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IMPROVEMENT IN DETECTION SENSITIVITY OF RARE DISEASE VARIANTS FOR LIQUID BIOPSY TESTING

DIAGNOSTICS

Method for generating large family size cell-free DNA while maintaining and improving test sensitivity.

TECHNOLOGY TYPE

Biomarkers
Cell-Free DNA

STAGE OF DEVELOPMENT

Verified with lung cancer clinical samples harboring rare variants.

IP PROTECTION

U.S. Utility Patent Pending
Size-Selection of Cell-Free DNA for Increasing Family Size During Next-Generation Sequencing
US20190106737A1

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TECHNOLOGY SUMMARY

Circulating tumor DNA and tumor-derived exosomes are becoming popular as non-invasive cancer diagnostic tools, termed "liquid" biopsy. Standard next-generation sequencing (NGS) DNA processing approaches enable broad identification of both known and unknown tumor-associated variants, including single nucleotide variants. However, even with the highest fidelity sequencing platforms, errors introduced at >0.1% limit identification of disease associated variants that occur at <1% frequency. This increases the risk of over-representation of false variants and diminishes the clinical relevance of such tests.

University of Utah researchers have developed a droplet digital PCR (ddPCR) approach for enhancing detection sensitivity. This ddPCR approach has the following proprietary intervening steps to enrich circulating tumor DNA: (1) high-throughput automated gel extraction to isolate subfractions of the mononucleosomal peak and (2) specific adapter sequences or molecular identifiers that allow grouping of PCR duplicates into "family sizes."

FEATURES AND BENEFITS

- Fraction preselection reduces sample complexity and yields larger PCR family sizes.
- Compatible with downstream NGS.
- Improved detection sensitivity of rare variant alleles in ddPCR.
- Reduces false positives.

RECENT PUBLICATIONS

Underhill HR, Kitzman JO, Hellwig S, Welker NC, Daza R, et al. (2016) Fragment length of circulating tumor DNA. *PLOS Genetics* *12*(7): e1006162. https://doi.org/10.1371/journal.pgen.1006162

INVENTOR PROFILE

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