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K-4CARE

K-4CARE Study Summary

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Integrated DNA–RNA Profiling with ctDNA-MRD Monitoring

Enables Comprehensive Biomarker Insights and Treatment Response Assessment

Current CGP that relies solely on FFPE DNA has important limitations: tumor-only analysis yields less accurate MSI/TMB/variant calls than tumor–normal testing; DNA-based fusion detection is less sensitive than mRNA profiling; and key biomarkers (CNV, HRD, germline) often necessitate additional assays.

K-4CARE integrates FFPE DNA–RNA profiling with liquid-biopsy ctDNA, providing a unified approach that addresses these gaps and enables comprehensive biomarker assessment plus on-treatment monitoring.

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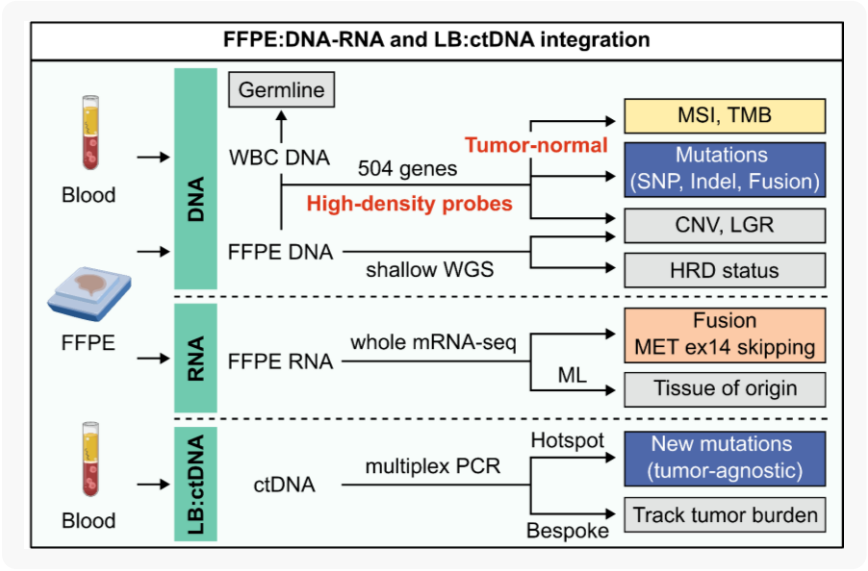
Key takeaways

- Unified FFPE DNA + whole-transcriptome RNA profiling with serial plasma ctDNA provides a tissue- and time-efficient pathway to detect actionable biomarkers and monitor clinical outcomes.
- High-density probe (HDP) design improves CNV detection at chromosome-, gene-, and exon-level.
- Combining DNA + RNA profiling maximizes fusion detection, addressing RNA quality variability in FFPE and capturing events such as *MET* exon 14 skipping.
- OriCUP tissue-of-origin model demonstrates high prediction accuracy for primary and metastatic tumors, aiding management of cancer of unknown primary (CUP).
- In stage-IV NSCLC, >50% ctDNA decrease from baseline is associated with markedly longer PFS versus non-responders; LOD ~0.01% achieved via multimodal ctDNA analysis.

K-4CARE – An AI-powered multi-omics, multi-modal assay

1. Tissue DNA (FFPE tumor + matched WBC; tumor–normal mode, 504-gene HDP panel) to report MSI, TMB, SNVs/indels, selected fusions, CNVs, and LGRs, plus shallow WGS on FFPE DNA for genome-wide CNV/LGR and HRD.
2. FFPE RNA-seq to improve fusion detection and enable ML-based tissue-of-origin prediction.
3. Plasma ctDNA (multiplex PCR) combining hotspot and patient-personalized tumor-informed variants to detect new tumor-agnostic alterations and longitudinally track tumor burden.



