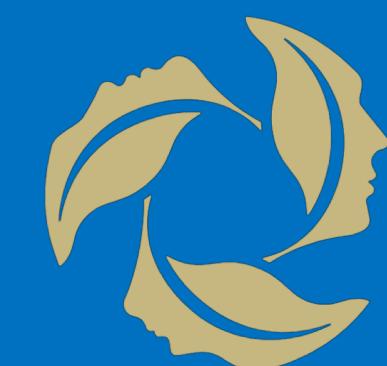




# Repurposing Cholesterol-Lowering Drugs to Personalize Breast Cancer Treatment

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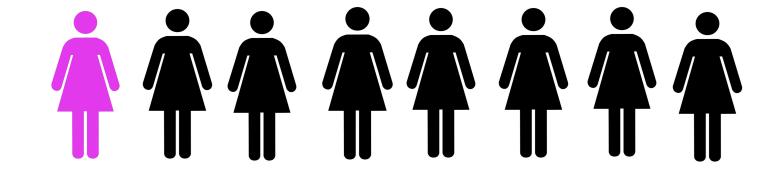


## Abstract

Data show that the statin family of cholesterol-lowering drugs can kill aggressive breast cancer cells; however, not all breast cancers respond equally. We propose to develop and validate a basal mRNA expression signature of statin sensitivity to facilitate the repurposing of these already-approved agents for the treatment of breast cancer.

## Background

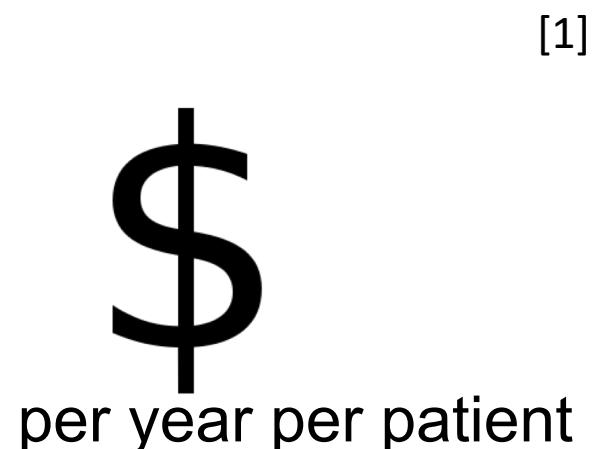
Breast cancer is the most common cancer in women worldwide.



