

Genomics driven oncology

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Gemelli

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GART

Advanced Radiation Therapy



CONFLICT OF INTEREST

- Travel support from MSD, Illumina, AZ, Menarini
- Honoraria from VEEVA, GSK, MSD, Altems, Guardant Health, Illumina

AGENDA

- 1. UNDERSTANDING CANCER:** did genomics have any role?
- 2. TREATING CANCER:** did genomics bring any clinically meaningful benefit?
- 3. FUTURE:** what is the role of genomics in future cancer care?

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UNDERSTANDING CANCER

Cancer is a genetic disease



0



1000



2000

BLACK BILE



Hippocrates of Kos (c. 460-370 BC)
Claudius Galen (130-200 BC)

Black bile caused incurable cancer,
whereas yellow bile caused curable
cancer



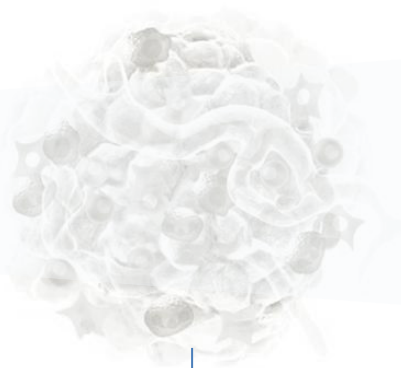
UNDERSTANDING CANCER

Cancer is a genetic disease

2000

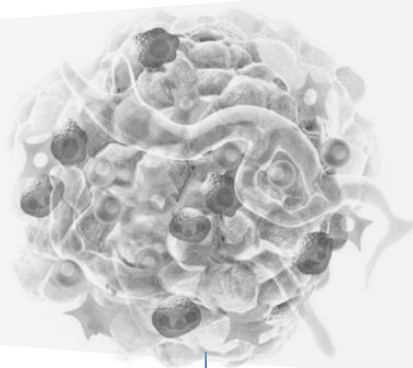
GENES

Level of understanding



Theodor Boveri (1902 AC)

Theorized that the underlying cause of cancer lies in chromosomal abnormalitie



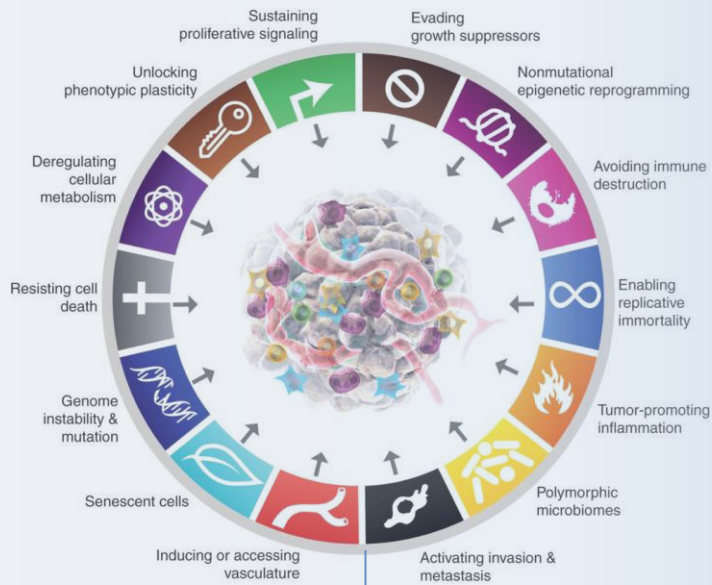
H. Varmus and M. Bishop (1989 AC)

Nobel Prize won: altered cellular genes could cause cancer



TGCA project (2003-2018 AC)

Pan cancer Atlas on 33 cancer types, more than 11,000 patients



Hallmark of cancer (2000-2022 AC)

Heuristic tool for distilling the vast complexity of cancer phenotypes and genotypes

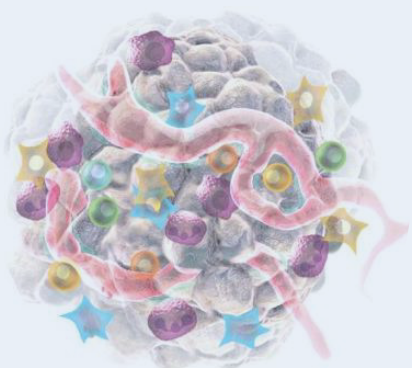
35° RESIDENTIAL COURSE

UNDERSTANDING CANCER

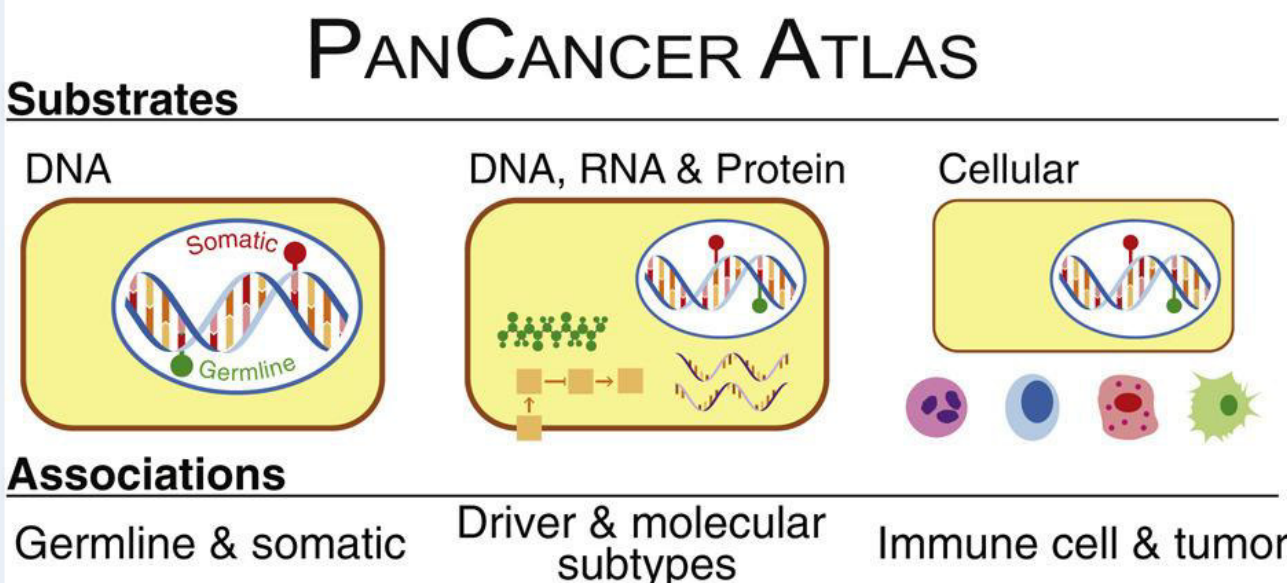
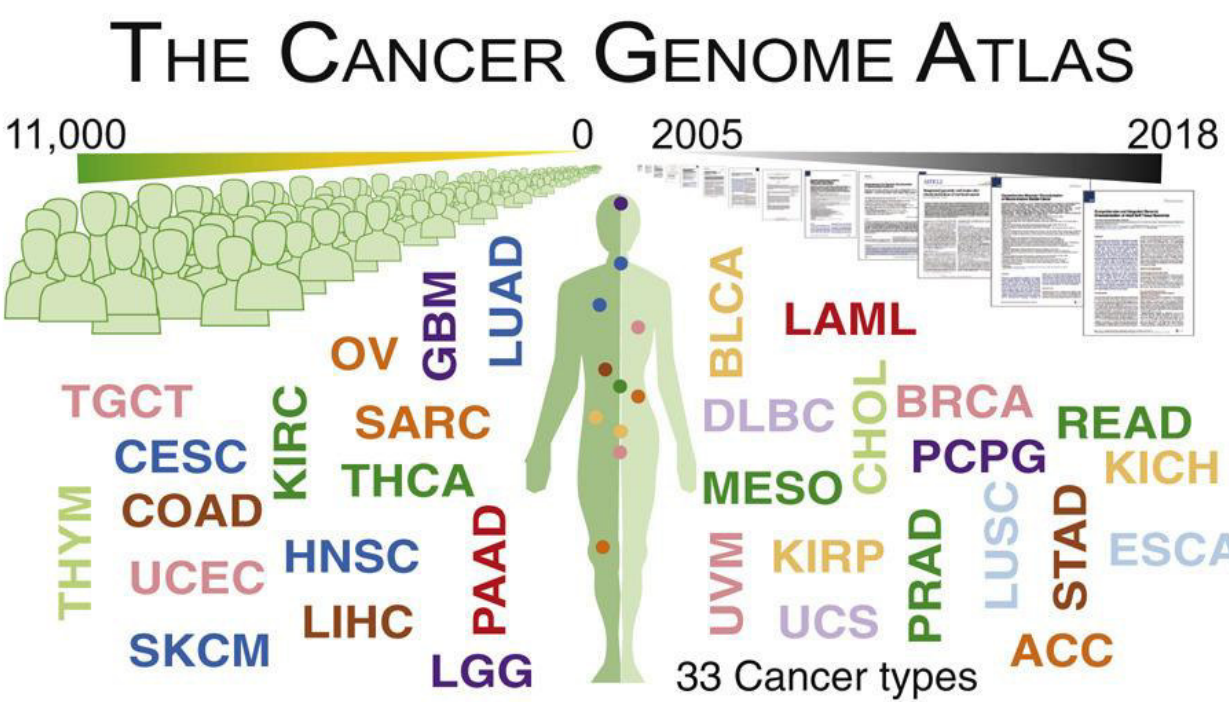
Cancer is a genetic disease

