OncoDNA®
THE CANCER THERANOSTIC COMPANY

International User Group Meeting

22nd and 23rd of April 2026

"OncoXPLORE: Advancing Liquid Biopsy into Clinical Practice. From academic development at KU Leuven to clinical implementation and commercialisation."

Gian Eeraerts, MD, PhD researcher

Overview

1. Liquid biopsy to overcome unmet clinical needs
2. Discovery of novel (epi)genomic biomarkers

3. OncoXPLORE: going beyond mutations
4. Technical & clinical performance of OncoXPLORE

5. Perspectives for future research

Disclaimer

No conflicts of interest to disclose

GIP*XPLORE*PLUZ/OncoXPLORE

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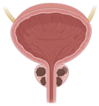
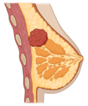
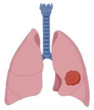
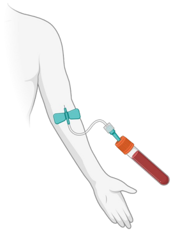
1. Liquid biopsy to overcome unmet clinical needs

Clinical use cases with unmet diagnostical needs

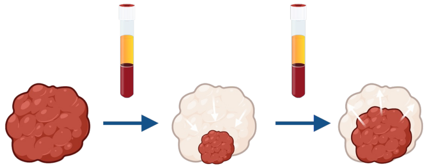
Cancer type	Actionable alterations	Limitations of tissue NGS
Metastatic castration-resistant prostate cancer (mCRPC) 	Mutations in *BRCA1/2* or other homologous recombination repair (HRR) genes	High failure rate of tissue biopsies: • **Bone metastases →** decalcification affects DNA • **Archival primary tissue** upon progression → old, degraded FFPE blocks
Hormone receptor positive, HER2-negative metastatic breast cancer 	*ESR1* variants, mutations in the PI3K pathway	Resistance mutations (*ESR1*) emerge under therapy pressure: • **Rebiopsy is invasive** and sometimes not feasible • Single-site biopsy may miss tumor **heterogeneity**
Non-small cell lung cancer (NSCLC) 	*EGFR, KRAS, BRAF, HER2* variants; *MET* exon 14 skipping events and *ROS1, ALK, RET* rearrangements	Lessions **not always accessible** for diagnostic biopsy

Advantages of liquid biopsy

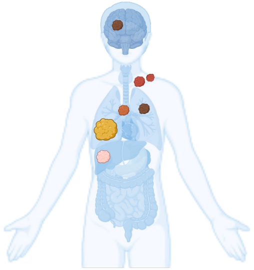
Minimally invasive alternative when tissue biopsy is not feasible or tissue NGS has failed



Allows serial monitoring to track emerging resistance mechanisms

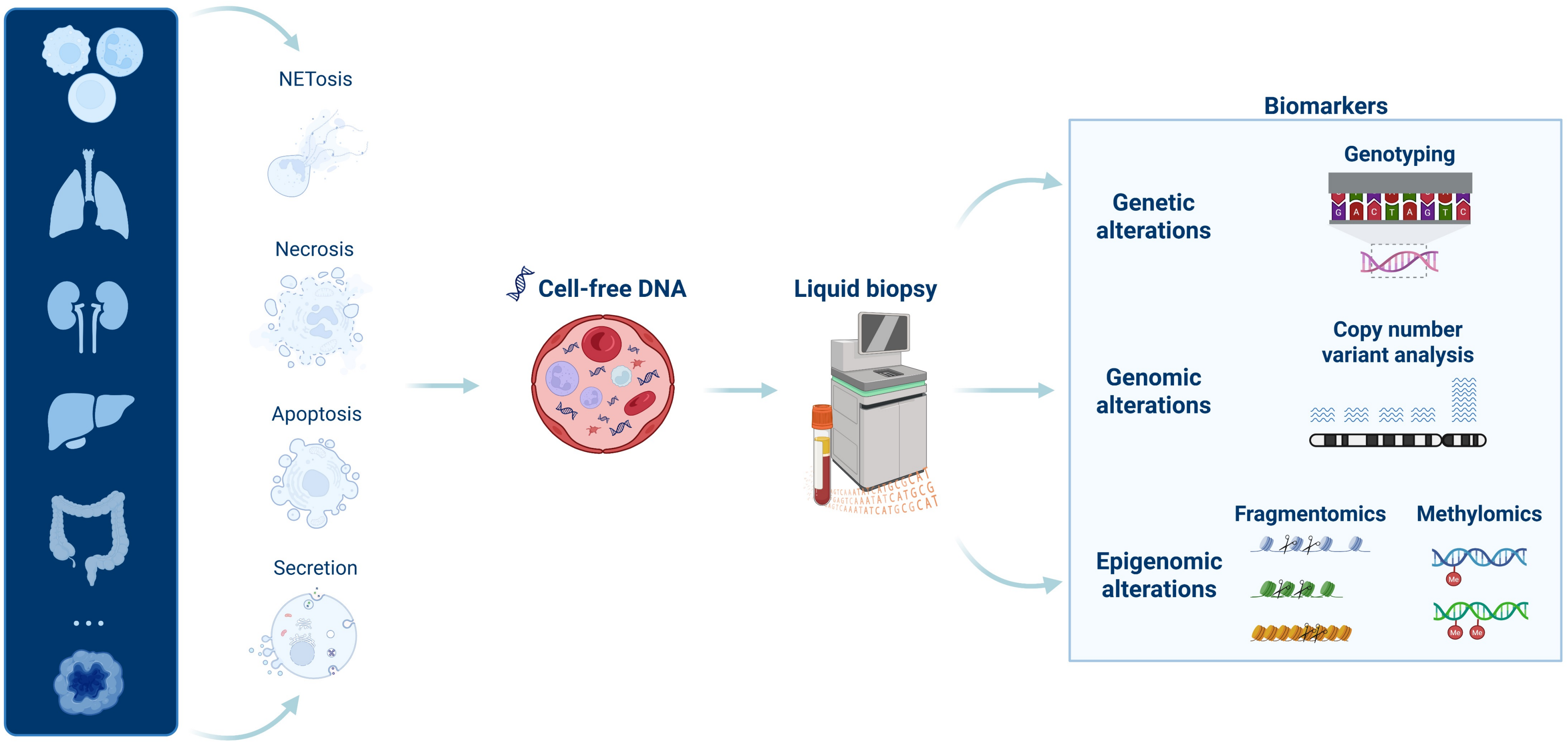


Captures tumor heterogeneity across multiple metastatic sites



2. Discovery of novel (epi)genomic biomarkers

Going beyond mutations: (epi)genomics



NETosis

Necrosis

Apoptosis

Secretion

Cell-free DNA

Liquid biopsy

Biomarkers

Genetic alterations

Genotyping

Genomic alterations

Copy number variant analysis

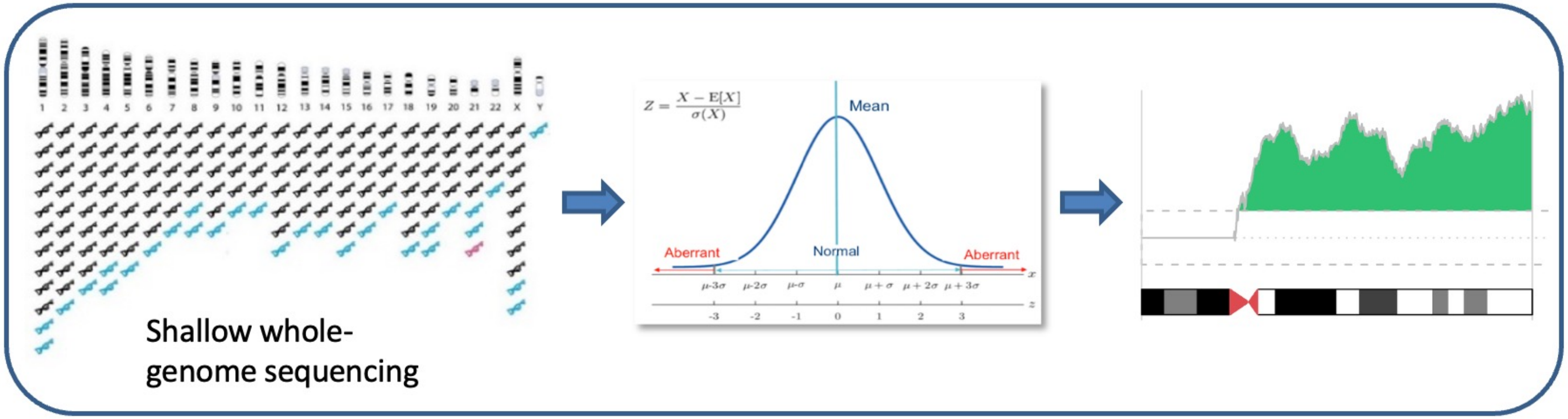
Epigenomic alterations

Fragmentomics

Methylomics

Going beyond mutations: genome-wide copy number alterations

Non-invasive prental testing with (NIPT) with GIPSeq:



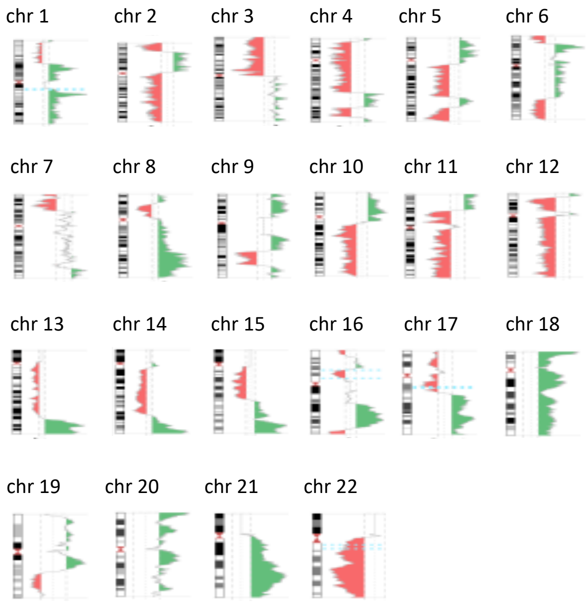
GIPSeq: Clinically implemented pipeline since 2013

