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MutantDx Looks to Outlicense Ultrasensitive Mutation Detection Tech for Early Cancer Detection

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NEW YORK – Fresh off receiving patents for its circulating tumor DNA collection tool earlier this month, molecular diagnostic startup MutantDx is actively seeking to license its liquid biopsy technology out to partners for cancer screening applications.

The Greensboro, North Carolina-based firm claims its PrimaCap multiplex liquid biopsy platform, which combines a proprietary nucleic acid amplification method with Sanger sequencing, can identify mutations in patient samples at "subclinical" concentrations, according to the patents.

Founded by CSO Thurai Moorthy and Medical Director Roger Hodkinson in 2018, MutantDx was established as the marketing arm of Canadian firm Bio-ID Diagnostics to commercialize its patented technologies for cancer applications. Bio-ID's subsidiary MultiGen Diagnostics, which had its CLIA labpurchased by Trovagene in 2012, developed an allele-specific multiplex sequencing (ASMS) technology that MutantDx is now marketing as TumorPlexfor analyzing solid tumor specimens.

Moorthy explained that PrimaCap detects asymmetric mutations in short DNA fragments of less than 100 nucleotides. He noted that the platform can be used with any type of body fluid – including urine and blood – that contains fragmented DNA.

MutantDx envisions that clinicians will be able to collect 1 to 5 ml of a patient's liquid sample and mail it to a CLIA-approved/CAP-accredited lab that licenses MutantDx's technologies. Researchers would then extract the ctDNA from the sample and perform PCR to amplify fragments into amplicons.

From there, Moorthy said that the team uses multiple proprietary primers to perform Sanger sequencing to detect tumor-specific biomarkers. While noting that PrimaCap can search for up to 20 biomarkers in a single panel, Moorthy said that team is considering adding the ability to detect more biomarkers in the future.

According to Moorthy, PrimaCap's overall workflow is similar to a standard clinical sequencing process; however, researchers use proprietary primers and accessory DNA to identify the biomarkers. He also noted that the assay only requires 8 to 10 hours to identify actionable cancer mutations from a liquid sample.

Moorthy explained that PrimaCap is mainly for smaller fragments and uses additional oligonucleotide DNA as its capture template. In contrast, TumorPlex is for larger fragments and uses traditional PCR. In order to increase sensitivity and specificity, both tools use ASMS and a "true internal control."MutantDx therefore believes that PrimaCap can simultaneously detect multiple biomarkers in ctDNA fragments as small as 30 base pairs at femtogram concentrations with high sensitivity.

"If you have a ctDNA fragment with a mutation within 30 bases of the end of the fragment, there is less of an ability for stringent binding of the PCR primers, leading to false results,"

Moorthy said. "Since part of the PrimaCap technology uses the ctDNA as a 'primer' itself, allowing for capture of these small fragments … we'll be able to identify the mutation without any false positives."

Moorthy highlighted that MutantDx's goal with its technology is not to identify cancer, but rather to identify patients at high risk of developing the disease.

"We are mainly screening for early-stage, asymptomatic populations with actionable mutations to see if something's going on so they could be followed up to identify high-risk patients," Moorthy explained.

Moorthy noted that somatic mutation detection is moving toward clinical sample types such as liquid biopsy, population screening, and early-stage cancers, and claimed that researchers and national regulatory agencies should re-evaluate the "efficacy of detection of somatic mutations."

Moorthy therefore proposes a new algorithm called "Detection Index" for measuring a test's sensitivity, which combines the lower limit of detection of a mutant allele and the ratio of copies of the mutant allele to the wild type. He believes the method would help standardize the detection of somatic mutations, as well as allow researchers to use the "appropriate amounts of DNA and assay conditions to achieve [the] desired detection index." By applying that method, Moorthy envisions researchers using PrimaCap to detect ctDNA at extremely low concentrations in a patient's liquid sample.

In a 2015 study, Moorthy and MultiGen researchers used TumorPlex to detect BRAF mutations using genomic DNA extracted from mutation-specific cell lines. Moorthy said that the firm is preparing to submit studies detailing PrimaCap's analytical sensitivity for detecting EGFR T790 mutations from spiked ctDNA plasma.

The recently awarded patents — US No. 10,351,899 and EP3049539 — both name parent company Bio-ID as the recipient and are specific to the PrimaCap technology. Moorthy said that Bio-ID has also received multiple patents related to TumorPlex, as well as a patent related to a technology for reducing cross-contamination that the firm believes eliminates false negative and false positives.

In addition to TumorPlex and PrimaCap, MutantDx is also developing a tool for microsatellite instability testing called RepSeqID. The tool generates a single electropherogram to detect gene deletions and gene fusions to potentially help clinicians select patients most likely to benefit from specific immunotherapy.

Within the cancer space, MutantDx envisions several licensing opportunities for larger firms to use its wide array of detection technologies. One important application is early-stage population cancer screening, as the firm has demonstrated the ability to detect and verify mutations in melanoma (BRAF), lung cancer (EGFR T790M), colorectal cancer (KRAS), and prostate cancer (ARV7).

In addition, MutantDx believes that researchers can use PrimaCap and TumorPlex to codevelop companion diagnostics for targeted treatment and patient selection for clinical trials. Moorthy envisions the tools as a way to help clinicians identify mutations for patient-specific chemotherapy, such as splice variants and checkpoint inhibitors.

"There is a trend going toward screening of asymptomatic people in the tests," Moorthy said. "As new mutations [are] characterized, those targets will be added to [our] screening tests."

Moorthy noted that PrimaCap's multiplexing ability will allow a lower price for users compared to similar technologies, but did not elaborate.

Moorthy also said that MutantDx has been on a shoestring budget since its founding but declined to comment further on the firm's plans for future funding. He noted that Bio-ID will also be promoting MutantDx's offerings in European markets.