

Progression & Resistance

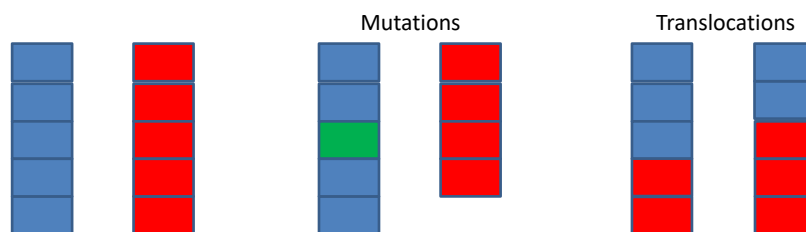
Progression. Now What? Necessary Testing, Common Mechanisms of EGFR-Dependent Resistance, and Possible Treatment Strategies

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Genetic Alterations Seen in Lung Cancer

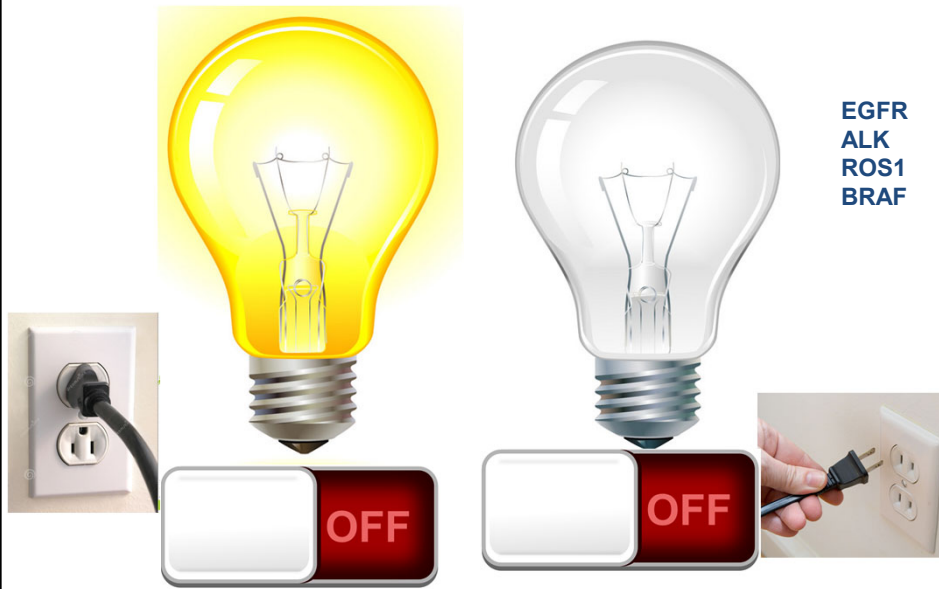
- Most are “somatic,” not “germline”
 - Not passed on through a family
- Generally seen everywhere throughout the tumor
 - Testing can be done on older tissue and mutations will still be there
- Most alterations seen are either a mutation or a translocation



Slide courtesy of Josh Bauml, MD

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Oncogene “On switch” altered



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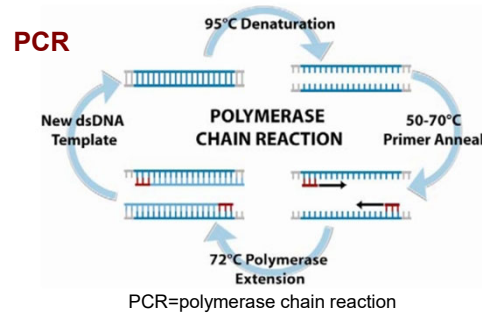
Tumor suppressor “Off switch” altered



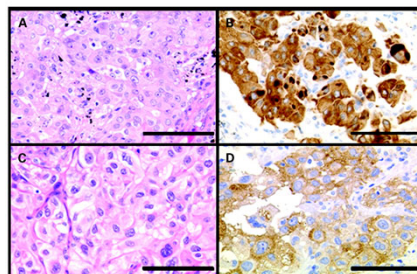
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How do we test for alterations?

