

# Progression & Resistance

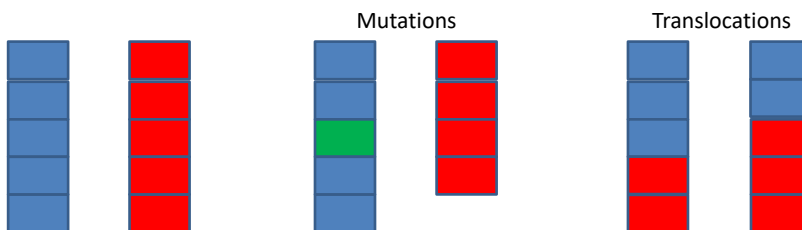
## Progression. Now What? Necessary Testing, Common Mechanisms of EGFR-Dependent Resistance, and Possible Treatment Strategies

Joshua Bauml, MD and Melina Marmarelis, MD, MSCE  
University of Pennsylvania, Philadelphia, PA



## Genetic Alterations Seen in Lung Cancer

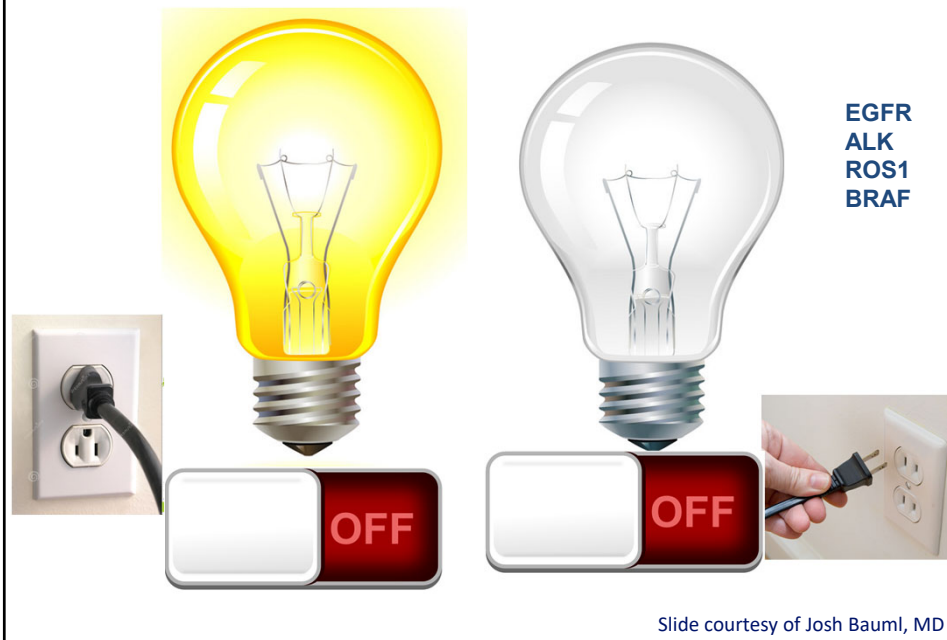
- Most are “somatic,” not “germline”
  - Not passed on through a family
- Generally seen everywhere throughout the tumor
  - Testing can be done on older tissue and mutations will still be there
- Most alterations seen are either a mutation or a translocation