1 in 8 women are diagnosed with breast cancer



5000 deaths in 2017

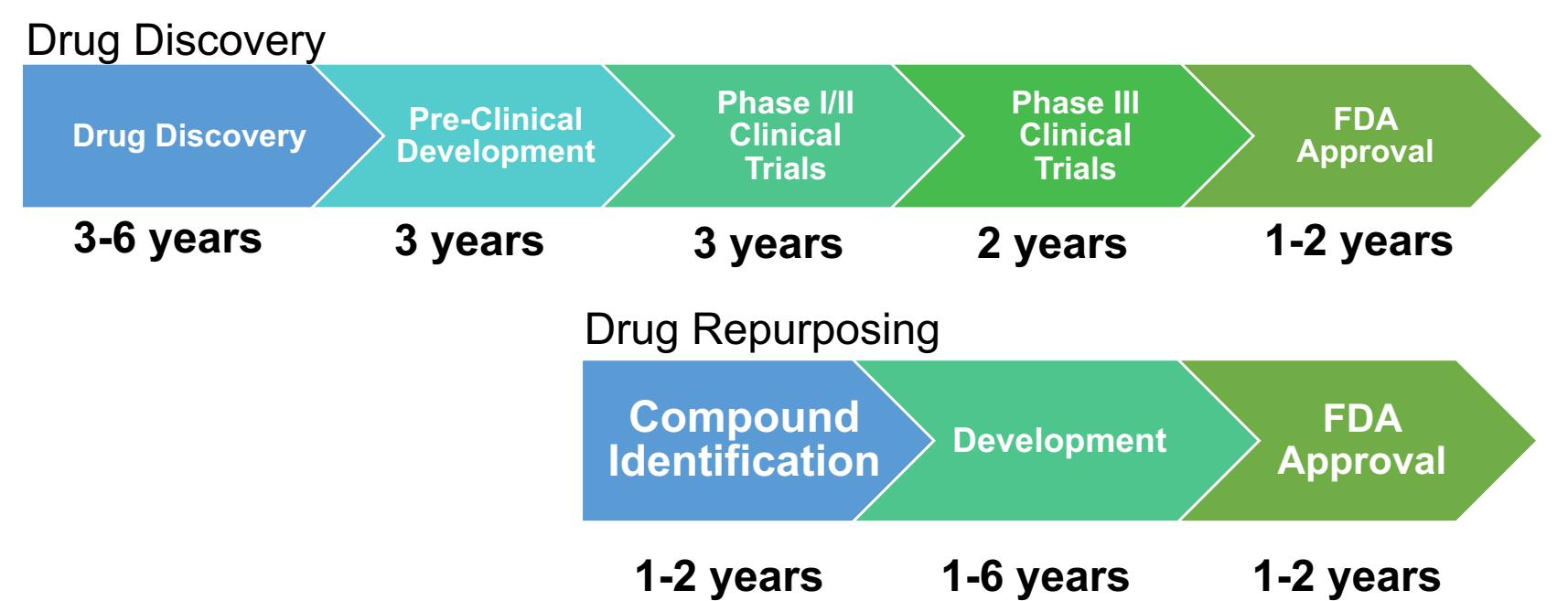


\$40,000 per year per patient

**There is an urgent demand for effective, inexpensive breast cancer treatment.**

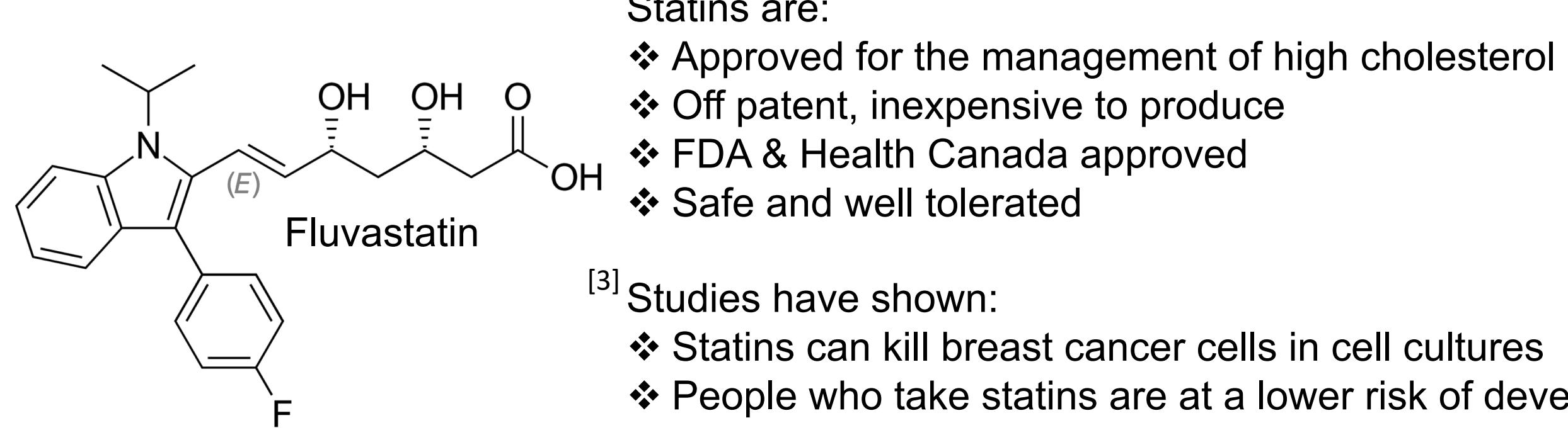
## Drug Repurposing

Drug discovery is a time-consuming, high-investment process. Drug repurposing is an alternative that has been shown to be much more efficient both cost and time wise.



