

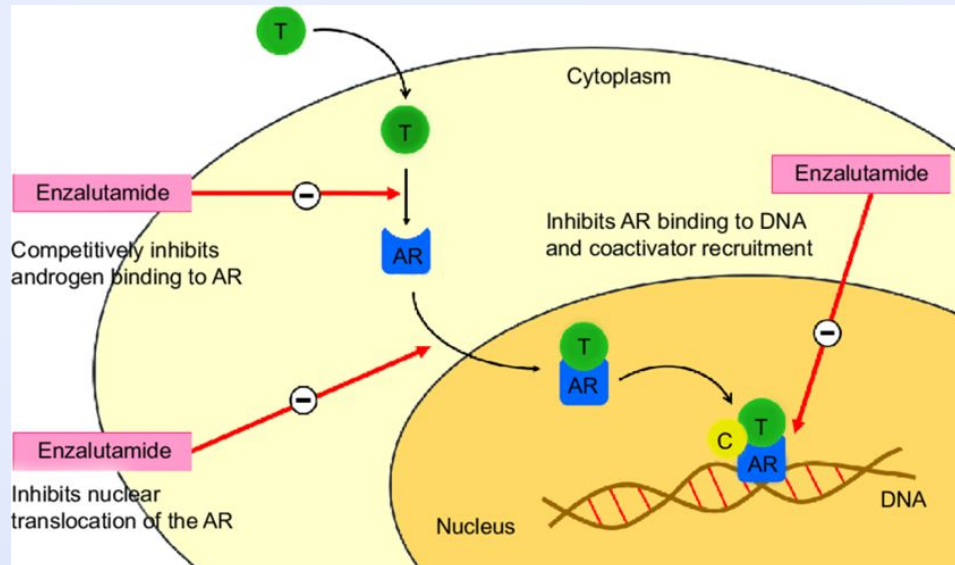
An abstract graphic featuring a network of interconnected nodes and lines, resembling a molecular structure or a data network. The nodes are represented by circles in various shades of blue, purple, and white, connected by thin, light blue lines. The background is a solid light blue. The graphic is positioned on the left and right sides of the slide, framing the central text.

Investigating Drug Resistance in Prostate Cancer

The Lab Rats
Cammy Kutter, Ethan Cohen,
and Sai Manikonda



Challenge Question

Can we identify druggable genes and pathways that contribute to enzalutamide resistance?





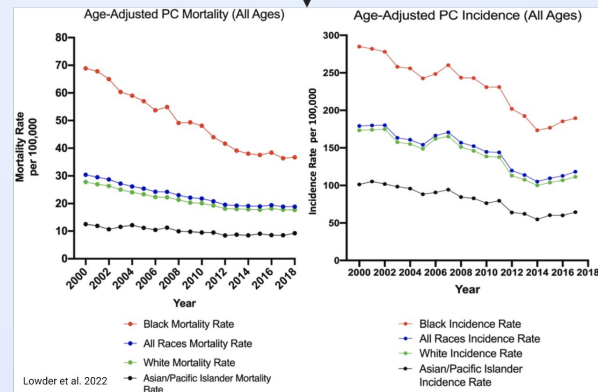
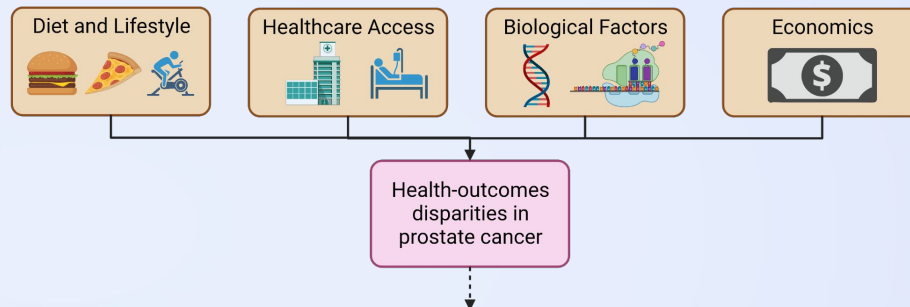
Prostate Cancer Data Exploration

