Identifying copy number alterations in high throughput sequencing of captured genomic material

Technology #2640

The genome is enriched for duplications that vary extensively in copy number. Variation in the copy number has been associated with recurrent genomic rearrangements as well as with a variety of diseases; and associating copy number alterations to a disease, such as cancer, can be an important step towards diagnosing and potential treatment of this disease.

New technologies have been developed to identify the copy number alterations, by capturing the genomic material from a biological sample, amplifying by PCR and then high throughput sequencing. An approach to identify copy number alterations in the sample is to analyze the depth/coverage produced by the sequencing. However, the main problem with this approach is that the capture, amplification and sequencing steps introduce biases in the coverage that are systematic artifacts of the process. For example, capture affinity of different genomic regions of the genome of the same organism can be non-homogeneous. Moreover, currently available technologies have limitations such as limited resolution, only applying to whole-genome sequencing, and not considering systematic errors of a previous capturing step, etc.

The technology provides a method to determine the absolute copy number for any genomic segment with great sensitivity and specificity, which presents an important step toward a comprehensive understanding of genomes and improved diagnosis of related diseases.

Computational method statistically assesses significance of genomic copy number

This technology presents a way of identifying copy number alterations by smoothing out the coverage in regions of the sample. Statistical methods have also been developed to assess the significance of the results.

Collaborative research is continuing on this project at Columbia University, to identify mutations in leukemia and lymphoma, using exon capture and pyrosequencing.

Lead Inventor:

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Applications:

- The technology provides a more accurate assessment of gene content and insight into functional constraint without the limitations of array-based technology
- Can be used to identify genomic alterations associated with diseases, e.g. cancer, autism, color blindness, psoriasis, HIV susceptibility, Crohn’s disease and lupus glomerulonephritis
- Can also be used to identify copy number variations in populations
- May extend existing capturing-sequencing pipelines to include a copy number analysis step

Advantages:

- Potentially high resolution and sensitivity limited only by the resolution of the capturing step
- The copy number analysis could be folded into a bigger mutation analysis, thus can reduce costs.
- The technology is compatible with existing capturing-sequencing protocol and facility, and can be integrated with other mutation / sequencing analysis

Patent Information:

Patent Pending

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