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DI MEDICINA

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AVIANO**



The **Liquid biopsy**
Research Group

PMAC
Precision Medicine Academic Consortium

Breast Journal Club, l'importanza della ricerca in oncologia – Napoli, 7 - 8 Marzo 2025

Liquid biopsy analysis with AI tools

Past is experience, present is experiment, future is expectation

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The Liquid Biopsy Research Group (LBRG)

Precision Medicine Academic Consortium (PMAC)



Conflict of Interest Disclosure Statement

 Last updated on 07.03.2025

Stock and Other Ownership Interests: None

Honoraria: None

Consulting or Advisory Role: AstraZeneca, Daiichi Sankyo, Eli Lilly, GlaxoSmithKline, Incyte, Novartis, Pfizer, Merck Sharp & Dohme, Menarini Stemline, Abbvie

Expert Testimony: None

Research Funding: None

Patents, Royalties, Other Intellectual Property: None

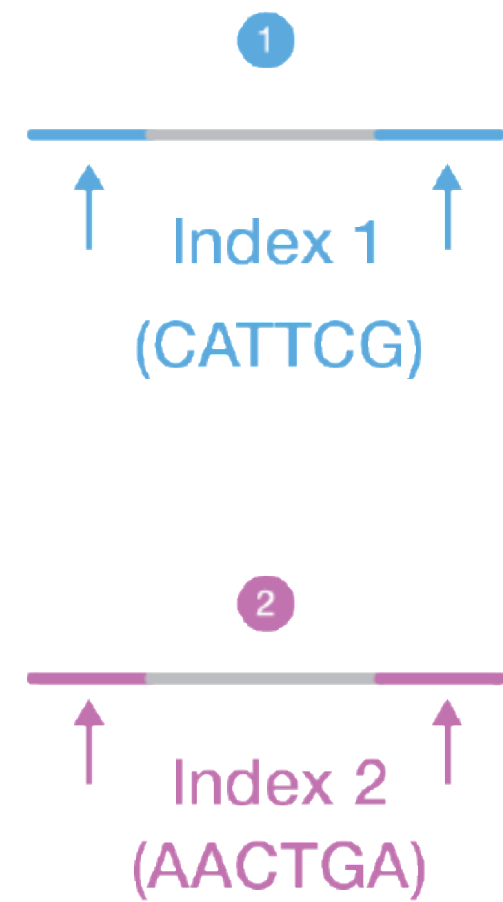
Travel Expenses: Menarini Stemline, Novartis, Gilead

AI likes to look for **patterns** in science and life

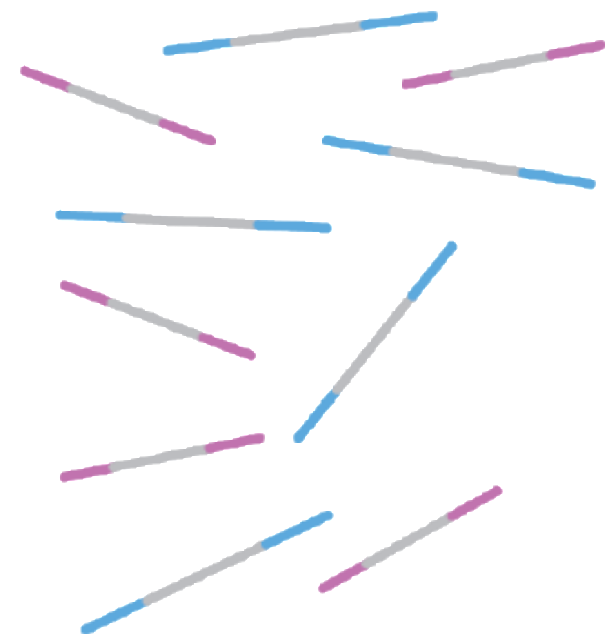
AI likes to look for patterns in science and life

