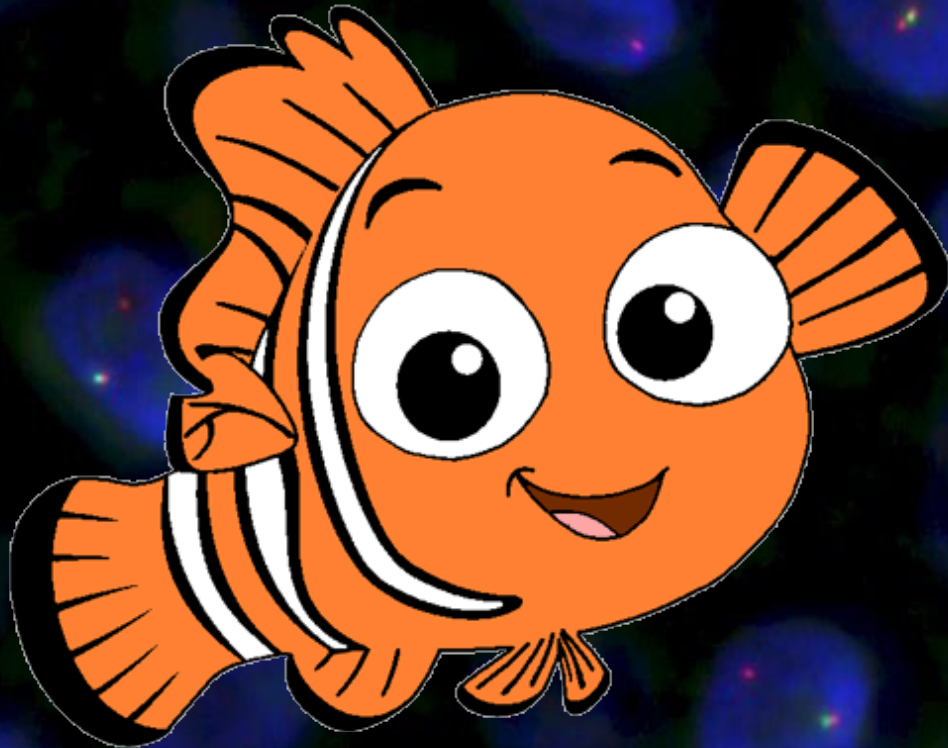


Non-Small Cell Lung Cancer FISH PANEL



Peter Mac
Peter MacCallum Cancer Centre
Victoria Australia

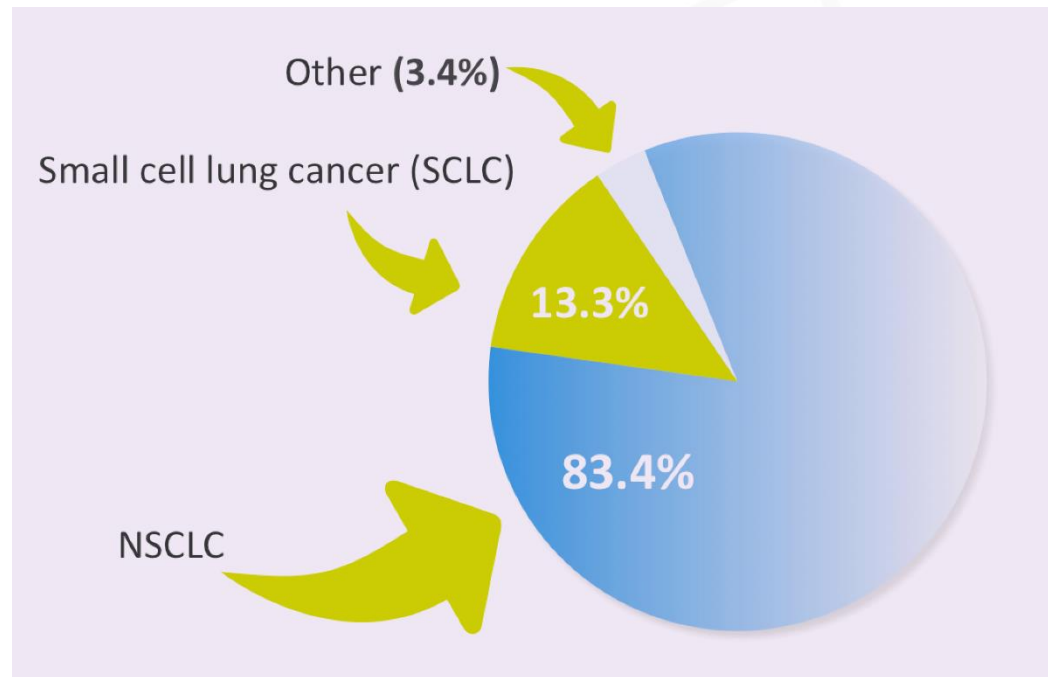
MEGHAN LEO

Overview

- Lung Cancer
- NSCLC Mutations
- FISH
- FISH Procedure
- Break-apart Probes
- ALK
- ROS
- RET
- Amplification Probes
- MET

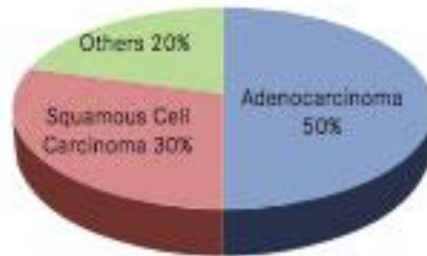
NON SMALL CELL LUNG CANCER (NSCLC)

