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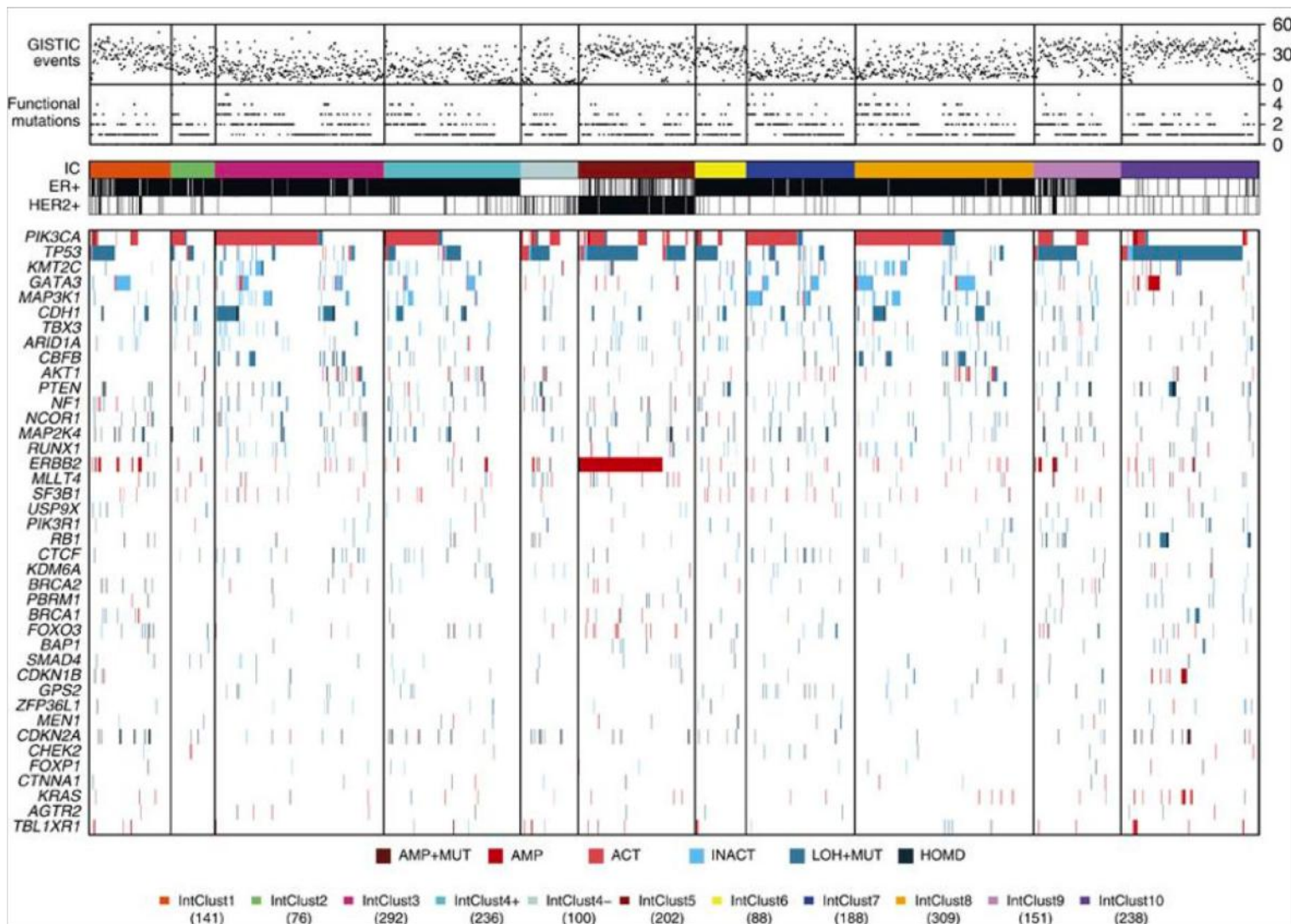


**CAMBRIDGE**  
CANCER GENOMICS

October 2018



# Presenting dense information in an easily readable way



Article | [OPEN](#) | Published: 10 May 2016

### The somatic mutation profiles of 2,433 breast cancers refine their genomic and transcriptomic landscapes

[Bernard Pereira](#), [Suet-Feung Chin](#) [...] [Carlos Caldas](#)

*Nature Communications* **7**, Article number: 11479 (2016) | [Download Citation](#)

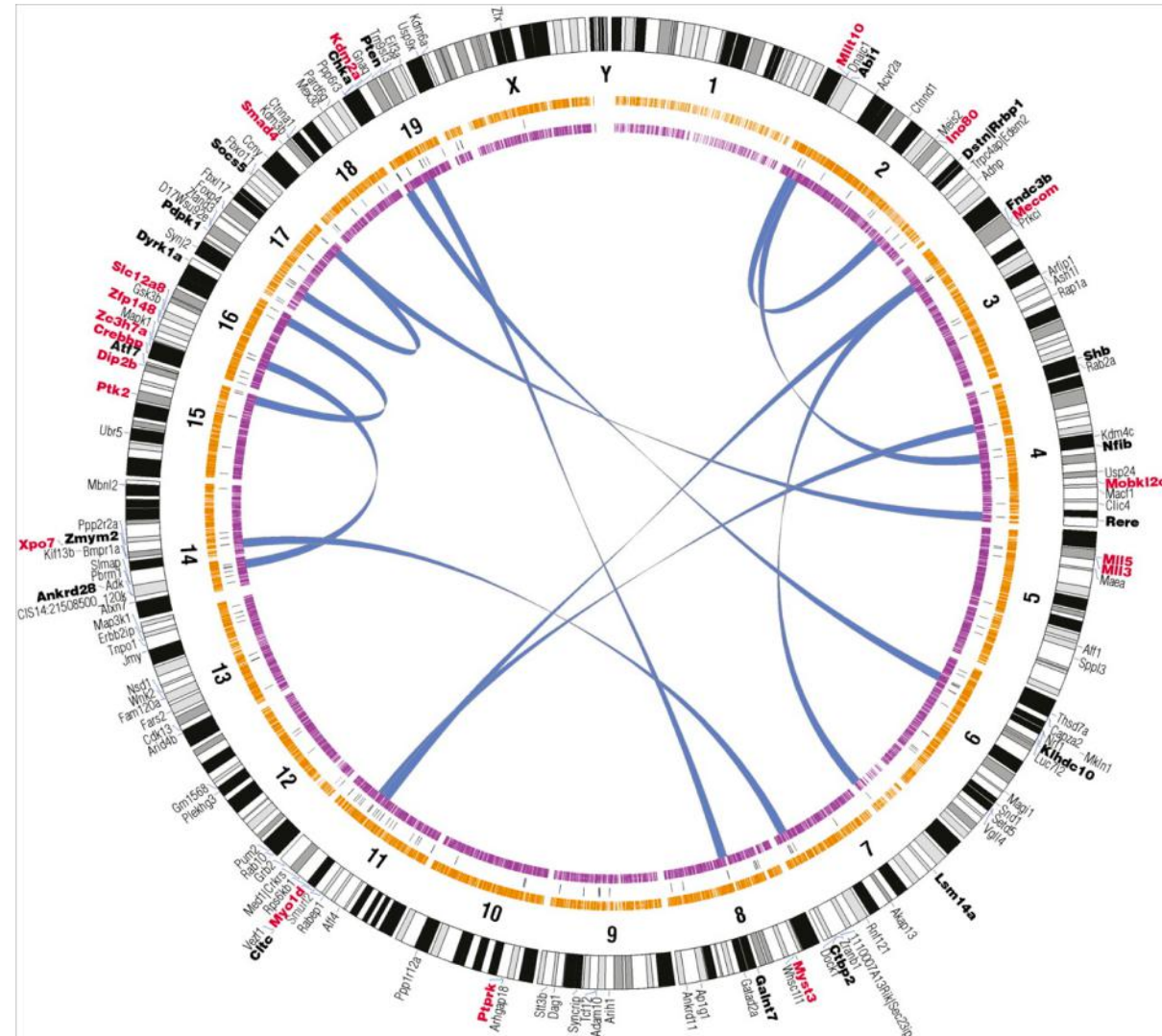
*Tumours with both mutation and copy number data available (n=2,021) are grouped by IntClust along the x-axis, and alterations in the 40 Mut-driver genes are indicated by coloured bars. For each tumour, the number of functional mutations in Mut-driver genes and the number of recurrent CNAs (as defined by GISTIC2) events are also shown. AMP, amplification; ACT, activating mutation; HOMD, homozygous deletion; INACT, inactivating mutation; LOH+MUT, mutation and hemizygous deletion.*

