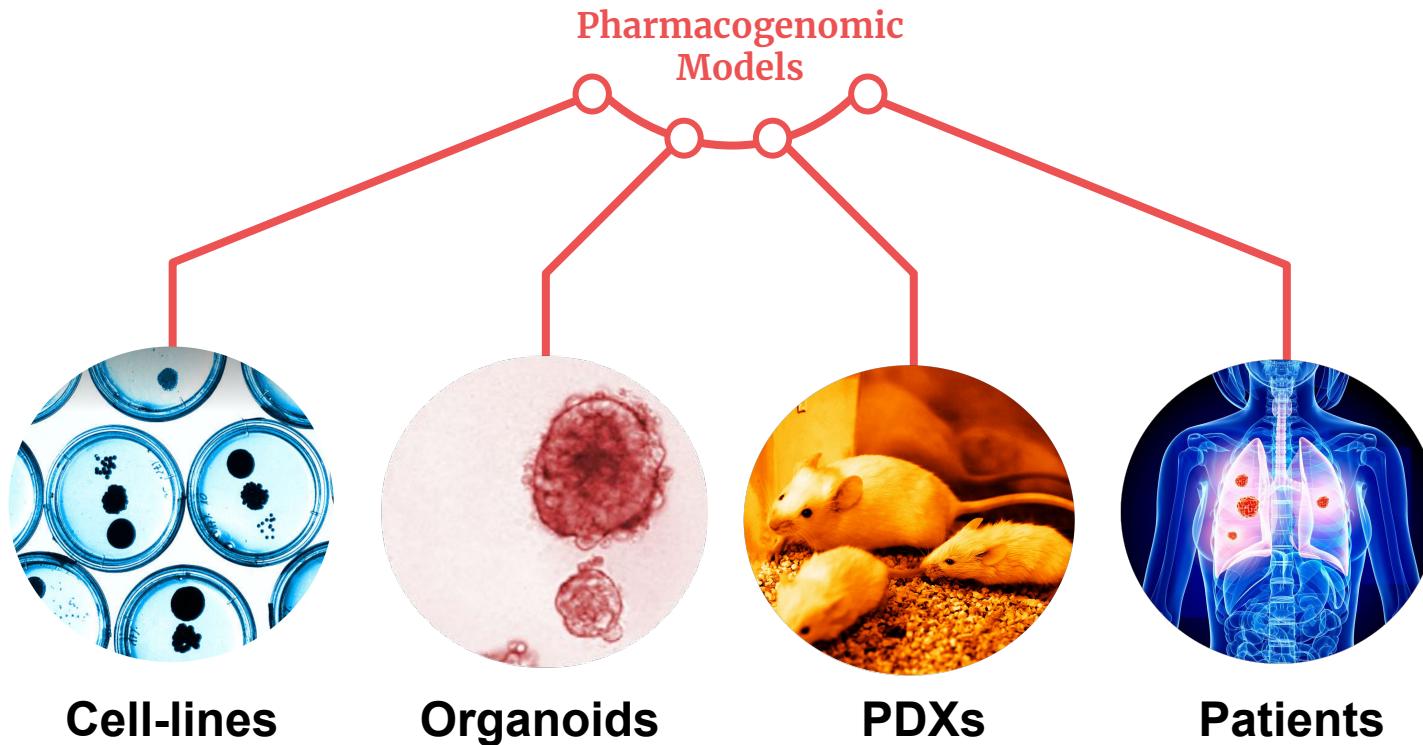


a.mer@utoronto.ca



@ArvidMer

# PHARMACOGENOMIC MODELS

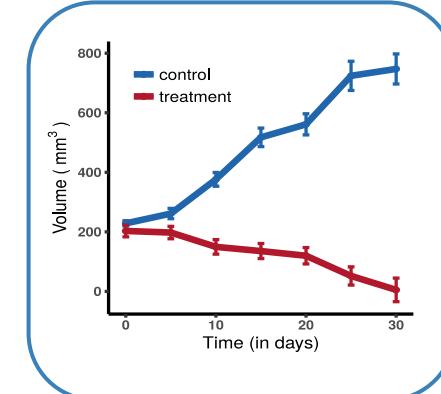
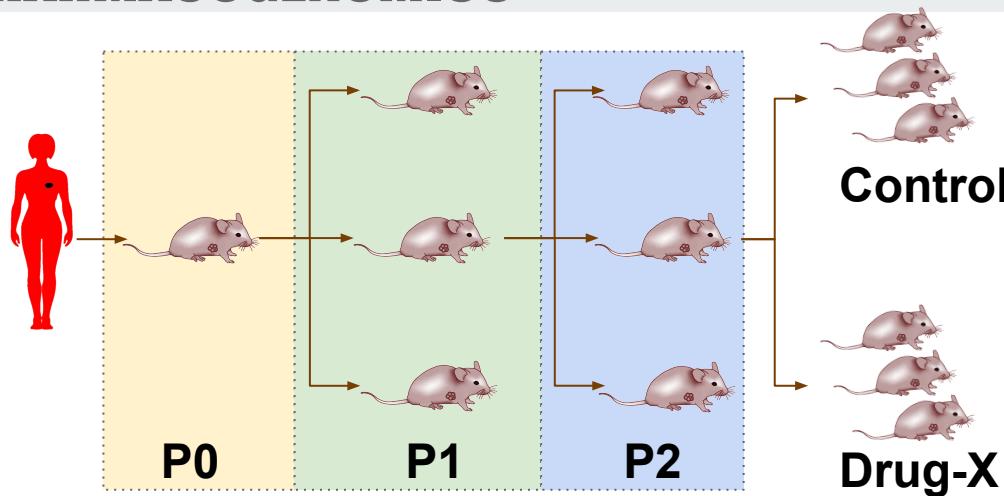




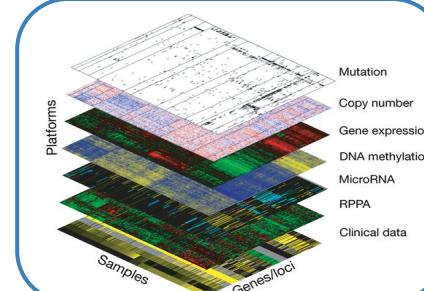
## Recommendations

- A. Establish a network for direct patient involvement
- B. Create a translational science network devoted to immunotherapy
- C. Develop ways to overcome resistance to therapy
- D. Build a national cancer data ecosystem
- E. Intensify research of the major drivers of childhood cancer
- F. Minimize cancer treatment's debilitating side effects
- G. Expand use of proven prevention and early detection strategies
- H. Mine past patient data to predict future patient outcomes
- I. **Develop a 3D cancer atlas**
- J. Develop new cancer technologies

