Using an integrated gene network technique to depict the genetic architecture of pediatric malignancies

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Abstract

Childhood malignancies have a mostly unknown genetic origin. It is critical, therefore, to develop fresh ways for deciphering the range of pediatric cancer genes. Statistical network modeling approaches have emerged as effective methods for inferring gene-disease associations and have been used to adult malignancies but not to pediatric malignancies. We used co-expression network analysis to get a multi-layer knowledge of pan-cancer transcriptome data from the Treehouse Childhood Cancer Initiative. Six modules were shown to be significantly correlated with pediatric tumor histotypes and to be functionally connected to developmental processes. Topological studies revealed that genes associated with childhood cancer propensity and prospective treatment targets were critical regulators of cancer-histotype-specific modules. A module with activities involved in DNA repair and cell cycle control was associated with several pediatric cancers. This canonical oncogenic module encapsulated the majority of the genes associated with pediatric cancer propensity and therapeutically actionable genes. The driver genes were co-expressed in a module associated with epigenetic and post-transcriptional processes in juvenile acute leukemias, indicating a key role for these pathways in the evolution of hematologic malignancies. This integrated pan-cancer analysis characterizes pediatric tumor-associated modules in detail and lays the groundwork for the investigation of new candidate genes implicated in juvenile carcinogenesis.

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