The extreme amount of data generated from NGS

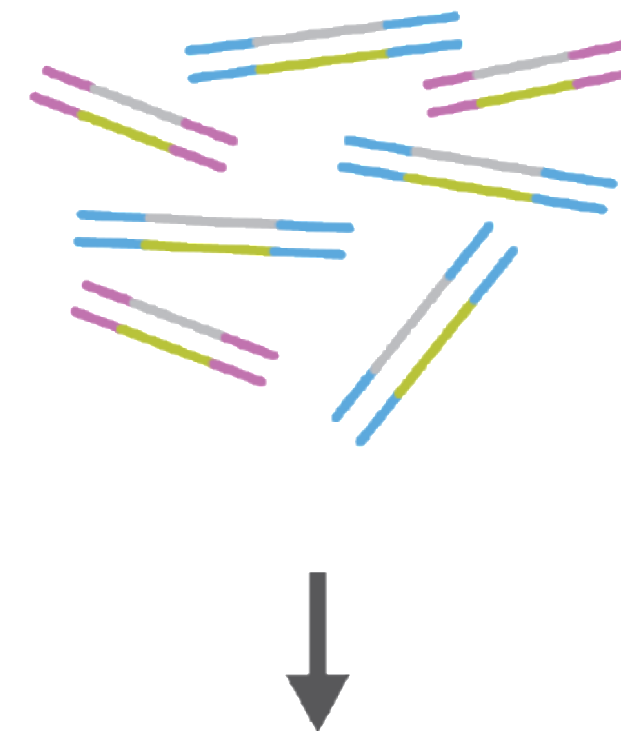
Library Preparation



Pool



Sequence



Sequence Output to Data File

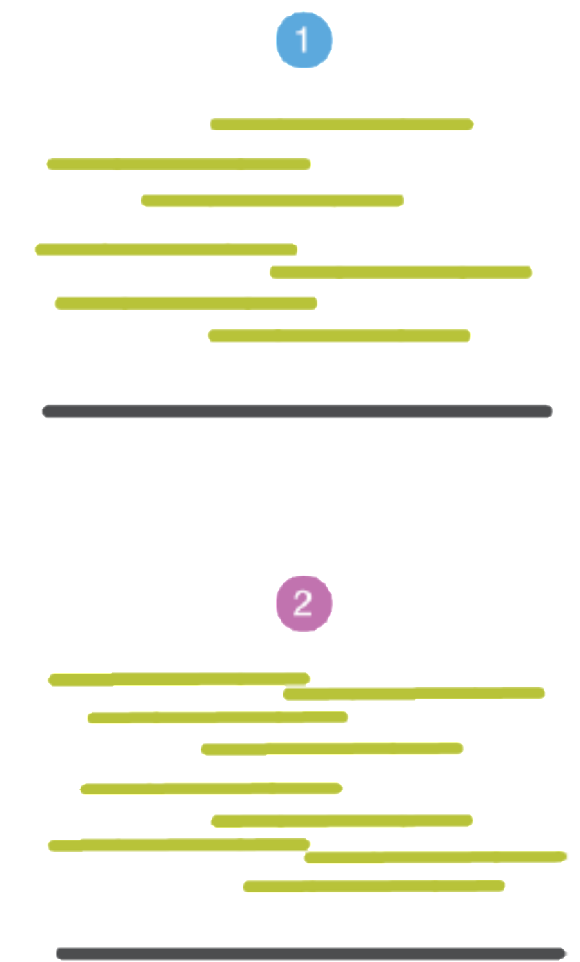
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AACT GATCGGATCC  
CATT CGTGGCAGTC  
AACT GAACCTGATG  
AACT GAGATTACAA  
CATT CGCAGTTCATT  
CATT CGAACTTCGA
```

Demultiplex

1
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CATT CGTGGCAGTC
CATT CGCAGTTCATT
CATT CGAACTTCGA

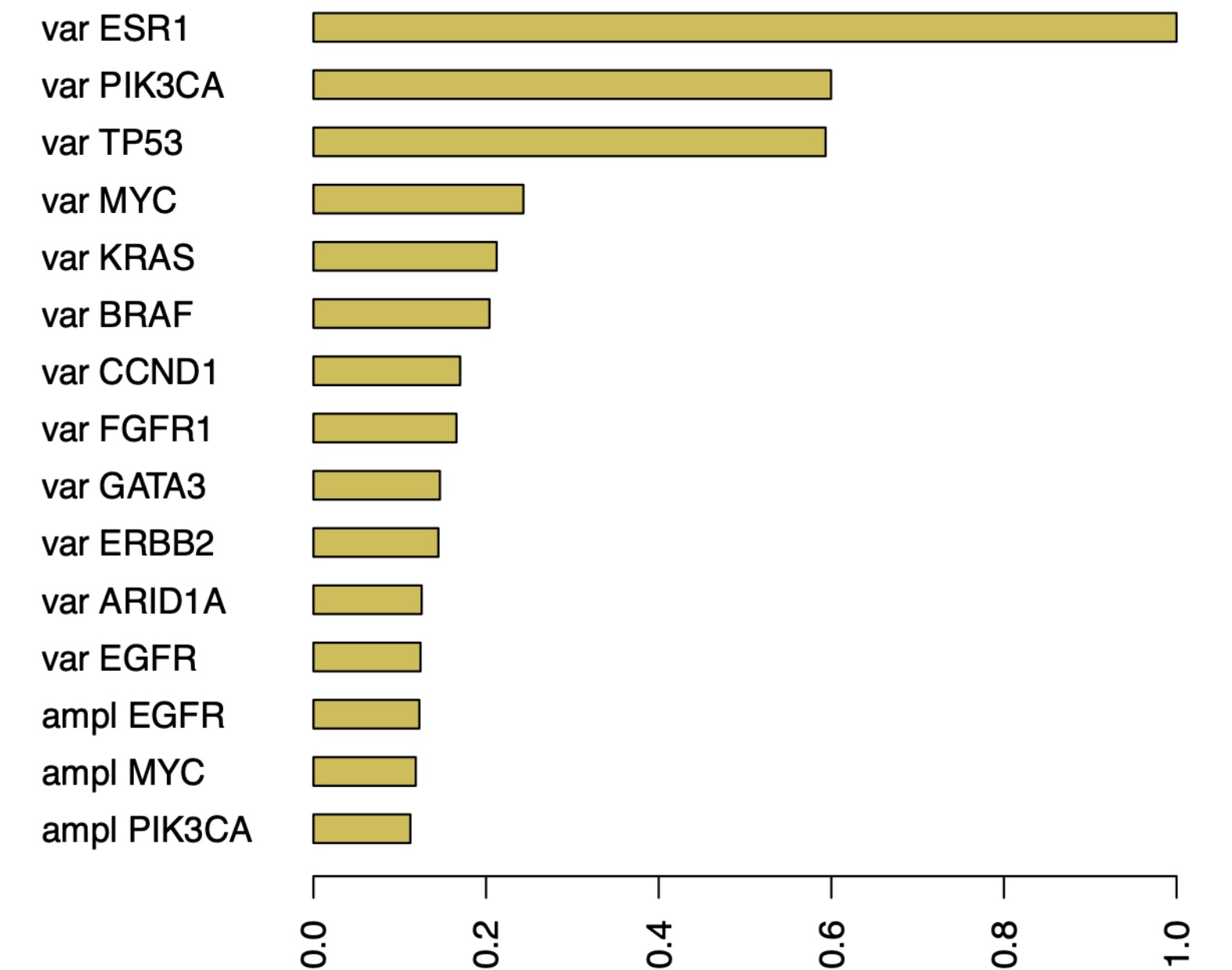
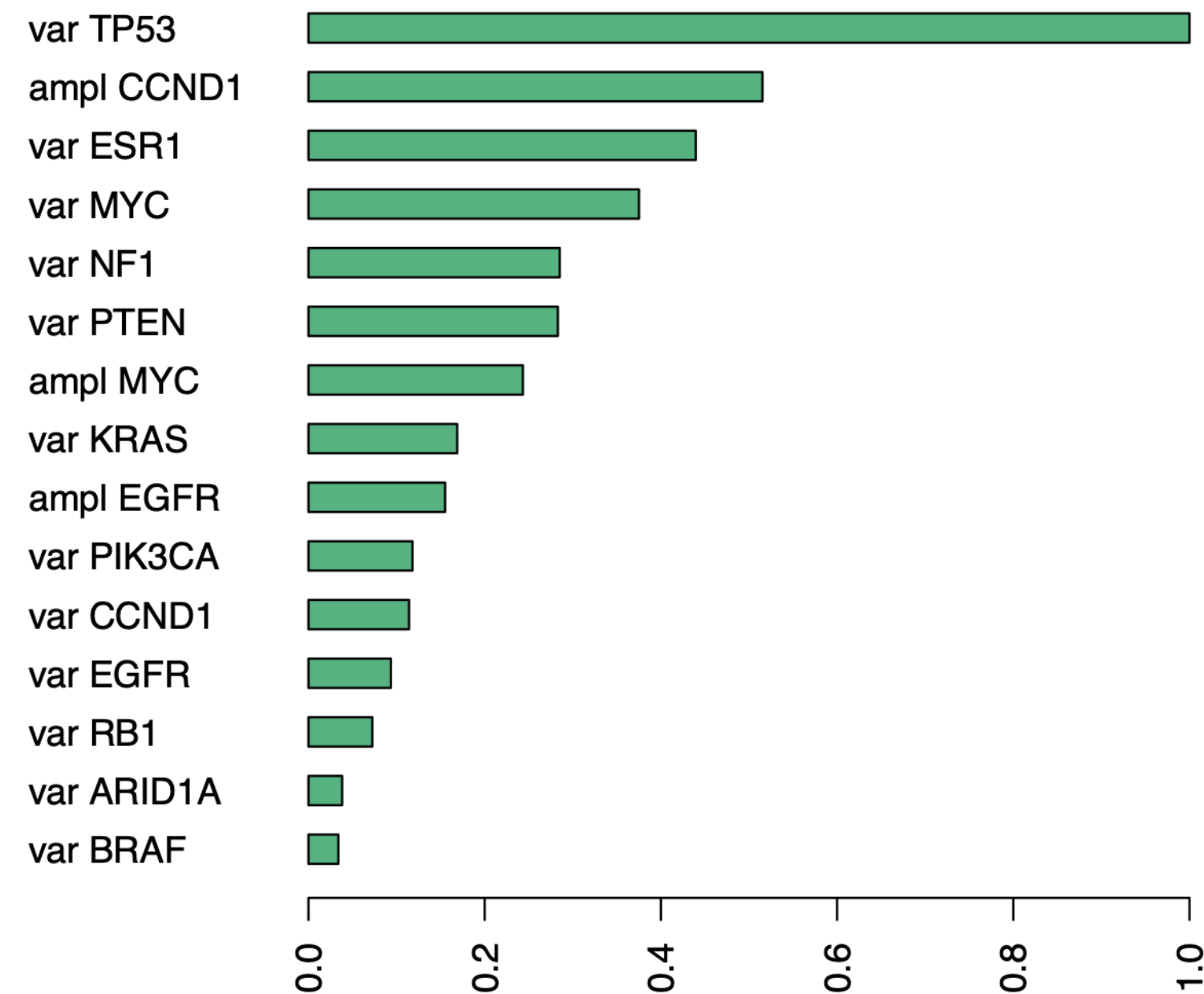
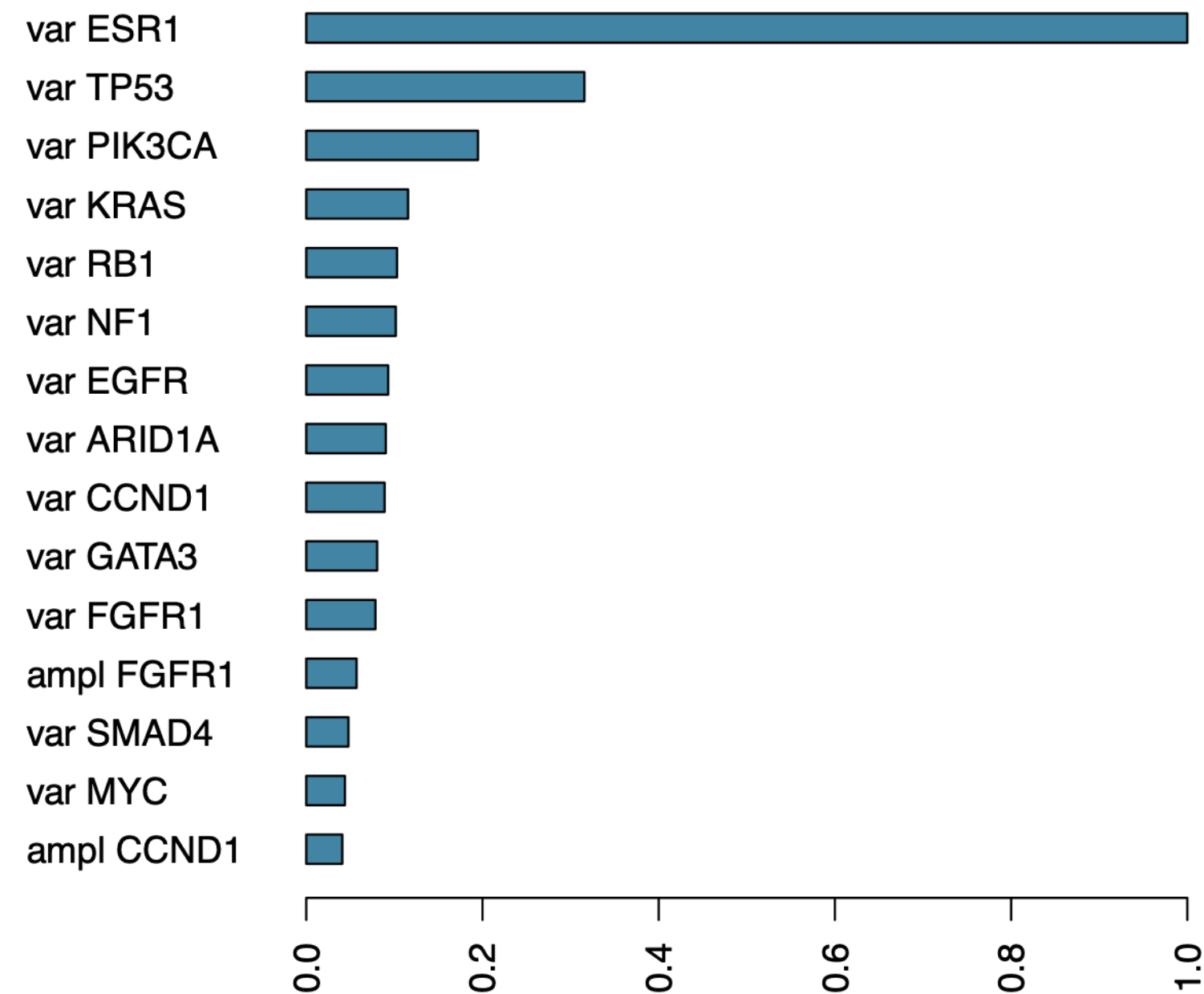
2
AACT GAGTCCGATA
AACT GATCGGATCC
AACT GAACCTGATG
AACT GAGATTACAA

Align



AI likes to look for patterns in science and life

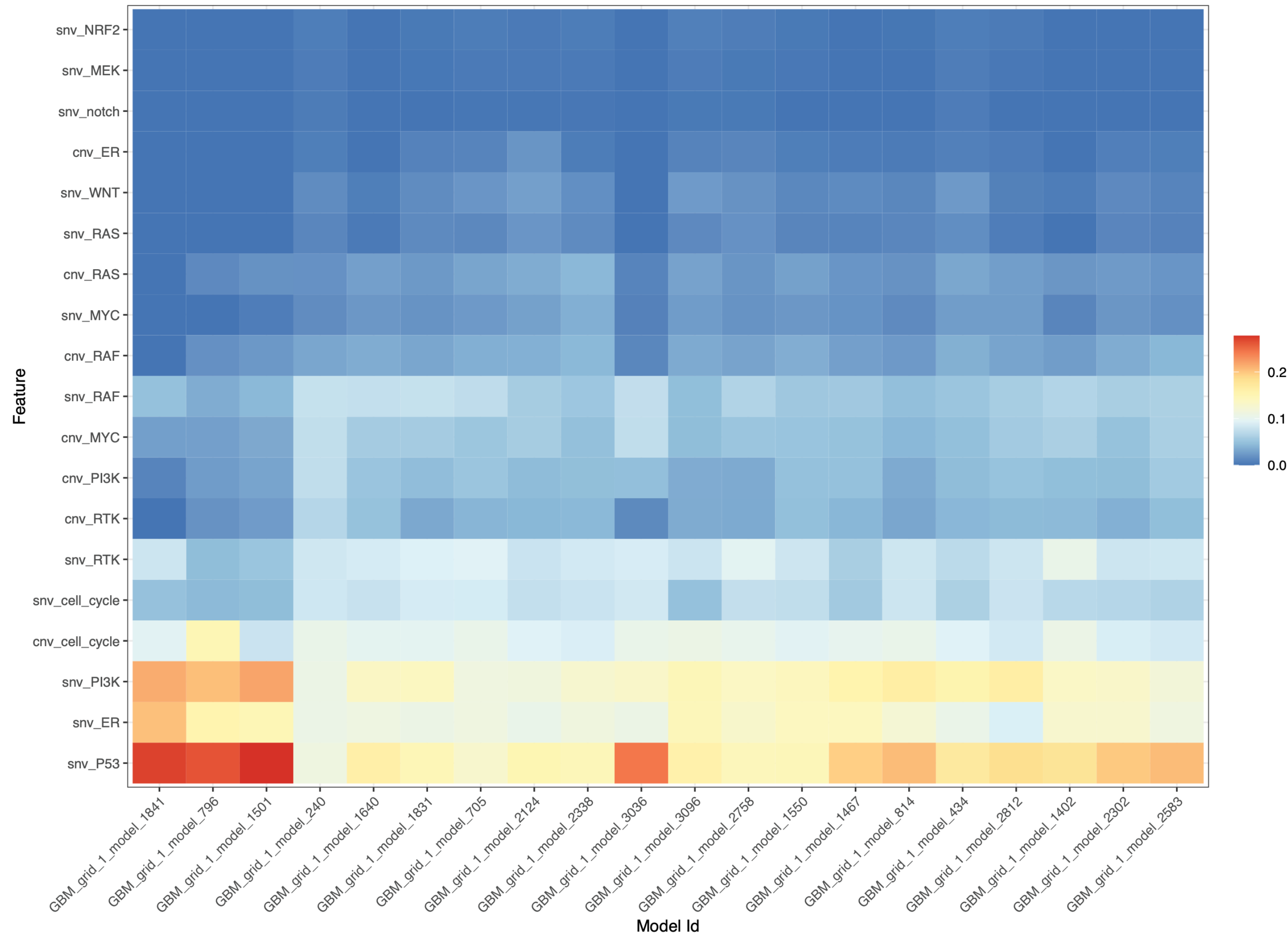
