Genomics in Cancer

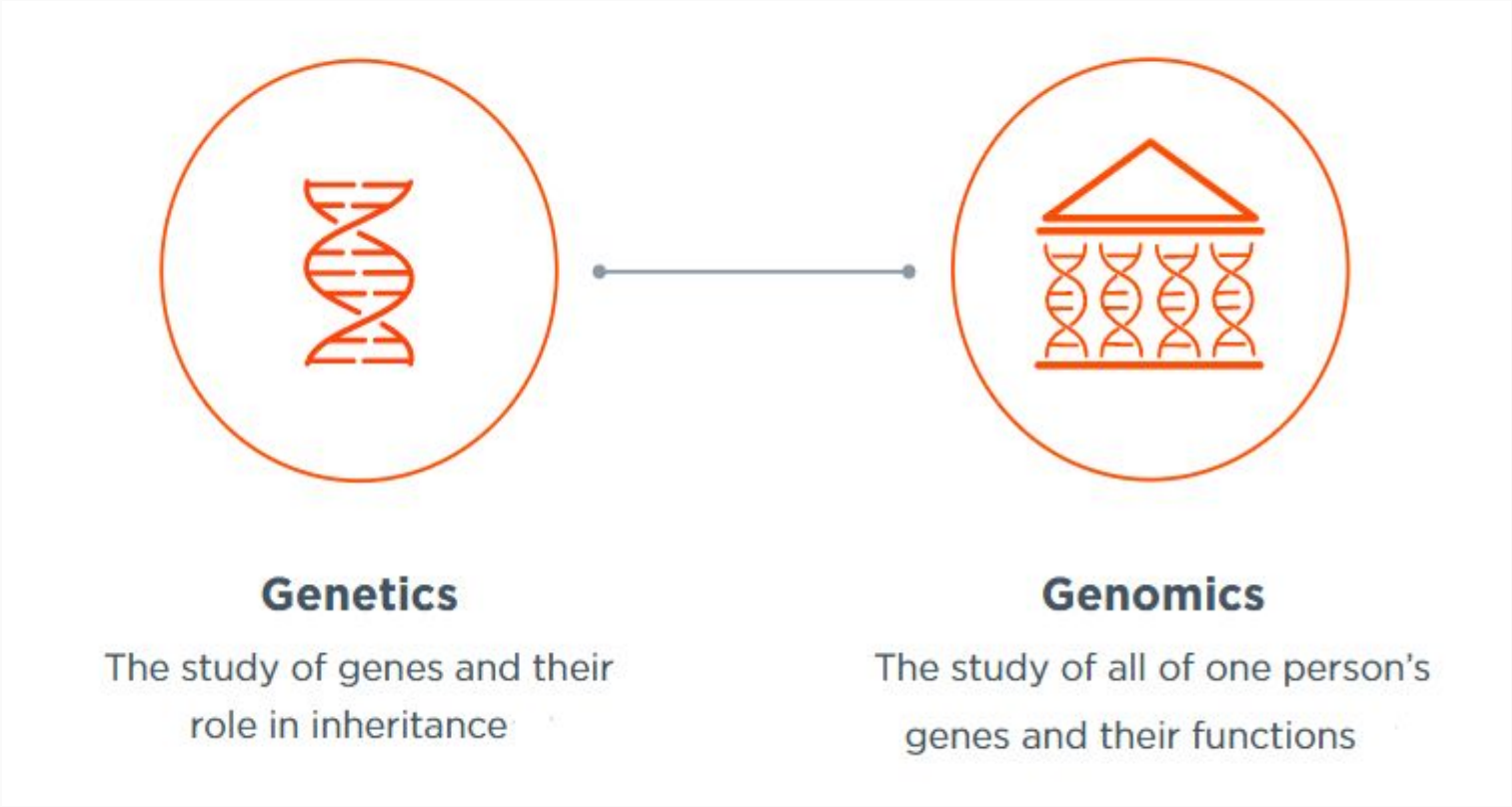
What is it? How is it done? Why is it important?