- Fifth most common cancer
- Highest rate of cancer deaths
- Low survival rate

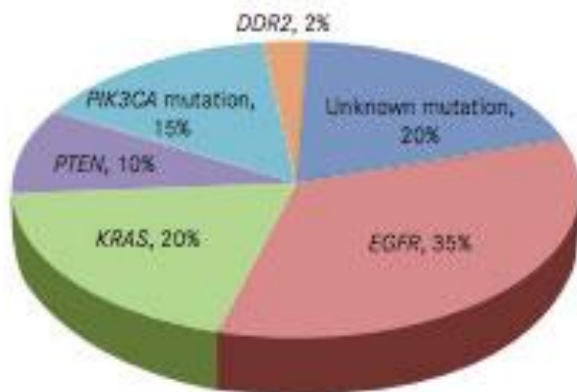


NSCLC Mutations

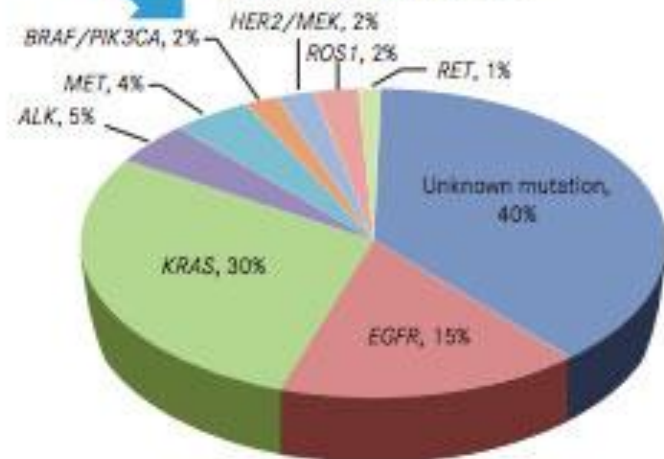
NSCLC by Histology



Squamous Cell Carcinoma

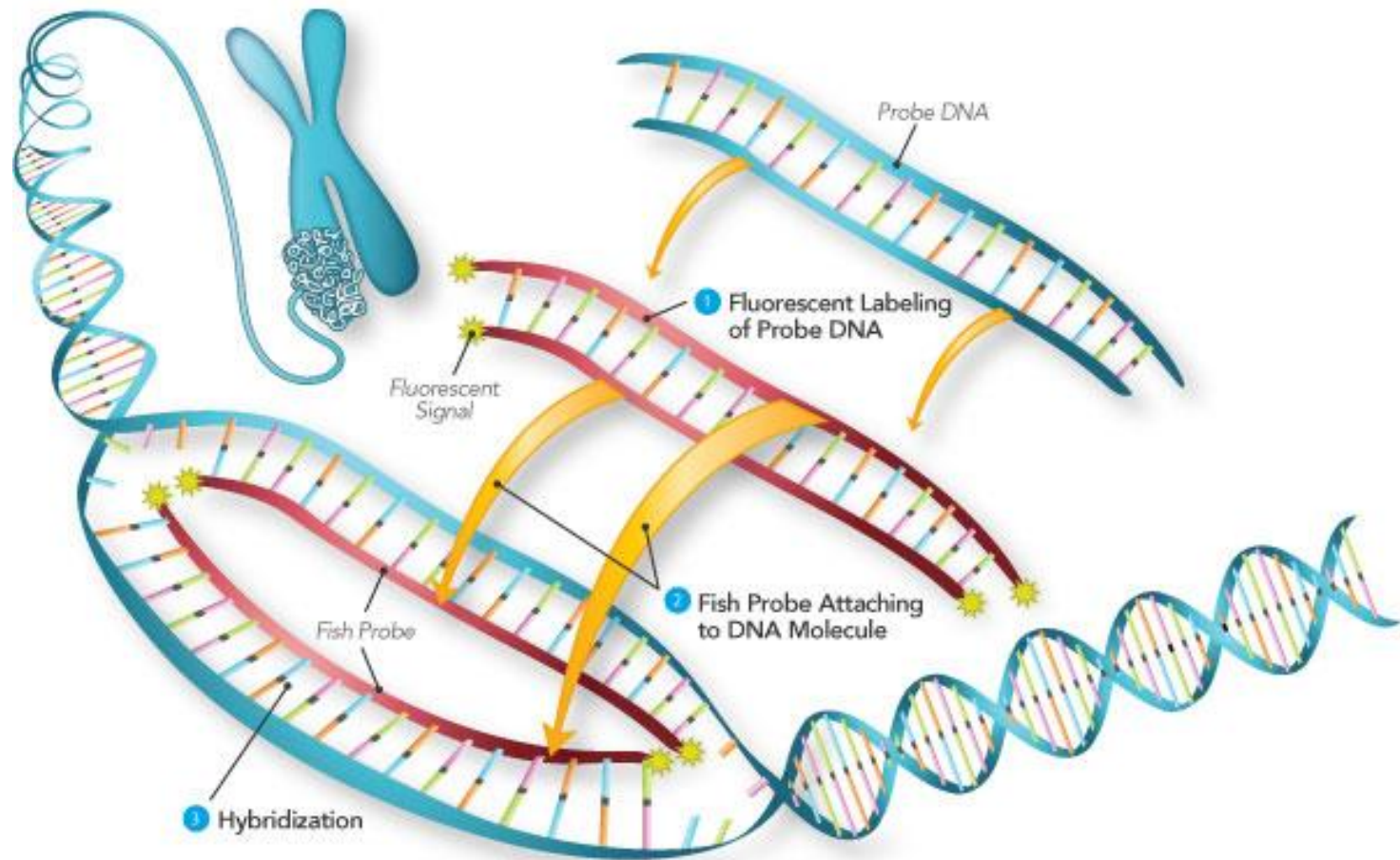


Adenocarcinoma

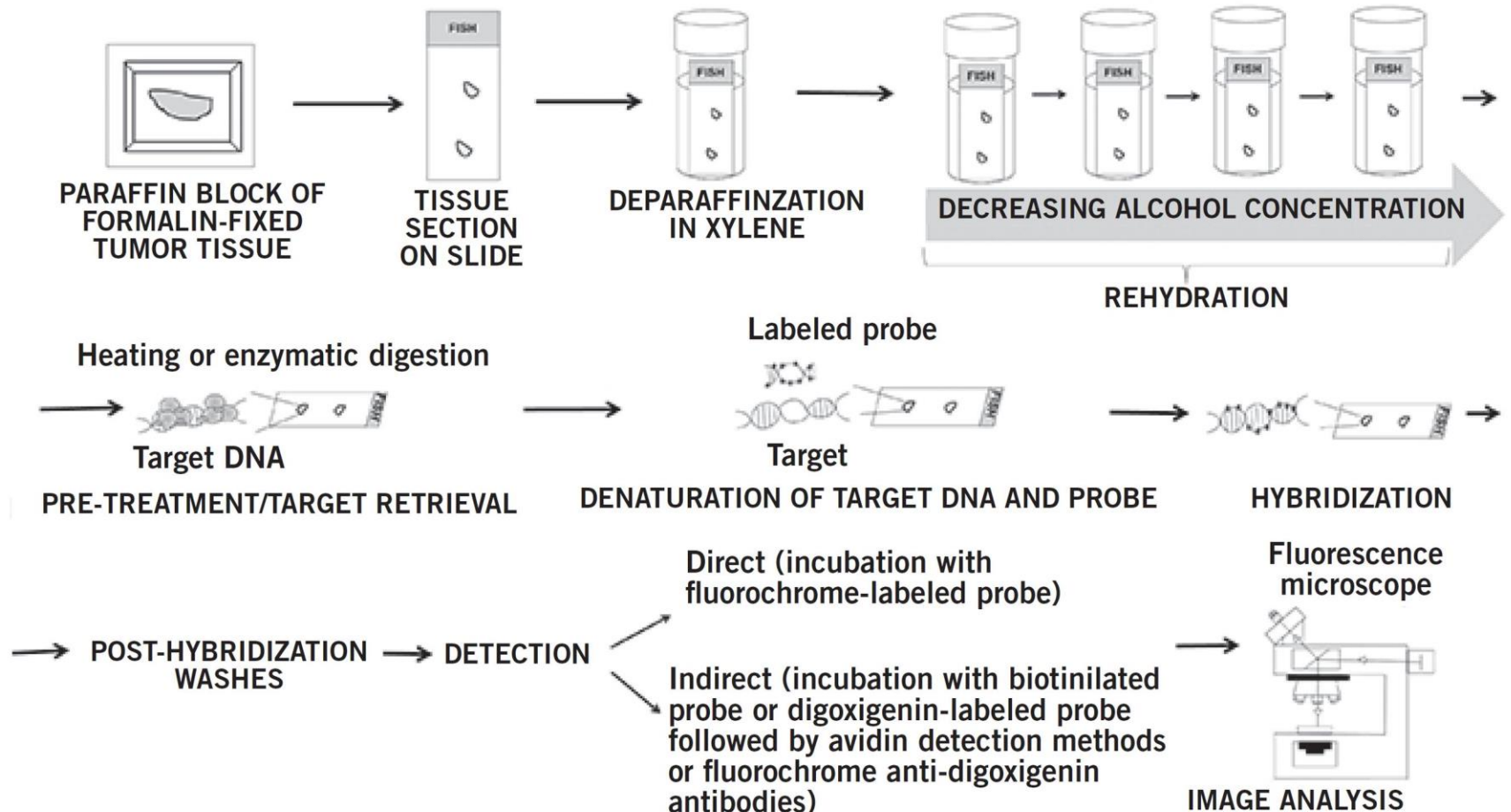


What is FISH?

