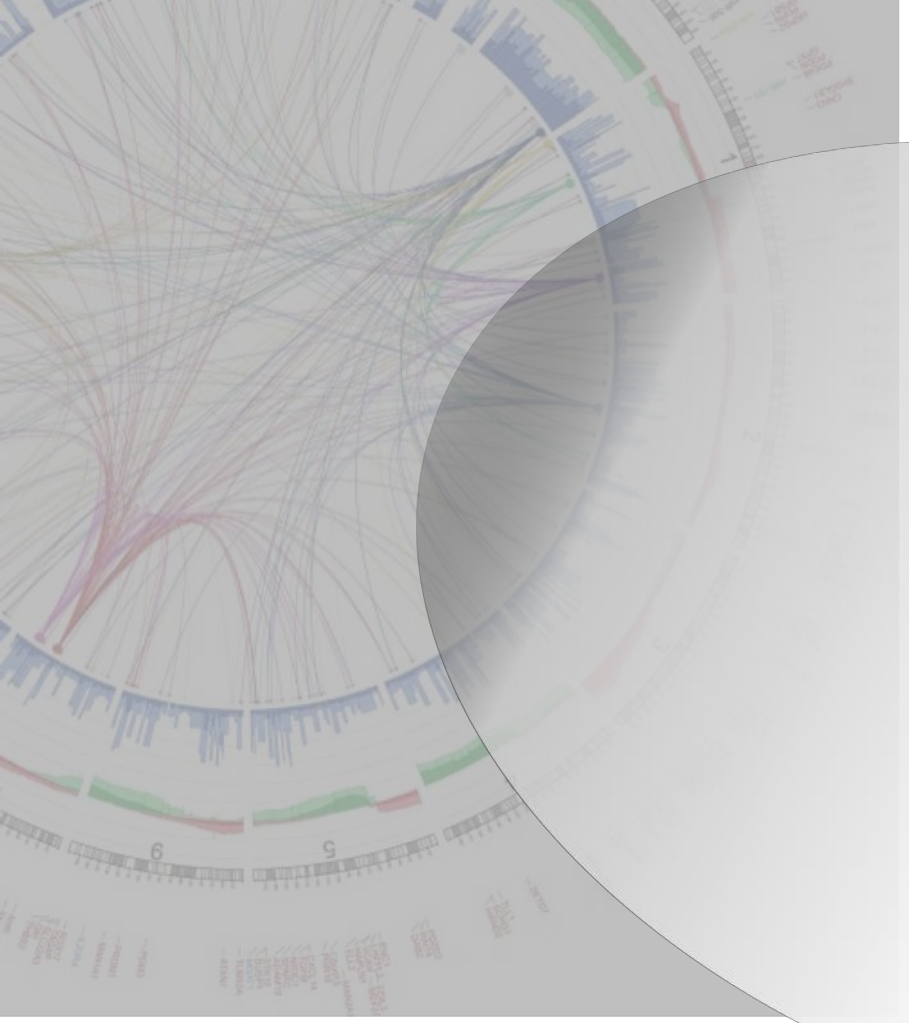


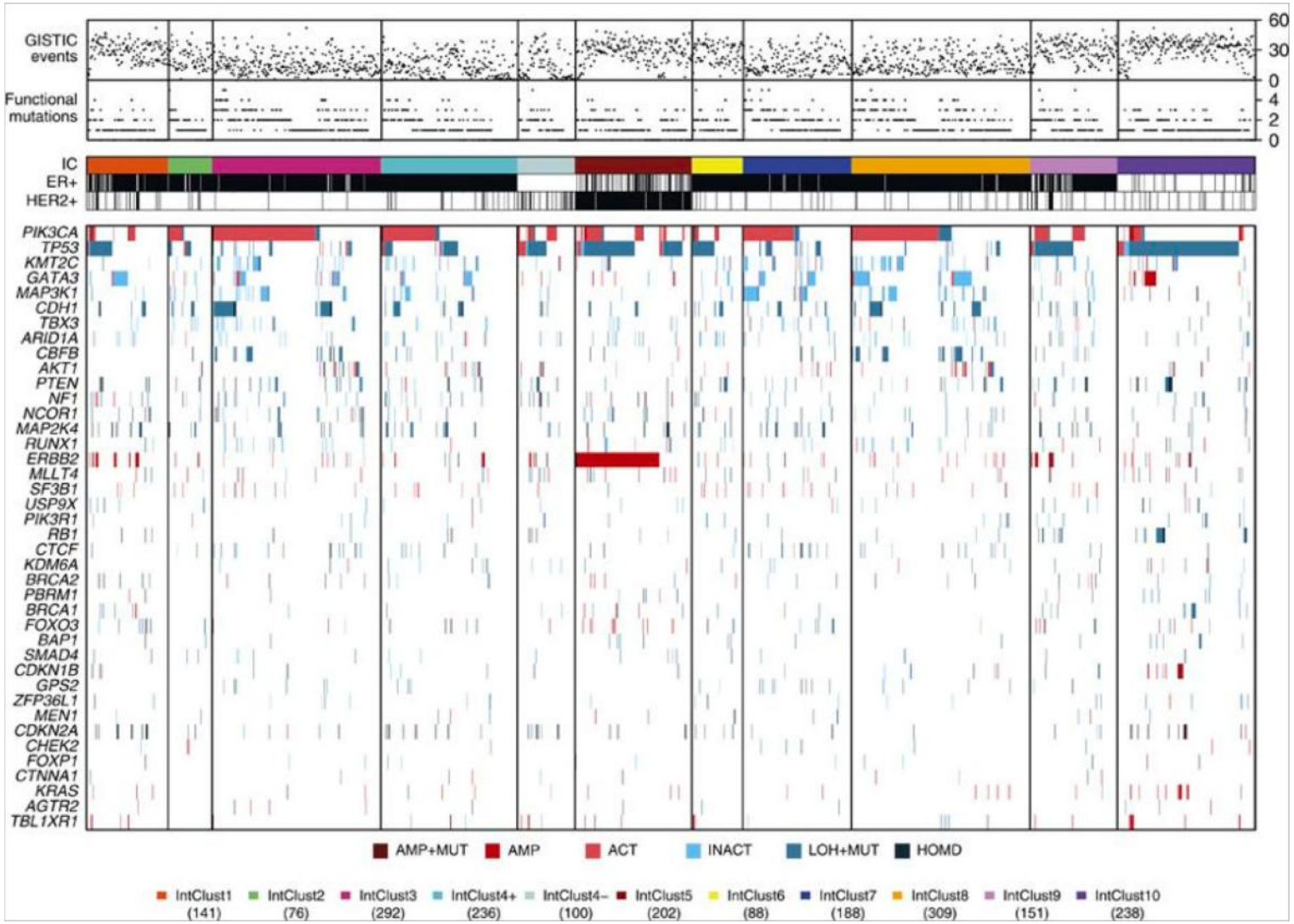
John W. Cassidy
Cofounder & CEO
John@CCG.ai

CAMBRIDGE
CANCER GENOMICS

October 2018

* Circos Plot visualization of tumour WGS.

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

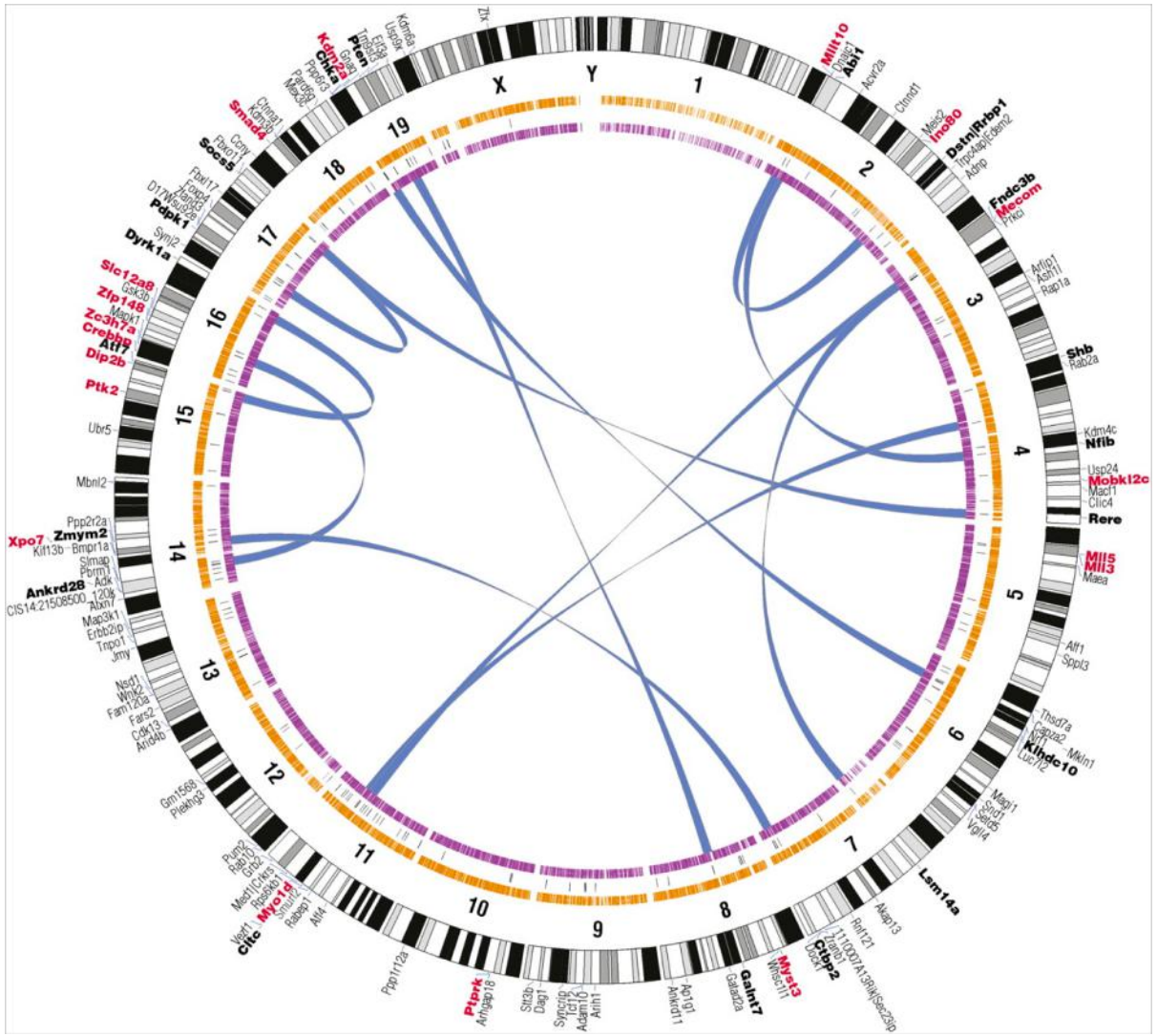
Nature Communications **7**, Article number: 11479 (2016) | Download Citation