2000

GENES



TCGA

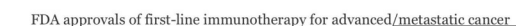


- 33 | different tumor types including 10 rare cancers
- 11,000 | patients (paired tumor-normal tissue sets)
- 7 | different data type
- 2.5 | Pentabytes of data
- 20 | Collaborative institutions within USA

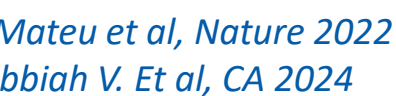
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Towards precision medicine



Genomically determined alterations can be targeted



TREATING CANCER

Genomically determined alterations can be targeted | OVARIAN CANCER

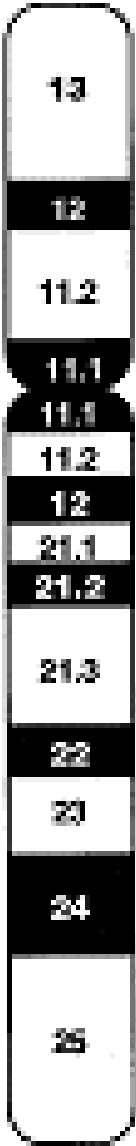
1900

1950

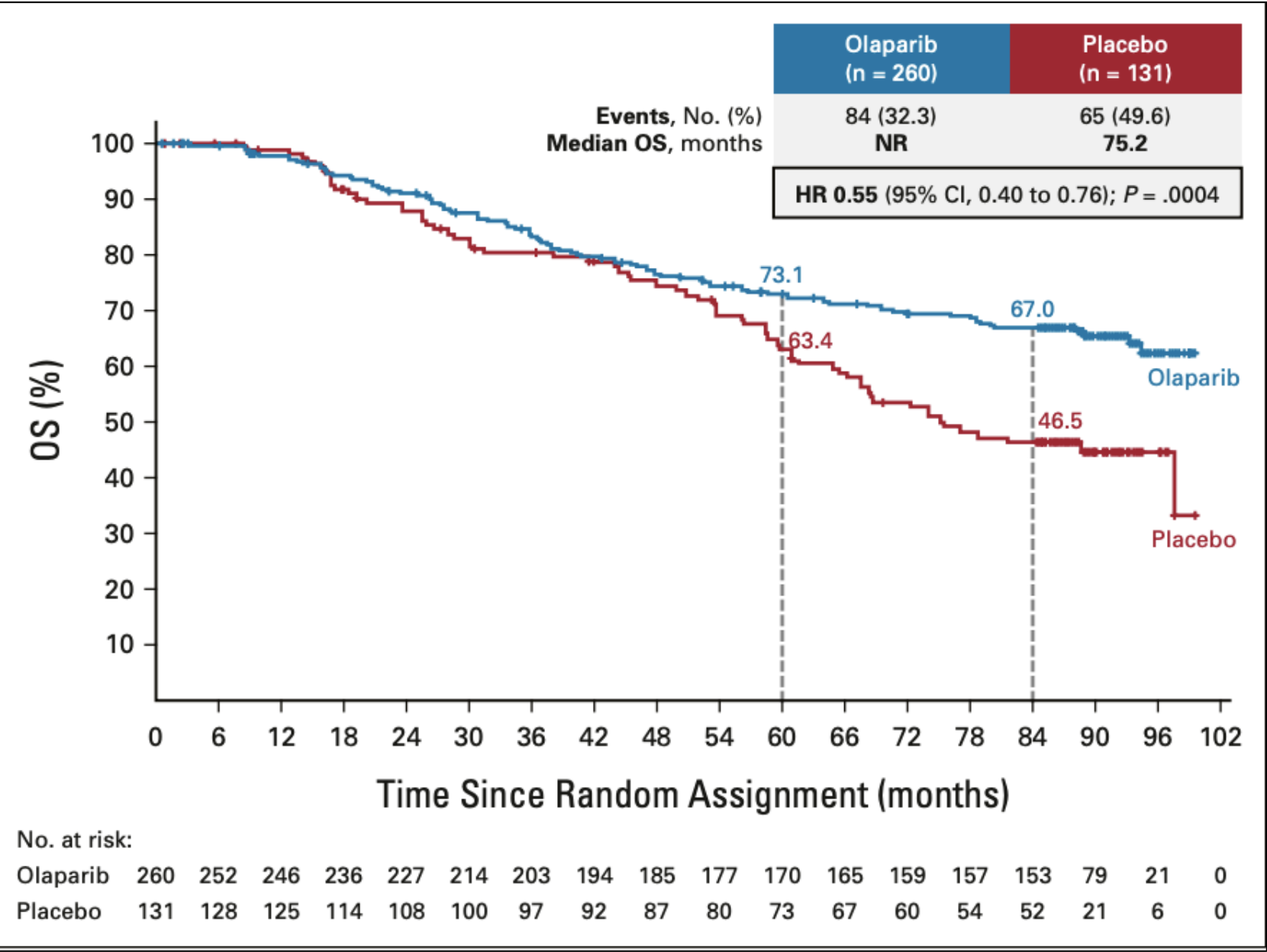
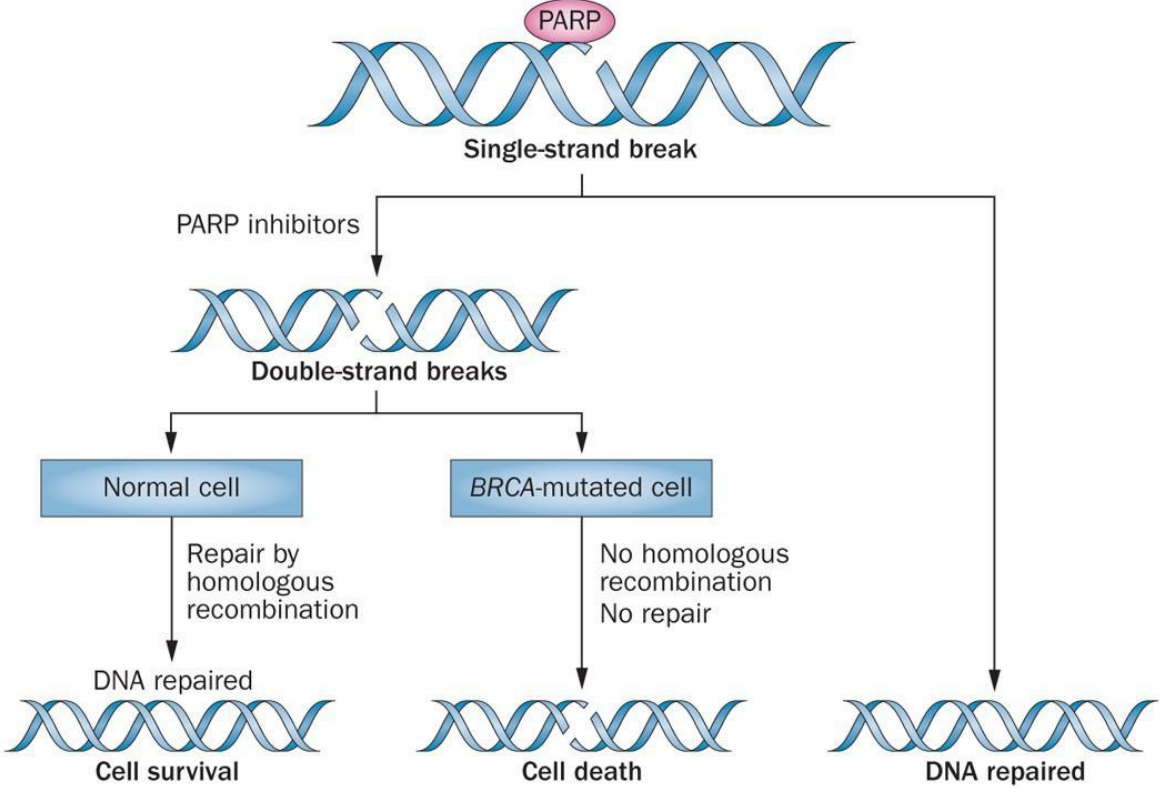
2000