Model training for single gene alterations



Best performing GBMs models for single gene alterations in the overall population (A), ET population (B) and population not treated with CDK4/6i (C)

AI likes to look for patterns in science and life

Top performing GBM models in the endocrine treated population

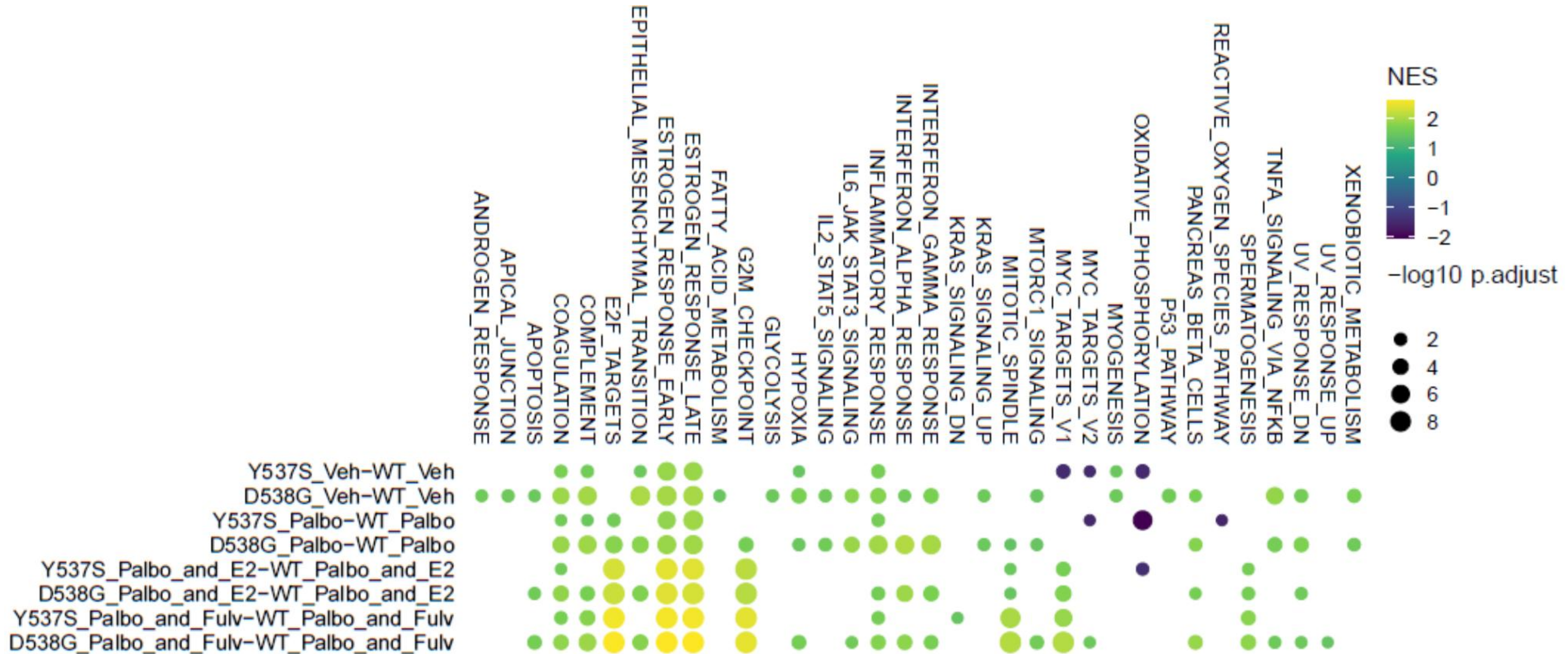


Top performing GBM models in the endocrine treated population predicting previous exposure to CDK4/6i

The highest RI was observed for P53 SNVs, PI3K SNVs, ER SNVs, Cell Cycle CNVs and RTK SNVs

AI likes to look for patterns in science and life

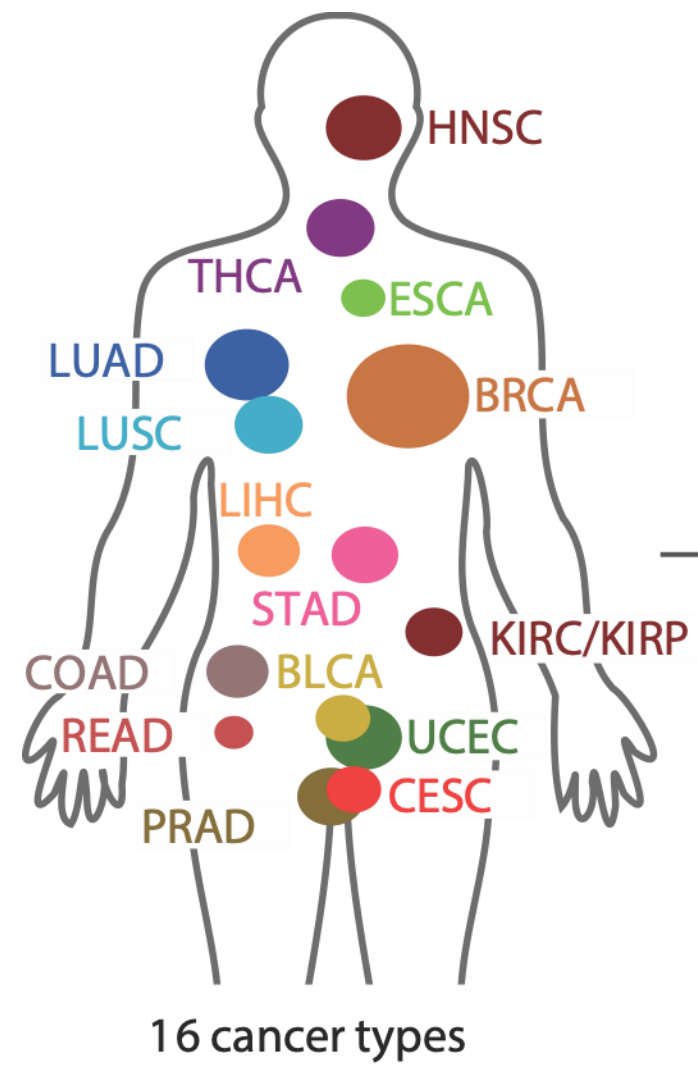
Top performing GBM models in the endocrine treated population



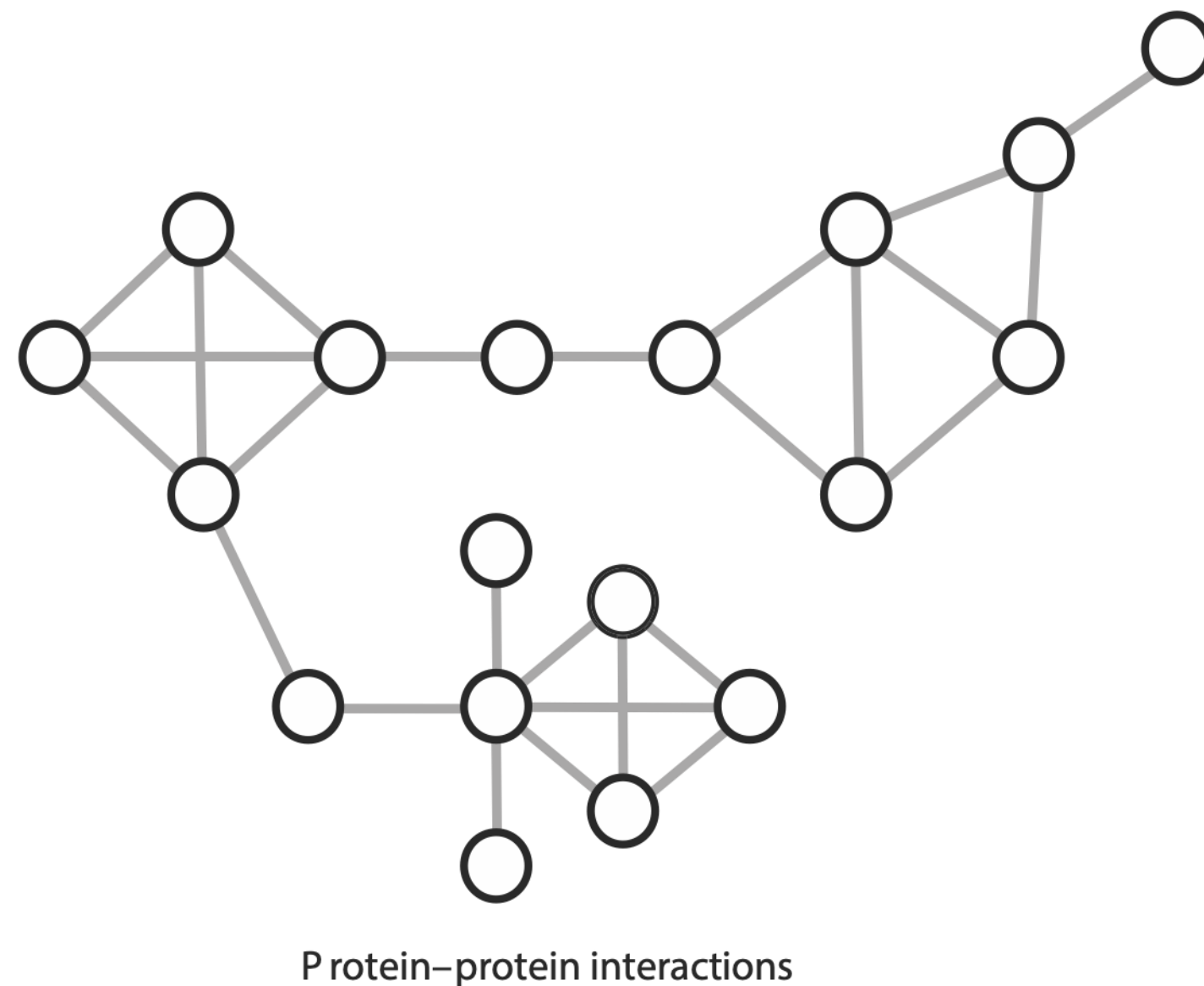
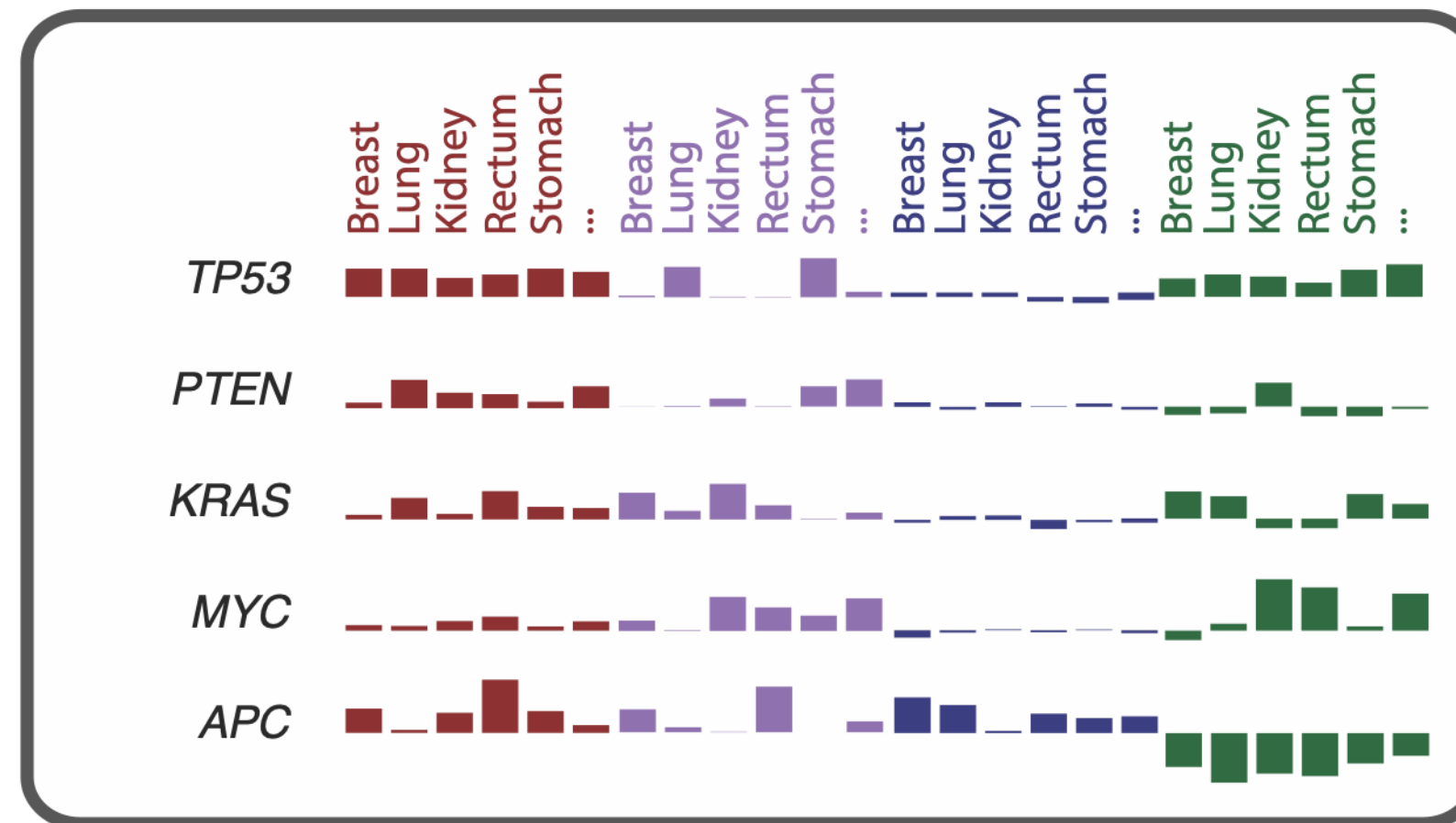
