Efficient Whole Genome Analysis System

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Inventors: David Schwartz, Konstantinos Potamousis, Shiguo Zhou, Steven Goldstein, Michael Newton, Rodney Runnheim, Daniel Forrest, Christopher Churas

The Wisconsin Alumni Research Foundation (WARF) is seeking commercial partners interested in developing a simple, rapid, comprehensive and cost-effective system for analyzing whole genomes.

Overview

In addition to simple nucleotide polymorphisms, the human genome includes intermediate structural variations, such as amplifications, insertions, deletions, inversions and complex rearrangements. While these types of genetic alterations have been studied using classical cytogenetics and more recently, by analysis of data from high-density arrays, whole genome approaches are needed to comprehensively analyze structural variation in the human genome.

The Invention

UW-Madison researchers have developed an efficient whole genome analysis system, called “Nanocoding,” which acquires sequence information from numerous large DNA molecules in new ways. Because large molecules are used, this system obtains information from heterochromatic regions, pinpoints structural variants and can even characterize aberrations associated with cancer cell genomes.

In this system, a new class of restriction endonucleases that cleaves just one strand of DNA is used to introduce sequence-specific nick sites into large genomic DNA molecules. After labeling, this action results in ordered restriction maps for the individual molecules. The barcoded maps can be aligned with reference maps to identify each molecule and reveal structural alterations, such as missing restriction sites, insertions or deletions.

A key component of this approach is the termination of DNA strand synthesis at a known distance away from a given nick site that has been mapped. This distance defines the breadth of a “neighborhood.” Labeled nucleotides are incorporated into each neighborhood between the nick and termination sites. The amount of label, which defines the measurable optical “signature” of the neighborhood, depends on the nucleotide sequence in the region. The set of all signatures within a given DNA molecule makes up its “barcode,” which is used to compare local sequence composition against that of a reference genome.

Applications

- Whole genome analysis, including comprehensive, high-resolution analysis of cancer cell genomes

Key Benefits

- Provides a comprehensive and cost-effective method of analyzing whole genomes
- Offers sequence information with resolution control approaching that of resequencing
- Uses no cycles of biochemical steps or imaging, and allows all biochemical steps to take place within a single reaction chamber
- Fosters simple, high throughput imaging schemes and sample handling

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- Because large DNA molecules are analyzed, this sequence acquisition scheme obtains information from heterochromatic regions, pinpoints structural variants in human genomes and characterizes aberrations associated with cancer genomes.
- Offers opportunities for linking sequence data from emerging sequencing platforms
- The Nanocoding system intrinsically links with physical maps to further enrich any acquired sequence data.
- Direct analysis of “raw” genomic DNA offers an unfiltered and relatively unbiased view of a genome, free from the common artifacts of clone libraries and PCR amplicons.
- Enables increased understanding of the variation within the human genome.
- To increase specificity, endogenous nicks in the DNA can be repaired before processing.

Stage of Development

The Nanocoding system is hardened for laboratory use.

Additional Information

For More Information About the Inventors

- David Schwartz
- Michael Newton

Publications

- Jo K., Dhingra D.M., Odijk T., de Pablo J.J., Graham M.D., Runnheim R., Forrest D. and Schwartz D.C. 2007. A Single-Molecule Barcoding System Using Nanoslits for DNA Analysis. Proc. Natl. Acad. Sci. USA 104, 2673-2678. PMCID: PMC1815240

Tech Fields

- Research Tools : Genomics & proteomics

For current licensing status, please contact Justin Anderson at janderson@warf.org or 608-960-9853

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