Nathan Healey was in the prime of his life, a successful tennis pro who had been a contender at the Australian Open, when his heart erupted. A seemingly healthy 32-year-old, he was puttering around his house in Reading, Pennsylvania, when he felt a tightness in his chest.

“All of a sudden, I felt dizzy and my heart rate was rising. I guess that is when something blew inside,” Healey, now 37, recalled recently from his home near Sydney, Australia.

An ambulance ferried him to the local emergency room, where doctors found that a hole had ruptured in the center of his heart, releasing a stream of blood into his system. Healey was transferred to the University of Pennsylvania medical center, where the cardiac surgeon on call, Joseph Woo, MD, greeted him before midnight with some grim news.

“I remember hearing Dr. Woo say, ‘Chances aren’t good, but I will see what I can do,’” Healey recalled.

Woo, now chair of cardiothoracic surgery at Stanford, discovered that Healey had been born with some previously undetected heart defects, including a weak spot that had progressively enlarged and finally burst open. He had other abnormalities in his aorta, including an aortic valve whose three flaps were of different sizes, making it hard for the valve to close properly.

In the operating room, Woo faced an urgent decision: Should he try to repair the defective valve, using Healey’s own tissue, or should he just replace it with a mechanical or animal valve, as was the more standard procedure?

Precision health in the clinic and operating room

Today, technological advances make it possible to identify subtle signs of disease early, even before symptoms occur, and to interfere in the process to prevent illness altogether. Cell and gene therapy, artificial intelligence, tests that reveal early signs of cancer or other diseases, and wearable devices that can detect heart and other problems are all among the tools empowering this growing movement, which we call precision health.

Precision health enables us not only to predict and prevent disease but also to treat it with precise therapies that are tailored to individual patients. In this issue of Stanford Medicine News, you will find several examples of precision health in action.

For instance, Stanford Medicine recently embarked on an innovative approach to health
SoundBites

“There were media people and reporters absolutely everywhere. Several very aggressive reporters actually crawled up the outside walls with cameras to get to the second floor intensive care unit to photograph the (patient). It was pretty exciting. And yeah, we did feel like we were on the brink of something pretty major.”

Cardiologist Sharon Hunt, MD, regarding the 50th anniversary of the first heart transplant at Stanford. Jan. 6

“Smartphone screens light up the same area of the brain as opioids and cannabis. The rewards pathways mediated by dopamine respond to screens in a very similar way to opioids.”

Addiction expert Anna Lembke, MD, associate professor of psychiatry and behavioral sciences, on what makes adolescents especially vulnerable to the addictive nature of smartphones. Jan. 9

“We are quadrupling the stroke treatment window today. It’s going to have a massive impact on how stroke is triaged and assessed.”

Neurologist Gregory Albers, MD, who directed a large-scale study that found patients could be effectively treated up to 16 hours or more after a stroke. Jan. 24

Massive study looks at overall health

Leslie Purchase describes herself as a data devotee. So when she heard about the Project Baseline study—one of the largest and most comprehensive on the basic underpinnings of health and disease—she jumped at the chance to participate.

“I’m so excited to be part of this effort to understand more about what makes the human body work,” said Purchase, 41, a former physician and mother of three who volunteers with the nonprofit Rotaplast International. “It’s an opportunity to help inform health and wellness on a scale that’s never before been attempted, and I think it’s a pretty easy way to do something good for the world.”

The study is an ambitious endeavor, with a potentially transformative payoff. Launched in April after years of design and planning by Verily, an Alphabet company, in partnership with Stanford Medicine and the Duke University School of Medicine, it aims to understand the molecular basis of health by collecting vast amounts of biomedical data from as many as 10,000 participants for at least four years. Stanford Medicine recently enrolled its 100th participant.

Observing how people’s health data change over time, regardless of whether they remain healthy or fall ill, could provide the first comprehensive atlas of what it means to be “well” at all stages of life. It could also help researchers learn the subtle signals given off by the body at the earliest stages of cancer, heart disease or other disorders.

The scope of the effort, and its potential to enable physicians to proactively monitor a person’s health and provide preemptive medical care—known as precision health—has captured the imagination of researchers for exploratory analysis such as characterizing the variation of the participants and identifying biomarkers of the transition from health to disease.