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

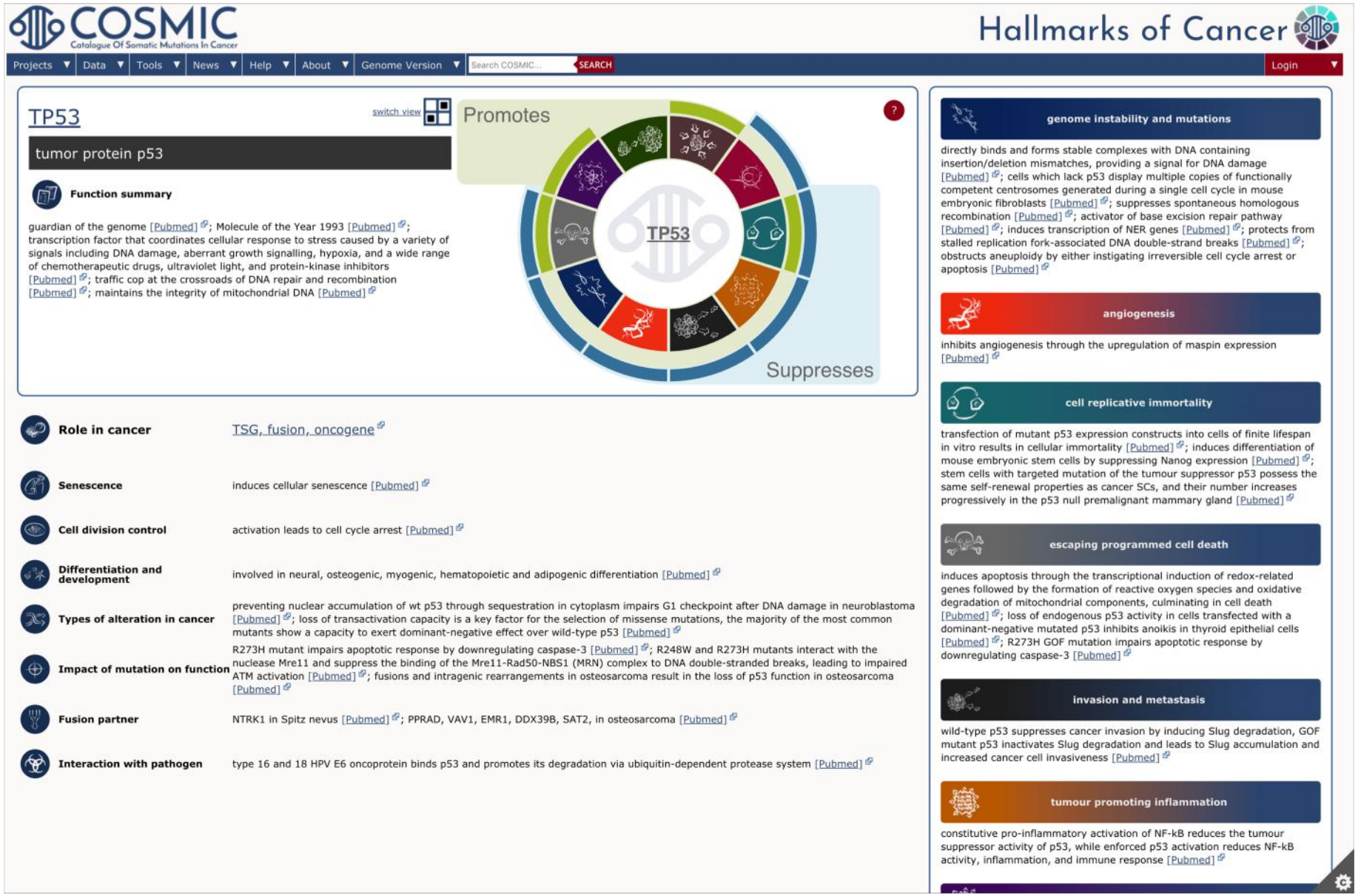
Sleeping Beauty mutagenesis reveals cooperating mutations and pathways in pancreatic adenocarcinoma

Karen M. Mann, Jerrold M. Ward, Christopher Chin Kuan Yew, Anne Kovochich, 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).