Karen Wood - Genomics Conditions Partner, Roche UK

Roche arranged session, with participation from Emma Kinloch (Salivary Gland Cancer UK) & Debra Montague (ALK +ive UK).
No financial contributions have been made to the presenters for this session.

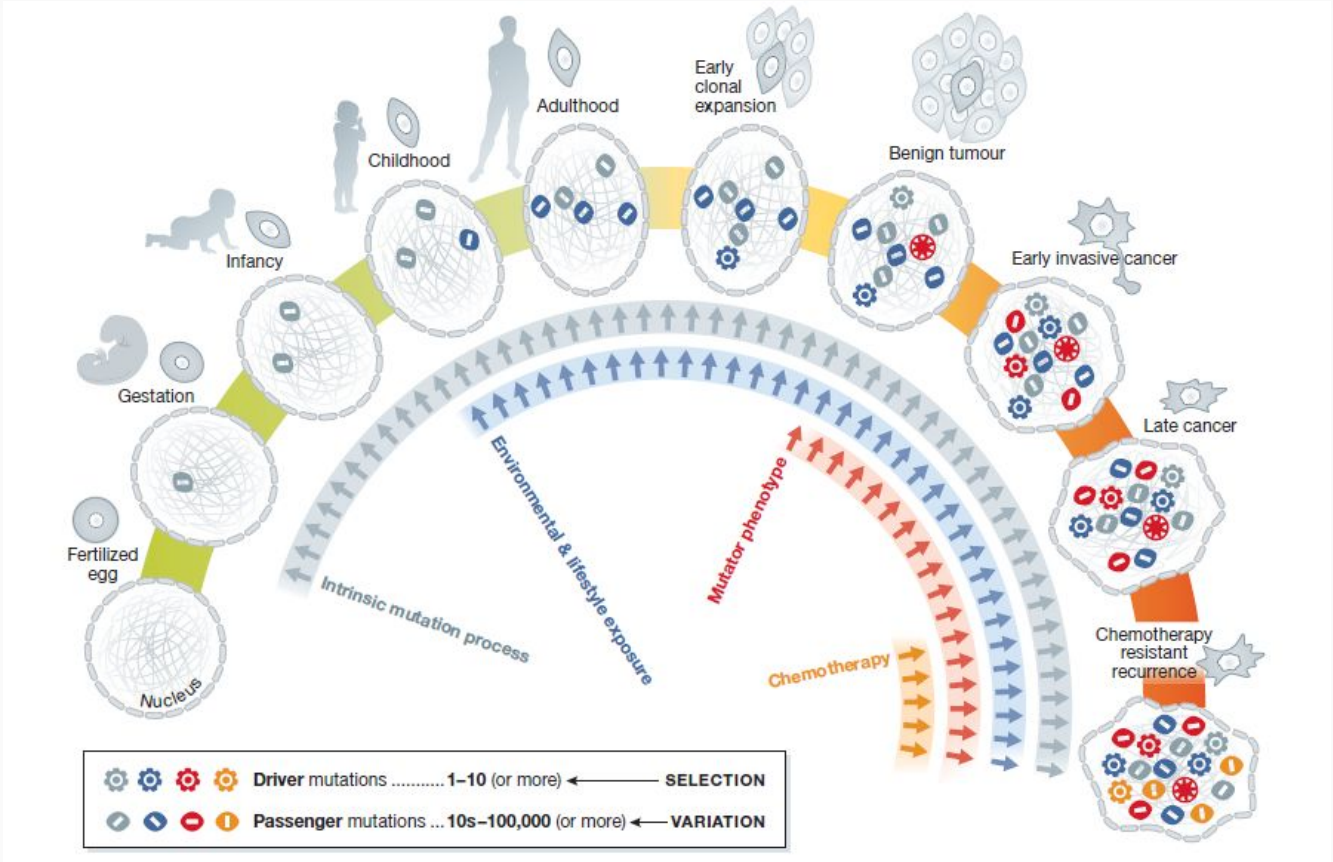
M-GB-00012053 April 2023

Genomics vs Genetics - what's the difference?