“We want to encourage anyone interested—particularly underrepresented minorities, the elderly and those at high risk for cancer or cardiovascular disease—to visit the website to learn more about the study and apply to participate,” said Gambhir, who is also the director of the Canary Center at Stanford for Cancer Early Detection.

“Once you truly understand what the study is attempting to accomplish,” said Purchase, “it almost feels like a moral obligation to participate. My youngest daughter is a brain cancer survivor and a huge motivating factor for me. Between my breast cancer and her brain cancer, we are desperate to move medical knowledge forward.”

People interested in participating in the study should visit www.projectbaseline.com or call 855-5-BASELINE or 855-522-7354.
Four years ago, Mukund Acharya spent a lot of time in the hospital while his wife struggled with terminal metastatic breast cancer. As her caregiver, he learned the ins and outs of hospital life and saw an opportunity to share his experience and offer feedback from a personal perspective. He asked to be part of the palliative care design team at the Stanford Cancer Center, where he worked alongside staff, physicians and other caregivers and families.

“My experience inspired me to act as a patient advocate for integrated palliative care,” said Acharya, a retired aerospace engineer. “I saw room for improvement in terms of helping patients learn their way around the system outside of its medical aspects, with a focus on the logistics of treatment and its psychosocial, financial and spiritual support. I felt like I could make a strong contribution to the team effort.”

Acharya later became a volunteer in the Patient and Family Partner Program at Stanford Health Care, representing the voices of other patients and families in improving programs and systems throughout the organization. He and his fellow volunteers meet with staff, faculty and administrators to share their unique perspectives on everything from floor plans to paperwork.

Integrating personal experience

Today, the Patient and Family Partner Program includes 120 members, who serve on 14 patient and family advisory councils covering specialties ranging from geriatrics to cancer, cystic fibrosis, emergency medicine and pain. The first group was launched in 2009 to integrate patients’ and caregivers’ firsthand experiences into the hospital’s programs and operations, as well as to help refine plans for Stanford Hospital, currently under construction, and outpatient centers such as the Neuroscience Health Center and Stanford Cancer Center South Bay.

“This program is about engaging patients and families to improve the patient experience,” said Mary Song, MPH, manager of the Patient and Family Partner Program and volunteer resources at Stanford Health Care. “No one understands what a patient needs better than someone who has lived that experience as a patient, caregiver or family member. They live it and breathe it every day. Our process is done with patients, not just for patients.”

Council members updated a brochure for new patients; helped reduce wait times through changes in the emergency department, mammography center and heart transplant clinic; suggested improvements to meals for hospitalized cancer patients; and created a Facebook page to build community among young cystic fibrosis patients. At the new Neuroscience Health Center on Quarry Road, they provided extensive input on a wide range of elements ranging from carpet colors to hallway handrails, lighting and a simplified check-in system, all to provide safer, more streamlined specialty care.

“Patient and family volunteers are instrumental throughout the organization. The program got its start with planning the new Stanford Hospital and new Lucile Packard Children’s Hospital almost 10 years ago,” said George Tingwald, MD, A1A, architect, physician and director of medical planning, design and construction for both hospitals. “The concept of indoor and outdoor respites with no clinical services, which are signatures of both new hospitals, stemmed from their own experiences when they sought a place to get away from the buzz of a busy hospital. They championed how important it was to provide space in all patient rooms for family members to sleep.”

Packard parent advocates

At the new Lucile Packard Children’s Hospital Stanford, the design team met first with patient families, who helped shape the details of patient rooms, services and amenities. From providing visitor sleeper beds to including bathtubs instead of showers, the new hospital features touches large and small that reflect insights from people who have spent large amounts of time by their child’s bedside.

“There are things you just don’t think about until you walk it from a patient or parent perspective,” said Diane Flynn, a Menlo Park mother of three who spent many nights by her youngest child’s bedside as he underwent a series of surgeries for a cleft lip. “A hospital needs to look at all aspects of how it provides family-centered care.”

Flynn became a member of Packard’s Family Advisory Council as a way to give back to the place that helped her son heal. She and other parents provided feedback on many of the new building’s design elements, from a family lounge, laundry facilities and family kitchen on every patient floor, to in-room phone chargers, kid-friendly interactive art and an overall focus on light and nature.

“Members of the Family Advisory Council are integral to our process of improving patient care because they are adept at converting their personal experiences into positive change,” said Karen Wayman, PhD, director of the hospital’s Family-Centered Care program.