# Going high-level

## ***Sleeping Beauty* mutagenesis reveals cooperating mutations and pathways in pancreatic adenocarcinoma**

Karen M. Mann, Jerrold M. Ward, Christopher Chin Kuan Yew, Anne Kovovich, David W. Dawson, Michael A. Black, Benjamin T. Brett, Todd E. Sheetz, Adam J. Dupuy, Australian Pancreatic Cancer Genome Initiative, David K. Chang, Andrew V. Biankin, Nicola Waddell, Karin S. Kassahn, Sean M. Grimmond, Alistair G. Rust, David J. Adams, Nancy A. Jenkins, and Neal G. Copeland

*Circos map of pancreatic cancer candidate cancer genes identified by the GKC method. Transposon insertions in the plus (orange lines) and minus (purple lines) strands show genome-wide coverage of mutagenesis. GKC CCGs are illustrated on the outer perimeter of the plot with their exact location denoted by a black line. Genes listed in red are mutated in human pancreatic cancer. The blue lines in the center connect bolded GKC CCGs that significantly co-occur in tumors (Fisher exact test,  $P < 0.0003$ ).*





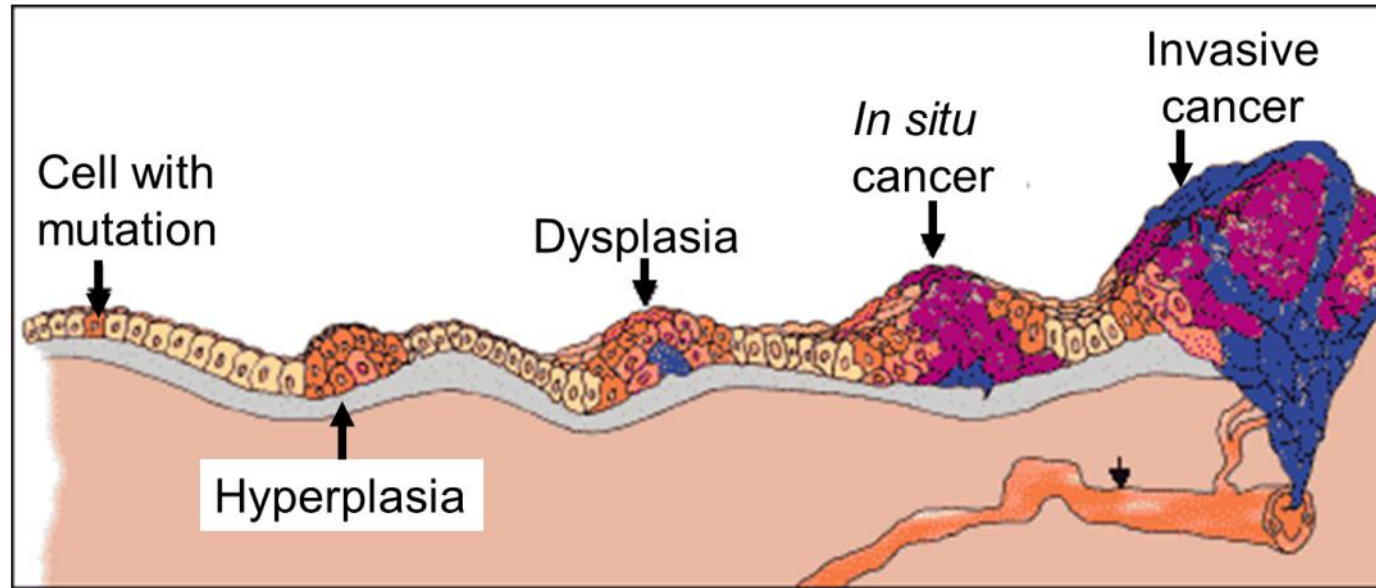


# Oncologists typically have 10mins to prep for a 15-30min consultation

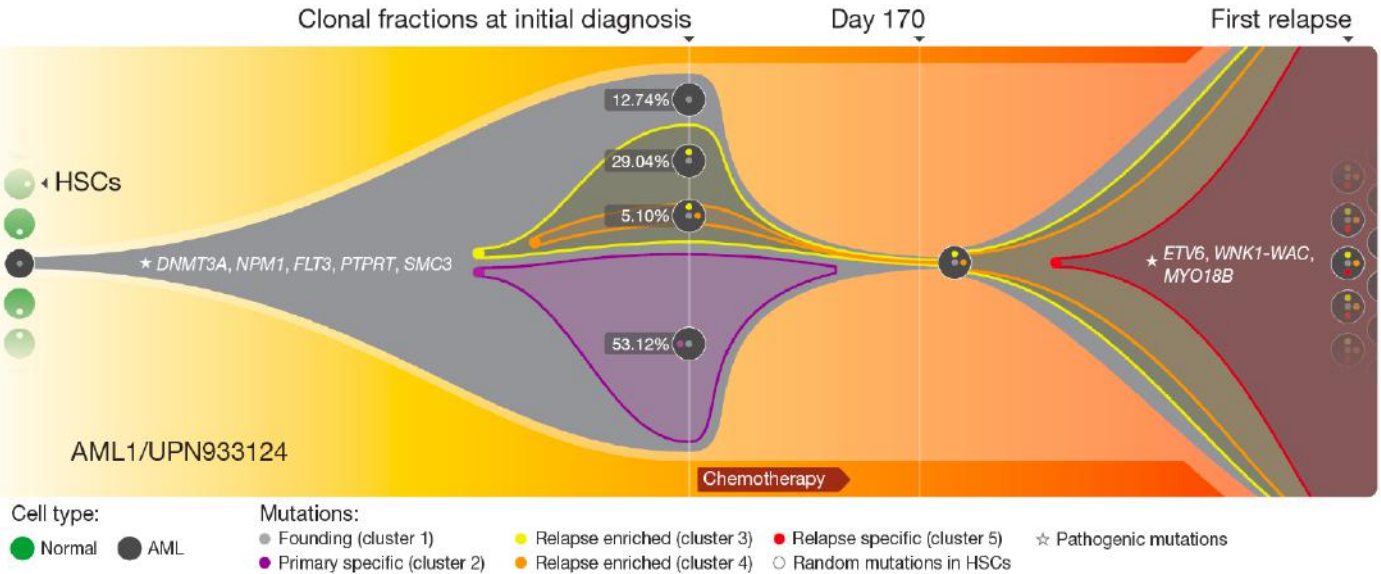
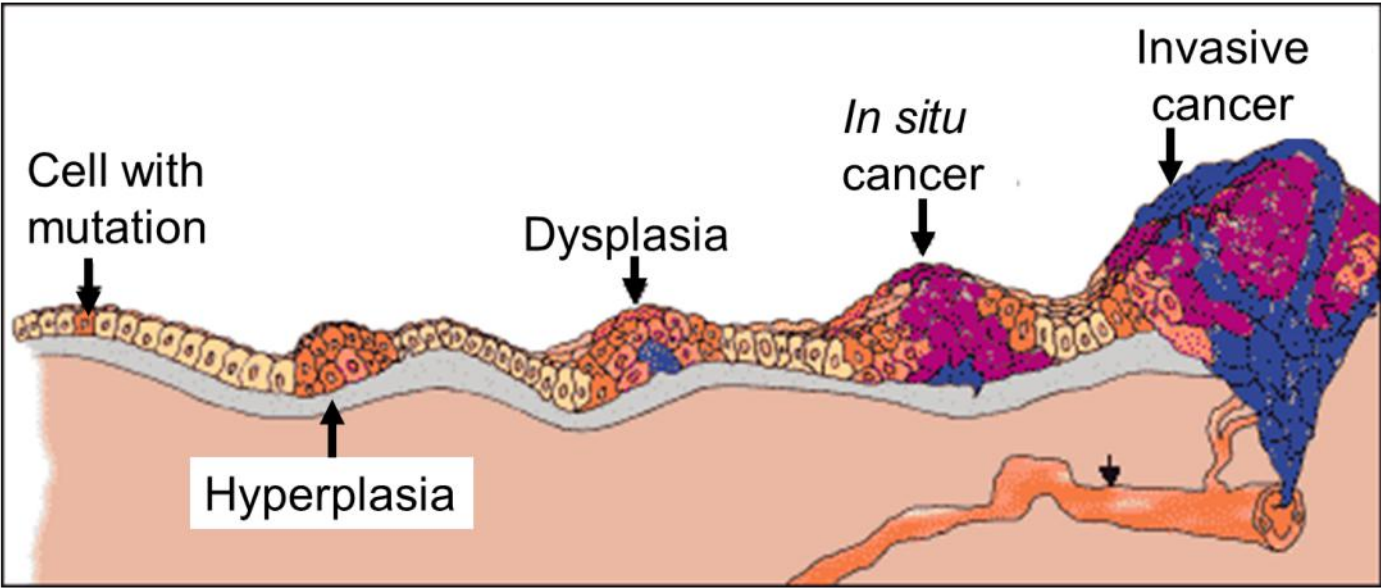
- Latest PET-MRI/CT scan results
- Pathology report
- Blood work & tox report
- MDT notes in EMR
- Current treatment regimen: Literature around resistance mechanisms and drug efficacy
- Genomic findings: Relevance and actionability