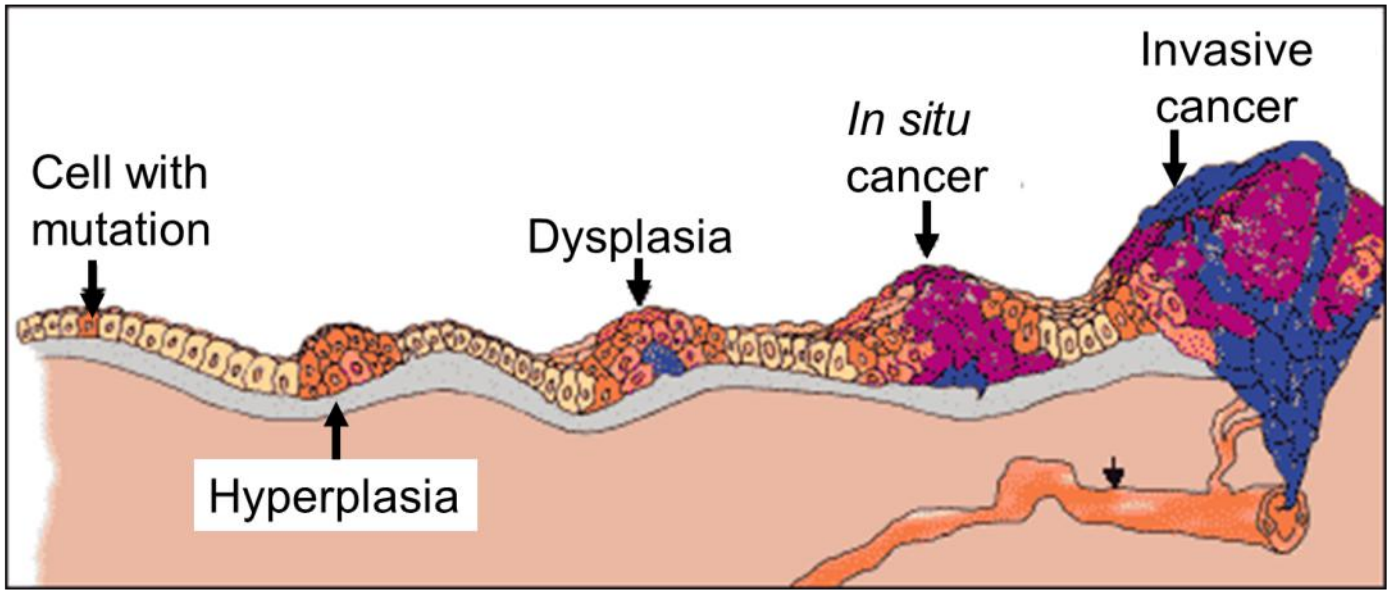
Granular and Detailed



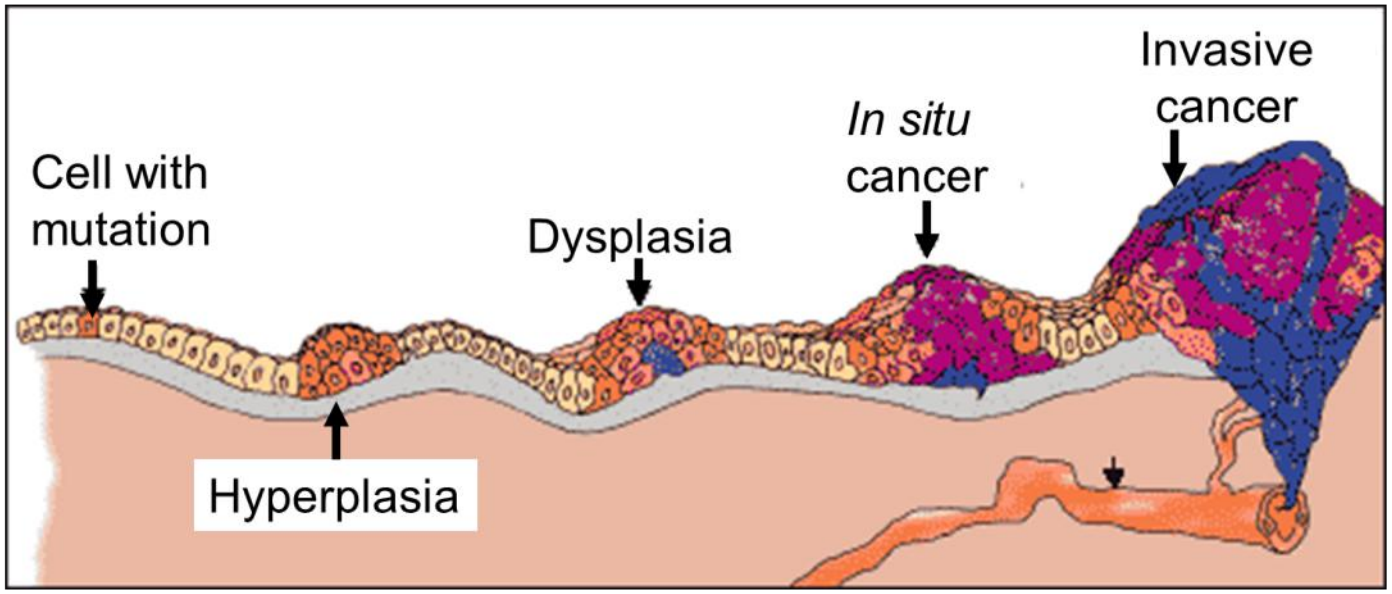
Oncologists typically have 10mins to prep for a 15-30min consultation

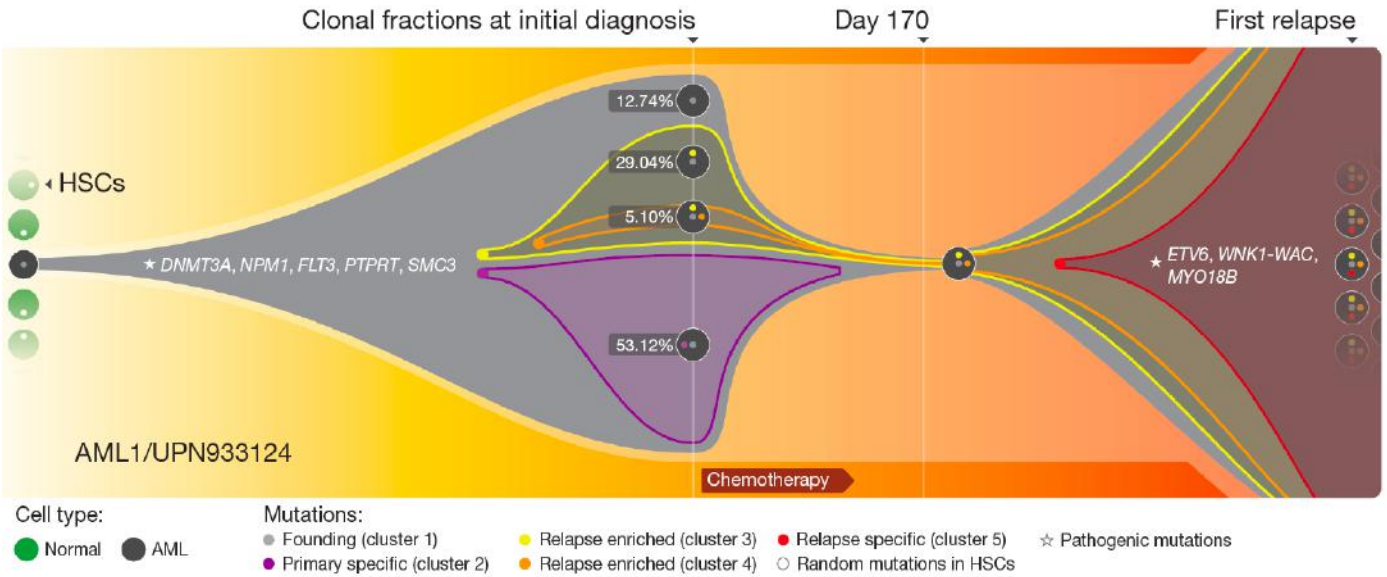
- Latest PET-MRI/CT scan results
- Pathology report
- Blood work & tox report
- MDT notes in EMR
- Current treatment regimen: Literature around resistance mechanisms and drug efficacy
- Genomic findings: Relevance and actionability