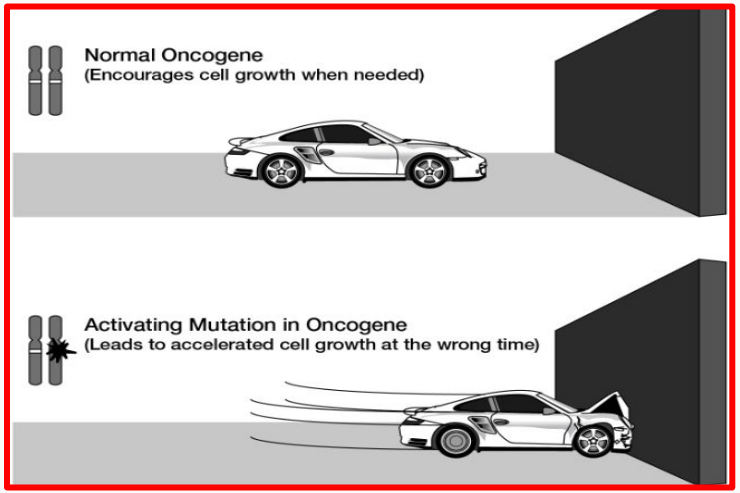
Available at: World Health Organisation definition of genetics and genomics
https://www.genome.gov/about-genomics/fact-sheets/Genetics-vs-Genomics

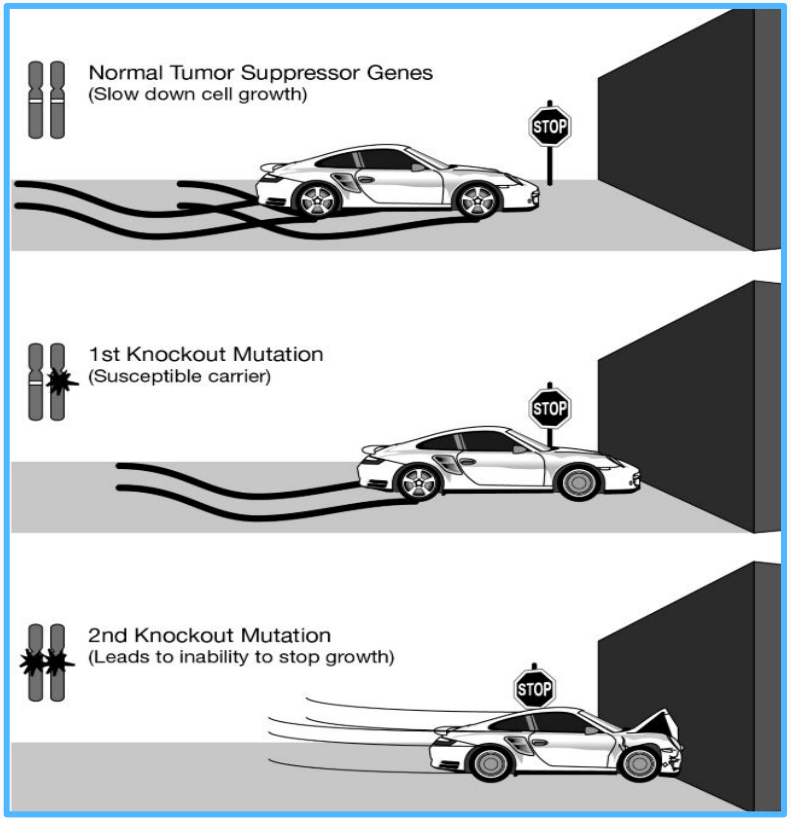
Cancer - ‘acquired’ changes can build up during our lifetime



