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Arporn Wangwiwatsin, PhD
Training Team Member

Introduction to Cancer Genomics:
Foundation and Frontier of Cancer Medicine

26th October 2025

Introduction to Cancer Genomics

Foundation and Frontier of Cancer Medicine

Presented by:
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Cancer Genome Analysis – Asia 2025

With presentation content mostly made by Nyasha Chambwe (Feinstein Institutes for Medical Research)

KKU KHON KAEN UNIVERSITY CARE Cholangiocarcinoma Research Institute MDKKU คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น FACULTY OF MEDICINE KHON KAEN UNIVERSITY

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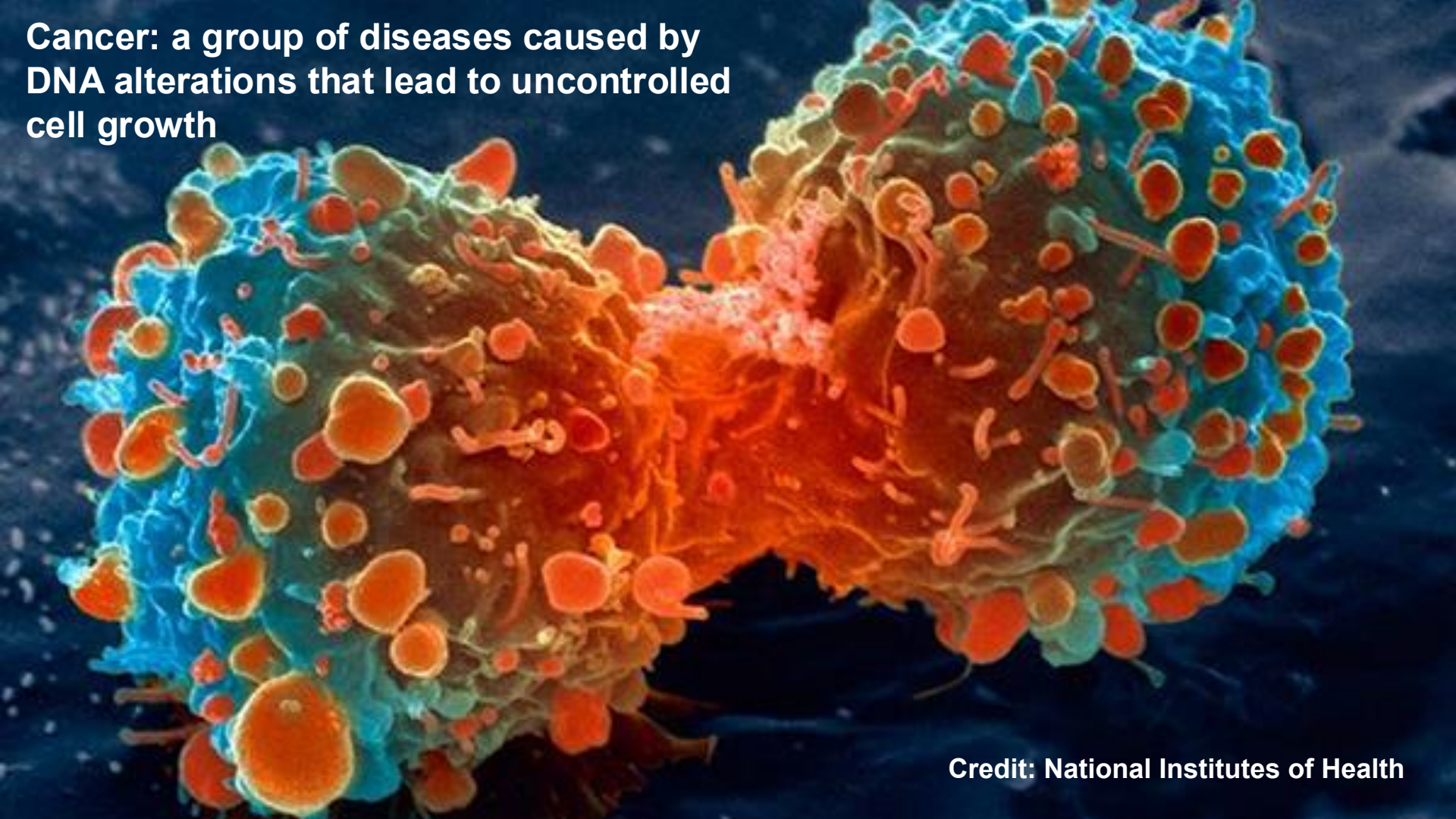
Overview and objectives

- Why cancer genomics matters
- How we decode cancer genomes
  - What to sequence – types of tissues, types of genomes
  - How to sequence
  - Finding meanings
- From genome to clinic
- Forward look


Cancer: a group of diseases caused by DNA alterations that lead to uncontrolled cell growth
Credit: National Institutes of Health

A Brief Guide to Genomics

NHGRI FACT SHEETS
genome.gov

- Biological field focused on studying **all the DNA of an organism** — that is, its genome
- Includes *identifying* and *characterizing* all the genes and functional elements in an organism's genome as well as *how they interact*

https://www.genome.gov/genetics-glossary/genomics

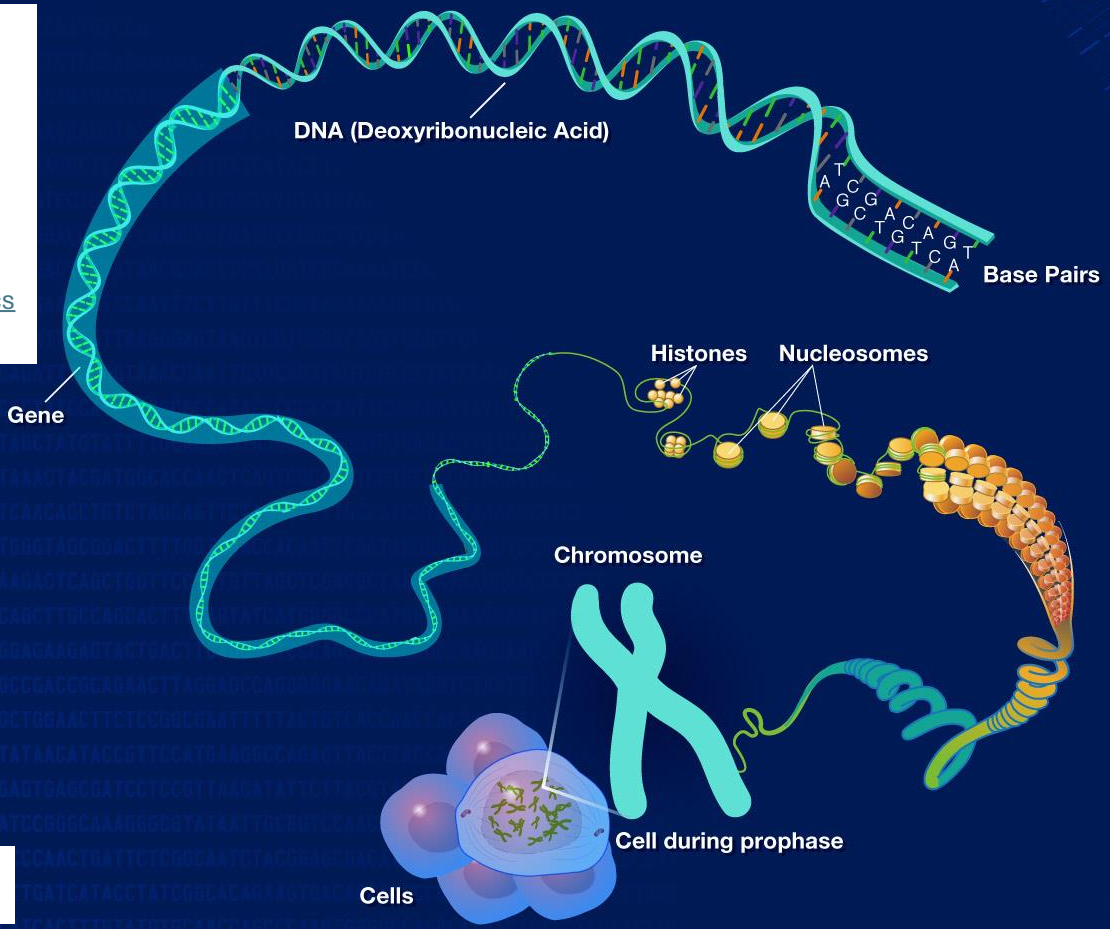
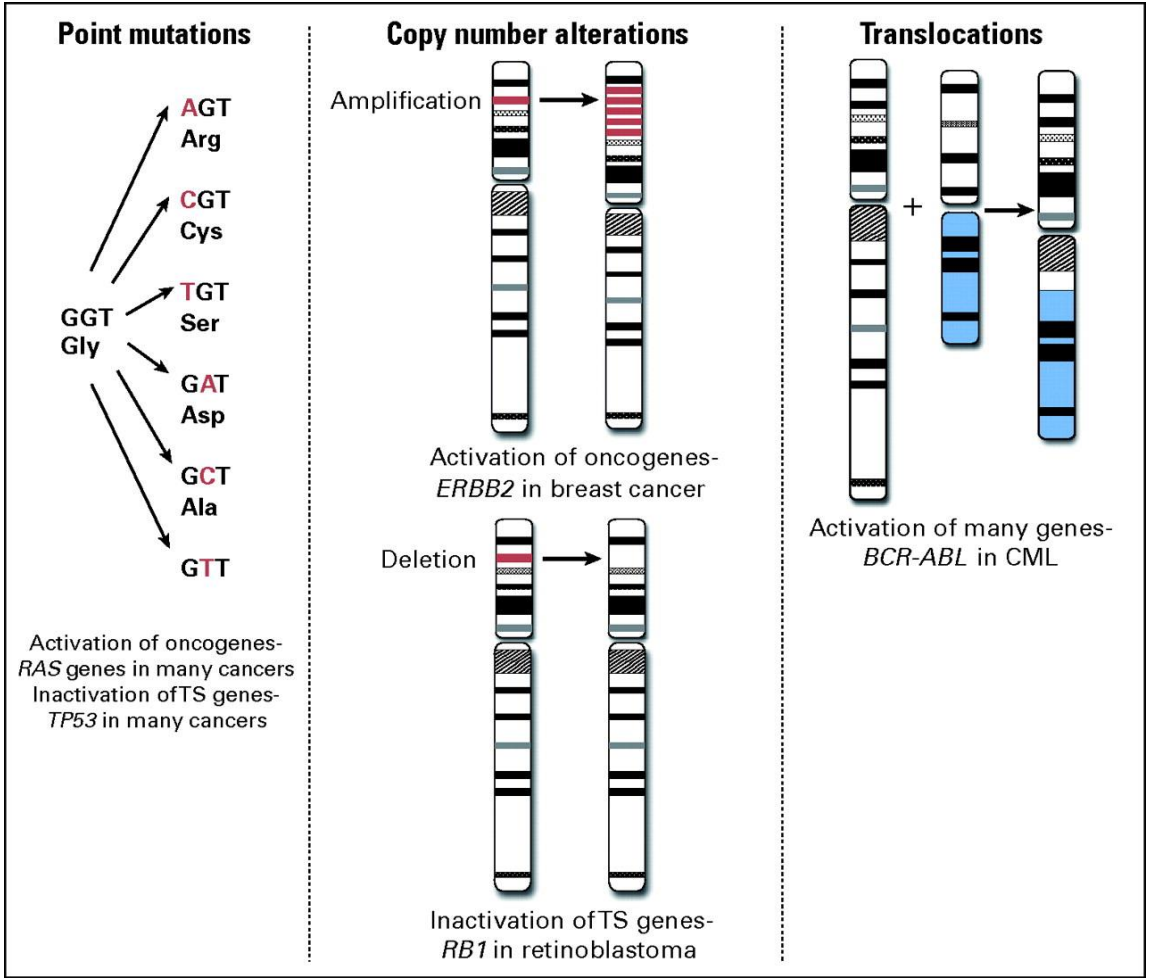