Modelling tumour evolution from longitudinal data

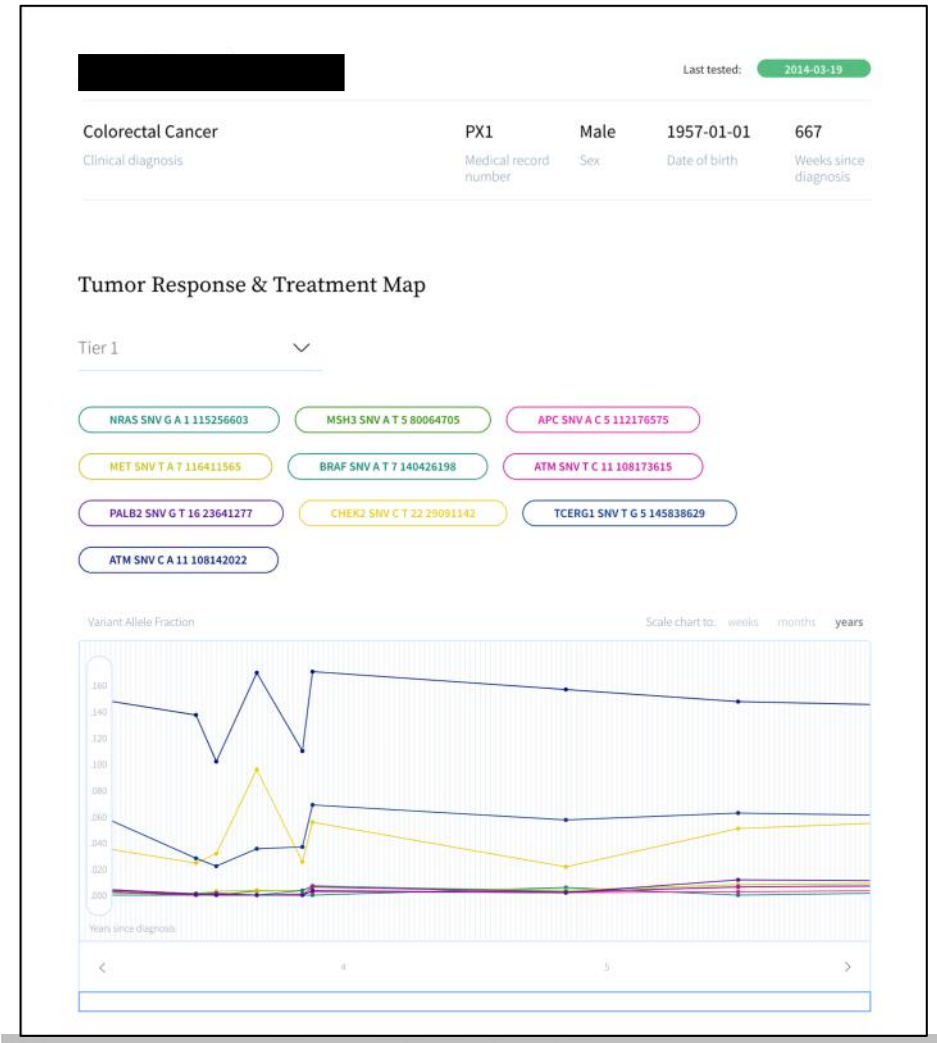


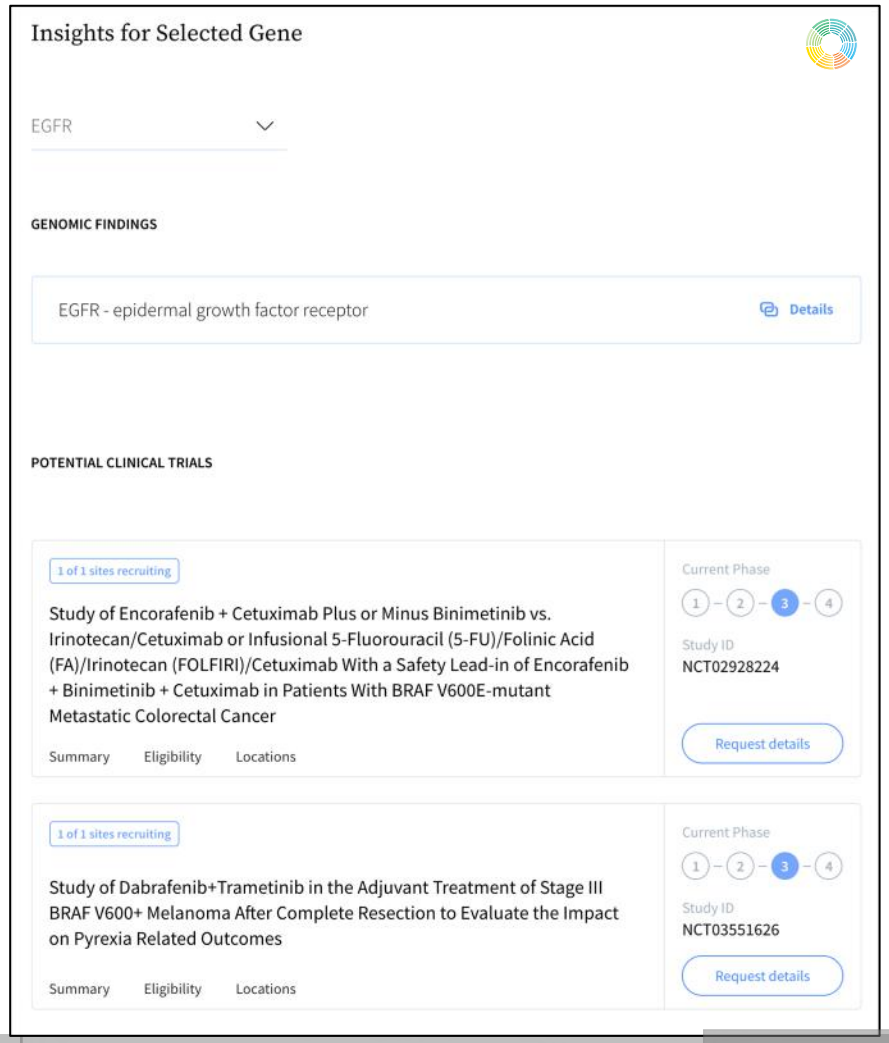
Modelling tumour evolution from longitudinal data

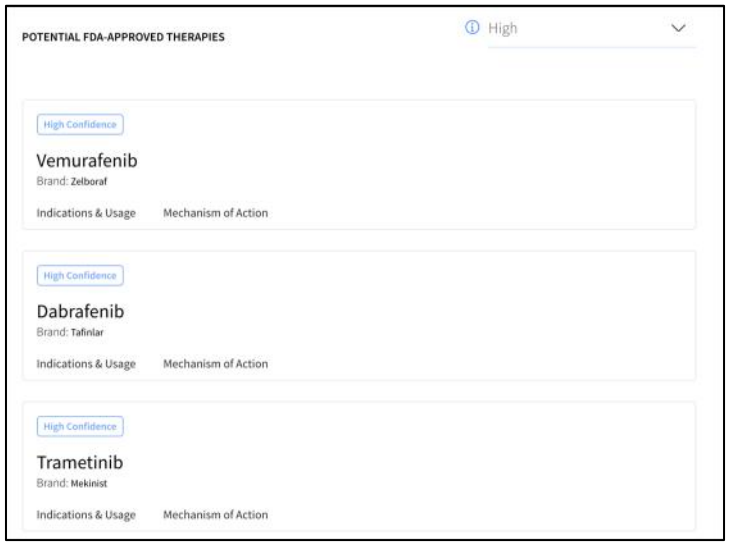


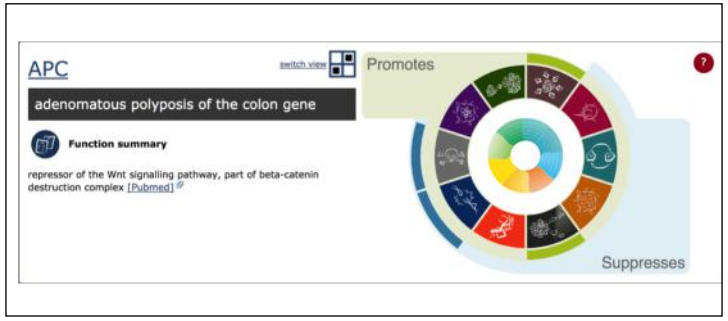


How we are thinking about data presentation in VAF Tracker

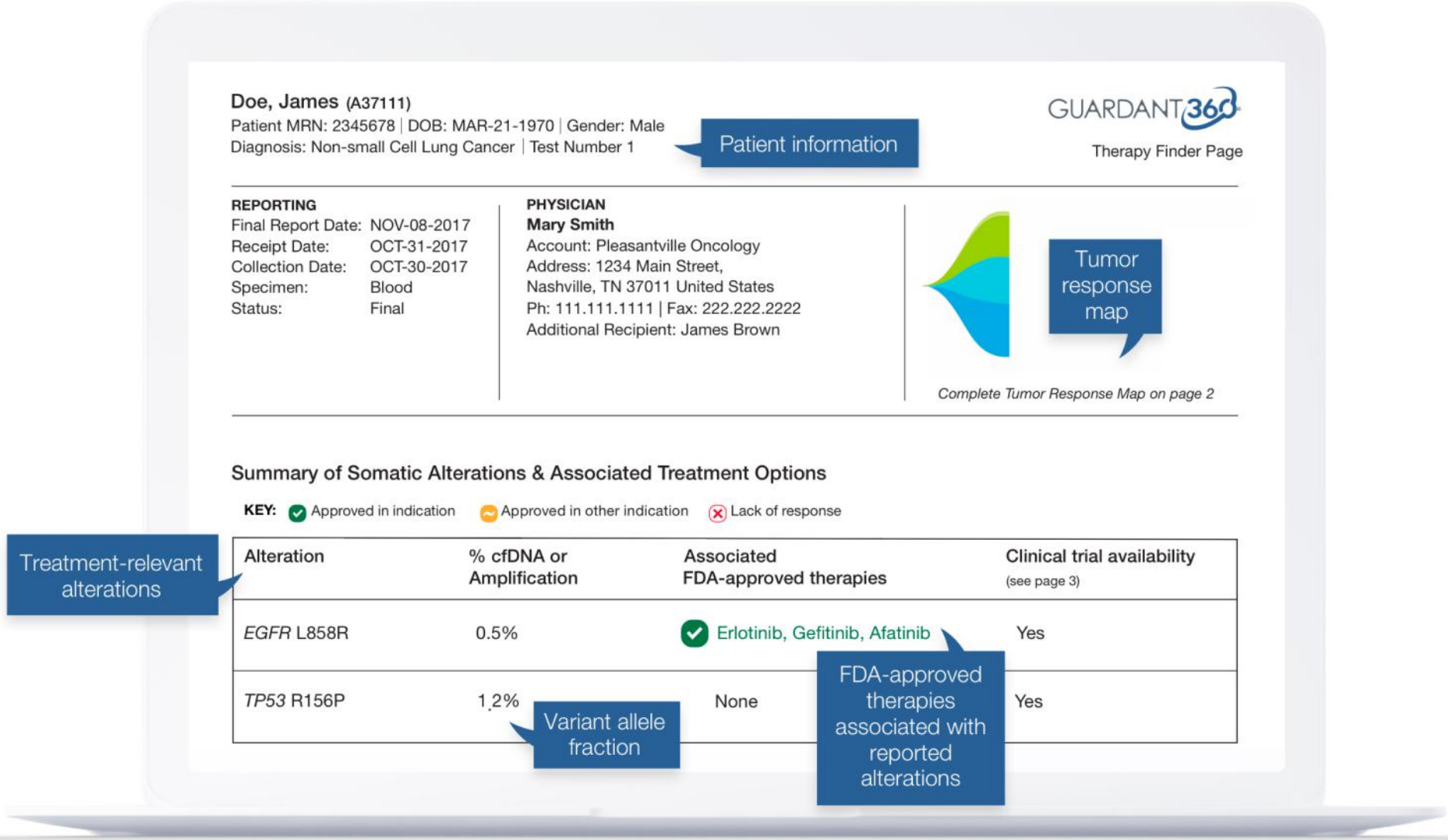








How others are thinking about presenting longitudinal genomic data



The Data

Molecular Taxonomy of Breast Cancer International Consortium (METABRIC)