- Drug Repurposing is beneficial as:
- ❖ Time efficient (3-10 years vs 12-16 years)
  - ❖ Saves money (\$20 million vs 1-2 billion)
  - ❖ Safety data available
  - ❖ Drugs are off-patent and affordable
  - ❖ Approved and available for clinical testing of different diseases

## Repurposing Statins as Anti-Breast Cancer Agents

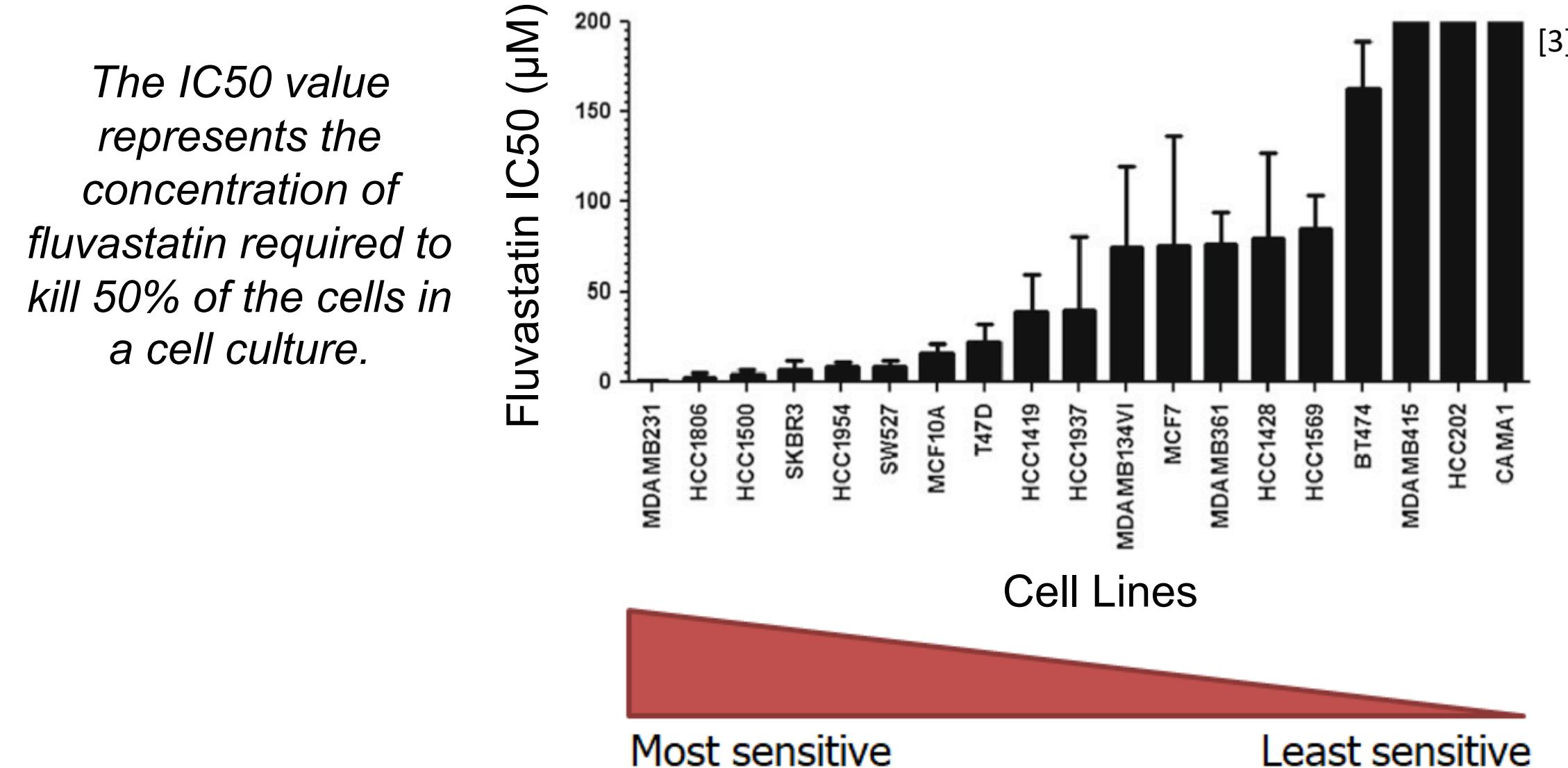


- [3] Studies have shown:
- ❖ Statins can kill breast cancer cells in cell cultures
  - ❖ People who take statins are at a lower risk of developing aggressive breast cancer

