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Analysis of Retinal Development and Diseases Using RNA-Seq

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Before the introduction of the high throughput mRNA sequencing method (RNA-seq), genome-wide gene expression studies largely relied on DNA microarray [1], SAGE (Serial Analysis of Gene Expression) [2], CAGE (Cap Analysis of Gene Expression) [3-5], and MPSS (Massively Parallel Signature Sequencing) [6], etc. These technologies were limited by their ability to analyze only a portion of the transcriptome [7]. RNA-seq analysis provides a new strategy for transcriptome profiling that can reveal more complex information on expression levels, differential splicing, allele-specific expression, RNA editing and fusion transcripts resulted from chromosome translocations, etc., [7,8]. With RNA-seq analysis, a complete genome-wide transcriptional architecture of genes can be characterized, which is central for the understanding of development, physiology and diseases.

This article focuses on applications of RNA-seq analysis in the study of development and diseases in the Central Nervous System (CNS). As an excellent model system for the study of the CNS, the vertebrate retina consists of seven major cell types: six types of neuronal cells and one type of glial cells [9-11]. Many studies have established that the development of the retina follows a defined temporal and spatial order, and many extrinsic and intrinsic factors have been identified to affect the differentiation of retinal stem/progenitor cells and cell survival at different stages [9,11-14].

Reports on applications of RNA-seq technology in retinal studies started to appear since last year. So far, only 5 publications were identified from the literature (using PubMed search). The first report [15] was a bioinformatic study focusing on the development of an algorithm to detect novel transcriptome features, e.g., novel exons and alternative splicing variants, in RNA-seq data from mouse retina. In the second report [16], mouse retinal transcriptome profiling by RNA-seq analysis was compared to microarray and quantitative reverse transcription polymerase chain reaction (qRT-PCR) methods to evaluate the optimal high-throughput data analysis. Results from this study demonstrated that RNA-seq analysis offers a more comprehensive and accurate quantitative and qualitative evaluation of the transcriptome within a cell or tissue; it accelerates genetic network analysis and allows the exploration of complex biologic functions. In the third report [17], developmental study of the adult mouse (postnatal day 21) retinal transcriptome analysis by RNA-seq revealed that retinal disease genes were among the most highly abundant. The data provides a resource for the research community. In the fourth report [18], RNA-seq analysis revealed transcriptome changes associated with diabetic retinopathy in a mouse model, and further molecular pathways by which pharmacological agents inhibit diabetic retinopathy. This study demonstrated that RNA-seq analysis is a powerful way for identifying disease-related genes, and for determining the efficacy of drug treatments. In the last and most recent report [19], RNA-seq analysis was applied to the study of age-related retinal degeneration. Changes in transcriptome signatures provided further understanding of the susceptible genetic loci that underlie pathogenic mechanisms of age-associated disorders, including human diseases that contribute to blindness. Together, these RNA-seq analyses have provided highly informative data that allowed a deeper understanding of the genetic regulation of retinal development and mechanisms underlying disease-related gene functions.

In conclusion, RNA-seq proves to be a powerful method for the studies of retinal development and diseases, which provides more precise evaluation of transcriptome than other methods. Despite many challenges associated with its applications, the recent advancement in RNA-seq technology makes it becoming a popular analysis tool in biomedical research.

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