Image source: https://bit.ly/3AMuwok

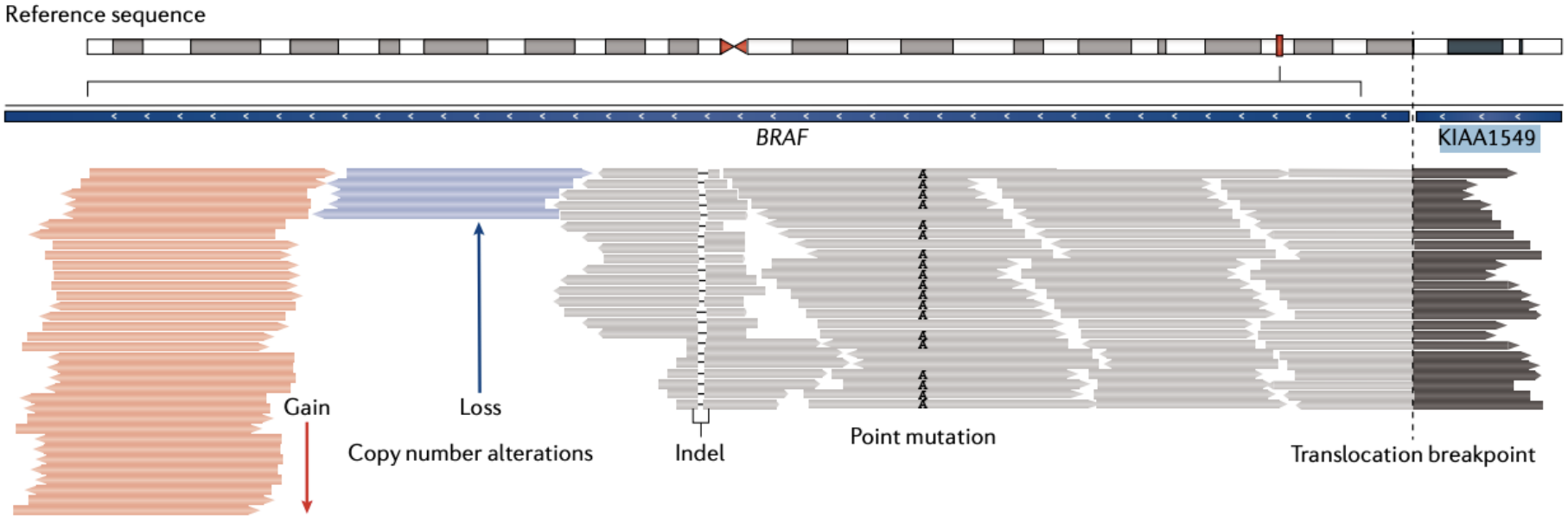
NIH National Human Genome Research Institute