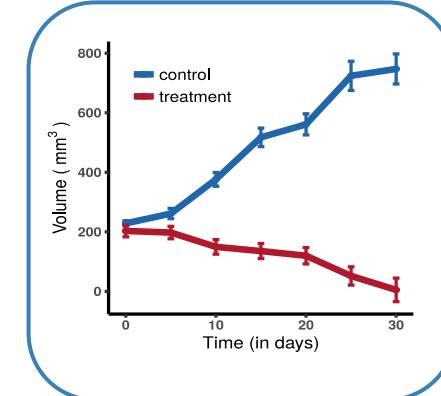
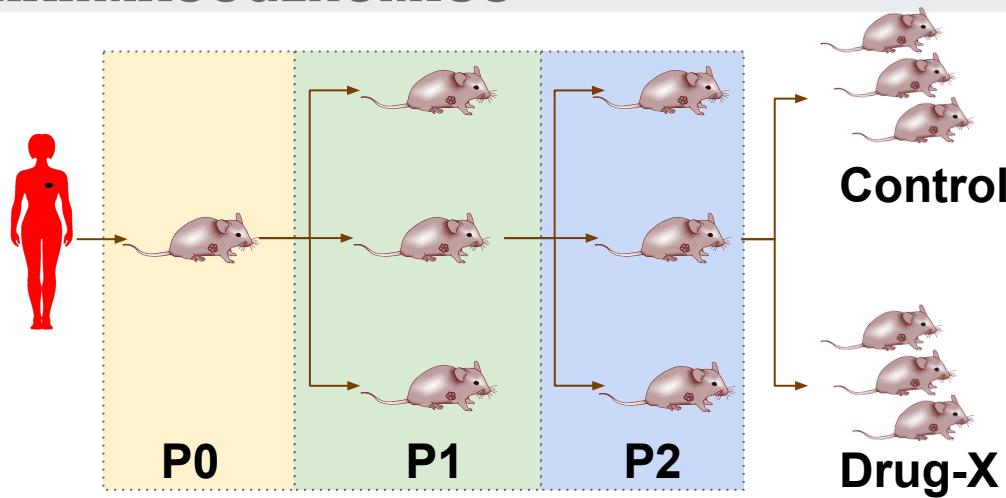
# PDX PHARMACOGENOMICS



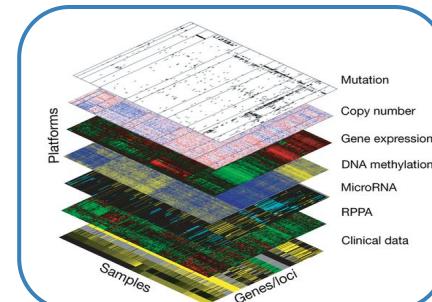
Biomarker discovery



# PDX PHARMACOGENOMICS



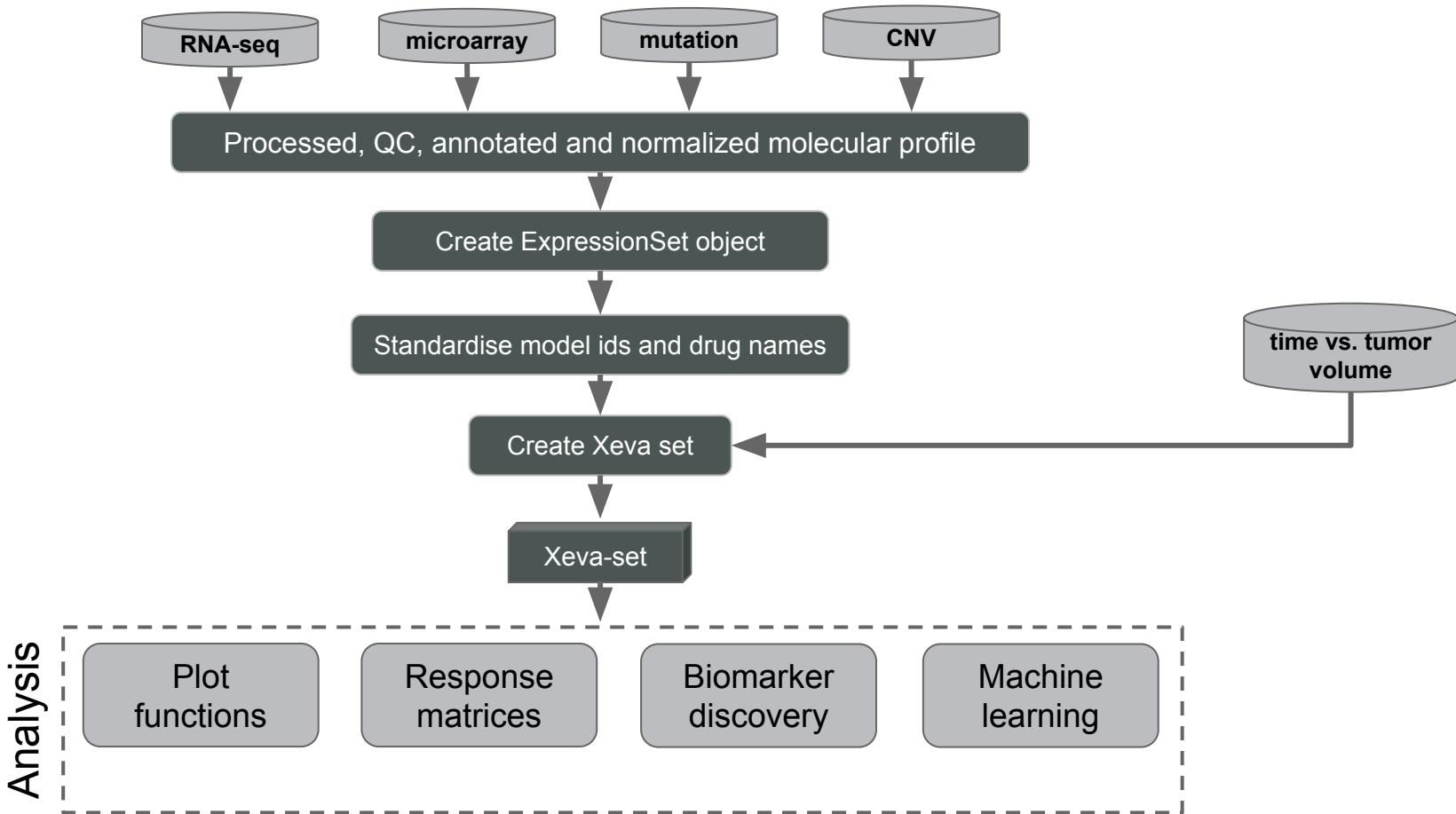
Biomarker discovery



# Xeva : XENOGRAFT VISUALIZATION & ANALYSIS

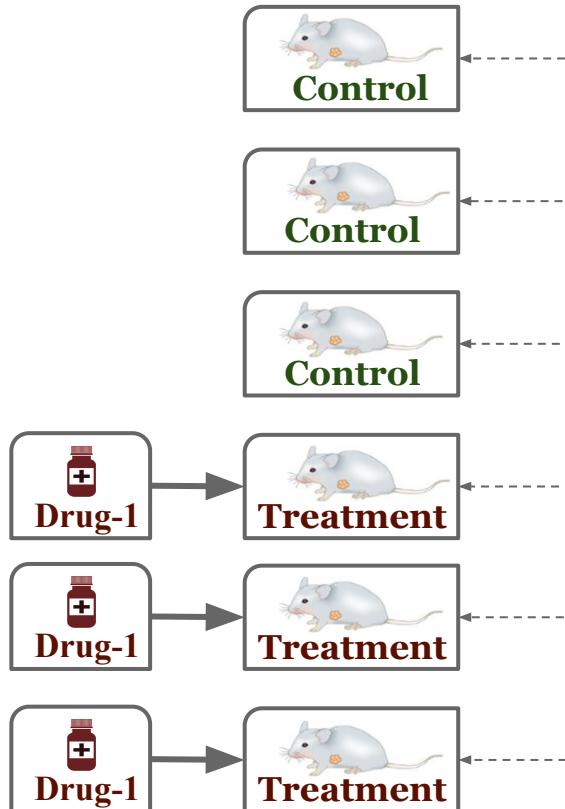
- ❑ Xeva (pronounced: *jīvaa*) an R package for patient derived xenograft data management and analysis
- ❑ PDX based pharmacogenomic data is inherently different than cell-line based data
- ❑ Drug response, experimental information and molecular profile annotated and stored in unified manner
- ❑ Function for PDX data analysis