- Locates specific DNA sequences

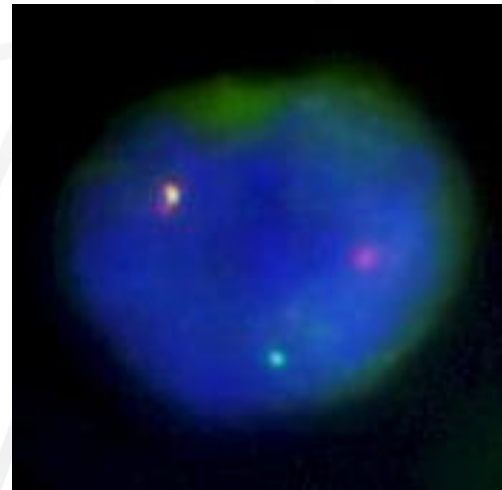
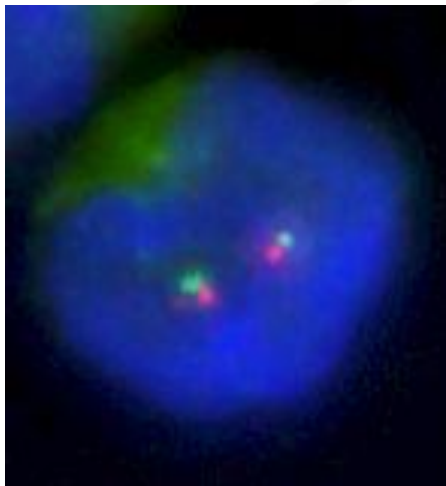
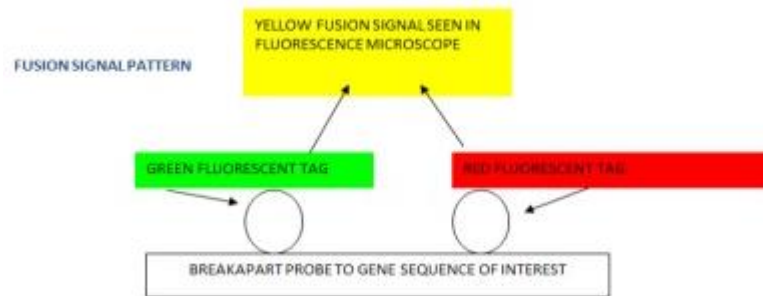


FISH Procedure



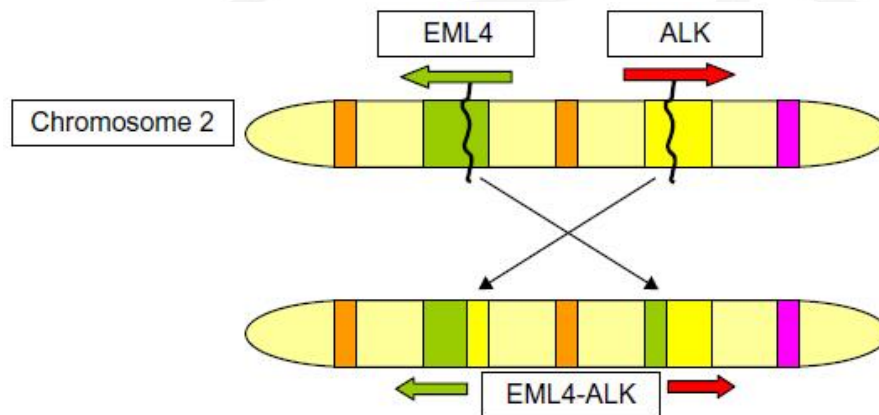
Break-apart Probes

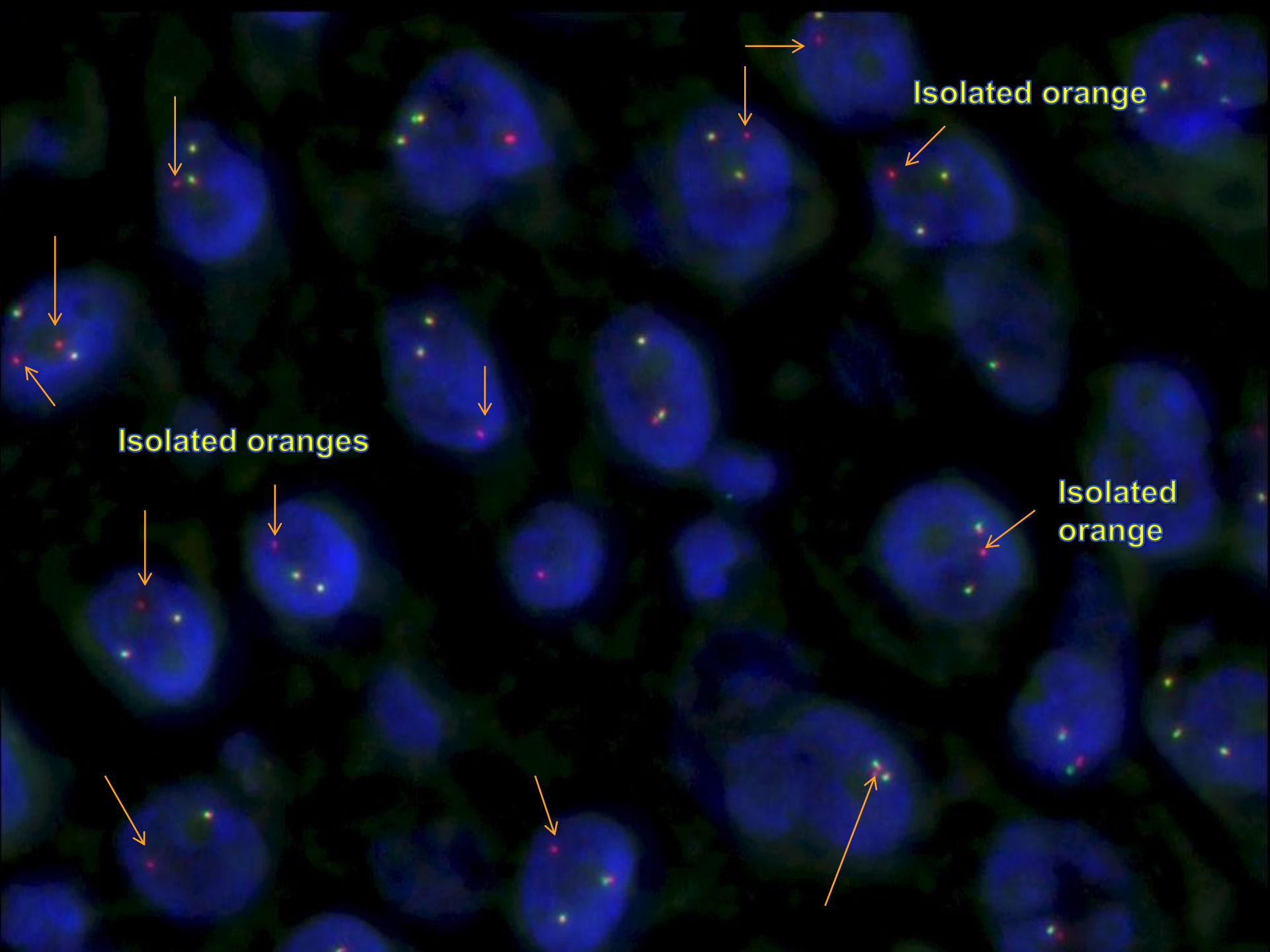
- Also known as translocation probes
- *ALK*, *ROS1* & *MET*



