Genomic DNA Mutation Assays and Uses Thereof

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The assays described can direct the power of next generation sequencing to the regions of the genome containing somatic mutations and/or germ line polymorphisms, which can be difficult to detect. The method use massively parallel sequencing technologies to determine the frequency of somatic mutations identified in a subject. By analyzing the frequency of a mutation or a set of mutations across an individual's genome, a disease or other physiological state of the subject can be determined.

Technology Overview

Mutations are the primary cause of genetic disorder and cancer. The ability to detect mutations in the genome holds the key to diagnosis, treatment, and prevention of the disease. Recent developments in novel sequencing technology have made efforts in sequencing hundreds of thousands of human genomes a reality. However, it remains challenging to identify somatic mutations, since they often present only in a trace amount in the sample, which makes it technically challenging to distinguish true mutations from sequencing errors. In addition, the low occurrence rate of somatic mutations means sequencing efforts for identifying somatic mutations often waste the majority of the sequencing reads on regions without mutations.

Dr. Wang has developed a method for identifying and positioning somatic mutations across the genome for a given individual sample without prior knowledge on these mutations or on the sample. The method takes advantage of the fact that when a mutant DNA strand base pairs with a complementary DNA strand without the corresponding mutation, a mismatch is induced. These mismatched DNA can be isolated using chemical or biological agents that bind specifically to the mismatches. The isolated DNA can then be used as templates for generating a sequencing library. By using a next generation sequencing method to sequence the library, the sequence reads generated can be mapped to a reference genome, mismatch variants can be identified, and the relative allele frequency (RAF) can be estimated and used to distinguish somatic mutation from parental polymorphisms. The somatic mutation information can be used to determine disease or other physiologic state.

Benefits/Technology Advantages

Comparing to other available technology for early detection of disease, this method has the potential to be minimally invasive, versatile (i.e. same assay for multiple diseases), and cost effective. Moreover, the rich and quantitative information obtained from sequencing somatic mutations could be further developed for disease prognosis and for suggesting therapeutic options.

Potential Applications

- Diagnosis of cancer through detection of cancer mutations in circulating DNA
- Monitoring organ transplant rejection through detection of foreign variants
- Genetic testing

Intellectual Property Status

Patent pending, U.S. Application No: 15/965,856

Available for licensing

Stage of Development

Pre-clinical

Associated Publications

N.A.

About the Investigator

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