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How an AI expert took on his toughest project ever: writing code to save his son's life

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BIRMINGHAM, Ala. — Cristina Might drew close to her son. He was listless and groggy after weeks of battling a puzzling illness that had filled his lungs with fluid and, hours earlier, stopped his breathing entirely. A code team had rushed to Buddy's bedside and jolted him back to life, but now the 11-year-old with the broad smile was gray, his eyes unable to focus. His mom leaned nearer still. It was time to say goodbye.

But Cristina's words to her son, a brown-eyed boy who loved dolphins and his aquarium, offered no hint of her desperation: "I was telling him it was all going to be OK, that his fishies couldn't wait to see him again and that he had to hurry up and come home."

Somehow, Buddy made it through that night this past May, allowing doctors at Children's Hospital of Alabama to insert a tube to drain his lungs. His illness had caused a frightening cascade of symptoms: a yellowish substance in his bones and a bulging abdomen, on top of the deluge of fluid. After weeks in and out of the hospital, no one had come up with a diagnosis, but the drainage tube would hopefully give them a few more days to find an answer.

Matt Might works at his son's bedside at Children's Hospital of Alabama in Birmingham. *Courtesy Matt Might*

Frustrated by the lack of progress, Matt Might, Buddy's father and a computer programmer who heads the Hugh Kaul Precision Medicine Institute[7] at the University of Alabama at Birmingham (UAB), began attacking the problem the only way he knew how — by writing code.

His work at the institute involves creating an artificial intelligence system capable of sifting and analyzing vast stores of biomedical information. Sitting at Buddy's bedside, he started building software to query the system for clues about what was causing his son's symptoms. It was a bit of a Hail Mary. The AI, dubbed mediKanren, is still experimental and used only by a small group of researchers at UAB.

It was developed as part of an ambitious project funded by the National Institutes of Health to link and make searchable decades worth of biomedical

data collected by universities and research labs on genes, proteins, disease symptoms, patient outcomes, drugs, and more. This information is now dispersed among hundreds of databases, in a confusing patchwork of formats and terminology that defies easy analysis. Might thinks of mediKanren as a kind of GPS that will allow doctors and researchers to navigate the data and search for connections that may help them understand the root causes of diseases and develop treatments.

On Memorial Day weekend, Buddy became mediKanren's first medical emergency, a test of whether its AI could help Might and his son's doctors unlock the answers to an illness that had brought Buddy to the brink. The series of events that followed showcases AI's power to produce dramatic results in health care. It also shows that the nature of AI's power is not to automate care, or to replace the judgement of doctors, but to give them crucial information — and a reason to change course — when it matters most.

After he typed in a half-dozen symptoms, Might's screen lit up with hundreds of results. They were grouped based on how many of Buddy's symptoms they explained. A handful of the closest matches floated to the top of the list, including cancers, autoimmune disorders, and infections.

By that point in his life, Buddy, whose given name is Bertrand, already had an extensive medical history. At age 4, after a diagnostic odyssey since chronicled[9] in the New Yorker, he was the first patient in the world found to have a double mutation in the NGLY1 gene, which encodes an enzyme that facilitates the recycling of cellular waste. Buddy's lack of that enzyme results in an untreatable neurodegenerative disease[10] that left him using a wheelchair and struggling with a constellation of symptoms, including seizure-like activity in the brain, severe developmental delays, and an inability to produce tears.

Given that background, Might was certain his son's latest illness was not cancer or one of the autoimmune conditions. He zeroed in on infection, a culprit in several of Buddy's previous hospitalizations. But why was this infection so debilitating and seemingly resistant to treatment? Could it even be

treated with conventional antibiotics?

He and his son's doctors needed more information — and time.

In the years after Buddy's NGLY1 diagnosis in 2010, Might's career became increasingly intertwined with his son's disease. His prior work had largely focused on cybersecurity and finding vulnerabilities in software. But he began using his programming knowledge to search for the biological pathways involved in Buddy's illness.

In the health care system, patients like Buddy are largely invisible. Because their genetic conditions are so rare, doctors know nothing about the underlying disease mechanisms, how to treat them, or how to marshal resources to change those realities. That work largely fell to his parents.

Might was well suited to the role, not only because he was then a computer science professor at the University of Utah, but also because of his stoicism. He rarely shows any emotion when talking about Buddy, answering questions about his son's medical challenges matter of factly, much like the AI system he has designed.