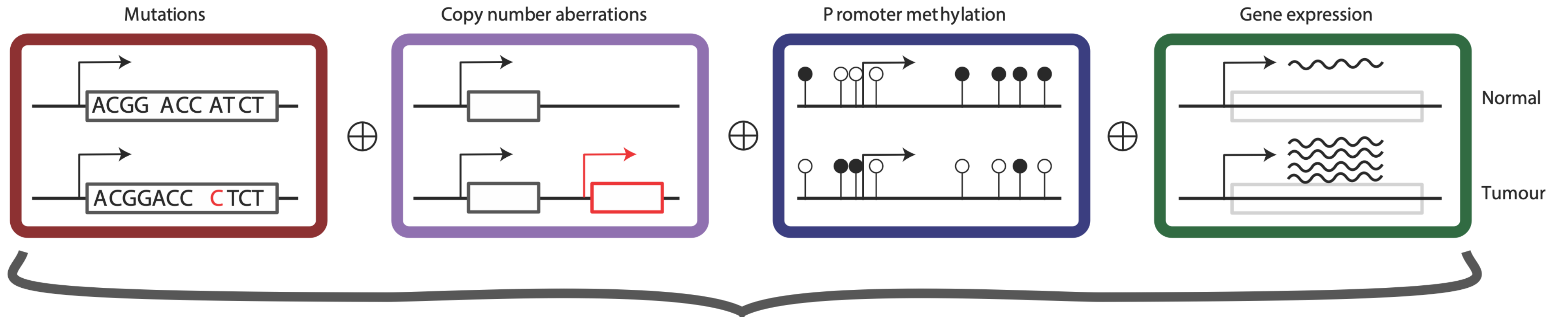
A step further: **neural networks**

A step further: neural networks

Integrate multiple omics to discover new cancer genes

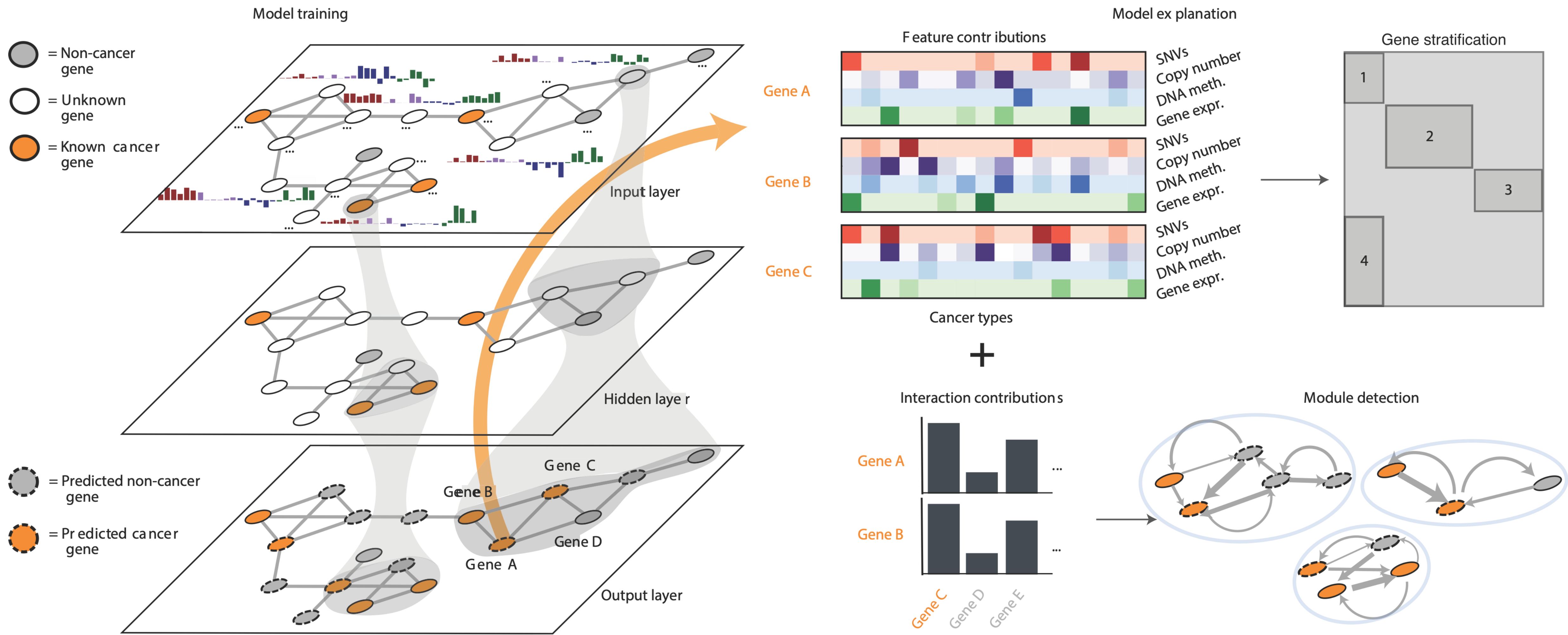


Multimomics data collection



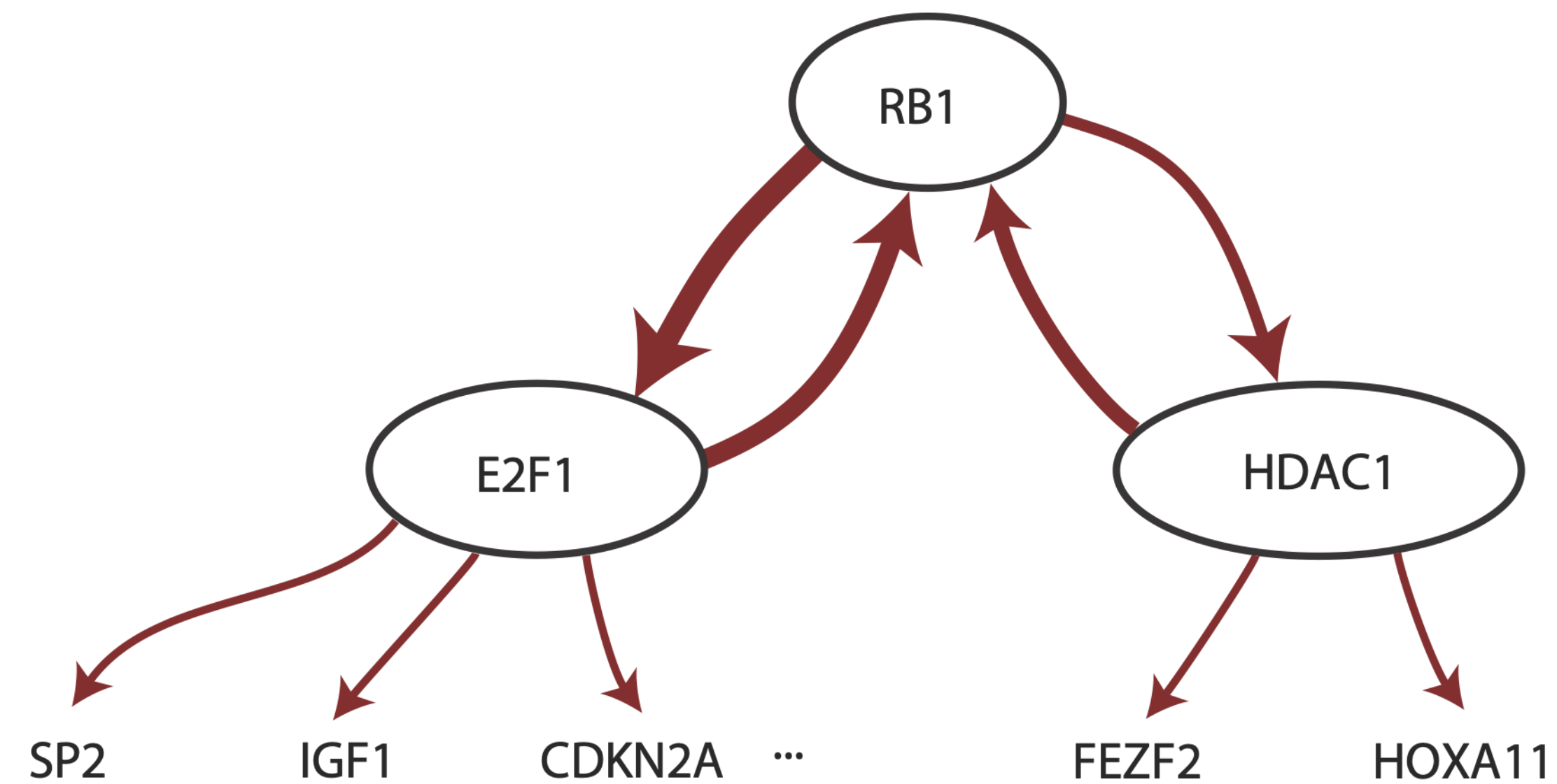
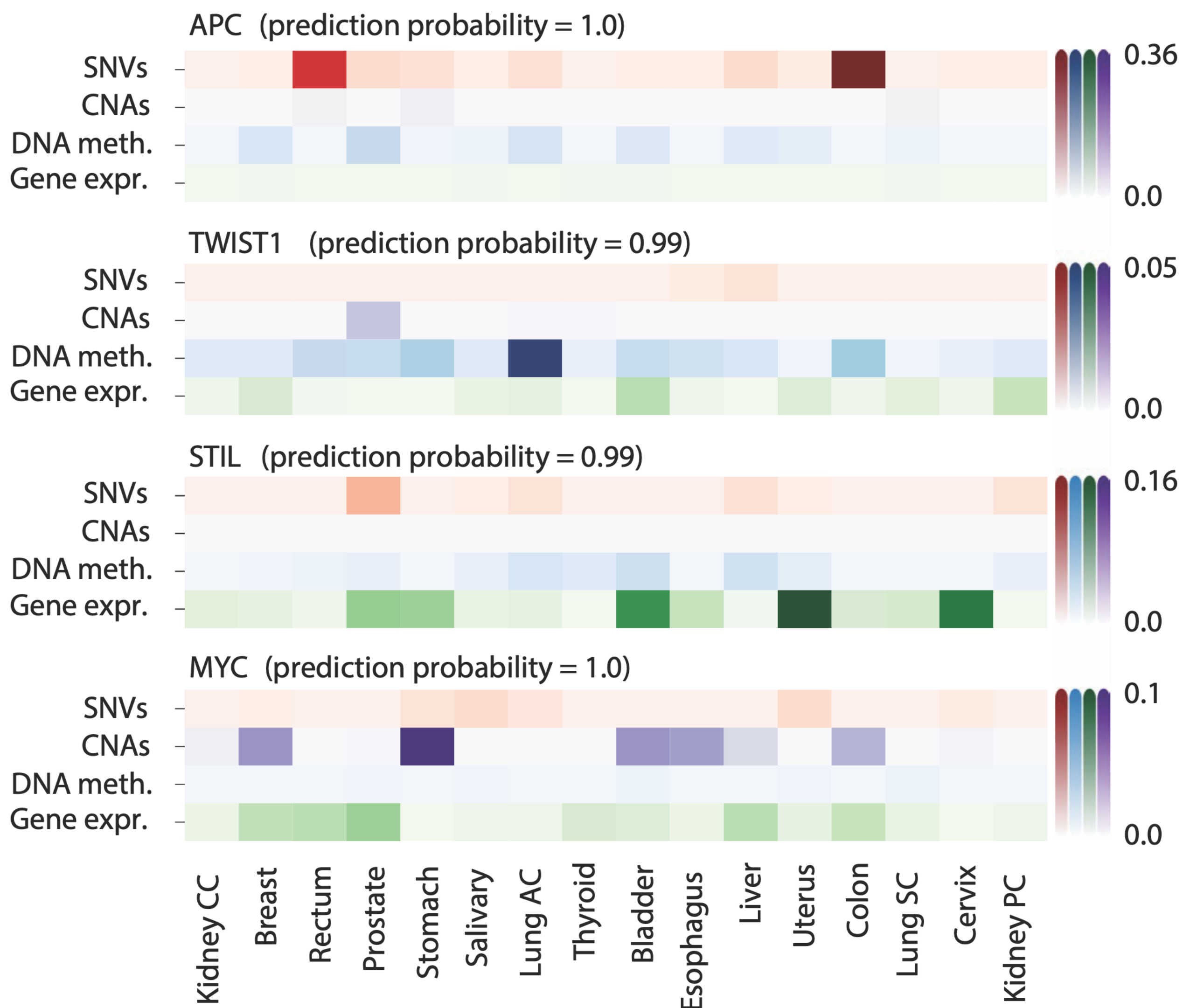
A step further: neural networks

Integrate multiple omics to discover new cancer genes



Integrate multiple omics to discover new cancer genes

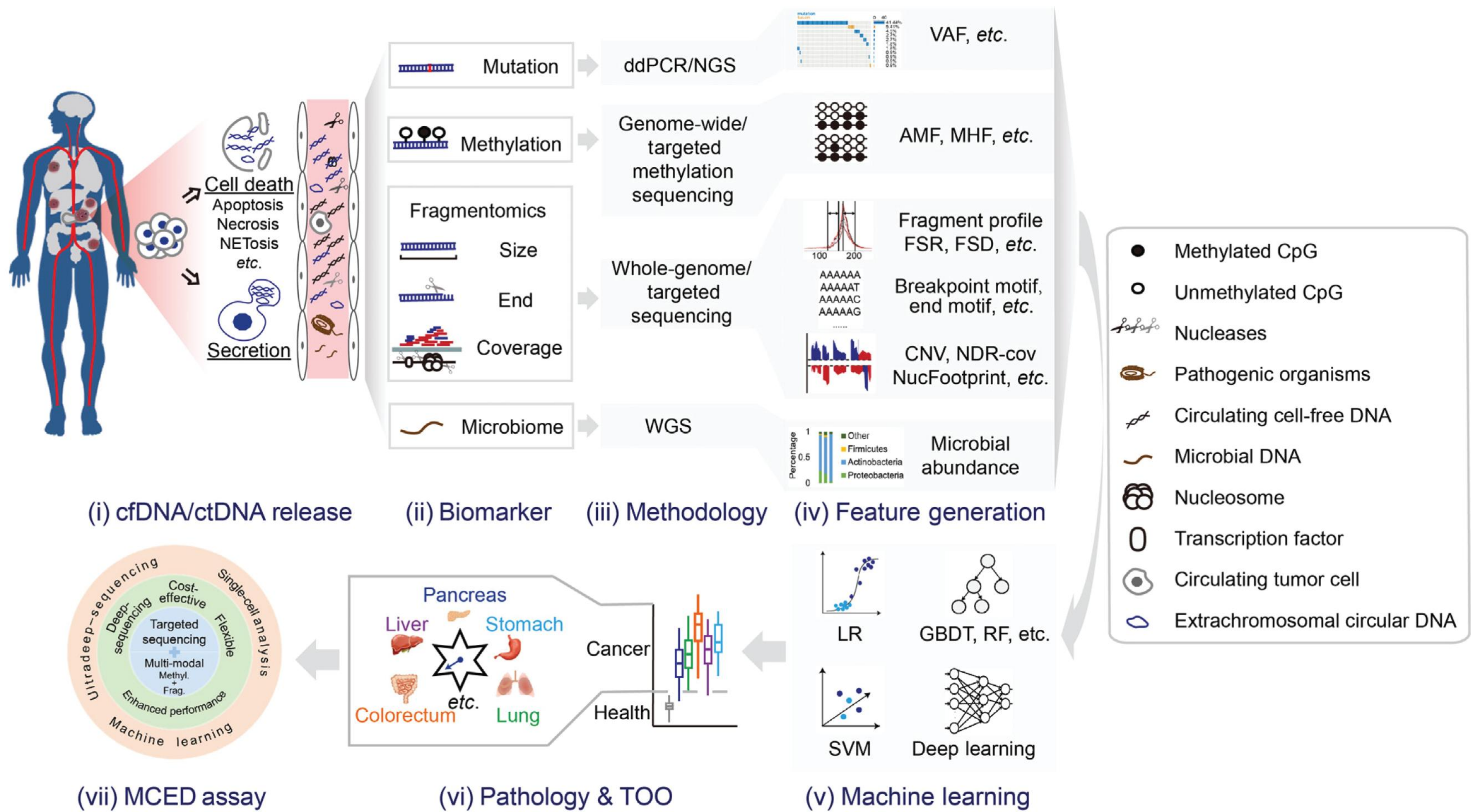
 The ground-proof



Fragmentomics: **following** the trail of crumbs

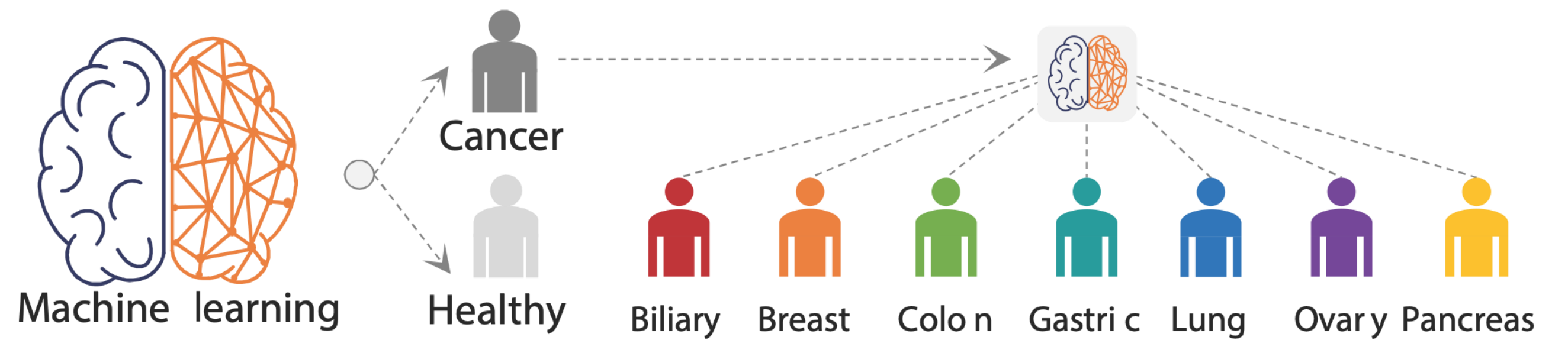
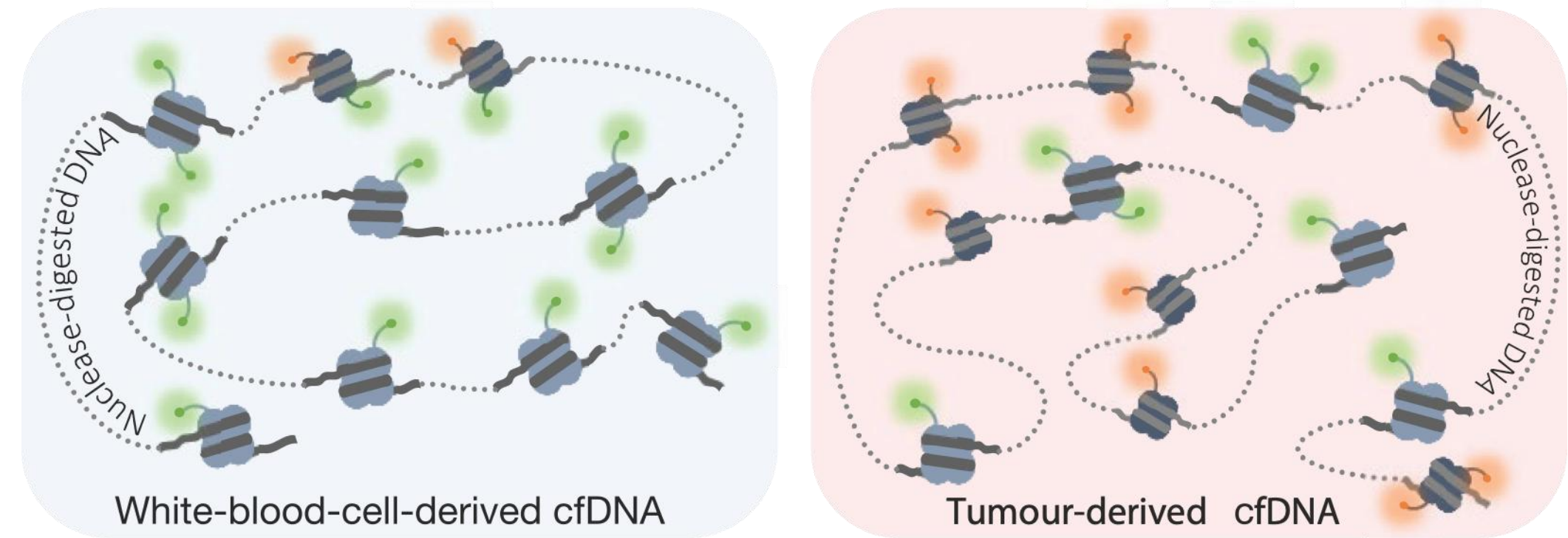
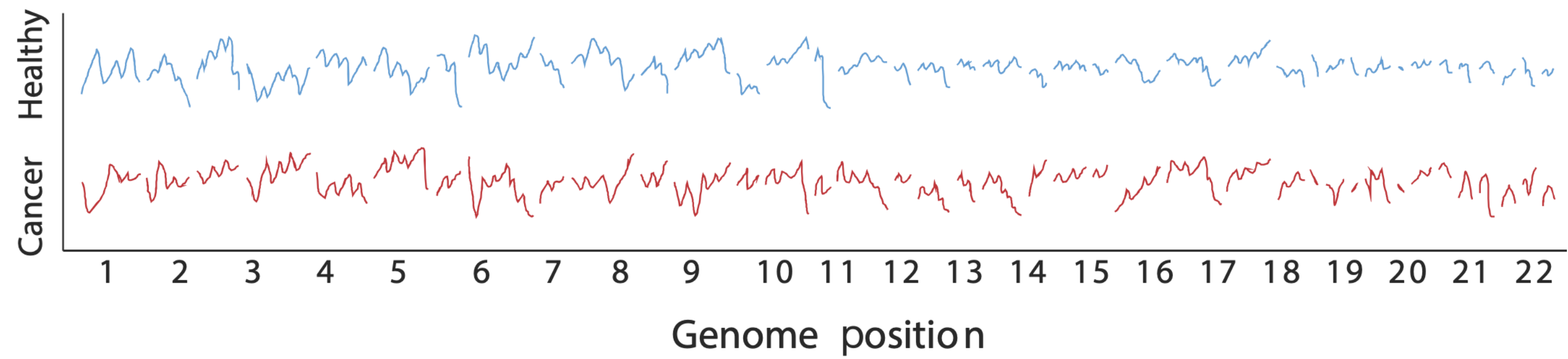
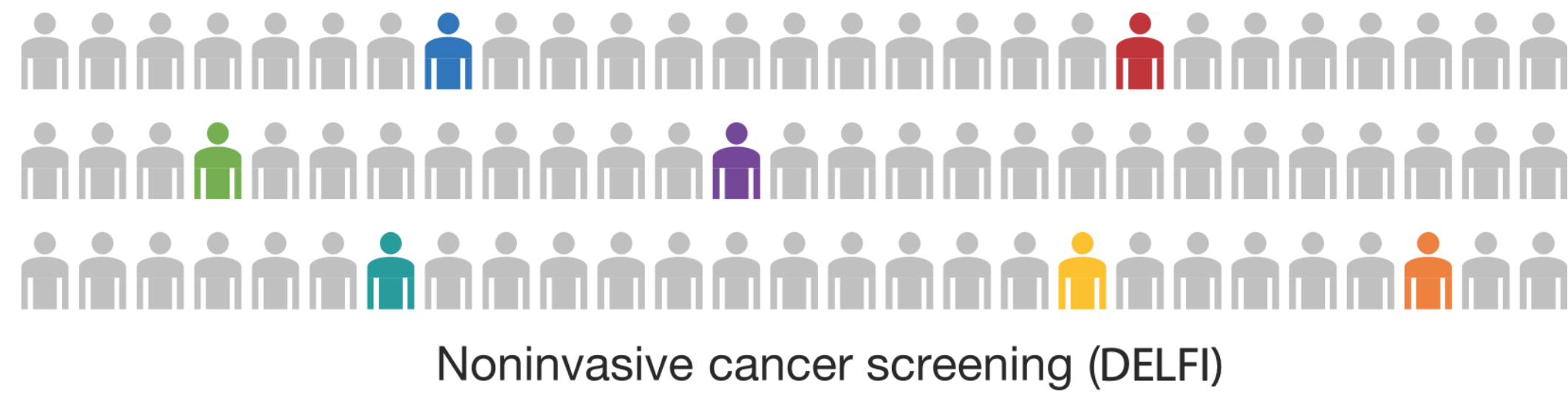
Fragmentomics: following the trail of crumbs

