

DELIVERING ON A PROMISE



# A New Blueprint

*Le Bonheur Heart Institute sets new vision, built on strong foundation*

- ▶ Study: Drug effective in reducing TS tumors
- ▶ Hotline aims to improve state breastfeeding rate



Many of you may know late Nephrologist Russell Chesney by his reputation. Russ was a tremendously respected researcher, educator and clinician. When he died in April, we lost not only a great academic mind, but a beloved mentor, colleague and friend.

Evidence of his brilliance and scientific prowess can be found in all the major specialty and subspecialty awards he earned – including the prestigious American Pediatric Society's John Howland Award.

But his legacy will also be remembered in his leadership and teaching. During his 23-year tenure as chair of the Department of Pediatrics at the University of Tennessee Health Science Center, Russ built a strong and cohesive faculty that continues to thrive and serve our community well. His leadership laid the foundation for the exponential growth that Le Bonheur Children's Hospital and the Department of Pediatrics are now experiencing.

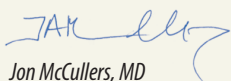
Russ had a great sense of humor and was kind to everyone he met. In addition to his sharp mind and quick wit, people were drawn to Russ for the warmth and sincere affection he bestowed on his friends, students, colleagues, patients and families. That affection, combined with the joy he had for life, gave him the ability to brighten a room.

Both his personal and professional attributes made Russ someone we wished to emulate. In many ways, he served as a role model for the kind of physicians – and people – we hope to be.

To honor Russ and his many contributions to Le Bonheur and the University of Tennessee, we have named our campus auditorium in his honor. We hope that all who come to learn and educate in this space will remember the remarkable legacy of our dear friend and colleague.



John Bissler, MD  
Chief of Pediatric Nephrology  
The University of Tennessee Health Science Center  
Le Bonheur Children's Hospital



Jon McCullers, MD  
Chair, The University of Tennessee Health Science Center  
Department of Pediatrics  
Pediatrician-in-Chief, Le Bonheur Children's Hospital







# Le Bonheur

Children's Hospital



Le Bonheur Children's Hospital in Memphis, Tenn., treats more than 250,000 children each year in regional clinics and a 255-bed hospital that features state-of-the-art technology and family-friendly resources. Our medical staff of more than 240 physicians provide care in 40 subspecialties.

## LE BONHEUR LEADERSHIP

Meri Armour – President and CEO  
Jon McCullers, MD – Pediatrician-in-Chief  
James "Trey" Eubanks, MD – Surgeon-in-Chief  
Harris Cohen, MD – Radiologist-in-Chief



The primary pediatric teaching affiliate of the University of Tennessee Health Science Center, College of Medicine

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#### THE COVER:

Late Pediatric Cardiovascular Surgeon Steven Goldberg was an educator who loved to teach with illustrations – whether he was explaining a diagnosis to families or teaching young doctors new concepts. "He used to get the young doctors together and say, 'What subject would you like to learn about today?'" said Le Bonheur Heart Institute Executive Co-Director and chief of Pediatric Cardiac Surgery Christopher Knott-Craig. "His knowledge spanned so wide that irrespective of what they chose, he could teach an hour-and-a-half lecture with diagrams. Pictured on the cover is an illustration of a normal heart that Dr. Goldberg drew while at Le Bonheur. Goldberg died in 2013 from cancer. He was 42.

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Le Bonheur Connect at 866-870-5570.



# A NEW --- BLUEPRINT





## *"Not compatible with life."*

Those words rang loud in Saralyn and Mark Crowell's ears just hours after their first child, Jack, was born on Thanksgiving Day 2012. Saralyn had a normal pregnancy and delivery, but after the third time that Jack struggled to eat, Saralyn and Mark, started to worry.

Then came the "looks" from Neonatal Intensive Care Unit nurses – the looks a mother never wants to get, the looks that assure you something is wrong.

Jack's diagnosis: Hypoplastic left heart Syndrome (HLHS), a congenital heart defect in which the left ventricle of the heart is underdeveloped, affecting normal blood flow. The defect is usually fatal unless treated within a few days or weeks after birth, and Jack was quickly transferred to Le Bonheur Children's Hospital. There, Cardiovascular Surgeon Christopher Knott-Craig, MD, prepared for a Norwood surgical procedure, the first of three planned surgeries Jack would need to "rewire" his heart.



When the Crowells learned their newborn son, Jack, had a rare congenital heart defect, they were relieved to learn that Le Bonheur Children's Hospital's Heart Institute, led by pioneer surgeon Christopher Knott-Craig, MD, was well-equipped to save their son's life.







### Christopher Knott-Craig, MD

Executive Co-Director of the Heart Institute,  
Le Bonheur Children's Hospital  
Medical Director of Cardiothoracic Surgery,  
Le Bonheur Children's Hospital  
Chief of Pediatric Cardiac Surgery,  
University of Tennessee Health Science Center



#### Education and Training

- University of Cape Town, Groote Schuur Hospital
- University of Stellenbosch, Tygerberg Hospital, South Africa, cardiothoracic surgery

#### Recent Experience

- Chief of Pediatric Cardiothoracic Surgery, University of Alabama at Birmingham (2006-2008)
- Chief of Pediatric Cardiac Surgery, Children's Hospital of Oklahoma (2000-2006)

#### Clinical and Research Focus

- Ambulatory thoracic surgery
- Cardiopulmonary bypass
- Cardiothoracic surgery
- Hyperhidrosis
- Pediatric congenital heart disease
- Minimally invasive valve surgery
- Neonatal/infant cardiac surgery
- Ebstein's anomaly

In a field of medicine where outcomes matter most, the Crowells quickly started studying up on HLHS and the Norwood operation. They rested easy knowing that Knott-Craig, a pioneer for some of the most complex congenital heart defect procedures, touted a 90 percent survival rate for the Norwood operation – far better than the Society for Thoracic Surgeons national average. Knott-Craig was surrounded by an experienced cardiology team who assured them that Jack had better than a fighting chance.