GENES

TARGETED THERAPIES



BRCA1 gene



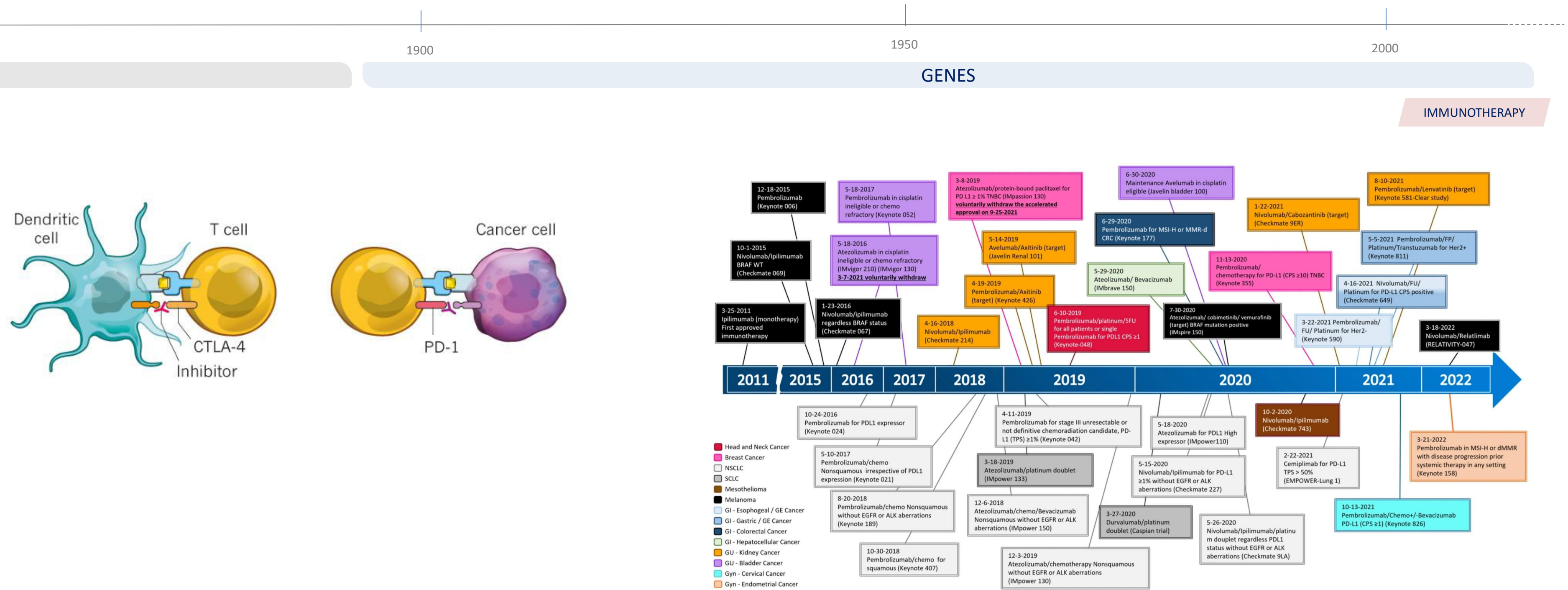
Mary-Claire King

DiSilvestro P et al, JCI 2022

Olaparib maintenance therapy provides about a 50% improvement in overall survival for patients with BRCA-mutated ovarian cancer

TREATING CANCER

The anti-cancer role of the immune system can be restored



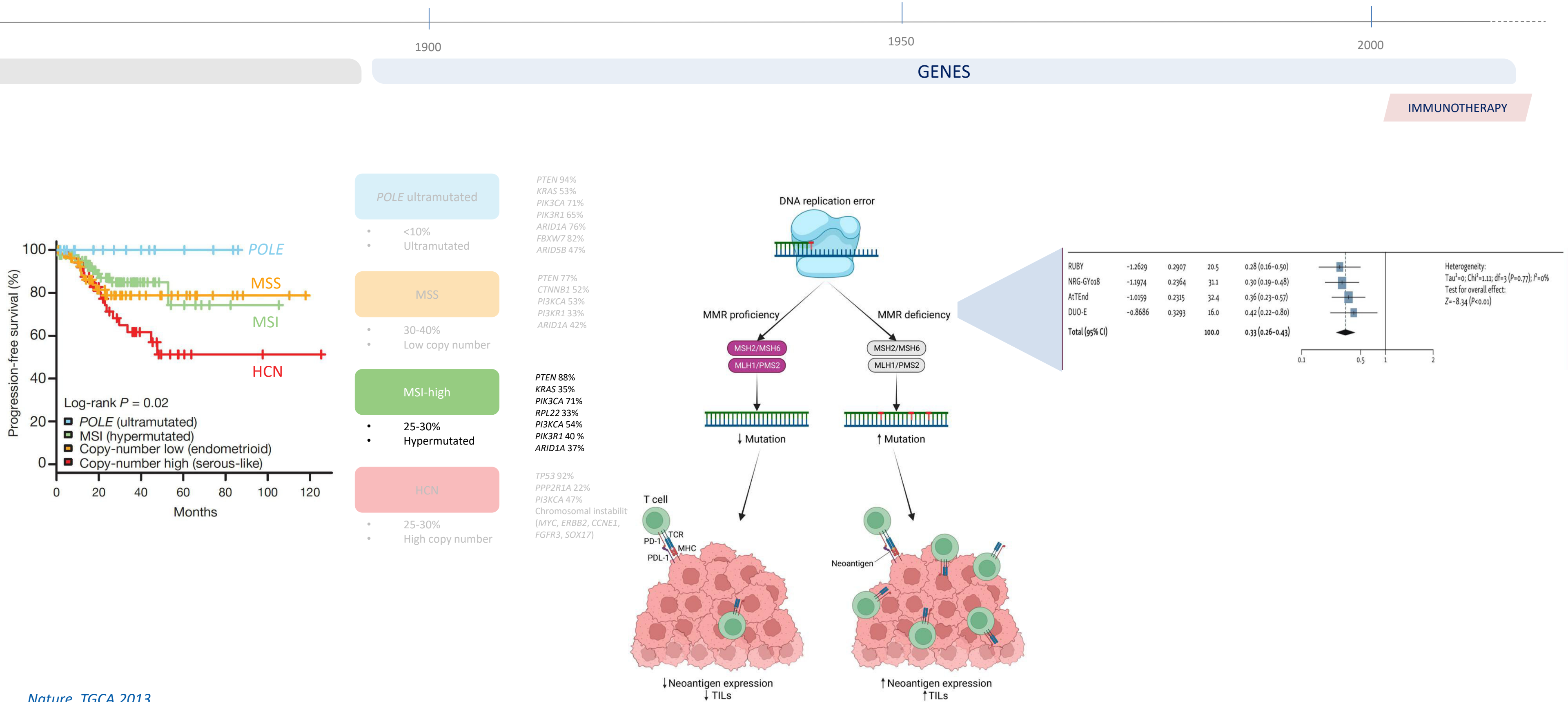
James P. Allison
Tasuku Honjo

FDA approvals of first-line immunotherapy for advanced/metastatic cancer

H. Ledford et al, Nature 2018
W. Ma et al, Exp Hem & Onco 2023

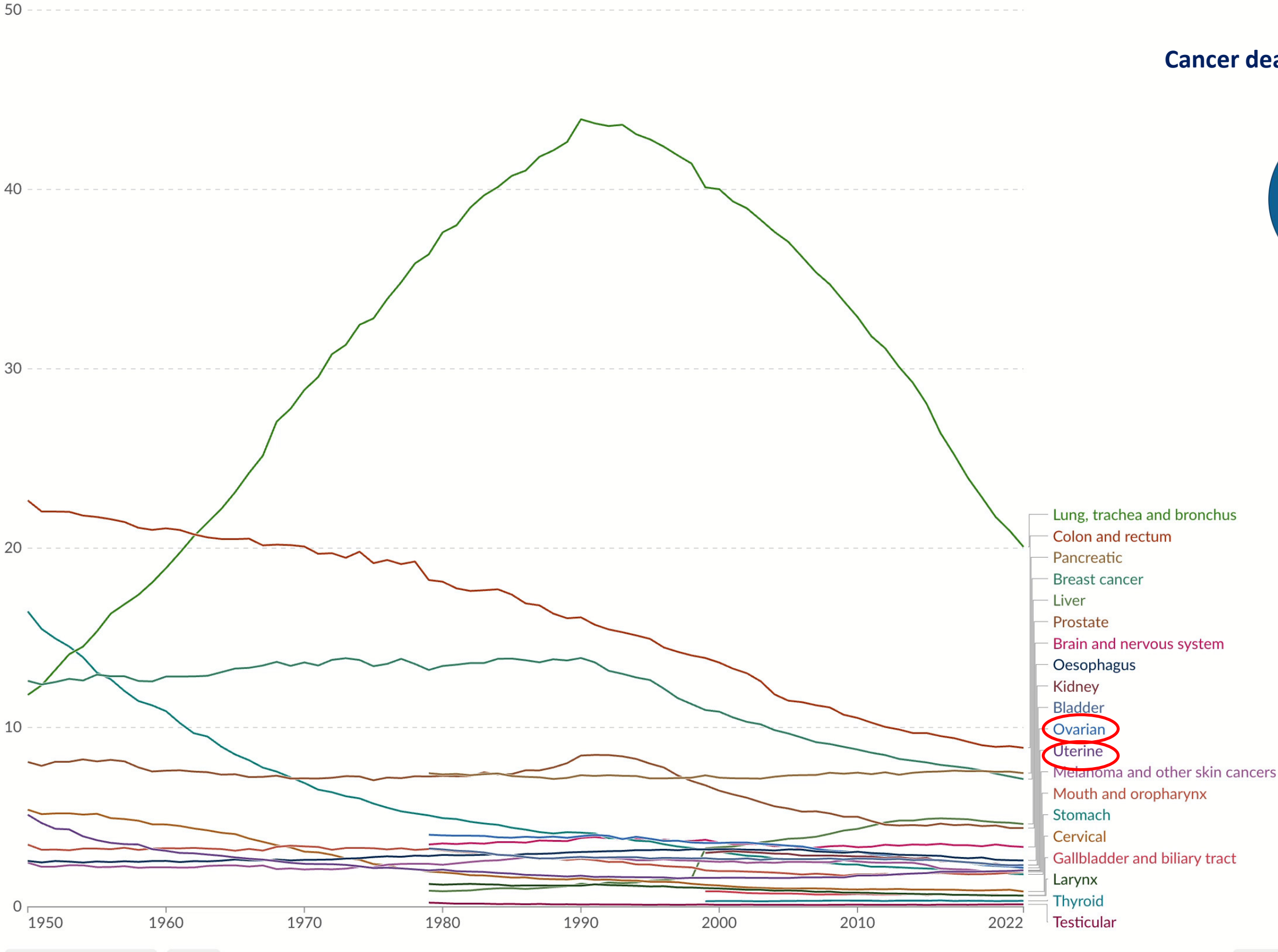
TREATING CANCER

The anti-cancer role of the immune system can be restored | ENDOMETRIAL CANCER

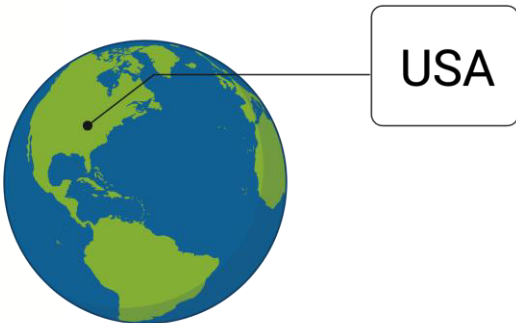


TREATING CANCER

Oncology mortality trends

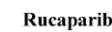
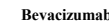
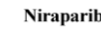