**These facts make statins an effective drug to be repurposed and immediately implemented as a treatment option to make a positive impact on breast cancer patients.**

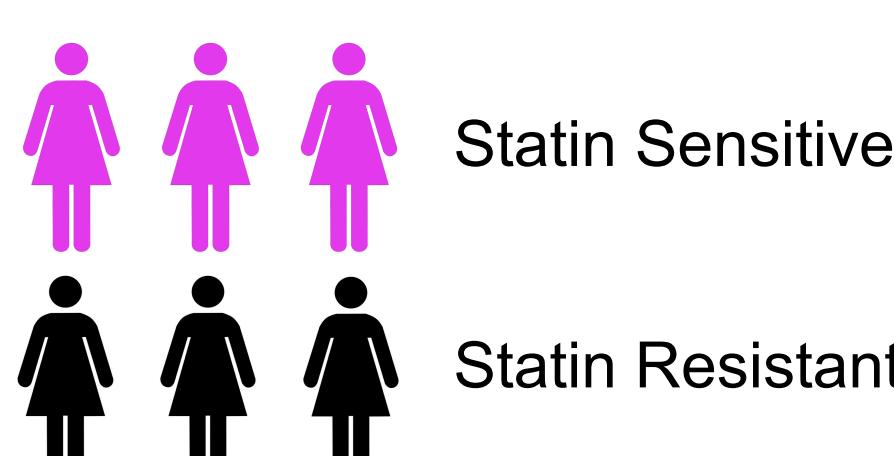
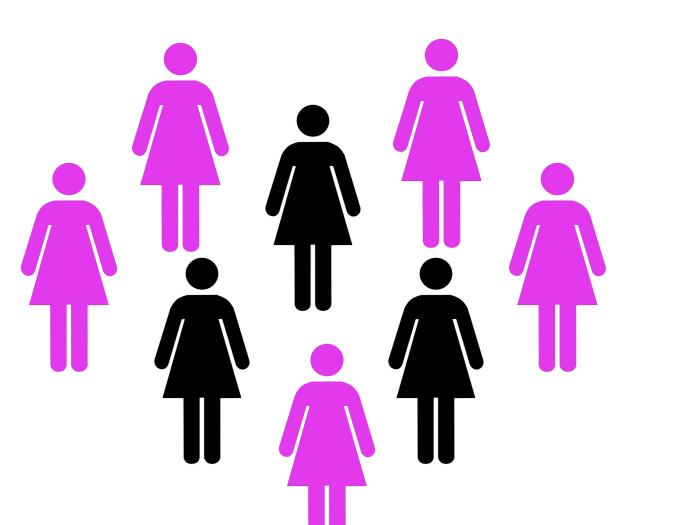
## Not all Breast Cancers are Sensitive to Statins

The variances in breast cancer cell sensitivity to fluvastatin provides an opportunity to discover characteristics that predict statin sensitivity.



## Project Objective

There is a definitive need for inexpensive, specialized treatment options for patients suffering from breast cancer as current forms of chemotherapy, radiotherapy and pan-cancer drugs are not as cost-effective.