# Xeva in a Nutshell

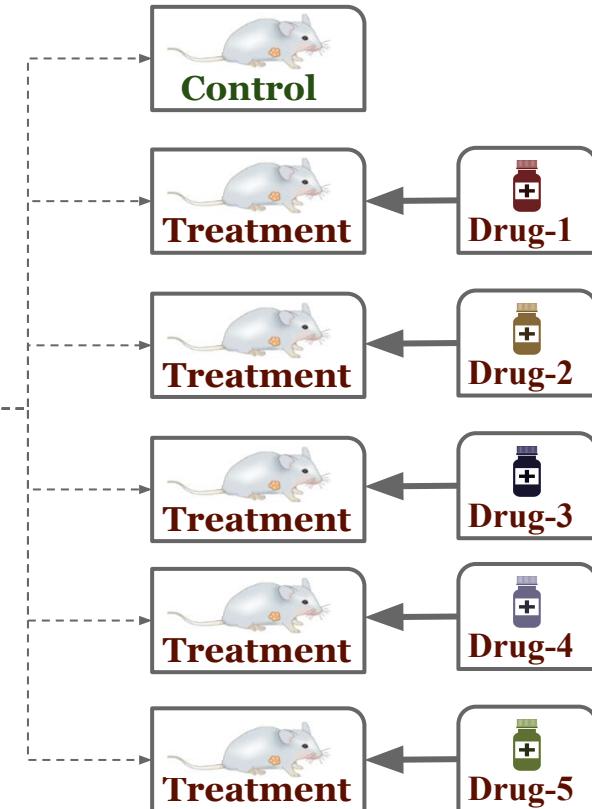


# PDX EXPERIMENT DESIGN

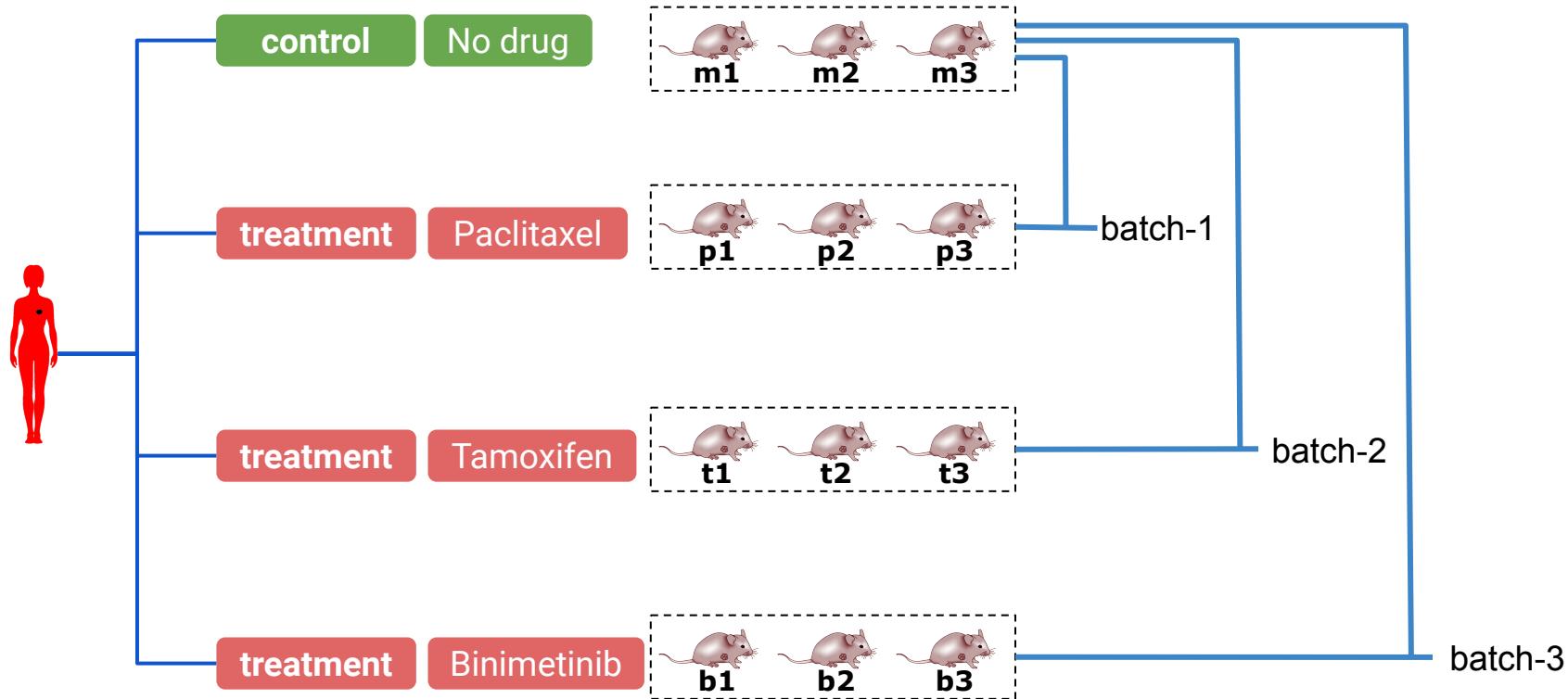
Traditional



1x1x1

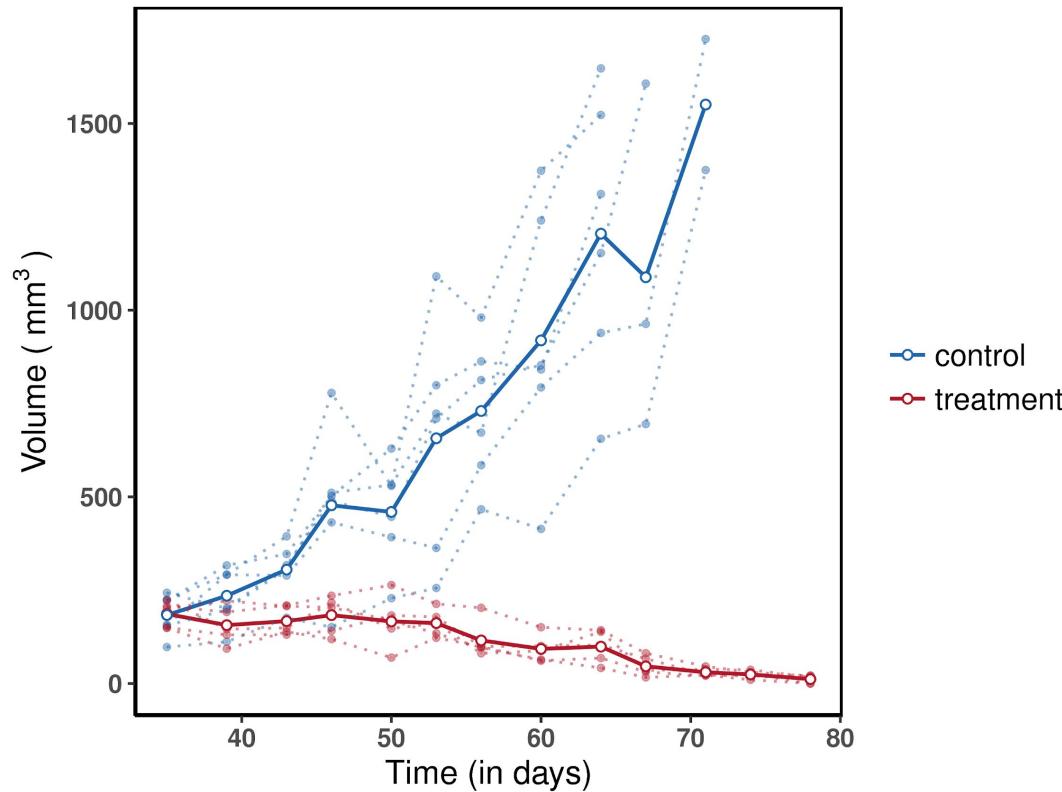


# MODEL AND BATCH ID



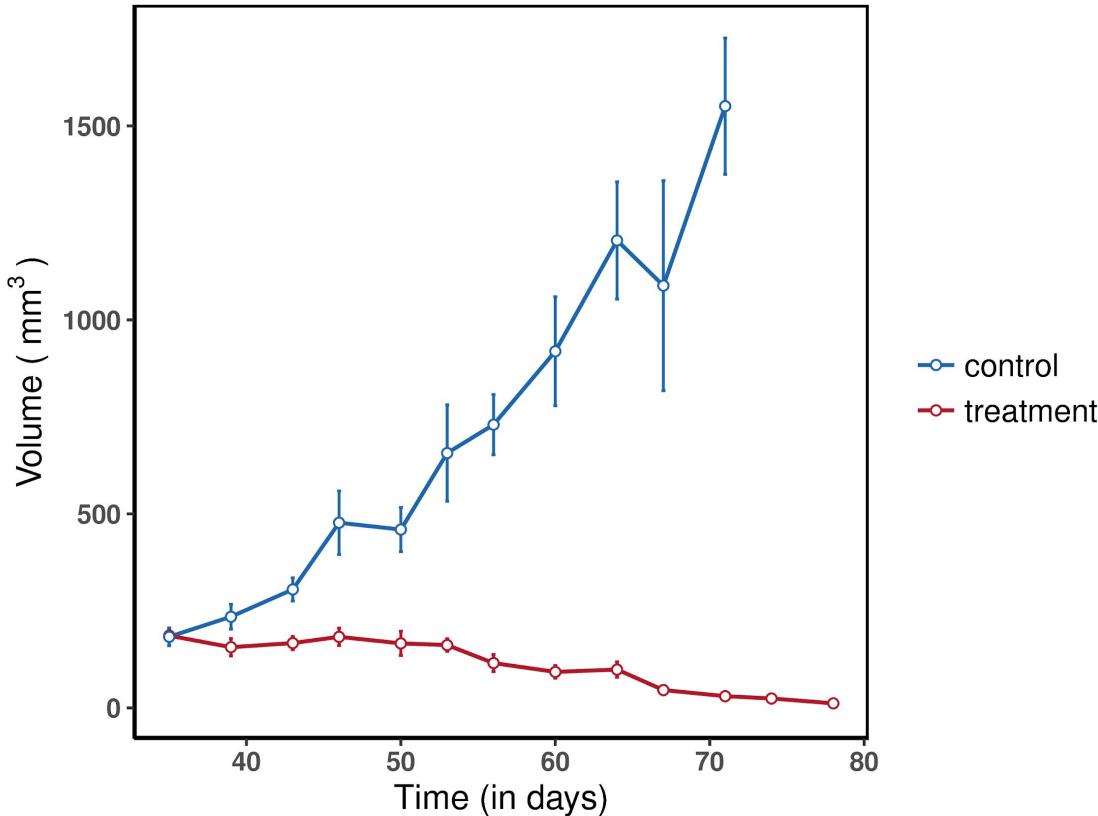