Stratton, M.R. (2013) *EMBO Mol Med* https://pubmed.ncbi.nlm.nih.gov/23339072/

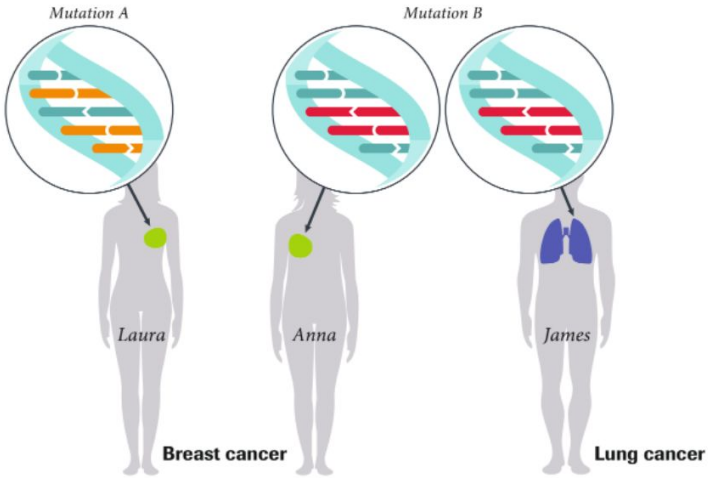
How can these changes lead to cancer?



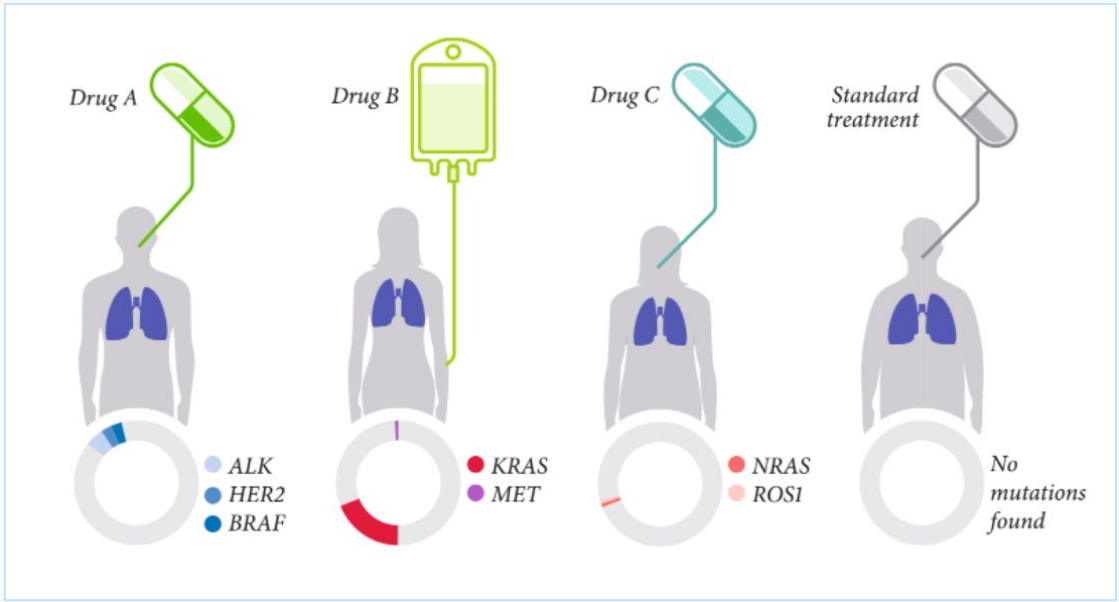


https://www.genome.gov/sites/default/files/tg/en/illustration/tumor_suppressor_gene.jpg