ALK

- Anaplastic lymphoma kinase
- Mutation – EML4-ALK fusion
- <40yrs, non-smoker, female, East Asian
- Alectinib & Crizotinib – longer survival time
- FISH positive
 - Breaks ≥ 2 signal widths
 - Isolated orange signal(s) with fused signal
 - Above cut-off threshold

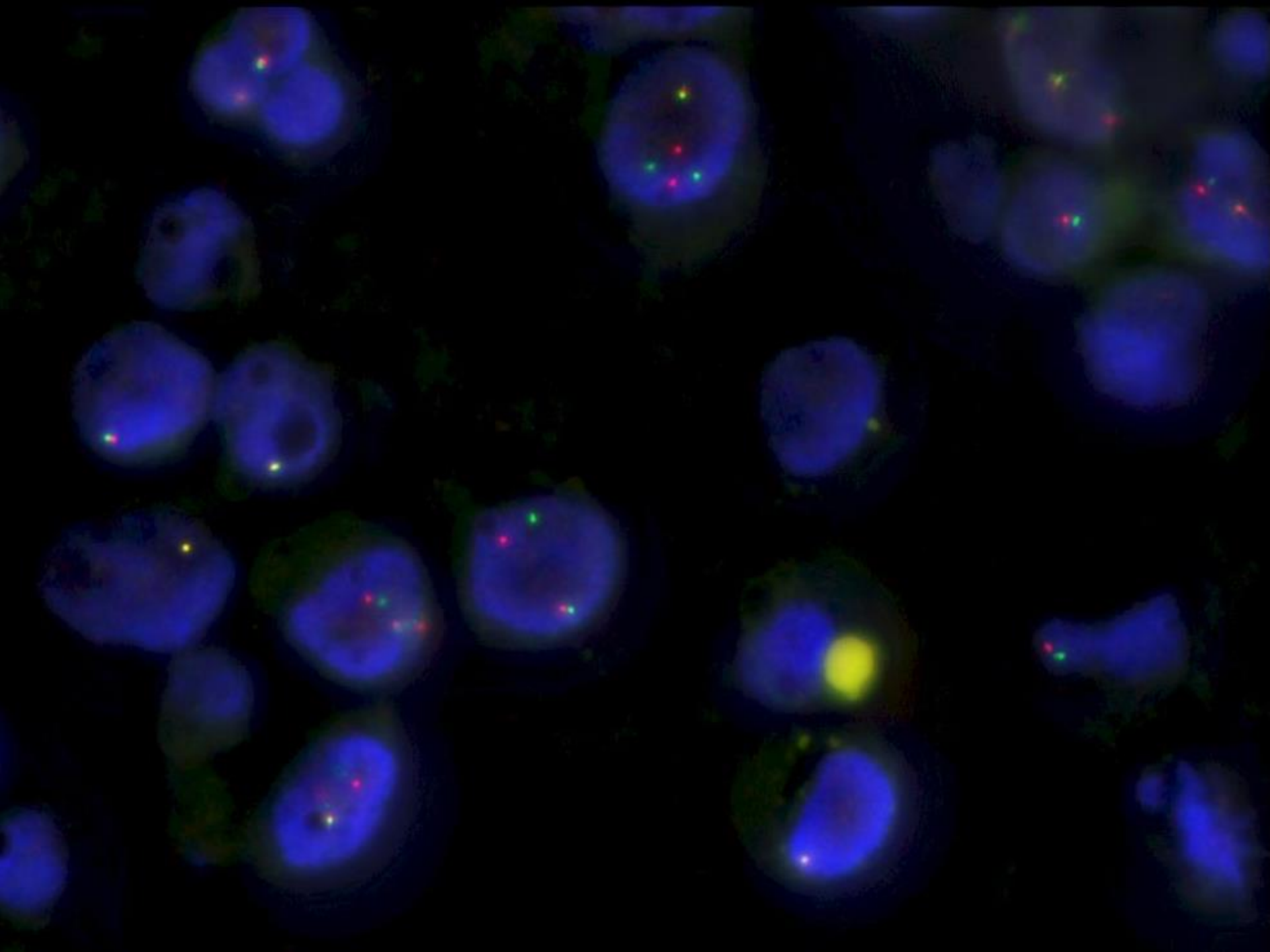


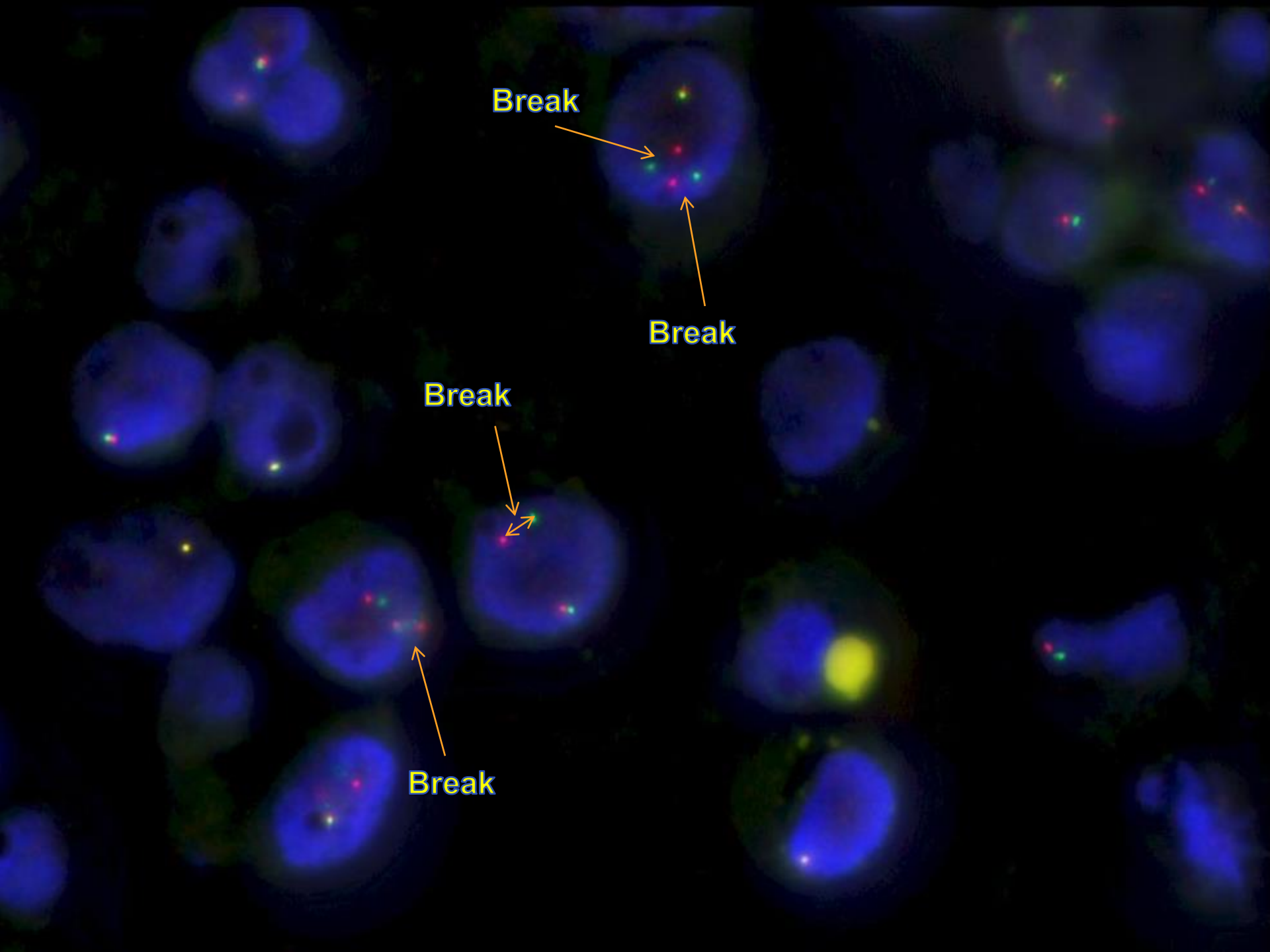


Isolated orange

Isolated orange