# TUMOR GROWTH CURVE

```
> plotPDX(tnbc, batch.name="drug.1",SE.plot ="all", treatment.only=TRUE)
```



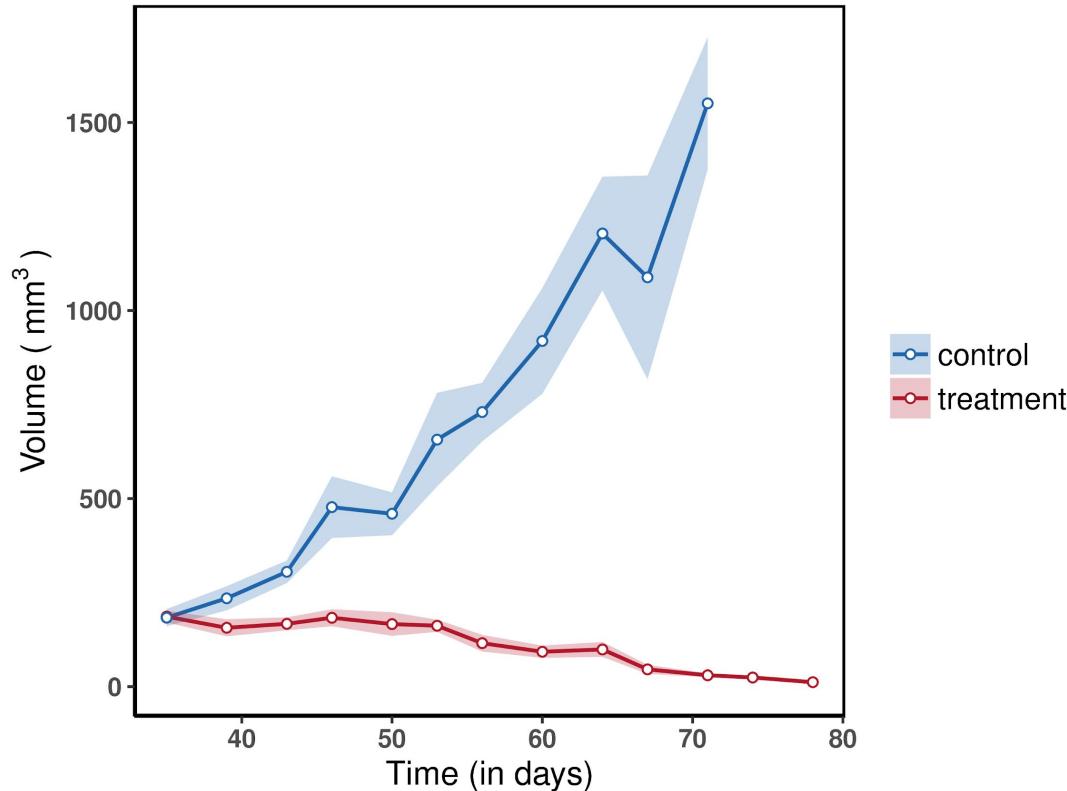
# TUMOR GROWTH CURVE

```
> plotPDX(tnbc, batch.name="drug.1",SE.plot ="errorbar", treatment.only=TRUE)
```