At Utah, Might struck up a partnership[11] with the pharmacy school to develop algorithms capable of identifying drugs that could be repurposed to address the genetic mutations afflicting his son and other patients.

The approach bore fruit for Buddy: Might's team found that Prevacid, normally used to treat stomach ulcers and acid reflux, eased his chronic lung problems and even appeared to improve his development trajectory, allowing him to communicate a little easier.

The project attracted top-flight partners, including Harvard University, Boston Children's Hospital, and Recursion Pharmaceuticals, a Utah-based company that uses artificial intelligence to develop drugs. Might's computational approach also caught the attention of the Obama administration.

He accepted an invitation to visit the White House in early 2015, though the exact purpose for the meeting was unclear. Might arrived on a Friday and was asked to wait in the Blue Room.

"About 30 minutes later, President Obama walked in and we chatted about what was soon to become known as the Precision Medicine Initiative," Might said. "He asked if I would help. I was stunned — of course I said yes."

Matt Might was tapped in 2015 as a strategic adviser on President Obama's Precision Medicine Initiative. *Pete Souza/The White House*

The work as an adviser was heady and hard and taxing on his family. Long days in the White House extended into long nights. By then the Mights had welcomed two other children, both born without the NGLY1 mutations. Meanwhile, Buddy suffered from developmental delays and could not feed or dress himself, or tell his mother when he wasn't feeling well. Occasional hospitalizations for infection or pneumonia broke up what was an otherwise happy, if challenging, routine.

After Might's work for the government ended in 2018, he accepted the job at UAB and the family moved to Birmingham. Buddy had developed an affinity for fish and marine life — he loved the movie "Dolphin Tale" — and his parents put a large fluorescent-lighted aquarium in his room. Seated in his wheelchair, Buddy would point at the shimmering schools of blood parrot cichlids as they darted through the water.

On a Saturday in mid-May, the family went to the local science museum for Star Wars day. Afterward, Cristina took the two younger children, Winston, 5, and Victoria, 8, to gymnastics while Matt went home with Buddy. Cristina started getting texts from her husband: Buddy had developed a fever and seemed unusually uncomfortable.

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How patient records from one Boston hospital fueled an explosion in AI research in medicine [12]

By the time she got home, his temperature was climbing and his oxygen level was dipping, a worrisome sign. Cristina grabbed Buddy's medications and packed a bag. She didn't know what had caused him to become so ill, but pattern recognition told her it was spiraling into a blow-through-the-stoplights emergency.

It is a 20-minute drive to Children's Hospital of Alabama in downtown Birmingham from the Mights' home in adjacent Mountain Brook. They arrived in less than nine.

During the ride, Buddy's temperature spiked to 106 and his blood pressure plummeted along with his oxygen saturation, which dropped below 70, then 60. Anything below 80 can cause brain damage. The emergency room doctors tried giving him oxygen through a mask, but it wasn't working. He had to be intubated.

"They could not get him to breathe," Cristina said. "It was so precipitous."

The doctors called for inserting a central line, a tube to deliver epinephrine to Buddy's heart. Matt and Cristina were stunned.

"We were like, OK, what's going on?" Cristina said. "The nurse who was with us said, 'This is septic shock. He's going into septic shock.'"

Might's team at the UAB Precision Medicine Institute functions like a cold case squad for patients like Buddy. It takes up the unsolved medical mysteries of people from around the country whose conditions have defied conventional treatments. Many have already seen multiple specialists and undergone countless tests, only to end up with the same symptoms and no answers.

On a recent Monday, the team piled into a conference room in downtown Birmingham to go through a case log with more than 100 patients. Might, wearing a solid black tie and royal blue blazer, sat at one end of the table while his head of operations, Andy Crause, occupied the other. In between were three premed students and Dr. Forest Huls, an expert diagnostician and pathologist who recently joined the team from the University of Michigan.

Among the most valuable members of the team is mediKanren, whose interface was open on laptops around the room. Its name is derived from the Japanese word kanren, which means connection, because it is programmed to search for hidden connections between different pieces of information — such as the molecular target of Prevacid and the genetic mutation that gave rise to Buddy's disease.

The system gets its data from an NIH project called Translator[15], in which scientists from around the country are working to combine disparate streams of biomedical information on diseases, patients, and drugs. The goal is to make this information searchable and facilitate a shift from symptom-based diagnosis

to a more precise process that classifies diseases based on molecular and cellular abnormalities that can be targeted by precision treatments.