Cancer death rates by type, United States



Data source: WHO Mortality Database (2025), <https://ourworldindata.org/>

BRCA genes and PARP inhibitors in ovarian cancer

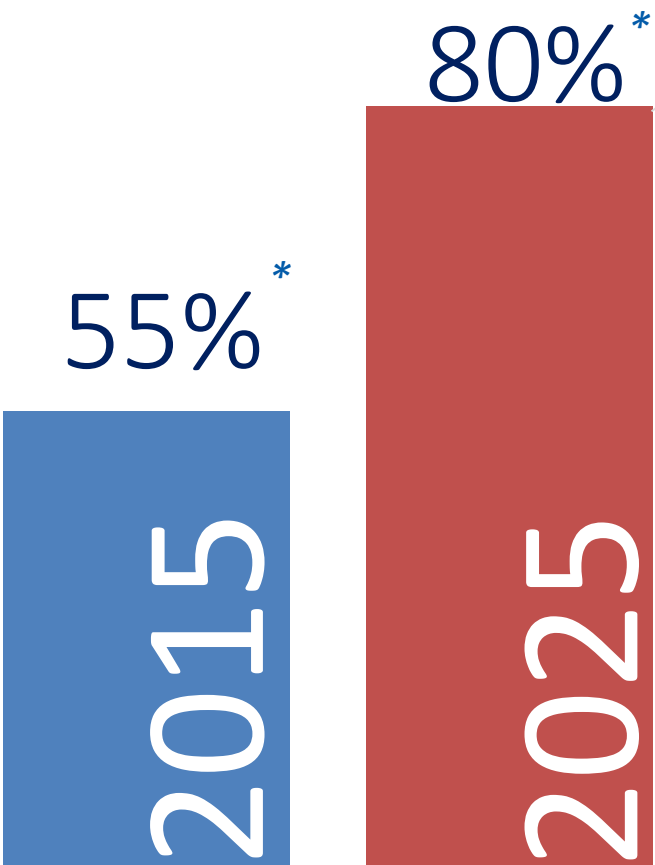


MRO .ART
MODERN RADIATION ONCOLOGY
35° RESIDENTIAL COURSE

SEER data
Banerjee S. et al. J Clin Oncol 2023; 41(4):626-63
González-Martín A. et al. Ann Oncol 2024; 35(6):575-586.
Ray-Coquard I. et al. Ann Oncol 2024; 35(2):136-147.
O'Malley D.M. et al. J Clin Oncol 2024 (online ahead of print).

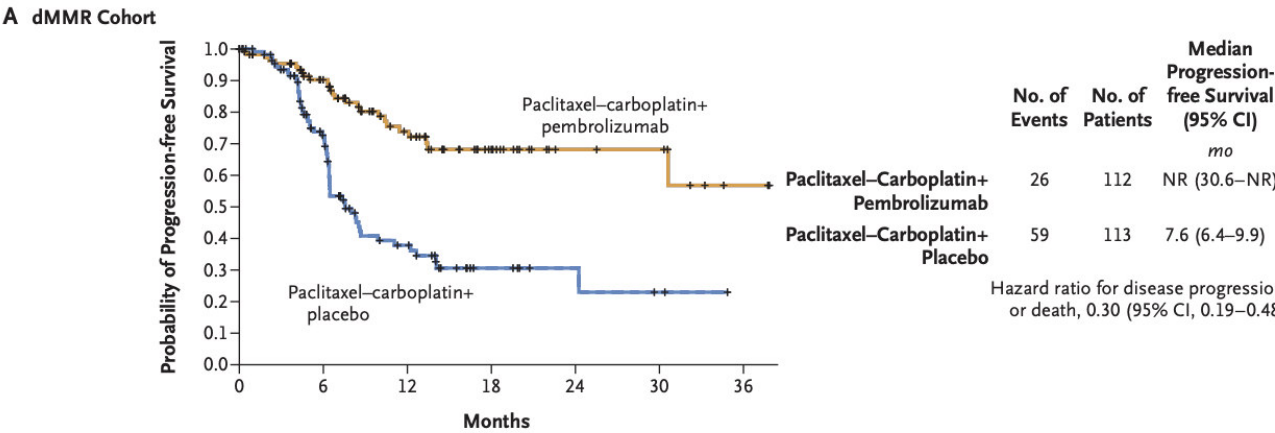
TREATING CANCER

Advanced/metastatic MSI-H/dMMR and ICI in endometrial cancer



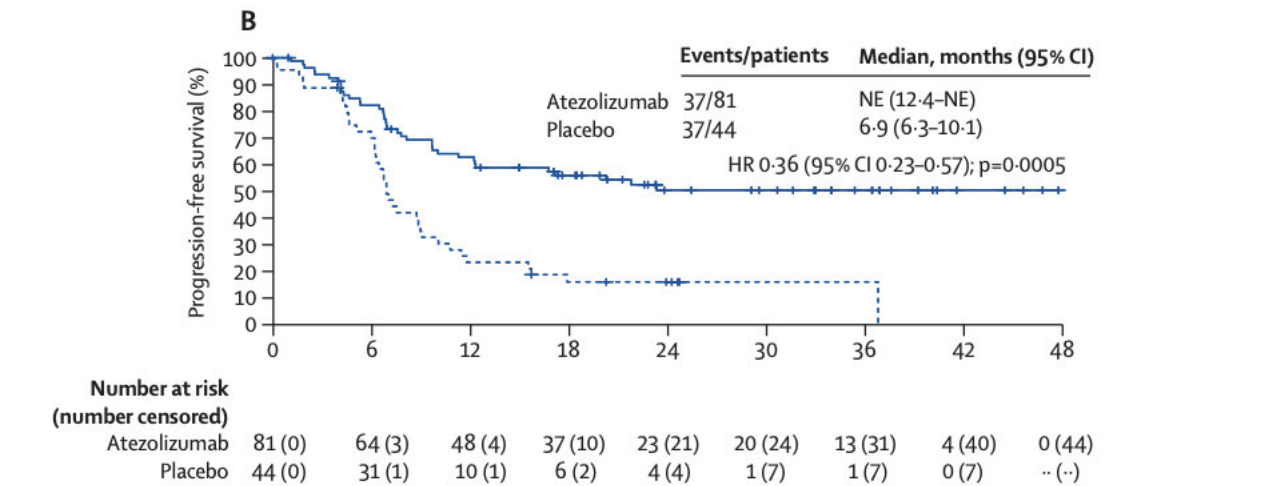
2-Y OS

*dMMR patients, ICI only
Data from Bogani G. et al, Ann Oncol 2024
Eskander et al, NEJM 2023
M.R. Mirza, N Engl J Med 2023
Colombo et al, Ann Oncol 2023



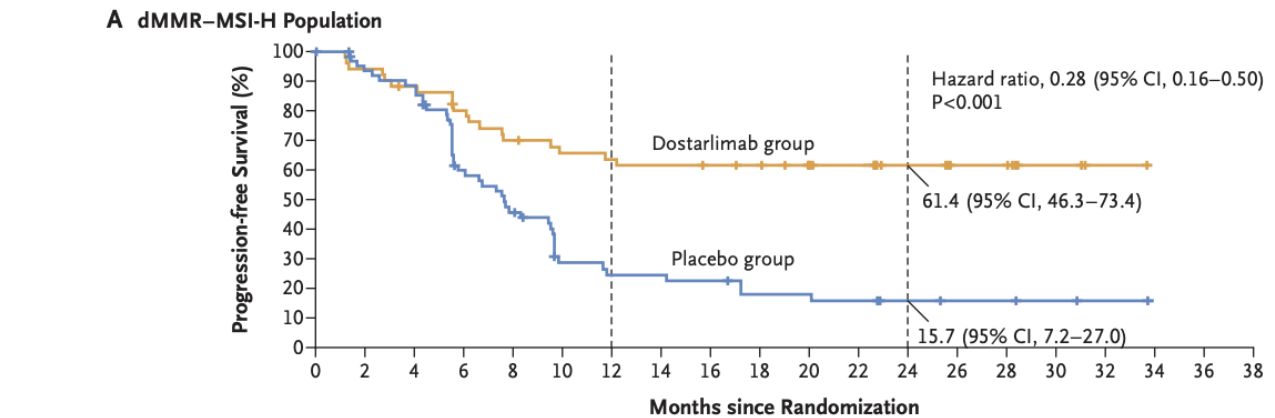
No. at Risk

	0	6	12	18	24	30	36
Paclitaxel-carboplatin+ pembrolizumab	112	80	44	22	9	8	2
Paclitaxel-carboplatin+ placebo	113	62	24	8	4	2	0



Number at risk (number censored)

	0	6	12	18	24	30	36	42	48
Atezolizumab	81 (0)	64 (3)	48 (4)	37 (10)	23 (21)	20 (24)	13 (31)	4 (40)	0 (44)
Placebo	44 (0)	31 (1)	10 (1)	6 (2)	4 (4)	1 (7)	1 (7)	0 (7)	.. (..)