Cancers are unique

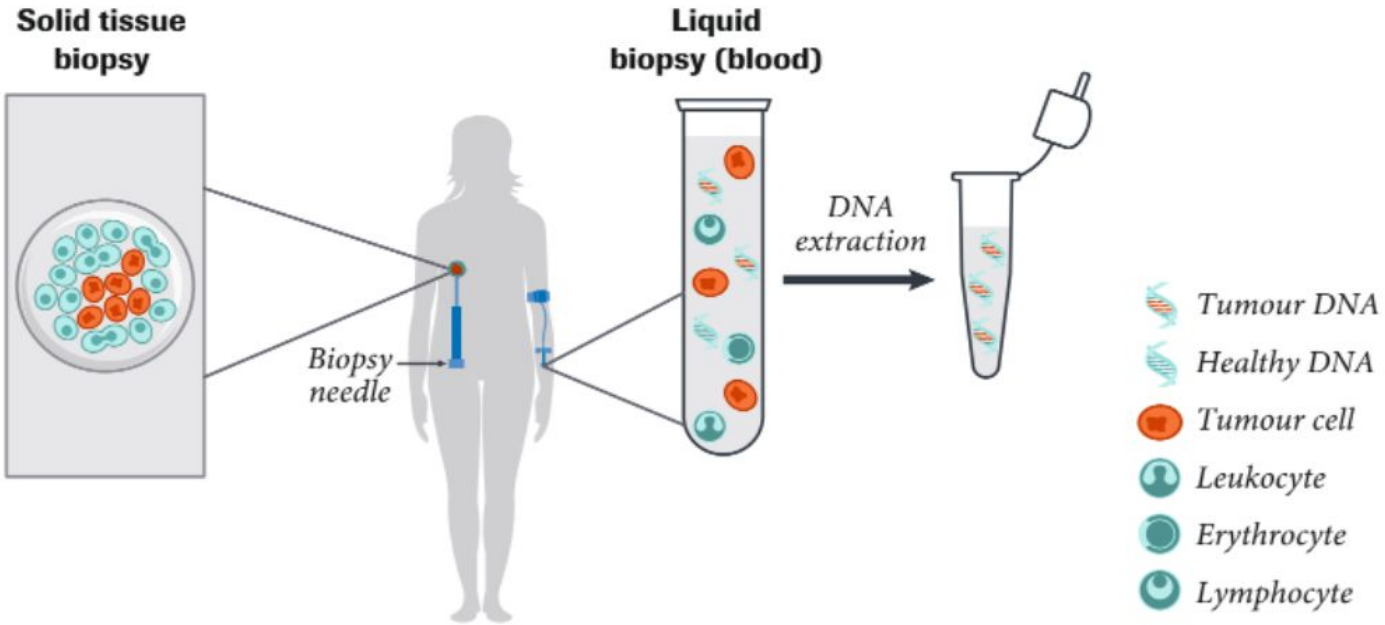


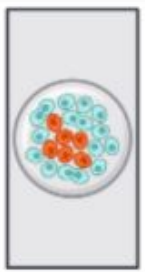
Heim, D., et al. (2014) Int J Cancer 135:2362-9.



NSCLC NCCN Guidelines for Patients 2018;NSCLC NCCN Guidelines. Version 4.2017; Ohashi, K,. et al. (2013) Clin Cancer Res 19:2584-91. Baumgart, M. (2015) Am J Hematol Oncol 11(6):10-13.

How do we test?

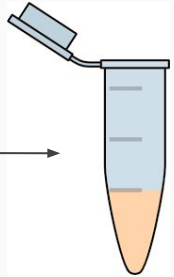




Tumour Sample - from surgery or biopsy

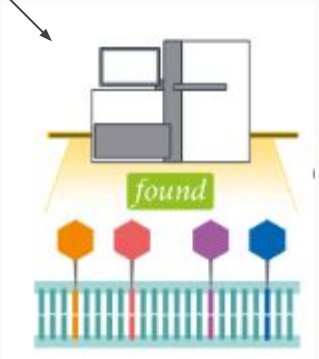
Liquid Sample - usually blood

Sample examined by a **pathologist to** ensure it is able to be 'profiled' (sufficient quantity/quality)



DNA is extracted

DNA is separated from all other cell parts.



Sample goes through **comprehensive genomic profiling-** normal cell DNA is compared to cancer DNA to find changes that could have caused the cancer

Genomic Profile

Data analysed - experts combine their knowledge with cancer information database to confirm and describe changes found