Packard’s Family Advisory Council includes about 40 parents and family members in nine councils who deal with key issues such as safety, oncology and transitioning to adult services. “The councils act as focus groups, build consensus and help brainstorm solutions,” Wayman said. “Their input is a real advantage in terms of helping to improve the care and safety of our young patients.”

Added Tingwald, “The patient, parent and caregiver groups are considered experts, and their comments are taken very seriously. I am constantly surprised by what they tell me, since they see things quite differently than staff or administrators. They are integral to all our efforts, and our design work is sharper because of their insights. Stanford has been a real leader in this movement, and I’m constantly asked how we make it work. My answer sounds simple: ‘We engage early, often and intensely, and we listen.’”
Woo knew that Healey’s athletic career would be over if he replaced the faulty valve, as the replacement options either would not be durable enough or would require him to take lifelong medications that would limit his physical activities.

He decided to take the extraordinary step of repairing the valve, doing some creative trimming and sculpting. He cut out one of the three oddly shaped flaps and used that tissue to fashion two flaps of equal size. He also rebuilt some of the surrounding tissues as part of the seven-hour procedure that saved Healey’s life and livelihood.

“It was an epiphany,” Woo said. “We’re always thinking, ‘How do you use what’s there and take advantage of it?’ That’s the fundamental concept to natural valve repair—to use what’s there in whatever creative manner you can to design something that works.”

That philosophy has put Woo in the forefront of the movement toward natural valve repair, which evolves as surgeons devise new techniques and gain experience.

**Valve history**
Modern-day valve treatment goes back to the 1950s, when the introduction of mechanical valves enabled doctors to replace the diseased tissues with a substitute made of mechanical parts, similar to the valves found in car engines, Woo says. Mechanical valves are effective and last a lifetime, but they have a major drawback in that blood tends to stick to them and form clots. As a result, patients have to take blood-thinning medications, which require regular monitoring for side effects, such as excessive bleeding and stroke.

In the 1970s, another alternative came to the fore: prosthetic valves taken from the cadavers of pigs or cows. These can work well but aren’t as durable, particularly when used in younger patients, who have greater heart demands. Animal valves can wear out in 10 to 15 years, so patients have to undergo a second replacement and endure the risks of another surgery. Because none of these replacement options are ideal, surgeons have turned to creatively restructuring damaged valves using the patient’s own tissue. Multiple studies have shown that patients who undergo mitral valve repair do better overall: They are more likely to survive, spend less time in the hospital, and suffer fewer complications, such as infection and stroke, compared with those who receive substitute valves, whether animal or mechanical.

**Fixing the aortic valve**
While mitral repair has gained greater acceptance, aortic valve repair is far less common, as the valve is very different in both form and function. For instance, while the mitral valve has two flaps, the aortic valve has three, so a surgeon has to effectively line up three flaps and used that tissue to fashion two flaps of equal size. He also rebuilt some of the surrounding tissues as part of the seven-hour procedure that saved Healey’s life and livelihood.

In the procedure, known as valve-sparing root replacement, surgeons cut out the diseased part of the aorta and replace it with a tube of Dacron polyester, known as a graft, which is stitched to the heart. Instead of cutting out the aortic valve, as was done in the past, surgeons preserve the patient’s tissue and reimplant it inside the new tube, sometimes refashioning the valve to fit the space.

**In the operating room**
One morning in the fall, Woo was called in to perform a variation on this procedure at Stanford Hospital for a man in his 50s who had endocarditis—a heart infection—which had damaged part of the aorta, including the valve. The patient was put on a heart-lung bypass machine, which took over the functions of his heart and lungs while the surgical team did their work. Before Woo began, he viewed the heart on an echocardiogram, displayed on a nearby screen. It showed the valve leaflets flopping back and forth, indicating significant destruction.

He and his team began by cutting out the defective root, then meticulously removing 20 fragments of diseased tissue from around the faulty valve. They replaced the aortic root with an inch-wide Dacron tube, which they anchored in place with multiple blue Gore-Tex sutures. Then came the most challenging part: sewing what remained of the patient’s valve back inside the tube.