Copy Number and RNA

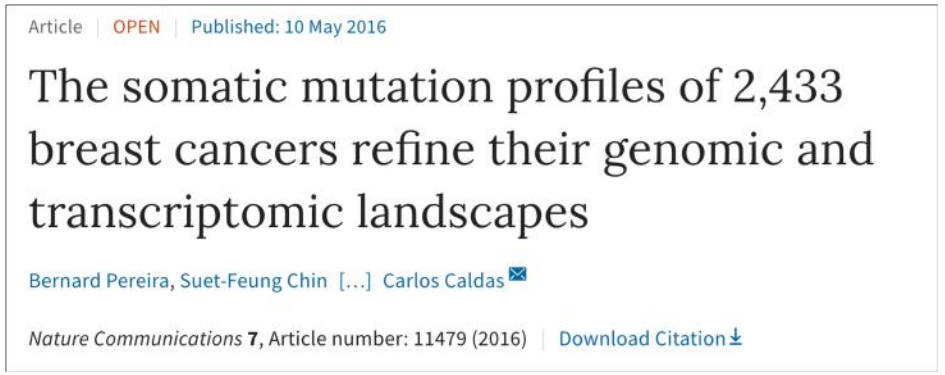
Article | Published: 18 April 2012

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



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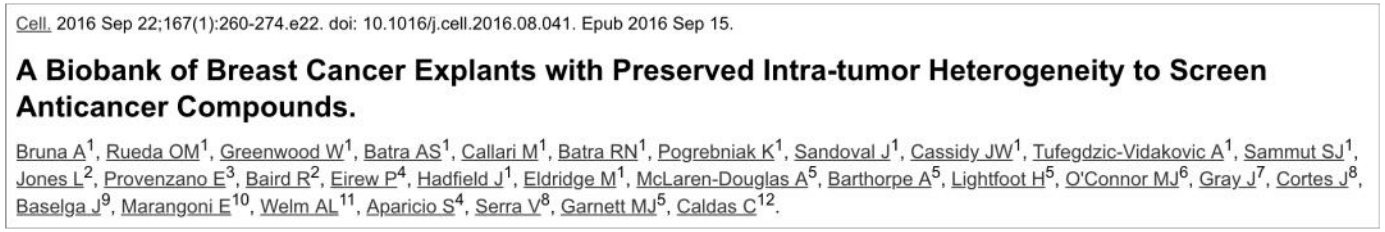
microRNA

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[1], Git A, Gräf S, Salmon-Divon M, Curtis C, Sottoriva A, Zhao Y, Hirst M, Armisen 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[1], Rueda OM[1], Greenwood W[1], Batra AS[1], Callari M[1], Batra RN[1], Pogrebniak K[1], Sandoval J[1], Cassidy JW[1], Tufegdzic-Vidakovic A[1], Sammut SJ[1], Jones L[2], Provenzano E[3], Baird R[2], Eirew P[4], Hadfield J[1], Eldridge M[1], McLaren-Douglas A[5], Barthorpe A[5], Lightfoot H[5], O'Connor MJ[6], Gray J[7], Cortes J[8], Baselga J[9], Marangoni E[10], Welm AL[11], Aparicio S[4], Serra V[8], Garnett MJ[5], Caldas C[12].

Article | Published: 18 April 2012

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

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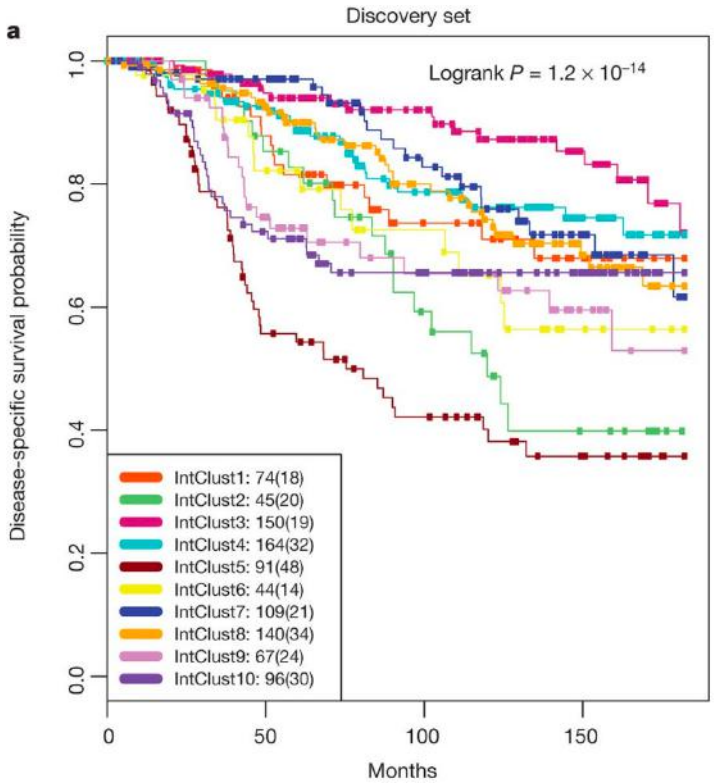
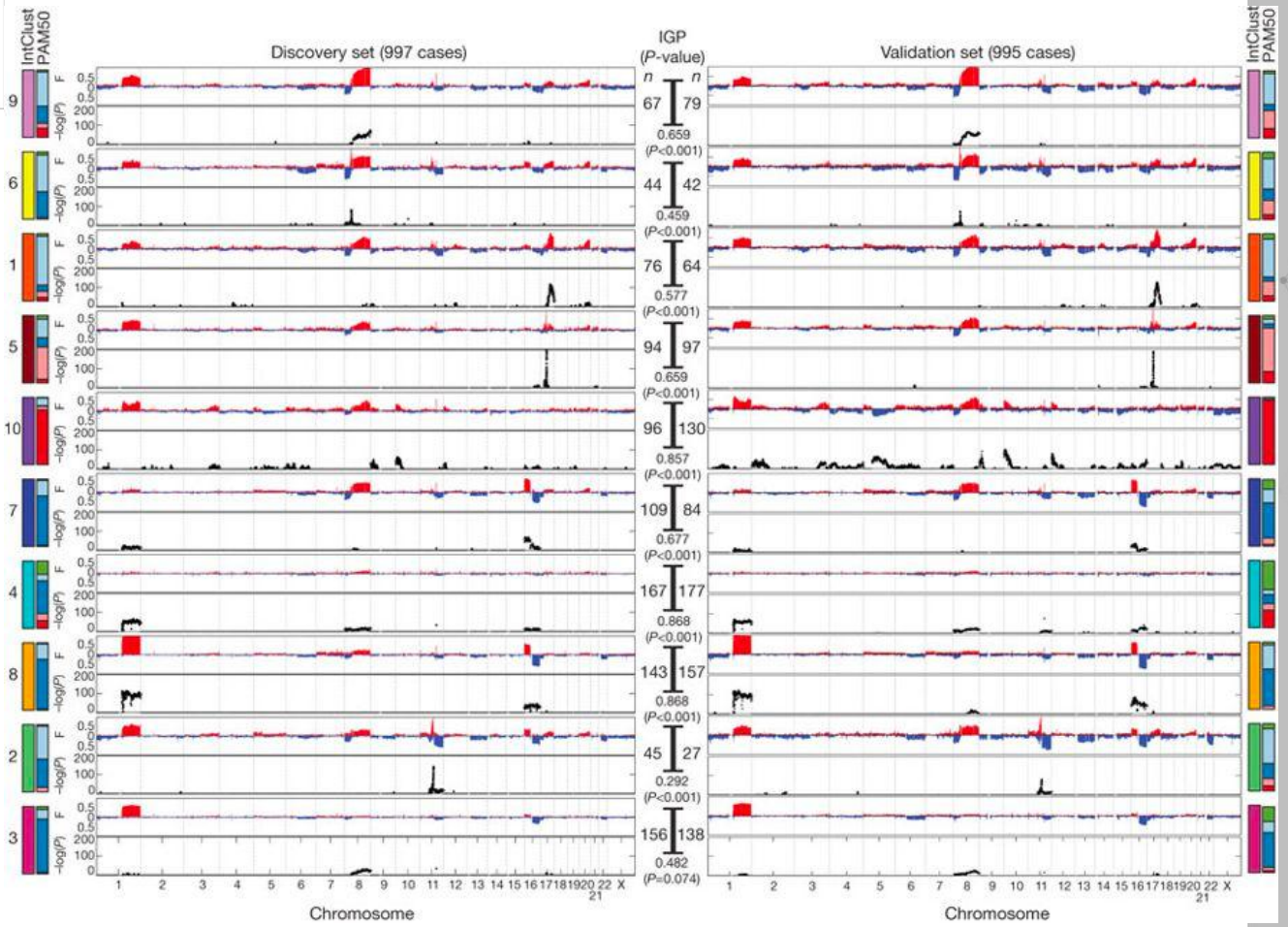
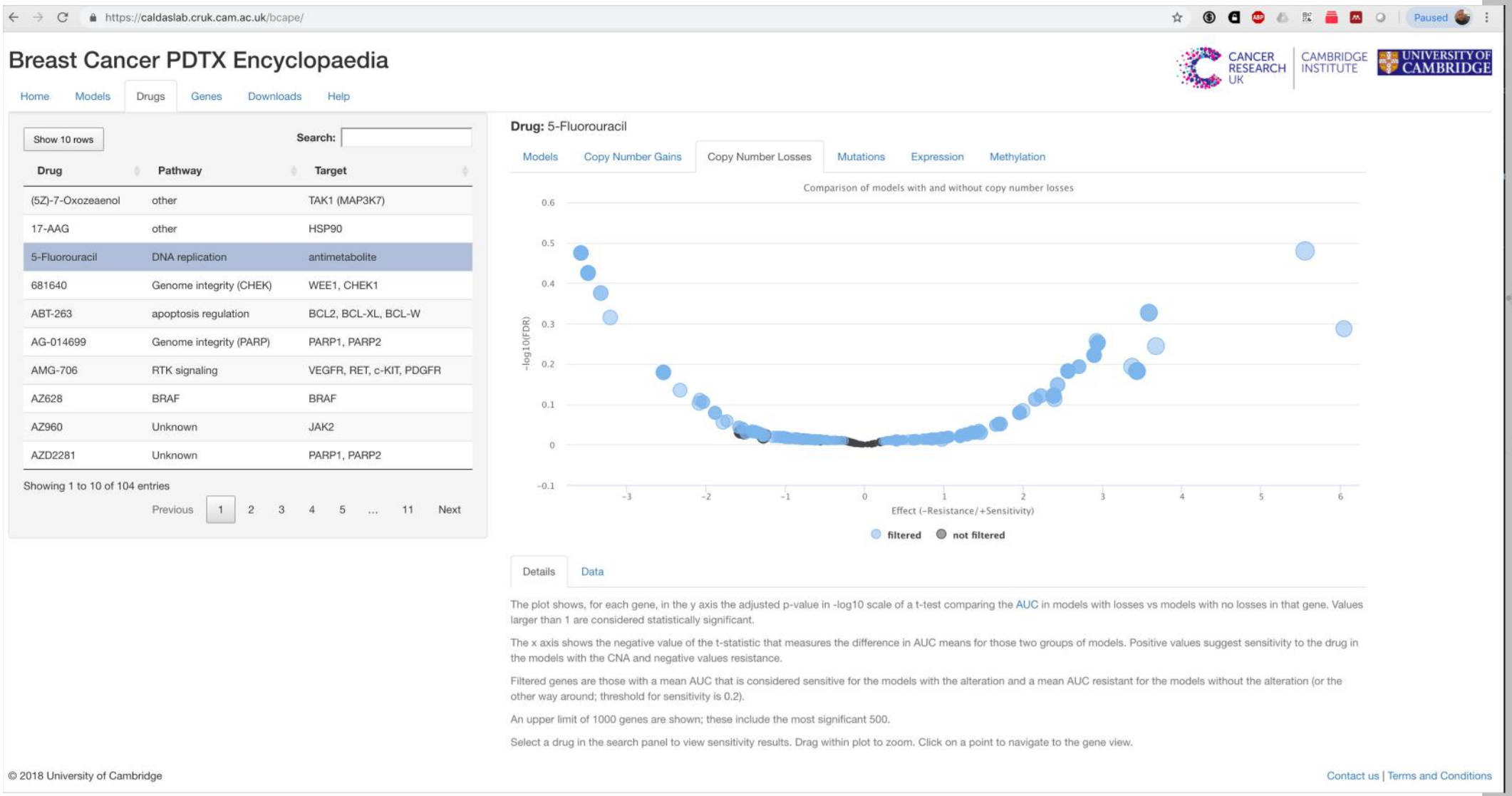




