Identify Tissue-of-Origin in Circulating Cell Free DNA by Inferred Epigenomic Pattern from Whole Genome Sequencing

Technology #18809

Applications

This technology is a novel technique for identifying the tissue-of-origin of circulating DNA with applications as a diagnostic for cancer, autoimmune disease, stroke, sepsis or myocardial infarction.

Problem Addressed

When cells die, they release cell-free DNA into the body. Cell-free circulating DNA (ctDNA) is an attractive diagnostic target because it is obtained through non-invasive blood draws, and could be applied to a wide variety of diseases with characteristic cell death, including cancer, autoimmune diseases, and myocardial infarction. However, identifying the ctDNA of interest remains challenging due to the large amount of circulating DNA that is irrelevant for detecting the disease. For example, in cancer less than 1% of the total circulating DNA arises from cancerous cells. Due to this high level of background noise, it is imperative that the tissue-of-origin of the ctDNA is correctly identified. Epigenetic modifications, such as nucleosome positioning or methylation patterns, are highly cell-type specific, but detecting these modifications in very small amounts of ctDNA is impractical with current technologies.

Technology

This technology is new method for determining tissue-of-origin of ctDNA using a novel assay to detect methylation patterns. Bisulfite sequencing is the standard method for detecting methylation patterns; however, it cannot be used to accurately measure ctDNA because of degradation issues with very low levels of input DNA. A recent study discovered that methylation status significantly influences DNA fragmentation patterns, and these inventors took advantage of this observation to generate a fragment-length algorithm to identify tissue-of-origin. To generate the computational model, the algorithm was trained to recognize methylation-dependent fragmentation patterns using whole genome bisulfite sequencing of DNA with a known methylation pattern. The algorithm can be used to identify tissue-of-origin of ctDNA by analyzing the fragmentation pattern of sequencing reads in the sample then using the fragment lengths to predict the methylation pattern of the ctDNA. Additionally, this technique can be used with ultra-low-pass sequencing of 0.1x, which significantly reduces sequencing costs.

Advantages

- Detect tissue-of-origin from low input ctDNA samples using a fragmentation algorithm
- Compatible with low-cost, ultra-low-pass sequencing at a read depth of only 0.1x

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Categories For This Invention:

Life Sciences
Biotechnology
Bioinformatics
Clinical Applications
Cardiovascular
Immunology
Infectious Disease
Inflammatory Disease
Oncology
Diagnostics
Markers

Intellectual Property:

Methods for genome characterization
PCT
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