Metabolic Gene Expression Changes in Neural Organoids During Key Timepoints in Development

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Introduction
Metabolism plays a crucial role in human development, especially in neural development, although the mechanisms regulating neurodevelopmental programs remain poorly understood. Existing research demonstrates that impaired glucose metabolism is associated with various neurodevelopmental diseases, such as ADHD and autism [1]. Highlighting its importance in early neurogenesis. Limited access to relevant biological information in human in vivo development contributes to this knowledge gap. Glucose metabolism is essential for the production of ATP, which is necessary for cells to perform their functions and energy production method can be utilized under either aerobic and anaerobic conditions. Studying the molecular mechanisms underlying brain development and the potential impact of altered glucose metabolism has the potential to enhance our understanding of the pathogenesis of neurodevelopmental disorders and identify new targets for therapeutic interventions. Neural organoids, which are cell culture models, derived from human induced pluripotent stem cells (iPSCs), serve as useful models for studying brain development. [2] They can be used to investigate the critical role glycolysis plays in development and to understand the metabolic programs employed by different neural cell types across neurogenesis.

Objectives
• Harvest the neural organoids at each developmental timepoint and extract total RNA using appropriate kits and protocols.
• Synthesize cDNA from the extracted RNA using reverse transcription.
• Perform qPCR analysis on the synthesized cDNA to quantify the expression levels of the glycolysis genes of interest (HK1, PKG1, ENO1, LDHA) using appropriate qPCR reagents, primers, and equipment.
• Analyze the qPCR data to determine the relative expression levels of the glycolysis genes of interest at each developmental timepoint.
• Interpret the results and draw conclusions about the changes in gene expression.

Experimental Methods

Results

Discussion
In our analysis of gene expression data, organoids derived from the three different cell lines (13234, H1, H28126) between week 8 and week 12 had notable trends across differentiation. For the glycolysis genes ENO1, LDHA, and PKG1, our findings revealed no significant differences in expression levels across time points in all cell lines. This consistency suggests a uniform regulation of these genes during neural organoid differentiation. However, a distinctive variation is evident in the case of HK1 expression. We observed a significant difference in HK1 expression between weeks 8 and 12 in the 13234 and H1 cell lines, as determined by a t-test analysis. This divergence in HK1 expression highlights the potential influence of early stages of glycolysis in neural differentiation. Additionally, the lack of change in LDHA, indicative of anaerobic glycolysis, suggests that cells are not transitioning between anaerobic vs aerobic respiration at this time. Further exploration of the underlying mechanisms governing HK1 differential regulation and its functional implications will be crucial for a comprehensive understanding of neural development.

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References