“That’s what saved Jack’s life,” said Mark Crowell. “All those people were in place the day we walked in the door. We were thankful for the foresight Le Bonheur had to put a team in place that could provide that level of care for our son.”

The Crowells benefited from a growing Le Bonheur Children’s Heart Institute team focused on transforming the way it cares for children and adults with congenital heart defects by providing a depth of talent, technology and research.

In the next five years, the Heart Institute will expand the foundation it has built by developing five



*Cardiothoracic Surgeon Christopher Knott-Craig, MD, came to Le Bonheur in 2008 with new, holistic approaches to surgical care.*



Learn more about The Heart Institute – [lebonheur.org/promise](http://lebonheur.org/promise).

to 10 new destination programs, recruiting another 25 faculty members, adding advanced specialty fellows and developing new areas of research.

The result: improved care that focuses on the changing needs of children and adults with congenital and acquired heart conditions.

## CREATING THE VISION

The recruitment of Heart Institute Executive Co-director Jeffrey A. Towbin, MD, in 2015 signaled the next step in the history of the Heart Institute at Le Bonheur Children's. Hospital leadership spent the past several years laying that foundation of which the Crowells speak – recruiting specialized cardiologists in fields like electrophysiology and adult congenital heart defects, adding advanced technology and operating rooms and delivering some of the best surgical outcomes in the country under the leadership of Knott-Craig.

### DESTINATION PROGRAMS

*The Heart Institute will expand destination programs in the next five years*

- Mechanical Circulatory Support
- Cardiomyopathy/Heart Failure
- Cardiovascular Genetics
- Adult Congenital Heart Disease
- Cardio-Oncology
- Heart Transplantation
- Neurodevelopment
- Single Ventricle Service
- Sports Cardiology
- Obesity

Towbin is working now to build on that foundation, focusing first on developing destination programs and recruiting sought-after experts to build them. He's starting



*Jeffrey A. Towbin, MD, was recruited to lead the Heart Institute at Le Bonheur Children's Hospital in 2015. Towbin's vision for the program includes building destination programs, recruiting specialized talent and adding advanced specialty fellows and developing new areas of research.*

with an area he knows well: cardiomyopathy and heart failure in children – a field in which he has spent more than 25 years of his career.

Towbin and the heart team also will focus on expanding super-specialized programs like:

- Mechanical Circulatory Support
- Cardiovascular Genetics
- Adult Congenital Heart Disease
- Heart Transplantation
- Neurodevelopment
- Single Ventricle
- Sports Cardiology
- Obesity
- Cardio-Oncology, in conjunction with St. Jude Children's Research Hospital, where he is also chief of Cardiology

“We have the surgical and medical teams in place to look beyond patient survival – now, it's about lifestyle and giving children and adults with congenital heart defects





## Jeffrey A. Towbin, MD

Executive Co-Director,  
Heart Institute at Le Bonheur Children's Hospital  
Chief of Cardiology, St. Jude Children's Research Hospital  
Chief of Pediatric Cardiology,  
The University of Tennessee Health Science Center



Vice Chair of Strategic Advancement, Le Bonheur  
Children's Hospital  
St. Jude Chair of Excellence in Cardiology, Le Bonheur Children's Hospital

### Education and Training

- University of Cincinnati, Cincinnati Children's Hospital Medical Center, pediatrics
- Baylor College of Medicine, Texas Children's Hospital, pediatric cardiology

### Recent Experience

- Executive Co-Director, The Heart Institute, Kindervelt-Samuel Kaplan Professor and Chief, Pediatric Cardiology (2009-2015)  
Director, Heart Failure Services and Cardiovascular Genetics (2009-2011), Cincinnati Children's Hospital Medical Center
- Chief, Pediatric Cardiology, Texas Children's Hospital, Baylor College of Medicine (2003-2009)  
Director, Heart Failure and Cardiovascular Genetics, Texas Children's Hospital (2003-2009)

### Clinical and Research Focus

- Diagnostic and therapeutic advancements for cardiomyopathies and sudden death
- Heart failure
- Mechanical circulatory support
- Heart transplantation
- Cardiovascular genetics

*Jeffrey A. Towbin, MD, has spent most of his career working with cardiomyopathy and heart failure in children. With a strong focus on research, Towbin hopes to grow Le Bonheur's research program to focus more on individualized medicine for congenital heart disease.*

and heart muscle diseases a great quality of life," said Towbin.

To build those programs, the Heart Institute expects to recruit 25 cardiologists in the next five years – five of those within the next few months.

Interventional Cardiologist Thomas Fagan, MD, moved his family to Memphis from Children's Hospital Colorado in Denver just three months after Towbin started calling. Towbin served as one of Fagan's mentors at Texas Children's Hospital and quickly sold him on his vision for the Heart Institute. Fagan, who became the medical director of the Catheterization Lab at Le Bonheur in August, says he was attracted to the "whole push to take things to the next level."