Estimated New Cases

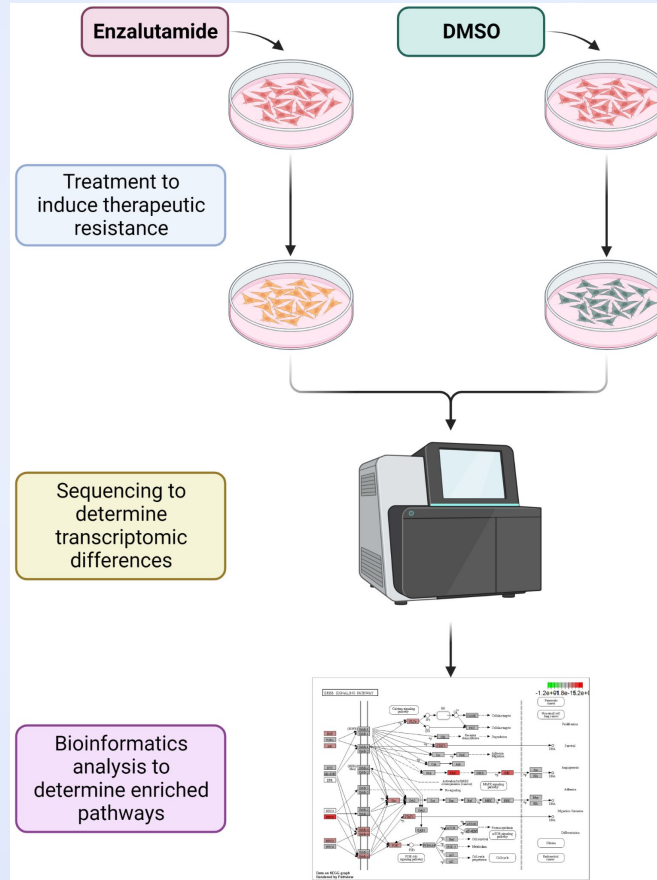
			Males	Females		
Prostate	288,300	29%			Breast	297,790 31%
Lung & bronchus	117,550	12%			Lung & bronchus	120,790 13%
Colon & rectum	81,860	8%			Colon & rectum	71,160 8%
Urinary bladder	62,420	6%			Uterine corpus	66,200 7%
Melanoma of the skin	58,120	6%			Melanoma of the skin	39,490 4%
Kidney & renal pelvis	52,360	5%			Non-Hodgkin lymphoma	35,670 4%
Non-Hodgkin lymphoma	44,880	4%			Thyroid	31,180 3%
Oral cavity & pharynx	39,290	4%			Pancreas	30,920 3%
Leukemia	35,670	4%			Kidney & renal pelvis	29,440 3%
Pancreas	33,130	3%			Leukemia	23,940 3%
All Sites	1,010,310	100%			All Sites	948,000 100%

Estimated Deaths

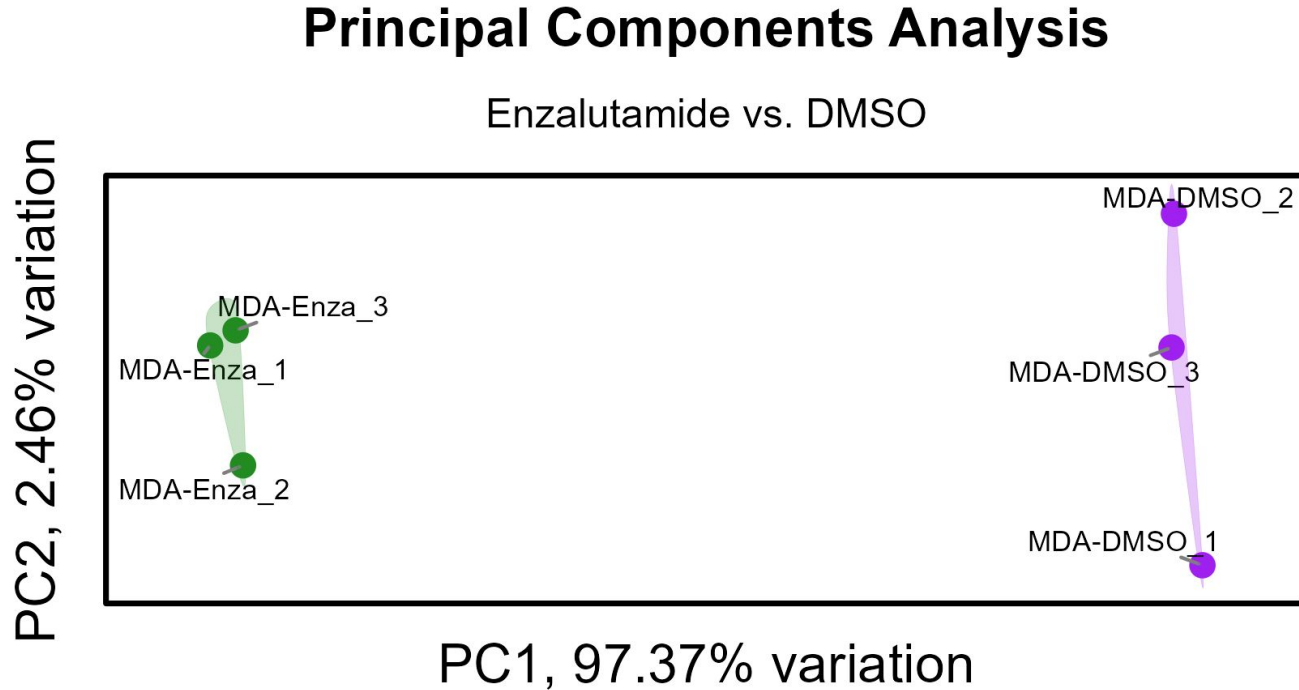
			Males	Females		
Lung & bronchus	67,160	21%			Lung & bronchus	59,910 21%
Prostate	34,700	11%			Breast	43,170 15%
Colon & rectum	28,470	9%			Colon & rectum	24,080 8%
Pancreas	26,620	8%			Pancreas	23,930 8%
Liver & intrahepatic bile duct	19,000	6%			Ovary	13,270 5%
Leukemia	13,900	4%			Uterine corpus	13,030 5%
Esophagus	12,920	4%			Liver & intrahepatic bile duct	10,380 4%
Urinary bladder	12,160	4%			Leukemia	9,810 3%
Non-Hodgkin lymphoma	11,780	4%			Non-Hodgkin lymphoma	8,400 3%
Brain & other nervous system	11,020	3%			Brain & other nervous system	7,970 3%
All Sites	322,080	100%			All Sites	287,740 100%