Integrating drug response data from caldaslab.cruk.cam.ac.uk/bcape

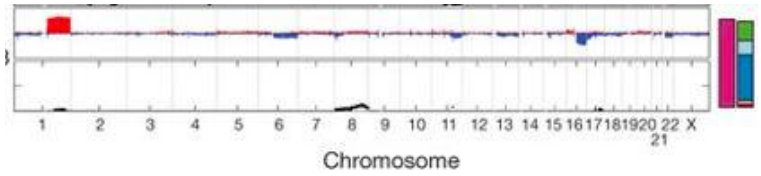


What should we present to clinicians?

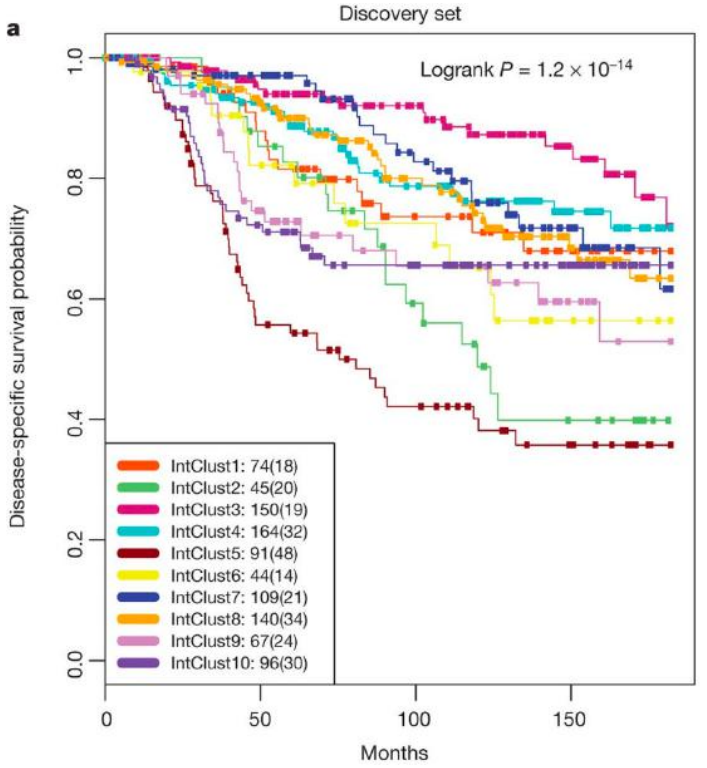
NB: for judging, we will assume that doctors have access to ipads/webapps/etc. so info can be interactive