"I know Jeff can build a program, and it became enticing – the thought of coming to help build and



move treatments and the science forward,” Fagan said.

Fagan is taking the reins from former Catheterization Lab medical director Rush Waller, MD. Waller, the new medical director of the institute’s Adult Congenital Program, is working to build a robust program that supports the ongoing and complex needs of adults living with congenital heart disease. He will lead the program with Cardiologist Ryan Jones and Umar Boston, the hospital’s new surgical director of Heart Transplant and Mechanical Circulatory Support.

Towbin also has begun hiring research scientists through Le Bonheur’s Children’s Foundation Research Institute to continue his work in gene discovery and

the mechanisms of cardiomyopathies, arrhythmias, sudden cardiac death, vascular disorders and congenital heart disease – as well as viral causes of myocarditis, cardiomyopathies, transplant rejection and transplant coronary disease.

Towbin pioneered the concept of pathway-focused candidate gene analysis using his “final common pathway hypothesis,” and calls his work in understanding how heart muscle turns into cardiomyopathy his most important research to date.

“Many years ago, my lab was able to identify a major gene for muscular dystrophy, the dystrophin gene, as a cause of just heart disease instead of heart and

## Paris Walker Rogers: trans-catheter patent ductus arteriosus closure



At 1 pound, 9 ounces at 25 weeks gestation, Paris Walker Rogers was born with a patent ductus arteriosus that caused her oxygen saturation to stay dangerously low.

Paris’ parents, Marquita and Edward, worried she was too small for a PDA ligation, or surgical repair. Cardiac Interventionalist Shyam Sathanandam, MD, proposed repairing the PDA with a transcatheter technique. At 2.03 kilograms (kg), Paris was half the size of many babies who undergo the procedure.

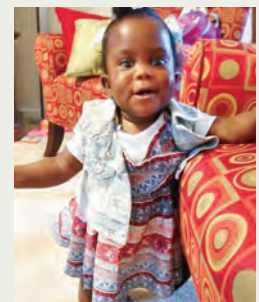
“Small preemie babies have tiny blood vessels which makes the trans-catheter device closure of PDA a challenging technique,” Shyam said.

Because the procedure is performed in the cath lab, preemies benefit from the less invasive procedure, which often shortens their length of stay in the hospital.

Today, Paris is a healthy, typical 15-month-old with no lasting effects of her early days in the hospital.

“We are so thankful for Dr. Shyam and the entire Le Bonheur staff. We believe this surgery saved her life,” said Marquita. “Her little body was just so fragile, I don’t believe she would have survived a more invasive surgery.”

To date, Shyam and his team have performed 17 PDA closures on children who weigh less than 2.5 kgs, eight of whom are between 1-1.5kg.





## Jack Crowell: 2, hypoplastic left heart



It's rare to miss a prenatal Hypoplastic Left Heart Syndrome diagnosis. But that was little comfort to Saralyn and Mark Crowell. The Crowells had expected a normal birth of their first child, Jack. Instead, shortly after his delivery, they were learning about hypoplastic left heart, a congenital defect that causes the left ventricle of the heart to be underdeveloped. He would need three surgeries to reconfigure blood flow to his heart.

At six days old, Jack underwent the first of those surgeries, a Norwood, which involves atrial septectomy and transection and ligation of the distal main pulmonary artery.

"Those first four months, we worried and were so concerned," said Saralyn. "Drs. Knott-Craig (Jack's surgeon) and Ballweg (Jack's cardiologist) gave us their phone numbers and helped us through that period. They were a huge security blanket."

At 4 months of age, Jack underwent the second surgery – a bi-directional Glenn – to divert half of the blood to the lungs, as circulation through the lungs no longer needed as much pressure from the ventricle. Jack's shunt to his pulmonary arteries was disconnected, and his right pulmonary artery was connected directly to the superior vena cava.

Finally, this past summer, when Jack was 2 ½ years old, he underwent the final procedure, a Fontan. In the Fontan, surgeons connected the inferior vena cava to the pulmonary artery by creating a channel to direct blood to the pulmonary artery. Now, all deoxygenated blood flows through the lungs passively.

One month post-surgery, Saralyn said she has already noticed Jack's appetite and energy improving.



Watch Jack's story –  
[www.lebonheur.org/promise](http://www.lebonheur.org/promise)

muscle disease," Towbin said. "We've used that to enable us to understand what other genes and proteins might be causative of cardiomyopathies, heart failure and sudden death."

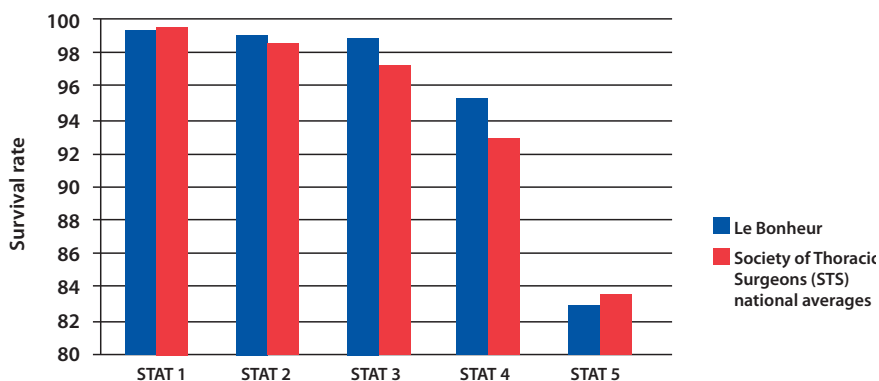
Towbin plans to grow the research program to focus more on personalized medicine for congenital heart disease and cardiomyopathies.