# Modelling tumour evolution from longitudinal data

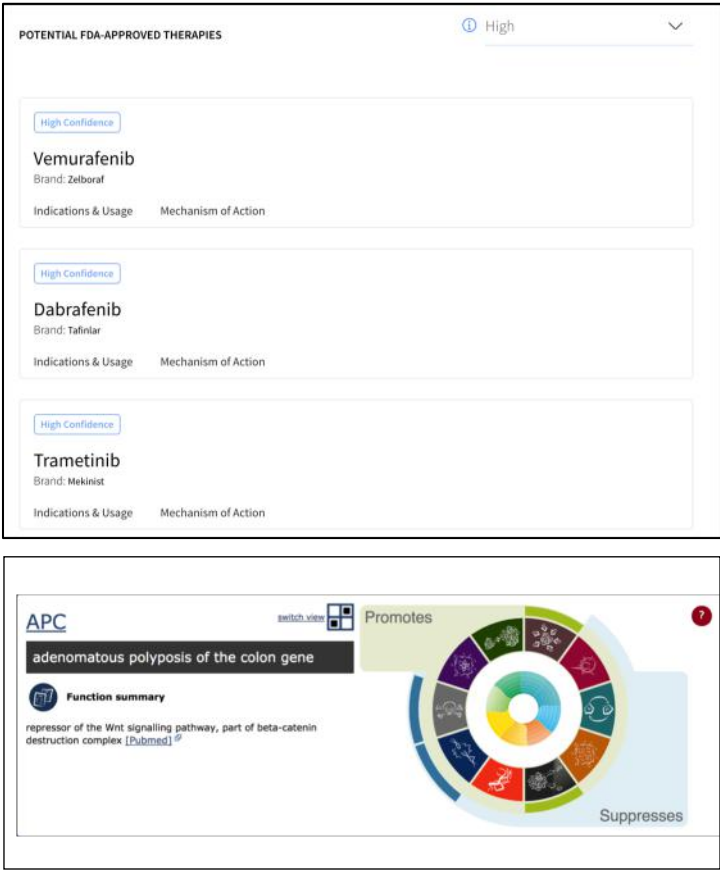
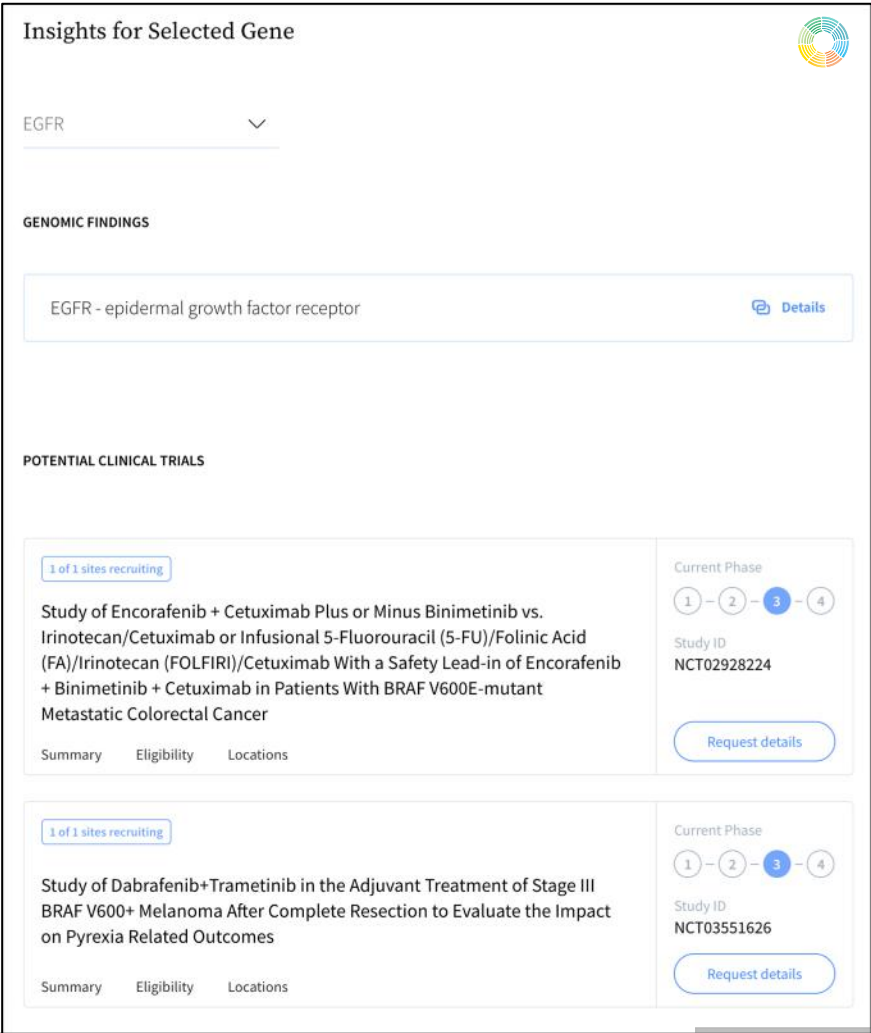
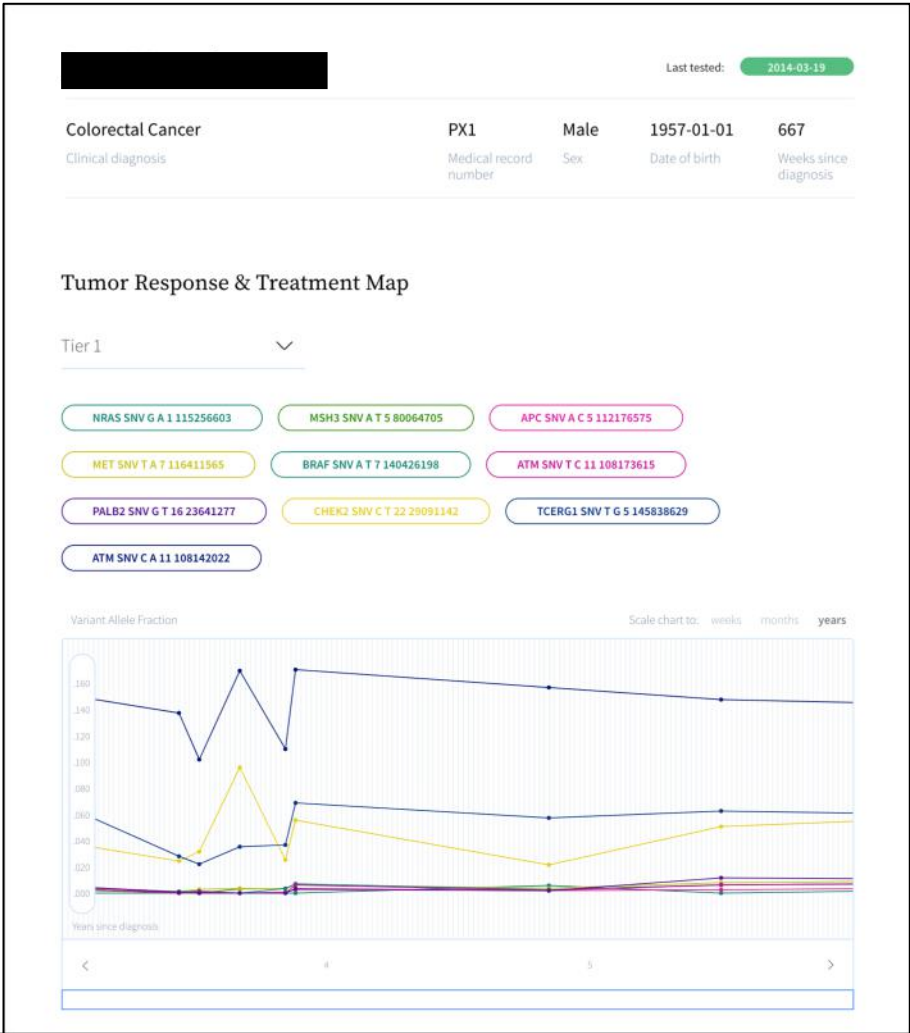