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

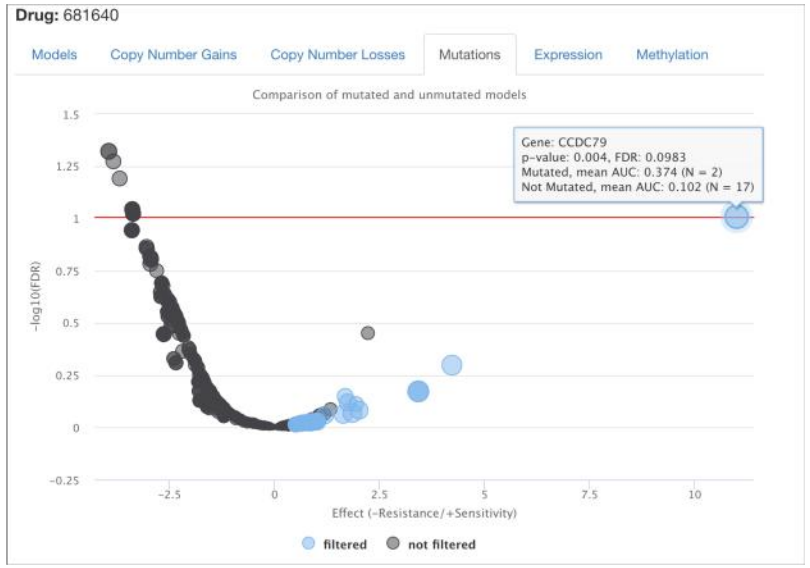
x



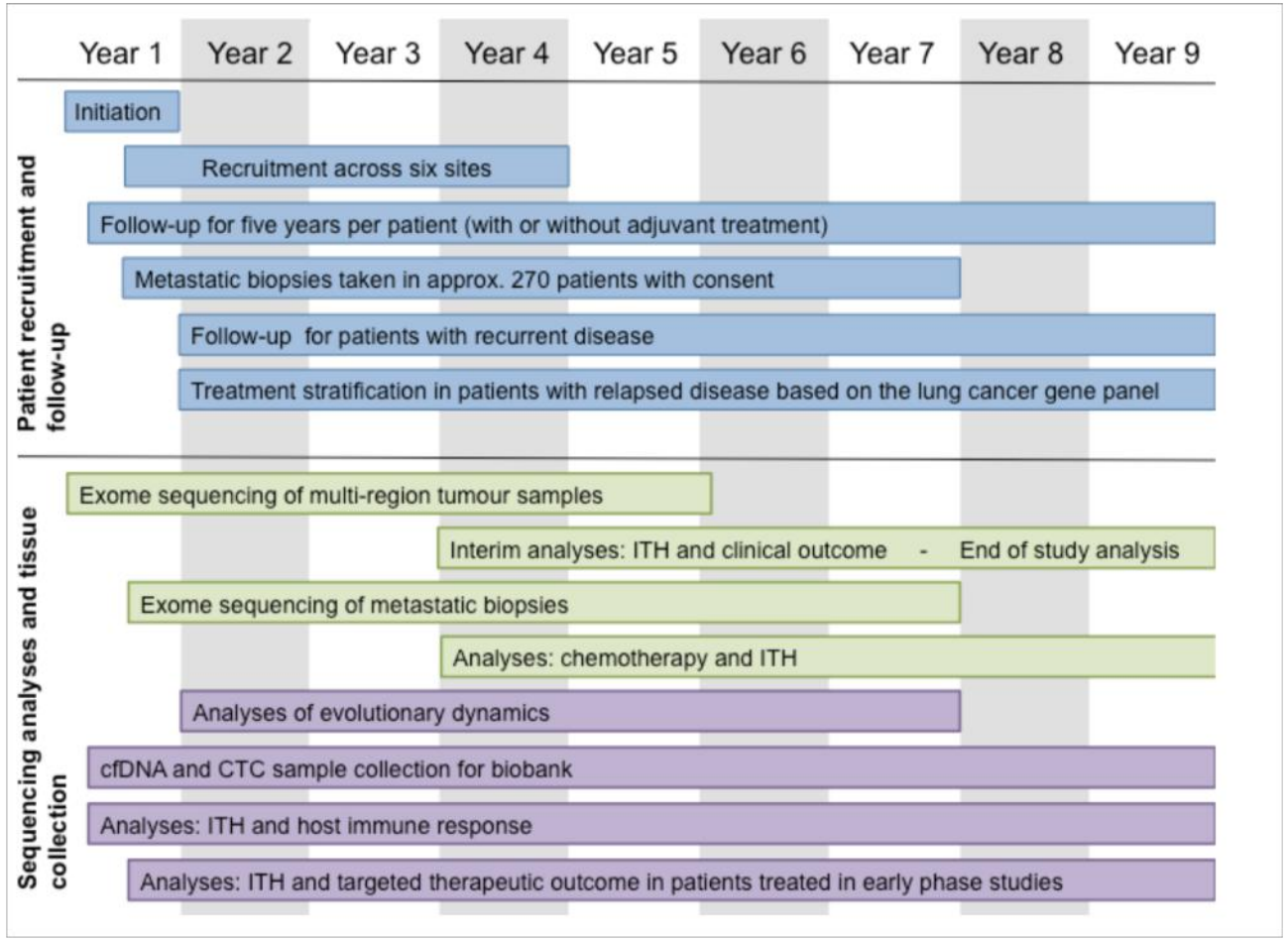
y



z



Tracking Cancer Evolution Through Therapy (Rx) (TRACERx)



TRACERx

tracerx.co.uk

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

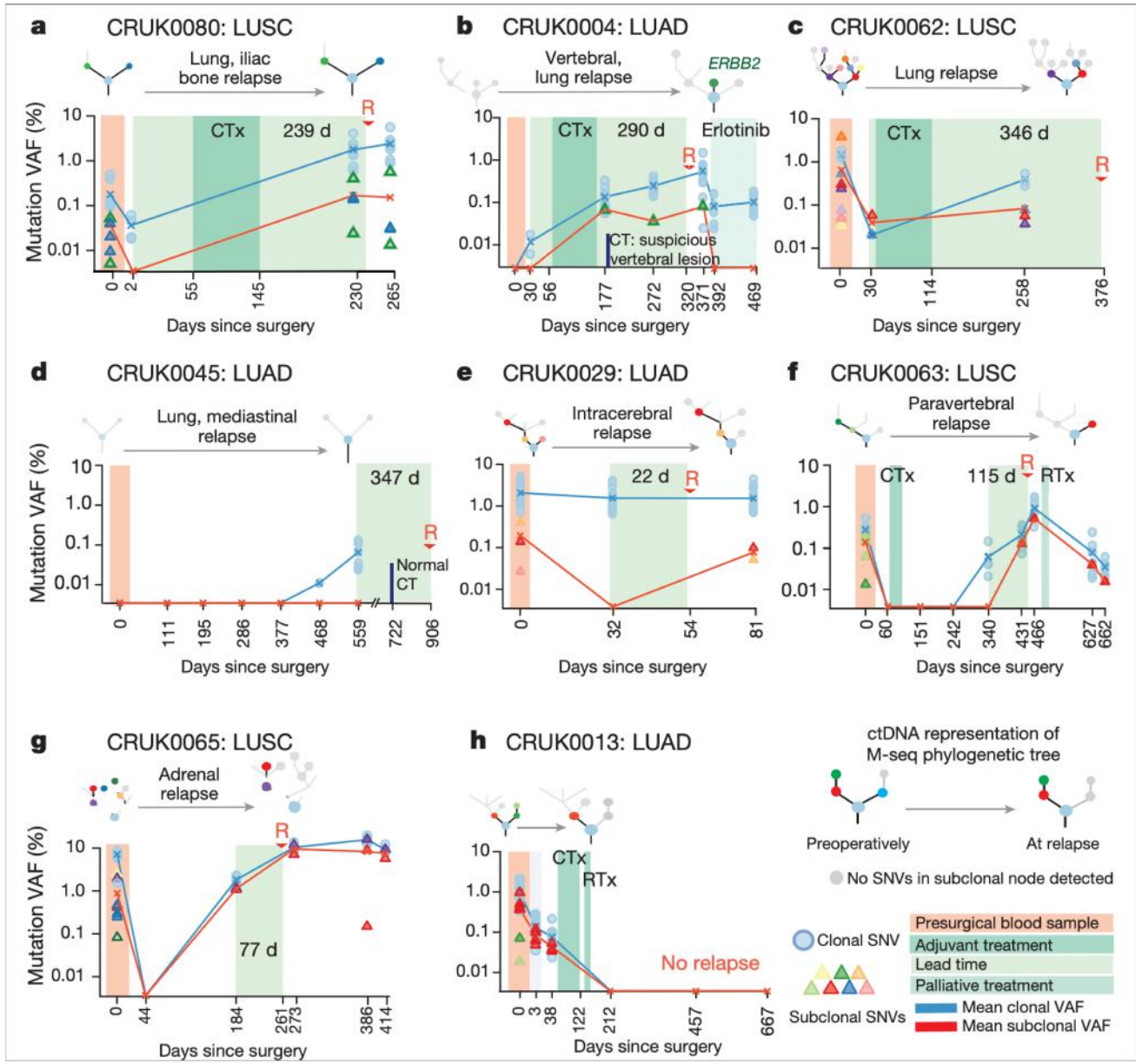
Clonal status of actionable driver events and the timing of mutational processes in cancer evolution

Nicholas McGranahan[1,2,*], Francesco Favero[3], Elza C. de Bruin[4], Nicolai Juul Birkbak[1,3,4,*], Zoltan Szallasi[3,5] and Charles S...

+ See all authors and affiliations

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

Modelling tumour evolution from longitudinal data



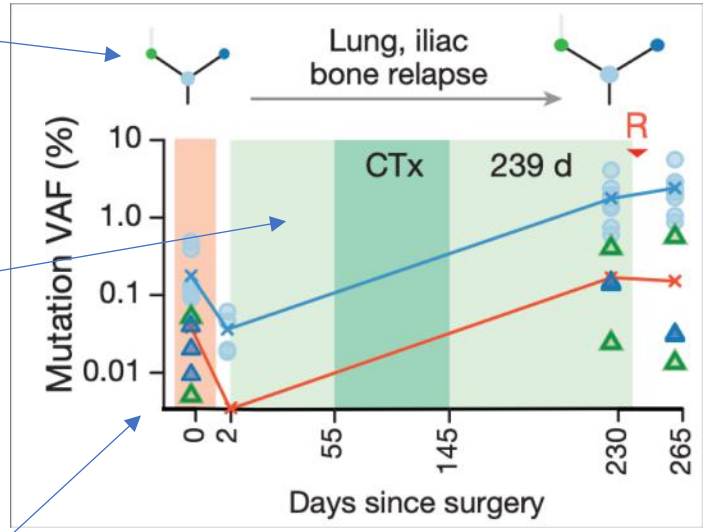
What should we present to clinicians?

