

The provided text discusses the challenges and limited treatment options for Hepatoblastoma (HB), the main pediatric liver cancer. Despite improvements in treatment, survivors often face long-term adverse effects. The text emphasizes the need for new therapeutic strategies, particularly for patients with advanced tumors. It introduces computational methods to predict drug sensitivity from a tumor's transcriptome, highlighting the success of these methods in common adult malignancies but noting the lack of specific efforts in pediatric cancers due to data scarcity. In this study, the researchers computationally screened the efficacy of drugs for HB patients with the aggressive C2 subtype and poor clinical outcomes based on their transcriptome. They utilized publicly available collections of pan-cancer transcriptional profiles and drug responses across various tumor types and compounds. The most effective drugs predicted by the computational screening were experimentally validated using patient-derived xenograft (PDX) models of HB, both in vitro and in vivo. Two CDK9 inhibitors, alvocidib and dinaciclib, were identified as potent inhibitors for the high-risk C2 molecular subtype. Additionally, the study found that high CDK9 tumor expression in a cohort of 46 HB patients was significantly associated with poor prognosis. The research demonstrates the utility of computational methods trained on pan-cancer datasets to reposition drugs in rare pediatric cancers like HB. The goal is to assist clinicians in choosing optimal treatment options for their patients.