“I imagine tailoring a suit but from inside the suit,” said Woo, as he worked inside the narrow tube, meticulously stitching the valve in place and shaping it so that the leaflets were evenly aligned. It’s a procedure many surgeons won’t attempt, as there is very little valve tissue left to work with. But for the patient’s sake, Woo was determined to make it happen. After more than five hours, he was satisfied with the results: “It’s opening up nicely and working beautifully. This guy will keep his own valve over time.”

**All-repair philosophy**
In general, Woo says, he likes to approach each patient as a potential candidate for repair, though he realizes it’s not always possible. For instance, in patients with aortic stenosis, or a narrowing of the vessel, the leaflets may be so thickened and damaged by calcium deposits that they can’t be manipulated and preserved. But he is nonetheless guided by an all-repair philosophy.

“We believe, in our hands, we can try to approach everyone as potentially repairable,” he says. “No one should be viewed as automatically not a candidate. Everyone should have an opportunity.”

He says he often gives talks to cardiologists and cardiac surgeons throughout the world, trying to promote the concept and techniques of repair. “It’s an ongoing challenge to educate the community that aortic valves can be repaired,” Woo says. “Either they have never heard of it or they’ve never seen it done effectively by a surgeon. Or they don’t want to try it out until there is long-term durability data,” which is not yet available.

As for Nathan Healey, he fully recovered from his marathon repair procedure after spending 10 days in the hospital. Woo implanted a pacemaker in his heart, as the rupture had disrupted its natural rhythm. Healey was able to return to professional tennis and three years later went on to try his hand in the 2015 U.S. Open—likely one of the few players with a pacemaker to compete at that level.

In the fall of 2016, he moved with his family back to his native Australia, where he now coaches tennis and competes in the occasional tennis tournament.

“I’m just incredibly grateful to be enjoying the life I’m living,” he says. “A lot of fortunate pieces fell into place that night. I was lucky to get the surgeon and I was lucky to get the repair.”
At age 58, Laura Hosking was unusually young to be in need of a new aortic heart valve. But her situation was not typical: As a teenager, she had received treatment for late-stage Hodgkin’s lymphoma, including full-body radiation, which put her at risk for problems with her heart and other disorders later in life.

A finance professional and mother of three, she began to feel the long-term effects when she was in her 40s. She tired easily and had difficulty walking and carrying groceries. She could no longer play her usual 18 holes of golf. As her condition worsened over the years, she sought the help of Stanford Medicine cardiologist Randall Vagelos, MD, who found that she was suffering from aortic stenosis, a narrowing of the aorta, which carries blood from the heart to the rest of the body. Her health was further compromised by the discovery in 2013 of lung cancer, which was brought under control with a combination of CyberKnife radiotherapy and localized surgery.

New alternative

Given these factors, Vagelos knew that Hosking might not be able to withstand open-heart surgery, so he offered her the option of a relatively new, minimally invasive heart valve procedure known as TAVR, or transcatheter aortic valve replacement. The procedure is considered by many in the field to be a game-changer. It was approved by the U.S. Food and Drug Administration in 2012 for use in patients who, like Hosking, are considered at high risk of complications or death from open-heart surgery.

“She had a fairly complex history going into the procedure, which made for a heart-team decision favoring the non-open surgical approach to her valve,” Vagelos said. “An open surgical approach to valve replacement in a patient so young is still the gold standard because a mechanical prosthetic valve can last a lifetime. But the global damage to her chest from childhood radiation made a non-open surgical approach to her aortic valve disease more attractive.”

Faster recovery

In a traditional aortic valve procedure, surgeons open the chest and use a heart-lung bypass machine to temporarily stop the heart, then remove the damaged valve and replace it with a new one. With TAVR, the new valve is compressed inside a thin catheter, which is inserted into a blood vessel in the leg, then threaded up through the aorta and into the heart. The new valve then is released from the catheter and expanded with a balloon. Once in place, it begins working immediately.

Patients usually recover after two or three days in the hospital, compared with five to seven days for open-heart surgery. Hosking, who was younger than a typical TAVR patient, recovered even more quickly. She was walking and talking the day after her procedure and was back home within two days. She had grown so accustomed to taking shallow breaths for years that she had to retrain herself to breathe normally, she said.

“TAVR gave me back my life in an immediate and profound way,” Hosking said. Today, she has returned to playing golf and clocking 10,000 steps a day. She continues to see her team at Stanford to monitor her new valve and her lungs and said that she is immensely grateful to her medical team. “Every birthday is such a gift,” she said.

