Survival Analysis of Pediatric Neuroblastoma Patients Using Gene Expression Data: Identification of Novel Neural Differentiation Related Biomarkers

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Of the over 100 types of cancers that together claim 2,000 lives in the United States daily, neuroblastoma is the most common in children under the age of two. This project seeks to identify novel prognostic biomarkers for neuroblastoma that can be used to develop faster/more efficient therapies and detection models, with a focus on the NEK2 gene and genes involved in neural differentiation (especially the Wnt and Notch signaling pathways). The gene expression and clinical data of 249 pediatric neuroblastoma patients was obtained from the TARGET database, and univariate Cox hazard regressions (a statistical survival analysis) were applied to each of the 23,000 genes to determine whether higher gene expression correlates with lower event-free survival time (prognosis). After applying univariate regression models, genes with a hazard ratio (comparison between probability of an event occurring based on a set variable such as gene expression) above 1.0 and p-value below 0.05 were researched for relevancy to the project purpose and novelty to neuroblastoma, and then individually put into multivariate Cox regression models (Cox regression factoring covariates such as age and gender) to determine whether the genes would still be significant prognostic markers. The hypothesis that NEK2 would be a prognostic biomarker was supported (with a multivariate hazard ratio of 1.368 and p-value of 0.0353), and additionally 16 other novel neural-differentiation related biomarkers were identified, which not only gives new insight into the pathways that neuroblastoma arises from, but also paves the way for novel, noninvasive gene therapies that minimize the chance of recurrence and rapid, preemptive cancer detection models to detect the cancer before metastasis.

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