LICENSING OPPORTUNITY

A Liquid Biopsy based Assay for Early Detection of Multi-Cancers using Cell-Free DNA Methylation

Here we present a diagnostic assay to detect and classify cancers based on CpG island hypermethylation signatures in plasma cell-free DNA. The cancer methylome is characterized by global hypomethylation and CpG islands-specific hypermethylation. CpG island hypermethylation has been described in almost every tumor type. Moffitt's diagnostic uses the differentially hypermethylated CpG islands in cell-free DNA for accurate cancer detection and multi-cancer classification. Using a methylation enrichment sequencing (cfMBD-seq) technique, Moffitt's diagnostic identifies a set of hypermethylated CpG islands that can be used as biomarkers for multiple cancer detection and classification.

COMMERCIAL OPPORTUNITY

- The American Cancer Society estimates 235,760, 104,270, and 60,430 new cases of lung, colorectal, and pancreatic cancer in the US in 2021. Early detection of cancer has been proven to significantly improve patient survival rates and quality of life, as well as to significantly reduce the cost and complexity of cancer treatment.
- One of well-known methylation biomarkers is the methylation of SEPT9 promoter, which is an FDA-approved biomarker for colorectal cancer (CRC) detection. A blood-based test for methylated SEPT9 (Epi proColon) has been applied to plasma cfDNA in patients undergoing CRC screening, however this test has low sensitivity for early-stage CRC detection. Nonetheless, CpG island hypermethylation has demonstrated its great versatility and potential for the detection and management of cancer.
- Currently, most studies use chemical treatment (sodium bisulfite) to examine cell-free DNA methylation level. However, this treatment further damages cfDNA and therefore, reduces sensitivity of methylation detection. Moffitt's technology uses a methylation enrichment sequencing technique (cfMBD-seq), which preferentially captures high CpG density regions, such as CpG islands. Using cfMBD-seq technique, the diagnostic identifies hypermethylated CpG islands that can be used as biomarkers for multiple cancer detection and classification.

TECHNOLOGY

A methylation enrichment sequencing technique (cfMBD-seq) was used to profile cell-free DNA methylome using plasma samples from cancer patients and non-cancer controls. 1,759, 1,783, and 1,548 differentially methylated CpG islands (DMCGIs) were identified in lung, colorectal and pancreatic cancer patients, respectively. The vast majority of DMCGIs were found to be hypermethylated and overlapped with aberrant methylation changes in corresponding tumor tissues, indicating that DMCGIs detected by cfMBD-seq were driven by tumor-specific DNA methylation patterns. From the overlapping DMCGIs, machine learning analyses identified a set of discriminating methylation signatures that showed robust performance in cancer detection and classification. These signatures include 3 DMCGIs for colon cancer, 16 DMCGIs for lung cancer and 6 DMCGIs for pancreatic cancer. Statistical models using these methylation signatures showed almost perfect separation among different cancer types and normal controls. Overall, cfDNA-based methylation signatures can be used as a powerful diagnostic tool for the multi-cancer detection and cancer type classification.

PUBLICATION/PATENT

1. Provisional application was filed for Dr. Liang Wang in 2021
2. Huang J et al. Cell-free DNA methylome profiling by MBD-seq with ultra-low input. Epigenetics 2021, 1-14.
3. Huang J et al. Cancer Detection and Classification by CpG Island Hypermethylation Signatures in Plasma Cell-Free DNA. Cancers. 2021; 13(22):5611. https://doi.org/10.3390/cancers13225611

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