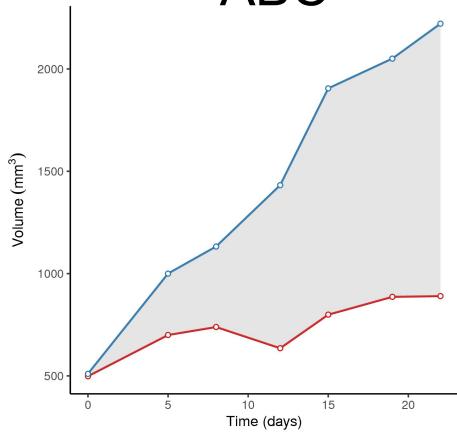
# TUMOR GROWTH CURVE

```
> plotPDX(tnbc, batch.name="drug.1",SE.plot ="ribbon", treatment.only=TRUE)
```

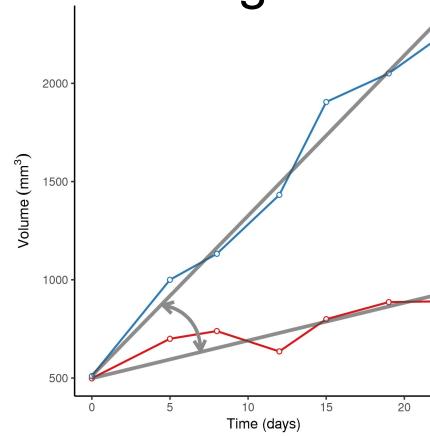


# RESPONSE MATRIX

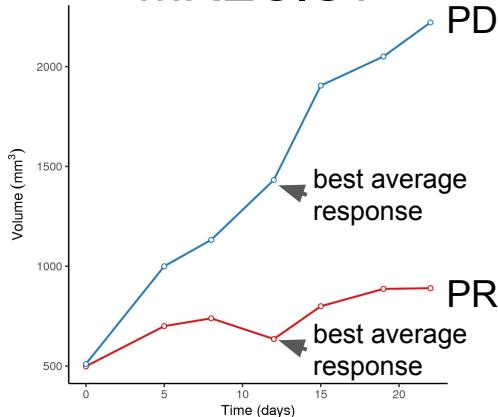
ABC



Angle



mRECIST



- Gaussian process modeling
- Linear mix model
- Treatment/control volume

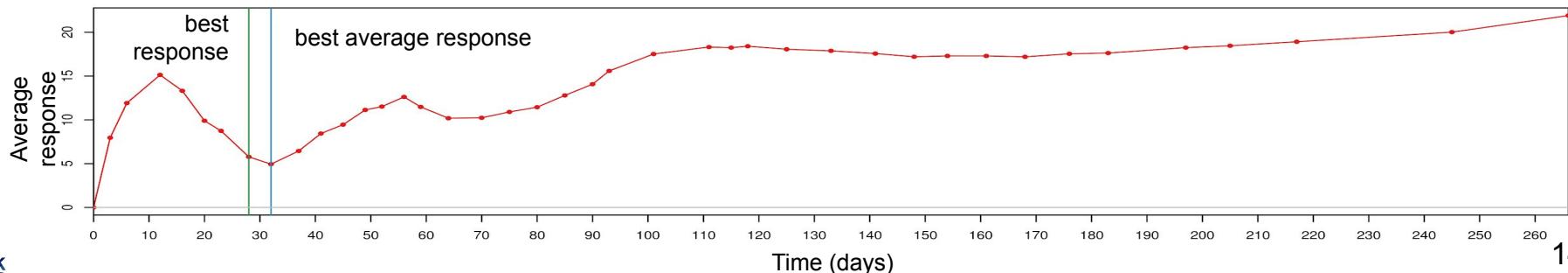
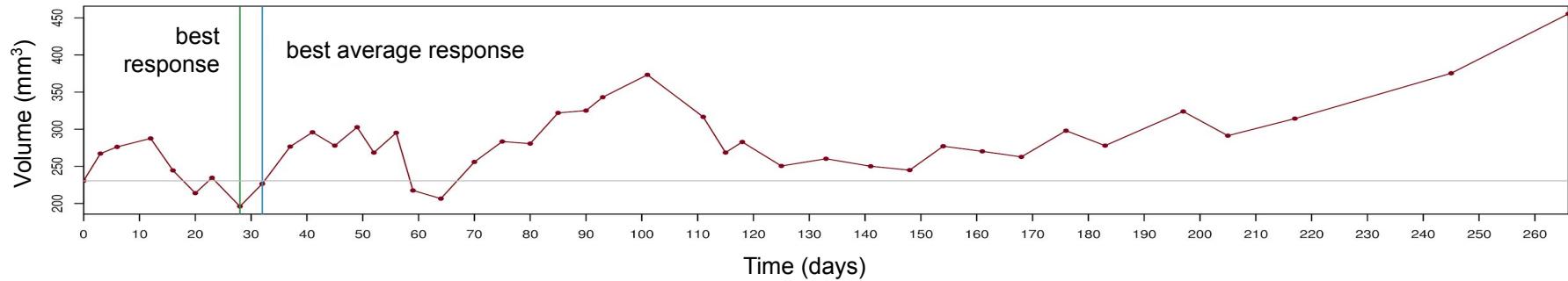
# mRECIST