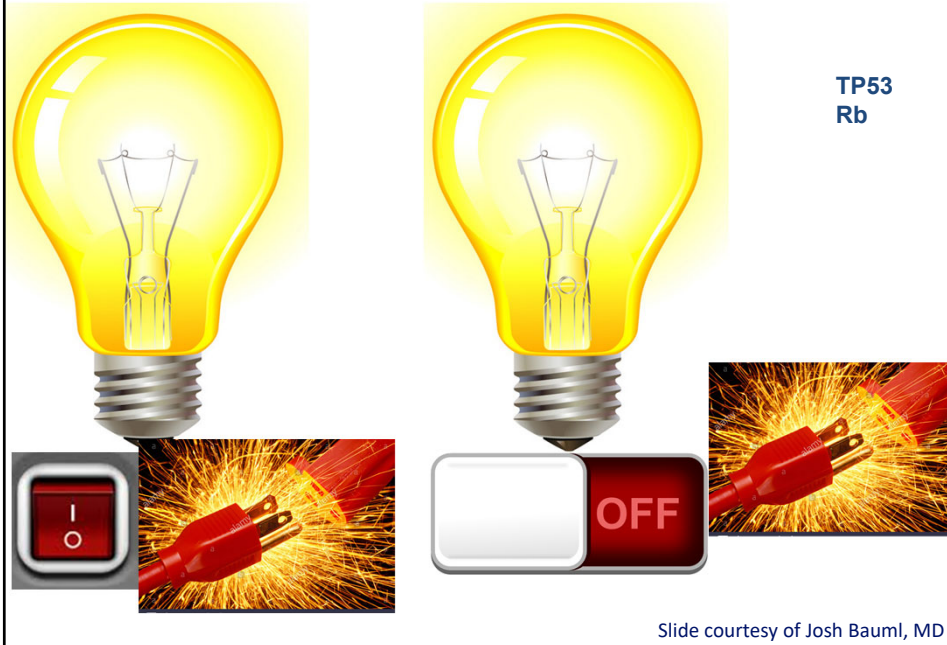
Slide courtesy of Josh Bauml, MD

# Progression & Resistance

## Oncogene “On switch” altered

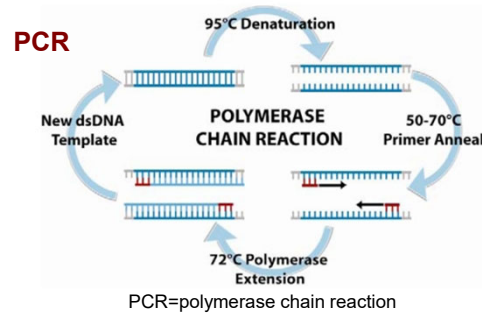


## Tumor suppressor “Off switch” altered

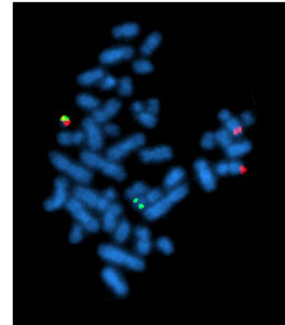


# Progression & Resistance

## How do we test for alterations?

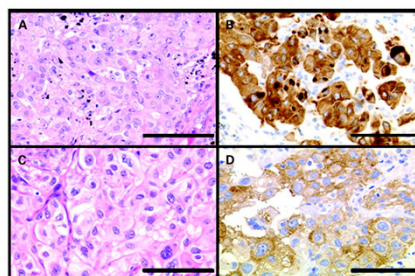


### FISH



FISH=fluorescent in situ hybridization

### IHC

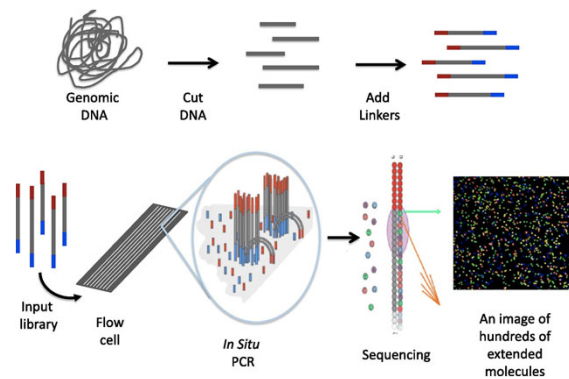


IHC=immunohistochemistry

Slide courtesy of Josh Bauml, MD

## Next Generation Sequencing

- ♦ **Older methods test for each gene one at a time**
  - Serial testing means we test for each gene, wait for the results and then test the next
  - Each test takes a little bit of tissue and a little bit of time
- ♦ **With NGS, problem is not tissue, but bioinformatics**