Bayindir et al., EJHG, 2015; Van Den Bogaert et al., Genetics in medicine, 2022

Incidental discovery of cancer in pregnant women during NIPT

Invasive breast ductal adenocarcinoma

cell-free plasma DNA



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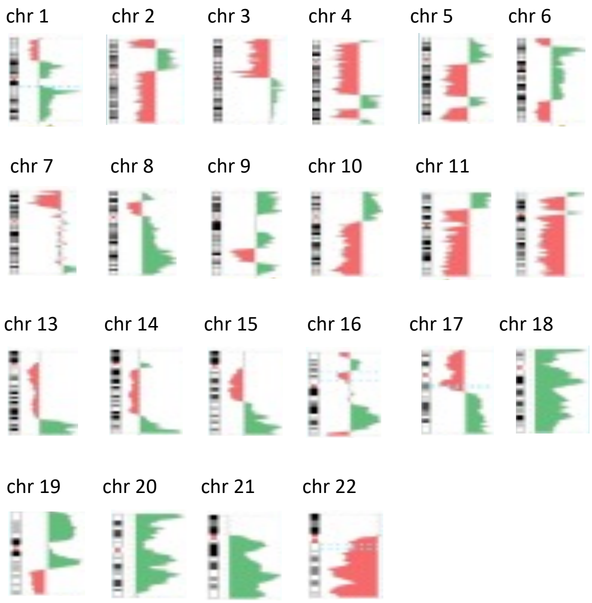
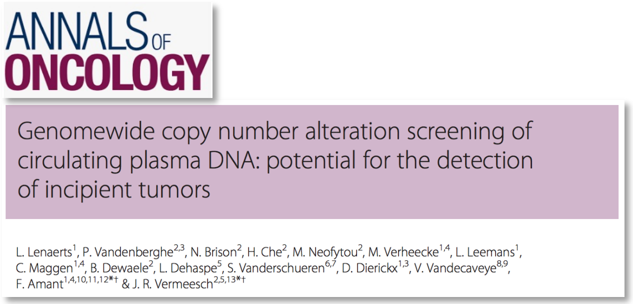
tumour DNA



Lenaerts et al., Clinical Chemistry, 2020

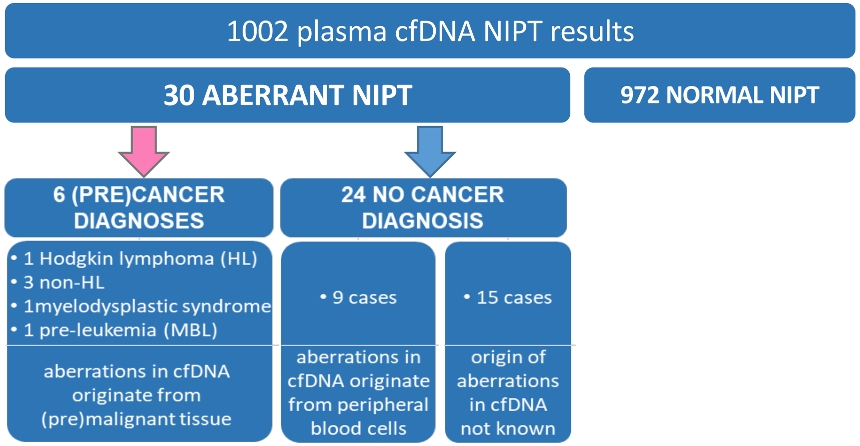
CNA profiling as a cancer screening tool in the elderly population?



ANNALS OF ONCOLOGY

Genomewide copy number alteration screening of circulating plasma DNA: potential for the detection of incipient tumors

L. Lenaerts[1], P. Vandenberghe[2,3], N. Brison[2], H. Che[2], M. Neofytou[2], M. Verheecke[1,4], L. Leemans[1], C. Maggen[1,4], B. Dewaele[2], L. Dehaspe[5], S. Vanderschueren[6,7], D. Dierickx[1,3], V. Vandecaveye[8,9], F. Amant[1,4,10,11,12*†] & J. R. Vermeesch[2,5,13*†]



1002 plasma cfDNA NIPT results

30 ABERRANT NIPT

972 NORMAL NIPT

6 (PRE)CANCER DIAGNOSES

- 1 Hodgkin lymphoma (HL)
- 3 non-HL
- 1myelodysplastic syndrome
- 1 pre-leukemia (MBL)

aberrations in cfDNA originate from (pre)malignant tissue

24 NO CANCER DIAGNOSIS

- 9 cases

aberrations in cfDNA originate from peripheral blood cells

- 15 cases

origin of aberrations in cfDNA not known

2015-2016 initiated study

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Lenaerts et al., Ann Oncol, 2019

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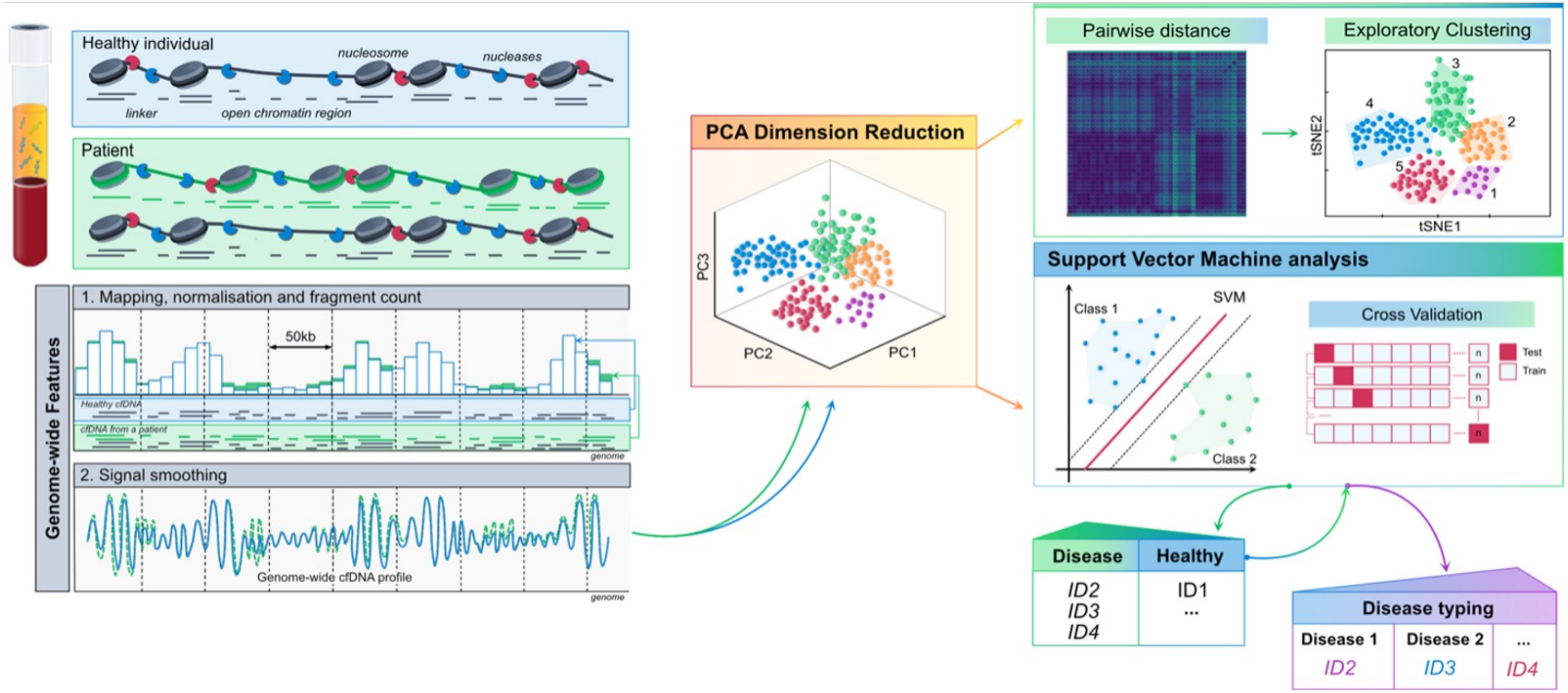
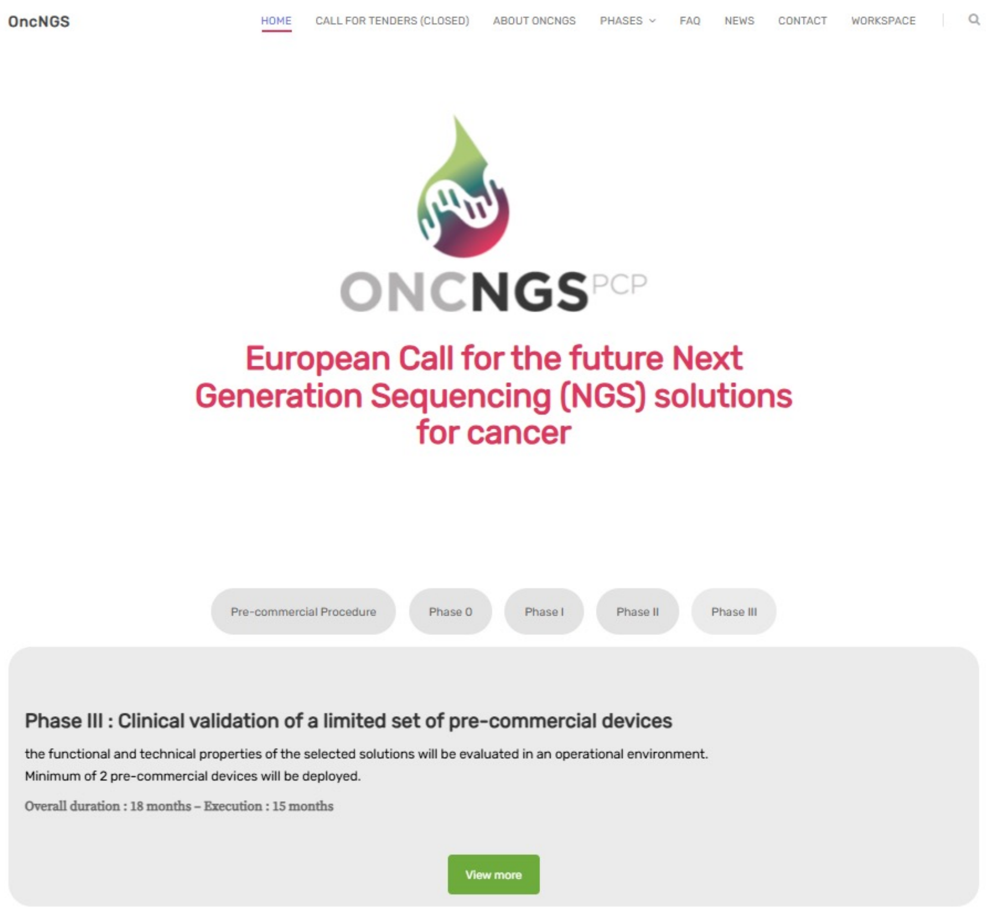
Identification of genome-wide cfDNA signatures



Che et al., Clinical Chemistry, 2022

3. OncoXPLORE: going beyond mutations

OncNGS consortium



European Call for the future Next Generation Sequencing (NGS) solutions for cancer

Phase III : Clinical validation of a limited set of pre-commercial devices

the functional and technical properties of the selected solutions will be evaluated in an operational environment.
Minimum of 2 pre-commercial devices will be deployed.