In addition to expanding research and destination programs, Le Bonheur will also develop a transplant program under the leadership of Dr. Towbin and newly recruited Boston, the surgical director of heart transplant and mechanical circulatory support. In August, Boston was named Le Bonheur's new surgical director of Heart Failure and Cardiac Transplantation and surgical director of the Adult Congenital Heart Disease program.

Boston comes to Le Bonheur from Washington University in St. Louis and St. Louis Children's Hospital, where he served as a pediatric cardiothoracic surgeon. His expertise is in heart transplantation, mechanical circulatory support, adult congenital heart disease and neonatal/childhood cardiac surgery.

"Drs. Fagan and Boston will help build services that we know children in our region and beyond need," Towbin said. "They are the first of several new physicians and physician scientists that we plan to bring to Memphis in the next few months."

Operative Survival by STAT Category, Jan. 2011 - Dec. 2014







## A FOUNDATION LAID

That willingness to look forward and find new approaches to care is what attracted Heart Institute Co-director and Cardiovascular Surgeon Christopher Knott-Craig, MD, to Le Bonheur in 2008. Knott-Craig, a pioneer in congenital heart repair in neonates, brought a holistic approach to post-surgical care that paid great attention to mitigating pain.

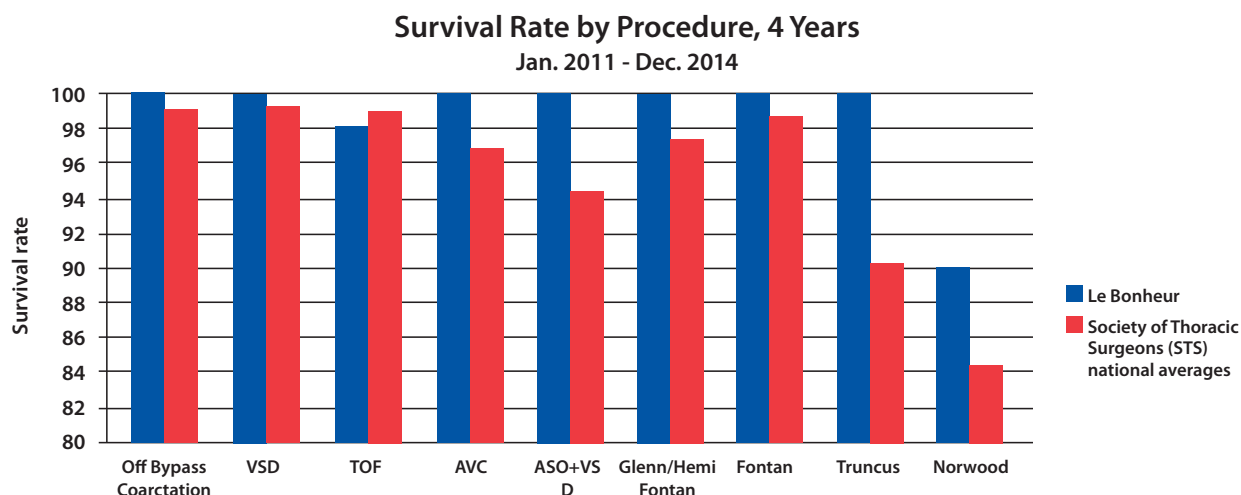
Expert surgical technique was coupled with great attention to the patient's five senses – lights were set low, classical music was often played, and parents were encouraged to climb into bed with their children to keep them calm. Patients also are given continuous infusions

of low-dose pain medications — all tactics that helped patients stay comfortable after surgery, and in turn, heal faster.

Meanwhile, in Le Bonheur's hybrid catheterization lab – where surgical and intravascular procedures occur sequentially or simultaneously — interventional specialists from cardiology, radiology and neurology are finding more ways to provide minimally invasive surgical interventions.

Those interventions include:

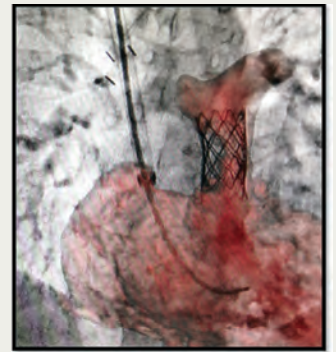
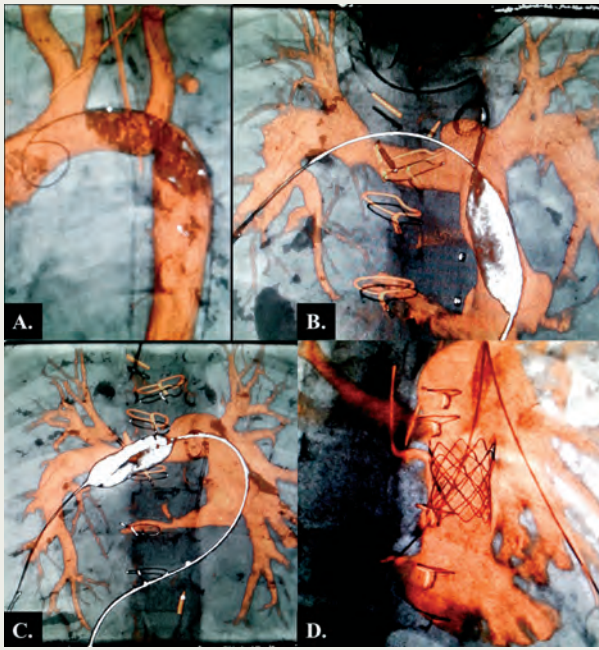
- Device insertions such as Melody® transcatheter pulmonary valve implantations and Pipeline® embolization for brain aneurysms
- Implantable loop recorders for long-term arrhythmia monitoring
- Embolization and sclerotherapy for vascular anomalies
- Complex Fontan stenting to redirect hepatic blood to the pulmonary arteries
- Device closure of patent ductus arteriosus in premature neonates
- Arrhythmia ablations
- Other complex endovascular interventions



*Le Bonheur's Heart Institute measures quality using data compiled by the Society of Thoracic Surgeons, or STS. STS collects data from other top pediatric heart programs in the country and publishes that information twice a year. The average survival rates for the majority of heart surgeries at Le Bonheur are higher than the national average — especially in the most complex procedures, like the Norwood.*



# Multi-Modality Fusion Imaging in the Cardiac Cath Lab



Fusion using 3D-MRI image on 2D-Fluoroscopic imaging can be used in stent implantation in right ventricle to pulmonary artery conduits. Multi-modality Fusion helps to show the difference in pre- and post-conduit diameters.

Multimodality fusion technology allows interventional cardiologists to reduce radiation exposure and accurately navigate in the cath lab.

Scans show images from:

- A.** Balloon angioplasty of recurrent coarctation of the aorta (LAO 60°)
- B.** Balloon angioplasty of stenosis in right ventricle to pulmonary artery conduit in a patient with tetralogy of Fallot (LAO 15° and Cranial 35°)
- C.** Balloon angioplasty of stenosis in the right pulmonary artery (RAO 15° and Cranial 15°)
- D.** Trans-catheter pulmonary valve implantation in a patient status post a Ross procedure with pulmonary homograft stenosis and regurgitation (RAO 10° and Cranial 40°)





“As technology develops, we want to bring more novel treatments into the cath lab,” Fagan said. “Technology is rapidly allowing us to change how we approach the care we offer there.”

Interventional Cardiologists Shyam Sathanandam, MD, and Rush Waller, MD, have also been working to reduce the amount of radiation patients undergo by using multimodality fusion technology that combines CT and MR images with fluoroscopic images. As a pilot site for Toshiba, Le Bonheur is helping develop the use of fusion imagery to allow real-time navigation in the catheterization lab for patients with congenital heart defects.

Heart Institute leaders expect exponential growth in the next few years, with the foundation of new approaches and the addition of new programs. They are currently developing expansion plans for a campus that include 10 additional CVICU beds, 20-30 more cardiology beds and two additional catheterization suites.

As children and adults living with congenital heart defects and cardiomyopathies look for subspecialized care, Le Bonheur will build programs that meet those needs.

That news is music to Memphian Mark Crowell’s ears. He thinks often of the care that Jack will need beyond today – and hopes for advancements in congenital heart defect medicine that can promise his son a long, healthy life. His hope, he says, is that those advancements can be found at Le Bonheur. And they’ll be waiting on Jack when he needs them most.



*Pediatric Cardiologist Mayte Figueroa, MD, is part of the team caring for a growing number of children and adults with congenital heart disease.*

## William Gomez: 6, hypertrophic cardiomyopathy



At 6 years old, William Gomez already has a medical history longer than most adults: NICU stay at birth; formal diagnosis of hypertrophic cardiomyopathy at 22 months of age; cardiac arrest at age 4. His parents, Rich and Anne Gomez of San Pedro, Calif., spent hours researching options for their son, as they grew to understand the complexity of his disease.

They would eventually hear a more official diagnosis: Hypertrophic/restrictive cardiomyopathy form of biventricular non-compaction cardiomyopathy with systolic and diastolic dysfunction and LV dilation.

William’s team of cardiologists is scattered across the country – pieced together to care for his complex and rare condition: an electrophysiologist, general pediatric cardiologist and even, for a time, a specialist in adult and adolescent cardiomyopathy. William needed something more, they decided. They asked other parents who are members of his Children’s Cardiomyopathy Foundation listserve for advice.

“I kept hearing the name of Dr. Towbin over and over again,” Rich said. “This is the guy we have got to go see. I called and talked to his nurse. In an hour, he called me back and talked to me for 40 minutes. The next thing you know, we have an appointment in Memphis.”

The Gomez family was immediately impressed with their interaction with Towbin and with his expertise in William’s condition. They were reassured that the trip across the country was a good decision.

Since that call, the Gomez family has visited Memphis and Dr. Towbin. William continues on a drug therapy aimed at improving the relaxation of the heart and improving its efficiency with the goal of not requiring heart transplantation and preventing sudden life-threatening events.