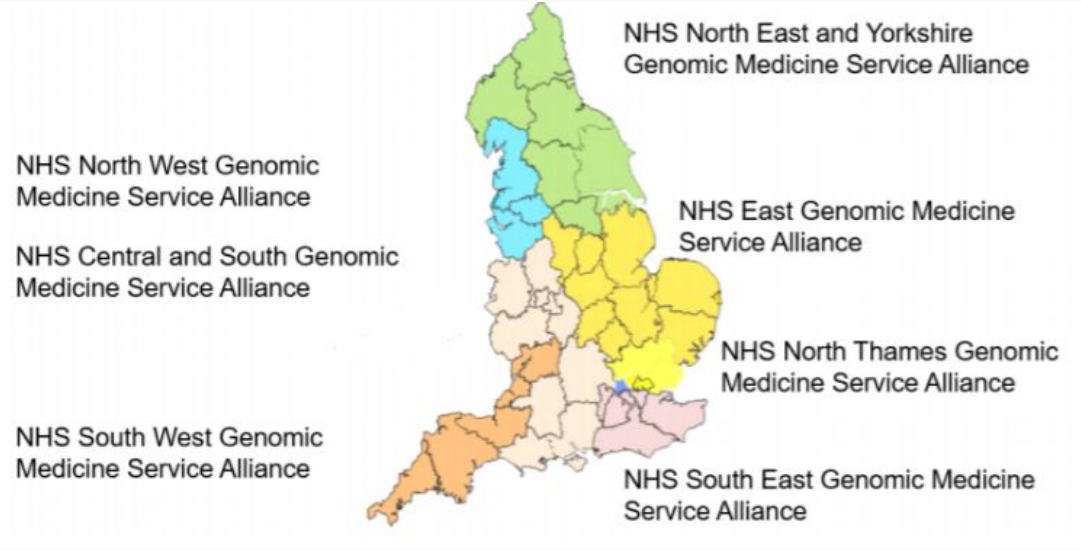
Report -sent to your doctor with changes found, and possible treatments or trials.

What tests and where do they happen?

Group	Specialist Test Group	CI Code	Clinical Indication Name	Test Code	Test Name	Target Gene(s) [essential]	Test Scope	Technology
Solid Tumours (Adult)	Core	M1	Colorectal Carcinoma	M1.1	Multi-target NGS panel - small variant (KRAS, NRAS, BRAF)	KRAS, NRAS, BRAF	Small variant detection	Panel
				M1.2	KRAS hotspot	KRAS	Small variant detection	Simple targeted mutation testing
				M1.3	NRAS hotspot	NRAS	Small variant detection	Simple targeted mutation testing
				M1.4	MSI Testing	N/A	Microsatellite instability analysis	Microsatellite instability
				M1.5	MLH1 promoter hypermethylation	MLH1	Methylation analysis	Targeted mutation testing
				M1.6	Multi-target NGS panel - structural variant (NTRK1, NTRK2, NTRK3)	NTRK1, NTRK2, NTRK3	Structural variant detection	Panel
				M1.7	DPYD hotspot	DPYD	Small variant detection	Simple targeted mutation testing
				M1.9	Multi-target NGS panel - small variant (MLH1, MSH2, MSH6, PMS2, POLE, POLD1)	MLH1, MSH2, MSH6, PMS2, POLE, POLD1	Small variant detection	Panel
Solid Tumours (Adult)	Core	M2	Ovarian Carcinoma	M2.1	Multi-target NGS panel - small variant (BRCA1, BRCA2, SMARCA4)	BRCA1, BRCA2, SMARCA4	Small variant detection	Panel
				M2.3	Multi-target NGS panel - structural variant (NTRK1, NTRK2, NTRK3)	NTRK1, NTRK2, NTRK3	Structural variant detection	Panel
				M2.5	HRD status (either positive for BRCA1 and/or 2, or HRD positive)	BRCA1/2 and/or genomic instability	Mutational signature detection	Panel
Solid Tumours (Adult)	Core (PILOT)	M233	High Grade Ovarian Carcinoma (WGS PILOT)	M233.1	WGS Germline and Tumour	All including burden / signature	All variant types	WGS

https://www.england.nhs.uk/publication/national-genomic-test-directories/

NHS Genomic Medicine Service



Devolved Nations Testing Services

AWMGS
ALL WALES MEDICAL GENOMICS SERVICE

Genomics service centralised in Cardiff for whole of Wales.
https://medicalgenomicswales.co.uk/

Genomics centre in Belfast for the whole of Northern Ireland.
https://www.qub.ac.uk/research-centres/PMC/Genomics/

NHS National Services Scotland

Four regional centres based in Aberdeen, Dundee, Edinburgh and Glasgow
https://www.nss.nhs.scot/specialist-healthcare/specialist-services/genetic-and-molecular-pathology-laboratories/

What is targeted therapy?