Example of genomic alterations that give rise to cancer

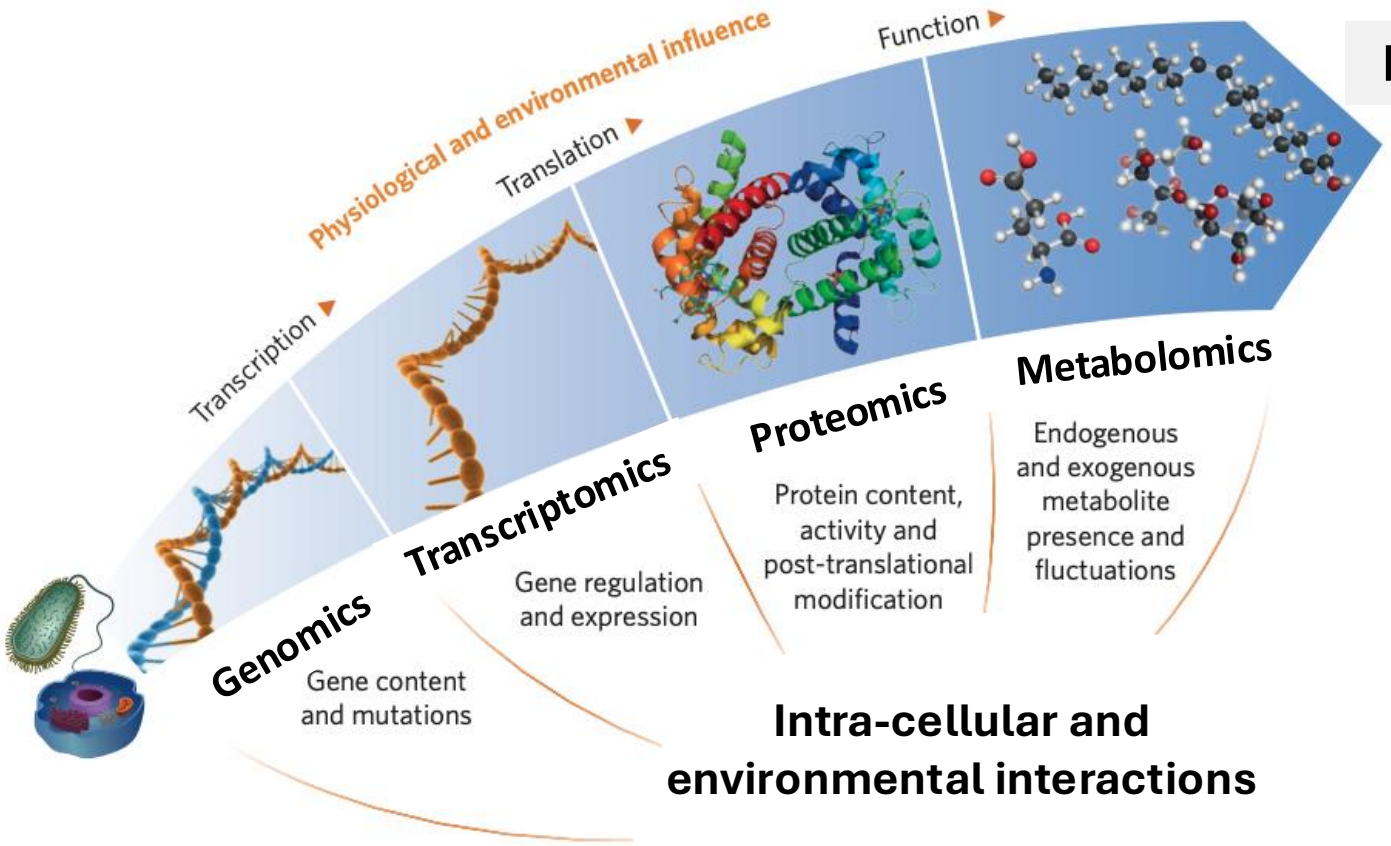


Macconaill LE, Garraway LA. J Clin Oncol. 2010

Example of genomic alterations that give rise to cancer

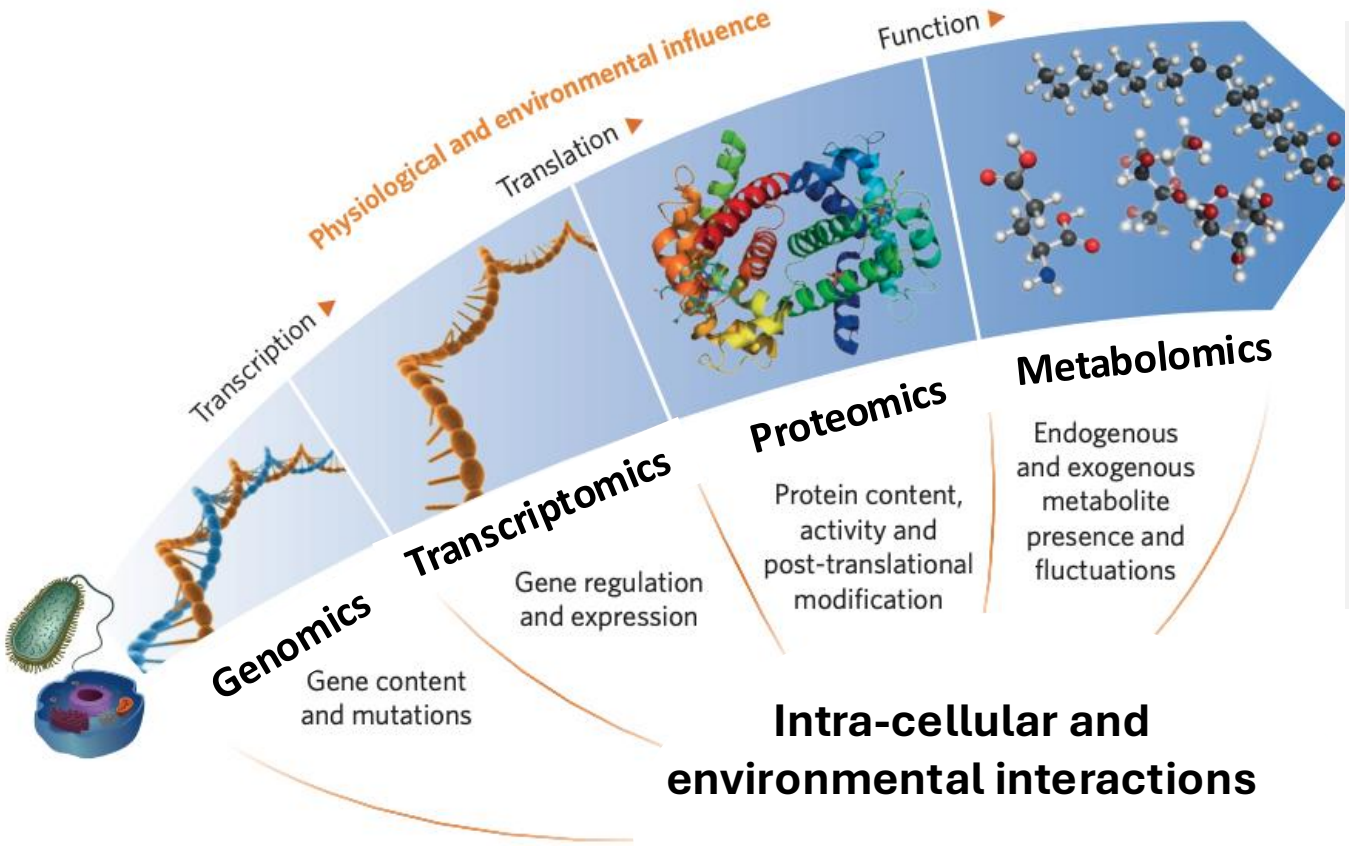


Chakravarty D et al. Nat Rev Genet. 2021



Disease outcomes

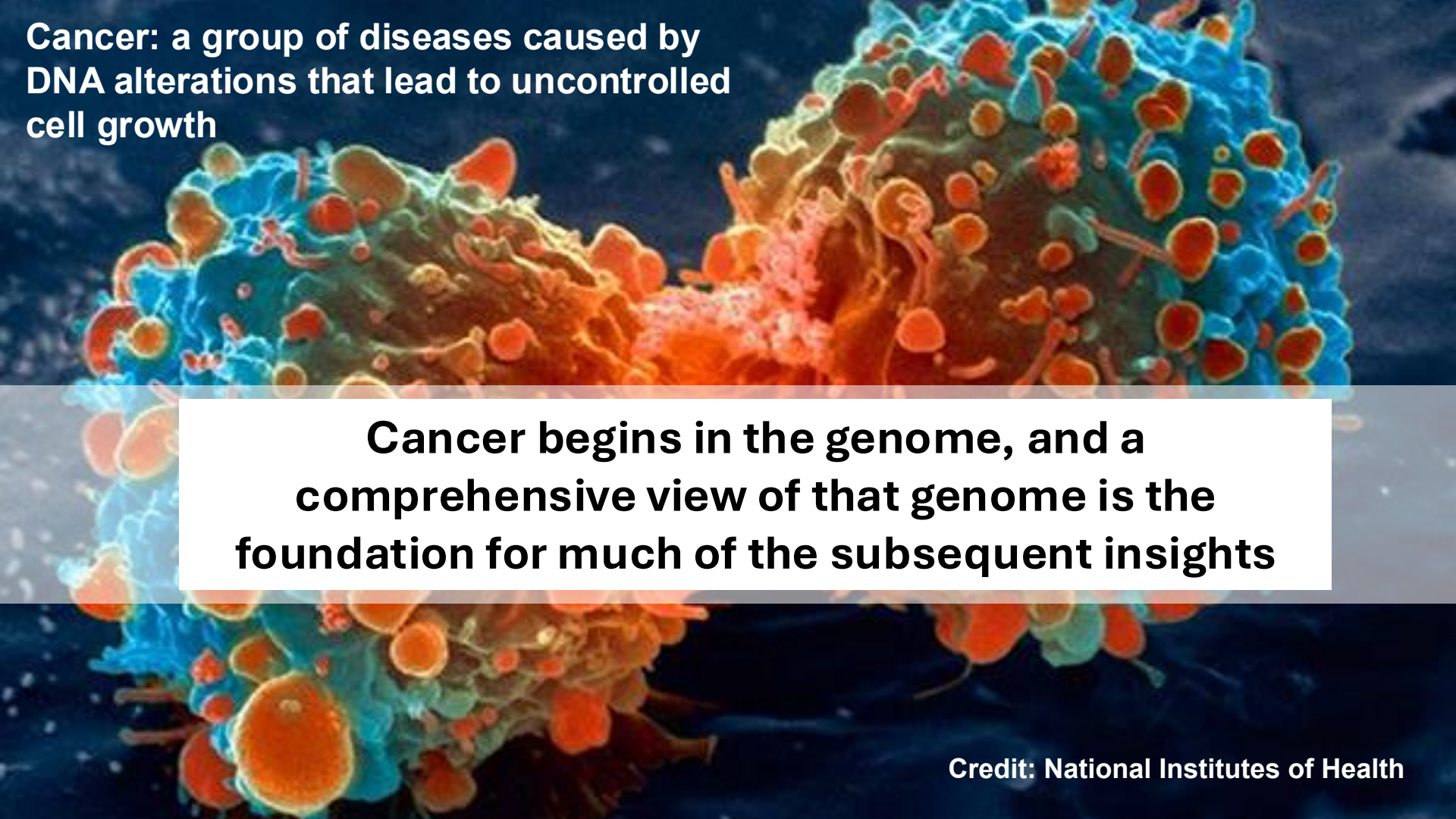
Jansson JK et al. Nat Microbiol. 2016



Disease outcomes

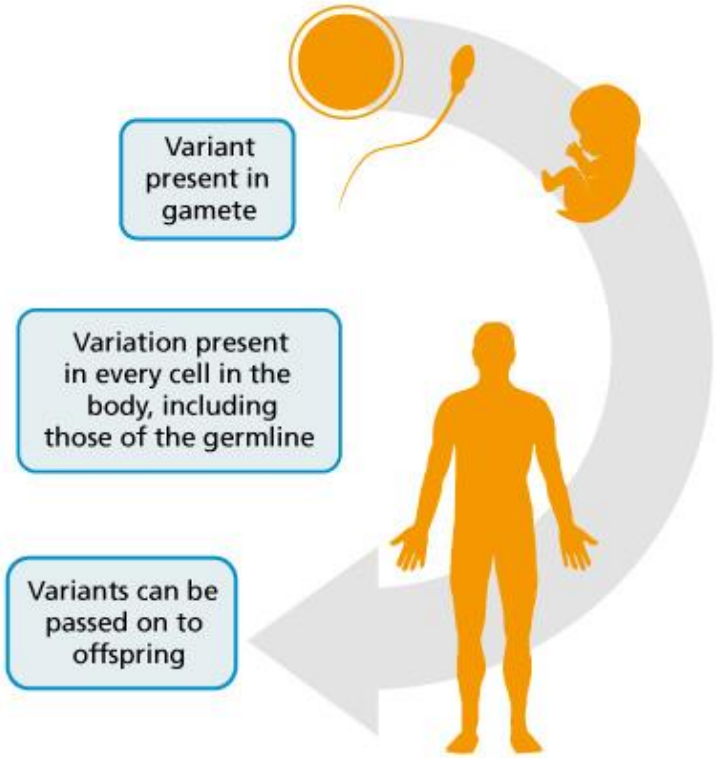
- **Cancer risk** (heredity predisposition)
- **Diagnosis and classification** (molecular taxonomy)
- **Therapeutic choice**
- **Prognosis and recurrence**

Jansson JK et al. Nat Microbiol. 2016


Cancer: a group of diseases caused by DNA alterations that lead to uncontrolled cell growth
Cancer begins in the genome, and a comprehensive view of that genome is the foundation for much of the subsequent insights
Credit: National Institutes of Health

What we mean by “Cancer Genome”

Inherited (germline) genomics variants vs acquired (somatic) variants



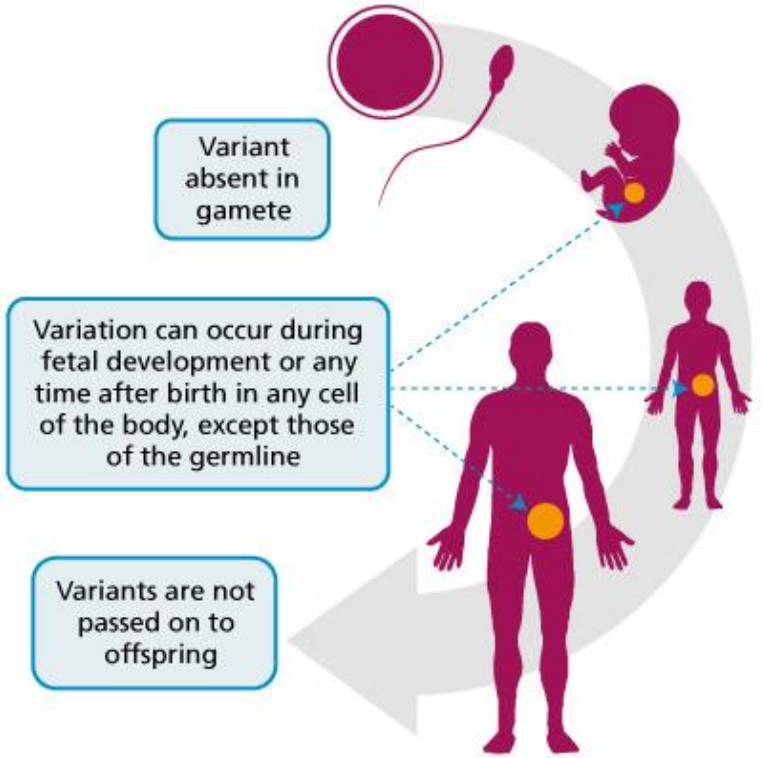
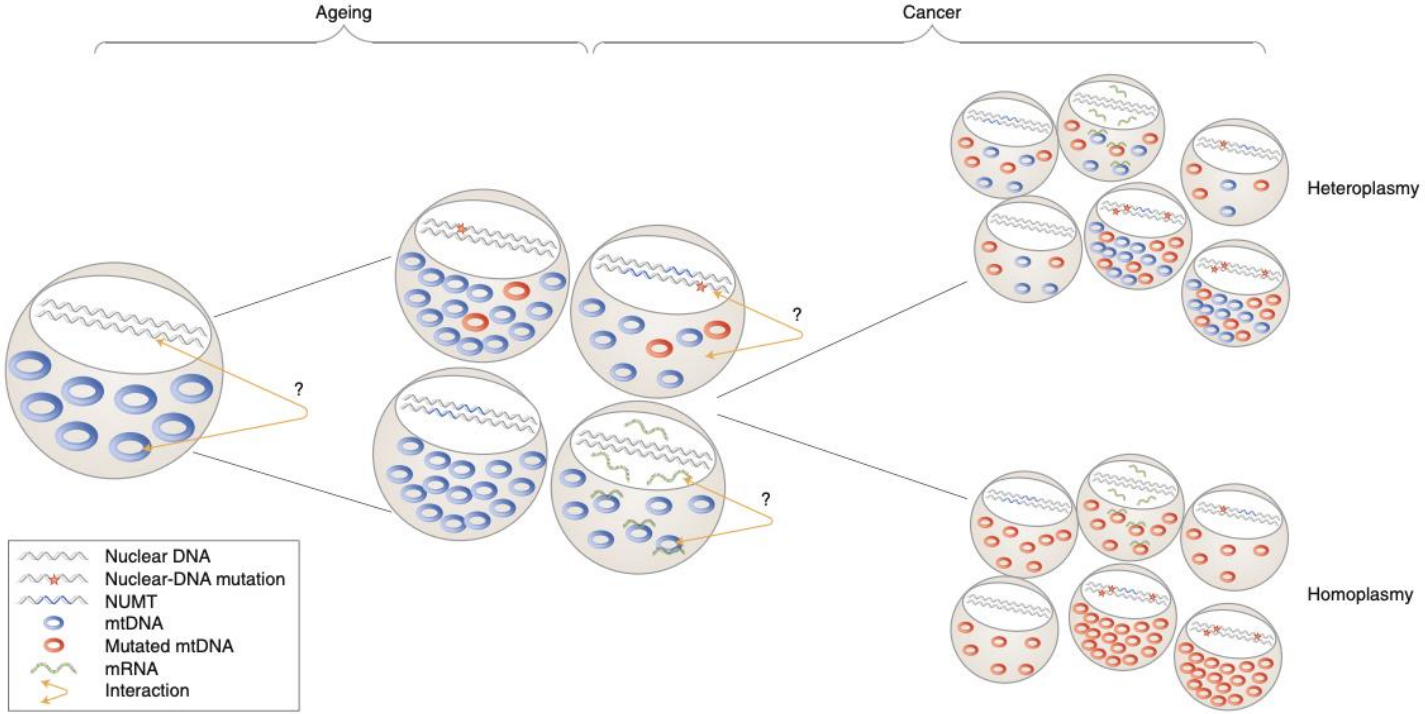


Image source: https://bit.ly/3cTawbZ

Beyond chromosomal DNA

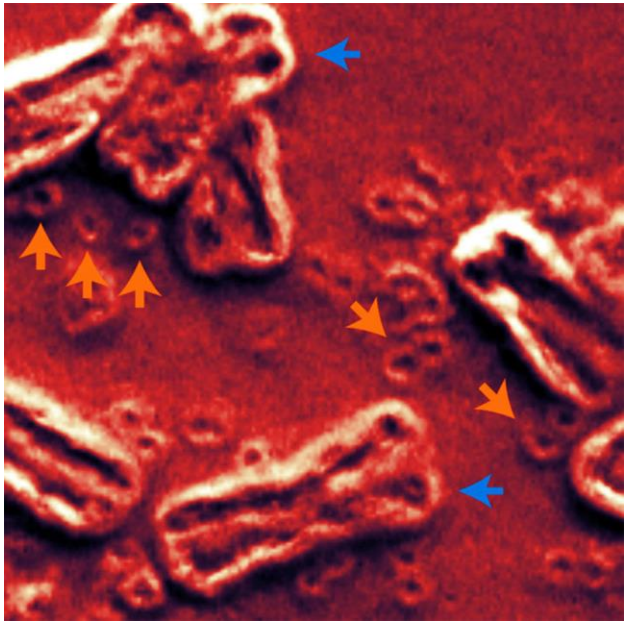
- mtDNA: mutations and heteroplasmy affect cell activities.

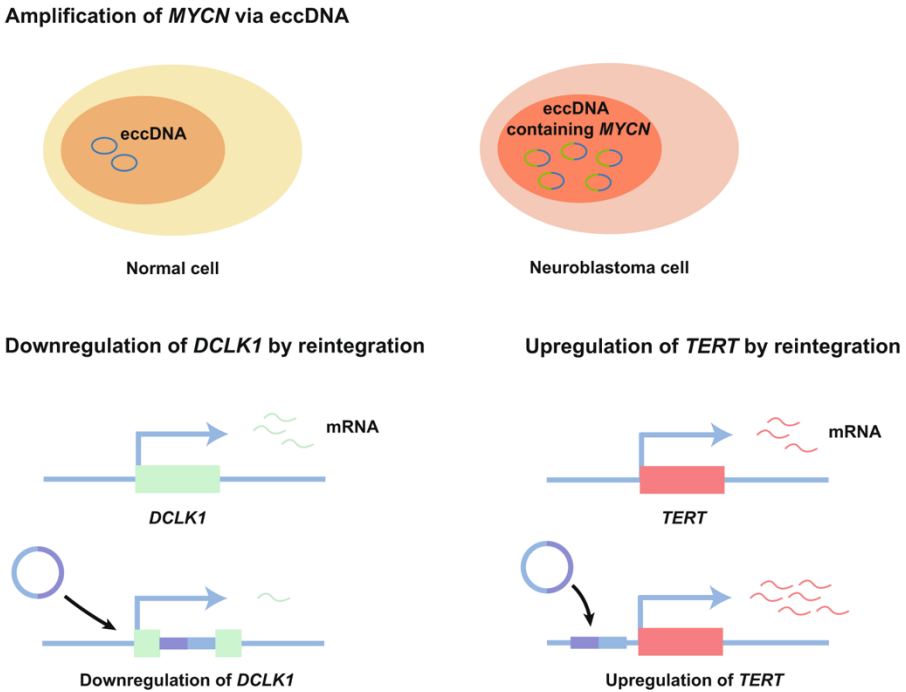


Wei W & Chinnery PF Nat Metab. 2020

Beyond chromosomal DNA

- eccDNA: amplified oncogenes or regulatory regions, linked to therapy resistance and relapse.