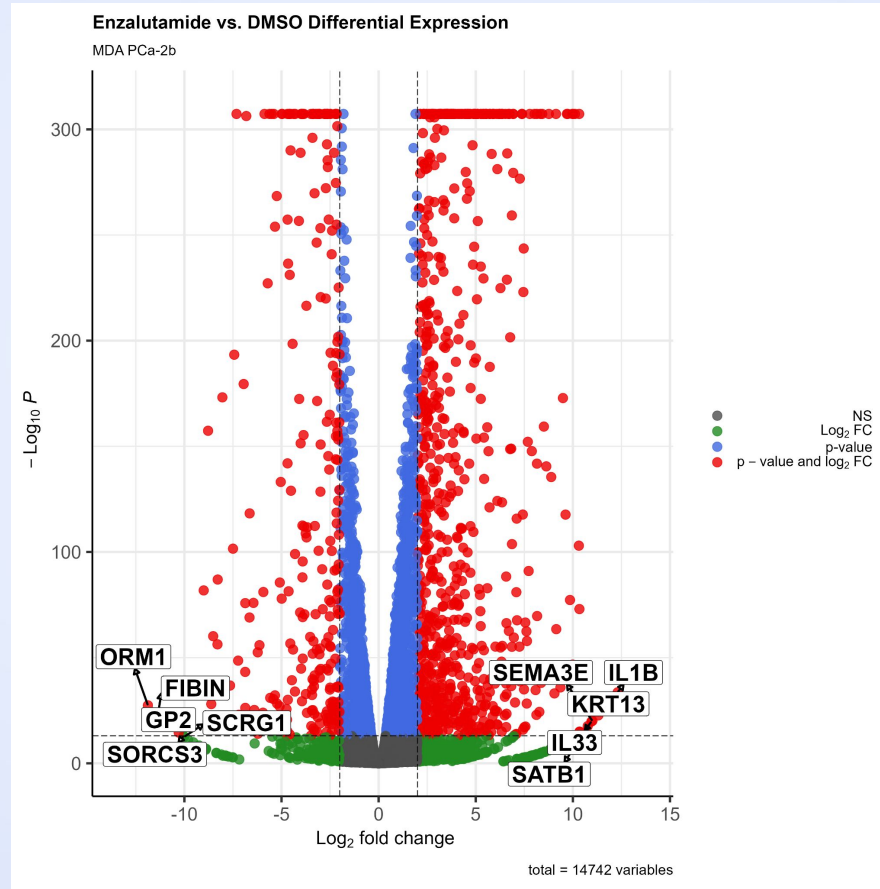
Data Production Experimental Design



Verifying differences between the conditions with PCA

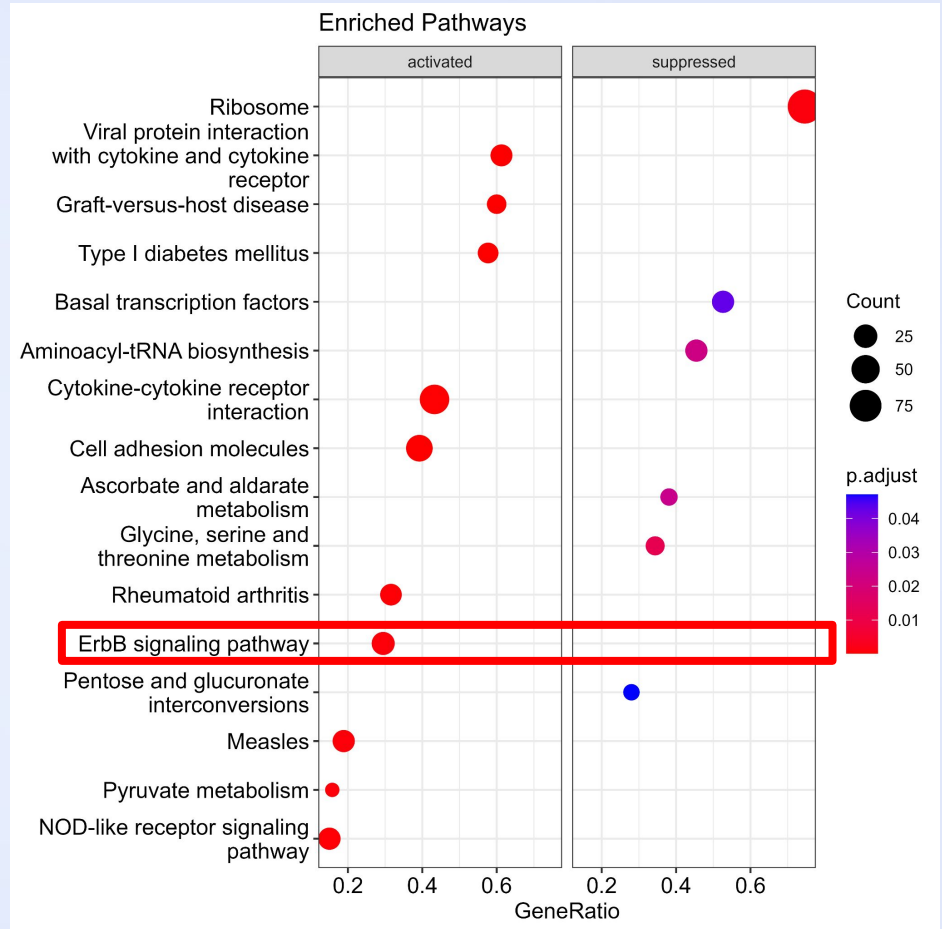


Differential Expression Analysis Reveals Druggable Genes

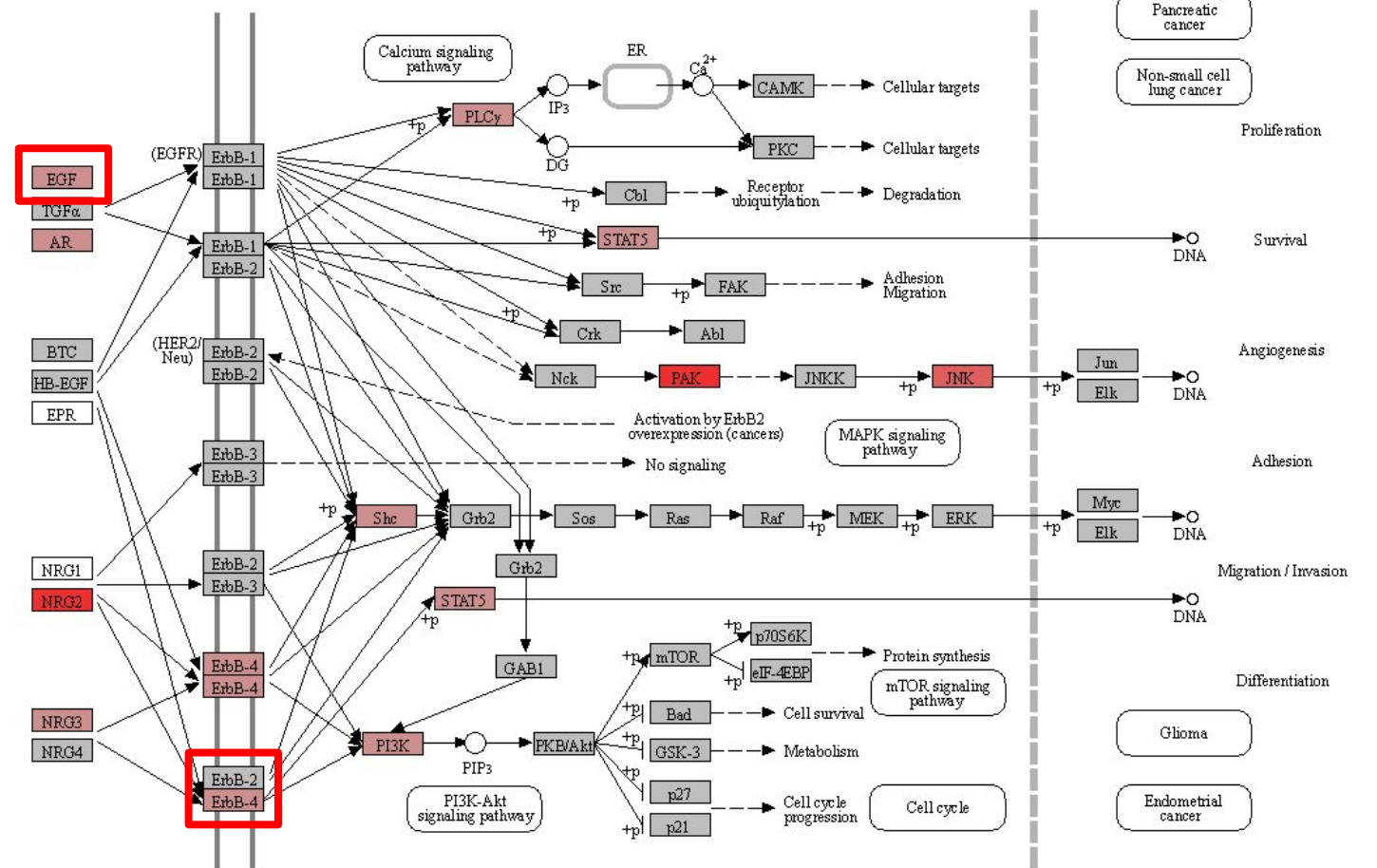


How can we use previously collected data to as motivation for new experimentation?

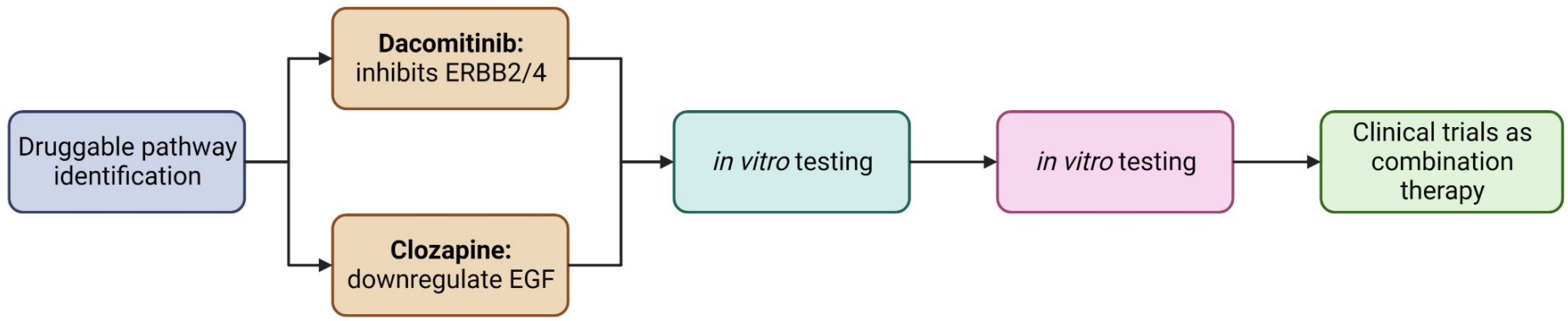
- Identify enriched pathways
- Narrow focus to one pathway
- Investigate the mechanisms of the chosen path



ERBB SIGNALING PATHWAY



Experimental Design



Advantages and Disadvantages of our Approach

Focus on a single pathway: ErbB

Easier to investigate potential mechanisms of progression

Other big data approaches to therapeutics discovery may be better

Principal component analysis on surface-level

Easy to visualize many dimensions in low-dimensional space

Analysis of PC's driving clustering could have yielded potential insights

Differential expression analysis done without knowledge of driver genes in prostate cancer

Allows us to approach data with an unbiased view

Experts may know genes/pathways that could be further investigated

References

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- Siegel, RL, Miller, KD, Wagle, NS, Jemal, A. Cancer statistics, 2023. CA Cancer J Clin. 2023; 73(1): 17-48. doi:10.3322/caac.21763\
- <https://www.selleckchem.com/products/pf299804.html>

Data and Code Availability: https://github.com/saipra003/mini-dream_nci_dcb_summer_2023



Questions?