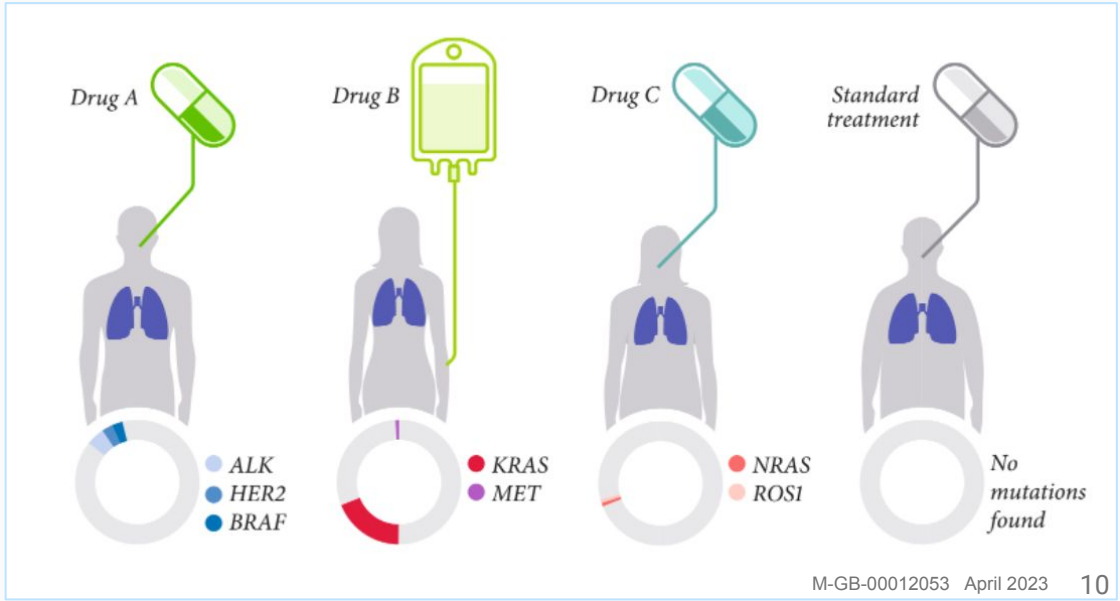
Personalised medicine can involve the use of targeted therapies

Targeted therapies work by **acting on specific DNA changes or proteins** involved in the growth, development and spread of cancer.

They can:

- Block/turn off the signals that tell cancer cells to grow and divide
- Stop making new blood vessels to feed the cancer cells
- Kill the cancer cells, by:

– Changing proteins within cancer cells
– Delivering a substance that kills cancer cells
– Triggering your immune system to kill cancer cells (also called Immunotherapy)



What will the results mean?

DNA changes found in the cancer may:

- Be linked to a licensed treatment *funded* by the NHS
- Be linked to a licensed treatment but *no funding* is available via the NHS
- Might indicate the possibility of a *trial* looking at treatments as yet unlicensed.
- Indicate *no suitable* targeted treatments or trials are available

- Even if a treatment is suggested, there are no guarantees that it will work.

- This is because cancer is a complex disease driven by multiple factors and responses to therapies can vary from patient to patient.

Links for further information for Patient Groups

‘From Testing to Targeted Treatments’ - Adaptable resources for Patient Groups including a question and answer guide for patients.

https://precisionmedicine.synapseconnect.org/resources/targeted-therapy-for-cancer-adaptable-resource

A Roche resource for Patient Groups including a slide kit on Personalised Cancer Care.

https://www.ieepo.com/en/useful-resources/phc-community-hub/PersonalisedCancerCareToolkit.html

Questions??

Why are genomics important to rare cancer patients?

http://www.salivaryglandcancer.uk/

Emma Kinloch, 3rd May 2023

Why is it important to you

Many rare cancers are poorly understood in terms of their biology, and so no targeted treatments are available

Understanding the genomic profile of your tumour can help drive forward research and understanding of your cancer. With more samples available to be studied, more patterns in cancers can be seen.