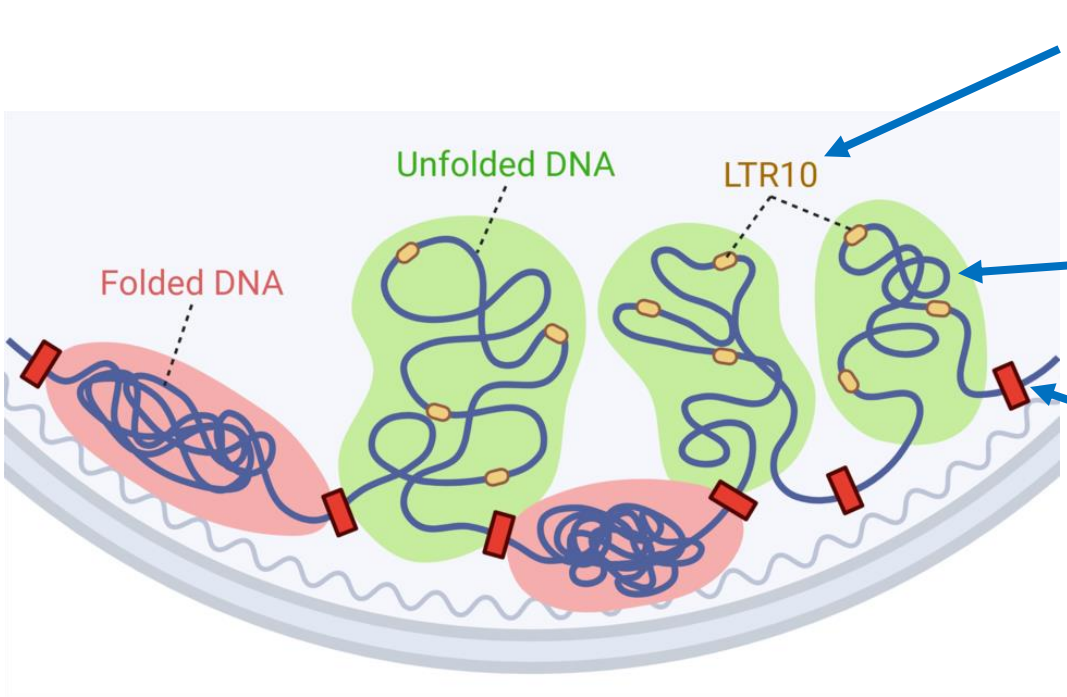




Yang L et al. Sig Transduct Target Ther. 2022
https://www.cancer.gov/news-events/cancer-currents-blog/2023/extrachromosomal-dna-barretts-esophageal-cancer

Beyond chromosomal DNA

- Viral DNA: integrated genomes as oncogenic drivers.



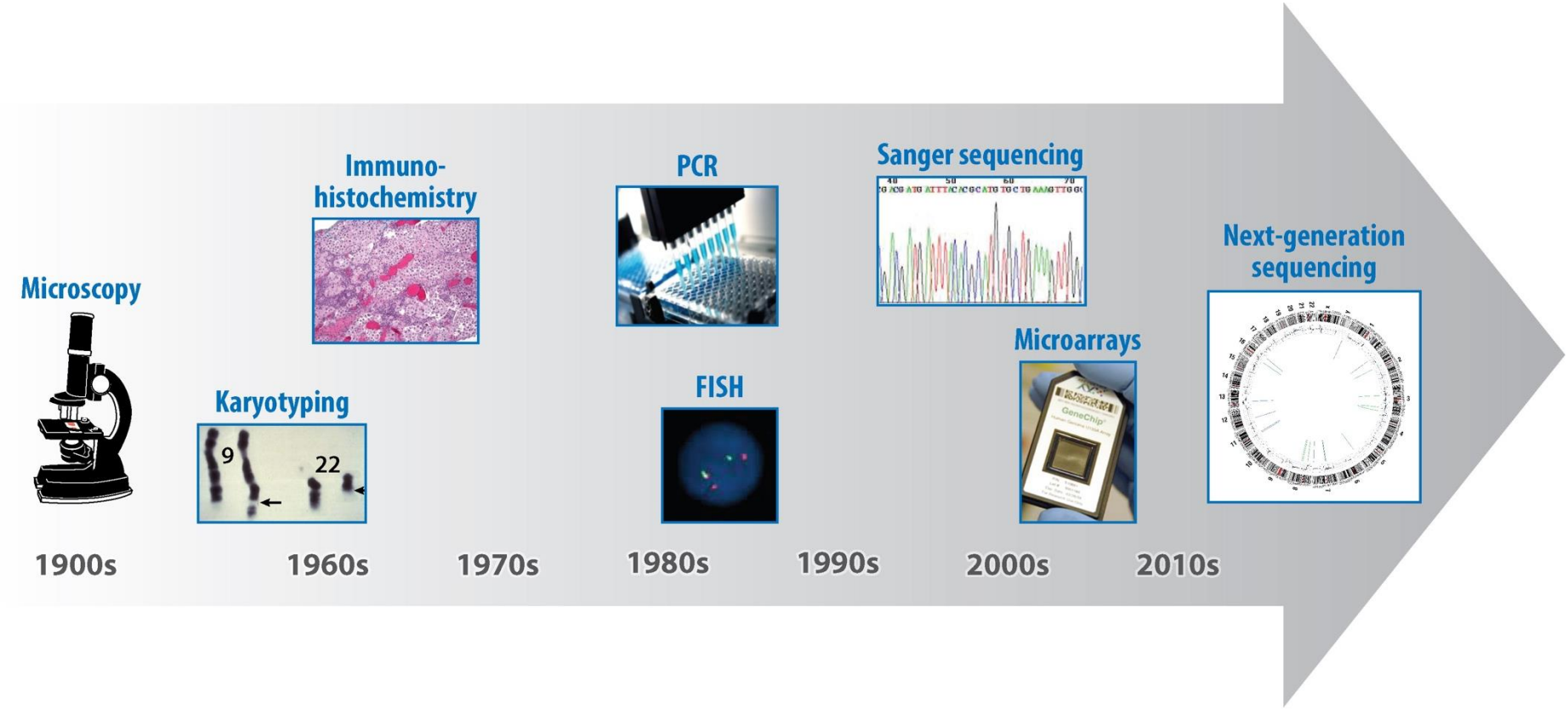
Fragment of DNA from endogenous retroviruses

Open chromatin

Access to transcription of an oncogene

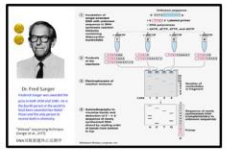
Ivancevic A et al. Sci Adv. 2024
https://www.cancer.gov/news-events/cancer-currents-blog/2024/ancient-retrovirus-dna-ltr10-cancer

Genomics is transforming how we study, diagnose and treat cancer



Yang A et al. Front Bioeng Biotechnol. 2020

Evolution of genomics data acquisition and large-scale genome projects



Sanger method

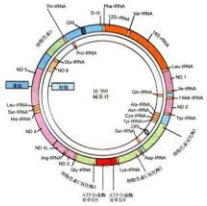
1977

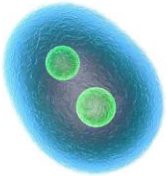
Human Genome Project

1981

1990

Human mitochondrial genome sequence





Complete eukaryotic genome

1995

1996

Complete cell genome

Second generation sequencer：454 GS20

2001

2005

Complete the Human Genome Project

Research Human Microbiome Project

2007

2008

Second generation sequencer：Genetic Analyzer 2

Nanospace sequencing

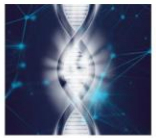
2011

2014

Third generation sequencer：PacBio RS

2019

The third stage Human microbiome project



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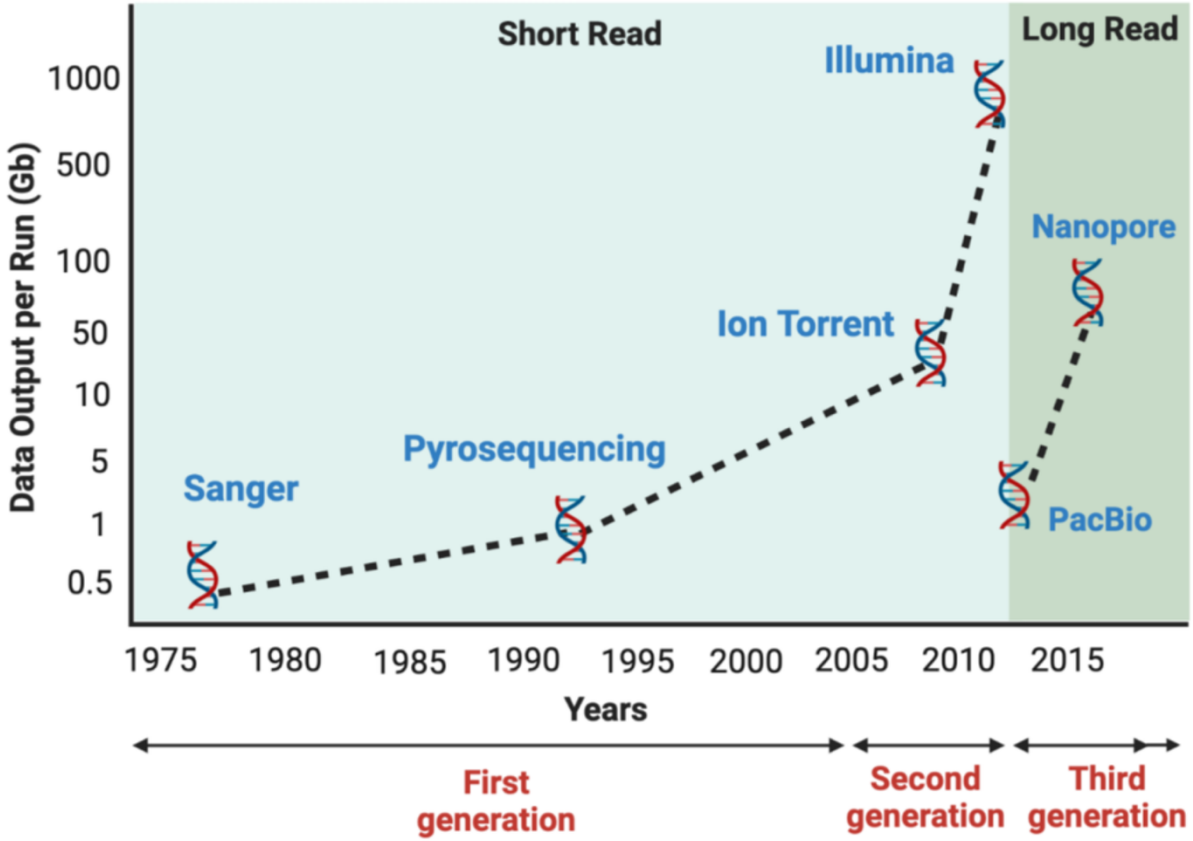
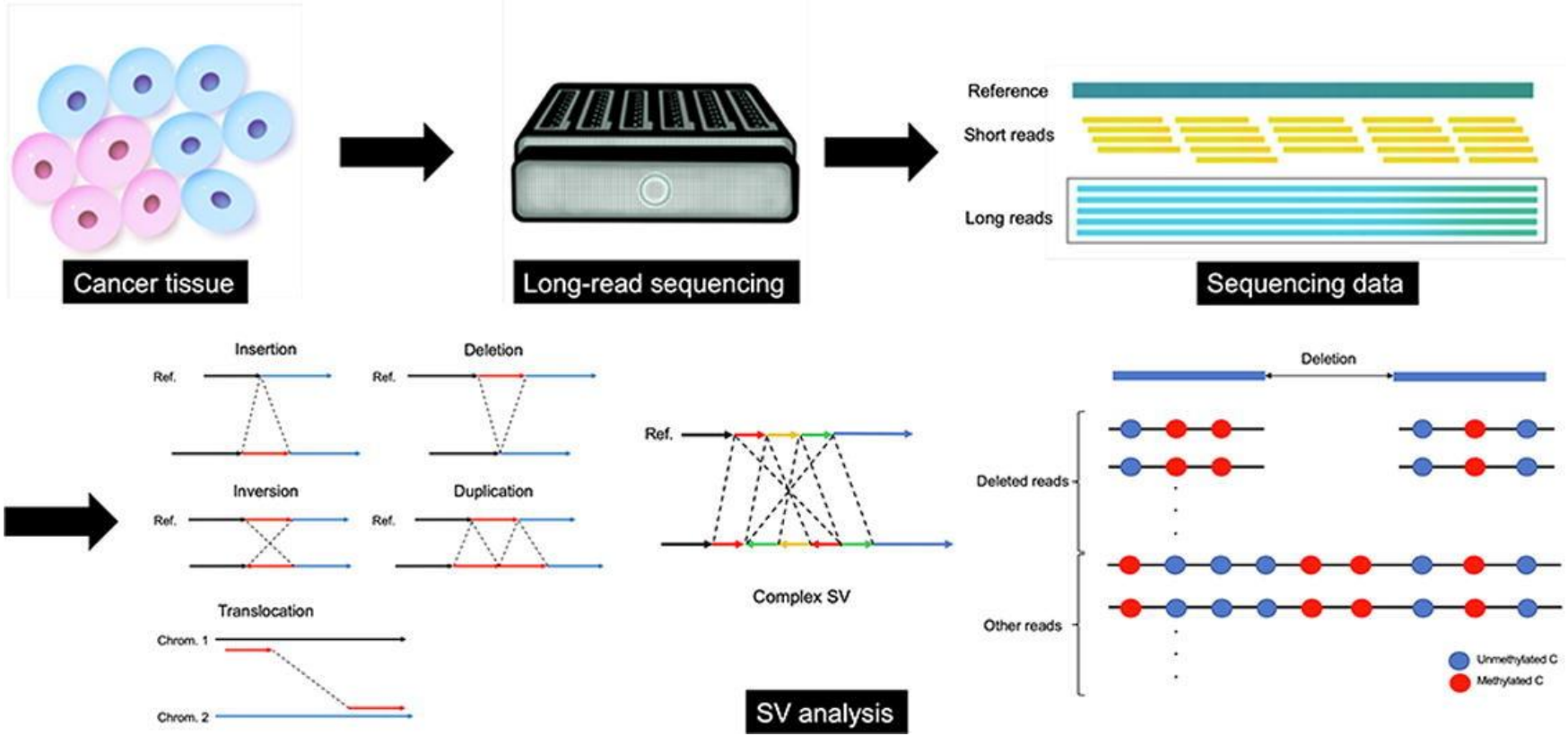


