Evaluation of Patient-Derived Xenograft Model Accuracy Using Differential Gene Expression Analysis for Cancer Modeling Optimization

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Patient-Derived Xenografts (PDX), a novel in vivo cancer modeling technique used in personalized medicine, has been shown to bypass typical constraints of in vitro tumor cell culture models. Through transfer of patient tumor tissue to immunocompromised mice, tumor development and effect on overall organismal function can be observed. However, PDX models, specifically colorectal cancer (CRC) models, currently exhibit faults, most notably model function inconsistencies caused by difference in consensus molecular subtype (CMS). By using open-source CRC patient gene count data from high-throughput RNA sequencing, differential gene analysis procedures based on the negative binomial distribution can be performed in order to highlight gene discrepancies between each of the four CMS. Then, a Gene Set Enrichment Analysis (GSEA) is used to categorize individual genes into Hallmark gene sets, which are each shown at various levels of up- or downregulation per CRC subtype. Further usage of Principal Component Analysis and Volcano plots reveal variance and magnitude of the differential expression, respectively, corroborating overall themes presented by the initial GSEA plot. These results illuminate specific cellular functions altered as a result of tumor cultivation in the PDX model, leading to a flawed representation of cancer behavior. This method enables further analysis of individual genes in crucial gene sets such as Epithelial Mesenchymal Transition, which will augment both cancer intensity and survival in a more precise future model. The specific genomic differences pinpointed by these methods are essential to the growing success of the PDX model and to cancer modeling as a whole.

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