Stanford Medicine doctors have performed more than 1,000 transcatheter aortic valve replacements, and Stanford Hospital is one of a handful of hospitals in Northern California to offer the procedure. Multiple studies have confirmed TAVR’s effectiveness in treating patients at intermediate to high surgical risk, and Stanford clinicians are continually evaluating more patients as potential candidates for the procedure. The Stanford team is also studying the use of the approach in patients at all risk levels who have asymptomatic aortic stenosis.
Multiple Sclerosis—The State of the Art

Neurologist Lucas Kipp, MD, will talk about current and emerging diagnostic and treatment protocols for this unpredictable and often disabling disease.

DATE: Thursday, March 8, 7 p.m.
LOCATION: Stanford Health Library, Hoover Pavilion, Suite 201, 211 Quarry Road, Palo Alto

To register, call 650-498-7826.

Dads of Daughters

Julie Metzger, RN, leads this seminar for fathers of girls in fourth through 12th grades.

DATE: Friday, May 4, 7 to 8:30 p.m.
LOCATION: Friedenrich Auditorium, Lucille Packard Children’s Hospital, 725 Welch Road, Palo Alto

Fee: $50. To register, call 650-724-4601.

Mothers of Sons

Robert Lehman, MD, leads this seminar for mothers of boys in the fourth through 12th grades.

DATE: Monday, May 7, 7 to 8:30 p.m.
LOCATION: Friedenrich Auditorium, Lucille Packard Children’s Hospital, 725 Welch Road, Palo Alto

Fee: $50. To register, call 650-724-4601.

Smart Sendoffs

Specialists in the Division of Adolescent Medicine at Lucile Packard Children’s Hospital Stanford provide guidance to high school seniors heading to college as well as their parents. They will discuss important health issues that can arise during the college years, including sleep, nutrition, stress management, mental health, sexual health, alcohol and drug use, and understanding consent and preventing sexual assault.

DATE: Sunday, May 20, 2 to 5 p.m.
LOCATION: Li Ka Shing Center for Learning and Knowledge, 291 Campus Drive, Palo Alto

Fee: $85. To register, call 650-724-4601.

Free health care fair

Stanford Medicine is hosting Health Matters on Saturday, May 19, a free community-wide event where participants can hear from world-renowned physicians on the latest medical innovations and get tips on healthy living. The event runs from 9 a.m. to 2 p.m. at the Li Ka Shing Center for Learning and Knowledge, 291 Campus Drive, on the medical school campus.

The day will include talks by distinguished faculty on subjects ranging from heart health and stroke prevention to hearing loss, palliative care, immunotherapy, genomics and obsessive-compulsive disorder. Throughout the day, a series of mini-talks will focus on nutrition and other important health issues. The event also will feature interactive, hands-on attractions and activities for the entire family.

High school students interested in pursuing a career in health care can participate in Med School Morning, featuring lectures, hands-on lab presentations and interactive activities on a variety of scientific topics. Advance registration for Med School Morning is required. Registration opens in mid-April.

For more information on the day’s events, visit: http://med.stanford.edu/health-matters.html.

COMMUNITY MATTERS FROM PAGE 1

through a study of some 10,000 people, known as Project Baseline (see story, page 2). A collaboration with Verily—an Alphabet company—and the Duke University School of Medicine, the study will amass voluminous molecular data from each participant with the goal of understanding the molecular factors associated with health at various stages of life. The study will help scientists understand what makes a person healthy and the forces that may send that person down the path to illness. Armed with this information, we could intervene to alter the course of events.

This winter, Stanford Medicine also is expected to open a new genomics lab that will enable physicians to examine an individual’s unique genetic blueprint, including use of a technique known as whole exome sequencing (see story, page 7). This technology will help clinicians identify genetic mutations in people with unexplained medical conditions, thus pointing the way to possible treatments. We are among a handful of medical centers in the country to offer this type of testing, which will benefit patients at both Stanford Children’s Health and Stanford Health Care.

Two other stories in this issue—one on natural heart valve repair and another on a bloodless heart surgery in an infant—provide examples of precise modes of treatment, tailored to the individual. With natural heart valve repair, Stanford Medicine cardiologists preserve and reshape a patient’s own valve tissues, rather than replace a damaged valve with a mechanical or animal version. With natural repair, the valve heals along with the patient, providing lifelong benefit without the need for additional drugs or surgeries. Stanford Medicine is among a select group of medical centers across the country that specialize in this type of valve repair, particularly for the aortic valve.