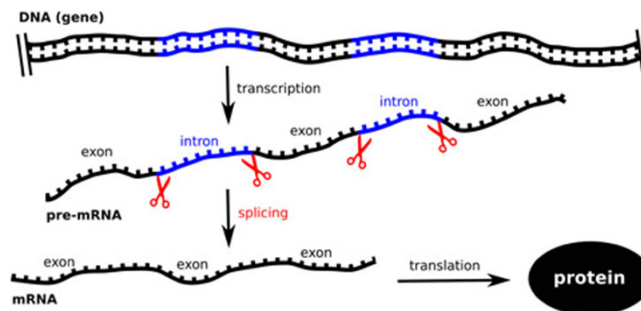
Slide courtesy of Josh Bauml, MD

EGFR RESISTERS ASK THE EXPERTS WEBINAR SERIES

# Progression & Resistance

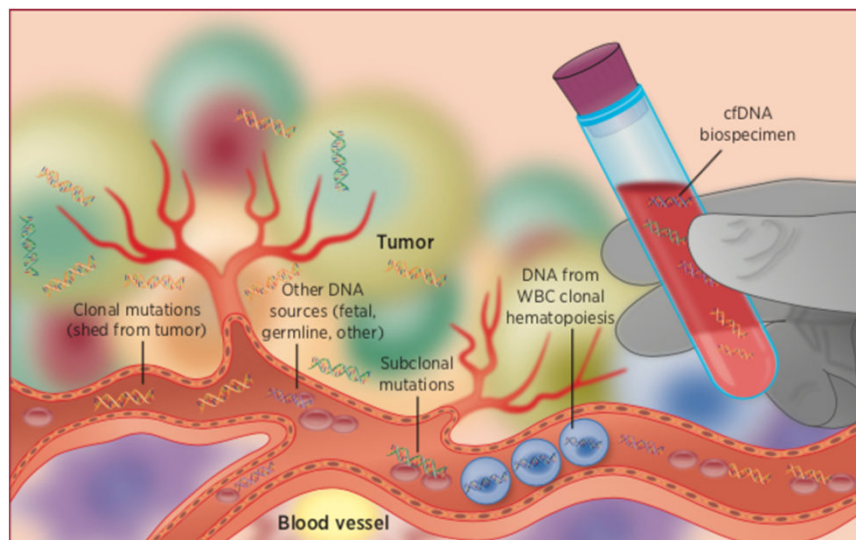
## DNA vs RNA Sequencing

- ◆ It is also important to know what type of NGS was done
- ◆ DNA based NGS can have difficulty identifying translocations
  - Introns can make this complex
- ◆ RNA based NGS (so called ARCHER assays) are better for translocations
  - Not done as frequently



Slide courtesy of Josh Bauml, MD

## What is a “liquid biopsy”?

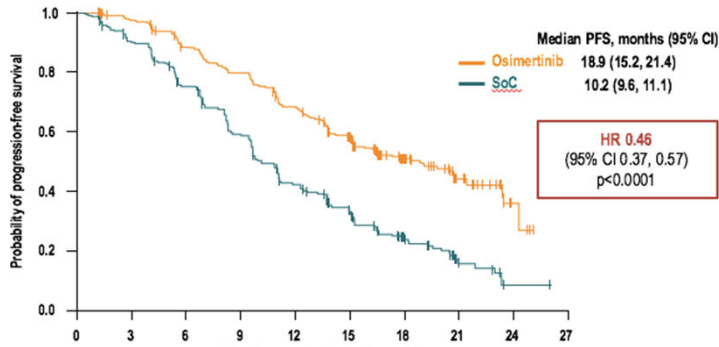


Slide courtesy of Josh Bauml, MD; Adapted from Bauml, et al. *Clin Cancer Res.* 2018