Overall duration : 18 months – Execution : 15 months

OncNGS consortium

8 BUYERS

6 SUPPORTING ENTITIES

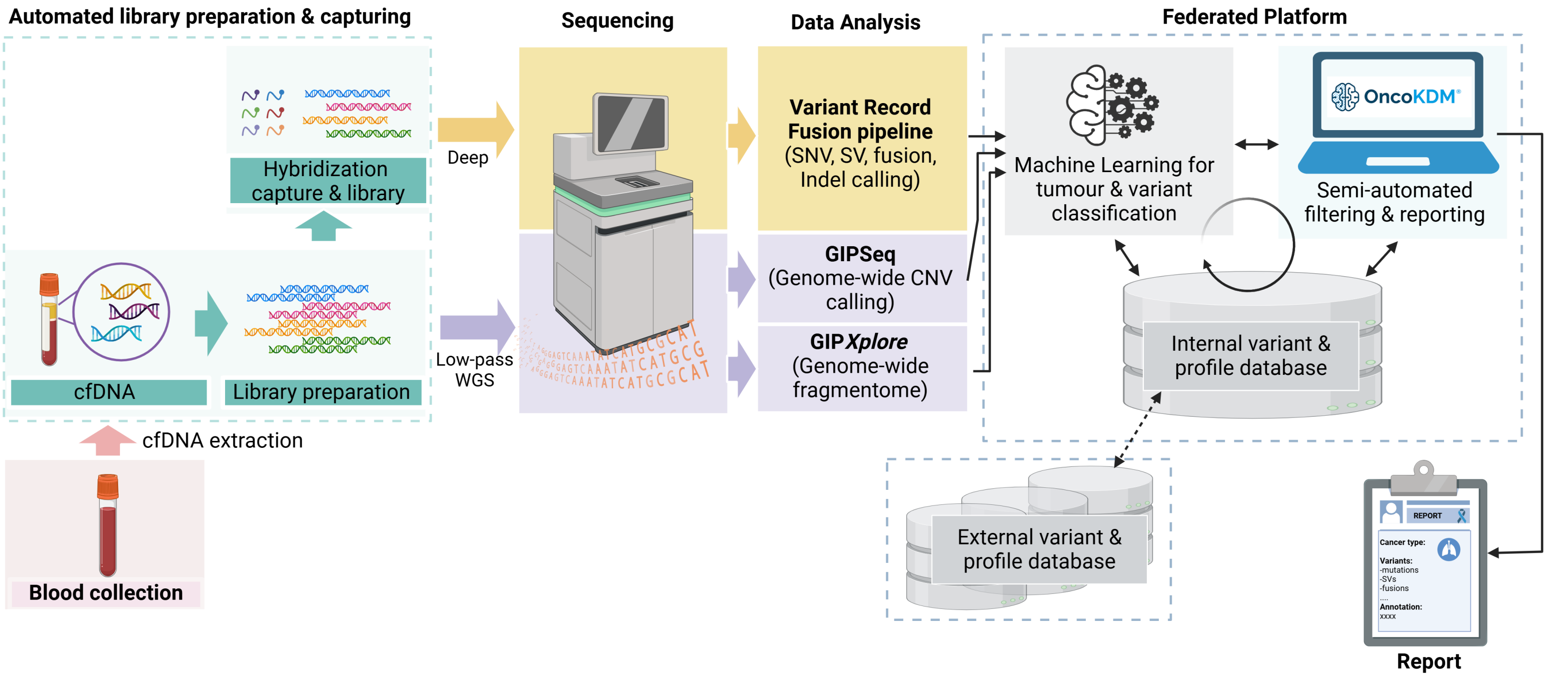
OncNGS is a strong consortium composed of 8 buyers from 5 member states

- Sciensano (Belgium)
- Institut Jules Bordet (Belgium)
- Institut Curie (France)
- Hospices Civils de Lyon (France)
- Charite Universitaetsmedizin (Germany)
- Ludwig Maximilians Universitaet Muenchen (Germany)
- Alleanza Contro il Cancro (Italy)
- Institut Catala d'Oncologia (Spain)

Supported by 6 entities with wide experience in their fields :

- Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS), expert in pre-commercial procurement (Spain)
- Belgian Cancer Registry, expert in cancer control (Belgium)
- Institut National du Cancer, expert in cancer control (France)
- Instituto de Investigación Biomédica de Salamanca, expert in biomedical research in the field of haematologic malignancies (Spain)
- Valle de Hebrón Instituto de Oncología, expert in biomedical research in the field of haematologic malignancies (Spain)
- De Clercq & Partners, expert in intellectual property rights and freedom to operate analysis (Belgium)

Cost-effective, scalable and fast off-the shelf solution



Automated library preparation & capturing

Hybridization capture & library

cfDNA

Library preparation

cfDNA extraction

Blood collection

Deep

Low-pass WGS

Sequencing

Data Analysis

Variant Record Fusion pipeline (SNV, SV, fusion, Indel calling)

GIPSeq (Genome-wide CNV calling)

GIP*Xplore* (Genome-wide fragmentome)

Federated Platform

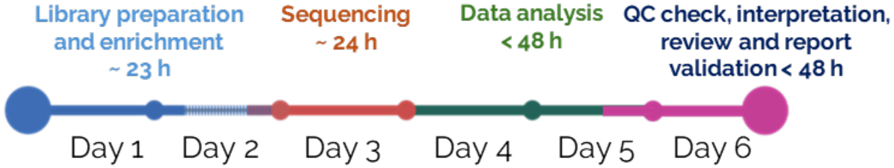
Machine Learning for tumour & variant classification

Semi-automated filtering & reporting

Internal variant & profile database

External variant & profile database

Report



Library preparation and enrichment ~ 23 h

Sequencing ~ 24 h

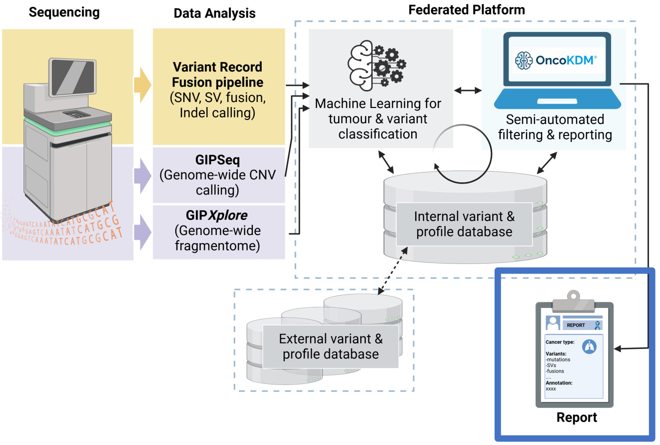
Data analysis < 48 h

QC check, interpretation, review and report validation < 48 h

Comprehensive genomic profiling with OncoXPLORE

Sequencing	Feature	Output
Targeted Module (120M PE reads)	SNV & INDEL	Somatic mutation allele frequency (AF) across **441 genes**
	Splicing variant	Splicing variants across 20bp intronic region on each exon with some introns (e.g. MET exon 14 skipping) receiving higher coverage
	MSI	MSI status based on ~300 loci
	TMB	Number of acquired non-synonymous variants per 1 Mb
	Translocation	Recurrent clinically relevant translocations: ALK, BRAF, EGFR, ETV6, EWSR1, FGFR2, FGFR3, NTRK1, NTRK2, PAX3, PAX8, RET, ROS1, TFE3 (solid); MYC, BCL2, BCL6, CCND1, IRF4 (haem)
	Focal CNV	CNV profiles to assess focal alterations
Low-Pass WGS Module (25M PE reads)	Large CNV (>1Mb)	Genome-wide aneuploidy detection
	Fragmentomics	Fragmentome-based cancer-type prediction

Clinical interpretation & reporting


Sequencing

Data Analysis

Federated Platform

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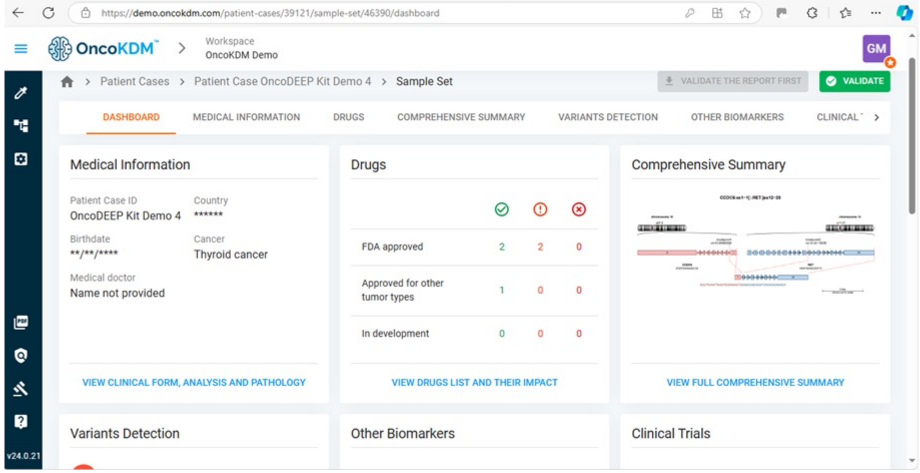

https://demo.oncokdm.com/patient-cases/39121/sample-set/46390/dashboard

Workspace
OncoKDM Demo

Patient Cases > Patient Case OncoDEEP Kit Demo 4 > Sample Set

DASHBOARD | MEDICAL INFORMATION | DRUGS | COMPREHENSIVE SUMMARY | VARIANTS DETECTION | OTHER BIOMARKERS | CLINICAL

Medical Information

Patient Case ID: OncoDEEP Kit Demo 4
Country: ******
Birthdate: **/**/****
Cancer: Thyroid cancer
Medical doctor: Name not provided