CR: BestResponse < -95% and BestAvgResponse < -40%

PR: BestResponse < -50% and BestAvgResponse < -20%

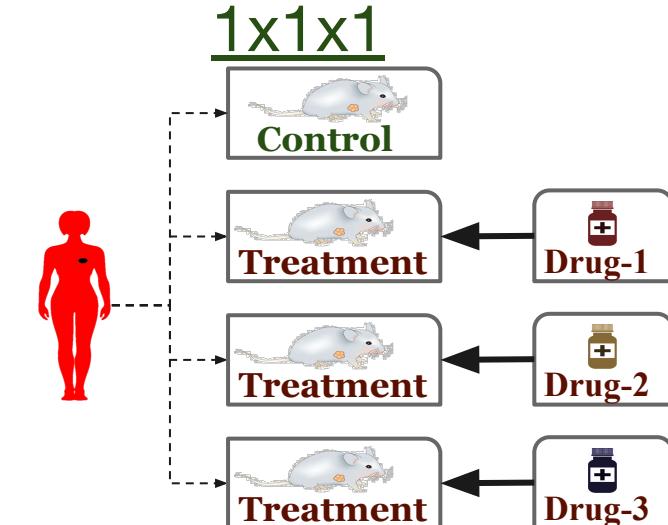
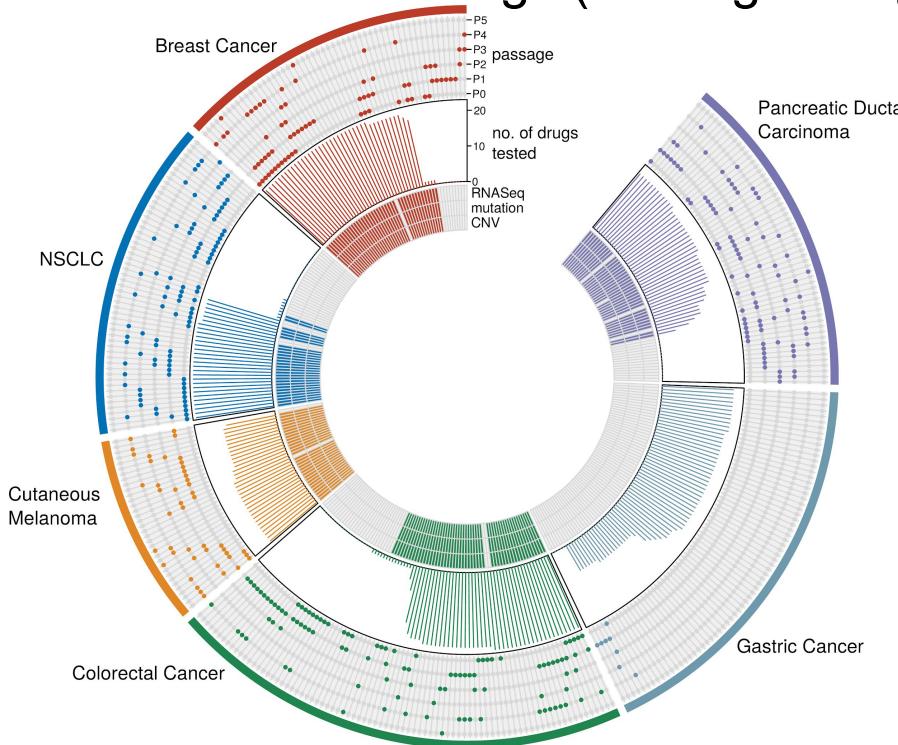
SD: BestResponse < 35% and BestAvgResponse < 30%

PD: not otherwise categorized



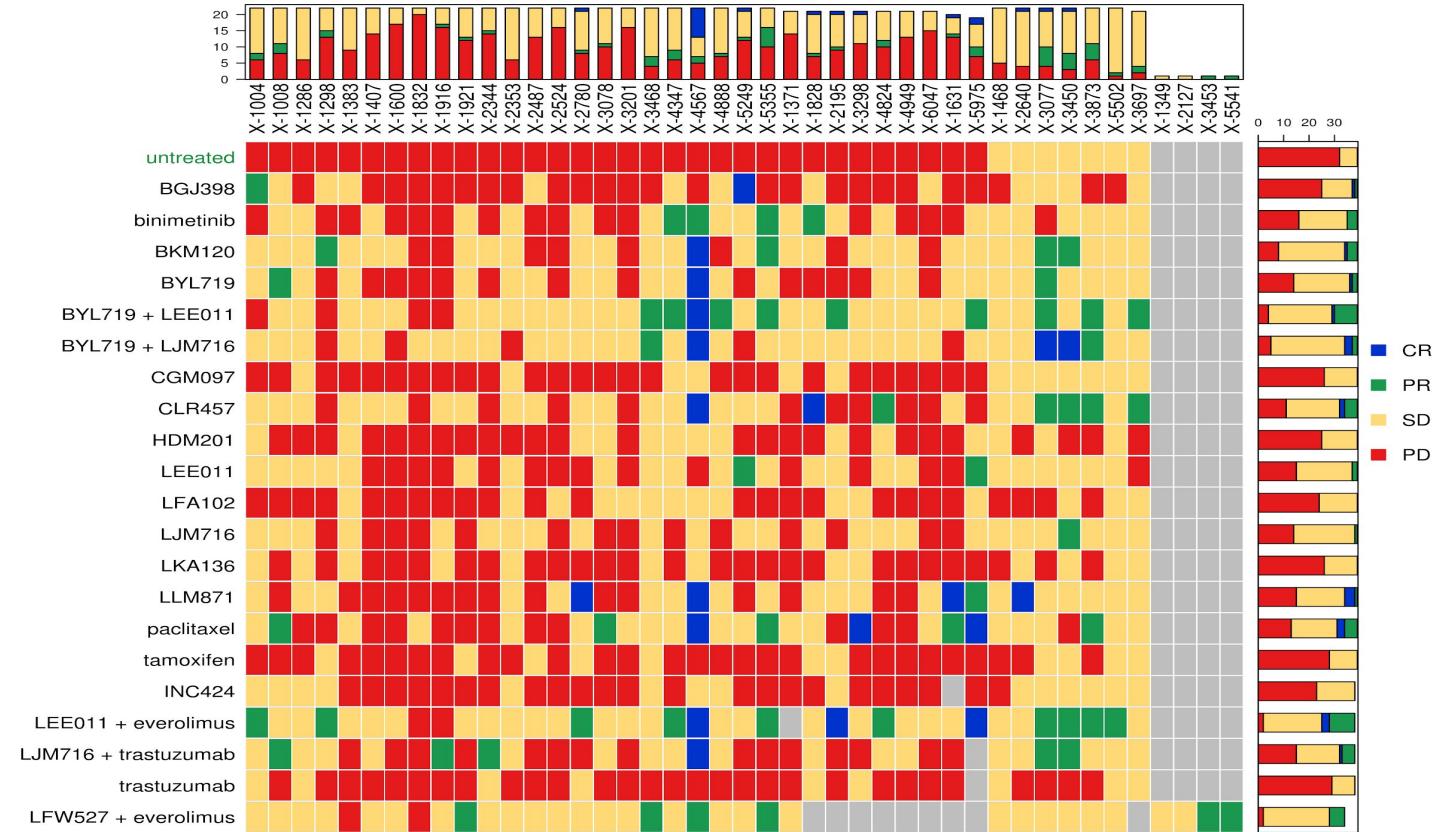
# Novartis PDXE DATA

- In 2015, Novartis generated 1,075 PDXs from 16 tissues along with molecular profiles (**PDXE**)
- 62 different drugs (38 single drugs and 24 combinations) were tested



# BREAST CANCER PDX RESPONSE

```
> brca <- summarizeResponse(pdxe, response.measure="mRECIST", tumor.type="BRCA")
> plotmRECIST(brca, control.name="untreated")
```