No. at Risk

	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38
Dostarlimab group	53	48	44	39	34	31	30	29	28	27	25	19	13	9	9	4	1	0		
Placebo group	65	57	54	34	26	14	12	12	11	8	8	7	4	3	3	2	1	0		

No. of Events

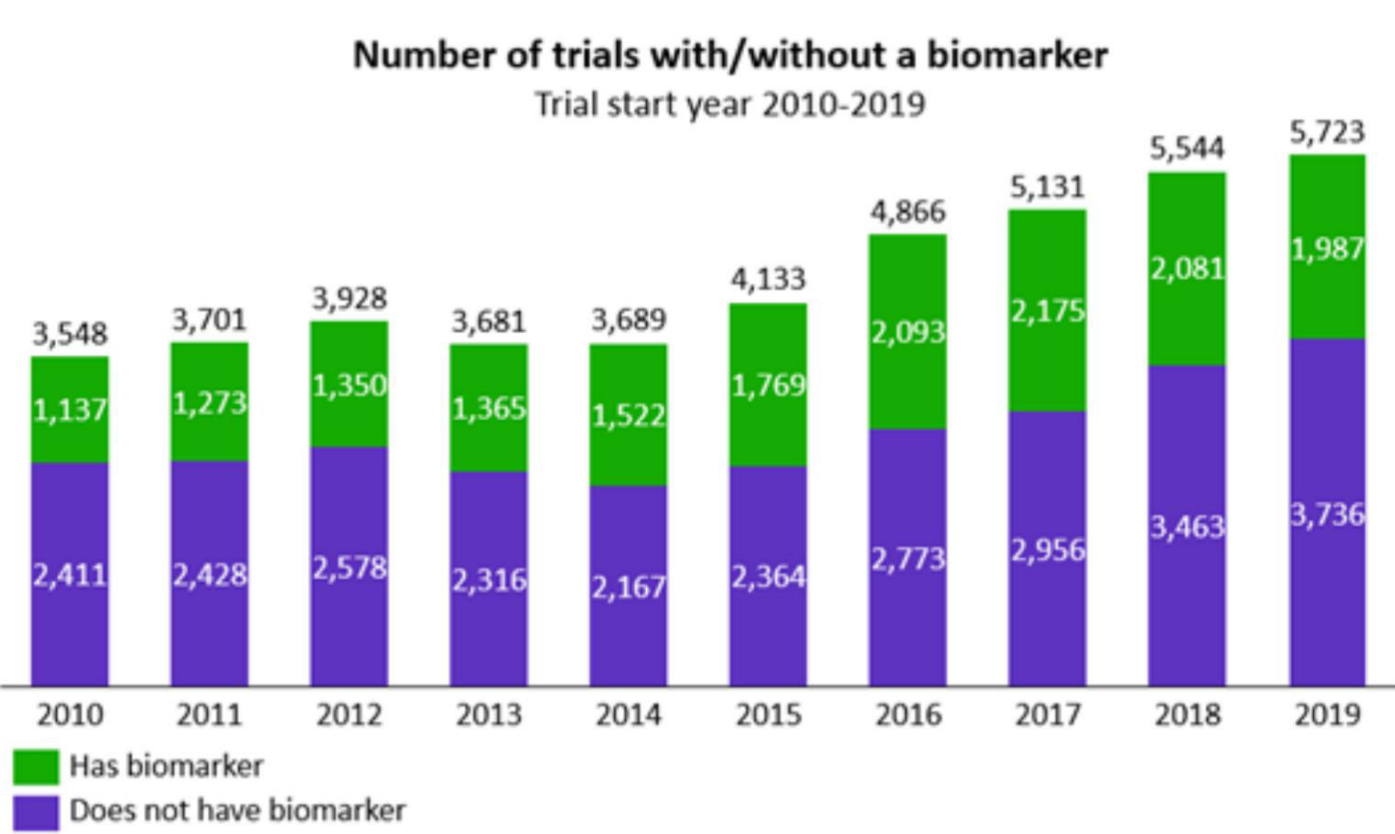
	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38
Dostarlimab group	0	3	6	10	15	17	18	19	19	19	19	19	19	19	19	19	19	19		
Placebo group	0	4	7	24	32	41	43	43	44	46	46	47	47	47	47	47	47	47		

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PRESENT AND FUTURE CHALLENGES

