November 23, 2011

Dr. Helen Blount
Editor, Genome Biology
BioMed Central Ltd
236 Gray's Inn Road
London WC1X 8HB
United Kingdom

Dear Dr. Blount,

I am submitting herewith a manuscript entitled "A Systematic Comparison and Evaluation of High Density Exon Arrays and RNA-seq technology in Unraveling the Peripheral Blood Transcriptome of Sickle Cell Disease" for consideration to publish in BMC Medical Genomics.

We describe in this manuscript the merits and limitations of high throughput genomic tools such as RNA-seq and high density microarrays for clinical genomic studies to identify disease biomarkers using a human sickle cell disease system. The current study unravels the sickle cell transcriptome using whole blood clinical specimens applying both the Affymetrix Human Exon 1.0 ST arrays and Illumina’s deep sequencing technologies. We report here a strong concordance (R=0.64) between exon array and RNA-seq in both gene level and exon level expression of transcripts. The magnitude of fold changes in the expression levels for the differentially expressed genes (p<0.05) was found to be
higher in RNA-seq than microarrays. However, the arrays outperformed the sequencing technology in the detection of low abundant transcripts. We also demonstrate herein the ability of RNA-seq technology to discover novel expression outside of the annotated genes and identify sequence variation in the expressed transcripts.

Our findings suggest that microarrays remain useful and accurate for transcriptomic analysis of clinical samples with low input requirements and RNA-seq technology complements and extends microarray measurements for novel discoveries. We think that this is the first report that has studied the expression of individual exons in a human sickle cell model on both the microarray and next gen sequencing platforms. We have also compared and evaluated both the technologies in an effort to determine the merits of each of these platforms for application in clinical studies.

We believe this manuscript will be of great interest to the readership of BMC Medical Genomics and will have a broad impact for clinical researchers and help them decide on the choice of tools in the form of arrays or RNA-seq for clinical transcriptomic studies.

Looking forward for a favorable response from you.

Thank You.

Sincerely

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