Precision medicine for pediatric cancer—considering the implications for diagnosis and treatment

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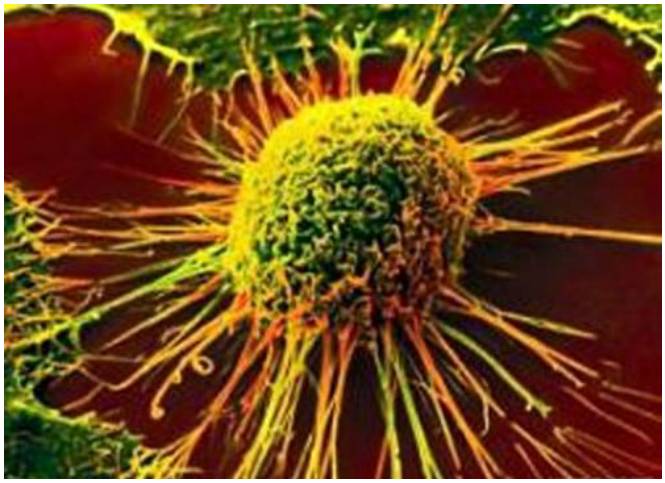

Research performed over the last several decades has led to an increased understanding of the genetics of cancer. The clinical application of this knowledge for pediatric cancer has lagged behind studies performed for adults. In a perspectives article published in the prestigious journal *Science*, Dr. Jaclyn Biegel, from Children's Hospital Los Angeles, and Dr. Alejandro Sweet-Cordero, of the University of California, San Francisco, survey the landscape of this young field and present opportunities for using genomic information to advance a new era of care for children with cancer.

Cancer arises from genetic changes, including DNA mutations, that are either present at birth, or are acquired over time. Many adult cancers are initiated by mutations acquired through exposure to substances like smoking and radiation or simply from aging. The tumors may contain hundreds of sequence alterations, and identifying which changes drive the growth of the tumors, and impact treatment response can be challenging. In contrast, pediatric malignancies often develop from a very small number of mutations, only some of which overlap with the types of mutations seen in adult cancers. Furthermore, an estimated 20% of pediatric cancers arise in children who have a genetic predisposition to malignancy. For this reason, the clinical genetic assays developed to inform prognosis and treatment decisions for adult cancers have not been as useful in pediatrics.

OncoKids was one of the first next-generation sequencing panels to detect DNA and RNA changes that characterize pediatric cancers. The panel was developed at Children's Hospital Los Angeles under the guidance of author Jaclyn Biegel, Ph.D., FACMG, Director of CHLA's Center for Personalized Medicine. The OncoKids panel provides a molecular diagnosis, informs prognosis, and highlights novel therapeutic targets across the broad spectrum of cancers in children, including leukemias, brain tumors and other solid tumors.

"To truly achieve personalized medicine in pediatric oncology, we need to be able to determine if a child is genetically predisposed to develop cancer," said Dr. Biegel. In addition to tumor testing, germline testing that uses a sample of a patient's blood, is critical for identifying those children who have a genetic risk for developing cancer in the future. Besides benefiting the patient, this information has implications for the entire family, since an abnormality that is passed down from parent to child can also raise the risk of developing cancer in siblings.

Although tremendous progress has been made in pediatric cancer care, treatment resistant disease and relapse continue to negatively impact patient outcomes. Genetic profiling of pediatric cancers is

typically done at the time of diagnosis or at the time of relapse to help determine treatment planning. According to Dr. Biegel, future studies that may be performed over the course of treatment and at remission have the potential to provide critical information about the mechanisms of tumor progression, treatment resistance and metastasis.

Tremendous opportunity exists for changing outcomes in children with cancer by using an integrated approach to evaluating children and their families that includes genomic medicine as a central component in their care.

More information: E. Alejandro Sweet-Cordero et al, The genomic landscape of pediatric cancers: Implications for diagnosis and treatment, *Science* (2019). DOI: 10.1126/science.aaw3535

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