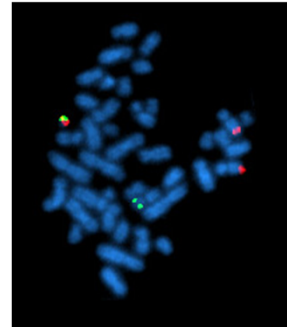


IHC



IHC=immunohistochemistry

FISH

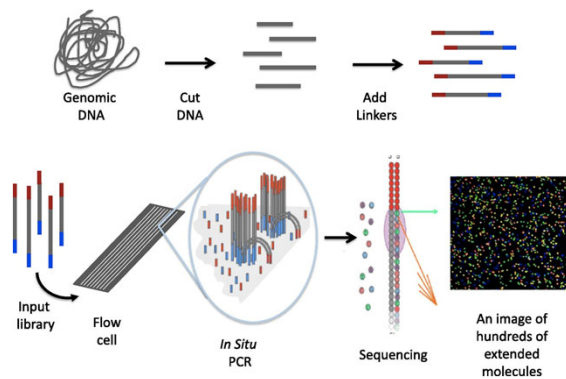


FISH=fluorescent in situ hybridization

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**

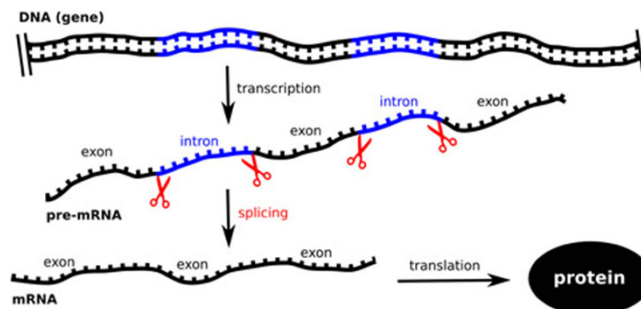


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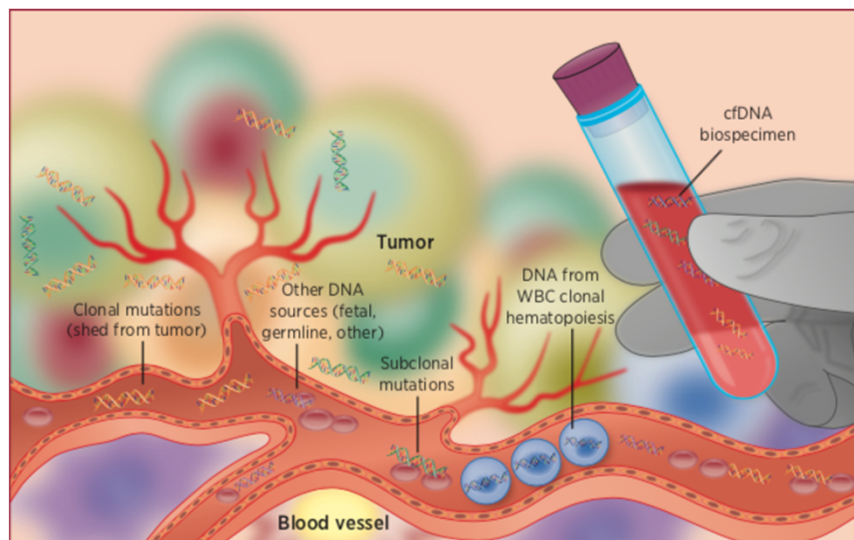
DNA vs RNA Sequencing

- ♦ 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”?