What's in our liquid-biopsy toolchain?



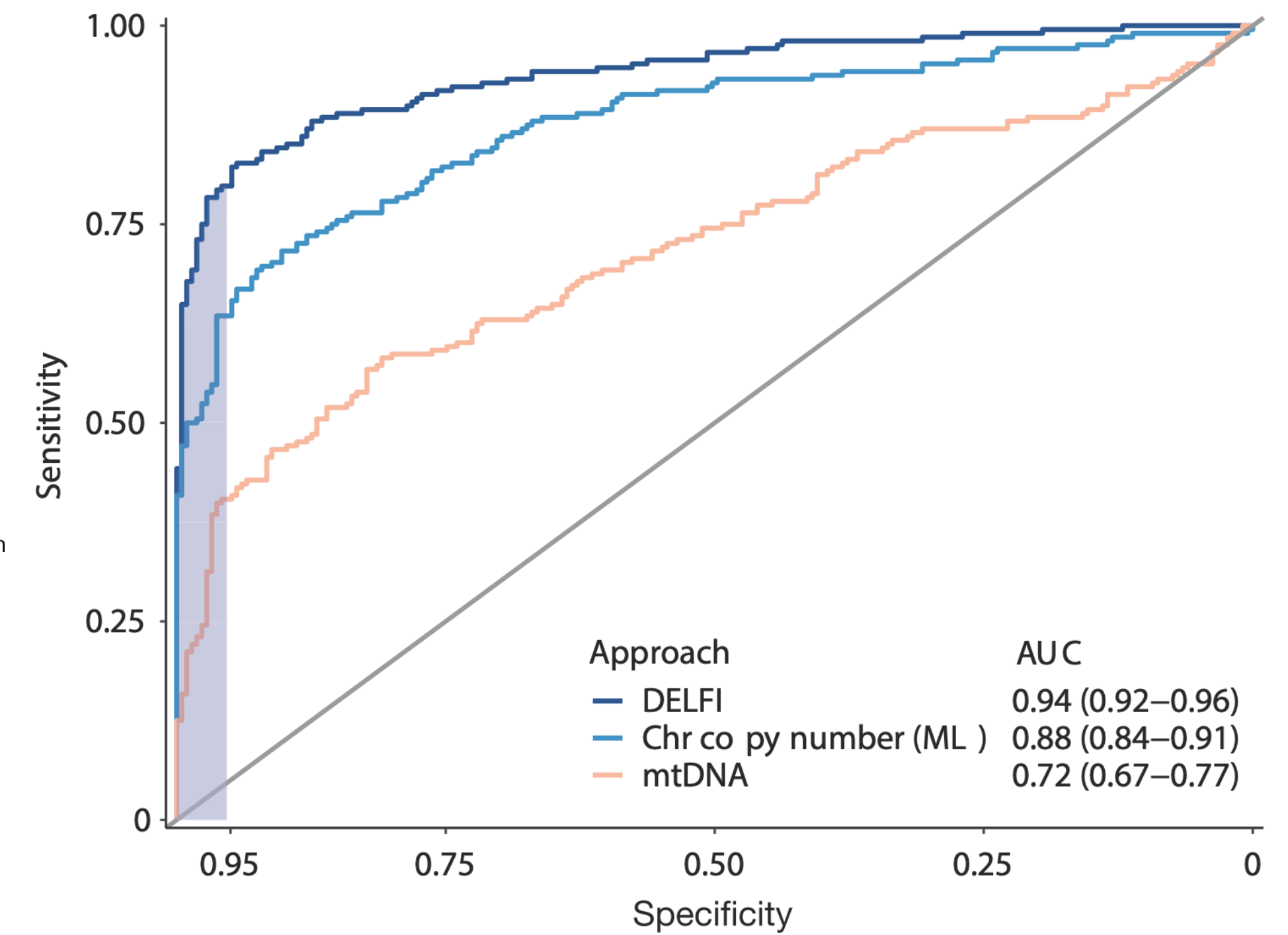
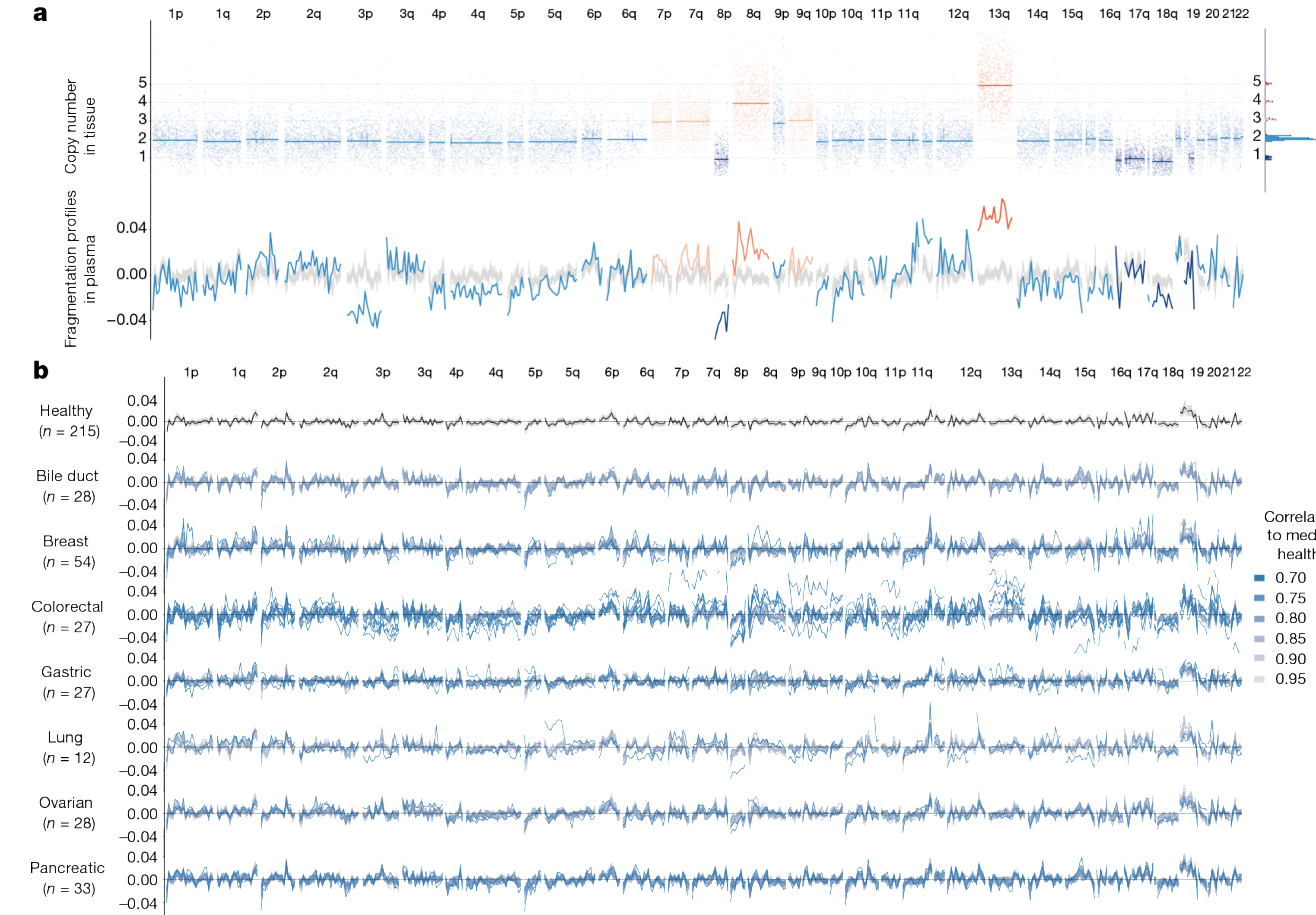
Genome-wide cfDNA fragmentation

DELFI: DNA evaluation of fragments for early interception



Genome-wide cfDNA fragmentation

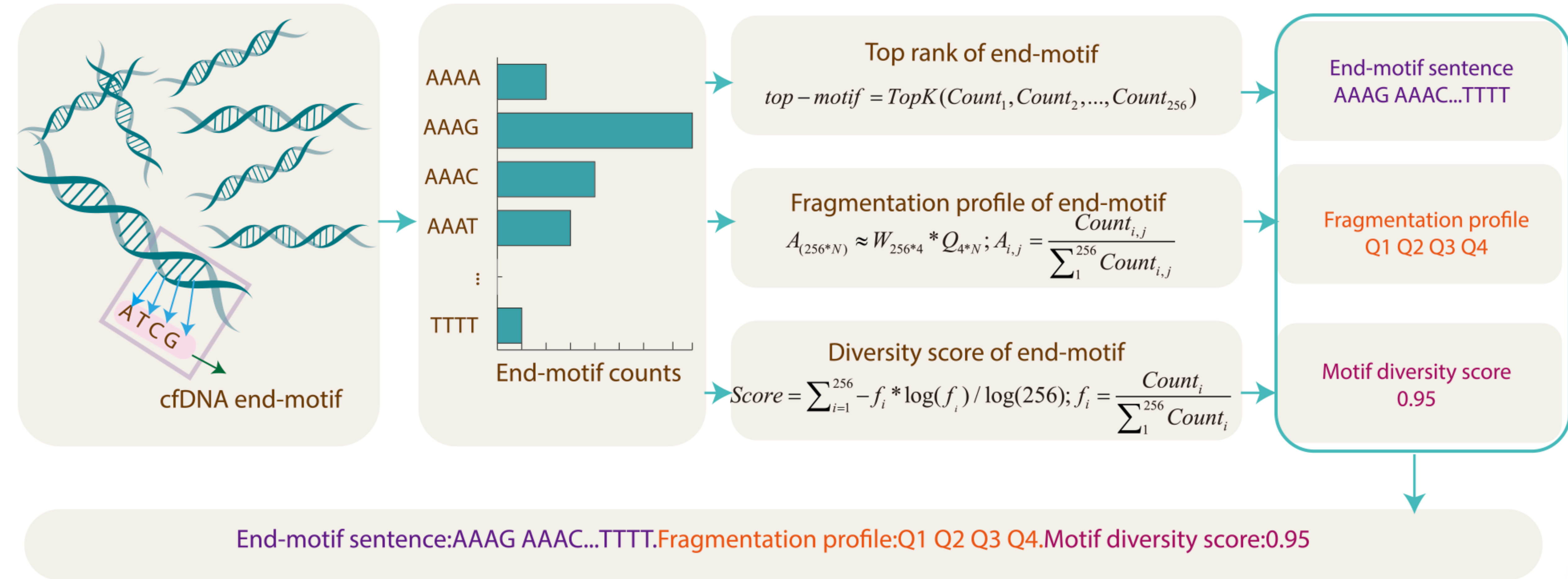
cfDNA fragmentation profiles in healthy individuals and patients with cancer



The next level: DNA is the **language of life**, after all

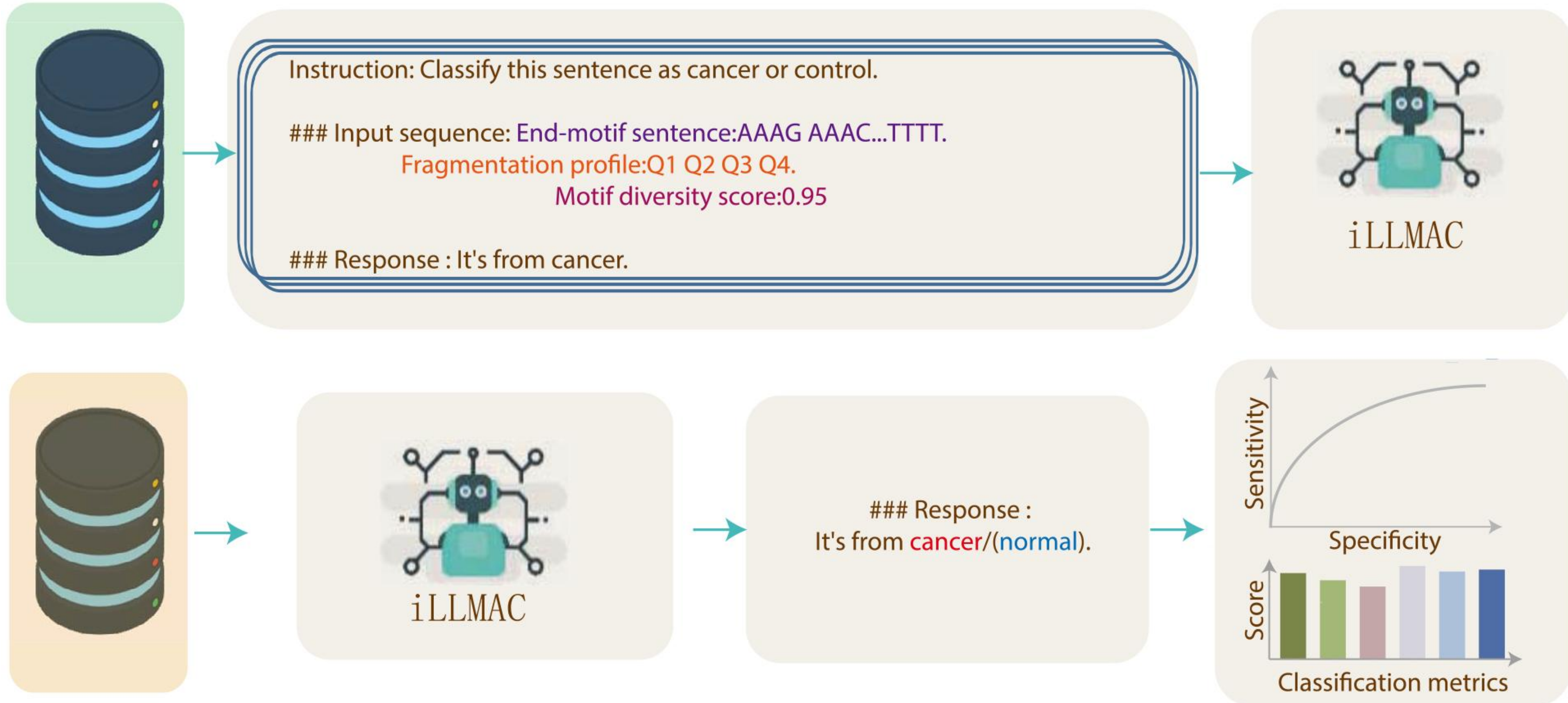
The next level: DNA is the language of life, after all

Large language models and end-motif profiles for cancer detection



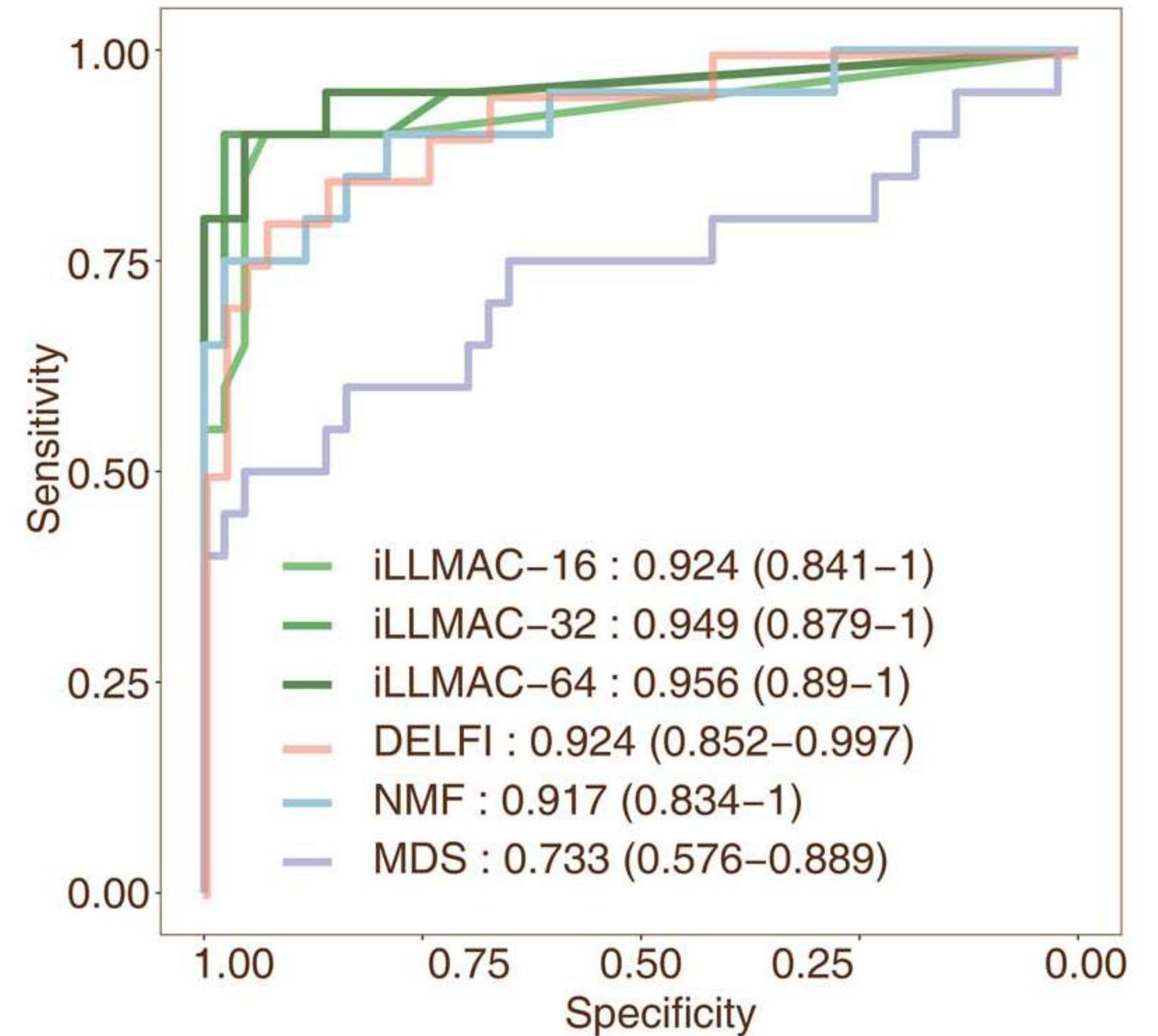
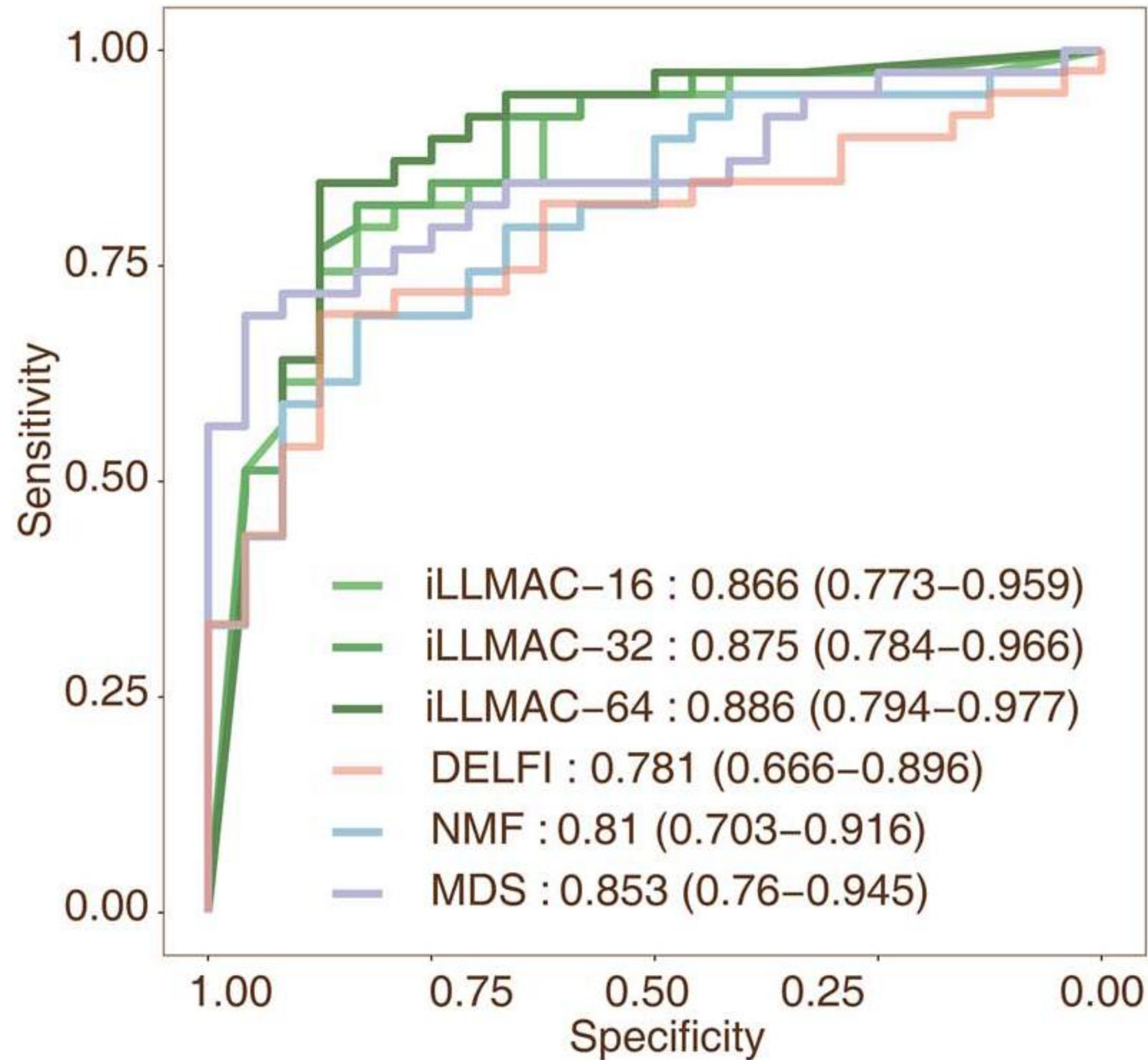
The next level: DNA is the language of life, after all

Instruction tuning LLM and inference for cancer detection



