RNA-Seq Analysis of the Parietal Cortex in Alzheimer's Disease Reveals Alternatively Spliced Isoforms Related to Lipid Metabolism, J. D. Mills, et. al.

Paper Report II
BMES 543: Quantitative Systems Biology Tony Kabilan Okeke

Summary

The paper discusses the results of an investigation into gene expression patterns in the parietal lobes of Alzheimer's patients. The expression patterns in the parietal lobe have thus far only been measured using microarrays which did not produce biologically significant findings; the goal of the study was to use RNA-Seq data to identify differentially expressed genes and isoforms of genes in Alzheimer's samples (compared to normal samples). The researchers were particularly interested in the differences in expression profiles of alternatively spliced isoforms of certain genes with respect to lipid metabolism. The researchers found that several genes associated with lipid metabolism were upregulated in the Alzheimer's samples. The researchers also found differences in the expression of different isoforms of the DBI gene which could potentially be responsible for changes in fatty acid metabolism and steroidogenesis in the Alzheimer's samples.

Strengths

- The use of quantitative real-time PCR of similar samples, as well as transcriptome sequencing studies of mouse somatosensory cortices to confirm their results increases confidence in the validity of their findings.
- Their discussion of the different enrichment maps for up and down regulated genes was useful in developing a clear understanding the biological significance of the results.

Limitations

- The distinction between genes and gene isoforms in the paper is not very clear which makes it difficult to follow along with their results.
- The small sample size used in the study (only 10 samples for RNA-Seq), as well as the inclusion of samples from only males could introduce bias in their findings.

Potential Improvements

- More samples should have been included in their analysis, including samples from female patients.
- The authors should have included further discussion on whether there were any noteworthy discrepancies between the RNA-Seq results and the qRT-PCR results.

What have Authors Done to Extend the Study

- The author (James D. Mills) has conducted subsequent studies involving transcriptomic and proteomic analyses of different parts of the brain.

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Multiple Choice Questions

Question: How were RNA-Seq differential expression patterns confirmed in the study?

a. qRT-PCR [Correct]
b. RNA-Seq
c. Next Generation Sequencing
d. Gene Set Enrichment Analysis

Question: Why was transcriptional activity higher in the AD sample?

a. Proteins hydrolyzing acyl-CoAs to free fatty acids
b. Simulation by beta-amyloid in astrocytes
c. Inflammatory processes in the parietal lobe [Correct]
d. Upregulation of DBI isoforms

Question: What was the maximum upregulated fold-change between the AD and normal samples?

a. 97.4
b. 89.4
c. 100.9
d. 90.4 [Correct]