At Lucile Packard Children’s Hospital Stanford, pediatric heart surgeons recently performed a technically challenging open-heart surgery in a newborn without use of blood products, out of respect for the family’s religious beliefs. Patients who undergo bloodless surgery are more likely to resist infection, avoid adverse immune responses and recover more quickly. This recent surgery is believed to be one of the first times in North America in which the operation, known as an arterial switch—or a rearrangement of two major heart arteries—was performed without a blood transfusion, providing a unique benefit to the patient and her family.

Precision health represents a new way of proactively focusing on the health and well-being of people and of addressing their individual needs. That is our commitment: to keep patients as healthy as possible and, when necessary, provide them with the most advanced and personalized care available.
en years is a long time in the life of a child. It is an eternity in the world of genomic sequencing. Within hours of her birth in 2003, Tessa Nye began having seizures. At the time, little was known about the cause of her severe form of epilepsy despite years of trial-and-error testing. Her birth came just a few months after the completion of the Human Genome Project, the first sequence of all 3 billion base pairs of human DNA. But broad genetic testing was not yet available to patients.

The Nye family spent years chasing a diagnosis for their daughter, who experienced hundreds of seizures a day, but doctors found no genetic cause for her disorder. The couple went on to have two healthy daughters, and their fears of a genetic basis for their firstborn’s disease dissipated. When Kim delivered her fourth child, Colton, that sense of security was shattered. Within 12 hours of his birth, Colton, a seemingly healthy baby boy, suffered a seizure.

But Colton was born in 2013, in an era when genetic sequencing had become available to patients. Gregory Enns, MD, a pediatric geneticist at Lucile Packard Children’s Hospital Stanford, ordered whole exome sequencing for Colton within days of his birth, the same test he had ordered for Tessa when it became clinically available in 2012. This blood test examines only the genes that code for proteins, approximately 1 to 2 percent of the genome, not the entire genome.

With two complete sets of genetic data to compare—Tessa’s and Colton’s—as well as the genetic data of both parents, Kim and Zach, the family’s doctors at Lucile Packard Children’s Hospital Stanford were able to identify a single-gene mutation that is the source of both children’s seizures. “That is the power of whole exome sequencing,” said Louanne Hudgins, MD, co-medical director of a new collaborative Clinical Genomics Program that will launch Feb. 28 at Stanford Health Care and Stanford Children’s Health. “It allows us to make accurate diagnoses in 25 to 30 percent of cases. This has been a total boon to what we do clinically. And it has been a total boon for gene discovery.”

The Clinical Genomics Program will offer whole exome sequencing and analysis to patients with undiagnosed genetic diseases. The whole exome sequencing will be conducted on site in a Stanford laboratory, rather than at another institution. Stanford Health Care and Stanford Children’s Health are two of a handful of hospitals nationwide to offer the entire sequencing process in-house. This improves coordination between the doctor requesting the test and the team performing the genetic analysis, helping pinpoint more precise diagnoses for patients, said Hudgins. The clinic will include genetic counselors to help families understand the implications of the results as well as financial consultants to help patients navigate insurance coverage for the test. The program will take referrals from physicians at both the adult and children’s hospitals.

In addition to conducting the initial whole exome sequencing, every year specialists at the Clinical Genomics Program will reanalyze results from patients whose whole exome sequencing did not uncover a genetic cause for their disease. New gene mutations are continually being identified: In Tessa’s case, for instance, whole exome sequencing initially came back normal. It was only through the ability to compare it with her brother’s and her parents’ exomes that the mutation was discovered. “With yearly reanalysis, we can continue to make diagnoses for years,” said Hudgins.

Whole exome sequencing does not look at all 3 billion base pairs of the human genome, but focuses instead on the approximately 21,000 protein-coding genes that have been found to be more causative of human disease. From those, the Stanford-built computational pipeline narrows down the results to 100 gene variants; each of these must be interpreted through 20 to 40 hours of manual analysis. This labor-intensive process is improved greatly when the lab scientist analyzing the results can work with the clinician who is familiar with patients’ symptoms and disease, said Hudgins. To improve that collaboration, referring physicians will attend weekly meetings to review active cases.