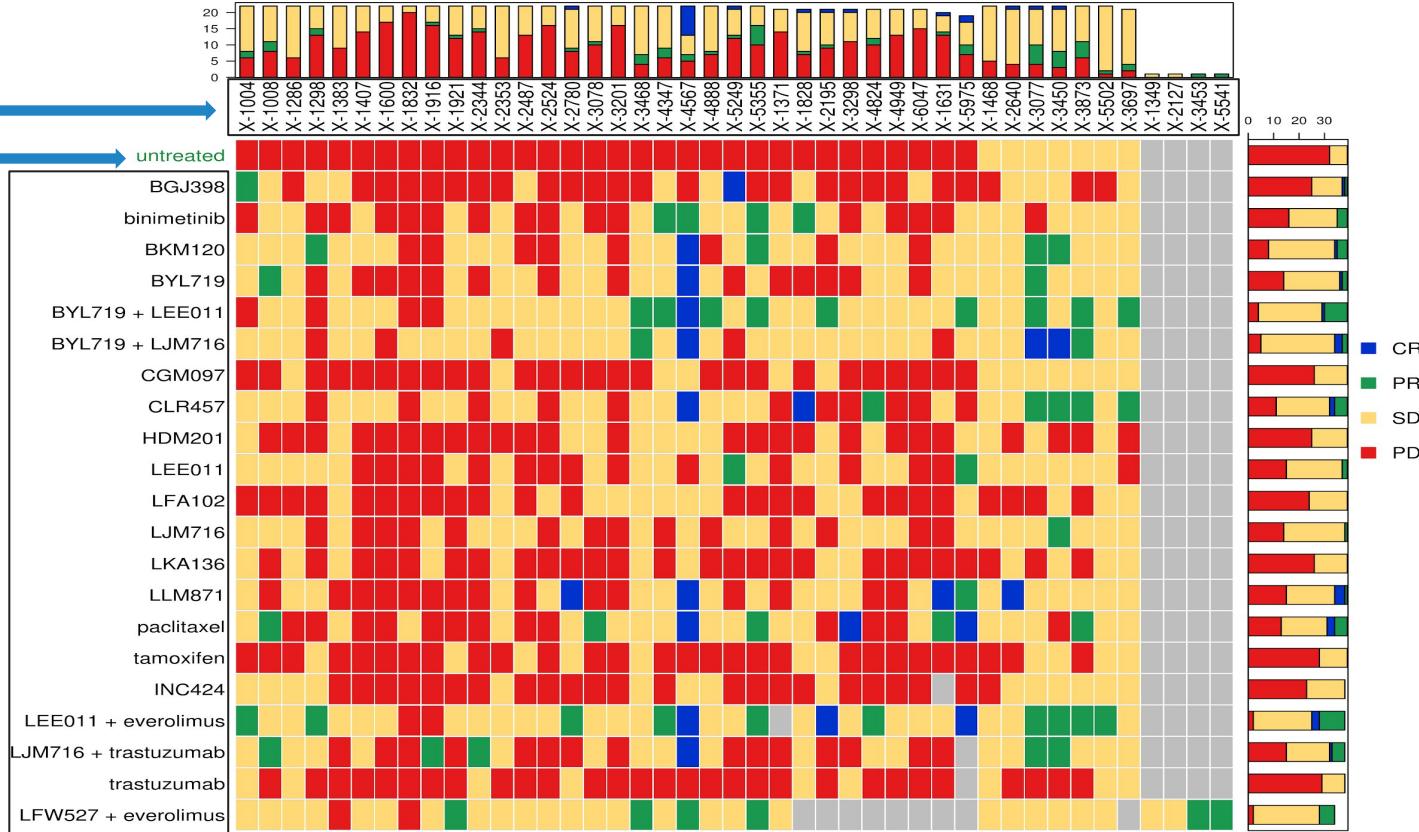


# BREAST CANCER PDX RESPONSE

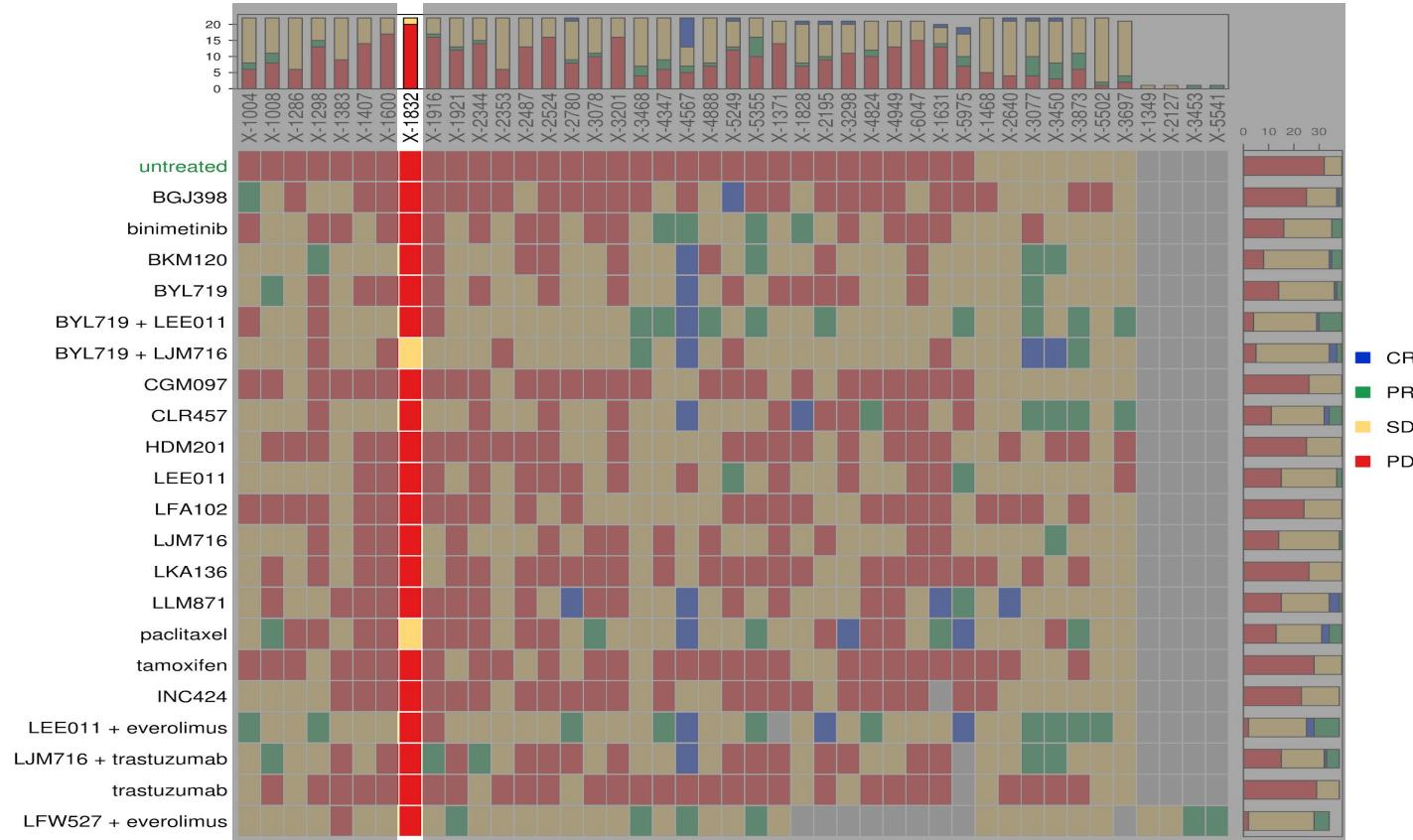
```
> brca <- summarizeResponse(pdxe, response.measure="mRECIST", tumor.type="BRCA")
> plotmRECIST(brca, control.name="untreated")
```