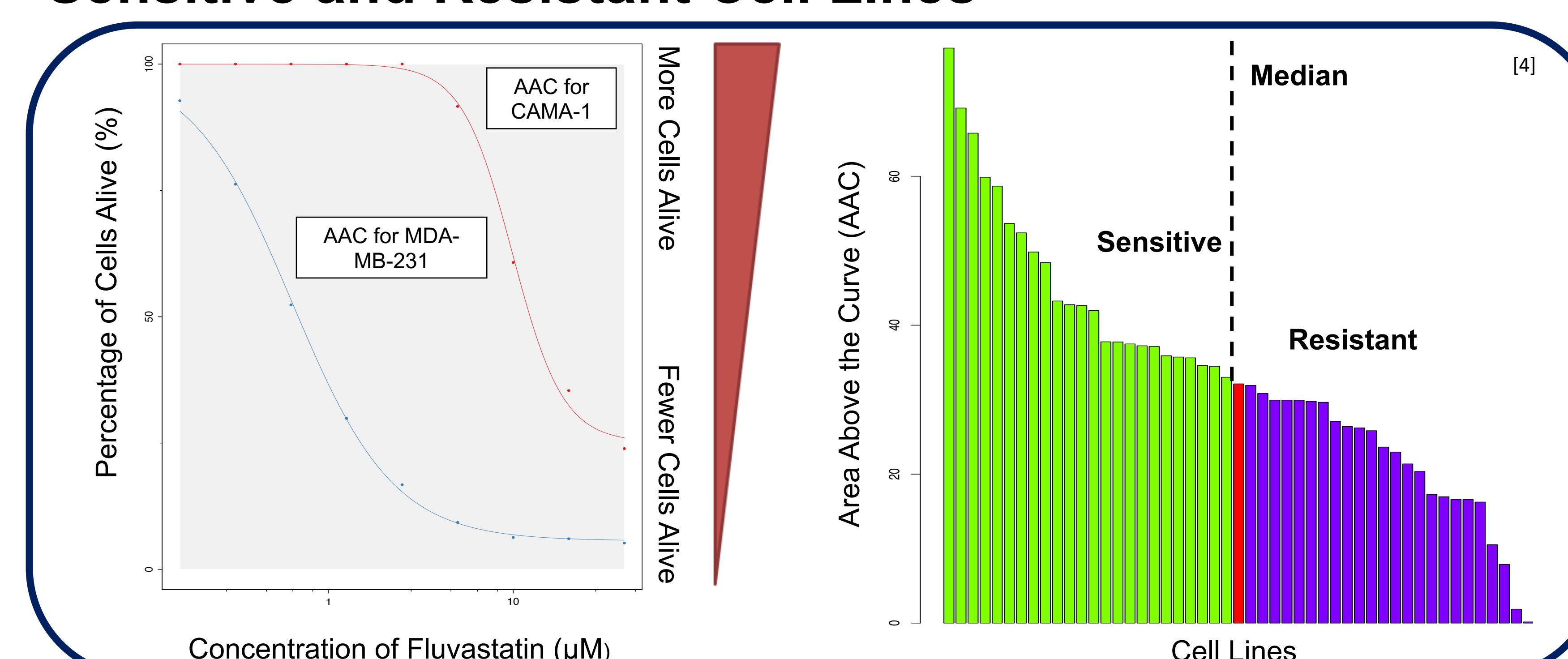


Statin Sensitive

Statin Resistant

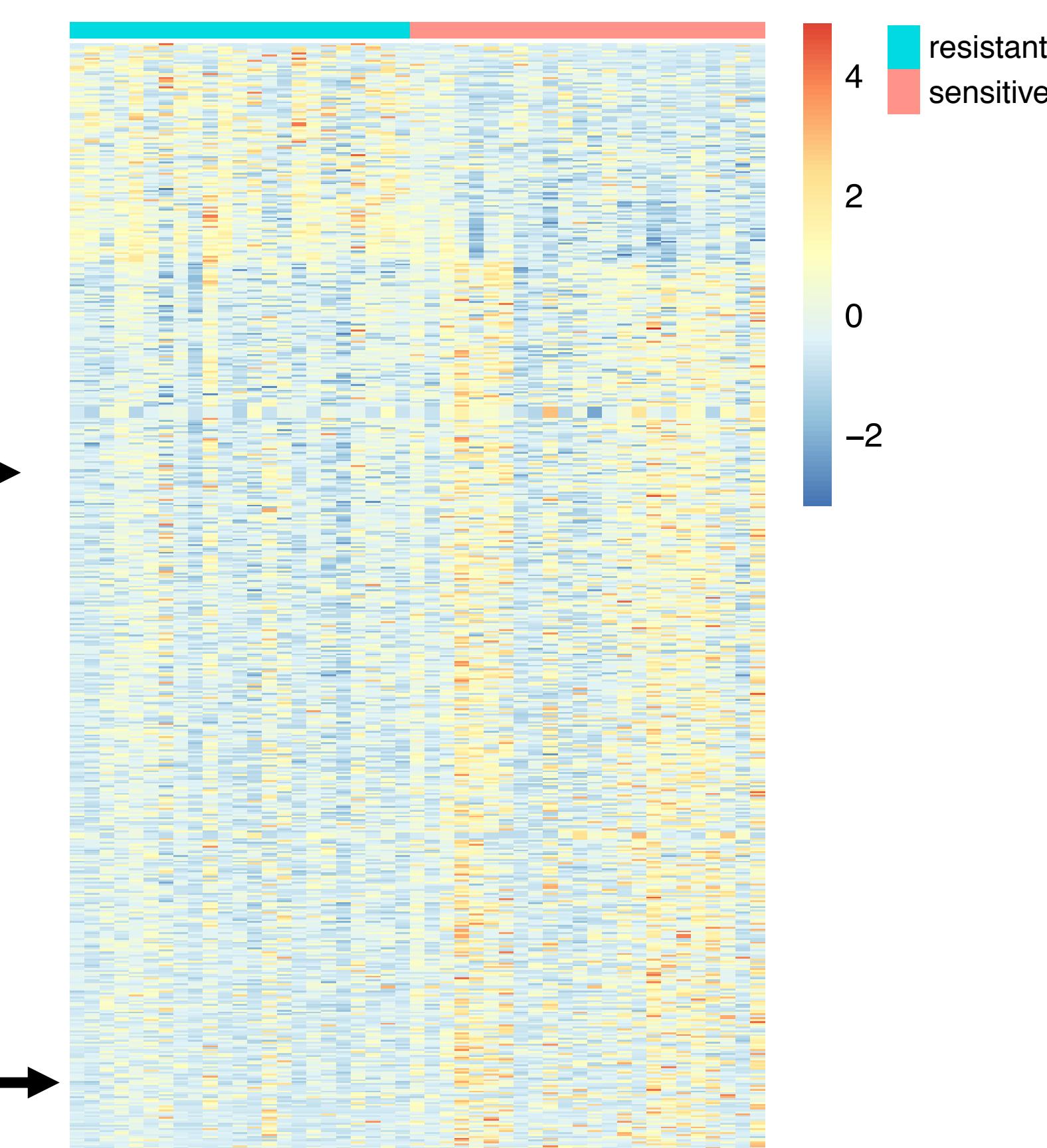
Statins have the potential to be repurposed for the treatment of breast cancer, however, not all patients are equally sensitive. Our project will identify and validate biological characteristics predictive of sensitivity to statins in breast cancer.

