Getting more from whole-transcript microarrays

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The widely-used Affymetrix Whole-Transcript Gene 1.0 ST (sense target) microarray platform, normally used to assay gene expression, can also be utilized to interrogate exon-specific splicing. Research published today in the open access journal *BMC Bioinformatics* shows scientists how to monitor alternative splicing activity on a genome-wide scale, without investing in new exon microarray technologies.

Alternative splicing produces a variety of mRNA transcripts from a single gene by splicing together different combinations of exons, which can give rise to alternative protein forms that are functionally distinct. Almost 90% of human genes are now considered to exhibit alternative splicing and to meet the demand to analyze this on a genome-wide scale, Affymetrix have developed their Exon 1.0 ST platform. However, this study by Mark Robinson and Terence Speed from the University of Melbourne and the Walter and Eliza Hall Institute of Medical Research in Australia suggests that the Gene platform can also do the job.

The scientists explored a publicly available dataset of 11 human tissues that were analyzed on both the Affymetrix Gene 1.0 ST and the Affymetrix Exon 1.0 ST chips. Robinson said, "Our intention was not to provide a detailed comparison between those platforms and to suggest that the Gene array should be used as a replacement for the Exon arrays. We simply wanted to demonstrate that researchers could get information about differential splicing from the Gene platform in certain circumstances at no additional experimental cost. We, therefore, provide added value to their collected data."

The authors acknowledge that the ability to detect differential splicing depends on various factors, including the number of probes covering the gene and the nature of the splicing event. They constructed a new statistical method, called FIRMAGene, that uses information about adjacent poorly fitting probes to calculate differential expression in the Gene arrays and showed that it provides comparable results to the Exon array analysis. The approach can only be used in well-annotated genes and can detect differential splicing involving multiple exons. However, they suggested that it should work particularly well for genes containing few exons, since for these genes the coverage of probes in the Gene platform can be greater than the Exon platform.

Dr Robinson added that, "To the best of our knowledge, this is the first statistical method that interrogates differential splicing using the Gene 1.0 ST platform. We have used this method for uncovering differential splicing in human tissues, where typically a small number of tissues exhibit a distinct pattern. However, we believe it could be useful in a variety of experimental settings." FIRMAGene can be applied to human, mouse and rat samples, for which the latest Affymetrix Gene 1.0 ST platforms are available, or any other whole-transcript microarray design.

More information: Differential splicing using whole-transcript microarrays, Mark D Robinson and Terence P Speed, *BMC Bioinformatics* (in press), www.biomedcentral.com/bmcbioinformatics/

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