# Gastroenterologist builds comprehensive program

**M**ark R. Corkins, MD, saw potential in Le Bonheur Children's Hospital's Pediatric Gastroenterology program. Hospital leadership knew the importance of growing the program, and much of the infrastructure – including a newly built hospital – was already in place. So he committed to lead the program and take it to the next level – moving from Riley Hospital for Children at Indiana University Health to Memphis, Tenn., in 2011.

Nearly five years later, Corkins – a veteran pediatric gastroenterologist with a special focus on nutrition – has expanded the program's research, teaching and clinical efforts, making it a sought-after program for pediatric gastrointestinal and liver issues.

"The idea of building and growing and developing and making something better, that's exciting to me. I love potential with a little challenge in it," Corkins said.

One of his first steps toward advancing the program was recruiting additional expertise, including three new physicians and a nurse practitioner trained in pediatric

gastroenterology care. This summer, the program welcomed its first pediatric gastroenterology fellow.

Under Corkins' leadership, the team has also added a handful of specialized clinics to the program's offerings, increasing access for children with gastrointestinal and liver disease and creating a more coordinated plan of care for patients.

Cary Cavender, MD, who joined the team in 2013, co-leads a newly formed multidisciplinary Eosinophilic Esophagitis Clinic. Cavender works alongside a Le Bonheur pediatric allergist/immunologist to care for children with this condi-

tion, which causes allergic inflammation of the esophagus.

For children with short bowel issues, CIRCLe (Children's Intestinal Rehab Clinic at Le Bonheur) Clinic



Division Chief of Pediatric Gastroenterology, Le Bonheur Children's Hospital  
and the University of Tennessee Health Science Center

Professor and Director, Pediatric Gastroenterology Fellowship,  
The University of Tennessee Health Science Center

Consultant, St. Jude Children's Research Hospital



offers patients access to a gastroenterologist, surgeon, dietitian and pharmacist – all in one setting. The CIRCLE Clinic was named the American Society for Parenteral and Enteral Nutrition (ASPEN)'s Clinical Nutrition Team of Distinction, an honor that recognizes excellence in interdisciplinary clinical nutrition practice.

Each of the program's clinics focuses on using more advanced forms of testing, including Bravo pH monitoring to measure acid reflux in the esophagus and the pill cam – a swallowable camera that captures images of the gastrointestinal tract.

A larger team and focused clinics have allowed the division to expand their research efforts as well. Le Bonheur is home to The Morgan Foundation, which supports the research of primary sclerosing cholangitis (PSC), a rare liver disease. Other current research projects include the

national Sustain™ database for patients on at-home nutrition support, the national Improve Care Now network for inflammatory bowel diseases and research focused on

better understanding of eosinophilic esophagitis.

"We're not only caring for our patients, but we're also improving that care and finding better ways to treat them," said Corkins.

As a Certified Nutrition Support Clinician®, Corkins has a special interest in nutrition issues,

which is woven into the care of every GI patient.

Next steps, says Corkins, include adding more physicians and nurse practitioners to the group. Corkins wants to grow the research infrastruc-

ture and with that, the opportunity to make big impacts for children living with gastrointestinal problems.

"When families come back to you and thank you for helping them – that's the rewarding part," said Corkins. "I tell them I'm just doing my job. I like being Dr. Mark."



*"The idea of building and growing and developing and making something better, that's exciting to me."*

Mark R. Corkins, MD

## Mark R. Corkins, MD

### Education and Training

- Medical School: University of Missouri, Columbia School of Medicine
- Pediatrics Residency: University of Iowa Hospital and Clinics
- Pediatric Gastroenterology Fellowship: University of Nebraska Medical Center/Creighton University

### Clinical and Research Focus

- nutrition
- short bowel syndrome
- nutrition monitoring and access issues





# FIRST LINE OF DEFENSE

*Researchers find long-term potential for tuberous sclerosis drug*

Pediatric Nephrologist John Bissler, MD, is changing the face of treatment for tuberous sclerosis patients living with tumors, elevating drug therapy to the top of the list of proven treatments.

A long-term, multi-center follow-up study of tuberous sclerosis (TS) and lymphangioleiomyomatosis (LAM) patients on mammalian target of rapamycin (mTOR) inhibitors for a renal

angiomyolipoma proves the drug is safe and effective in continuing to reduce tumor volume. The recent placebo-controlled trial, published in *Nephrology Dialysis Transplantation*, served as an



*Tuberous sclerosis patient Cynthia Allen, 29, was diagnosed in 1995. From Gore, Okla., Allen travels to Memphis for regular check-ups with Nephrologist John Bissler, MD. Allen has been taking AFINITOR® since February for tubers on her kidneys and liver.*

open-label extension of a primary analysis of mTOR inhibitor treatment for renal angiomyolipoma. Bissler is a principal author of the study.

Bissler serves as co-director of

Le Bonheur Children's TS Center of Excellence and has long been focused on clinical trials. His tumor therapy work began 10 years ago with the discovery that mTOR could successfully reduce the volume of a renal angiomyolipoma. The type of tumor, found in 80 percent of patients with TS, poses a risk

of aneurysm and hemorrhage if left untreated. The drug had a similar effect on subependymal giant cell astrocytoma (SEGA) brain tumors and on patients with sporadic lymphangioleiomyomatosis (LAM), a rare lung disease that, like TS, causes benign tumor growth. The original trial was published by Bissler in the

*New England Journal of Medicine* in 2008 and followed patients on sirolimus. In a 2013 follow-up *Lancet* study, more than 40 percent of patients achieved at least a 50 percent reduction in tumor volume

angiomyolipoma. Patients initially were prescribed a daily 10-milligram dose and adjusted based on tolerability.

