Open-source science helps father's genetic quest

October 26 2012, by Lisa M. Krieger, San Jose Mercury News

One tiny flaw in one gene in one little girl. That explains why Beatrice Rienhoff, 8, is so lean and leggy.

But it took the communal contributions of many researchers - in an open-ended, open-source scientific search, led by her father - to solve Bea's singular mystery.

Most medical research is secret and proprietary. At Saturday's Open Science Summit in Mountain View, Calif., however, Bea's father, Hugh, described a needle-in-a-haystack quest made possible by the pitchforks of so many.

"We used materials that are public, freely available," said Rienhoff, a physician and scientist, as Beatrice frolicked nearby. "And everything we've learned we've put back out there, in the public domain. It's for the patient's good, and the public good."

Born with small, weak muscles, long feet and curled fingers, Beatrice confounded all the experts.

No one else in her family had such a syndrome. In fact, apparently no one else in the world did either.

Rienhoff - a biotech consultant trained in math, medicine and genetics at Harvard, Johns Hopkins and the Fred Hutchinson Cancer Research Center in Seattle - launched a search.

He combed the publicly available medical literature, researching diseases, while jotting down each new clue or theory. Because her ailment is so rare, he knew no big labs or advocacy groups would be interested.

He did some of his own lab work in his San Carlos, Calif., home, borrowing tools or buying them used online. A few commercial labs, like the San Diego-based biotech Illumina, offered him help for free. And a wide array of pediatricians, geneticists and neurologists volunteered their opinions.

Over time, he zeroed in on a stretch of genes that control a growth hormone responsible for muscle cell size and number. And he knew he could further target his search - saving time and money by not sequencing Bea's entire genome, but only the exomes, which are the genes that code for proteins.

Eventually, he needed to interpret all that genetic data. For that, he turned to a public genetic reference library, stored on the University of California-Santa Cruz computers.

Rienhoff's tale of searching and sharing genetic information is one just one facet of the so-called "Open Science" movement.

At the conference, held at the Computer History Museum, other speakers - from efforts such as Figshare, Collaborative Drug Discovery, Ayaski, the Personal Genome Project and Syapse - described how they enlist big public databases to do pharmaceutical and genomic research.

There are other examples. Open access journals, like the University of California-San Francisco-based Public Library of Science, don't require ultra-expensive subscriptions. And open-source software and hardware are driving down the cost of science because amateurs can build their

own lab equipment.

"Napster disrupted the music industry, but now we're seeing changes across many different fields - including biology," said conference founder and organizer Joseph Jackson, a Harvard-educated philosopher. Biology is becoming more data-driven and better coordinated, and costs are plummeting, he said.

"Dr. Rienhoff is an early adopter of DIY-genetics, out of necessity, not choice," Jackson said. "Our hope is to scale that up."

Using such shared resources, Rienhoff sequenced his family's exomes. He discovered that all five of Bea's family members - himself; his wife, Lisa Hane; and two brothers - carry the standard identical sequence of amino acids within a specific gene. It's an important gene, regulating a growth hormone needed for normal muscle development.

The same sequence was even found in worms, fishes and other primitive animals - unchanged, despite 600,000 years of evolution.

But in Bea, he was startled to find that the sequence was different. She is missing an amino acid called cystine. In its place is a different amino acid, called tyrosine.

This single genetic quirk is responsible for Bea's maladies, he believes.

What went wrong? He thinks that when she was very young - just a 1- or 2-week-old embryo - the faulty gene sequence caused too little growth hormone to be produced, so her muscles failed to build enough cells.

Bea is otherwise healthy and loves music. She plays the violin and piano.

"We found it. We found the gene," he said. "It's very satisfying."

His work continues. Now he's collaborating with an Arizona lab to induce the identical defect in the genes of mice.

Soon there will be a whole colony of mice with Beatrice-like syndromes.

Hugh Rienhoff and other scientists aim to study their embryonic development, so they can better understand her genetic error. They'll watch the mice age and die, for a glimpse of her future.

And he'll freely share what they learn with the entire scientific community to construct a better understanding of muscular architecture.

It's his turn to give back, Rienhoff said.

"Beatrice may not be the beneficiary," he said. "But somebody will."