Precision Medicine for Pediatric Cancer

In likely the first study of its kind in children, researchers used genomic sequencing data from patients’ advanced and rare cancers to suggest effective treatment options. The findings demonstrate the feasibility of incorporating genomic information into the clinical management of pediatric patients.

In the single-site, observational study, 91 children and young adults with relapsed, refractory, or rare cancers underwent whole-exome and transcriptome sequencing. The data were then interpreted and analyzed by a tumor board made up of oncologists, geneticists, and other experts. Actionable findings were reported for 42 of the patients—including 15 of 28 patients with hematologic malignancies and 27 of 63 with solid tumors. Based on the data, physicians changed the treatment for 14 patients, nine of whom went into partial or complete remission (JAMA 2015;314:913–25).

“this is one of the first comprehensive DNA/RNA sequencing platforms implemented in pediatric patients with advanced cancer,” says the study’s senior author, Arul Chinnaiyan, MD, PhD, director of the Michigan Center for Translational Pathology at the University of Michigan in Ann Arbor.

“We showed that it is possible to carry this out in a regimented fashion and to impact the individual management of patients in terms of the potential clinical use of targeted therapeutic agents.”

Investigators defined actionable findings as somatic mutations targetable with an alternative therapy; molecular aberrations leading to changes in a patient’s diagnosis; or cancer-related germline mutations that could inform genetic counseling.

However, many patients with actionable findings experienced tumor progression before the results could be acted upon, partly due to the time it took to convene the tumor board and interpret the findings. The median time from biopsy to sequencing analysis and treatment recommendations was more than 6 weeks.

Access to targeted therapies was another limiting factor, says Chinnaiyan.

In some cases, patients with potentially actionable mutations could not access treatment due to exclusion criteria for a clinical trial or lack of pediatric dosing information for a drug approved for adults.

“The pediatric oncology community will need to completely rethink models of drug development in the genomic era as rare diseases become even more rare based on genetically defined subsets,” notes an accompanying editorial (JAMA 2015;314:881–3). “Academic, federal, and industry leaders must overcome the current risk-aversion mentality that interferes with translational innovation and develop new mechanisms to more adeptly develop and deliver drugs to children with cancer.”

The study has several limitations, the authors acknowledged, including lack of a control group to distinguish whether treatment changes based on the study actually improved outcomes compared with standard of care. In addition, because some tumors were sequenced from archival material, any new mutations that emerged during treatment would have been missed.

Although this study focused on patients with advanced cancer, the goal is to incorporate clinical sequencing earlier in the disease process, says Chinnaiyan.

“It’s exceedingly difficult to treat patients who have gone through many different therapeutic regimens because the tumor has developed so many resistance mechanisms,” he says. “Clinical sequencing efforts have the potential to improve clinical management if we can bring them in earlier in the course of cancer development.”

Researchers Win Coveted Lasker Awards

Three renowned scientists who made discoveries that advanced understanding of genetics and biology—and that led to the development of new cancer therapies—have been honored for their work with prestigious prizes from the Albert and Mary Lasker Foundation. Among the most coveted honors in medicine, the awards each carry an honorarium of $250,000.

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