VIEW CLINICAL FORM, ANALYSIS AND PATHOLOGY

Drugs

	✓	!	⊗
FDA approved	2	2	0
Approved for other tumor types	1	0	0
In development	0	0	0

VIEW DRUGS LIST AND THEIR IMPACT

Comprehensive Summary

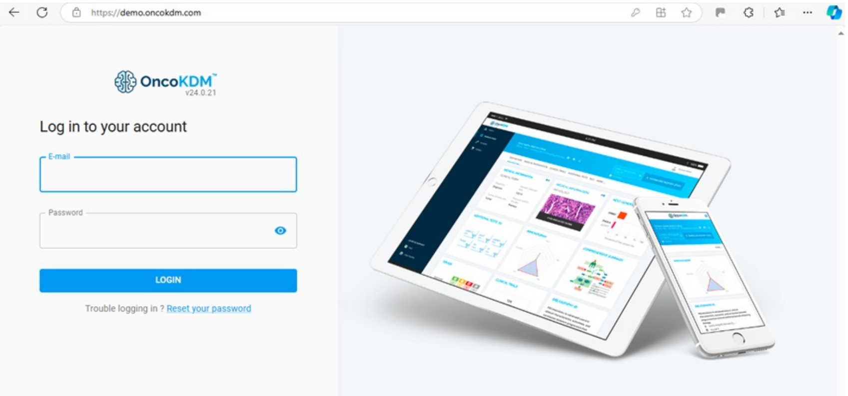
VIEW FULL COMPREHENSIVE SUMMARY

Variants Detection

Other Biomarkers

Clinical Trials

OncoKDM platform as a main user interface and reporting tool


https://demo.oncokdm.com

Log in to your account

E-mail:

Password:

Trouble logging in ? Reset your password

4. Technical & clinical performance of OncoXPLORE

Multicentric technical validation

7 Sites

6 Twist Pan-cancer cfDNA reference sets: **0%, 0.25%, 0.5%, 1% VAF**

2 Validation samples with known variants

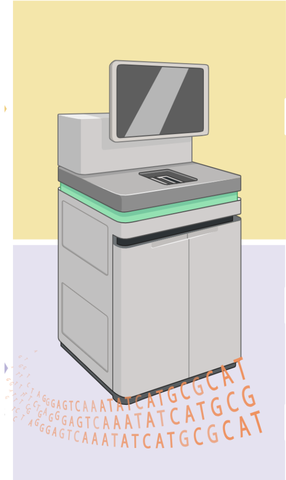
20 ng as input material

Variant class	N of variants
SNVs	220
InDel	203
SVs (Fusions)	5
Total	**430**

Twist Pan-cancer cfDNA reference variant overview

Targeted sequencing module

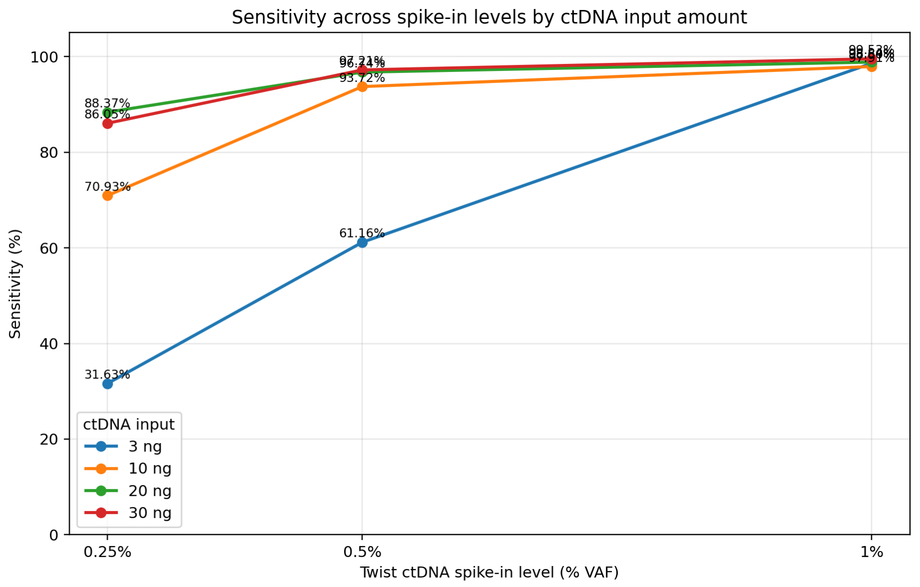
Sequencing



Data Analysis

Variant Record
Fusion pipeline
(SNV, SV, fusion,
Indel calling)

Performance characteristics for SNVs and InDels



Internal validation using Twist Pan-cancer cfDNA V2 Reference set

≥ 96.7% Sensitivity

For detection of SNVs/InDels at 0.5% VAF at 20-30 ng input

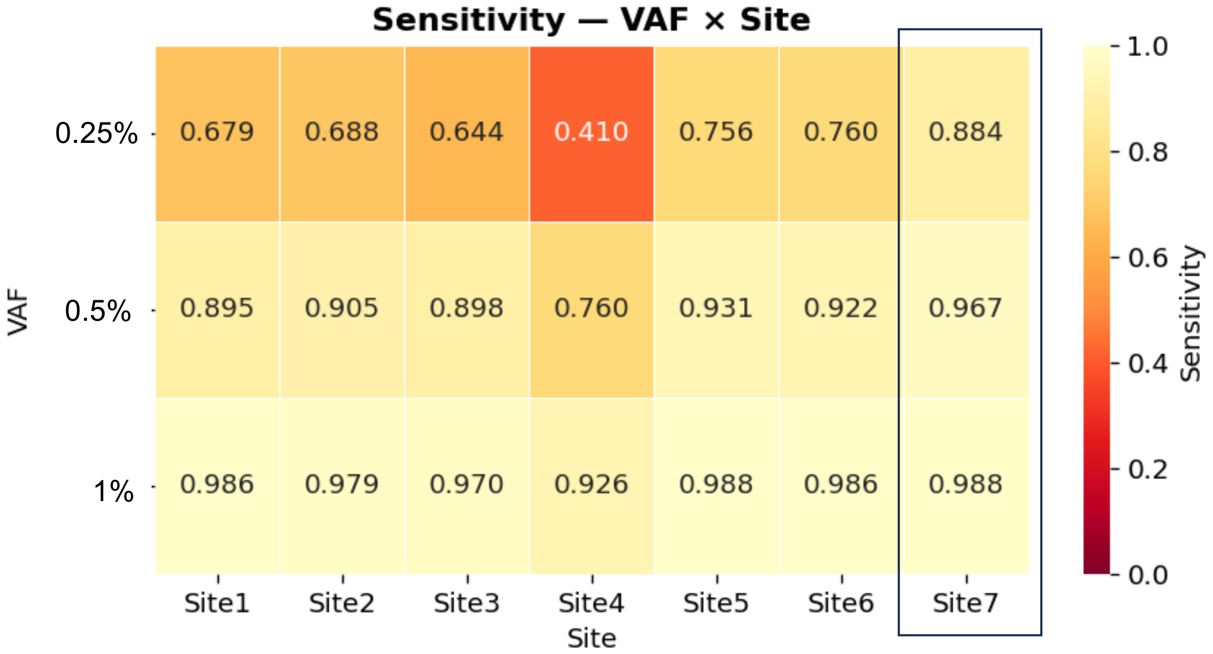
≥ 99.99% Specificity

For detection of SNVs/InDels across all tested inputs

0.5% LoD

At ≥ 95% sensitivity (LoD95) for detection of SNVs/Indels at 10-30 ng input

Multicentric validation for SNV/indel detection


Sensitivity — VAF × Site

VAF	Site1	Site2	Site3	Site4	Site5	Site6	Site7
0.25%	0.679	0.688	0.644	0.410	0.756	0.760	0.884
0.5%	0.895	0.905	0.898	0.760	0.931	0.922	0.967
1%	0.986	0.979	0.970	0.926	0.988	0.986	0.988