Satam H et. al. Biology (Basel). 2023

Long Read Sequencing Allows Resolution of Complicated Structural Variants



Sakamoto Y et. al. Comput Struct Biotechnol J. 2021

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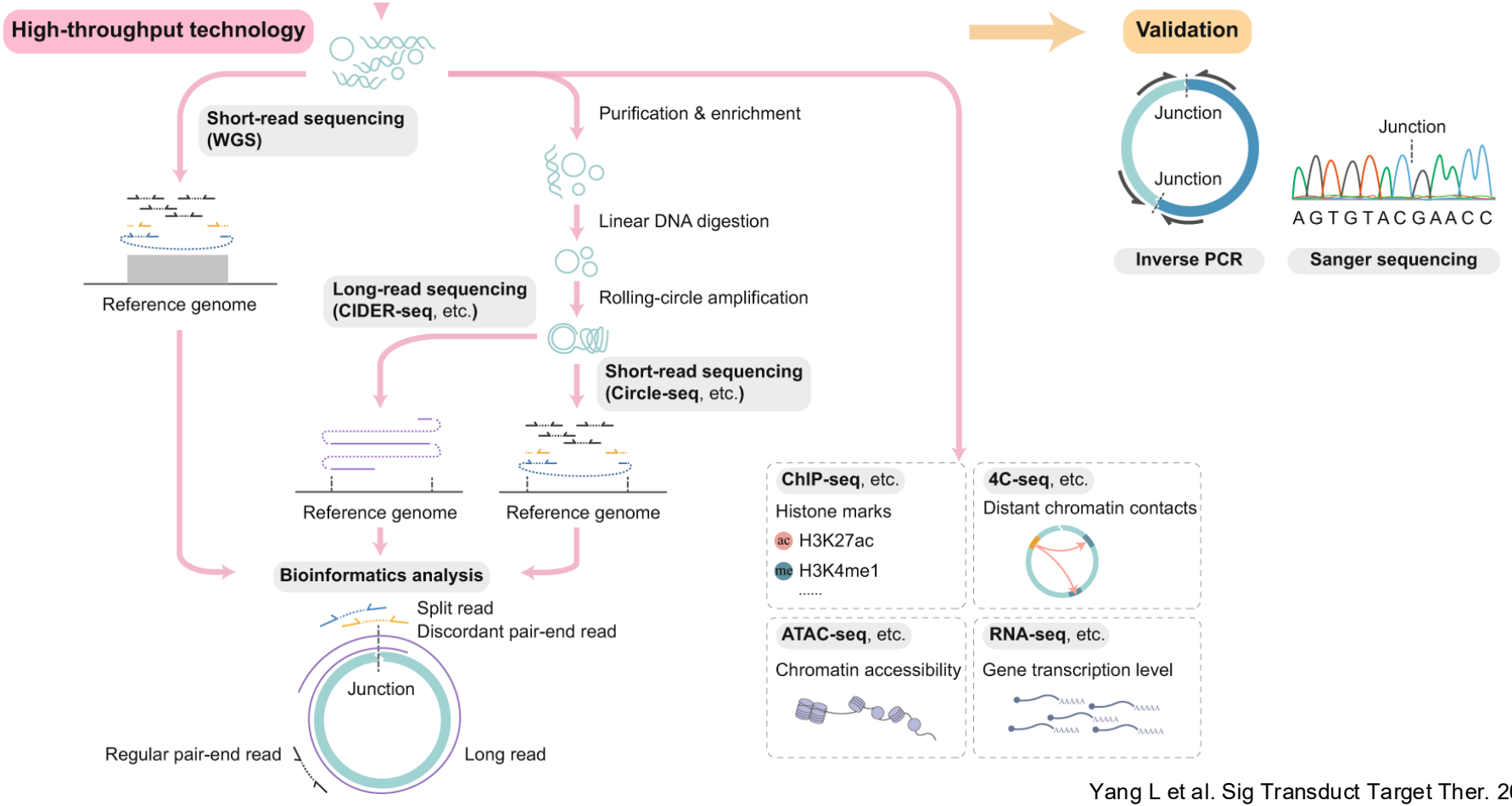
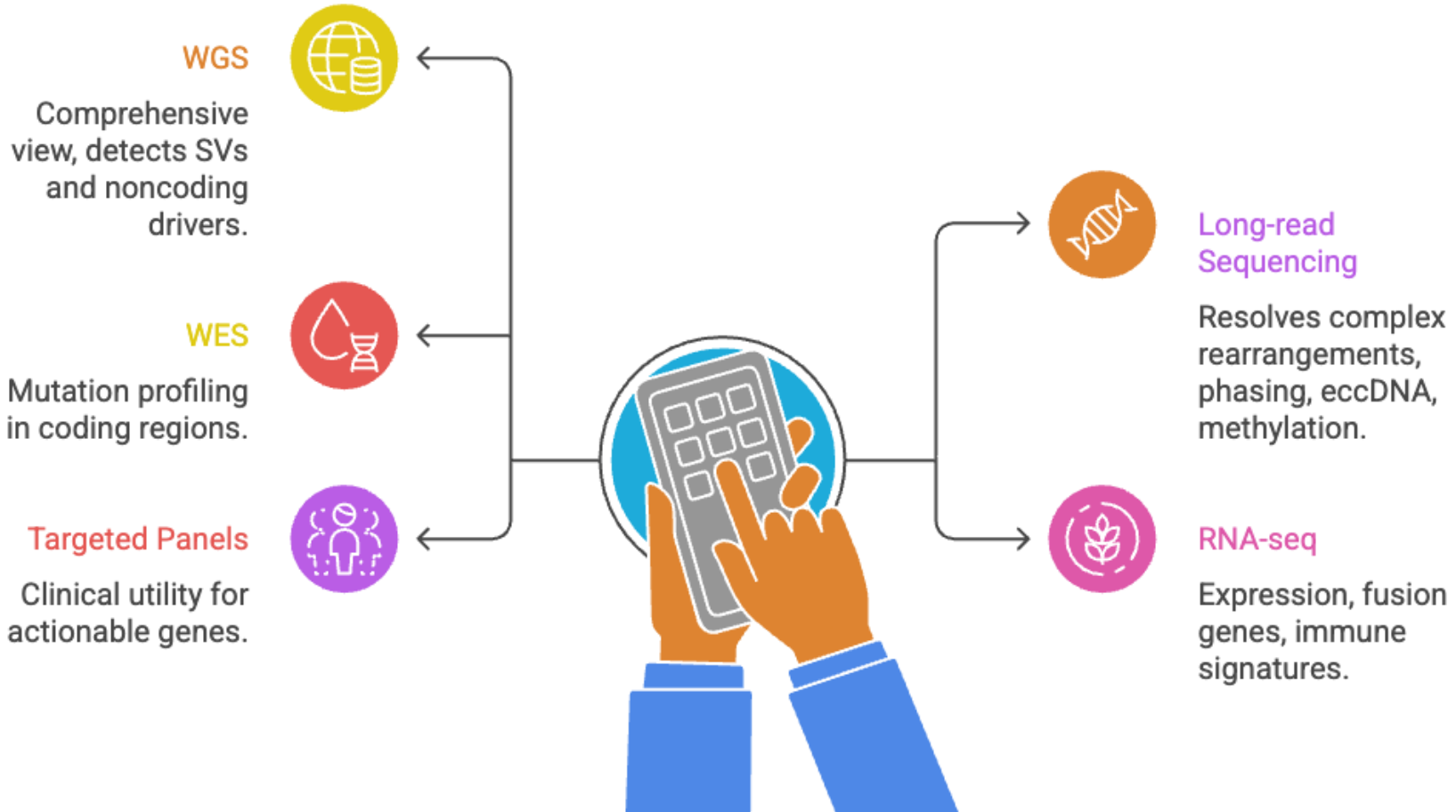
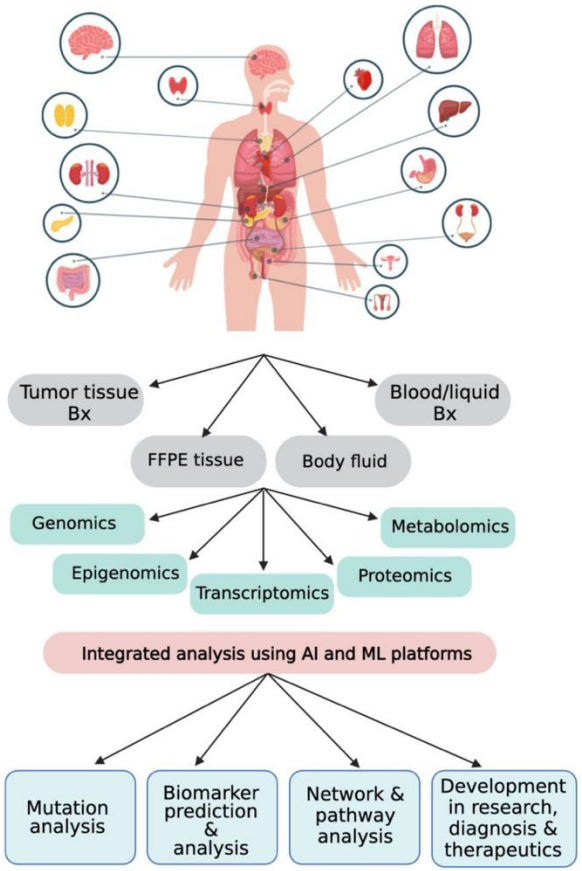