Isolated oranges





ROS1

- Receptor tyrosine kinase activity
- Driver mutation
- Crizotinib – great response
- FISH positive
 - Breaks ≥ 1 signal width
 - Isolated green signal(s) with fused signal
 - Above cut-off threshold

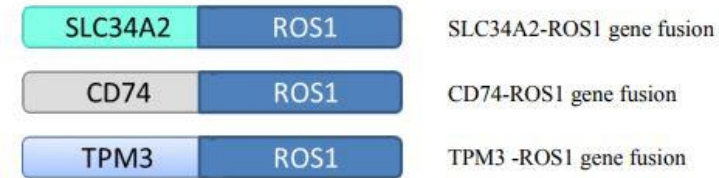
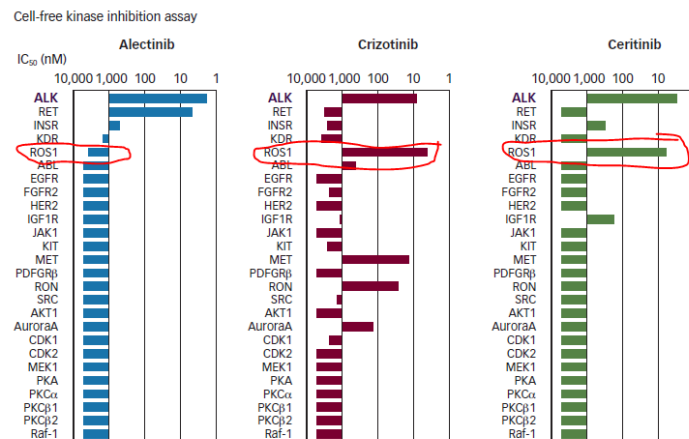
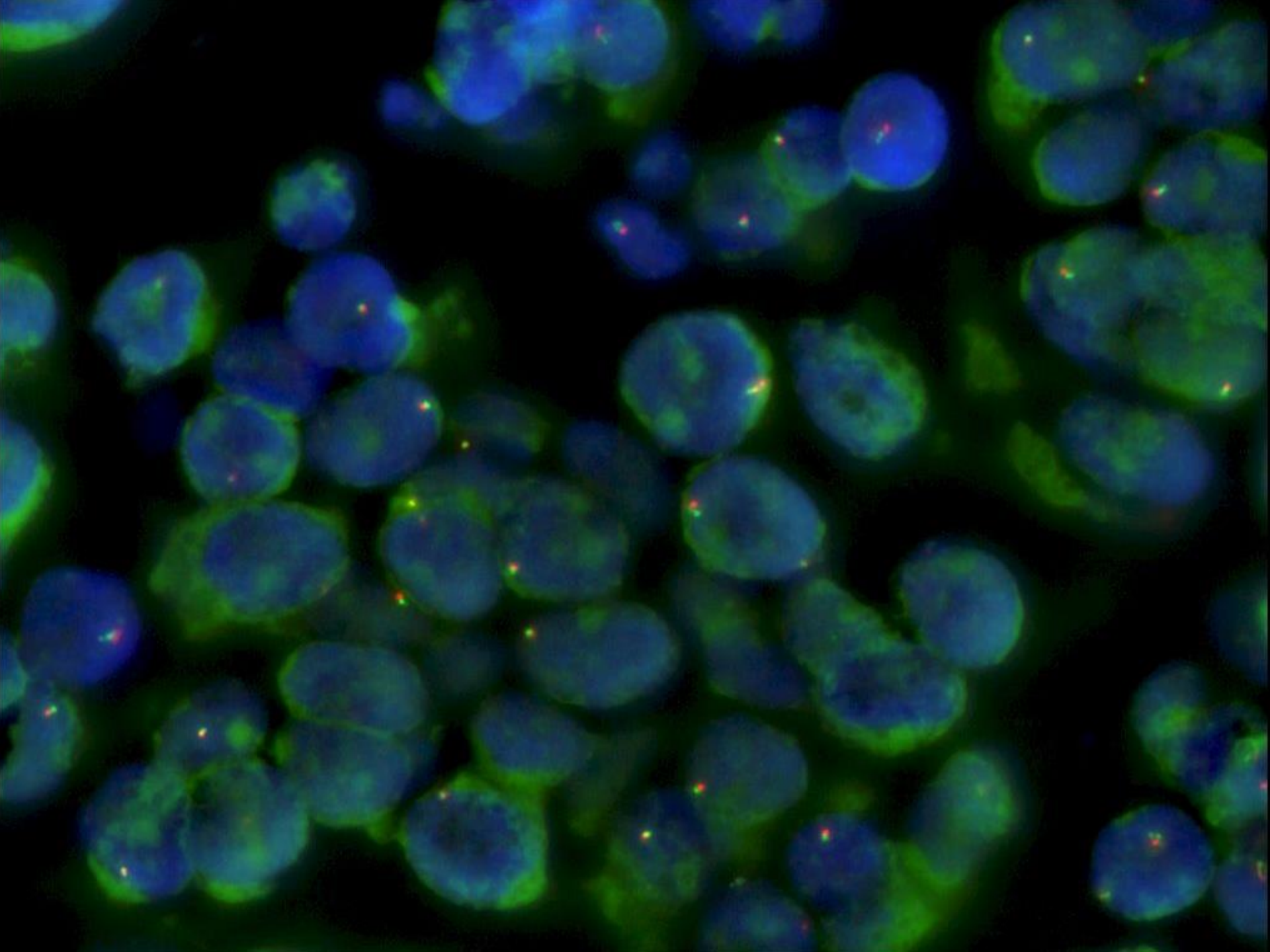
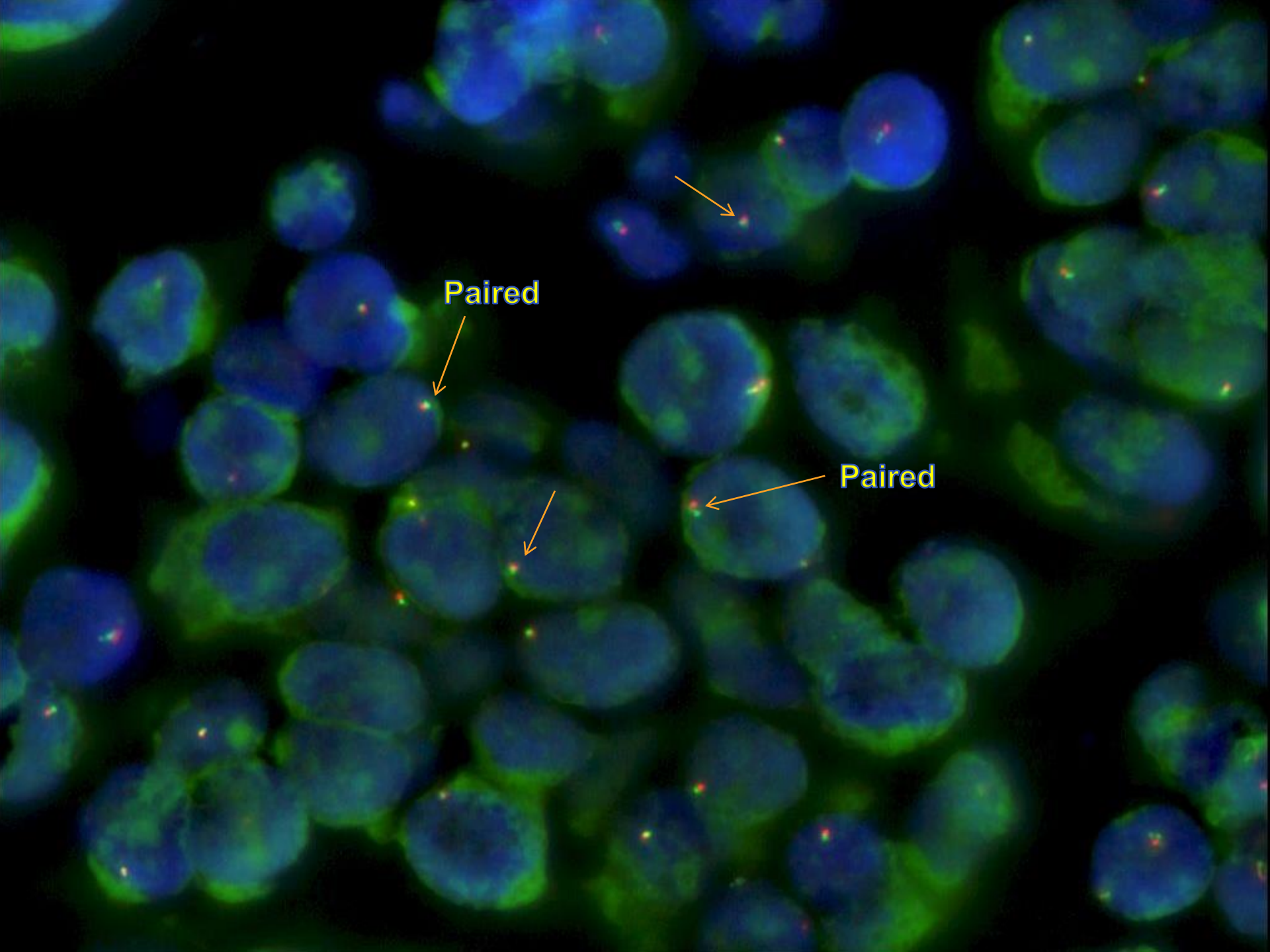