The next level: DNA is the language of life, after all

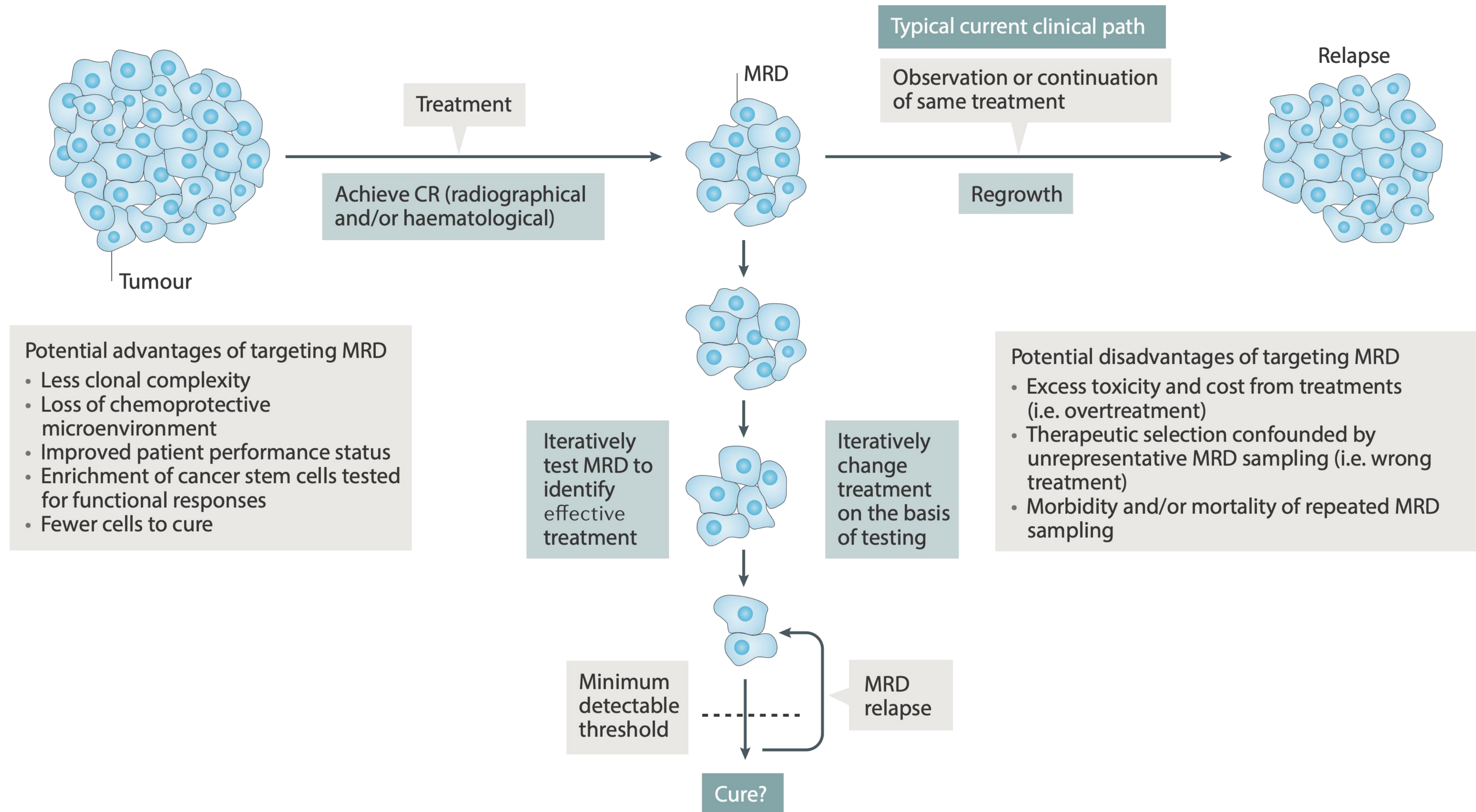
■ Different number of end-motifs and benchmarked baseline methods in the diagnosis of cancer



Is it just about **research and a future** far away?

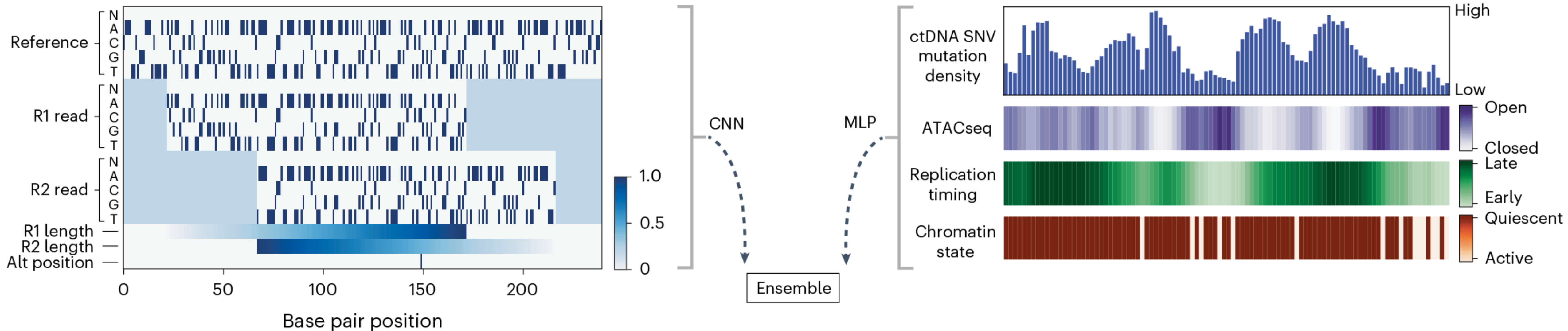
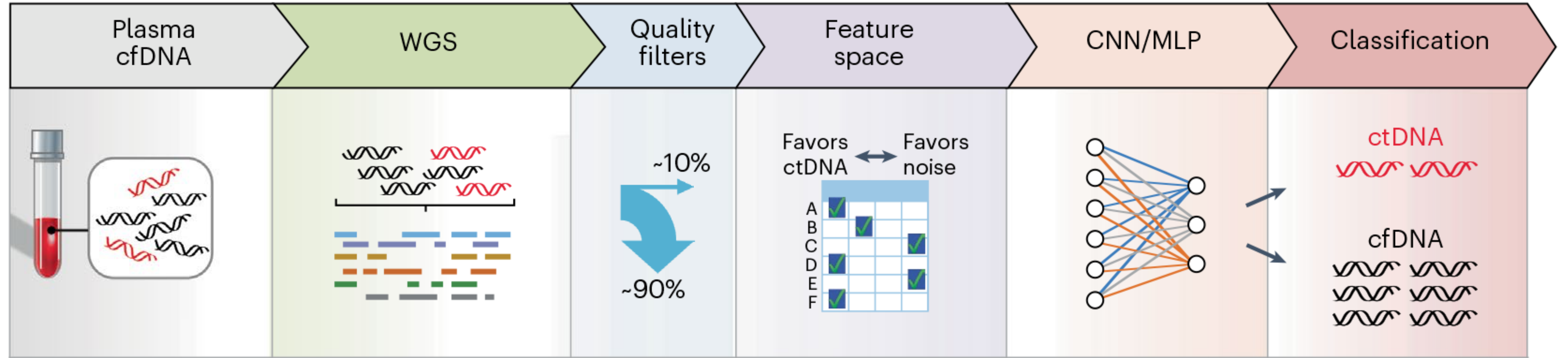
Is it just about research and a future far away?

Targeting what you cannot see: Minimal residual disease and treatment intensity



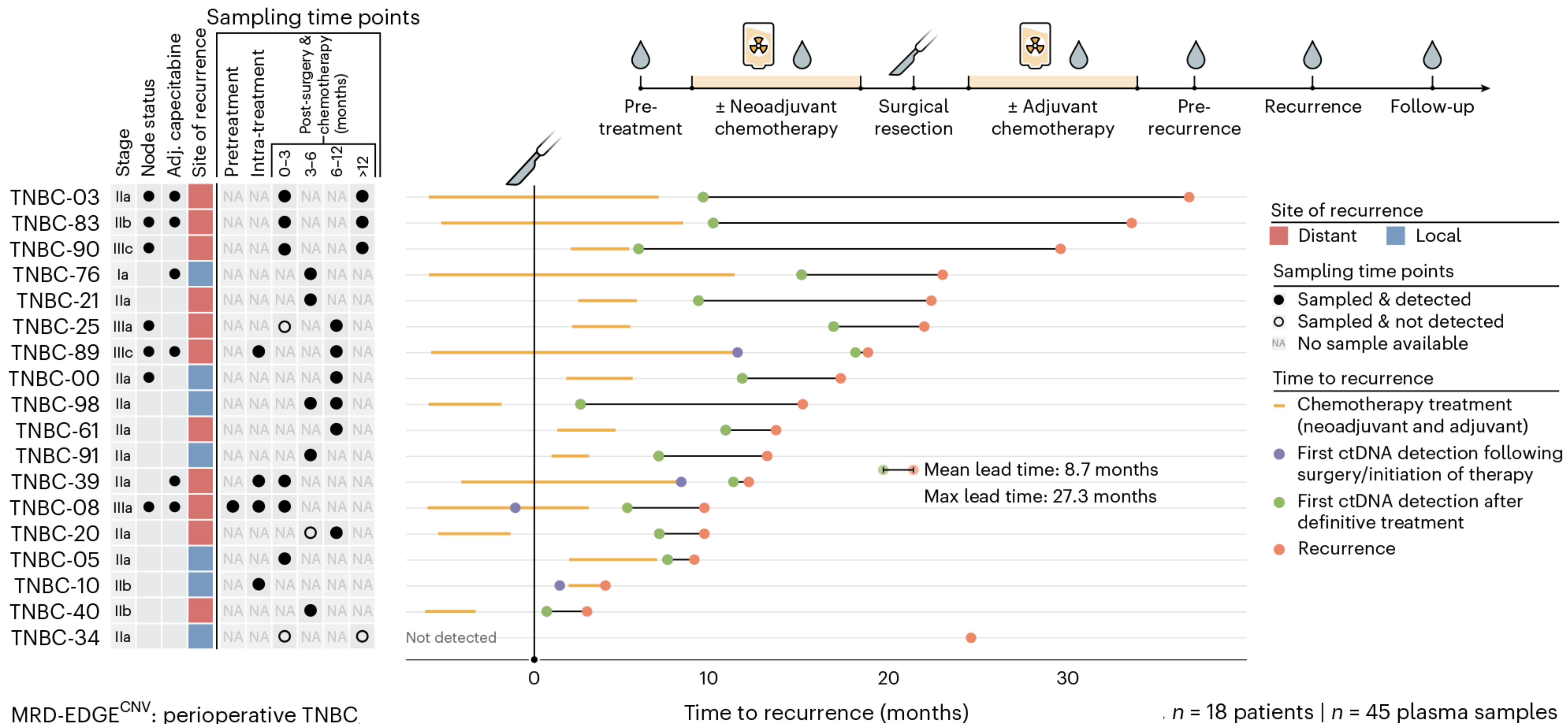
Is it just about research and a future far away?

The sound of noise: the deeper you go the higher it gets



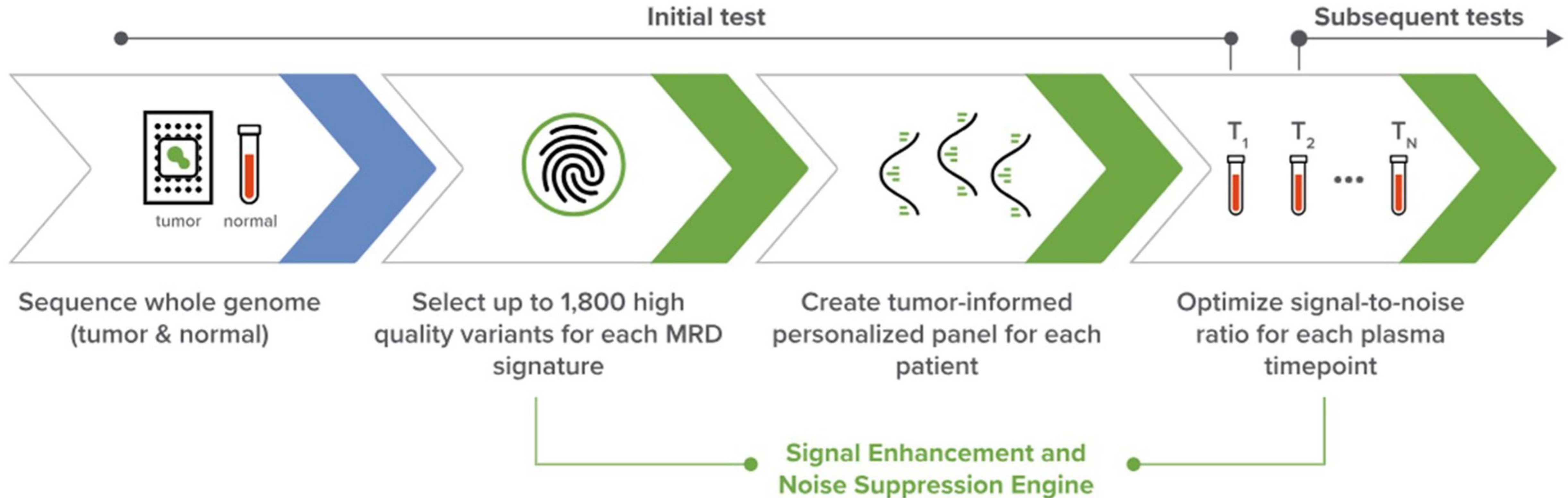
The power of a classifier of classifiers

A multi-cancer early detection model based on liquid biopsy of multi-omics biomarkers