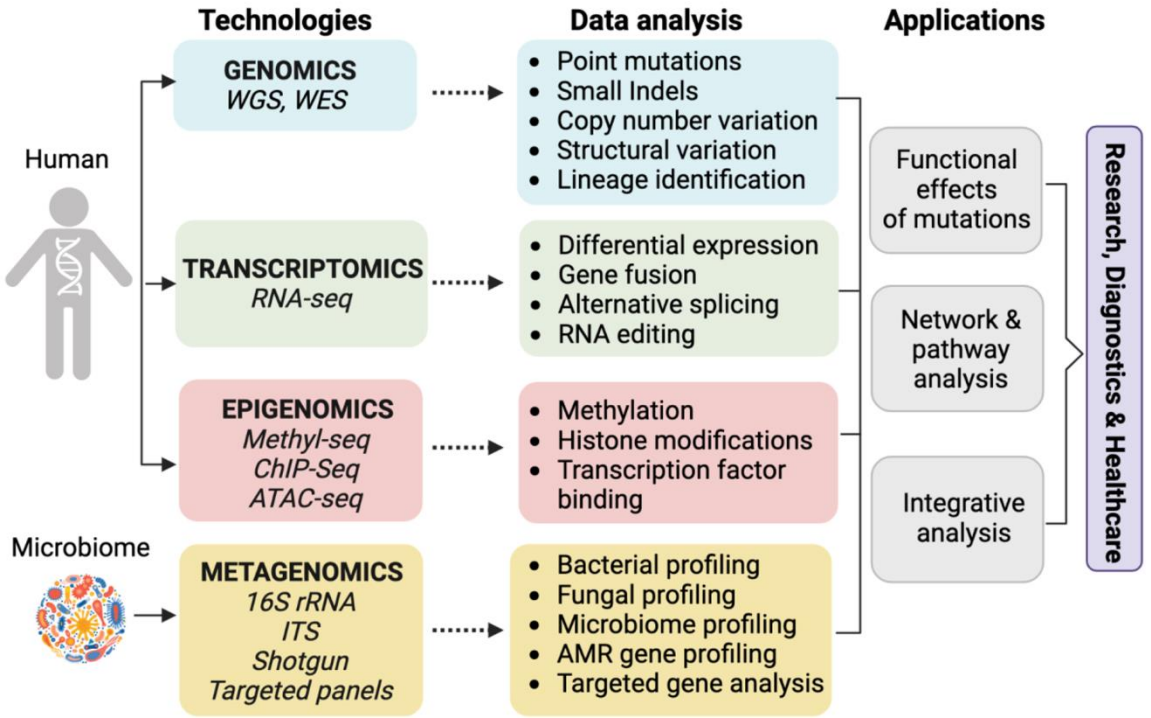
Yang L et al. Sig Transduct Target Ther. 2022

Sequencing the genome: many options



Role of NGS Technology in Cancer Diagnosis, Prognosis, and Therapeutics

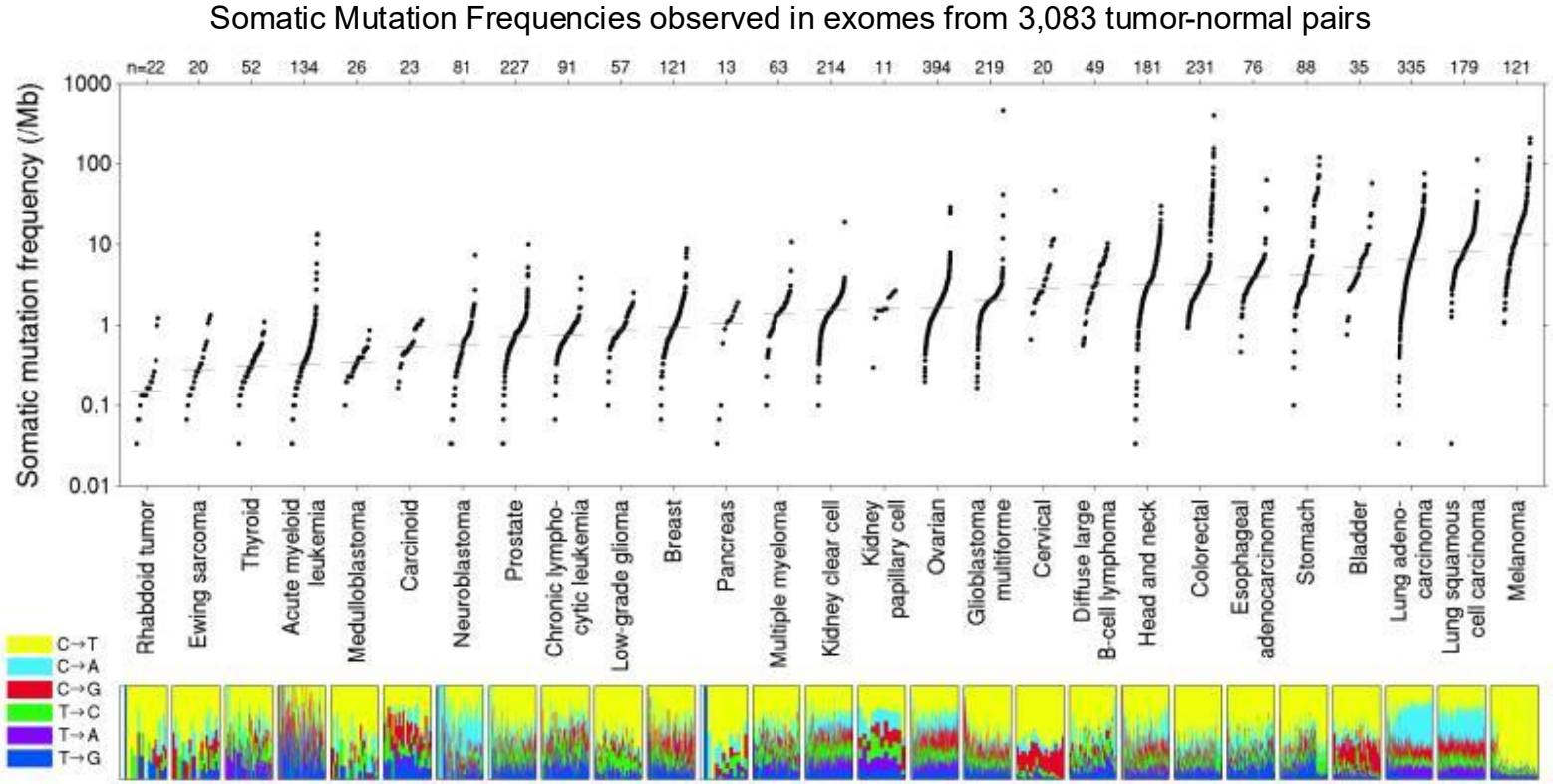




Satam H et. al. Biology (Basel). 2023

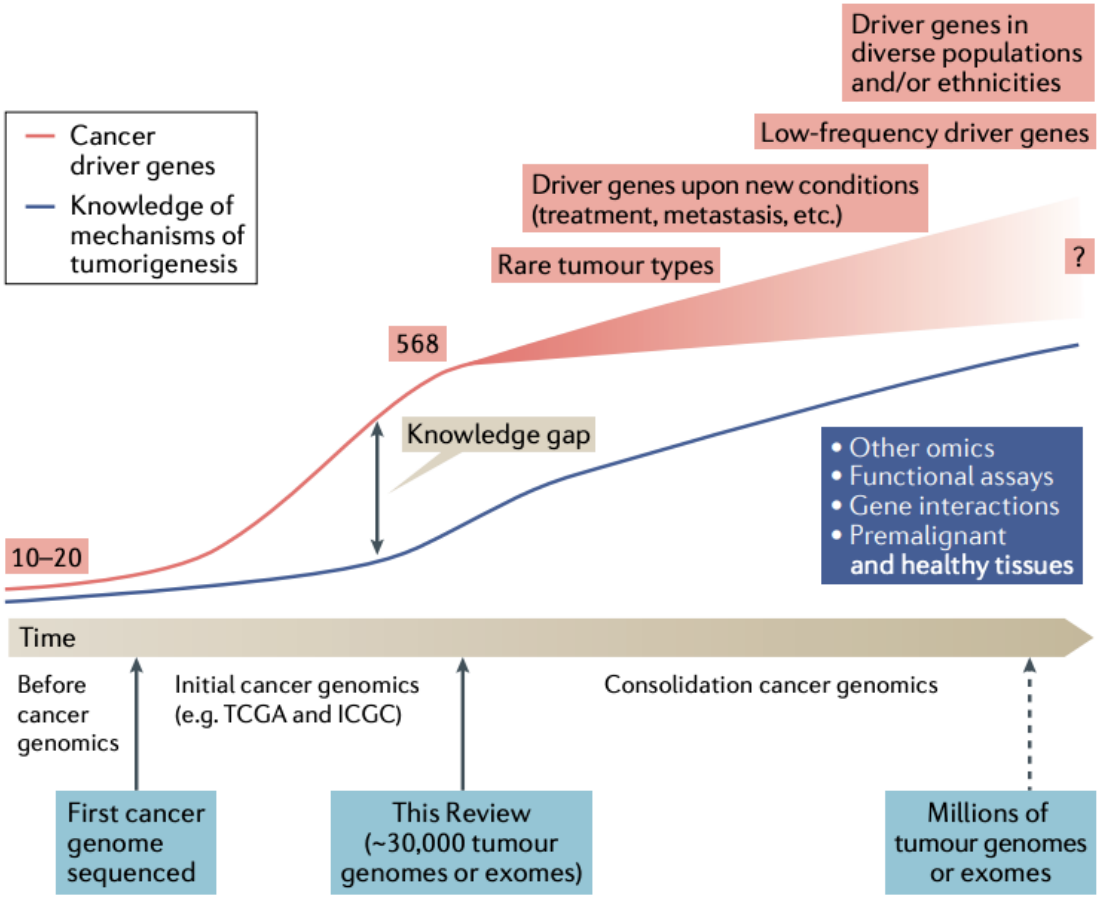
FFPE, formalin-fixed paraffin-embedded; Bx, biopsy; AI, artificial intelligence; Ml, machine learning.

Improved understanding of the cancer phenotypes that drive oncogenesis



Lawrence M.S. et al. Nature 2013

Improved understanding of the cancer phenotypes that drive oncogenesis

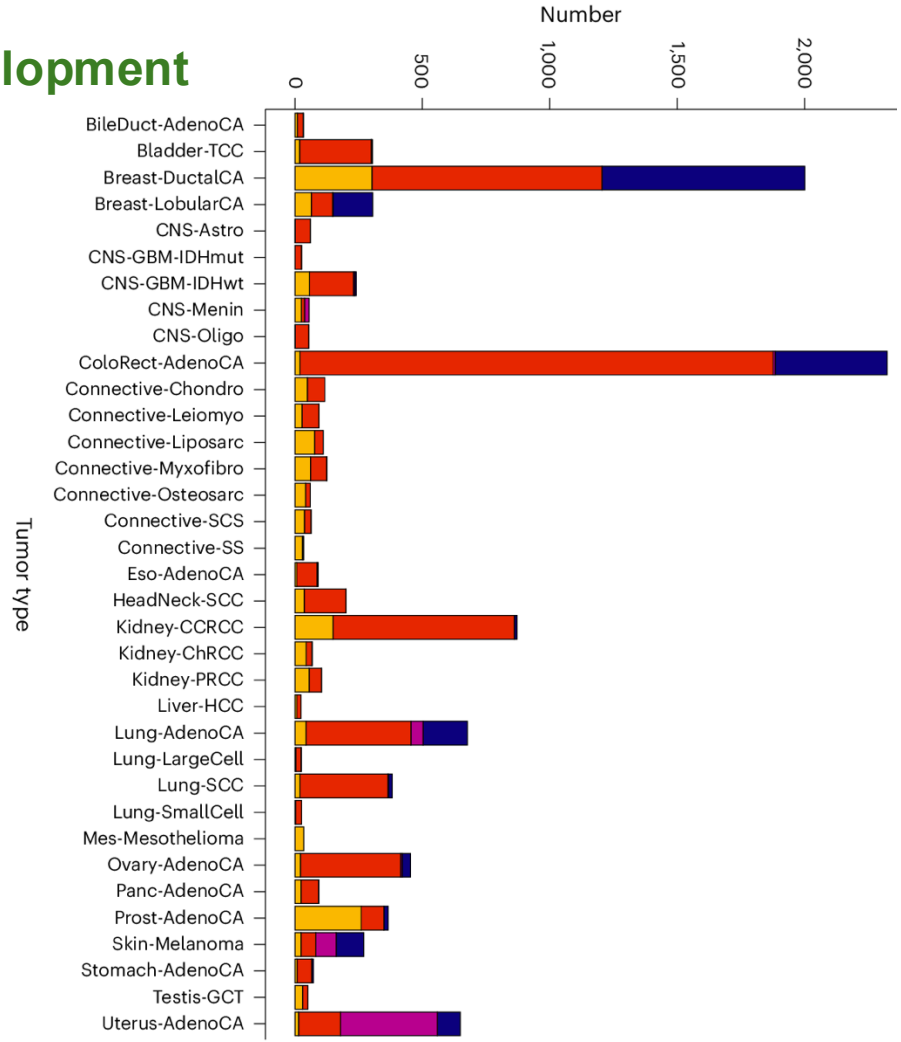


Martínez-Jiménez F et al. Nat Rev Cancer. 2020

Prioritise candidate target for drug development

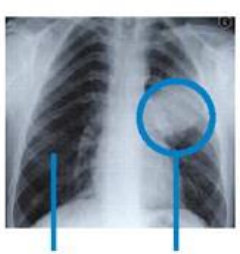
COSMIC actionability

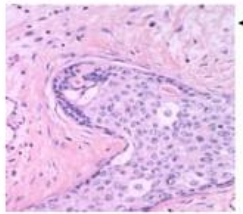
1	Approved marketed drug with demonstrated efficacy at the mutation
2	Phase 2/3 clinical results meet primary outcome measures
3	Drug in ongoing clinical trials
0	None