“Sequencing the genomes of patients and families represents the state of the art in genetic testing for patients today,” said Euan Ashley, MD, co-medical director of the Clinical Genomics Program. “It is the essence of precision health, understanding disease at a deeper level so that we can treat it more precisely. You are essentially looking at someone’s DNA and figuring out exactly what is wrong with them.”

For the Nye family, whole exome sequencing gave them the answer they had sought for years. “As a parent, it was very meaningful to get a diagnosis,” said Kim Nye. “We spent a full 10 years trying to figure out what was going on with our daughter. It’s heartbreaking to see your child’s health totally fail and have nobody be able to tell you why.”

Ultimately, the goal will be to use this information to understand the underlying molecular basis for disease and help develop targeted therapies, Hudgins said.

“We haven’t found our miracle cure yet, but whole exome sequencing has absolutely had an impact on suggesting new treatment options,” said Kim Nye. “At some point, there will be a breakthrough based on the underlying genetic
A 10-day-old girl was the smallest infant in North America to undergo open-heart surgery without a blood transfusion in a procedure performed by specialists at Lucile Packard Children's Hospital Stanford.

The child, born in October with a severe heart defect, made a quick recovery from the operation, which required meticulous planning and execution to overcome the technical challenges of avoiding the use of blood products.

“If you can do surgery safely and effectively without transfusion, there are several medical benefits,” said Frank Hanley, MD, chief of pediatric cardiac surgery at the hospital’s Betty Irene Moore Children’s Heart Center and one of two surgeons on the case. He said that patients who do not receive blood products have fewer post-surgical complications, provided they do not lose too much blood. “You have to be able to do the surgery safely and not have the patient’s red blood cell count drop too low,” Hanley said.

A severe heart defect

From the moment of her birth on Oct. 21, little Lola Garcia struggled to breathe. She and her parents, Felisa and Jared Garcia of Hemet, California, were rushed to a children’s hospital near their home.

Lola was diagnosed with transposition of the great arteries, a rare condition in which the heart’s major arteries are not connected correctly. Normally, the blood follows a single figure-eight-shaped circuit through the heart and lungs, then back to the heart and out to the body to supply oxygen to the internal organs and the brain. In Lola’s heart, the blood made two separate circuits—from the heart to the lungs and back, and from the heart to the body and back. As a result, her brain and other organs received too little oxygen.

“They said she would definitely need heart surgery, and most likely a blood transfusion, to correct the problem,” said Felisa. “We were happy there was a solution, but when they said ‘transfusion,’ my heart dropped.” The Garcia family are Jehovah’s Witnesses; they requested that Lola’s surgery be done without a blood transfusion because of their religious beliefs.

Although many hospitals offer bloodless surgery for adults, avoiding transfusion is more difficult in newborns. Several hospitals around the country turned the family down. But the Packard Children’s offered to attempt baby Lola’s operation without transfusing blood.

Technical hurdles

During the surgery, performed by a team led by Hanley and cardiothoracic surgeon Kazuhide Maeda, MD, Lola needed to be connected to a heart-lung machine, which would pump her blood through a circuit of tubing and membranes for re-oxygenation.

The machine carries a solution of saline that mixes with the patient’s blood. For an adult, the volume of saline in a heart-lung machine does not dilute the blood much, but a seven-pound newborn has less blood to begin with. Connecting Lola to a standard heart-lung circuit would have dangerously lowered her red blood cell count.

In the past, the problem has been solved by transfusing blood. For Lola, the Packard Children’s team took a different approach.

“We used a miniaturized heart-lung circuit with a much lower priming volume of saline,” Hanley said. The medical team also planned every step of Lola’s care to minimize blood loss, including her blood draws, surgical techniques and materials.

Still, the team could not guarantee that Lola would not need a transfusion. California state law gives physicians authority to administer blood to minors in emergencies, even if the parents disagree. Before surgery, the physicians explained to the parents how they would monitor Lola.

During and after the seven-hour surgery, Lola’s red blood cell count stayed in the safe range; no transfusion was required. She recovered more quickly than expected, which her doctors say may be due to avoiding transfusion.

“I couldn’t believe how fast she was healing,” Jared said. “We went home in less than two weeks. It was great.”

“Lola is doing fantastic; she looks phenomenal,” Hanley said. “Our team is excited to build this bloodless surgery program that will help many other children and families in the future.”