# Modelling tumour evolution from longitudinal data





# How we are thinking about data presentation in VAF Tracker





## How others are thinking about presenting longitudinal genomic data

**Doe, James (A37111)**

Patient MRN: 2345678 | DOB: MAR-21-1970 | Gender: Male

Diagnosis: Non-small Cell Lung Cancer | Test Number 1

Therapy Finder Page

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**REPORTING**

Final Report Date: NOV-08-2017

Receipt Date: OCT-31-2017

Collection Date: OCT-30-2017

Specimen: Blood

Status: Final

**PHYSICIAN**

**Mary Smith**

Account: Pleasantville Oncology

Address: 1234 Main Street,  
Nashville, TN 37011 United States

Ph: 111.111.1111 | Fax: 222.222.2222

Additional Recipient: James Brown

Tumor  
response  
map

*Complete Tumor Response Map on page 2*

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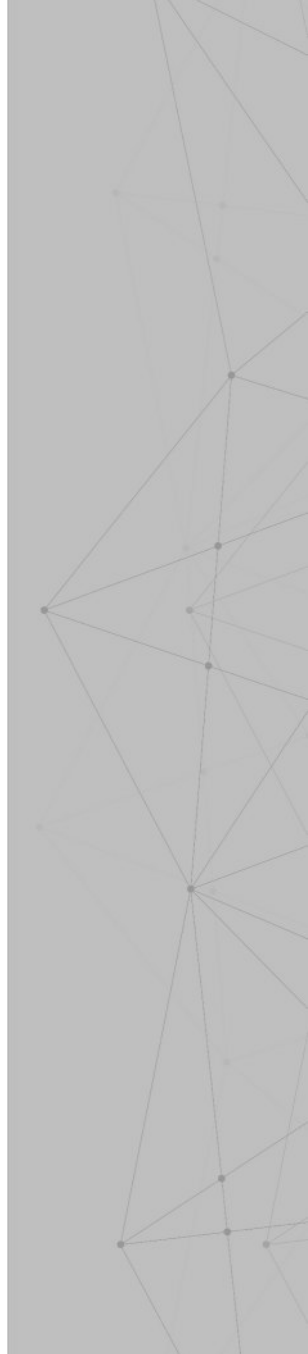
### Summary of Somatic Alterations & Associated Treatment Options

**KEY:** ✔ Approved in indication    ~ Approved in other indication    ✘ Lack of response

Alteration	% cfDNA or Amplification	Associated FDA-approved therapies	Clinical trial availability <small>(see page 3)</small>
EGFR L858R	0.5%	<span style="color: green;">✔</span> Erlotinib, Gefitinib, Afatinib	Yes
TP53 R156P	1.2%	None	Yes



# The Data



# Molecular Taxonomy of Breast Cancer International Consortium (METABRIC)

## Copy Number and RNA

Article | Published: 18 April 2012

**The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups**

Christina Curtis, Sohrab P. Shah [...] Samuel Aparicio ✉

*Nature* **486**, 346–352 (21 June 2012) | [Download Citation](#) ↓

## Targeted DNA sequencing

Article | OPEN | Published: 10 May 2016

**The somatic mutation profiles of 2,433 breast cancers refine their genomic and transcriptomic landscapes**

Bernard Pereira, Suet-Feung Chin [...] Carlos Caldas ✉

*Nature Communications* **7**, Article number: 11479 (2016) | [Download Citation](#) ↓

## microRNA

*Nature*, 2013 May 16;497(7449):378–82. doi: 10.1038/nature12108. Epub 2013 May 5.

**The shaping and functional consequences of the microRNA landscape in breast cancer.**

Dvinge H<sup>1</sup>, Git A, Gräf S, Salmon-Divon M, Curtis C, Sottoriva A, Zhao Y, Hirst M, Armitage J, Miska EA, Chin SF, Provenzano E, Turashvili G, Green A, Ellis I, Aparicio S, Caldas C.

## Experimental Models

*Cell*, 2016 Sep 22;167(1):260–274.e22. doi: 10.1016/j.cell.2016.08.041. Epub 2016 Sep 15.