"Patients were continuing to achieve tumor reduction on the drug,"

said Bissler. "The longer patients were on treatment, the more their tumor shrank."

Nearly 82 percent of patients saw an angiomyolipoma reduction of 30 percent or more, and 64.5 percent of patients achieved tumor reduction of 50 percent or more by week 96. Side effects on the drug were minimal and



*John Bissler, MD, has spent much of his career working to find treatment options for patients like Chloe Bredeson, 9, with tuberous sclerosis. His latest clinical trials have focused on mTOR inhibitors for the treatment of renal and other tumors.*

on everolimus after a 12-week period.

"We knew this type of treatment works. We wanted to determine efficacy and tolerability in the long term," said Bissler.

Bissler's most recent trial examined long-term results (average 28.9 months) for 112 patients on everolimus for an

manageable.

Families like the Bredesons of South Carolina can attest to the effectiveness of the treatment. Their 9-year-old daughter, Chloe, began seeing Bissler after she was diagnosed with TS in 2010 and has been taking AFINITOR® (everolimus) since 2012. The drug has



## Case study: Chloe Bredeson, 9

### *Tuberous sclerosis, polycystic kidney disease*

The seizures started just before her fourth birthday.

"Her eye would twitch, and her mouth pulled up," said Amy Bredeson, mom to tuberous sclerosis patient Chloe.

The Bredesons spent four days at a children's hospital near their South Carolina home as doctors ran tests to determine the cause. An MRI revealed tubers in Chloe's brain. Her diagnosis: tuberous sclerosis complex. A disease the family had never heard of before.

When they posted an update to Facebook with Chloe's new diagnosis, they asked family and friends to go easy on the questions.

"It was overwhelming. We did a lot of online research," said Amy.

The Bredesons were eventually referred to Pediatric Nephrologist John Bissler, MD, at Cincinnati Children's Hospital Medical Center. The family followed him to Le Bonheur Children's, where he was recruited to lead the hospital's TSC Center of Excellence in 2013.

"Chloe loved Dr. Bissler right away. When we heard he was leaving Cincinnati, it was a pretty easy decision to follow him to Memphis. Chloe's kidneys are much more affected than any other part of her body, and we knew Dr. Bissler was the best in the field. I had also heard that Dr. Wheless was a wonderful neurologist, so it was a no-brainer," said Amy.

Chloe has five tubers, several subependymal nodules and one subependymal giant cell astrocytoma (SEGA). She also has polycystic kidney disease – a condition that will eventually cause her to need a kidney transplant. Chloe started taking AFINITOR® in 2012 to prevent the SEGA from growing. Bissler also credits the drug for improving her polycystic kidneys.

"At first we thought Chloe might need a kidney transplant by her teens or 20s," said Amy. "Now we might have until her 30s. Her kidneys are looking better and better."



Her parents and clinicians call her Super Chloe. Chloe Bredeson, 9, was diagnosed with tuberous sclerosis five years ago, but with her spirit and attitude, you'd never know, says mom Amy. "She's brave. Instead of being scared to go to the hospital, she looks forward to seeing her doctors and nurses," Amy said.

prevented further growth of a SEGA in Chloe's brain and has helped improve her polycystic kidneys.

"Chloe has done very well, and the treatment has really helped her," Bissler said.

Bissler says the drug is also thought to help improve seizure activity and improve neurocognition in patients with TS. Now that the drug has received Food and Drug Administration approval as a first line of treatment for TS, researchers are working toward the next step: finding a less invasive way to measure tumor volume.

"As the genetic and cell biology of tuberous sclerosis complex becomes more understood, therapies like mTORC1 inhibitors emerge. Finding better treatments and preventive therapies for patients is a critical goal of the TS Center of Excellence," said Bissler.

Bissler JJ, Kingswood JC, Radzikowska E, Zonnenberg BA, Frost M, Belousova E, Sauter M, Nonomura N, Brakemeier S, de Vries PJ, Berkowitz N, Miao S, Segal S, Peyrard S, Budde K. Everolimus for renal angiomyolipoma in patients with tuberous sclerosis complex or sporadic lymphangioleiomyomatosis: extension of a randomized controlled trial. *Nephrol Dial Transplant*. 2015 Jul 8. [Epub ahead of print].





Nashville mom Leslie Meehan used the Tennessee Breastfeeding Hotline as a resource throughout the first eight months of her son, Ethan's, life. She credits the hotline's lactation consultants for helping her meet her goal: to breastfeed Ethan for at least one year.

# CALLING FOR SUPPORT

*24-hour hotline aims to improve state's breastfeeding rate*

**V**eteran mom Leslie Meehan made her first call to the Tennessee Breastfeeding Hotline at 2 a.m. After successfully breastfeeding her first-born son for 13 months, she was surprised to have such a different experience with her 4-day-old son, Ethan. She wasn't producing enough milk and started to panic.

"My son was having a hard time transferring milk and wasn't getting much. My supply started to suffer and I worried about dehydration," said Meehan.