Comprehensive characterisation of the genomic alterations using matched clinical information with genomic data, can help detection of changes which could be potentially targeted by therapeutics
e.g. Tumour Mutational Burden (‘TMB’).

Having your tumour genomic information stored in a central place
e.g. a specialist Hub with a biobank, or patient registry, means you are contributing to this understanding.

Salivary Gland Cancer .UK

Why is it important to you

When new 'targets' or drugs to 'target the targets' become available, how will you know and be included in any trials?

Having your tumour genomic information stored in a central place e.g. a specialist Hub with a biobank, or patient registry, means you can be found, and recalled for a trial.

Whole genome sequencing is now available on the NHS – but there is not a guaranteed recall mechanism currently.

If you go into a clinical trial then part of the pre-screen will include a genomic test but it's important to understand what panel is being used.

Cancer vaccines.

Salivary Gland Cancer .UK

Why is it important to you

What else do your patients need to know?
e.g. how do they get referred?

Strongly encourage information specific to your cancer, to be available to your patients.

SGC UK put downloadable co-designed leaflets on our website:

Salivary Gland Cancer .UK

Gene profiling or tumour profiling or genomic testing - Salivary Gland Cancer UK

Thank you for listening

Any Questions?

www.salivaryglandcancer.uk

emma.kinloch@salivaryglandcancer.uk

Twitter/FB/Insta: @SGCancerUK

www.salivaryglandcancer.uk/get-involved/join-our-network/

ALK Positive Lung Cancer (UK)

A patient-focused charity that

SUPPORTS **EMPOWERS** **ADVOCATES**

ALK Positive Lung Cancer (UK)

A patient-focused charity that

Supports Empowers Advocates

- Patients progress on targeted treatments
  - Progression due to either –
    - The treatment stops working
    - Oncogene driver mutates to another oncogene driver
- Inconsistent ability to access a re-biopsy across the UK
- Patients needed confidence to challenge their Oncologist
  - Need a resource to understand Biomarkers

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ORIGINAL RESEARCH

Biomarker Testing

DO I HAVE THE RIGHT TO BIOMARKER TESTING?

As a patient, you have the right to:

- **Receive optimal care and engage in shared decision-making** with your healthcare team when discussing your personalised treatment plan.
- **Access and understand your biomarker test results,** which have critical information about whether you may respond to treatment.
- **Request a print or electronic copy of your biomarker testing report** for your medical records; they can be helpful in seeking a second opinion.
- **Seek a second opinion** about your treatment options.

WHAT QUESTIONS SHOULD I ASK MY HEALTHCARE TEAM BEFORE AND AFTER BIOMARKER TESTING?

Understanding diagnostic procedures

- What diagnostic tests do you recommend for my condition and why? What can the test results tell me about my condition?
- What will the tests involve? Are they available to me? How much time/energy will it require from me?
- When and where will I have my testing completed? Will all testing be completed now or will some be done later?
- Is there a waiting period to have any tests done? How long will it take to get the results?
- How will I be given my results? Who can help me understand them? Can I have a copy of my test results?

Understanding treatment options

- What does each treatment aim to do and how effective is it likely to be? Is there anything I can do myself to help?
- Do I need to have further tests before initiating the treatment? Will I have to wait to get all the test results back before starting treatment?
- When will the treatment start? Is there time to wait and see, and time for me to consider my options?
- What are the potential side effects of the recommended treatments? How might they affect my quality of life? What can we do to manage them?
- Will the recommended treatment interact with other medications I am taking for my condition or vice versa? How can we manage this?
- How do I take my treatment and how often? How long will it last?
- I would like to get a second opinion before I commit to my treatment plan. Can you suggest a suitable specialist?
- Is there any psychological/social/emotional support or tools available during my treatment to support me and/or my family members?
- Will I need to contribute financially towards my tests? If so, are there financial assistance programs or resources you can recommend (in countries where relevant)?

HOW DO I GET ADDITIONAL RESOURCES AND SUPPORT?

You might like to contact the charity ALK Positive Lung Cancer (UK) via their website at www.alkpositive.org.uk.

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