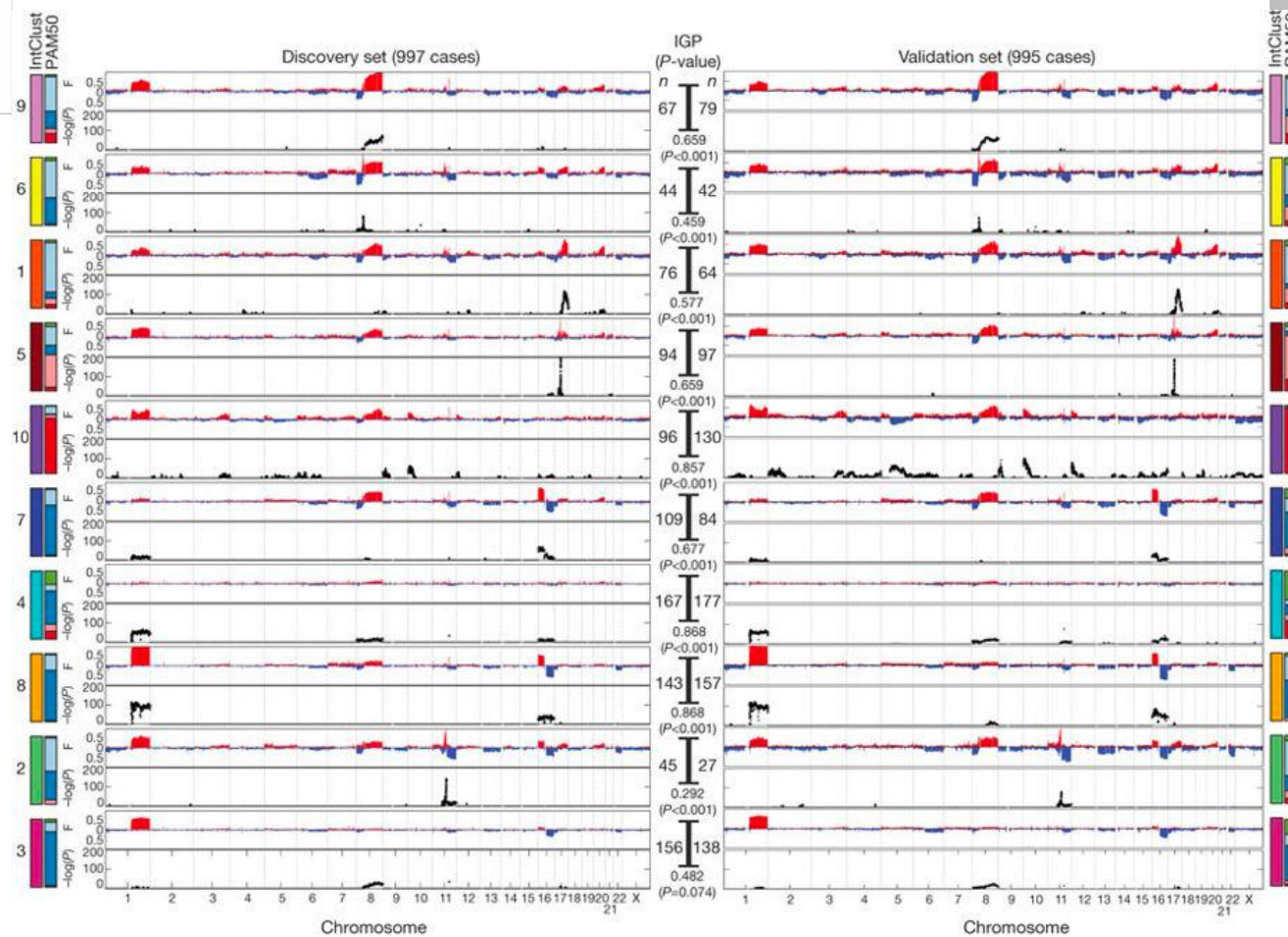
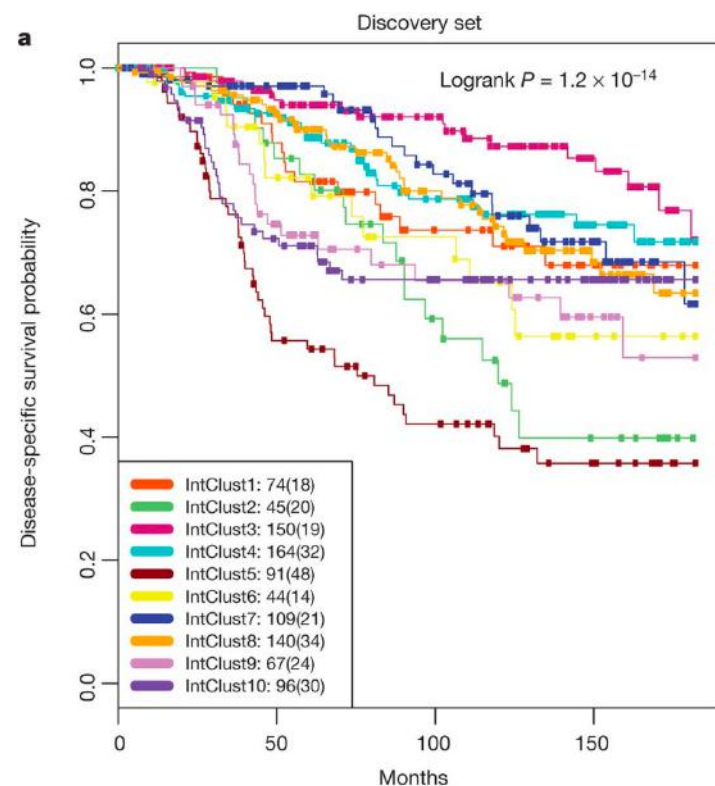
**A Biobank of Breast Cancer Explants with Preserved Intra-tumor Heterogeneity to Screen Anticancer Compounds.**

Bruna A<sup>1</sup>, Rueda OM<sup>1</sup>, Greenwood W<sup>1</sup>, Batra AS<sup>1</sup>, Callari M<sup>1</sup>, Batra RN<sup>1</sup>, Pogrebniak K<sup>1</sup>, Sandoval J<sup>1</sup>, Cassidy JW<sup>1</sup>, Tufegdžić-Vidaković A<sup>1</sup>, Sammut SJ<sup>1</sup>, Jones L<sup>2</sup>, Provenzano E<sup>3</sup>, Baird R<sup>2</sup>, Eirew P<sup>4</sup>, Hadfield J<sup>1</sup>, Eldridge M<sup>1</sup>, McLaren-Douglas A<sup>5</sup>, Barthorpe A<sup>5</sup>, Lightfoot H<sup>5</sup>, O'Connor MJ<sup>6</sup>, Gray J<sup>7</sup>, Cortes J<sup>8</sup>, Baselga J<sup>9</sup>, Marangoni E<sup>10</sup>, Welton AL<sup>11</sup>, Aparicio S<sup>4</sup>, Serra V<sup>8</sup>, Garnett MJ<sup>5</sup>, Caldas C<sup>12</sup>.





*Nature* **486**, 346–352 (21 June 2012) | [Download Citation](#) 



# Integrating drug response data from caldaslab.cruk.cam.ac.uk/bcape

← → ↻ https://caldaslab.cruk.cam.ac.uk/bcape/

Breast Cancer PDTX Encyclopaedia

Home Models Drugs Genes Downloads Help

Show 10 rows

Search:

Drug	Pathway	Target
(5Z)-7-Oxozeaenol	other	TAK1 (MAP3K7)
17-AAG	other	HSP90
5-Fluorouracil	DNA replication	antimetabolite
681640	Genome integrity (CHEK)	WEE1, CHEK1
ABT-263	apoptosis regulation	BCL2, BCL-XL, BCL-W
AG-014699	Genome integrity (PARP)	PARP1, PARP2
AMG-706	RTK signaling	VEGFR, RET, c-KIT, PDGFR
AZ628	BRAF	BRAF
AZ960	Unknown	JAK2
AZD2281	Unknown	PARP1, PARP2

Showing 1 to 10 of 104 entries

Previous 1 2 3 4 5 ... 11 Next

Drug: 5-Fluorouracil

Models Copy Number Gains Copy Number Losses Mutations Expression Methylation

Comparison of models with and without copy number losses

Details Data

The plot shows, for each gene, in the y axis the adjusted p-value in -log10 scale of a t-test comparing the AUC in models with losses vs models with no losses in that gene. Values larger than 1 are considered statistically significant.

The x axis shows the negative value of the t-statistic that measures the difference in AUC means for those two groups of models. Positive values suggest sensitivity to the drug in the models with the CNA and negative values resistance.

Filtered genes are those with a mean AUC that is considered sensitive for the models with the alteration and a mean AUC resistant for the models without the alteration (or the other way around; threshold for sensitivity is 0.2).

An upper limit of 1000 genes are shown; these include the most significant 500.

Select a drug in the search panel to view sensitivity results. Drag within plot to zoom. Click on a point to navigate to the gene view.

