Docket #: S10-233

Fast, direct DNA capture and sequencing

Researchers in Prof. Hanlee Ji's laboratory have developed an automated method to capture and directly sequence target DNA with next-generation sequencing. Next gen sequencing has been combined with targeted DNA capture for clinical and research applications where deep sequencing of specific regions is required. Currently, targeted sequencing requires capturing specific genomic DNA regions, preparing the sequencing library and then sequencing the template DNA. This process is complex, error prone and requires extensive optimization. To overcome these complexities, the inventors have developed an automated approach that integrates these steps by using an immobilized primer lawn on a solid support of a fluidic system to allow direct capture, preparation and sequencing of target DNA. This technology provides an automated, flexible and efficient targeted sequencing method - one only has to program the sequencer to analyze specific genomic targets.

Stage of Research
The inventors have used this method to cover up to 1421 genes with a total coverage of 5.5 Megabases (Mb); sequence continuous genomic loci up to 1.5 Mb while simultaneously genotyping single nucleotide polymorphisms (SNPs) and genes; detect low minor allele fraction variants; and determine the exact breakpoint sequence of cancer rearrangements.

Ongoing Research
The inventors continue to optimize and add functionality to the method.

Applications

- Research tool for genomic studies:
    - Identify genetic and epigenetic variants in:

        - Eukaryotic genomes
        - Microbial genomes
        - Viral RNA and DNA
    - Analyze candidate genes
    - Detect variants in genetic mixtures
    - Detect cancer mutations
    - Delineate sequence of structural variation breakpoints
    - Analyze Mb size contiguous loci from the human genome
    - Genotype specific SNPs
    - DNA copy number profiling
    - Sequencing the transcriptome
    - Profile methylation patterns

Advantages

- Fully automated workflow- target enrichment and flow cell preparation take place on a standard fluidic device
- Fast
- High performance for selective sequencing of genome targets
- Configuration flexibility- can be configured for multiple applications across a wide variety of genomic targets from any organism
- Refined primer probe design
    - Improved uniformity of targeting
    - High on-target sequence yield
- Minimal experimental hands on time required
    - Saves money
    - Reduces error

Publications

- Erik S. Hopmans, Georges Natsoulis, John M. Bell, Susan M. Grimes, Weiva Sieh and Hanlee P. Ji, A programmable method for massively parallel targeted sequencing, Nucleic Acids Research, Vol. 42, No. 10, published online April 29, 2014.
- S. Myllykangas, JD Buenrostro, G. Natsoulis, JM Bell, HP Ji , Efficient targeted resequencing of human germline and cancer genomes by oligonucleotide-

selective sequencing, Nature Biotechnology, published online Oct. 23, 2011.
- US Patent Application Publication No. 20150017635

Patents

- Published Application: 20120157322
- Published Application: WO2012040387
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- Issued: 9,309,556 (USA)
- Issued: 10,072,283 (USA)

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