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Teen Helped Research Her Own Disease

Rare Cancer May Be Linked to Gene Mutation

By **Ron Winslow**
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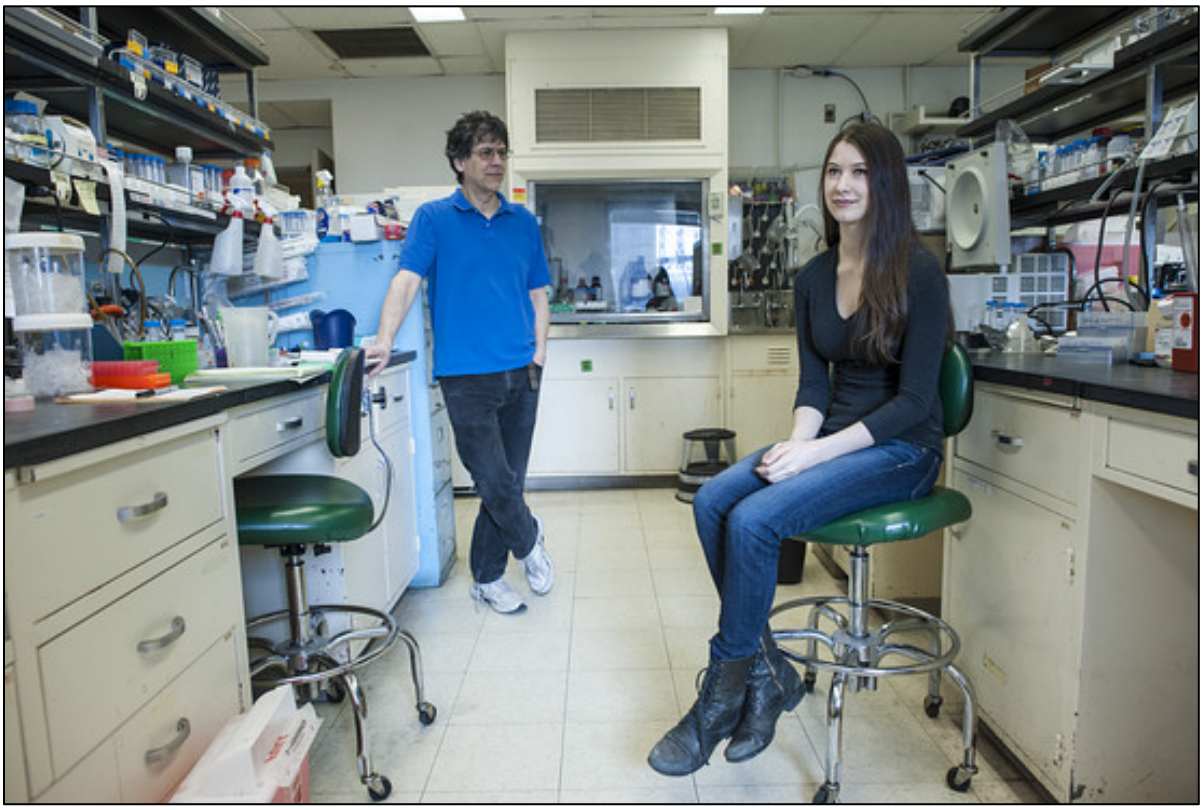

Elana Simon, a dancer and acrobat, helped researchers find a possible genetic basis for her disease.

When Elana Simon was 12 years old, she was diagnosed with a rare form of cancer that required an operation to remove much of her liver.

Now 18, Ms. Simon, a high school senior, dancer and aerial acrobat, is deemed cancer-free. She also is a key member of a research team that has identified a genetic abnormality that may be a cause of the mysterious cancer, which afflicts about 200 adolescents and young adults a year world-wide.

Ms. Simon initiated the study and worked closely with scientists at Rockefeller University, where her father runs a laboratory, as well as at Memorial Sloan-Kettering Cancer Center and New York Genome Center, all in New York, to conduct genetic sequencing and other analyses. The findings were published Thursday in the journal Science.

The disease, called fibrolamellar hepatocellular carcinoma, has no effective drug treatments, and without surgery, prognosis for patients is poor.

The genetic anomaly Ms. Simon and her colleagues found is a fusion of parts of two different genes. It turned up in tumor tissue taken from all 15 patients they studied, while it wasn't present in any normal liver tissue removed from the same patients—a strong signal that the mutant gene could be a culprit, researchers said.

"This is the milestone on research in that cancer type," said Bert Vogelstein, head of the Ludwig Center for Cancer Genetics & Therapeutics at Johns Hopkins University School of Medicine in Baltimore, who wasn't involved in the study. "It's the mountain everybody wants to find when they do these cancer genome sequencing studies."

Finding such a mutation doesn't mean it definitely causes the cancer and more research needs to be done to establish its role, said Michael La Quaglia, chief of pediatric surgery at Memorial Sloan-Kettering and a co-author of the study.

But assuming a clear link is determined, the findings could lead to a diagnostic test and perhaps a treatment.

Beyond showcasing the ingenuity and determination of a teenager eager to learn about her own disease, the research underscores the growing impact genome sequencing and other technologies are having on rare diseases and cancer.

These analytical tools are part of a "perfect storm" that make science more accessible, even to young people like Ms. Simon, said her father, Sanford Simon, who heads a biophysics laboratory at Rockefeller where much of the work on the new study was done.

Ms. Simon, who had suffered stomach cramps as a child, was diagnosed with lactose intolerance, stress, appendicitis and a possible bacterial infection before doctors determined the source of her symptoms was liver cancer. Ms. Simon went to the Internet to learn what she could about this disease.

"The more I found the less encouraging things became," she said. "People didn't know that much about it and people didn't seem to be doing much about it."

When she turned 16, she landed an internship at a lab at Mount Sinai School of Medicine in New York through a science program at the Dalton School, a private school in Manhattan where she is a student. "I wanted to go off and be my own scientist," she said of the idea, which she pursued without consulting her father.

Her project: to compare genetic data sequenced from tissue from eight pancreatic cancer patients to hunt for mutations that might separate cancerous samples from normal ones. But the tissue was from older patients who through normal aging had accumulated thousands of harmless mutations that made spotting one or two potentially meaningful ones difficult.

For Ms. Simon, a light went on. Younger people have far fewer potentially confounding mutations. Maybe performing a similar study on tissue from young fibrolamellar patients would yield the genetic secrets of the disease.

She proposed the idea Dr. La Quaglia, who was also her surgeon. He led the effort to collect tumor samples from fibrolamellar patients he operated on and assigned research fellows from his lab at Sloan-Kettering to work with Ms. Simon and Dr. Simon and other researchers at Rockefeller.

The effort was supported by a grant from the Fibrolamellar Cancer Foundation of Greenwich, Conn., established by the parents of Tucker Lowe Davis, who died of the disease in 2010.

What began to emerge from the sequencing data was what researchers call a deletion, a spot where a significant segment was missing on the strand of DNA. The strand was joined by the fusion of two different genes.

When it became clear that the fusion was showing up in all of the tumor samples, other scientists in Dr. Simon's lab pitched in to help confirm the function of the aberrant genes. Joshua Honeyman, a fellow from Dr. La Quaglia's lab, was co-first author with Ms. Simon on the study.

Ms. Simon is currently at work on a second paper about the research. She plans to attend Harvard University in the fall, with a major in computer science.

"Initially I didn't think we'd find anything that could actually help people," she said. "It's awesome that things are coming together and the research is doing well."