MRD-EDGE: Ultra-Sensitive Detection of Circulating Tumor DNA for Cancer Screening and Diagnosis

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**Background & Unmet Need**

- Liquid biopsy is an emerging noninvasive method for cancer diagnosis and monitoring which involves sequencing blood plasma cell-free DNA (cfDNA) to identify circulating tumor DNA (ctDNA)
- ctDNA detection is of particular interest for evaluating minimal residual disease (MRD), which indicates the lingering presence of cancerous cells after an initial cancer treatment
- Current ctDNA detection methods have inadequate sensitivity in low volume cancer due to the sparsity of ctDNA in blood and usually require a matched tumor sample, which may not be feasible in many clinical settings
- **Unmet Need:** A sensitive noninvasive liquid biopsy platform to accurately detect residual tumor in blood samples at low tumor burden in the tumor-informed or tumor-naïve context

**Technology Overview**

- **The Technology:** MRD-EDGE is an ultra-sensitive machine learning-guided ctDNA analysis platform for MRD detection in low tumor fraction cancers
- MRD-EDGE incorporates simultaneous profiling of single nucleotide variants (SNV) and copy number variants (CNV) to enhance ctDNA detection
- The deep learning SNV classifier integrates properties of somatic mutations to distinguish ctDNA from sequencing error, enabling ctDNA detection even in the parts per million range and below
- The CNV module couples read-depth denoising with fragmentomics and an allelic imbalance classifier to detect ctDNA even at low aneuploidy levels
- **PoC Data:** MRD-EDGE enabled tracking tumor burden changes in response to immunotherapy in non-small cell lung cancer (NSCLC), ctDNA shedding in precancerous colorectal adenomas, and de novo mutation calling in melanoma, yielding clinically informative tumor fraction monitoring

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- Minita Shah
- Cole Khamnei
- Jacob Bass

**Patents:**
- PCT Application Filed
- PCT Application Filed

**Publications:**

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**Cornell Reference:**
- D-9641
- D-10093
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Technology Applications

- Ultrasensitive MRD detection following surgical resection of cancer
- Noninvasive liquid biopsy for cancer screening
- Real-time serial monitoring of therapy response to inform therapeutic optimization
- Patient monitoring during remission for early detection of relapse
- Applicability in a wide range of solid tumors

Technology Advantages

- Ultra-sensitive SNV and CNV detection due to advanced error suppression and radical amplification of ctDNA signal
- ctDNA detection in tumor-informed or tumor-naïve context (without matched tumor tissue)
- Simple Whole Genome Sequencing (WGS) workflow does not require custom panel creation or molecular barcodes and can work with limited input material

Supporting Data / Figures

Figure 1: ctDNA analysis workflow with MRD-EDGE.

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Supporting Data / Figures

A

Reference
R1 read
R2 read
R1 length
R2 length
All position

SNV Classification

Base pair position
SNV mutation density
DNase
Replication timing
Chromatin state

B

Copy number
denoising

Tumor / Normal
Read Depth Ratio

MRD-EDGE SNV combines a novel fragment-level deep learning architecture with epigenetic features to classify fragments as ctDNA. (B) MRD-EDGE CNV integrates machine learning-based read-depth denoising with allelic imbalance and fragmentomics for ultrasensitive ctDNA detection.

Figure 2: (A) MRD-EDGE SNV combines a novel fragment-level deep learning architecture with epigenetic features to classify fragments as ctDNA. (B) MRD-EDGE CNV integrates machine learning-based read-depth denoising with allelic imbalance and fragmentomics for ultrasensitive ctDNA detection.

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Figure 3: A-D. Serial tumor burden monitoring with MRD-EDGE in a neoadjuvant non-small cell lung cancer (NSCLC) clinical treatment protocol (A) demonstrates lack of response to immune checkpoint inhibitor therapy in two patients (B, C), while evidence of MRD above detection threshold after surgical removal predicts disease recurrence (C, D). In patient D, MRD-EDGE captures residual disease following stereotactic body radiation therapy (SBRT) on Day 3.

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Figure 4. (A) Tumor-informed post-operative ctDNA detection in early-stage colorectal cancer is associated with shorter progression-free survival. (B) Serial tumor-naive ctDNA monitoring with MRD-EDGE reflects changes seen on imaging.

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