Kinnersley B et al. Nat Genet. 2024

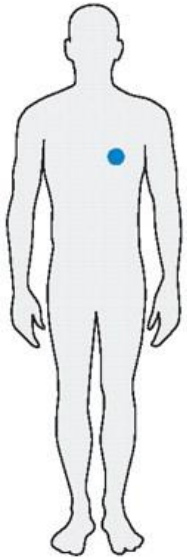
Toward treatment guideline based on gene mutational profile



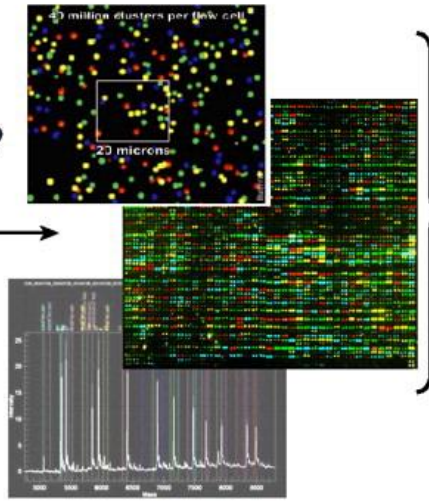


Cancerous

Tumor traditionally classified by histology, tissue site



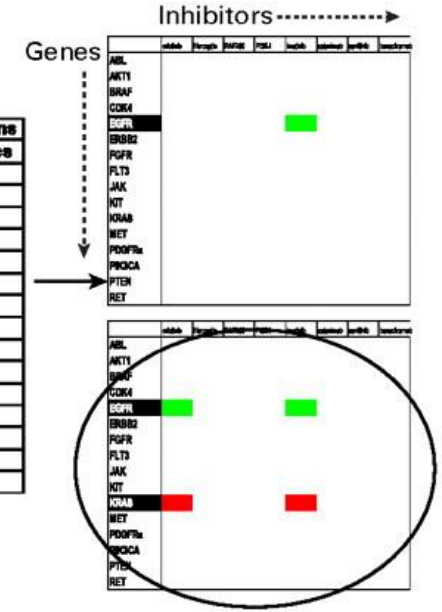
Extract tumor biopsy



Extract DNA from tumor to profile for somatic alterations

Gene	Mut	Amp	Del	Trans
ABL				yes
AKT1				
BRAF				
CDK4				
EGFR	yes			
ERBB2				
FGFR				
FLT3				
JAK				
KIT				
KRAS				
MET				
PDGFRa				
PIK3CA				
PTEN				
RET				

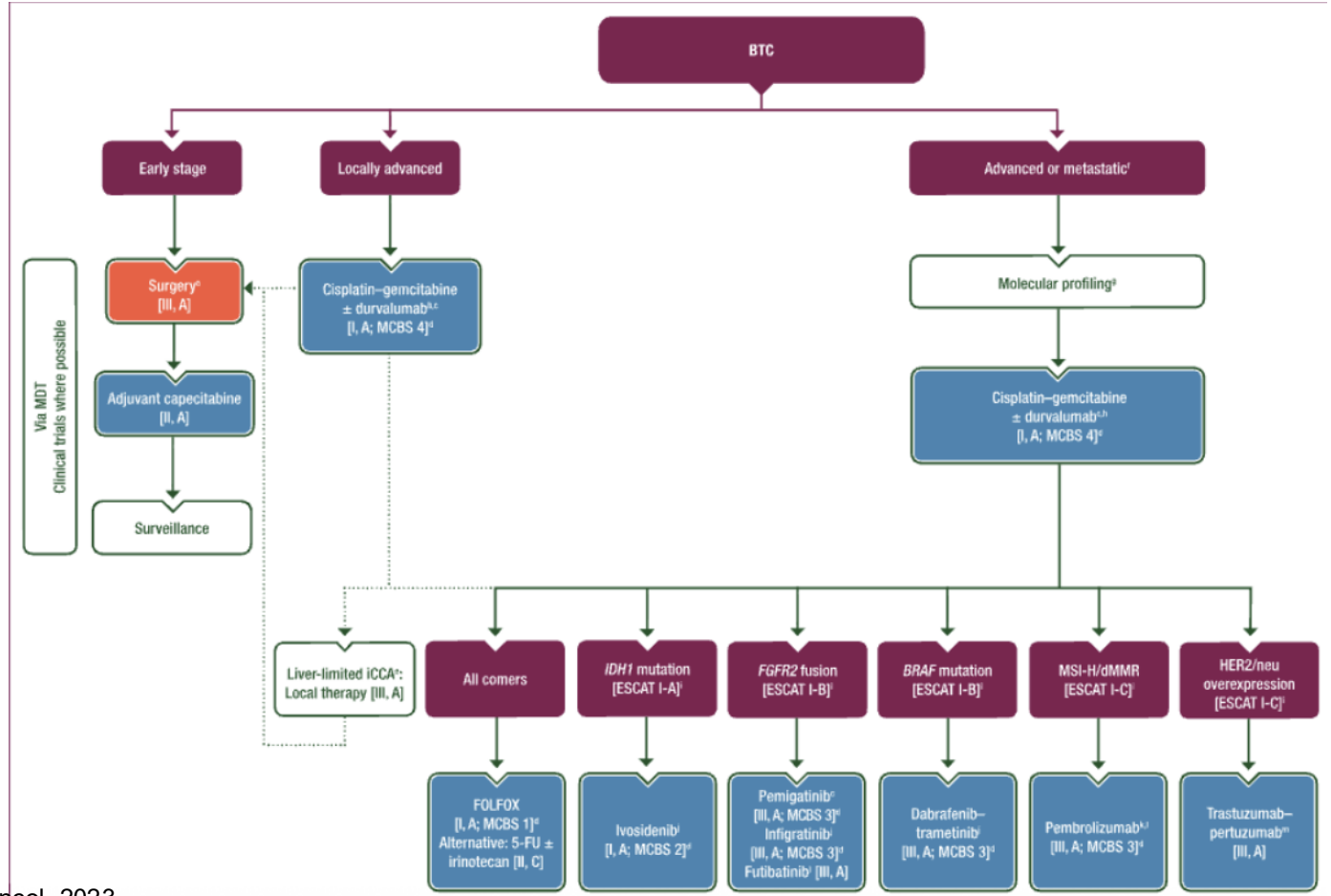
Define "actionable" mutation profile of tumor



Use genetic alteration profile to choose individualized targeted therapeutic

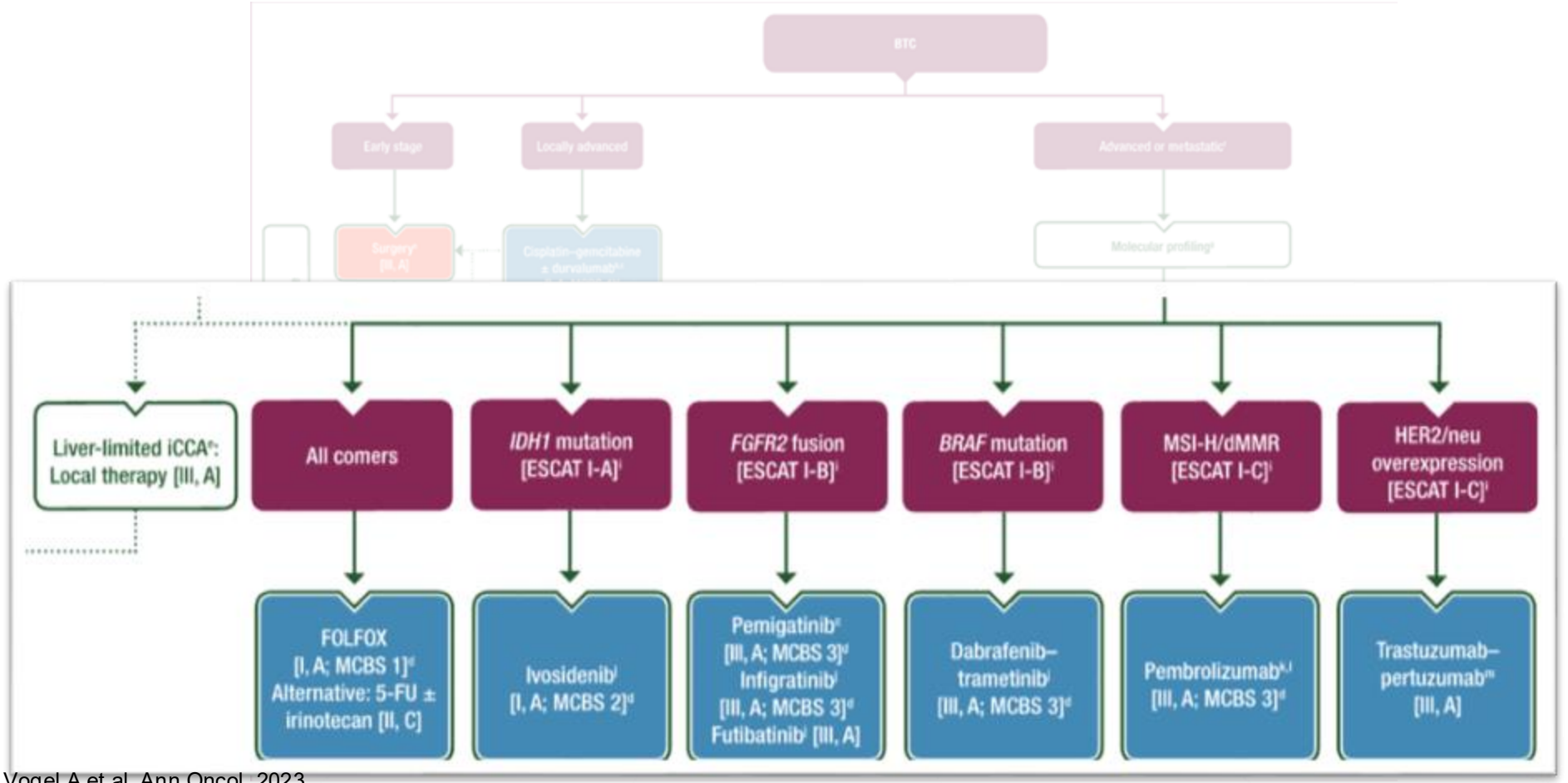
Macconaill LE, Garraway LA. J Clin Oncol. 2010