## Sensitive and Resistant Cell Lines



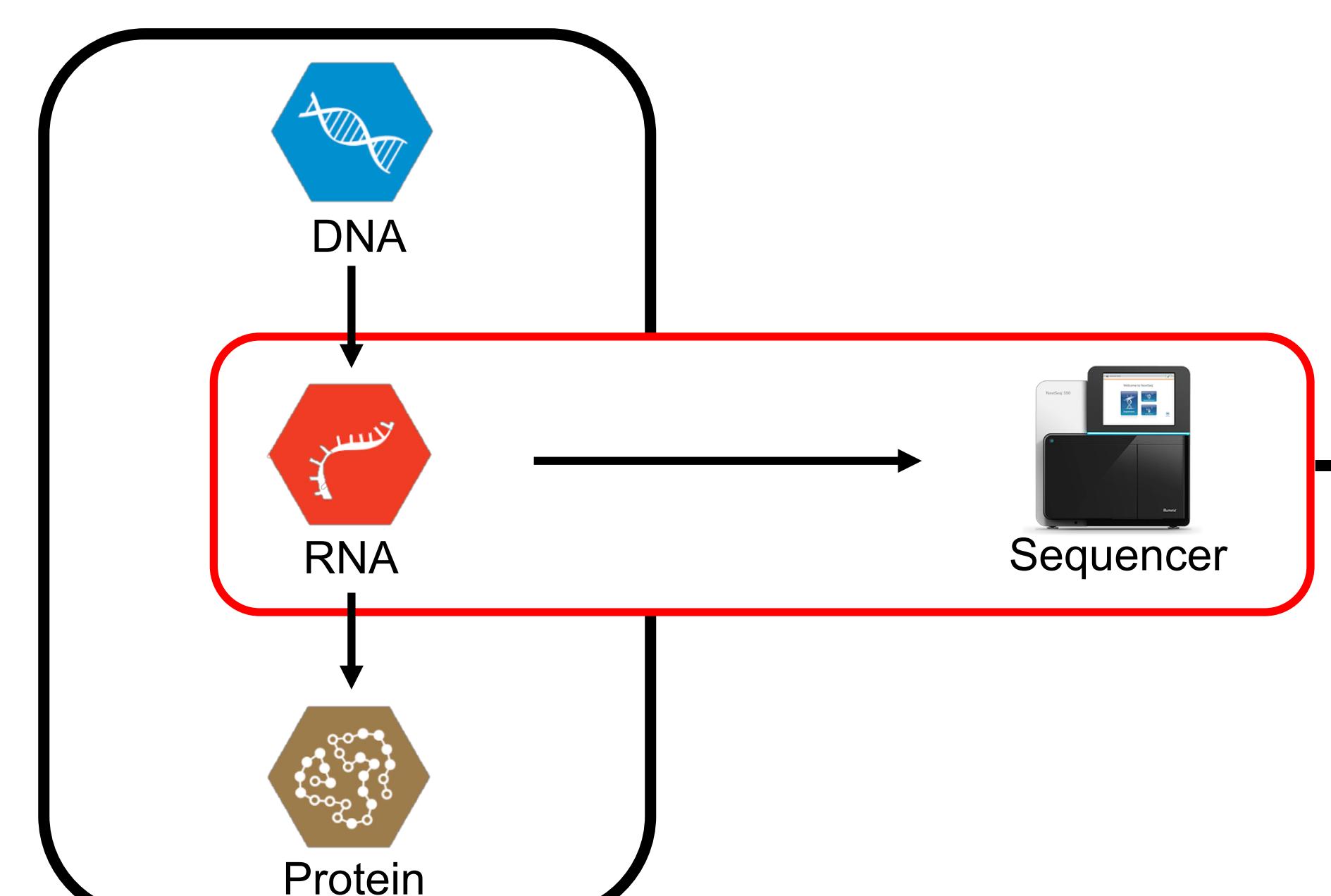
## Methods

## Differentially Expressed Genes



## Breast Cancer Cell Lines (44 Cell Lines)

## RNA Sequencing

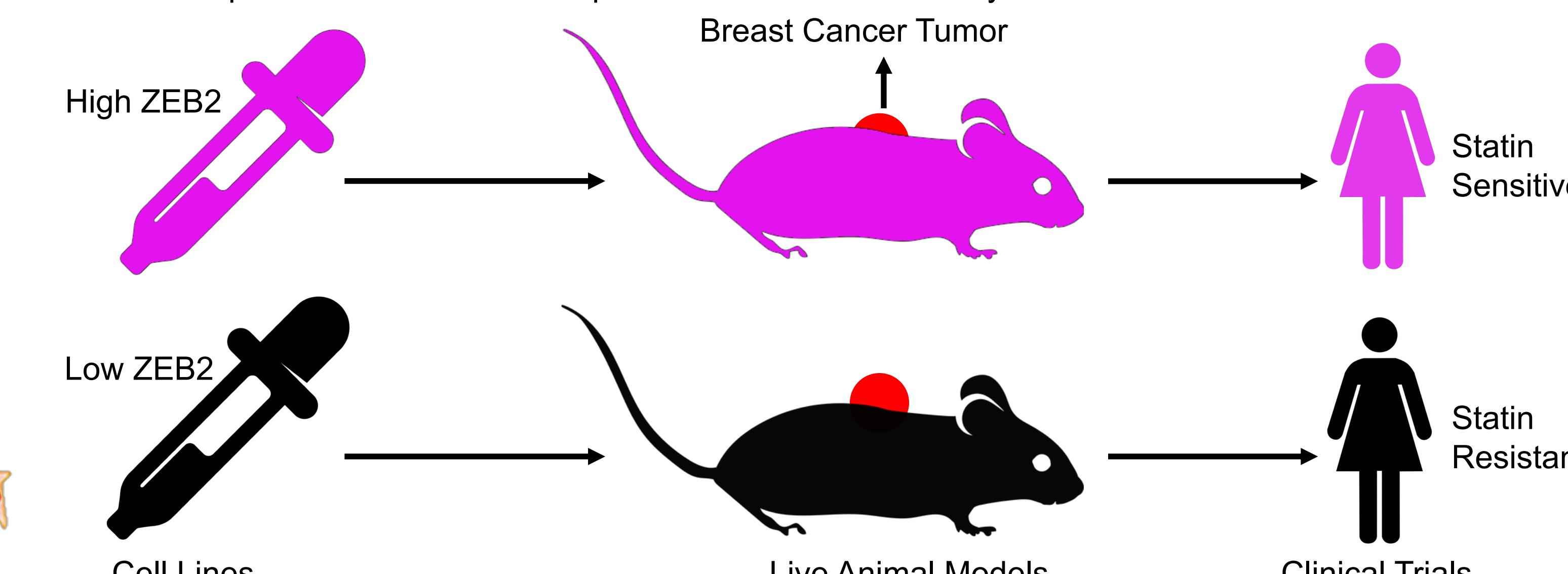


## Validation with External Dataset (34 Cell Lines)

## Zinc Finger E-box Binding Homeobox 2 (ZEB2)

## Future Directions

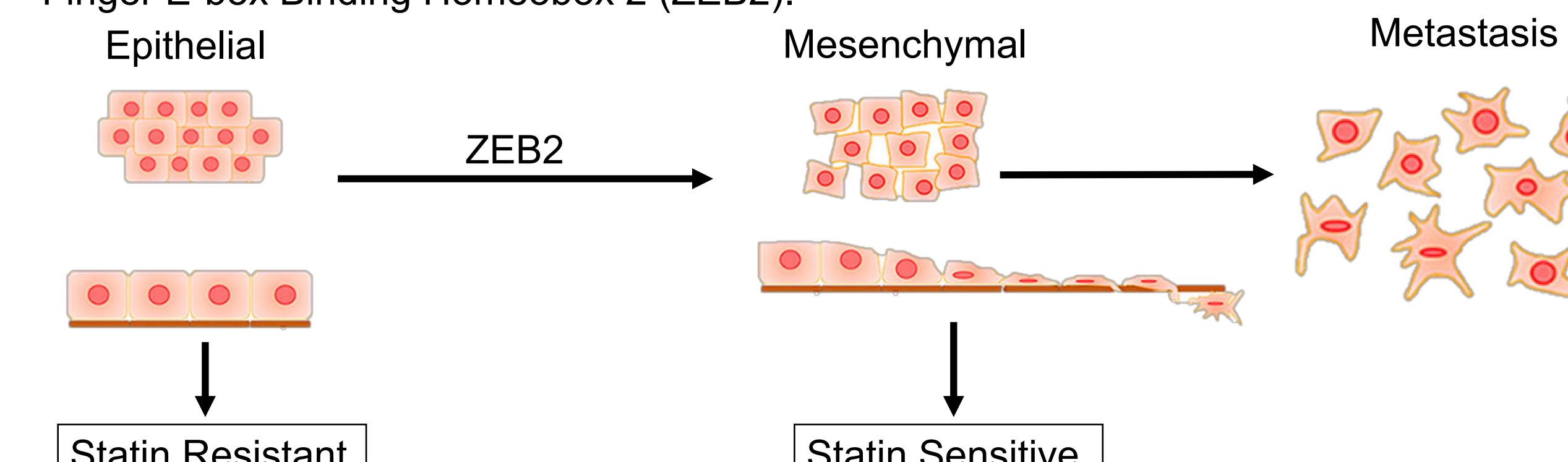
The next step is to validate if ZEB2 is predictive of statin sensitivity in:



By doing so, it is possible to repurpose statins for the treatment of breast cancer in a timely, cost-effective manner.

## Discussion

A notable gene identified out of the list of differentially expressed genes is Zinc Finger E-box Binding Homeobox 2 (ZEB2).



High expression of ZEB2 was notable in statin sensitive breast cancer cell lines. ZEB2 prevents the production of proteins that enable cells to adhere to one another. This allows for epithelial breast cancer cells to become mesenchymal-like and diverge from their origin, spreading to other organs.

## Acknowledgements

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## Citations

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