Internal Validation data

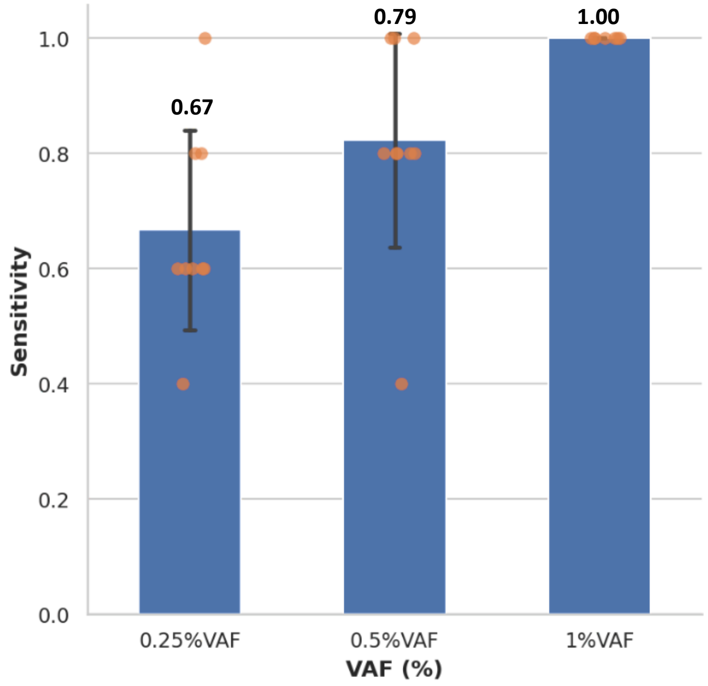
≥ 99.99 Specificity

*Tested at 20ng input

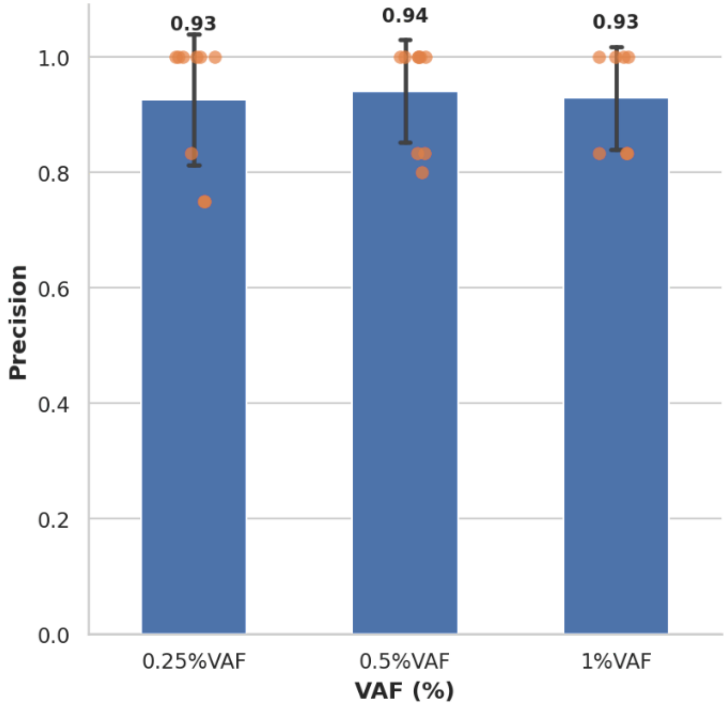
*Site 4 did not PASS the data QC

Multicentric validation for fusion detection

Sensitivity



PPV



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*Tested at 20ng input

*One site did not PASS the data QC

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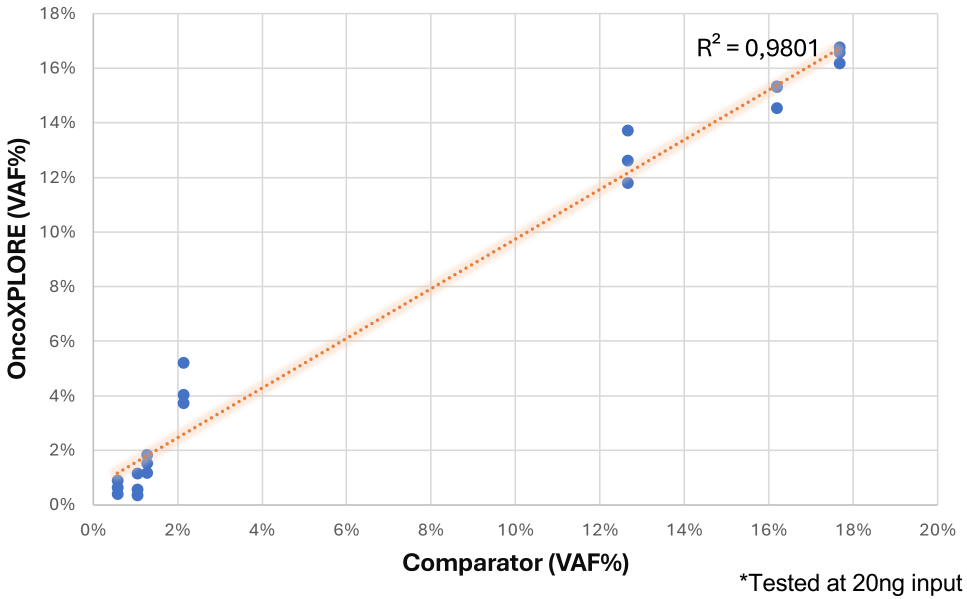
High quantitative accuracy in variant allele frequency



*Tested at 20ng input

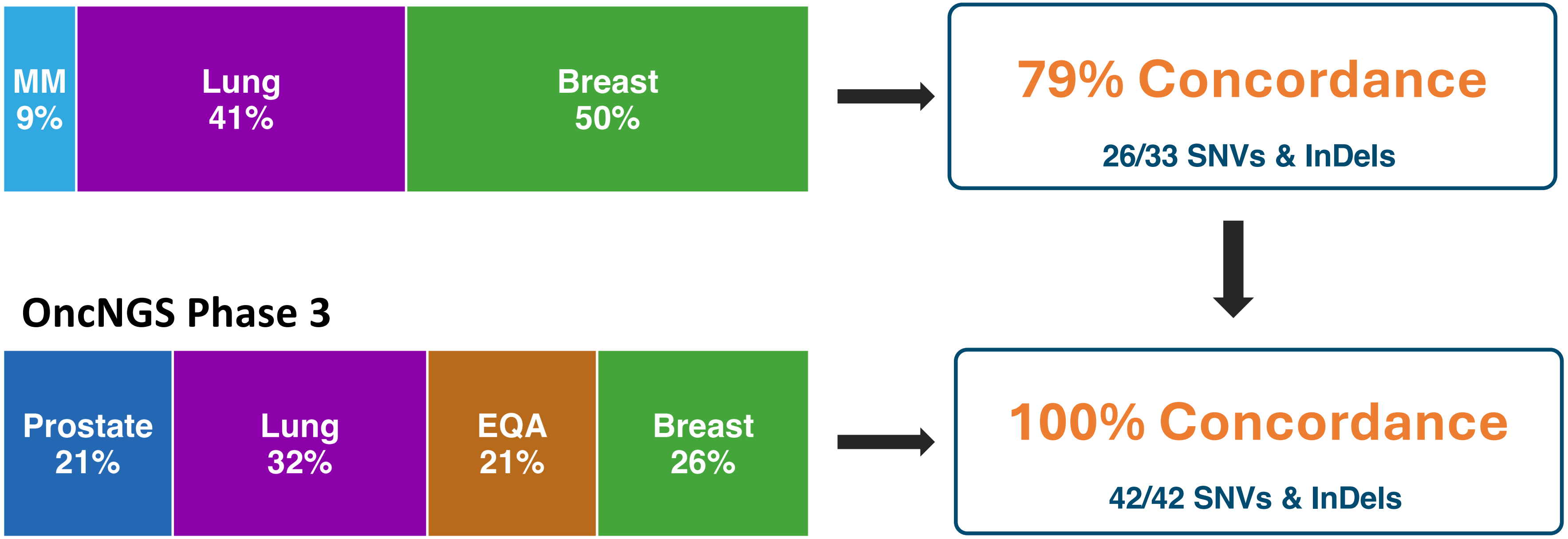
100% **Positive Percent Agreement (PPA)**

For detection of known variants in validation samples

R^2=0.98 **High quantitative accuracy**

OncoXPLORE vs orthogonal liquid NGS comparator

Improved variant detection in clinical samples



OncNGS Phase 2

79% Concordance

26/33 SNVs & InDels

OncNGS Phase 3

100% Concordance

42/42 SNVs & InDels

KU LEUVEN *plasma ddPCR and tissue NGS as comparator, internal validation

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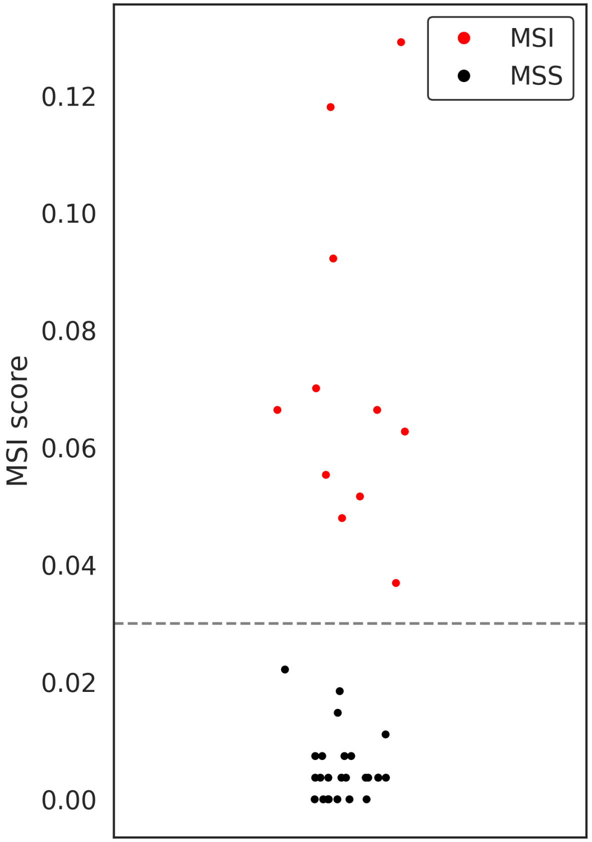
Microsatellite Instability (MSI)