Toward treatment guideline based on gene mutational profile



Vogel A et al. Ann Oncol. 2023

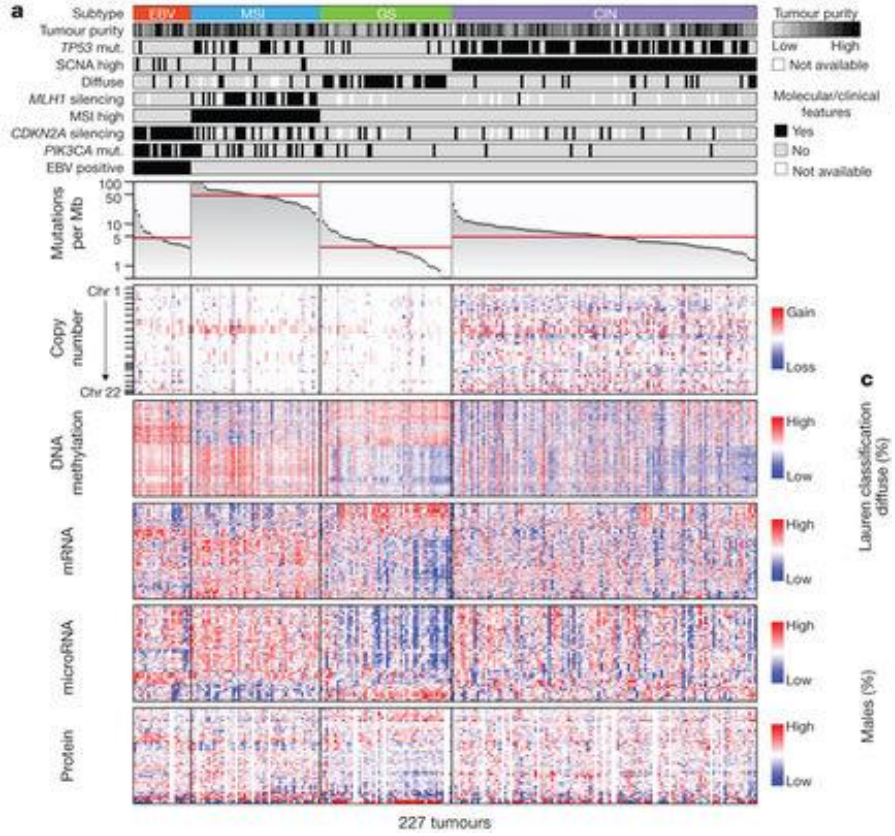
Toward treatment guideline based on gene mutational profile

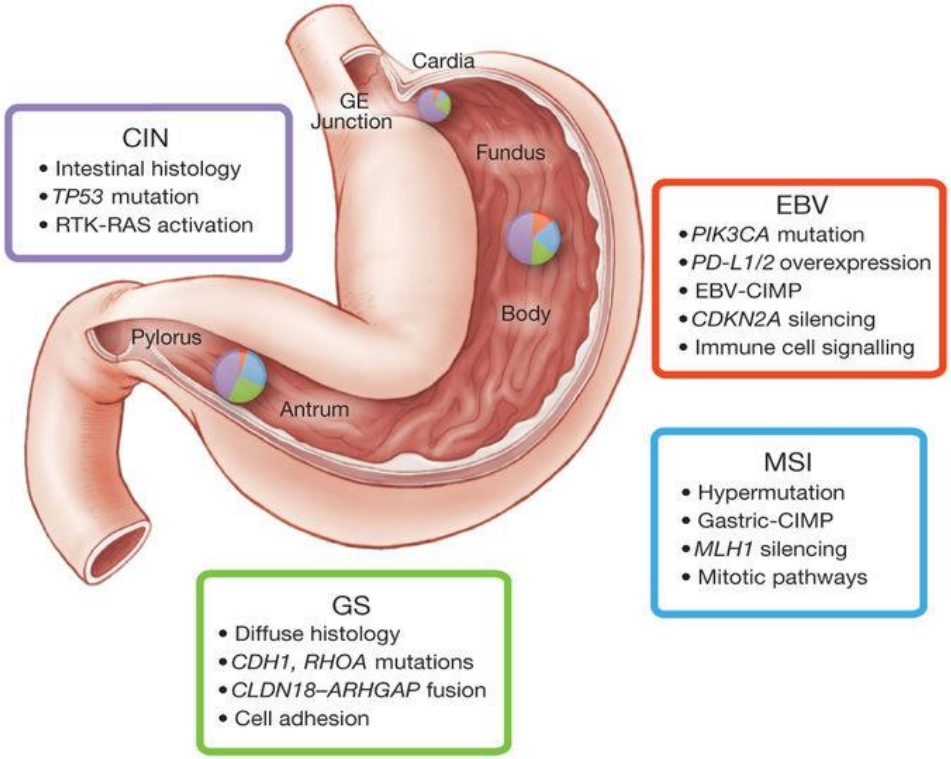


Vogel A et al. Ann Oncol. 2023

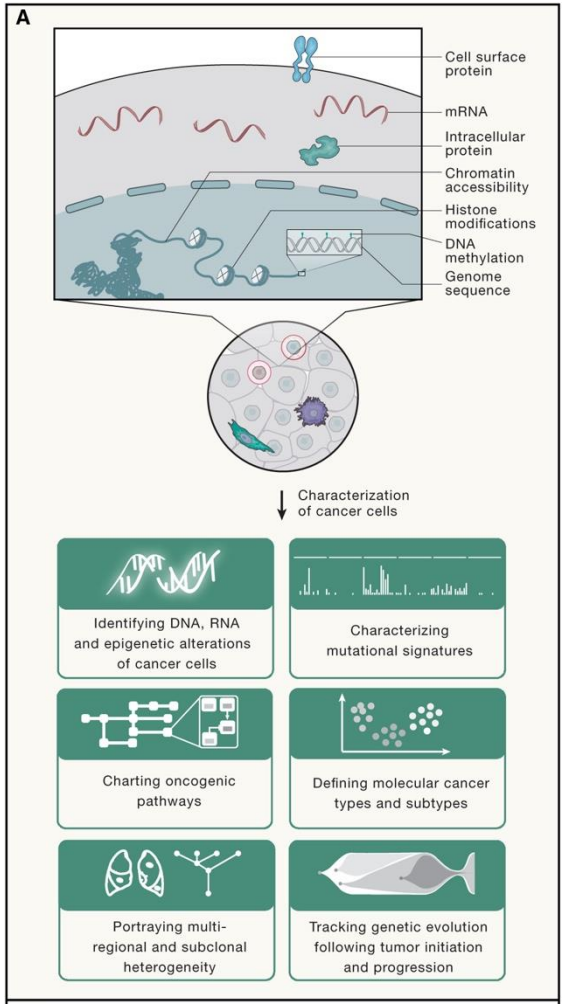
Classification of cancer, prognosis, and response to treatments

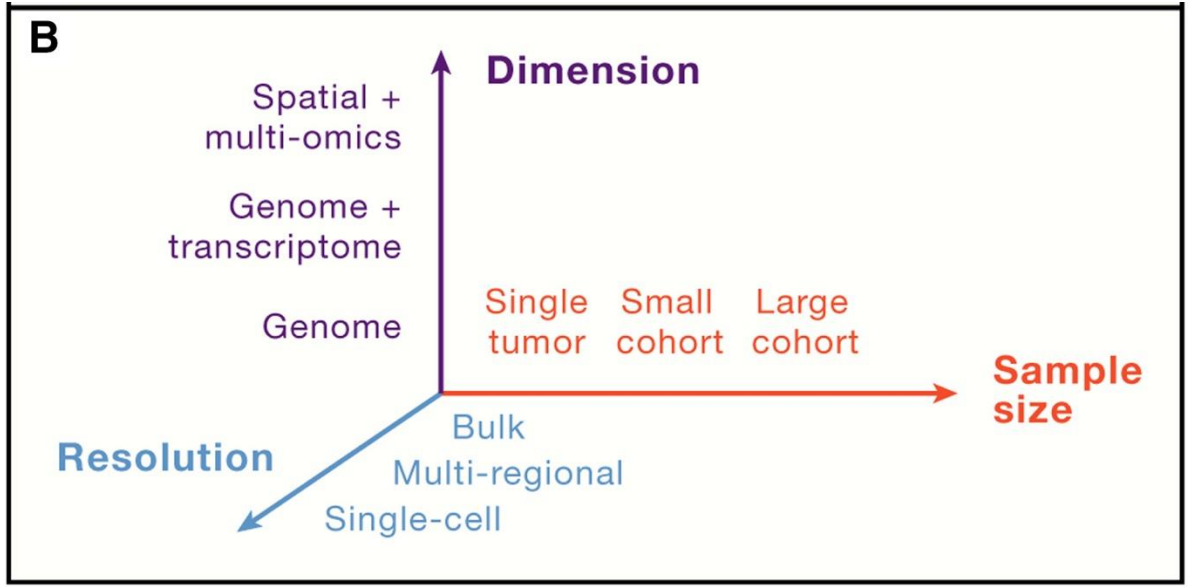
Comprehensive molecular characterization of gastric adenocarcinoma



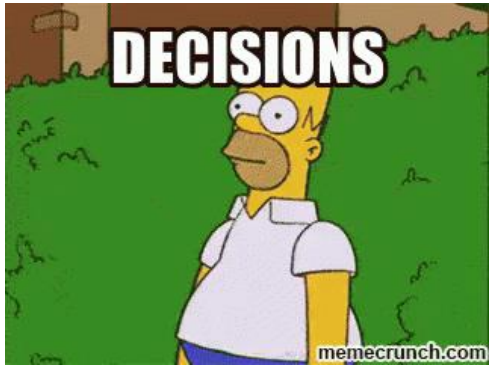


TCGA Research Network Nature Genetics 2014



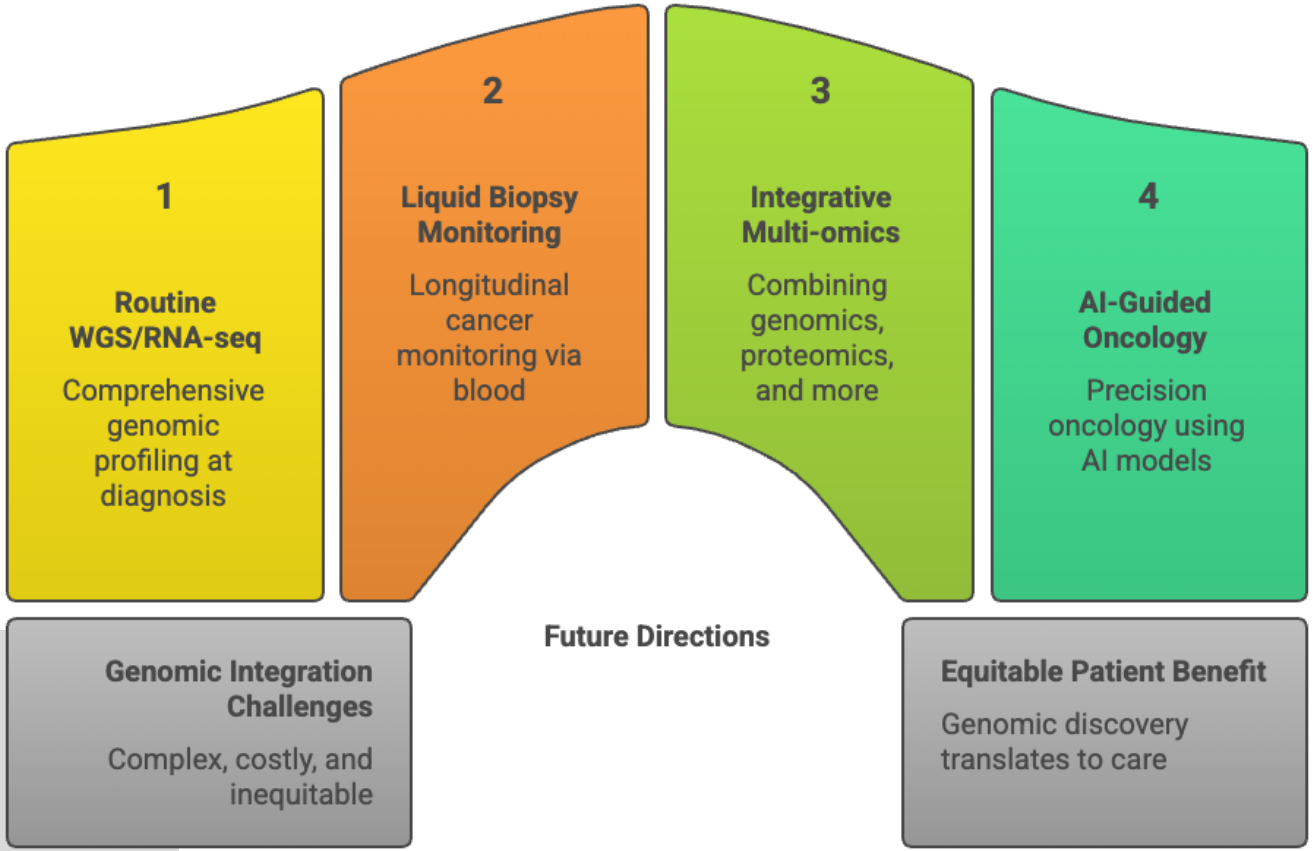


Wang D, et. al. Cell. 2023 Apr 13;186(8):1755-1771



Challenges and looking forward in cancer genomics

- Tumor heterogeneity
- High cost
- Turnaround time
- Unvalidated variants
- Complexity of data integration
- Genomics literacy
- Inconsistent reporting standards
- Data privacy



Where is cancer genomics in patient care