© 2018 University of Cambridge

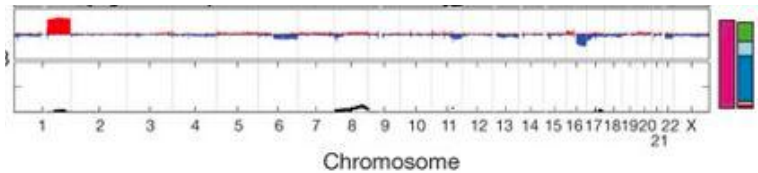
Contact us | Terms and Conditions

# What should we present to clinicians?

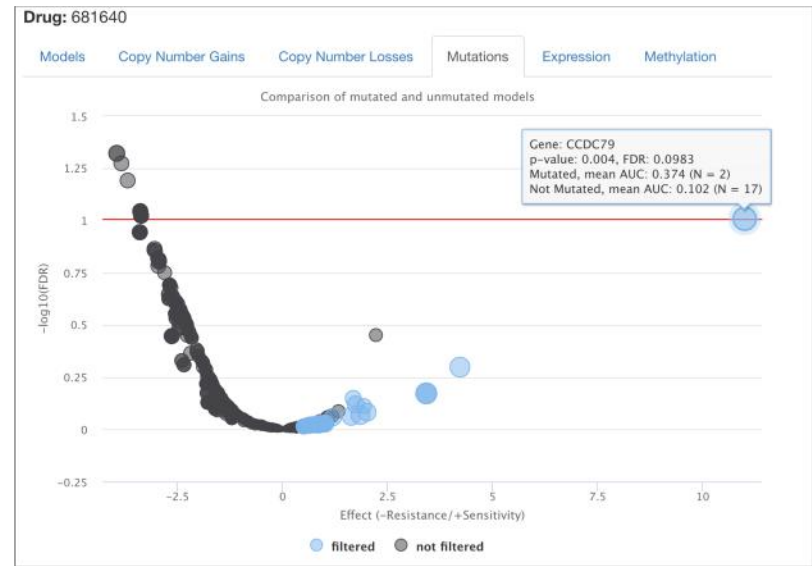
NB: for judging, we will assume that doctors have access to ipads/webapps/etc. so info can be interactive

*“Patient is IntCluster x, with a median survival of y months, and has copy number gains associated with z drug resistance”*

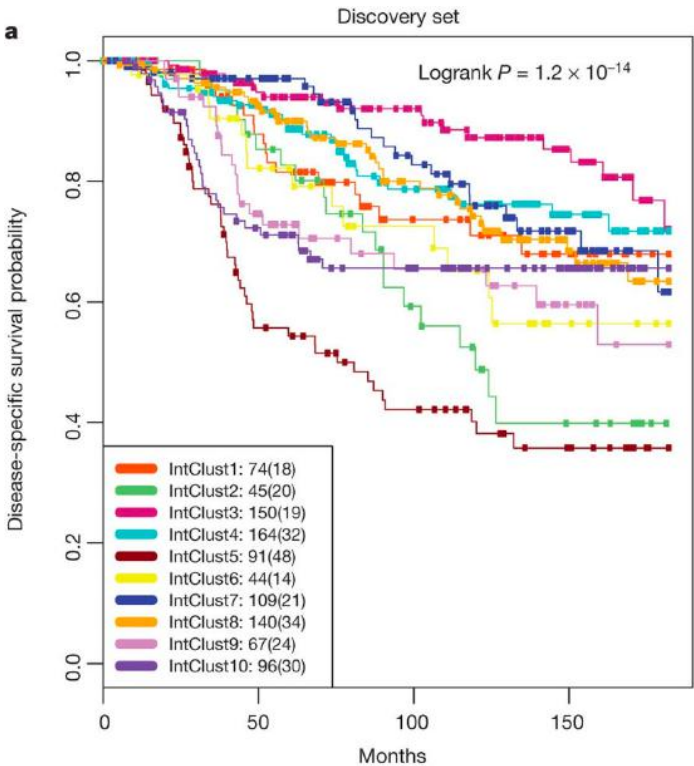
X



Z

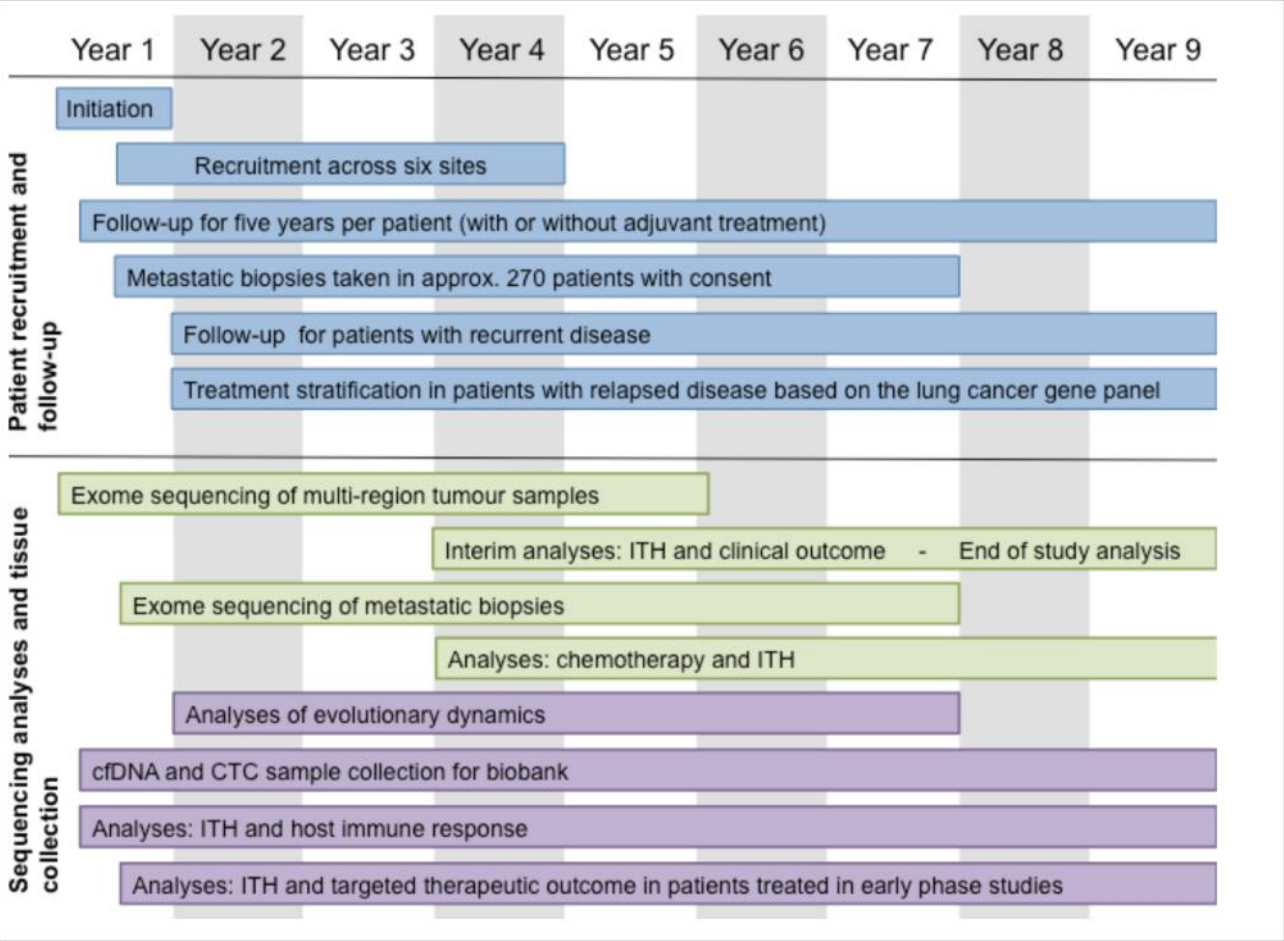


y





# Tracking Cancer Evolution Through Therapy (Rx) (TRACERx)



## ARTICLE

doi:10.1038/nature22364

### Phylogenetic ctDNA analysis depicts early-stage lung cancer evolution

A list of authors and their affiliations appears in the online version of the paper.

