Gene Profiling Identifies Drugs For Childhood Cancers But Access A Problem

20 Sep 2019 | **NEWS**

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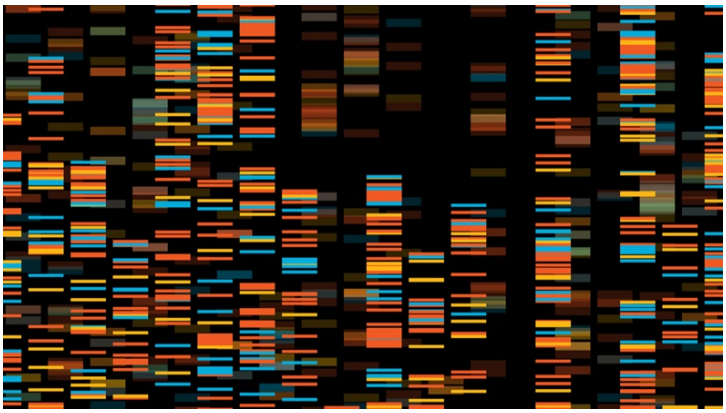
Executive Summary

Lack of infrastructure for identifying mutations and access routes is holding back use of targeted medicines in children with cancer



NEXT GENERATION SEQUENCING IDENTIFIES TARGETABLE MUTATIONS *Source: Shutterstock*

A new study has shown that genetic testing can help match children with cancer to targeted drug treatments, opening up hope of improved outcomes for young patients with hard-to-treat conditions.

The test developed by The Institute of Cancer Research (ICR) in London is a first for pediatric cancer treatment and could prove to be a foundation stone in making precision medicine a reality in the UK.

But in highlighting the potential of genetic testing, the study also made clear how England's National Health Service (NHS) currently lacks an infrastructure for identifying these mutations and ensuring these patients have the chance to access targeted medicines.

Led by ICR and The Royal Marsden NHS Foundation Trust, researchers used a gene panel test to read the DNA sequence of 91 genes that drive cancer's growth and spread from 223 children's tumor biopsies, looking for mutations treatable with targeted drug therapy.

At least one genetic mutation was detected in 70% of samples processed by the next generation sequencing (NGS) panel, and overall 51% were clinically actionable. However the study found only 7% of those with targetable mutations were able to access the appropriate drug licensed for use in adults.

Researchers found a number of reasons for this, including a lack of available clinical trials, difficulties accessing novel drugs on a compassionate-use basis and/or clinical deterioration of the patient.

The children involved in the study had a range of solid tumors, including neuroblastoma, rhabdomysarcoma, glioma and other non-CNS solid tumors.

Although many patients had relapsed/refractory disease, many were still on either first-line therapy or proven standard relapse therapies at the time of sequencing. A number of patients were also enrolled in available Phase I/II trials that did not require biomarker screening.

The most common potentially treatable mutations were in the genes ATRX, CDKN2A and CTNNB1, each found in 12 children's tumors. MYCN mutations were found in 11 tumors and PI3K3CA mutations in 10 tumors.

Three children had BRAF gene mutations, common in melanoma skin cancers and treated using Novartis AG's targeted combination therapy of Tafinlar (dabrafenib) and Mekinist (trametinib). (Also see "Novartis' Growth Driver Tafinlar/Mekinist Picks Up New Melanoma, Thyroid Indications" - Scrip, 7 May, 2018.)

Using this combination, one of the children had their brain tumor held in check for 13 months before developing resistance. Another was on the drug for nine months with no progression of disease. The third child could not tolerate the combination but had a response to dabrafenib for 15 months.

This illustrates the potential benefit to a wider population of children with cancer and study author Sally George, a consultant pediatric oncologist at The Royal Marsden, said, "Children deserve the very best cancer treatments, so they can live as long as possible and as well as possible. We desperately need better, more intelligently designed treatments which can give children longer with their families with fewer side effects.

"By testing tumors for specific gene mutations, we have shown it's possible to identify new smarter, kinder treatment options for children, which may potentially give these patients much longer with their families after conventional therapies have failed.

"But our study also exposes the desperately frustrating barriers that children still face in receiving new treatments - barriers which lie in the regulations controlling how drugs for children are developed and approved."

Plans to address the need for routine genetic testing and access to targeted medicines is addressed in the NHS Long Term Plan, which was published in January 2019.

It includes a pledge to make the NHS the first health service in the world to offer whole genome sequencing for children with cancer and young people who have a rare genetic disorder, in addition to adults suffering from certain rare conditions or specific cancers.