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Differential Gene Expression of Neuroblastoma Cell Differentiation

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Differential Gene Expression of Neuroblastoma Cell Differentiation

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Abstract: The human body is composed of nearly 400 distinct cell types. This great cellular diversity allows us to perform a number of physiological functions, yet all of this is encoded in the same single genome. The difference between all these specialized cells is what parts of the genome they use and how they use the genome to drive cellular differentiation and development. The molecular changes that accompany differentiation are poorly understood. We seek to characterize the functional and molecular alterations that accompany a distinct cellular change. As a model, we use human neuroblastoma cells grown in culture. We show that neuroblastoma cells differentiate into neuronal-like cells upon retinoic acid treatment and characterize the morphological changes using confocal microscopy. To assess the neuronal state of differentiated cells, we performed electrophysiological measurements and show that retinoic acid treatment results in an increased action potential representative of a neuronal phenotype. Together, these results demonstrate that retinoic acid drives cellular differentiation of neuroblastoma cells into a functionally distinct neuronal-like cell. To understand the changes in gene expression that accompany this cellular differentiation, we performed differential gene expression analysis using transcriptomic data from untreated and retinoic acid-treated neuroblastoma cells. We hypothesize that specific groups of genes containing neuronal classifications are upregulated in retinoic acid treated cells compared to the control treatments. To understand the regulatory mechanisms controlling transcriptional silencing of retinoic acid repressed genes, we analyzed whole genome epigenetic datasets and correlate the association with repressive chromatin marks around silenced genes to help define a genetic signature of neuronal differentiation. Overall, this work provides a model for cellular differentiation and will offer mechanistic detail towards the understanding of the molecular events that drive cell fate decisions.