So far, mediKanren has ingested about 80 databases and all the research published through PubMed, a federal government compilation of more than 29 million medical articles. It can query that information to provide doctors and researchers with something of a biological roadmap to diseases. For example, if a user is trying to research treatments for a rare form of asthma, mediKanren can surface any documented information on the molecular and genetic features that have given rise to the disease in previous patients, and how those patients were treated. That information can be used to examine how existing drugs might be used to target disease mechanisms, or aid in the search for a novel therapy.

Informatics experts said a key attribute of the system is its ability to highlight the sources from which it derives information, so that researchers can trace its logic through published literature and the information in the databases.

“Part of what’s so exciting about Matt Might’s system is that it seems to have a deep respect for causality and the role of the human analyst,” said John Bowers, an artificial intelligence researcher at the Berkman Klein Center for Internet and Society at Harvard University. “It shows how a human analyst can benefit from the giant troves of associational predictions and data, but it doesn’t subjugate the analyst to the machinations of the AI system.”

During the Monday case review, mediKanren served as an all-knowing medical reference librarian, quickly chasing down key pieces of information to support the institute’s investigations. The team took up a wide array of cases: a girl with tremors related to a rare mutation in a gene known as ADCY5; a boy suffering from repeated bouts of unexplained seizures; and a man struggling to find the cause of an unusual constellation of symptoms that included excruciating chest pain, severe headaches, buzzing in his ears, and cold sweats. His problems had persisted despite visits to two dozen hospitals.

In the latter case, Huls, the pathologist and diagnostician, theorized that the man was suffering from a slow leak of cerebrospinal fluid stemming from a prior head injury. The leak, he suggested, was caused by a type of intracranial pressure that could explain all of the man's symptoms.

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MediKanren surfaced another interesting piece of the puzzle, noting that caffeine is one of many substances known to increase production of cerebrospinal fluid. Huls said he noticed from the patient's chart that he had an unusual habit of drinking between five and six cups of coffee a day.

"I think he's been treating himself inadvertently," said Huls, who planned to write a report about his theory for the patient's doctors. If he's correct, he said, the man's condition could be treated fairly simply by injecting blood into his spinal column to plug the leak.

"I hope this guy gets his life back," Huls said, "because it's been half a decade of driving from one place to another and being disappointed at every turn."

In that case, as in most taken up by the UAB team, mediKanren served a supporting role, connecting dots that the team members may have missed without a nudge from the machine.

In the case of Kelsea Sauer, mediKanren provided an even bigger push.

Sauer, 21, reached out to the institute last year after suffering from bouts of vomiting and nausea for most of her life. The condition eventually caused her weight to drop to 77 pounds, requiring a 2 1/2-week hospital stay last October. She had cycled through six or seven doctors who ran repeated tests but could not offer a clear diagnosis or an effective treatment.

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At UAB, an initial search of mediKanren turned up dozens of possible therapies. Might and his team focused on a group of treatments that hadn't been tried on Kelsea — a zone of mediKanren results they call the known unknowns. These are treatments that are documented in the literature but might be hard to find without an algorithm that can nearly instantly search the totality of information published on a subject.

MediKanren found three papers suggesting that nasal inhalation of isopropyl alcohol could counteract nausea in similar patients. Sauer's doctors agreed to try it.

"It was pretty much a night and day difference," Sauer said of the treatment's impact. She said she keeps alcohol pads at her bedside and in her purse, and inhales whenever she feels an episode coming on. After beginning treatment, her weight increased to 123 pounds and in April, she got married and moved to California.

"Every once in a while, I will have a very small episode where I'll be down for like a day," Sauer said. "But it's very rare now. And I know how to get rid of it."

Cases like Sauer's show mediKanren's potential. But could it help in the type of emergency circumstances facing Buddy, whose rapidly deteriorating condition left almost no room for error?

After a perilous night in the pediatric ICU, Buddy slowly began to recover from septic shock, a sharp drop in blood pressure that can lead to organ failure and death. He was able to watch movies and play with stuffed animals in his bed. But the roller coaster was just beginning.

After being discharged, Buddy returned to the hospital within 24 hours, this time suffering from excruciating leg pain at the site of a former break. Doctors performed two surgeries, scraping a yellowish substance from his femur. His

arms swelled up and fluid began filling his lungs.

The initial infection that had plunged him into septic shock was mounting another attack. On May 23, a Thursday, his parents went home to sleep for a few hours before a planned surgery the next day to drain Buddy's lungs.

Then the phone rang.