Biormakers driven trials



MORE OPTIONS, LESS TOOLS TO CHOOSE

Source: Cortellis Clinical Trials Intelligence

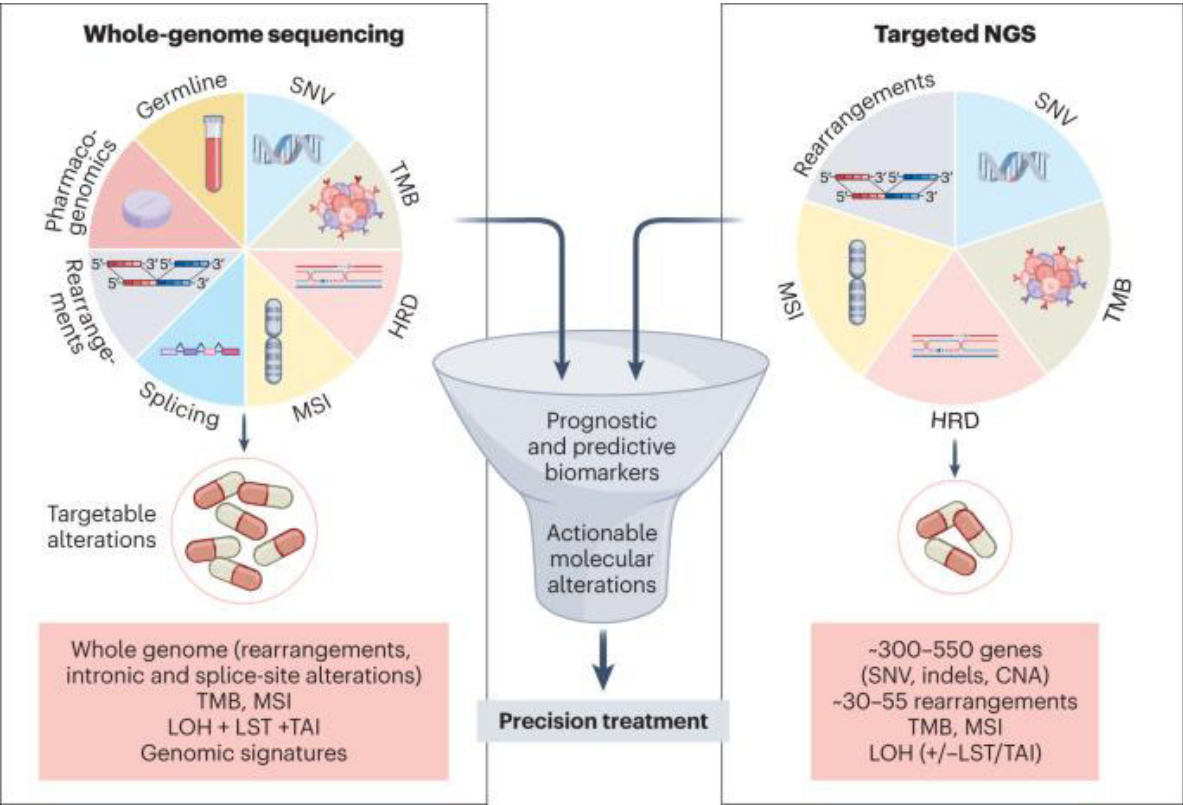
FUTURE PERSPECTIVES

From genomics to -omics



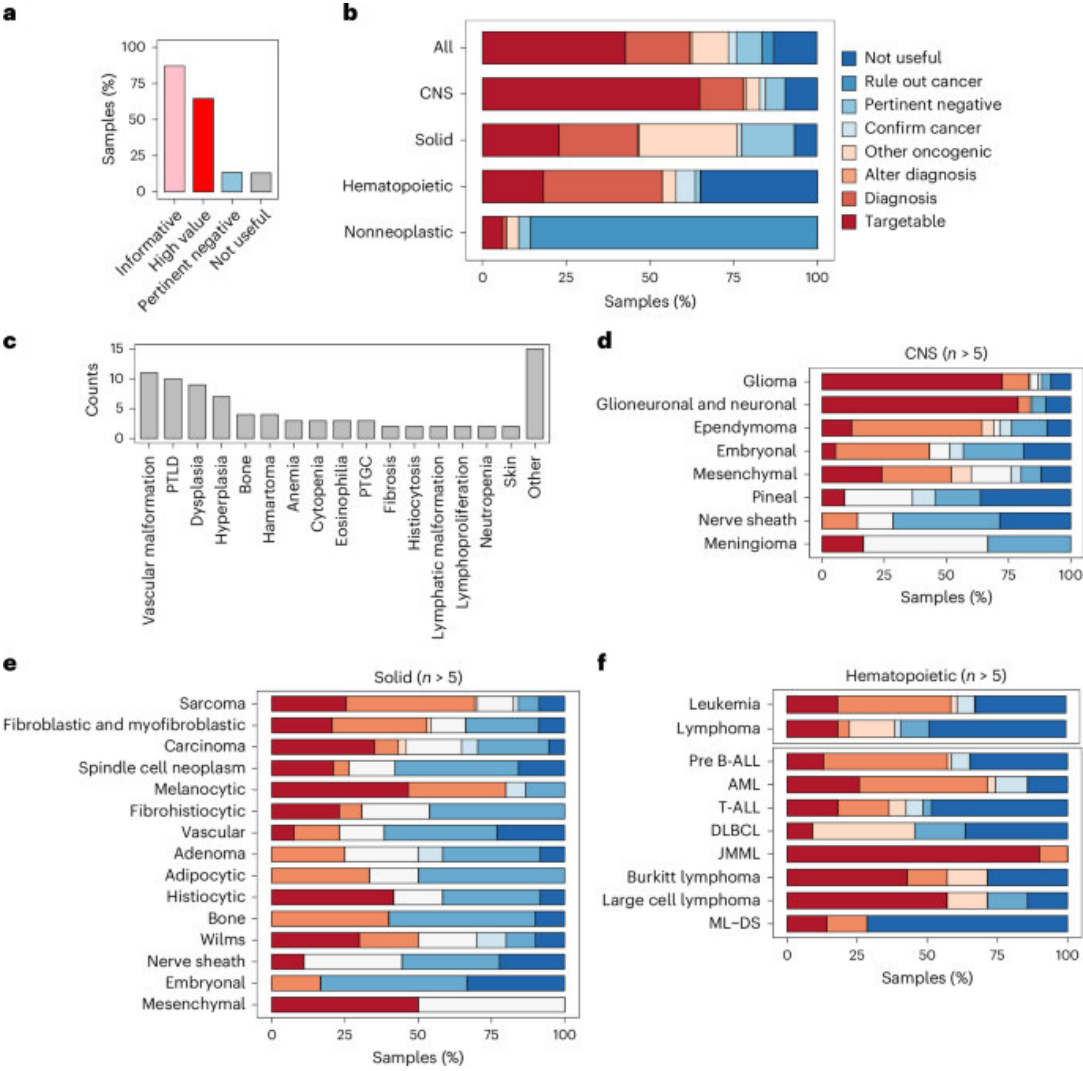
LARGER

DNA



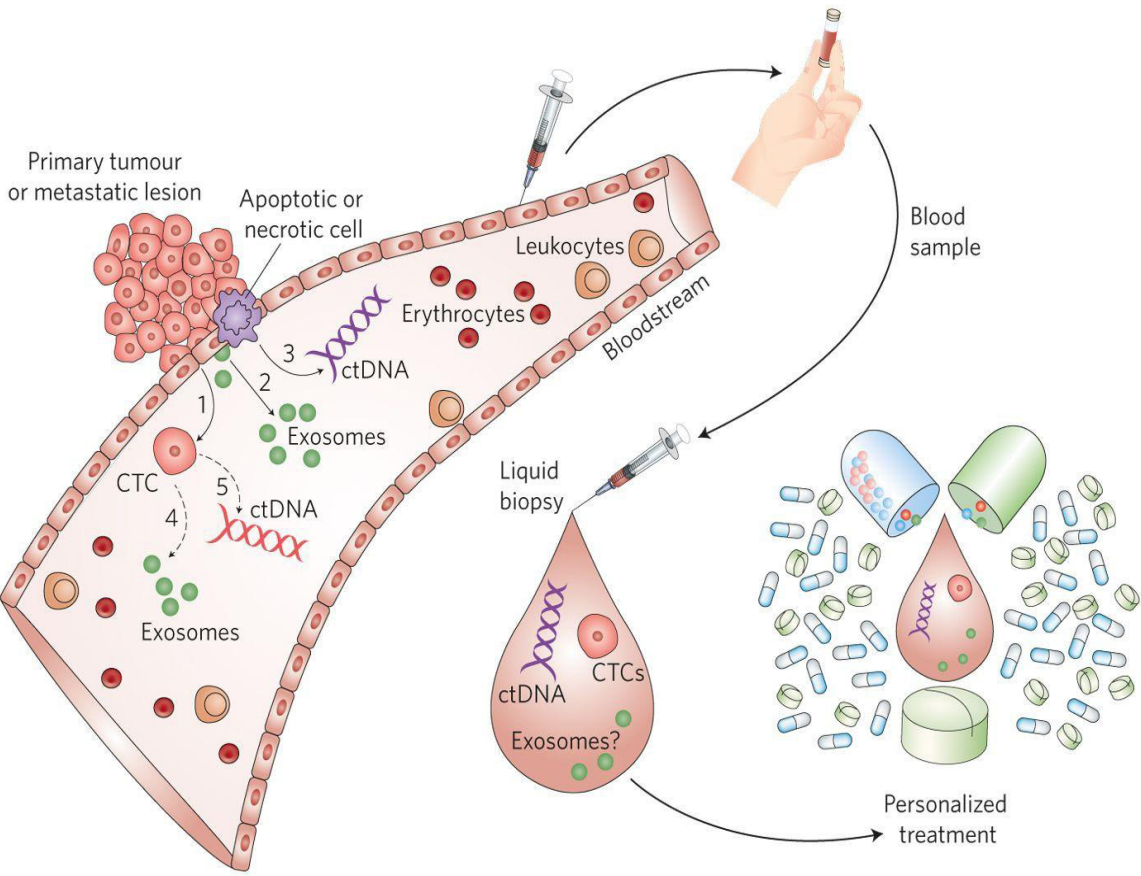
WIDER

RNA/PROTEINE



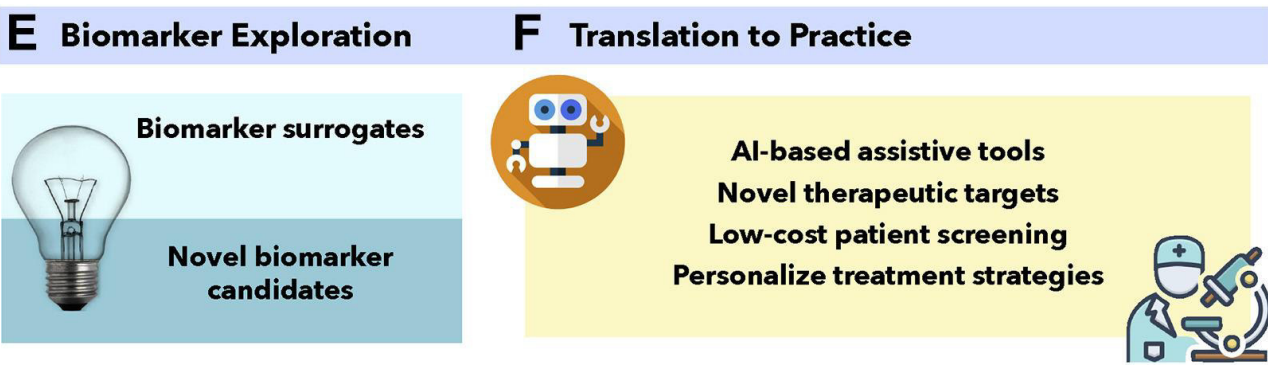
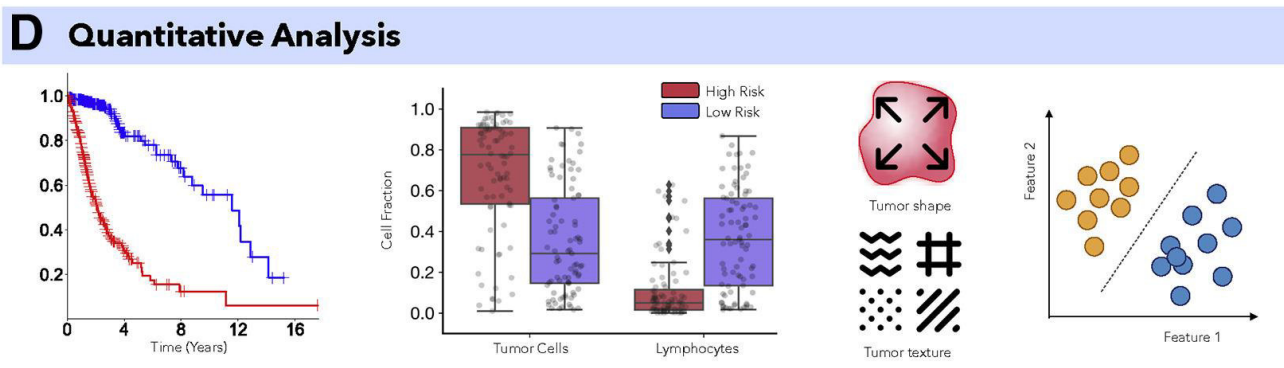