11/11 MSI high samples correctly classified

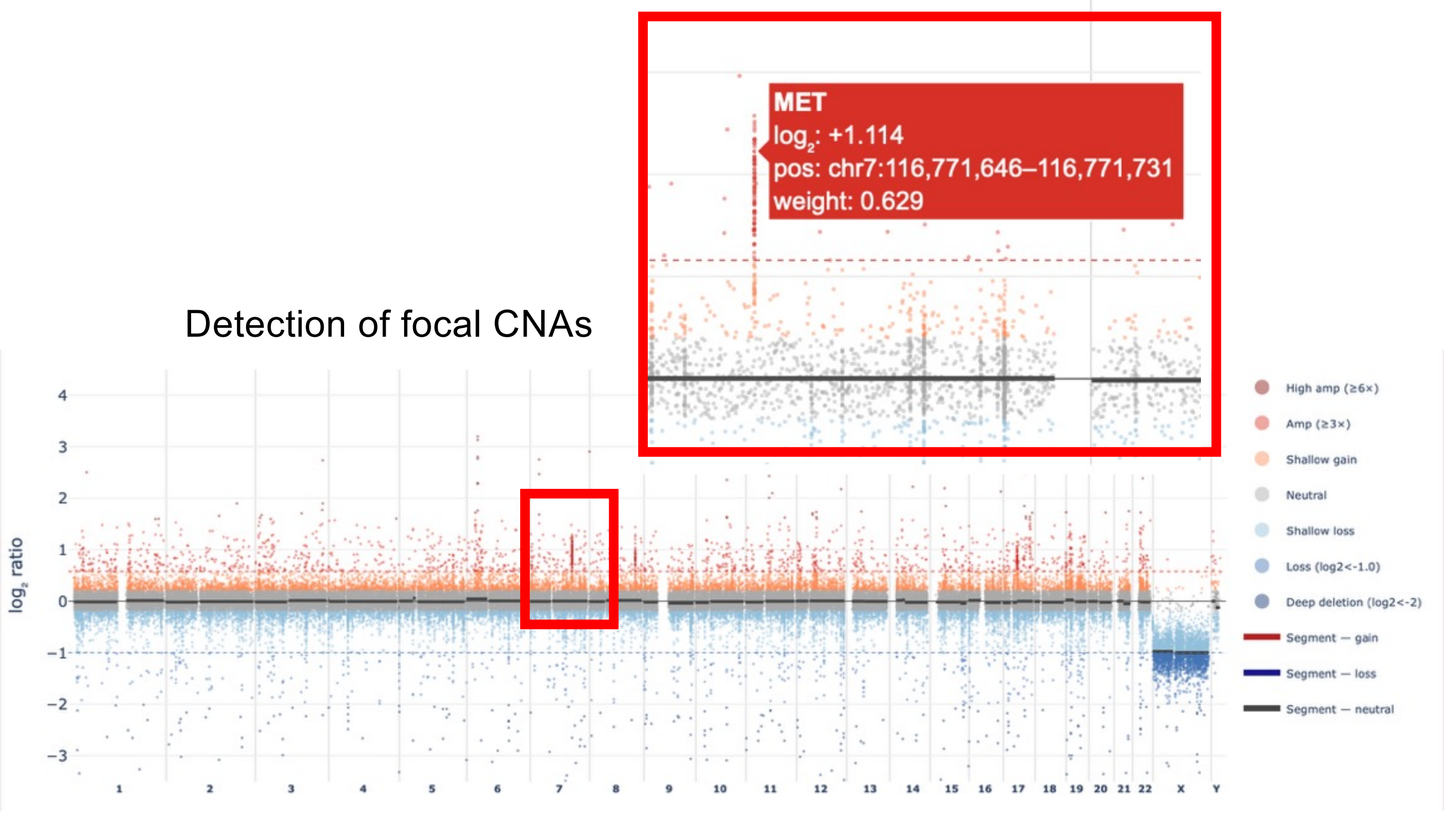


26/26 MSS samples correctly classified

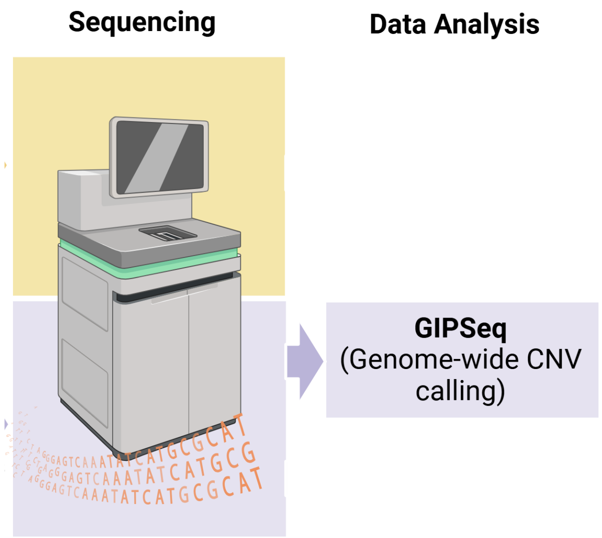
*tissue PCR as comparator

Genome-wide copy-number alterations (CNAs) from targeted data

Detection of focal CNAs



Low-pass whole genome sequencing module



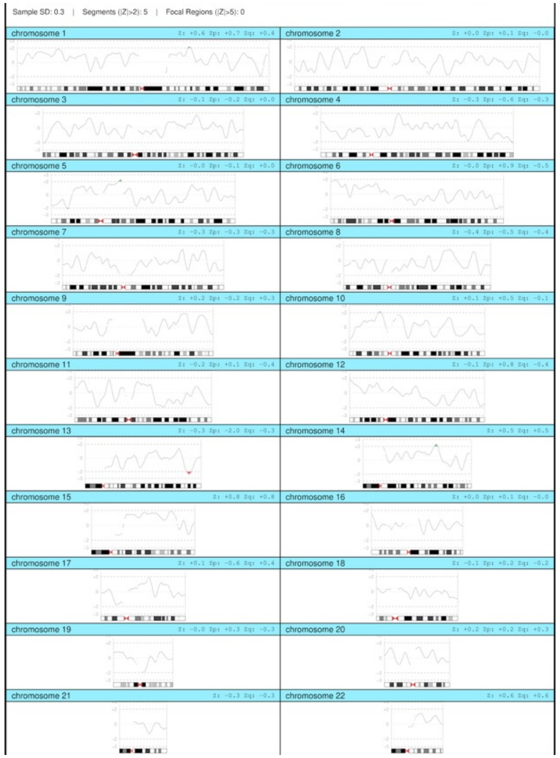
Sequencing

Data Analysis

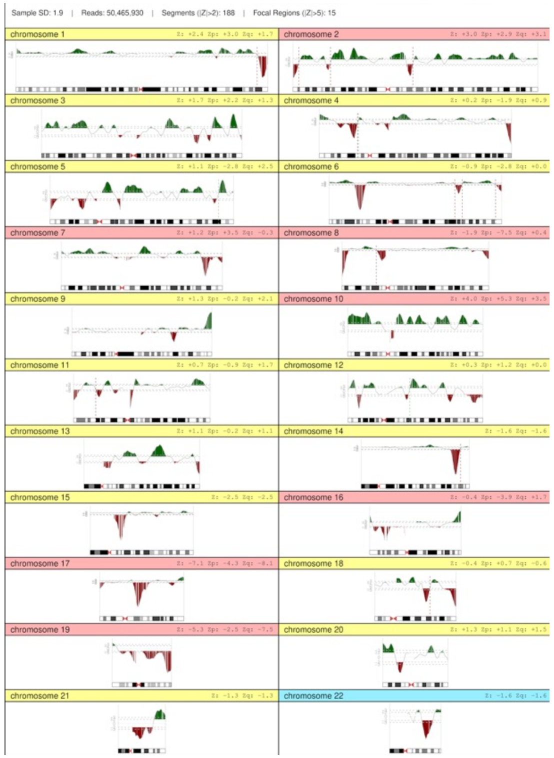
GIPSeq
(Genome-wide CNV calling)

Genome-wide copy number alterations (CNAs)