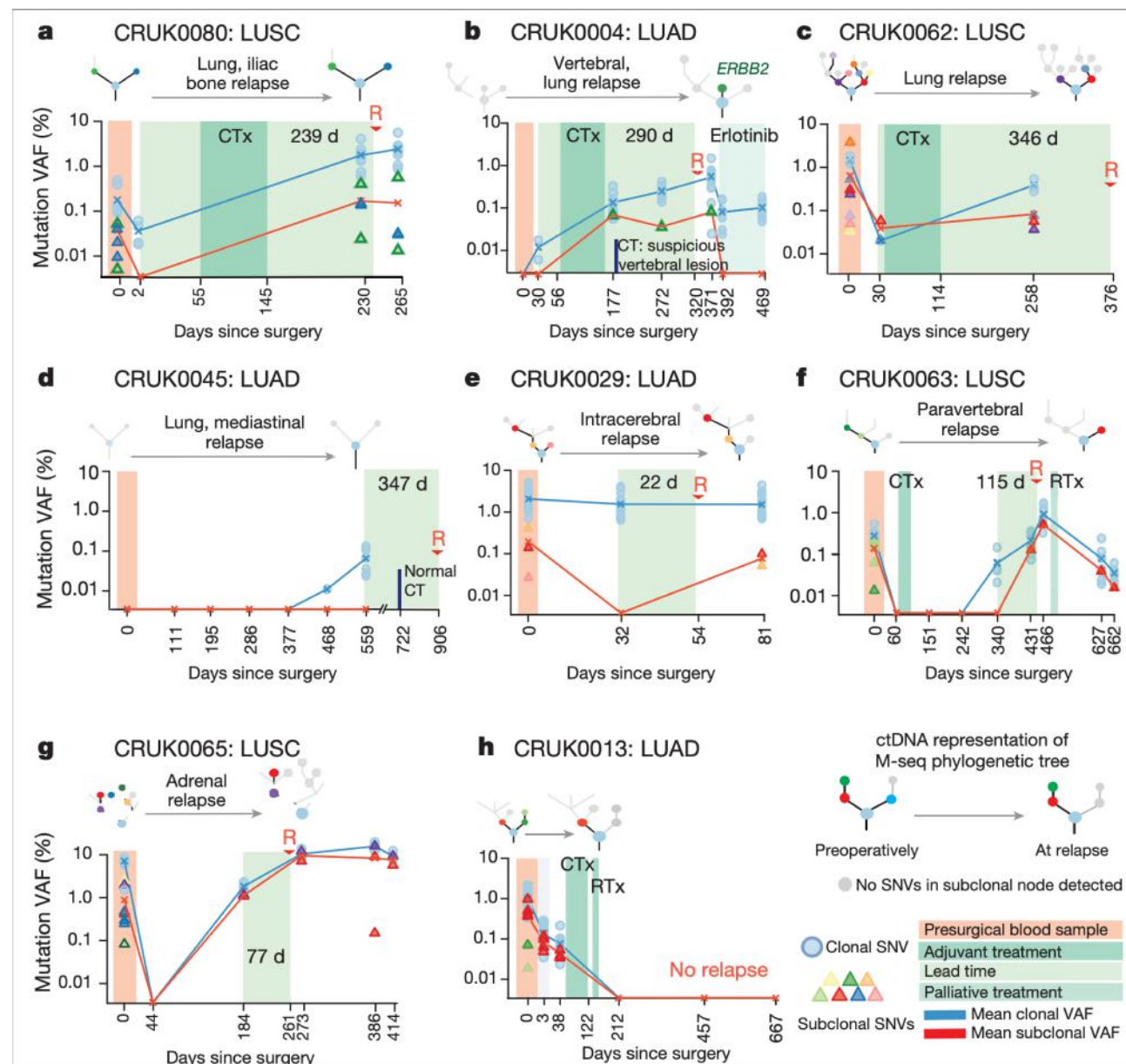
RESEARCH ARTICLE | CANCER

### Clonal status of actionable driver events and the timing of mutational processes in cancer evolution

Nicholas McGranahan<sup>1,2,\*</sup>, Francesco Favero<sup>3</sup>, Elza C. de Bruin<sup>4</sup>, Nicolai Juul Birkbak<sup>1,3,4,\*</sup>, Zoltan Szallasi<sup>3,5</sup> and Charles S...

Science Translational Medicine 15 Apr 2015:  
Vol. 7, Issue 283, pp. 283ra54  
DOI: 10.1126/scitranslmed.aaa1408

# Modelling tumour evolution from longitudinal data

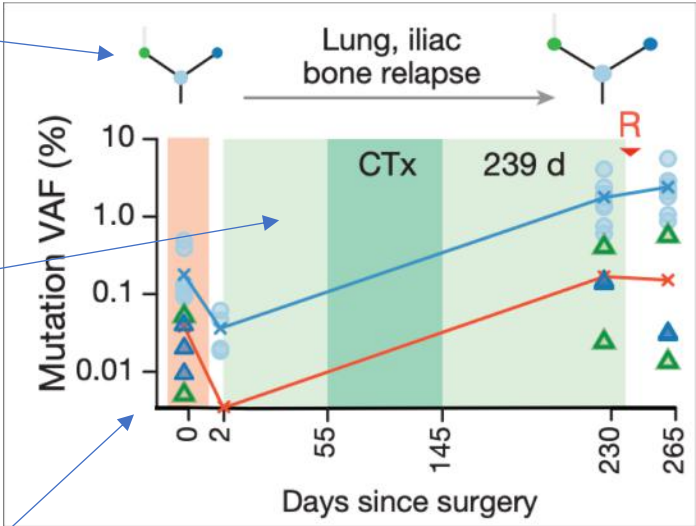


# What should we present to clinicians?

Evolution and metastasis

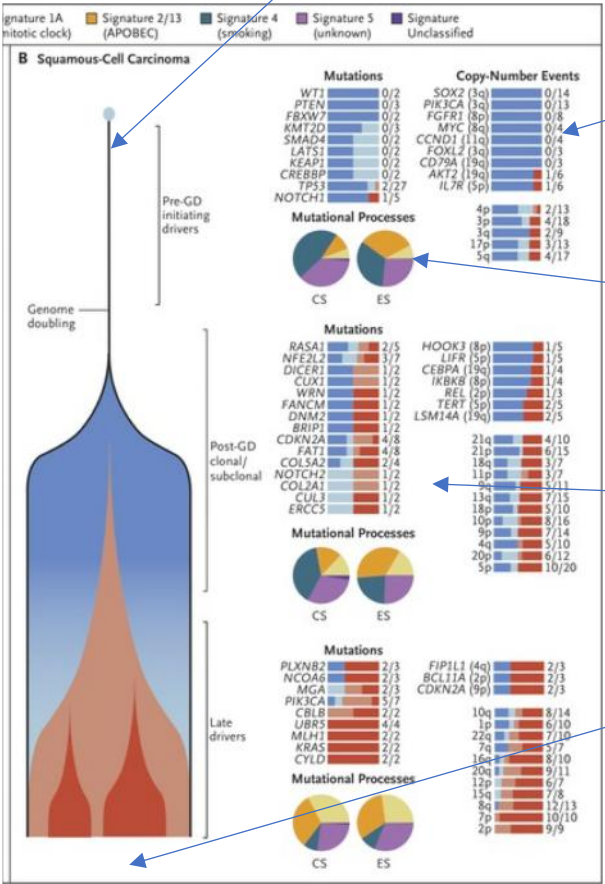
Colours = treatment regimen

Granular info CNA/SNV associated with drugs and/or clinical trials?