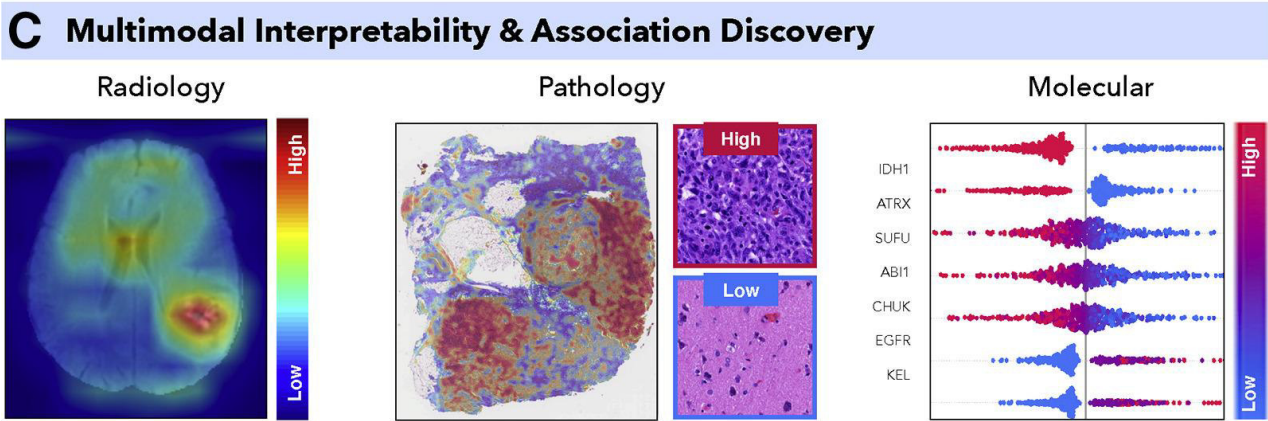
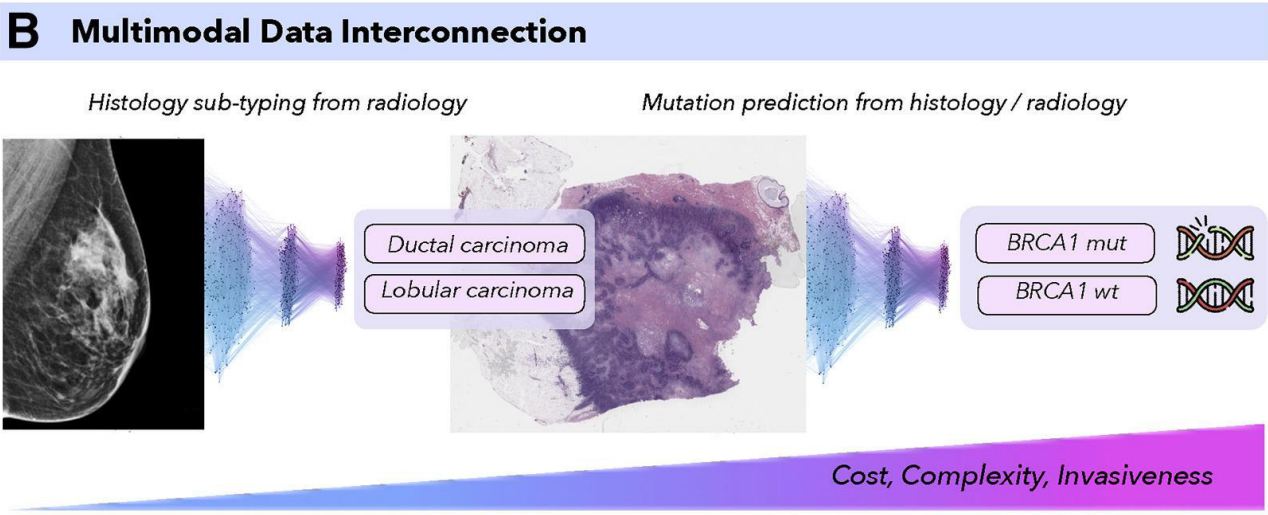
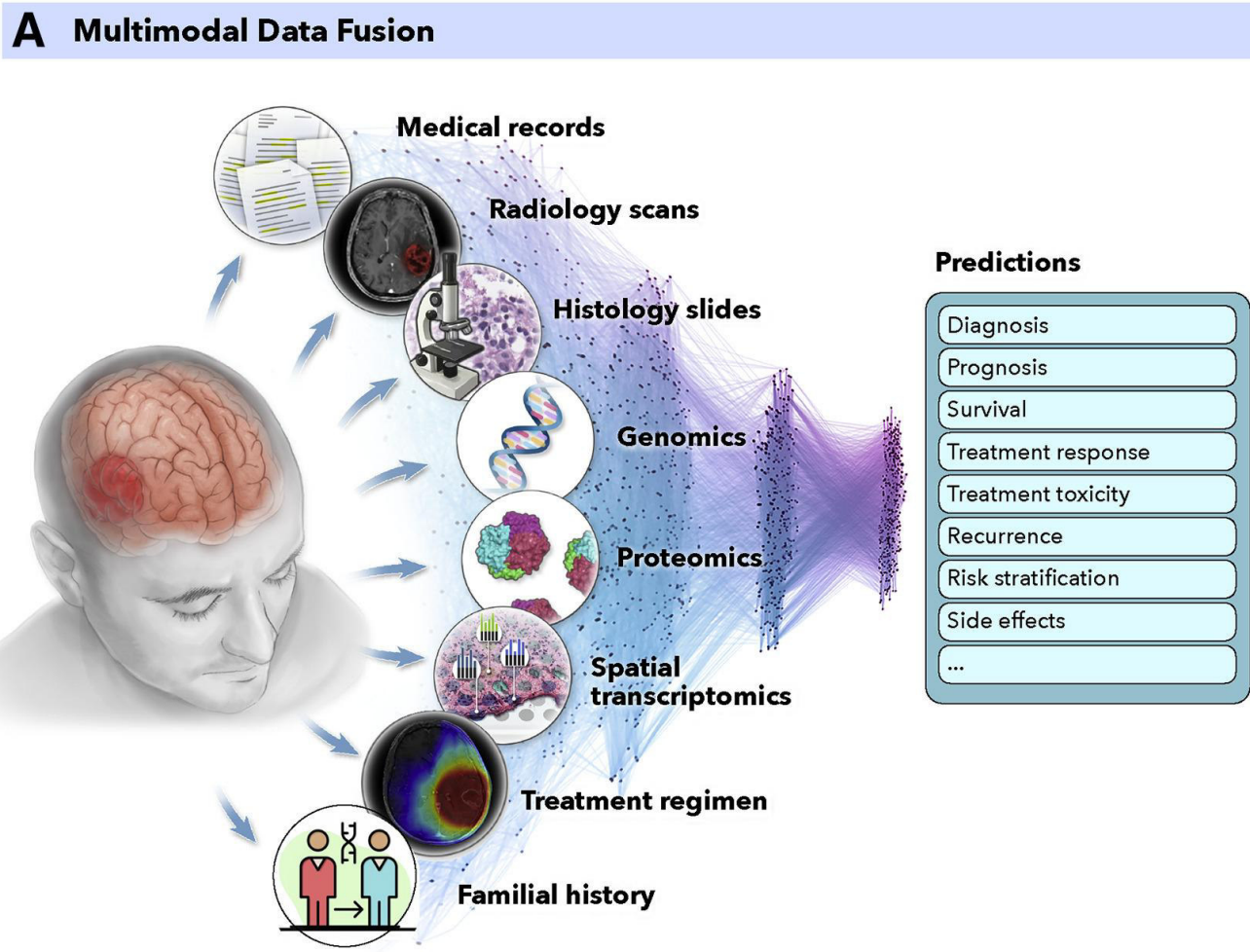
MORE FREQUENT

ctDNA/CTCs

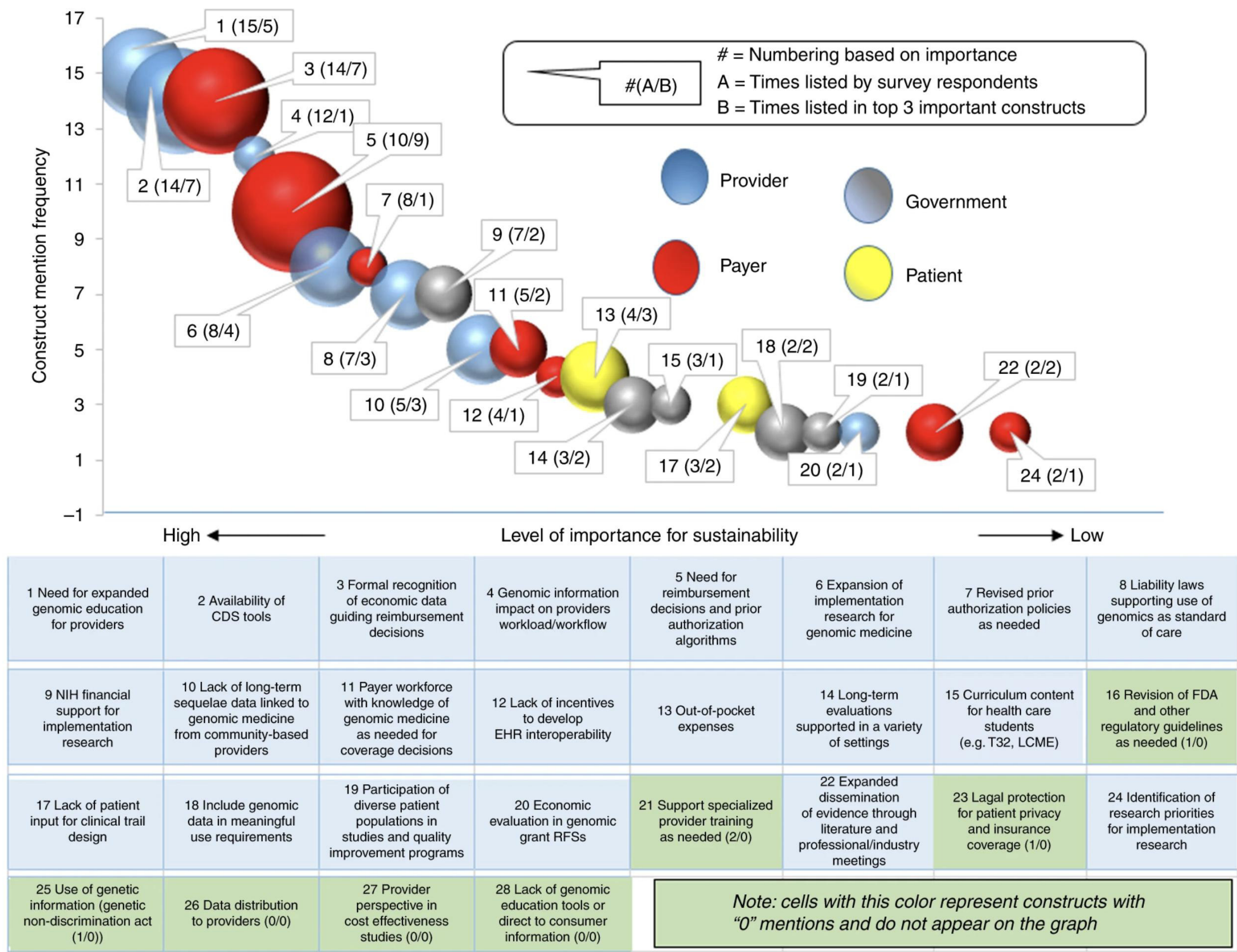


FUTURE PERSPECTIVES

Data integration



SUSTAINABILITY



Constructs weighted by frequency selected as being important in genomic sustainability (a), and frequency weighted in top three of importance (b).