AI denoising in an assay near you

■ ■ ■ Increase sensitivity to enhance detection

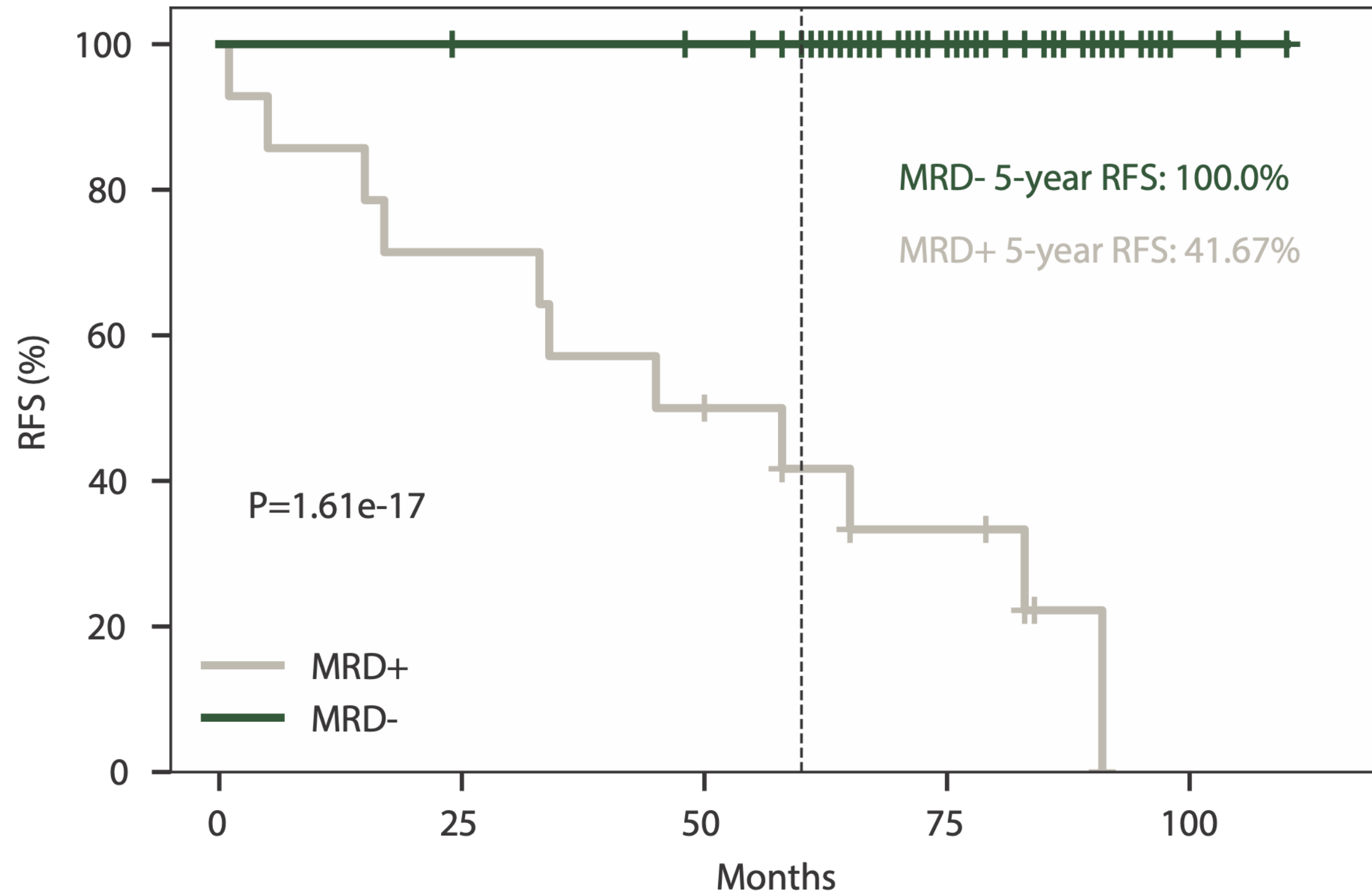


Matched tumor FFPE DNA/germline samples were **WGS sequenced to a median depth of 38x**

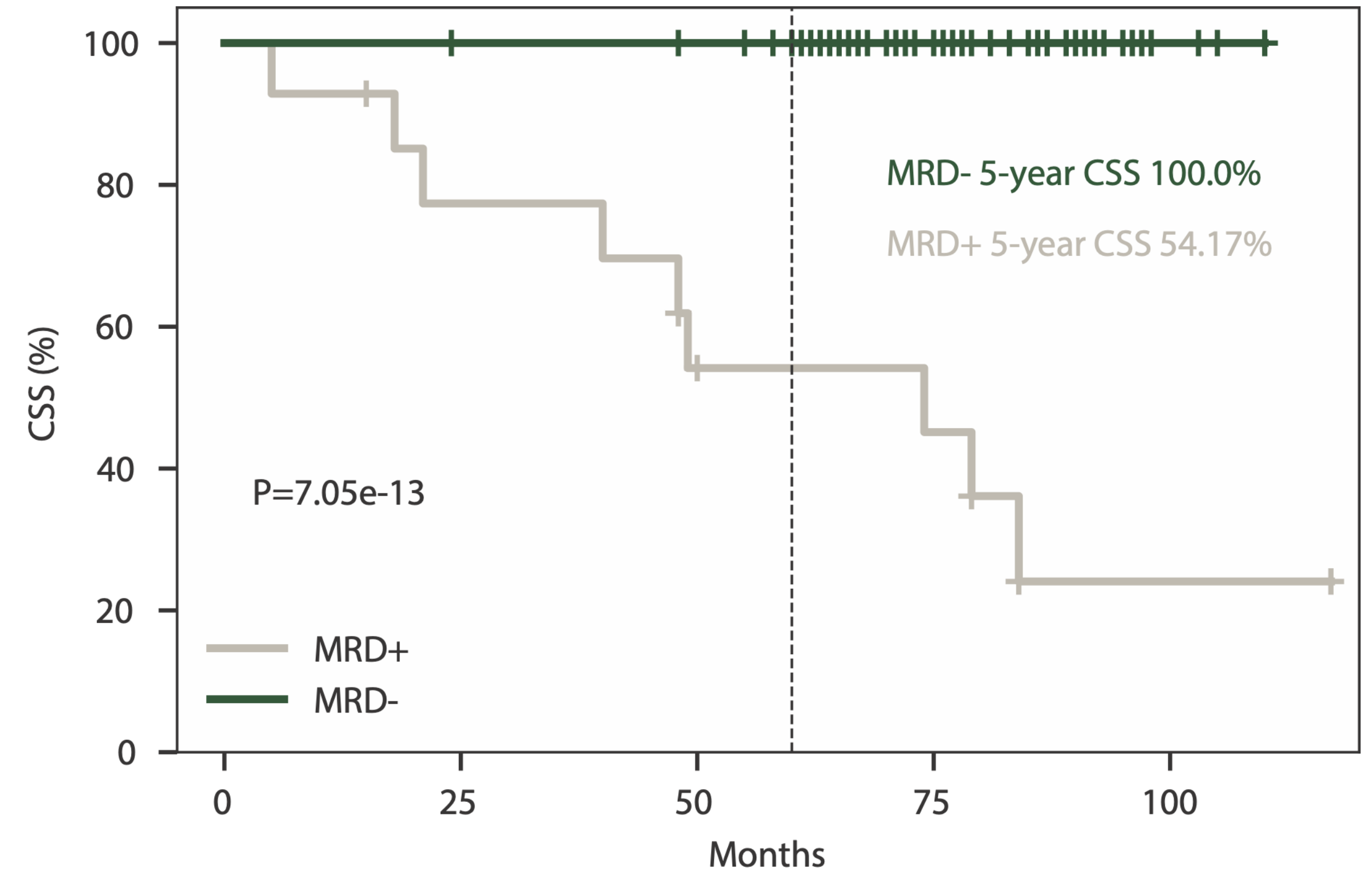
cfDNA was extracted from a median volume of 3.3 ml of plasma (range 1-4.8 ml) and panels designed contained a **median of 1421 variants/panel** (range 706-1,934/panel)

AI denoising in an assay near you

 The added value: longitudinal monitoring



MRD-	60	59	58	32	4
MRD+	14	10	6	4	0



MRD-	60	59	58	32	4
MRD+	14	10	6	5	1

Median Lead Time 15 months (range 4-41 months) over clinical relapse

Wrapping up

Use your experience in your experiments to achieve your expectations

1

Artificial intelligence has a great potential in Medical Oncology

- AI's capability to detect patterns can be of pivotal importance to assist Big data
- Filtering and enhancing tool will be the cornerstone of highly complex diagnostic technologies

2

Machine learning as a support for interpreting multi-parameter datasets

- High throughput technologies generate a high quantity of data that are not readily interpretable
- Latent patterns can be used to generate new hypothesis and assist clinical trial design

3

And we are just scraping the surface

- ctDNA is not just about mutations, epigenetics and fragmentomics are complementary biomarkers
- New downstream analyses for CTCs (e.g. RNAseq, WGS) will unlock a even higher amount of data



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