EGFR RESISTERS ASK THE EXPERTS WEBINAR SERIES

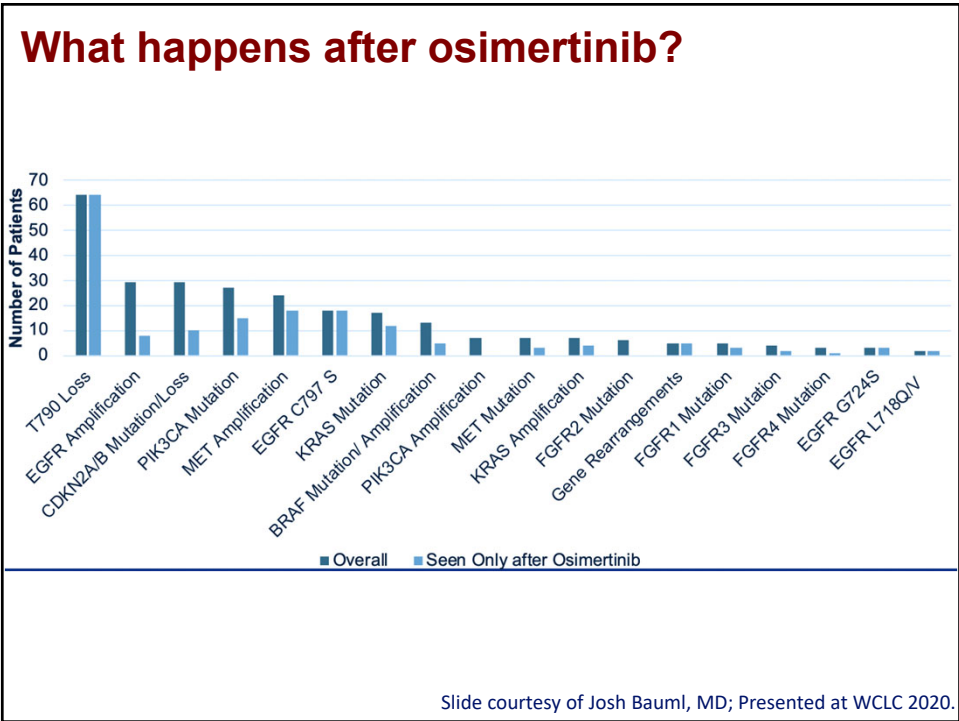
# Progression & Resistance

## FLAURA Results



	Osimertinib	SOC
Rash	25%	48%
Diarrhea	58%	57%
Stomatitis	29%	20%

Ramalingam S, et al. Presented at ESMO 2017.

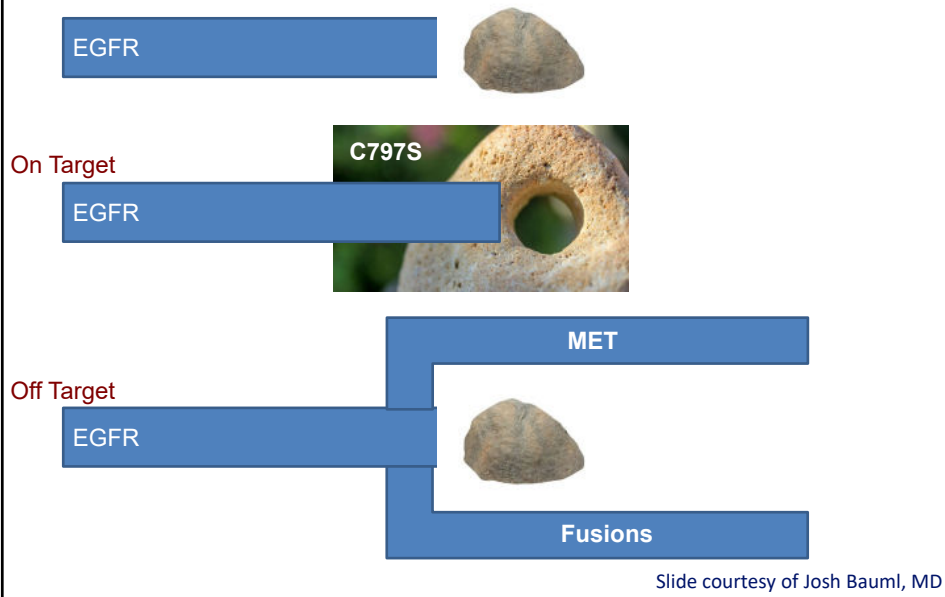


Slide courtesy of Josh Bauml, MD; Presented at WCLC 2020.



# Progression & Resistance

## What does “on target” vs “off target mean?”



## How do we measure changes in gene expression?

### Overexpression



### Gene Copy Number Change



### Amplification



Slide courtesy of Josh Bauml, MD