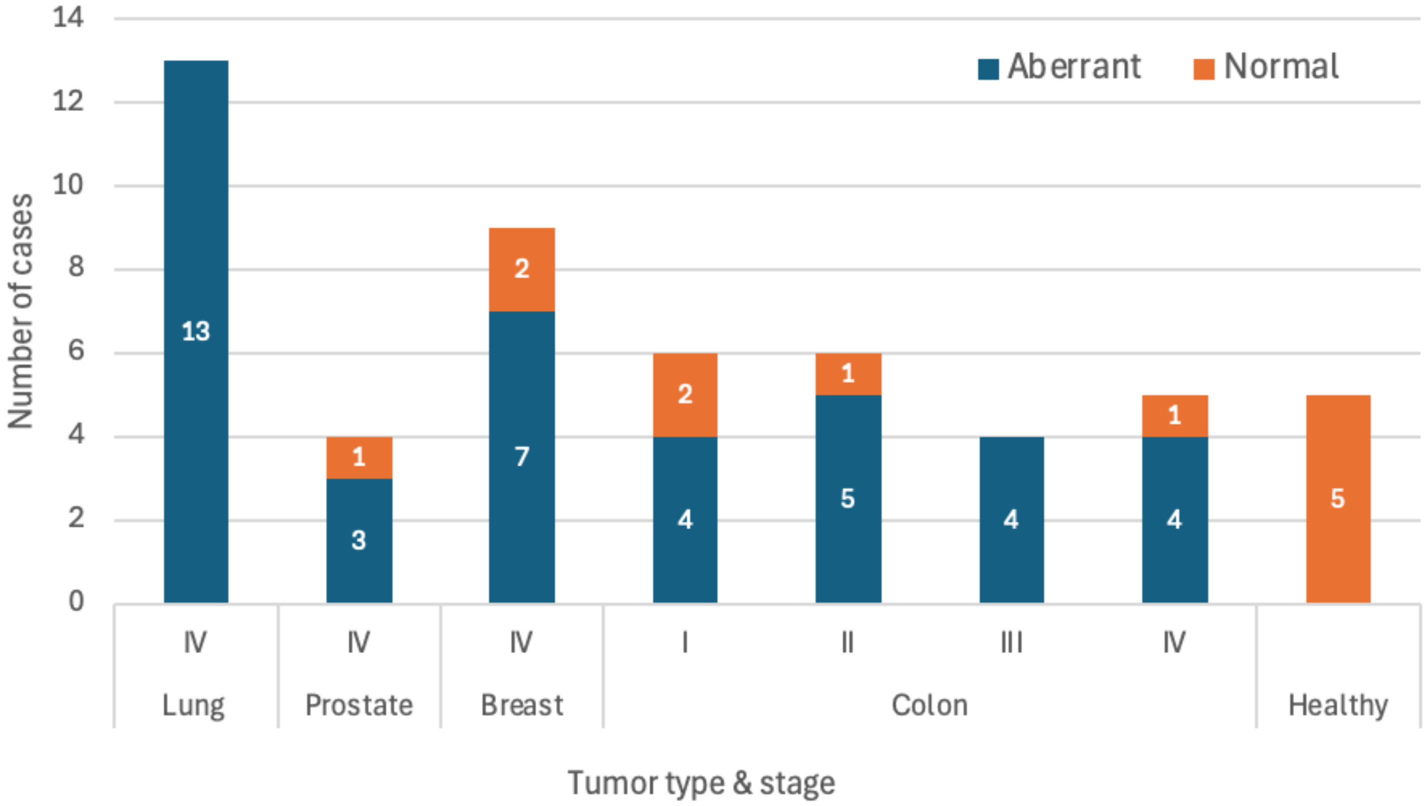
Normal profile



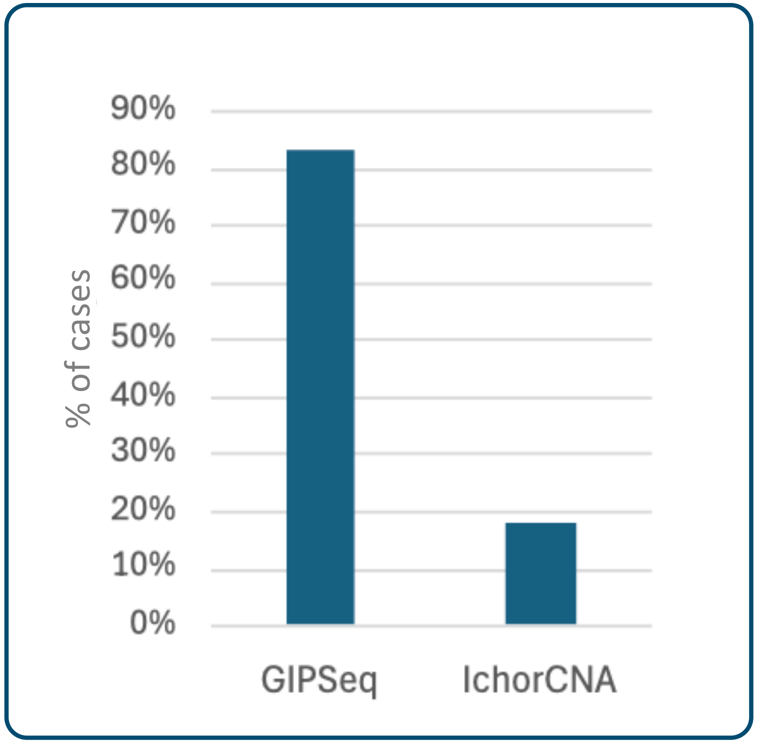
Cancer profile



Cancer signal detection with genome-wide CNA analyses



GIPSeq has a sensitivity well below 3% tumour fraction



>80% **Samples with detectable cancer signal**

OncoXPLORE vs IchorCNA as comparator

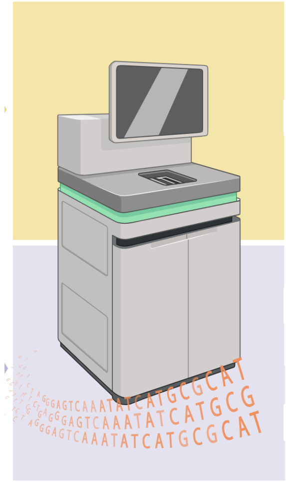
<3%TF **Sensitive cancer signal detection**

as estimated using IchorCNA

Low-pass whole genome sequencing module

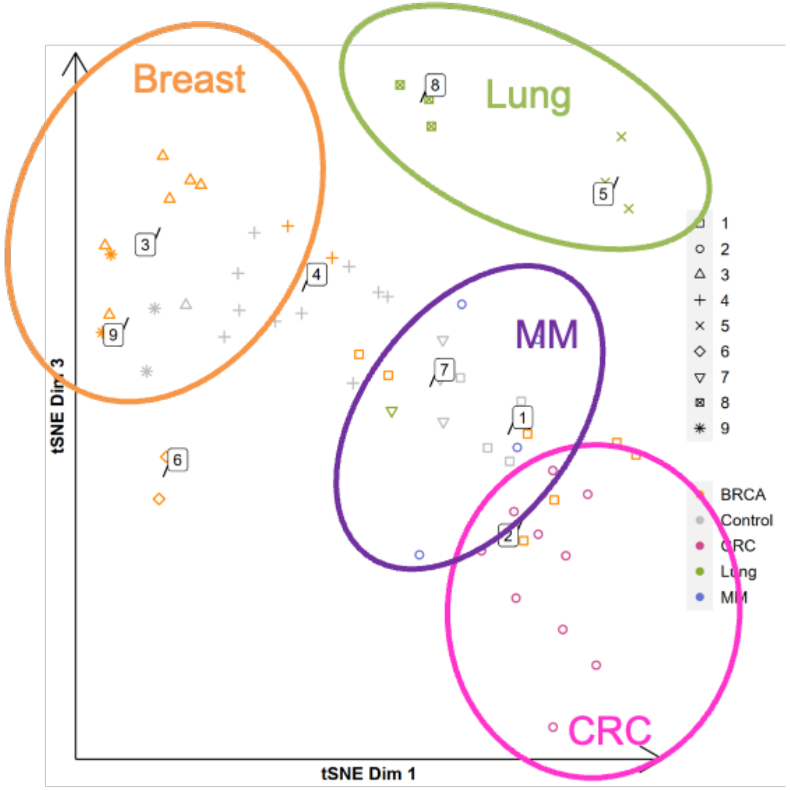
Sequencing

Data Analysis

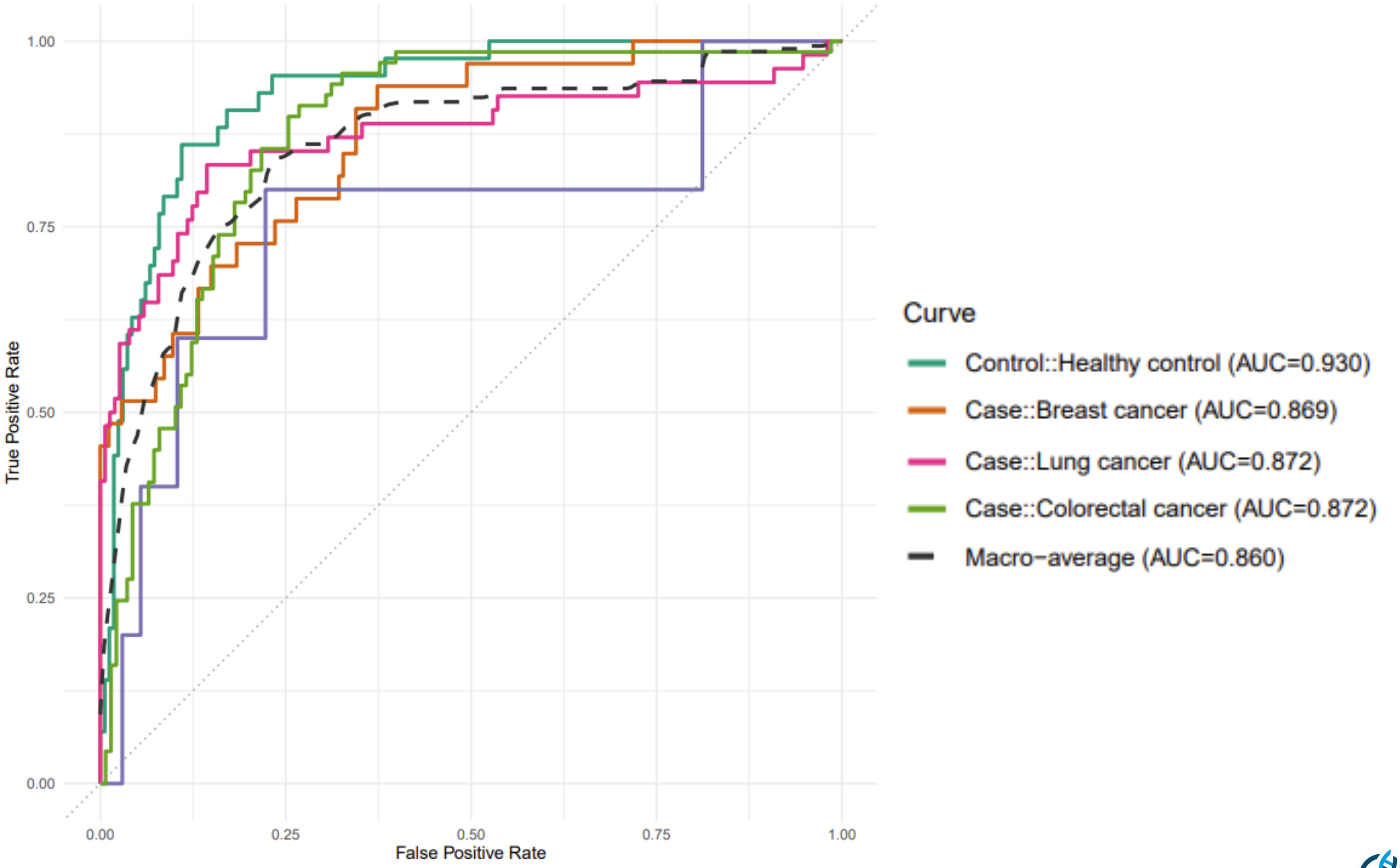


GIP*Xplore*
(Genome-wide
fragmentome)

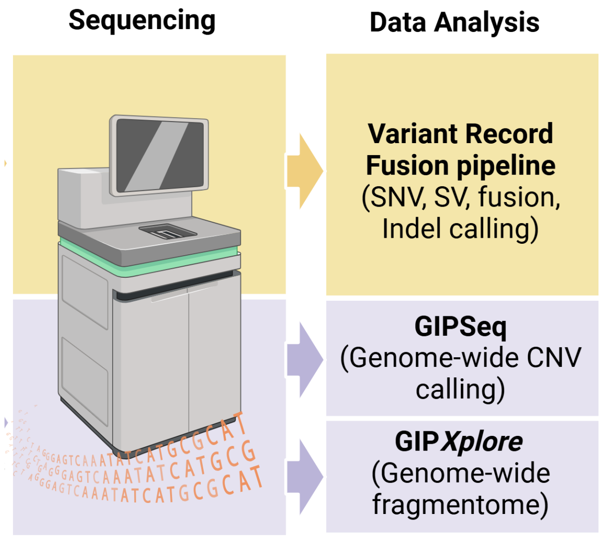
Multicentric evaluation of cfDNA fragmentome profiles (Phase 2)



Genome-wide cfDNA profiles carry cancer type-specific patterns



OncoXPLORE solution: Integrating all the data



Sequencing

Data Analysis

Variant Record Fusion pipeline
(SNV, SV, fusion, Indel calling)

GIPSeq
(Genome-wide CNV calling)