Superior CNV sensitivity with high-density probes (HDP) panel

Chromosome-level	Clearer hallmark events like 1p/19q co-deletion, chr10 loss
Gene-level	Amplification signals more pronounced. Quantitative accuracy/precision: Absolute copy-number deviation for reference samples was 0.1–0.4 copies with HDP vs. up to 1.5 copies with STD.
Exon-level (LGRs)	Sensitivity for *BRCA1/2* exon-level LGRs: HDP = 100% vs. STD = 81.8%.
Broader HRD assessment	55% HRD+: many HRD+ were wGI+ without mBRCA (33.7%)

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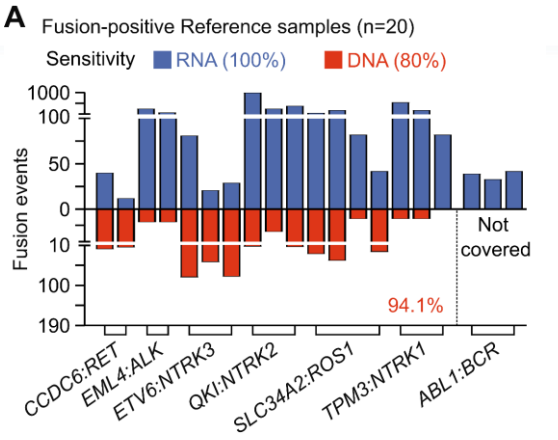
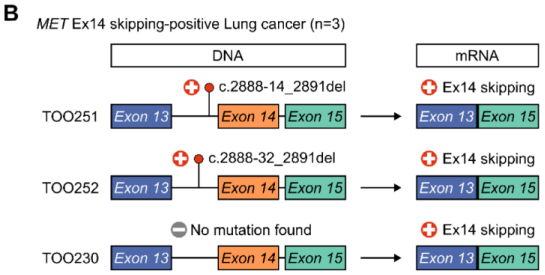
RNA (transcriptomic) reveals what DNA may miss: fusions and *MET* exon 14 skipping





In fusion-positive reference samples, **mRNA profiling achieved 100% sensitivity to capture all fusion variants**, while DNA profiling detected 80% of them.

Real-world FFPE RNA can be limiting 35% of clinical FFPE samples had low RNA quality (DV200 <30%), **supporting the practical need to combine DNA and mRNA to maximize actionable fusion detection.**

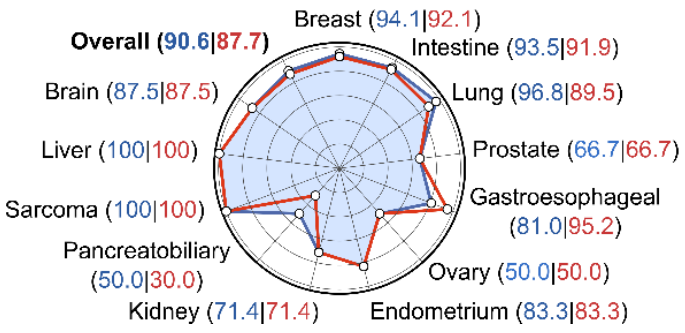
mRNA profiling could detect *MET* Ex14 skipping when no DNA mutation was identified in lung cancer samples.

Detection performance: **>99% sensitivity and >99% specificity** (positivity threshold ≥ 10 junction reads).

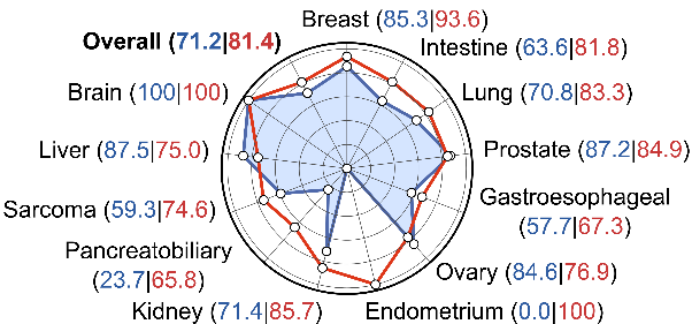
High accuracy (up to 87.7%) for predicting cancer Tissue of Origin (TOO) using mRNA profiling and AI

For metastatic tumors, **K-4CARE's OriCUP demonstrated ~10% higher overall accuracy in** comparison developed algorithm. **T**he largest differences were found in lung and gastrointestinal cancers.