"They called us and told us to come back. They said Buddy coded," Cristina said. An emergency response team rushed to Buddy's room and was able to get him breathing again. The next hours brought a desperate scramble: a blood transfusion, then surgery to insert a tube in his lungs. Buddy coded again, this time in front of the pulmonary team, and then a larger tube was inserted to siphon the fluid faster.

He finally began to stabilize, but the cause of the infection was still a mystery. All the blood cultures had come back negative.

Matt Might's queries of mediKanren, however, produced a crucial lead: a list of possible microbes, including a type of bacteria called Pseudomonas. Most people experience only minor symptoms from Pseudomonas infection, but its impact can be more severe for patients like Buddy with compromised immune systems. Might forwarded the results to Buddy's doctors, asking for more testing to figure out what was wrong.

Might proposed to do metagenomic analysis on his son, a way of diagnosing infection by comparing the genetic material in Buddy's blood and lung fluid to a database of thousands of bacteria, viruses, and other pathogens.

Crause, his operations manager, found a lab in Huntsville[19] that could perform the analysis in a matter of hours. So on Memorial Day, Might packed his son's specimens in a cooler and raced up Interstate 65. Crause met him at a Jack in the Box restaurant off the highway, where Might handed over the cooler so Crause could take it to a researcher who had agreed to do the test.

After analyzing the results, a striking change jumped out: The level of Pseudomonas bacteria in Buddy's lung fluid had gone from 2% to 13%. The test also turned up E. coli, as had a separate analysis conducted by Children's of Alabama. It had also turned up on the list generated by mediKanren.

The results pointed Buddy's doctors to a treatment: They prescribed a course of meropenem, an antibiotic that can eradicate both Pseudomonas and E. coli but is used sparingly because of its high costs and a desire to avoid the development of drug-resistant bacteria.

"Once they put him on it, he was visibly different," Cristina said. "His eyes were open and he was looking at our faces. By the next day, he was a different child."

A few days later, Matt and Cristina kept a promise they'd made at Buddy's bedside: They took him to swim with dolphins in Jupiter Beach, Fla. As Matt and Cristina held him in the swimming pool, a dolphin's nose just inches away, a broad smile swept across Buddy's face.

Buddy's medical journey, and his parents' willingness to talk about it publicly, has opened doors for other patients. Following his NGLY1 diagnosis, more than 70 other people were diagnosed with the condition, resulting in the formation of a worldwide community of patients and families.

Buddy's ninth birthday was celebrated with a bowling party at the White House with other rare disease patients whose struggles had finally begun to find an official audience.

And this latest hospitalization showcased the increasing capacity of AI to spur scientific inquiry, and find answers, even in desperate circumstances. Might spoke about the role of AI in his son's recovery at a recent precision medicine event at Harvard, telling an audience of entrepreneurs and scientists that he'd been mistaken years earlier when he'd proclaimed that data would be the greatest drug of the 21st century.

"I think I said that somewhat naively and wrongly at the time," Might told the crowd. "The truth is, it already was the greatest drug. The only thing that's ever been a limiting reagent in this case was reasoning — our ability to use artificial intelligence to manipulate the sea of data that's always been out there."

After his release from the hospital, Matt and Cristina Might took Buddy swimming with dolphins in Jupiter Beach, Fla. *Courtesy Might family*

UAB is now working to incorporate Might's team, and mediKanren, into clinical care, so it can be called upon to assist physicians with challenging cases, a crucial step forward in the use of AI.

But Buddy's future does not look as bright as the science his life has enabled. Sitting on her screened-in porch last month, Cristina said her son has not been the same since returning home. He hasn't sat up on his own or been able to use his hands to play with toys.

"Any time he has an episode in the hospital, he'll get back up to 90% of what he was before, but he never gets to 100%," she said. "Each time it takes so much out of him."

Buddy is entering puberty, when patients with NGLY1 disorder typically

decline more rapidly. Cristina said her hope for her son is that he will be able to live out his life happily and free from suffering, but she knows the cold realities he's facing.

"He's already in overtime," she said. "He was 14 months old when they told me he had a two- to three-year life expectancy, so every second, every single day is a gift, every time I get to read him a bedtime story or snuggle him is a gift."

But it is hard, she said, her voice quavering, to see Buddy struggle as he did during his last emergency and to carry on knowing that it may keep happening.

"It feels unfair to continually by extreme measures extend his life when I can't promise him a better tomorrow," she said. "We're trying. I'm very proud of him. I love him so much. He's an amazing little boy."

Ruth Hailu contributed reporting.

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