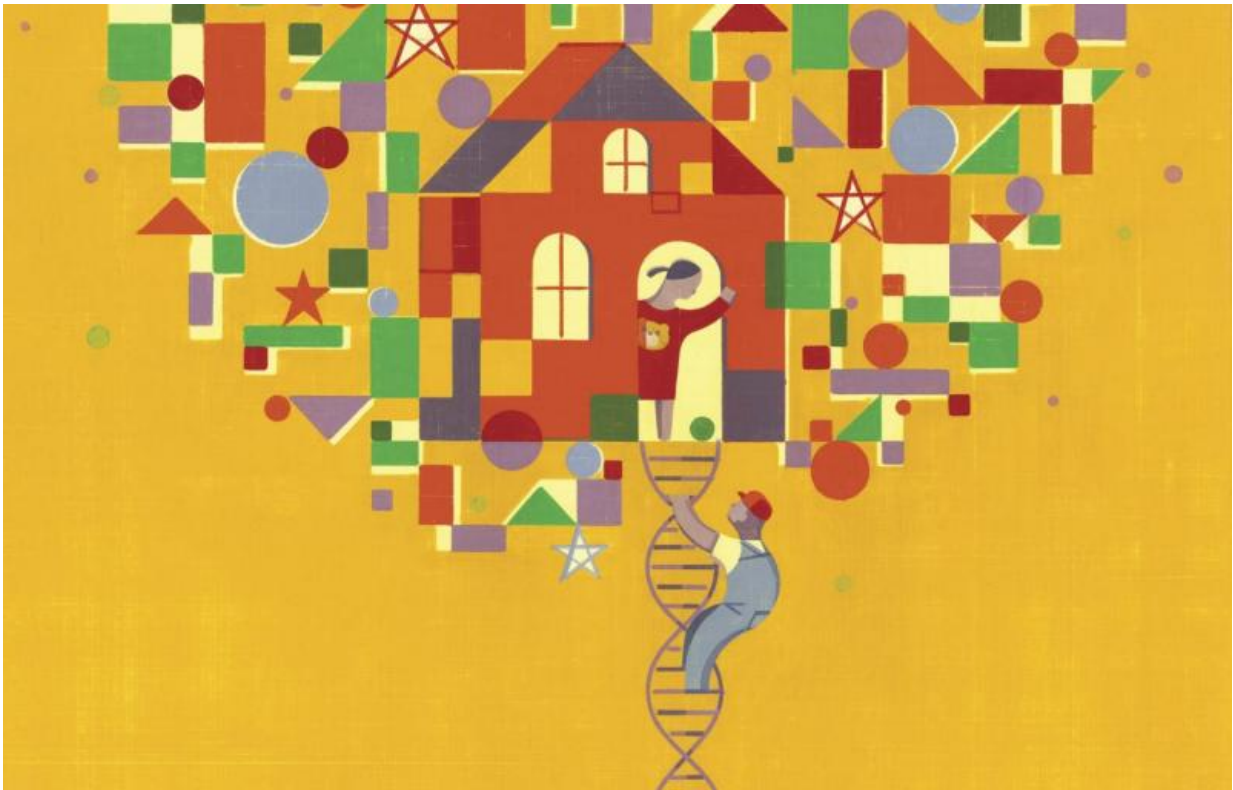


Researchers opening a new front in the battle against childhood cancer

April 1 2016, by Dan White



There can be no more heartbreaking diagnosis for a child than that of cancer. It doesn't seem possible—or fair—that someone so young can be afflicted with a disease we often associate with aging.

And yet, cancer kills more children in the United States than any other disease.

A cancer diagnosis used to be a death sentence for young children. Doctors could offer very little to their youthful patients, aside from words of comfort.

But a team of researchers from the UC Santa Cruz Genomics Institute is using a unique combination of high-tech networking and data sharing to open up a new front in the battle against pediatric cancer, while looking into effective, targeted alternatives to the harsh treatments of the past.

"Using genomics to help guide therapy in a patient is not new," said Olena Morozova, a postdoctoral scholar at UC Santa Cruz's Center for Biomolecular Science and Engineering, and a lead researcher for California Kids Cancer Comparison, a project that aims to fight pediatric cancer by comparing cancer data from young patients across the globe. "What is new is our vision to share and consolidate all the cancer genomic data so that we can use the knowledge and the world's data for the benefit of each new patient. We are literally learning and improving our approach with every patient."



This cancer comparison project is a clinical pilot for the UC Santa Cruz Genomic Institute's ongoing Treehouse Childhood Cancer Project, which supplies oncologists with genomic data that will help them choose targeted treatment options for cancer patients.

The "Treehouse" name comes from Lu Haussler, wife of UC Santa Cruz Distinguished Professor of Biomolecular Engineering David Haussler. She chose it as a visual metaphor for a branching project that is also a house, or destination, for gathering and sharing all pediatric cancer genomes.

"The long-term dream for the oncology field is to eventually replace all the aggressive, brute-force therapies like chemo and radiation with therapies tailored to the cells inside a patient's cancer," Morozova said.

Seeking a cure for 'incurable' cancer

Morozova did not expect the research-based cancer project to apply to a clinical setting anytime in the near future. But last year, when Morozova and her teammates began to study the genes of a rare sarcoma growing inside the lungs of an 8-year-old boy whose family had exhausted all the standard treatments, the project expanded its scope. Suddenly, the Treehouse was in a position to save a life—not at some distant point in the future, but right away.

