It was the longest 30 minutes of his life. Sitting in his office in the ground floor of the UVM Medical Center’s main campus, Michael Towle stared at his computer while, in the office just down the hall, Debra Leonard, M.D., Ph.D., chair of pathology and laboratory medicine at the Larner College of Medicine, studied his genetic blueprint. Leonard was looking to see if Towle had the mutation for frontotemporal dementia (FTD), a devastating disease that strikes early.

A half-hour later, Leonard called him in to her office to tell him the good news: he did not have the mutation. Then, together, they cried.

A few years earlier, spurred on by the record of dementia and cancer in his family, Towle had decided to have his genome sequenced. After his mother began showing symptoms of FTD, the family asked William Pendlebury, M.D., professor emeritus of pathology and laboratory medicine at the Larner College of Medicine, to recommend and order genetic testing for their mother to try to identify the mutation causing FTD in their family. That information, along with the sequencing of Towle’s genome, gave Leonard the scientific crystal ball she needed to predict Towle’s chances of getting the disease.
To the cycle. It was powerful."

"I was doubting myself, then I was sure it was the right thing to do, then I was doubting myself again—it was an endless loop of uncertainty. Finding out put an end to the cycle. It was powerful."

PLAYING THE HAND YOU’RE DEALT

In poker, as in life, many of us think in terms of doing the best with what we have. By that way of thinking, what if you could learn your lifetime risks for disease... and act accordingly?

That’s the idea behind the genetic testing currently being offered to patients at select UVM Medical Center primary care offices. The test, provided at no cost as part of each patient's preventive health care, identifies your lifetime risks for disease. ...and act accordingly?

A WINDOW ON THE FUTURE

Using just two teaspoons of blood, the two-part test provides two things. First, a genetic health screen of 147 genes for cancer and cardiovascular risk. These are mostly genetically dominant “disorders,” so if a person has a positive result, they have an increased risk of having or developing the condition, and each of their children has a 50 percent chance of inheriting the same increased risk.

Secondly, the testing provides a carrier screen that targets 300 genes for genetically recessive conditions like cystic fibrosis. Most people are carriers of at least three recessive health conditions, most of them rare. Carriers have one altered copy of the gene, and one “normal” copy which prevents the disease. To have the disease a person needs to have received an altered gene copy from each of their parents. Thus, if you are a carrier, only if your partner also is a carrier would you have a chance of having a child affected by the condition. If both partners are identified as carriers, there’s a 1 in 4 chance for each child to have the disease.

Each patient receives a full report of their test results and an action plan created by genomic medicine experts at UVM Medical Center and a group of patient and family advisors. The team also includes Timothy Lahey, M.D., professor of medicine at the Larner College of Medicine and director of clinical ethics at UVM Medical Center.

The care pathways provide common language for every aspect of the experience, from obtaining informed consent to guiding patients on next steps, such as which specialist a patient should be referred to and what kind of further testing the patient might need before seeing the specialist.

“We’re learning a lot about genes as we get more information,” says Christine Giunno, a genetic counselor involved with the program. “It’s important for the family medical doctors counseling these patients to have the information they need about further specialty care and testing so that they can advise accordingly. We have created the Genomic Medicine Resource Center to answer questions and provide resources for providers and patients.”

Giunno notes that the care pathways’ work is an evolving process; the team continues to adjust the pathways as patients and providers report on their experience, and as clinical evidence in the medical literature advances. Striking the right ethical balance has also been a key focus. Ethical guidelines have helped shape the informed consent process so patients have a clear understanding of what the program offers, what the results can mean—and what kind of control they have over their information.

Further, says Lahey, the ethical implications of knowing what your future holds have influenced the architecture of the pilot project. “We’ve been very careful. We don’t want to give scattered bits of information that might lead to increased anxiety and unnecessary testing that ultimately isn’t helpful. We want to offer information that is clearly connected to evidence-based pathways of care.”

Community members who bring the patient and family voice to health care have played a role in ensuring that all the information materials are understandable for patients and their families. Says Patient and
Some patients have no signs or symptoms of a disease, and others learn about their genetic difference after an injury or illness that turns out to be genetic in nature. Genetic testing can help identify disease risks and missed diagnoses, get to the right treatments faster and avoid ineffective tests and treatments.

— ROBERT WILDIN, M.D.

As a physician and a scientist, he was drawn in—and then there was the personal: with a history of cardiovascular disease in his family, he wanted to know if additional risk for that was in store for him as well. “I had some distrust,” he says. “But it wasn’t too daunting.”

To look into what may be your future can be daunting, and information revealed through genetic testing can lead to more uncertainty. “Genetic testing is one of many examples of how our technology sometimes outpaces our understanding,” he says. “We have to be mindful of how we use it.”

His own results were encouraging—and useful. Not only was there nothing especially concerning, but the sequencing revealed important information about how his body metabolizes medication. Further, he says, “I have a unique level of confidence knowing that my entire genome is stored on a thumb drive.”

OneCare Vermont, says he’s proud of the program’s success. “Our overarching goal is to do no harm. We always want to make sure our processes are safe and effective—and that patients have control over the use of their personal health information.”

Lahey is encouraged by the careful, toe-in-the-water way the Genomic Medicine Program is wading into this work. “The focus is pragmatic, the goal is to be evidence-based, and the aim is to use genetic information thoughtfully.”

THE GENOME AND VERMONT’S HEALTH CARE LANDSCAPE

If a patient who has no signs or symptoms learns they have a genetic difference that indicates the potential for lurking heart disease, the physician would order an echocardiogram. It’s likely that this test wouldn’t have been ordered in patients without recognized symptoms. How will these cause-and-effect ramifications of genetic testing impact our statewide effort to reduce the overall cost of health care? How will we prove, in the long run, that genetic testing has helped prevent future disease, impact our statewide efforts to reduce the overall cost of health care?

In college, a mysterious new symptom appeared: he felt like he had a bowling ball rolling around his stomach. This, too, came and went, with no apparent cause. MRI and upper GI studies revealed nothing. His doctors told him he needed a vacation.

Flash forward four decades. Merhar and his wife Debra Leonard, M.D., Ph.D., the founder of UVM Health Network’s Genomic Medicine Program, decided it would be romantic if they gave each other their genome sequences for Christmas.

As it turned out, for Merhar, this was a life-altering gift. The sequencing revealed that he has a genetic mutation on chromosome 16. With a little sleuthing, he also learned he fits the profile for Familial Mediterranean Fever (FMF), a condition in which his body doesn’t produce any or enough of a protein that is involved in helping to regulate the process of inflammation.

“Basically, any inflammatory event, I just blow up,” he says.

Within a few days, he had a prescription for Colchicine. He took it Friday night. Saturday morning he woke up feeling like “a tight switch had gone off.” Sunday morning, he lay in bed and thought, “I have no pain.”

Merhar points out that because he doesn’t look like someone of Mediterranean heritage, it wasn’t a diagnosis that would have occurred to the many physicians who saw him over the years. “In that way I’m kind of the poster child for genetic testing,” he says. “That was the key to my diagnosis.”

Today, Merhar is still running. And every step of the way, with every passing year, the image of a man beset by pain recedes into the rear view mirror.

An avid runner, Greg Merhar sprinted through his early years before he became plagued by pain and intermittent fatigue.

“The only thing that helped was to sit in a bathtub. I used to sit in a bathtub for hours at a time. I just blow up,” he says.

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Greg Merhar and his doctor, Aaron Butler, M.D.

WITH THE FLICK OF A SWITCH

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A PHYSICIAN’S EXPERIENCE

Tom Peterson, M.D.

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