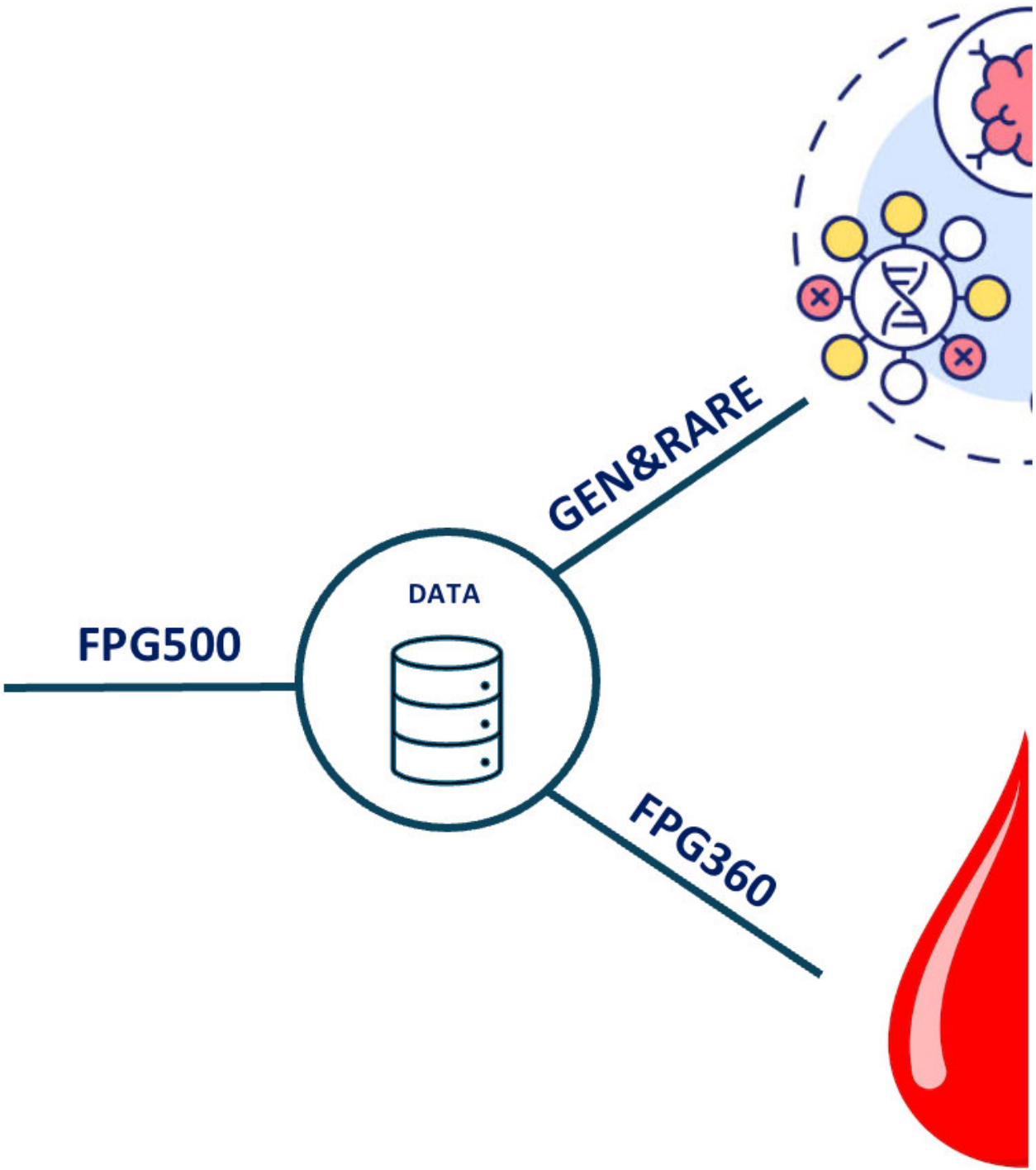
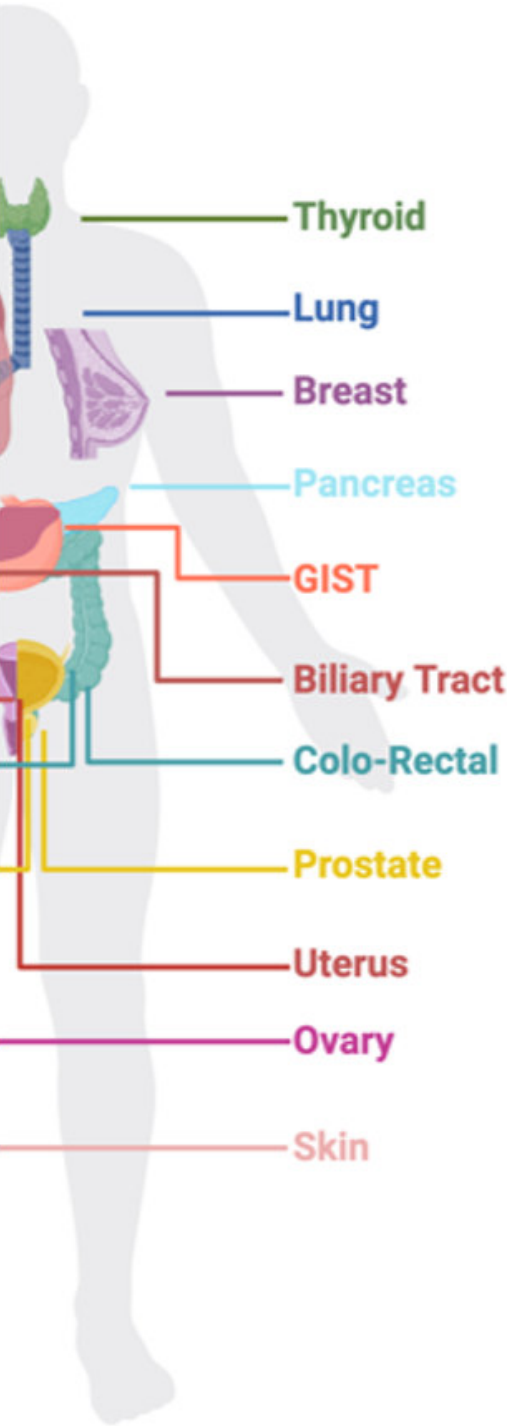
FPG CHOICE

COMPREHENSIVE GENOMIC PROFILING PROGRAM

Turning a standard diagnostic Step into an opportunity to generate research data

 Total
6164 pts

since Jan 2022 



RARE GENETIC DISEASE CHARACTERIZATION PROGRAM

Exploring the whole exome to identify rare genetic defects

 Total
460 pts

 since Jan 2025



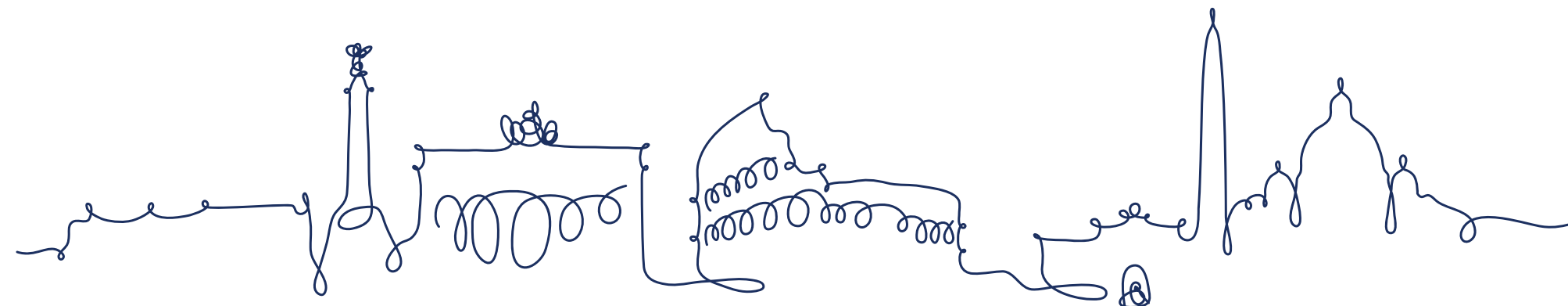
LIQUID BIOPSY PROGRAM IN ONCOLOGY

Technology to capture the temporal dimension of tumors

Powered by  GUARDANT™

 since Oct 2025





Genomics driven oncology

Genomics drives cancer