87.7% in primary tumors



81.4% in metastatic tumors



CUP-AI-Dx model
817 genes

OriCUP model
2000 genes

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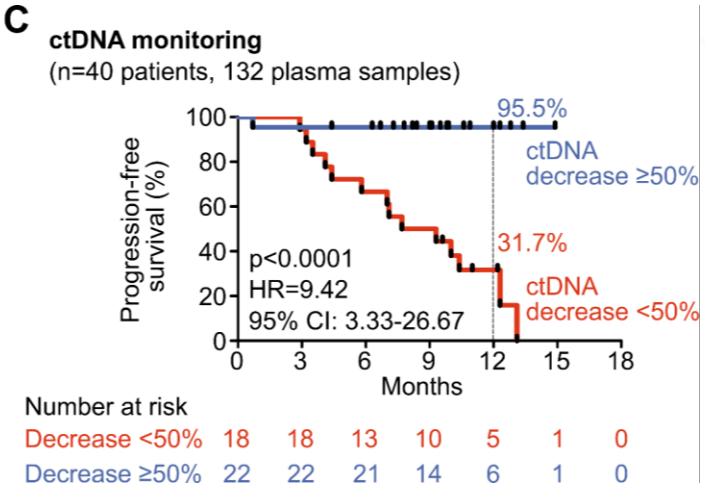
ctDNA dynamics are strongly prognostic and treatment-informative



In **40 patients** with serial testing on **TKIs or ICIs**, a **>50% ctDNA drop** ("molecular responder") was linked to markedly longer PFS (**HR 9.42; p<0.0001**) with **12-month PFS 95.5% vs 31.7%**

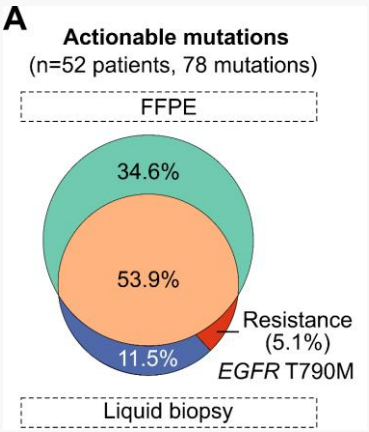
Concordance with clinical response: **84.0% (21/25)** of molecular responders achieved **CR/PR**, while **93.3% (14/15)** of molecular non-responders had confirmed **progressive disease -** positioning ctDNA as a practical, real-time response indicator.

0.01% ctDNA Limit of Detection

Integrates **mutation + non-mutation features** (including CNV and fragmentomics) - enabling ultra-sensitive monitoring

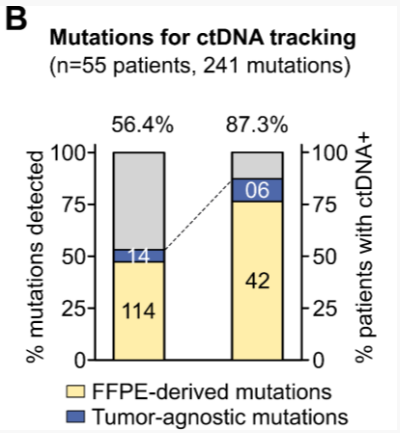
Innovative integration provides more insight and higer precision

+11.5% more actionable mutations



LB-ctDNA profiling contributed additional actionable and resistance findings beyond tissue analysis in advanced lung cancer (including EGFR T790M).

87.3% baseline ctDNA detectability



The addition of a hotspot panel, combined with FFPE-derived mutations, increased the baseline ctDNA detection rate by >10%.