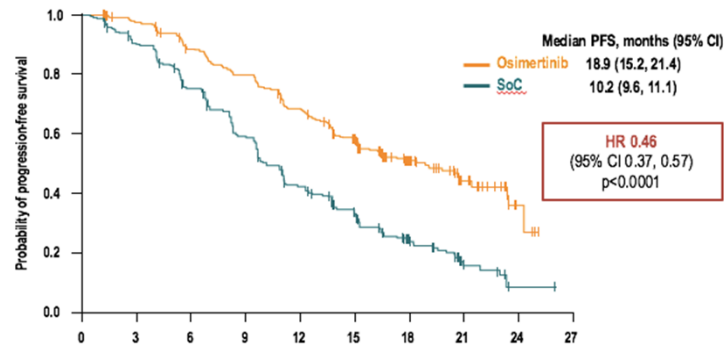


Slide courtesy of Josh Bauml, MD; Adapted from Bauml, et al. *Clin Cancer Res.* 2018

EGFR RESISTERS ASK THE EXPERTS WEBINAR SERIES

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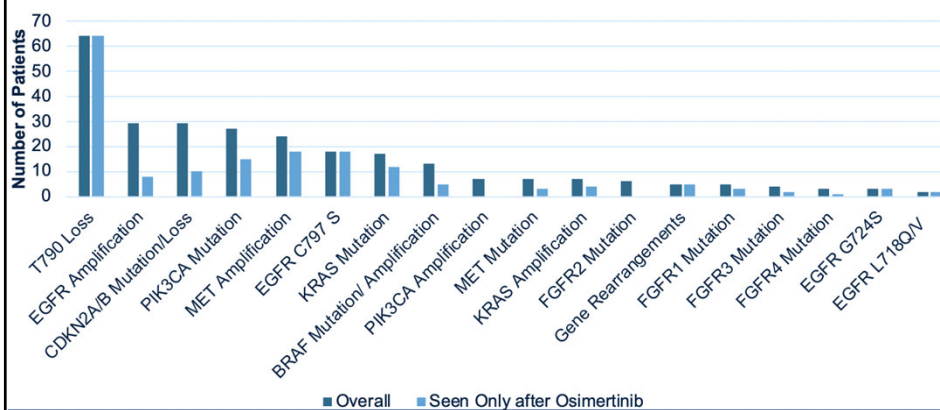
FLAURA Results



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

Ramalingam S, et al. Presented at ESMO 2017.

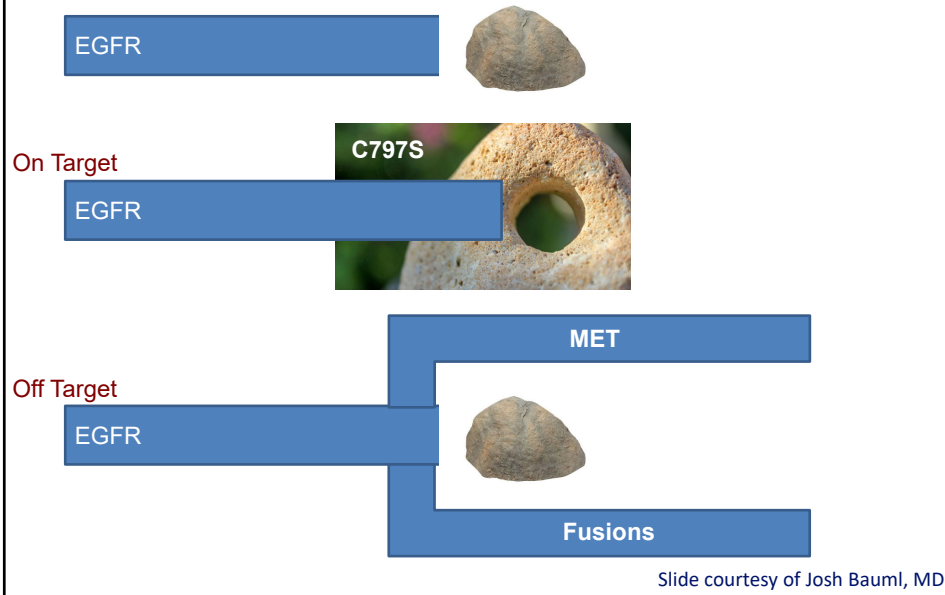
What happens after osimertinib?



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



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