Clinical timelines

The tumours evolutionary history



CNA/SNV associated with drugs and/or clinical trials?

What mutational processes caused this cancer? Eg smoking?

The second stage of this tumours evolution

What can we predict about the future?





**CAMBRIDGE**  
CANCER GENOMICS

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*blood testing for better cancer treatment*

Cambridge Cancer Genomics  
Future Business Centre,  
Kings Hedges Road,  
Cambridge, UK, CB42HY

# How we are thinking about data presentation in VAF Tracker

Clinical info at a glance

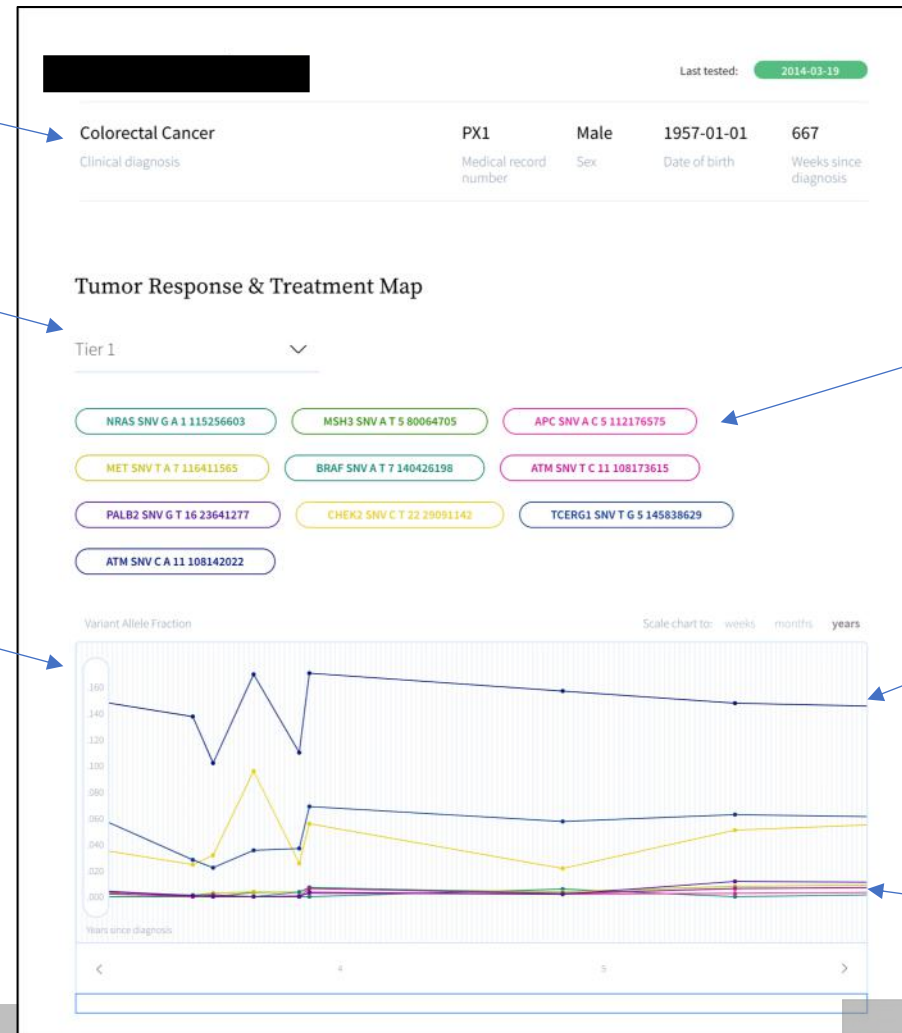
Mutations tiered based on importance

VAF plot (with minimal noise filtering)

Each individual mutation can be isolated for further info

Dominant mutation present in most of tumour cells

Subclonal mutations not very prevalent in tumour but still potentially important (e.g. drug resistance alleles)



# How we are thinking about data presentation in VAF Tracker

Simple dropdowns to avoid page clutter with lots of genomic info

Matches genomic info and clinical records with e.g. ClinicalTrials.gov and MolMatch

High level summary for clinicians info

The screenshot displays the 'Insights for Selected Gene' interface. At the top, there is a dropdown menu for 'EGFR'. Below this, the 'GENOMIC FINDINGS' section shows 'EGFR - epidermal growth factor receptor' with a 'Details' link. The 'POTENTIAL CLINICAL TRIALS' section lists two trials. The first trial is 'Study of Encorafenib + Cetuximab Plus or Minus Binimetinib vs. Irinotecan/Cetuximab or Infusional 5-Fluorouracil (5-FU)/Folinic Acid (FA)/Irinotecan (FOLFIRI)/Cetuximab With a Safety Lead-in of Encorafenib + Binimetinib + Cetuximab in Patients With BRAF V600E-mutant Metastatic Colorectal Cancer', with Study ID NCT02928224. The second trial is 'Study of Dabrafenib+Trametinib in the Adjuvant Treatment of Stage III BRAF V600+ Melanoma After Complete Resection to Evaluate the Impact on Pyrexia Related Outcomes', with Study ID NCT03551626. Both trials show a 'Current Phase' indicator with phases 1, 2, 3, and 4, where phase 3 is highlighted. A 'Request details' button is present for each trial. The interface also includes a 'Summary' tab and 'Locations' information for each trial.

Much more granular data is only ever one click away

Simple process to make requests to recruiting centres

Simple trial enquiry and visual representation of scale of trial (phase)



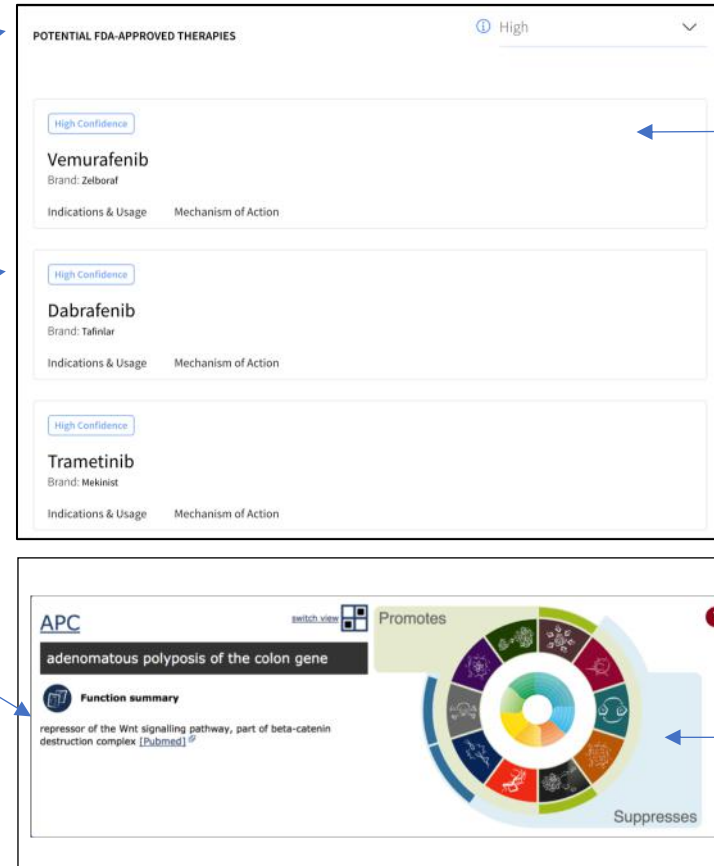


# How we are thinking about data presentation in VAF Tracker

Soft language and guidance only

A level of confidence to aid in clinical decision process

Links to more papers/studies



Matches genomic info and clinical records with curated databases of approved drugs

Granular info pulled from COSMIC API