The boy's doctors had given him the usual battery of "standard aggressive therapy" including chemotherapy, radiation, and a bone-marrow transplant, but it was not enough to stop the tumor from returning two years later. "The patient was out of treatment options and pretty much going on hospice," Morozova said.

That spring, a new clinical trial at the British Columbia Children's Hospital in Vancouver gave the boy and his family a reason for cautious optimism. The trial explores the use of genomic analysis as a pathway to treatments that doctors had not yet considered. The boy's doctor asked the Treehouse team to scan through the genetic material extracted from cancer patients all over the world and do a "cancer comparison approach."

Ph.D. candidate Yulia Newton, a key researcher on the Treehouse team, said that when researchers look at a tumor in relation to "a larger cohort" of tumors, it is possible to pinpoint certain signatures in the cancer, with high-tech assistance from a tumor map program that is quite similar to the look and feel of Google Maps. Instead of exploring streetscapes, it peers into the cartography of diseases.

The researchers examined the genetic material in the tumor, with the key computational analysis provided by Newton, who works in Professor

Josh Stuart's bioinformatics lab. Stuart said the detailed maps of tumors can sometimes yield valuable "signposts" that clinicians can use for clues to suggest treatments.

After this process, researchers can then build detailed tumor maps that suggest relationships between tumors. This information can help clinicians identify the best treatment for a particular patient's tumor.

That is what happened after the Treehouse researchers ran data from the Vancouver patient. In the process, they discovered that his tumor was similar to another kind of pediatric tumor. Because there are common properties or pathways affected in cancers, the same treatments can work in multiple patients, even if their diagnoses, and the organs where the cancers occurred, are different.

"Since all of us are different genetically, the cancers we get, even if it is the same exact diagnosis, are different, too," Morozova said. "No two cancer patients are exactly identical, and we really need to read the genetic code of a patient's tumor to fully understand the disease in each patient."

Armed with this new information, the oncologist in Vancouver decided to hit the child's sarcoma with two FDA-approved drugs that had been used in adult lung cancer and blood cancer patients but are not typically considered for a pediatric sarcoma patient, Morozova said.

The Treehouse project has heard that the boy, as of late summer, was doing well. "The clinical trials and the boy have already affected the direction and the scope of the Treehouse project dramatically," Morozova said.

Looking toward the future

In their comparative cancer project, UC Santa Cruz researchers have a valuable tool at their disposal: MedBook, a high-tech "workbench" for cancer data analysis.

Informally known as "the Facebook of Cancer," the application brings together the findings from patient tumor samples and connects scientists to help them work collaboratively while matching patients with targeted treatments.

"Using big data along with big (computing), our group can decode the molecular nature of cancer," said alumnus Ted Goldstein (Stevenson and Oakes '83, computer and information sciences; Ph.D. '13 bioinformatics/biomolecular engineering), who is also a UC Santa Cruz Foundation trustee. Goldstein is assisting the Treehouse project.

MedBook was inspired by modern web metaphors of social networking and content sharing pioneered by Facebook, enabling clinicians and researchers to rapidly analyze and treat an individual patient's cancer.

Meanwhile, the genomic databases and intellectual firepower at the UC Santa Cruz Genomics Institute is also serving as a foundation for Treehouse's work. Major technological breakthroughs in DNA sequencing—including the historic full mapping of a human genome at UC Santa Cruz in 2000—allow researchers to "read" DNA like never before and share their information with oncologists.

A resourceful enemy

The Treehouse pilot project is part of a wider effort to use genomic analysis against tumors that are now thought to be incurable. Treehouse will build on pediatric clinical trials, similar to the one in Vancouver, popping up across the nation.

Such projects are one reason why childhood cancer in the 21st century is not quite as devastating as it would have been in the 1950s.

Cancer is a genetic-based disease that arises from defects in human DNA. This damage to the DNA can happen over a lifetime of exposure to toxins or result from other causes, such as inherited mutations and environmental factors that result in an error in normal development.

About one in 300 children in the U.S. will get cancer by the time they are 20 years old, Morozova said. Childhood cancer consists of at least 12 unique diseases including brain tumors, sarcomas, neuroblastomas, and various kinds of leukemias and lymphomas.

About 50 years ago, only one out of every 10 children diagnosed with cancer could expect to survive longer than a couple of months. Today, doctors expect 80 percent of children to survive at least five years past diagnosis.

But there is much work to be done.

"When people hear the 80 percent survival statistic they immediately think that the [pediatric cancer](#) problem is solved, which is absolutely not the case," Morozova said.

She points out that doctors ramped up the survival percentage by using heavy-duty treatments that can have "devastating long-term consequences," including, in some cases, fatal secondary cancers caused by the treatments.

Even now, some cancers remain unbeatable. A type of brain cancer called diffuse intrinsic pontine glioma (DIPG) is uniformly lethal. DIPG—which killed astronaut Neil Armstrong's daughter—is as deadly now as it was a half-century ago.

Oncologists also face another daunting challenge: If children undergo an aggressive therapy regimen such as radiation but the cancer reappears anyhow, that resurgent disease is usually fatal. Such hard-to-treat patients are now the primary focus of the California Kids Cancer Comparison initiative.

The team's goal is to bring genome-based medicine to every child with "difficult-to-treat" or terminal cancer.

These children are "completely out of treatment options today," said Morozova.

"Eventually we would like to bring genomics to every child with [cancer](#) at diagnosis, but the more immediate goal is difficult-to-treat patients," Morozova said. "We would like to start with them."

Provided by University of California - Santa Cruz

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