Patient  
Control

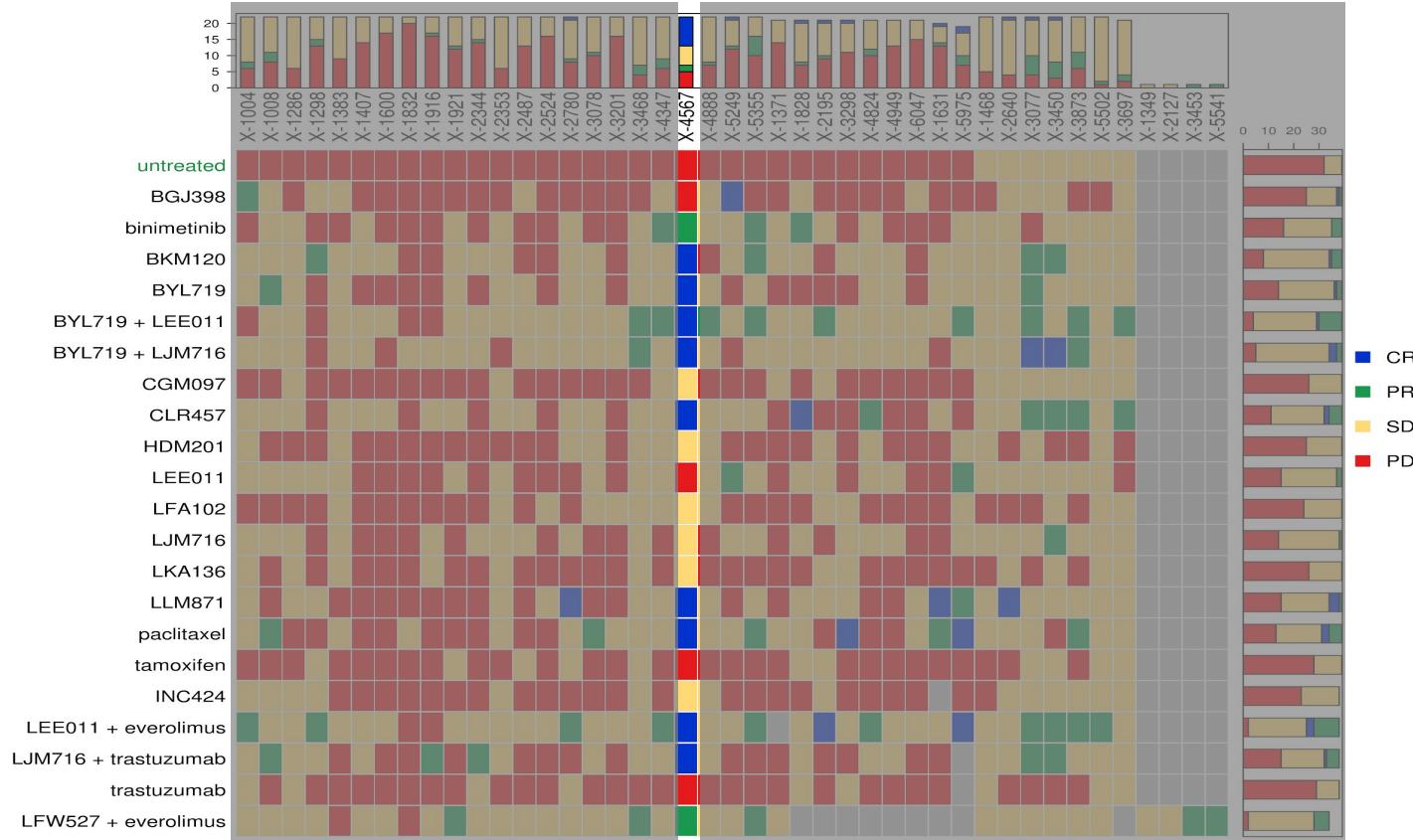
Drugs →



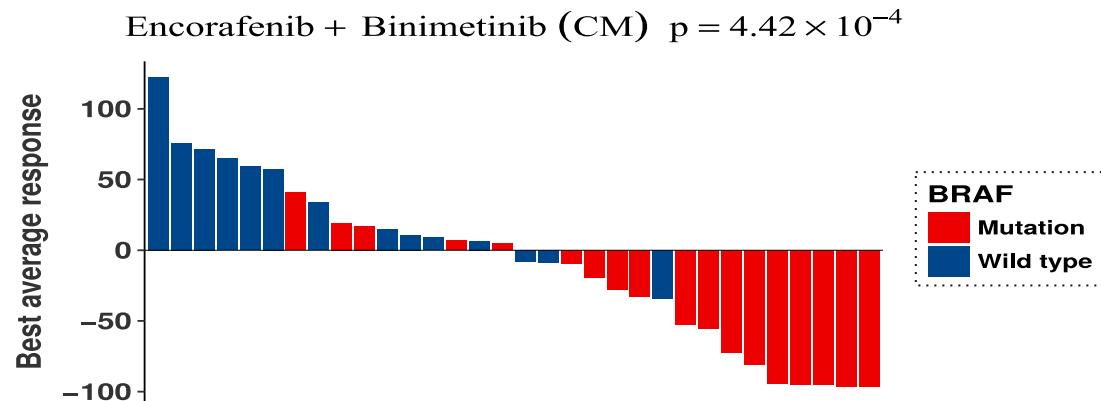
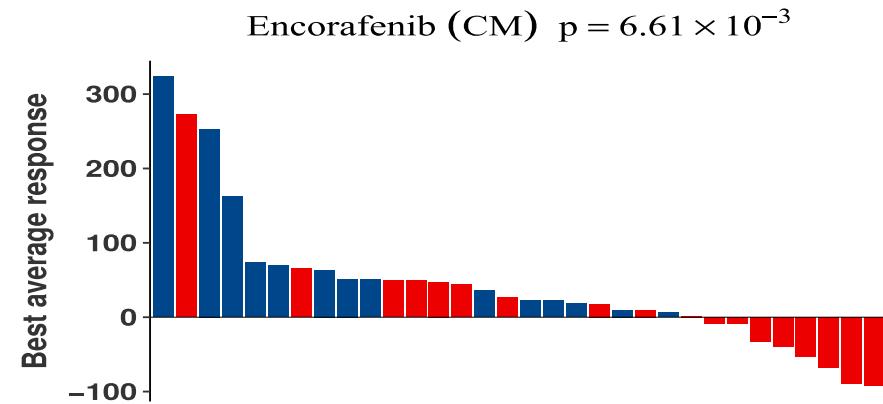
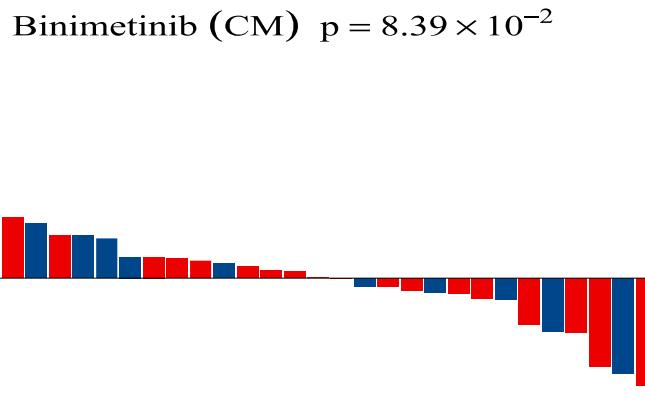
# BREAST CANCER PDX RESPONSE



# BREAST CANCER PDX RESPONSE



# Biomarkers in PDXE



Let's do some hands-on exercise