Evolution and metastasis

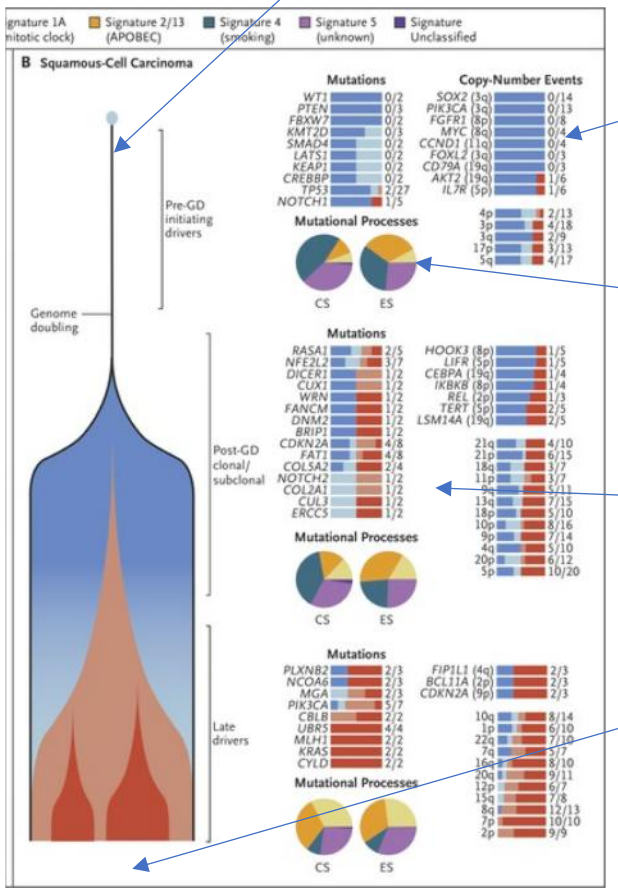
Colours = treatment regimen

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

blood testing for better cancer treatment

John W Cassidy
Co-founder & CEO
John@CCG.ai

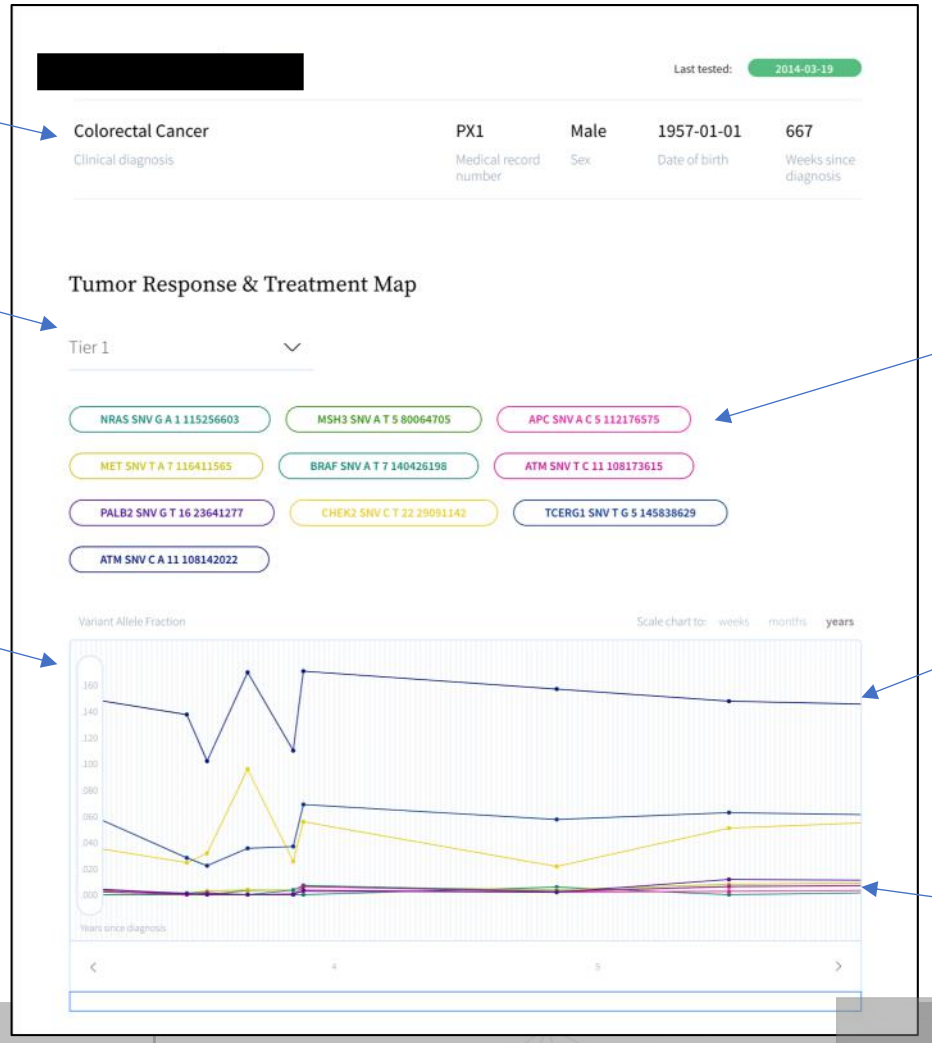
Cambridge Cancer Genomics
Future Business Centre,
Kings Hedges Road,
Cambridge, UK, CB42HY

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

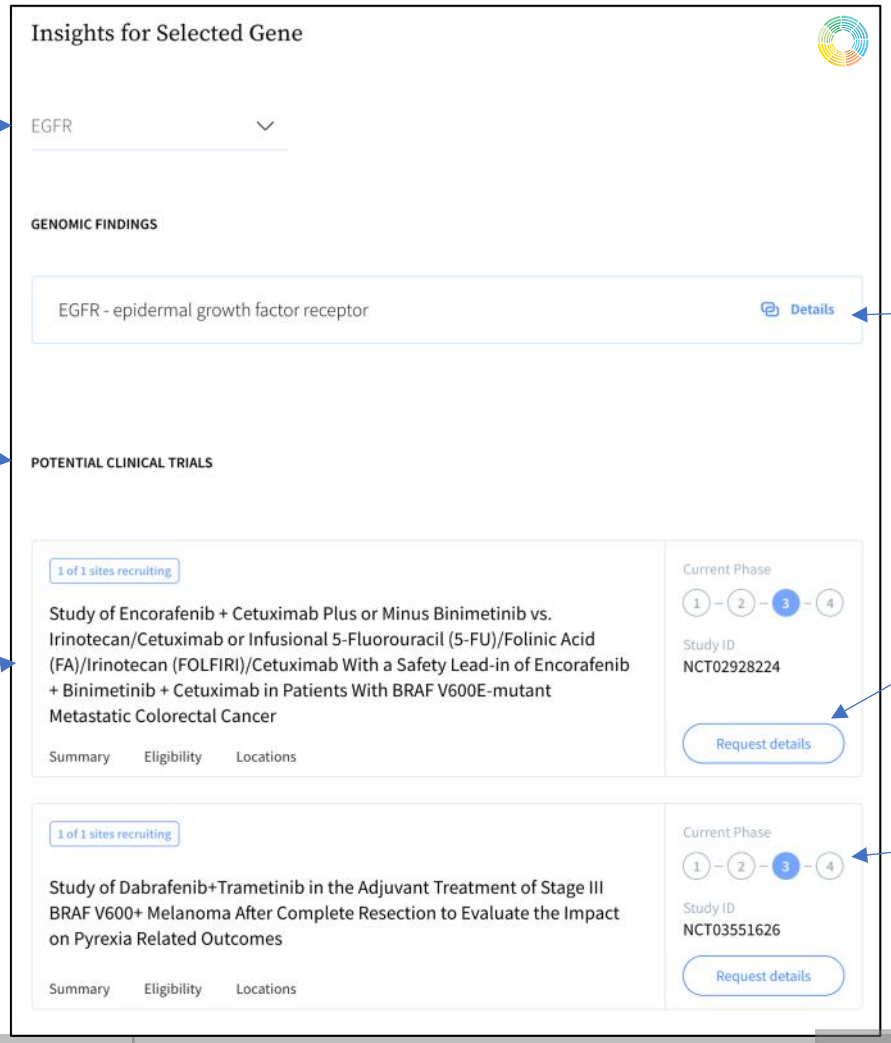
Subclonal mutations not very prevelant in tumour but still potentially important (e.g. drug resistance alleles

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



Much more granular data is only ever one click away

Simple process to make requests to recruiting centres

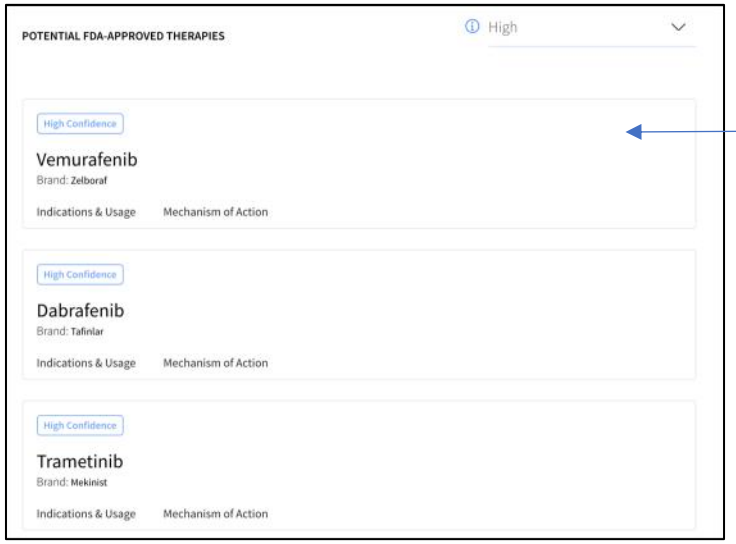
Simple trial enquiry and visual representation of scale of trial (phase)

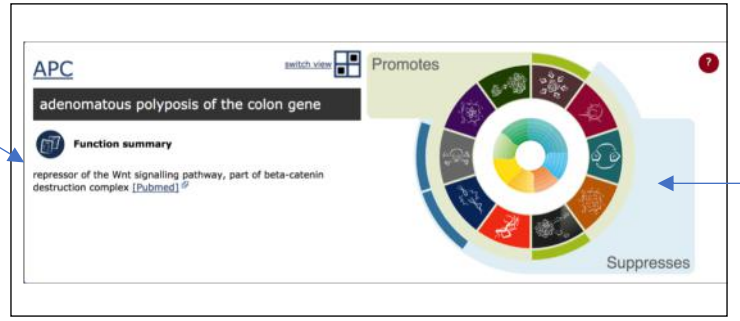
How we are thinking about data presentation in VAF Tracker

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