Figure 1: Kinase Inhibitor Selectivity Assessment of Currently Approved ALK Inhibitors



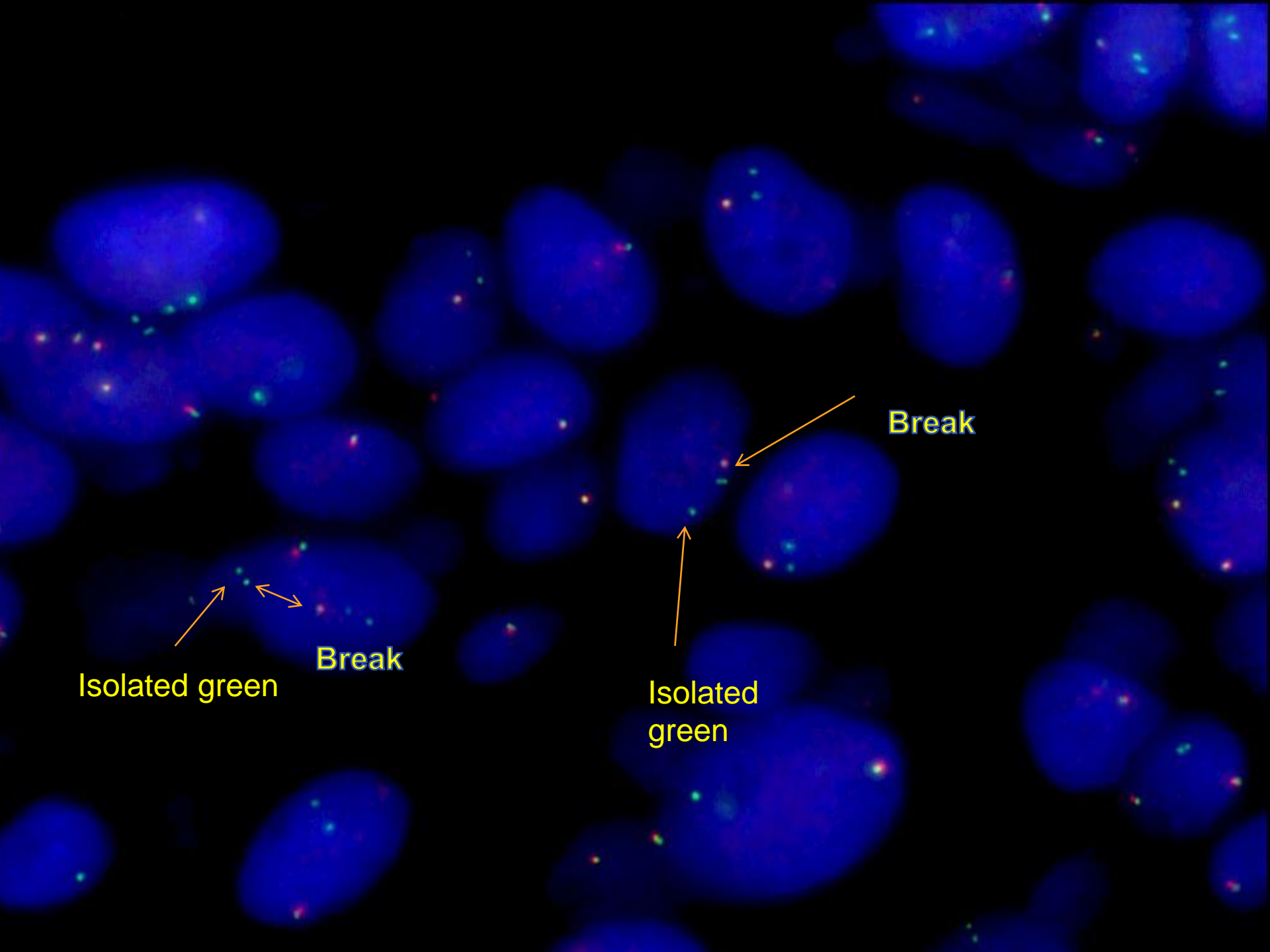
Data source: Sakamoto et al., 2011.⁴⁹



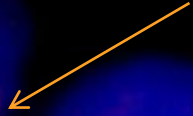


Paired

Paired



Break



Isolated green