GIP*Xplore*
(Genome-wide fragmentome)

OncoXPLORE comprehensive sample view

Targeted module:

Variant data:
ESR1 p.D538G
0.72% VAF

Fusions:

No actionable SVs found

MSI status:

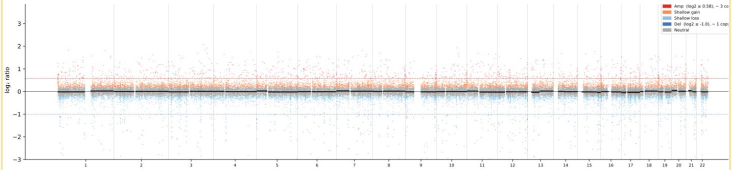
Stable

(b)TMB score:

6.0 Mut/Mb

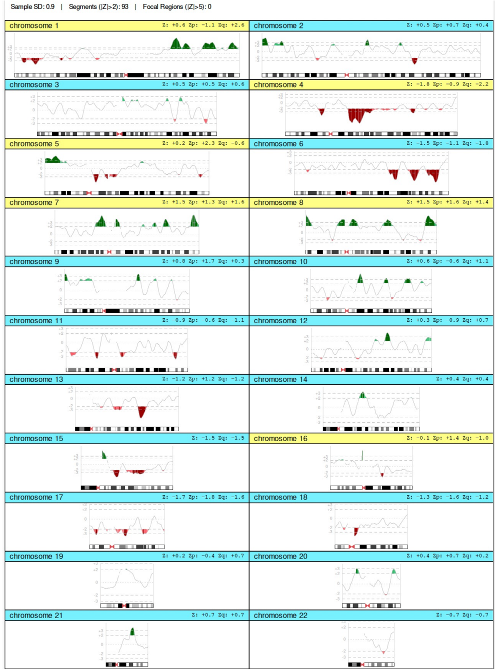
CNAs:

-



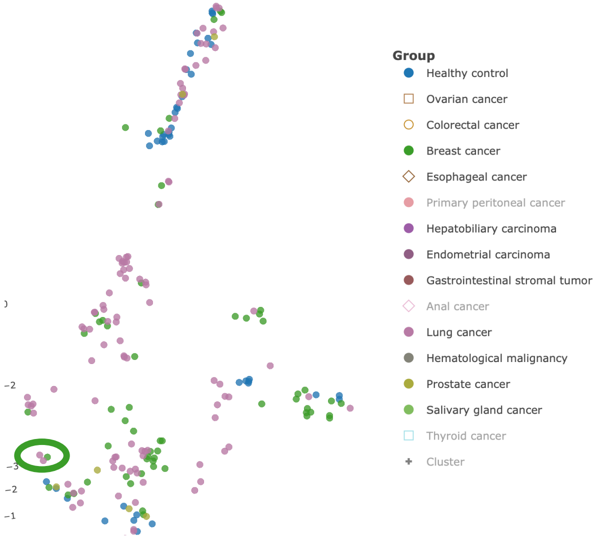
Low-pass WGS module:

Genome-wide CNA profile



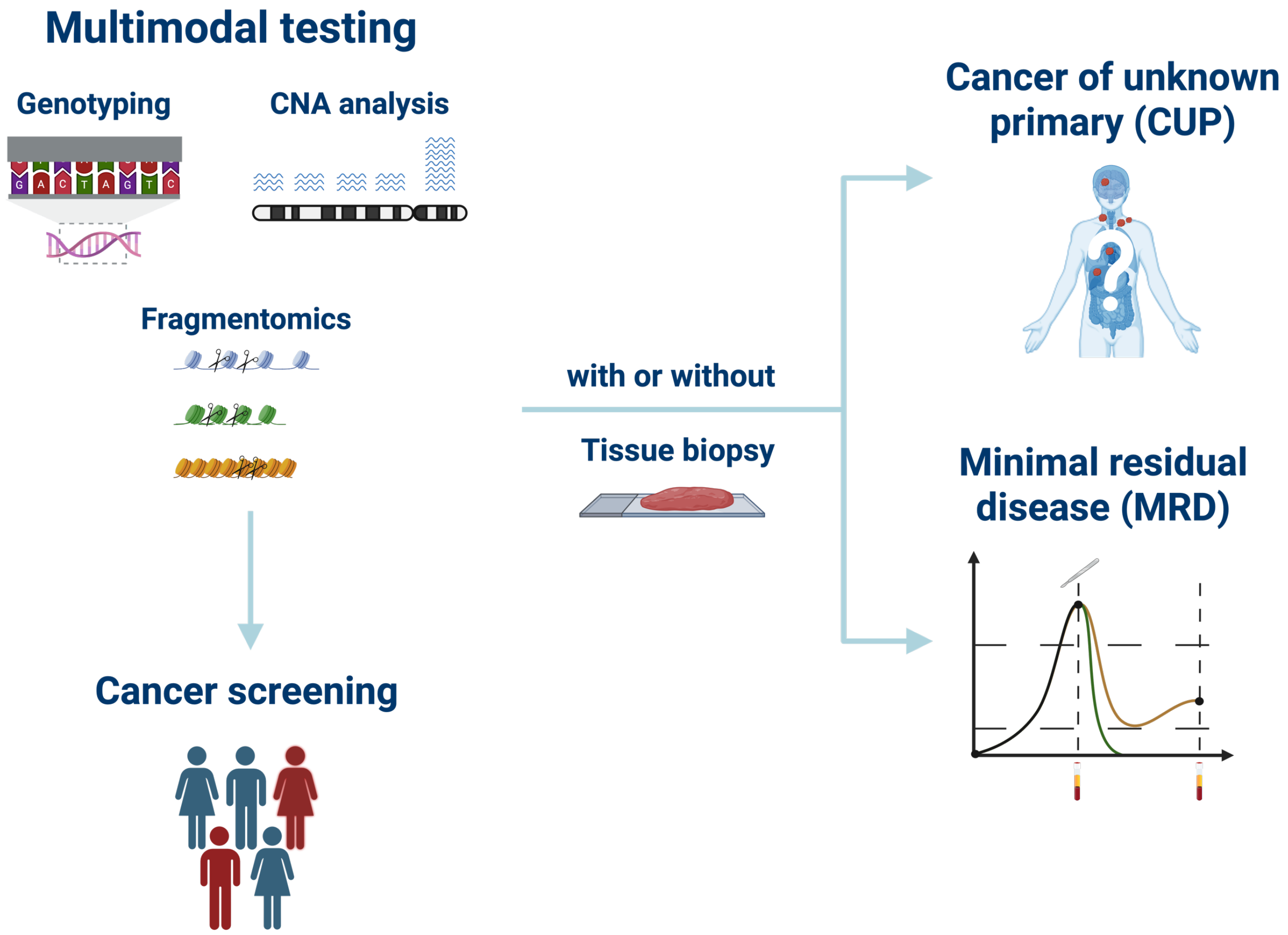
Fragmentome-based site-of-origin prediction

Case vs control	Tumor type
Case	Breast cancer



5. Perspectives for future research

Multimodal testing



Genotyping

CNA analysis

Fragmentomics

Cancer screening

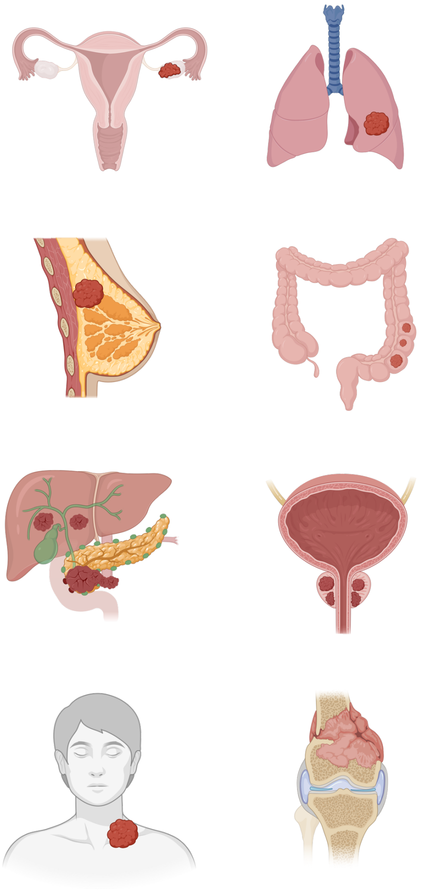
with or without

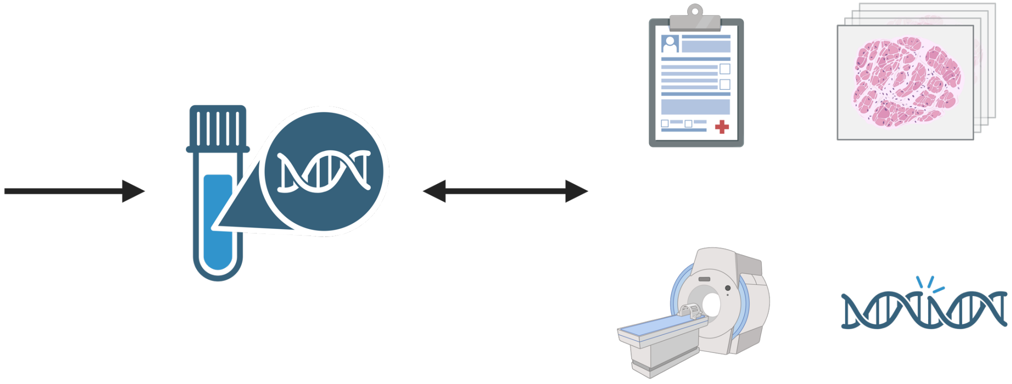
Tissue biopsy

Cancer of unknown primary (CUP)

Minimal residual disease (MRD)

Need for further clinical validation to increase knowledge about fragmentome profiles in multiple tumor types





Let’s EXPLORE the future of ONCOdiagnostics together!

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- **OncoXPLORE** is able to detect actionable alterations with **high sensitivity in clinical use cases** with unmet diagnostic needs
- **Cost-effective, scalable and fast** (<7 TAT) off-the shelf solution
- **(Epi)genomics** improves cancer signal detection and profiling
- **Need for** further **clinical validation and collaboration** to increase knowledge about (epi)genomic profiles in multiple tumor types

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