Break

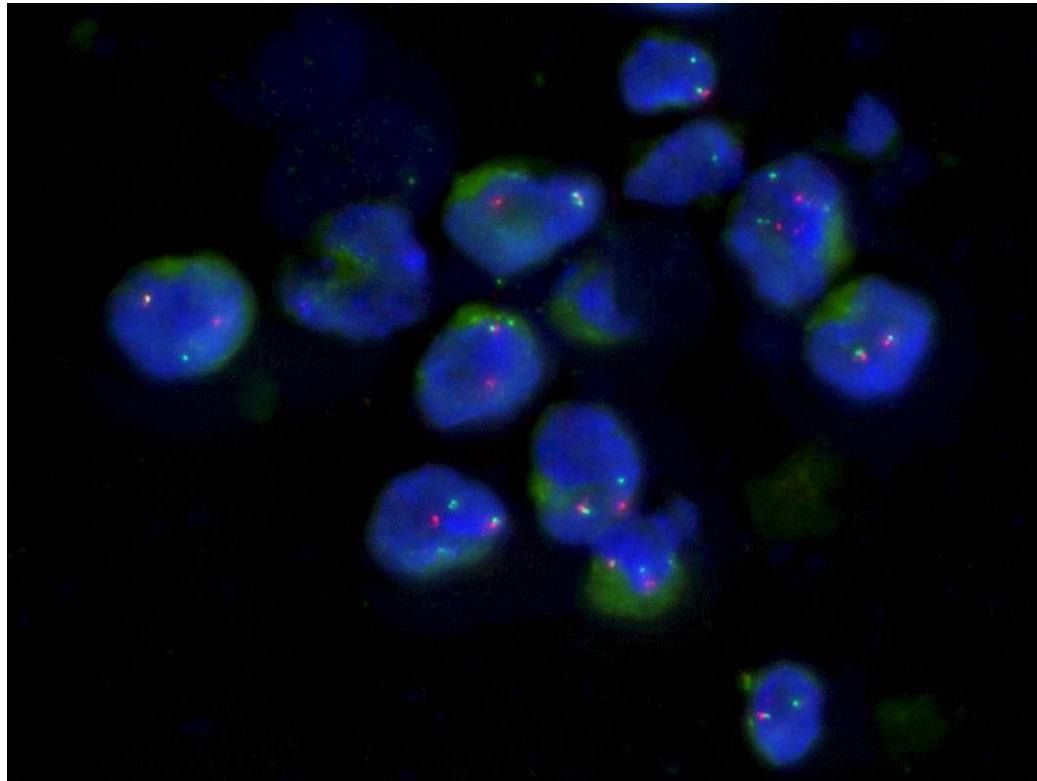


Isolated green



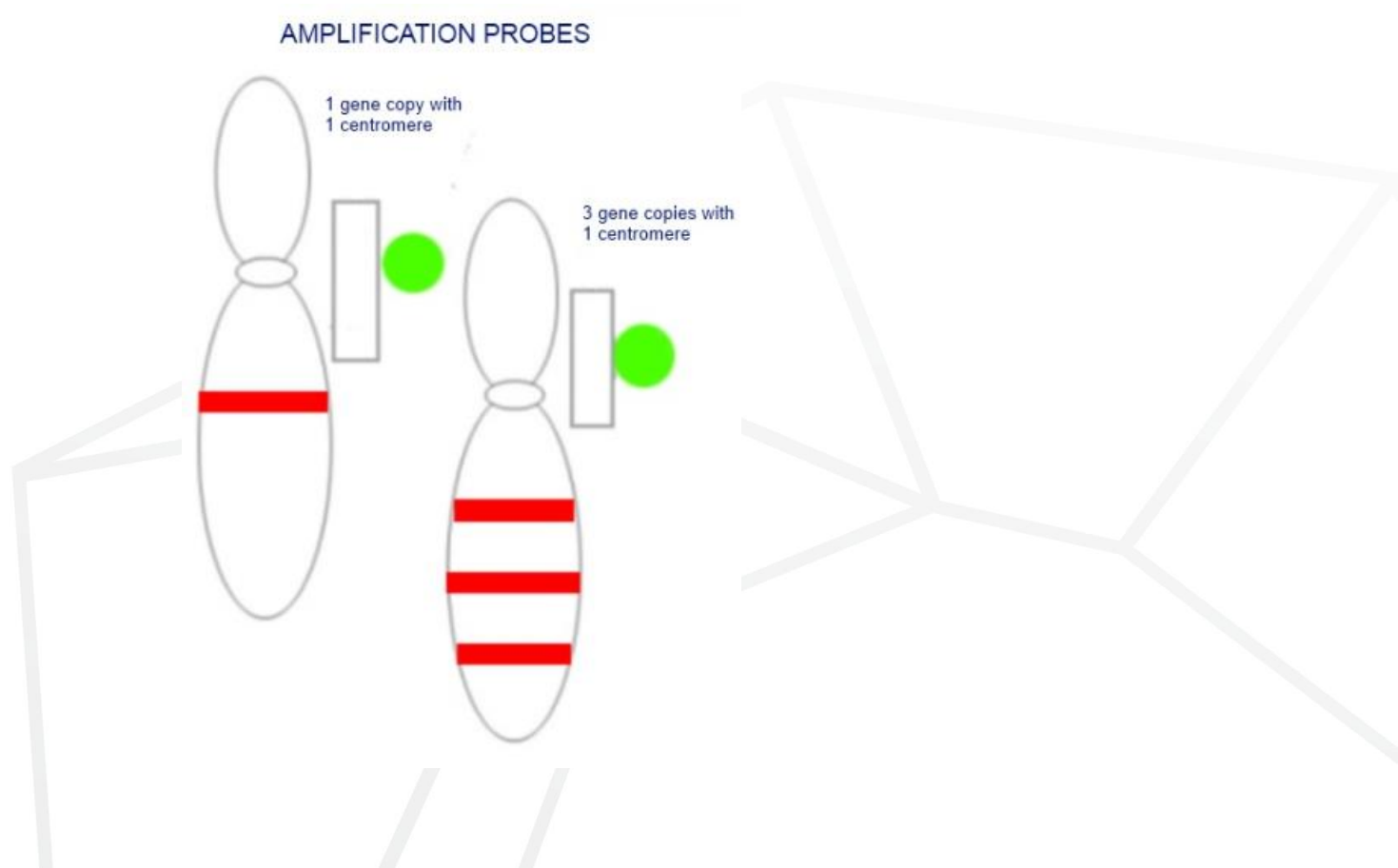
RET

- Shown to fuse with 8 different genes
- Clinical trials underway
- FISH positive
 - Breaks ≥ 1 signal width
 - Above cut-off threshold



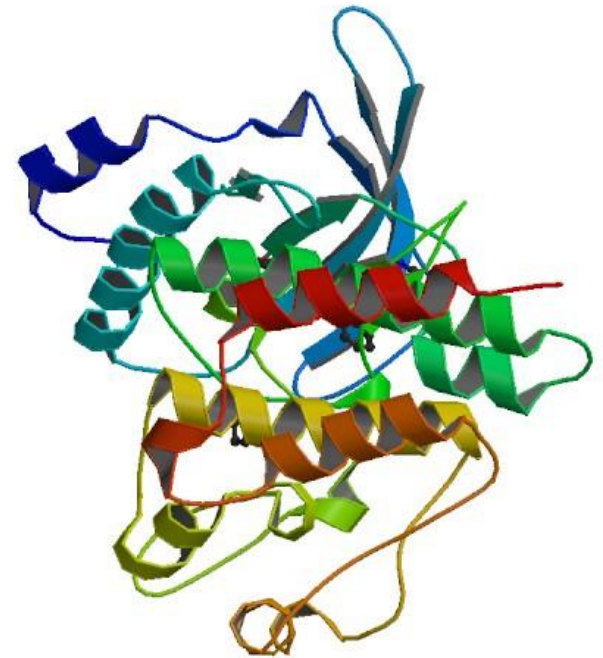
Amplification Probes

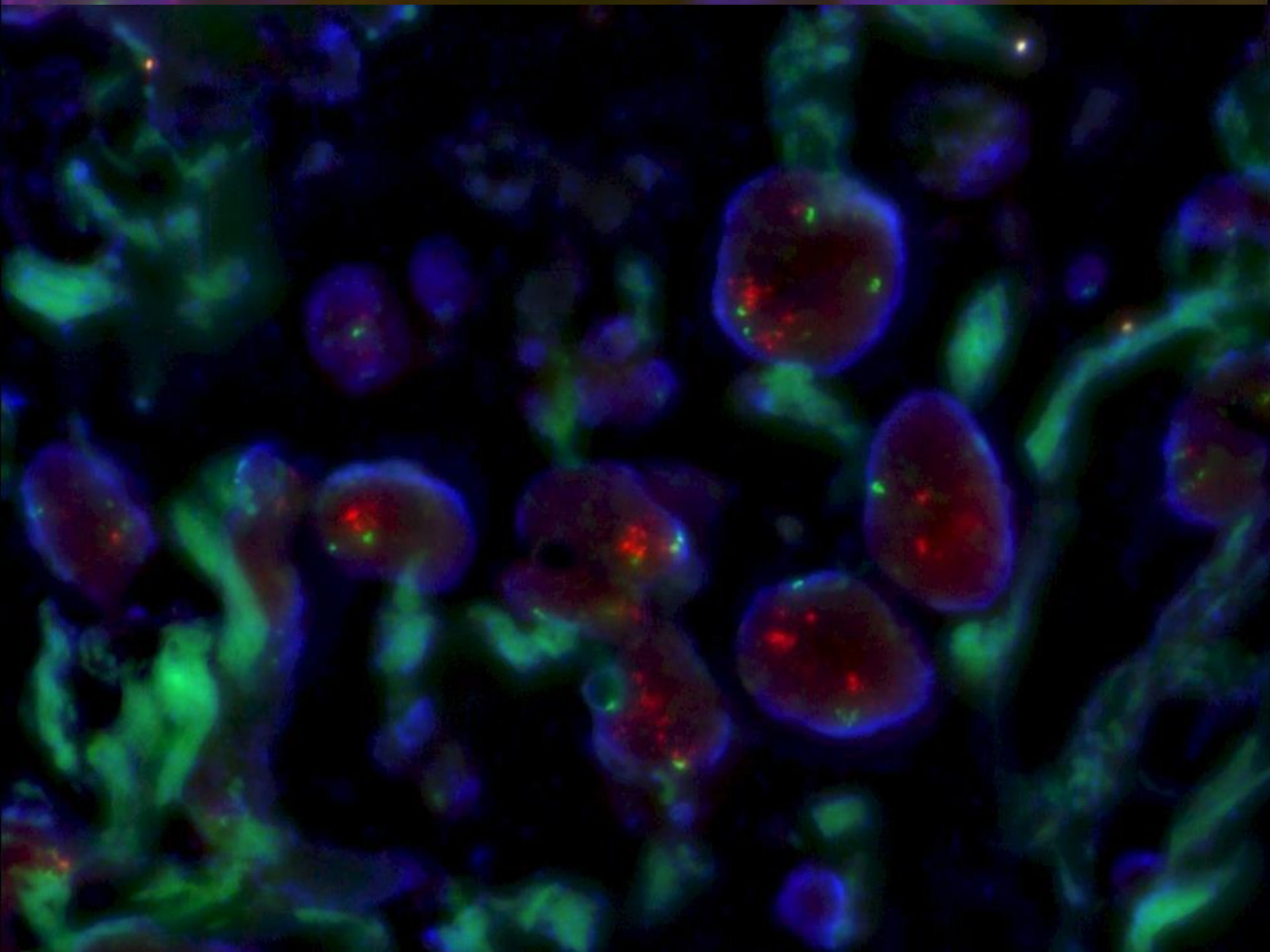
- Locus-specific probes
- Amplification determined by ratio and/or copy number




MET

- Tyrosine-protein kinases Met or hepatocyte growth factor receptor (HGFR)
- Proto-oncogene
- Amplification associated with poor prognosis
- Crizotinib
- FISH:
 - Ratio ≥ 2
 - Copy number per cell ≥ 5





Acknowledgements

- Toni-Marie Rogers
 - Vicky Nastevski
 - Angela Kam
 - Dr. Owen Prall
 - Dr. Christine Khoo
 - Dr. Christopher Angel
 - NHC Organising Committee
 - NHC Attendees
- 
- An abstract graphic in the bottom right corner consisting of several light gray lines forming a series of interconnected triangles and polygons, creating a geometric pattern.

REFERENCES

- Rogers *et al.*, Comparison of methods in the detection of *ALK* and *ROS1* rearrangements in lung cancer. *J Thorac Oncol* 2015; 10:611-618
- Takeuchi *et al.*, *RET*, *ROS1* and *ALK* fusions in lung cancer. *Nat Med* 2012;3:378-381
- Beau-Faller *et al.*, *MET* Gene Copy Number in Non-small Cell Lung cancer: Molecular Analysis in a Targeted Tyrosine Kinase Inhibitor Naïve Cohort. *J Thorac Oncol* 2008; 4:331-339

IT'S NOT GOODBYE



IT'S SEE YOU LATER

memegenerator.net