Meehan, who learned about the hotline on a

***"It was such a relief to know that I could call from anywhere at any time of day or night and on the weekends."***

Leslie Meehan

brochure she was given in her hospital's labor and delivery unit, continued to use the hotline – staffed solely

with Le Bonheur Children's Hospital certified lactation consultants – for the next eight months. She credits the consultants for offering the evidence-based information and moral support she needed to continue breastfeeding

her son for the first year of his life. She's one of thousands of mothers and caregivers across the state turning to Tennessee's free, 24-hour telephonic breastfeeding support program to help them tackle the challenges of

breastfeeding.

Le Bonheur Children's Hospital is using a five-year grant from the Tennessee Department of Health to operate the Tennessee Breastfeeding Hotline, which launched in September 2013. Tennessee breastfeeding rates are significantly below the national average. In Tennessee, only 14.8 percent of mothers were breastfeeding at 12 months, compared to a national average of 26.7 percent. The service provides nursing mothers, their families and partners, expectant parents and health care providers 24-hour access to certified lactation consultants and counselors. Those counselors offer strategies to empower clients to breastfeed, identify barriers to successful breastfeeding and provide techniques to cope with and overcome barriers to breastfeeding.

"We know breastfeeding is important because babies who are breastfed tend to have fewer infections and are at a lower risk for asthma, type I and type II diabetes and other issues," said Allison Stiles, MD, the program's medical consultant.

The hotline has received more than 5,200 calls for help with issues ranging from medication use to breast or nipple pain and latching.

While most of the calls are from first-time callers, 25 to 30 percent of callers, like Meehan, use the hotline repeatedly.

"Our hotline is continually being used for a variety of breastfeeding issues and challenges. Mothers and caregivers are showing they need this type of support,"

said Helen Scott, RN/IBCLC/RLC, hotline program coordinator.

After the hotline's lactation counselors helped her overcome the supply issue that prompted the first call, Meehan had more questions weeks later when a prescribed medication left her unable to exclusively breastfeed Ethan. And then more questions months later when she returned to work and began using a breast pump and bottle feeding. A lactation consultant was there each time to offer support and strategies to resolve her issues – sometimes on the weekends, and sometimes in the middle of the night.

"It was such a relief to know that I could call from



Allison Stiles, MD, serves as the hotline's medical consultant. In her role, Stiles reviews a select number of callers' charts each month.

anywhere at any time of day or night and on the weekends," said Meehan. "The medical advice I was given is one thing, but you can't put a value on the moral support the hotline provided me."



## REMOVING BARRIERS TO BREASTFEEDING

With her first child, Sean, Meehan visited a lactation consultant near her home. She had to pay out-of-pocket for the visit; it cost her \$150. At the time, she wondered what she would do if she couldn't afford such a service. Considered educational by many insurance companies, lactation consultation is not a covered benefit of many insurance carriers in the state.

"If a woman wants to visit a lactation consultant, she must make an appointment, prepare to spend \$150 for each visit out-of-pocket, and must take her child to the appointment, during which time the baby may be asleep or not hungry," said Meehan. "The Tennessee Breastfeeding Hotline alleviates the financial, scheduling and transportation burdens. Women can call 24 hours a day."

Le Bonheur staffs the hotline with a team of 10 international board-certified lactation consultants (IBCLC) and certified lactation counselors (CLC). They work in four-, eight- and 12-hour shifts on weekdays, weekends and nights, answering calls in the office and at home. It's a rewarding job, says Victoria Roselli, BS, IBCLC, RLC, who became an international board-certified lactation consultant in 2010.

Like others on her team, Roselli has a passion for maternal and child health. She worked in a hospital labor and delivery unit while finishing school and is a trained doula and Lamaze instructor.

"I know the benefits of breastfeeding for both mothers and babies, and it's incredibly rewarding to know you're helping support a mother's breastfeeding goals. Moms need that support," said Roselli.

When necessary, lactation consultants are able to refer callers to additional resources or to a physician for further help. The hotline offers interpretive services



Le Bonheur Children's Hospital staffs the hotline with a team of 10 international board-certified lactation consultants (IBCLC) and certified lactation counselors (CLC). Staff members like Lactation Counselor Crystal Gilreath, MS, CLS, ensure the calls are answered around the clock and that each caller receives at least one follow-up call.

for more than 200 languages, and special operators are available to assist hearing-impaired callers.

## TRACKING IMPROVEMENTS

Le Bonheur tracks data from each call, recording information like the reason for the call, the baby's age and method of delivery, as well as the caller's age, location and ethnicity. Consultants provide a follow-up to each mom at four-, eight- and 12-weeks after the initial call. Some callers whose issues require additional support and encouragement receive a follow-up call after 24 hours. Follow-ups gauge a client's confidence in breastfeeding, intent to continue breastfeeding and whether their issue has improved. The caller is asked two survey questions: "How satisfied are you with the hotline?" and "How likely are you to refer someone to the hotline?"

Results, thus far, are promising. In the program's seventh quarter, 77.7 percent of clients were still breastfeeding 12 weeks after their initial call, and 90 percent of callers said they felt an increased confidence and

comfort level with breastfeeding. Data also showed that the majority of callers' issues improved with the lactation consultant's advice.

Only in its second year, the Tennessee Breastfeeding Hotline will continue to track data to ensure the state is making strides in its primary goal: to foster the healthy development of children by promoting and supporting the practice of breastfeeding in Tennessee.

"Breastfeeding is widely accepted as an effective

strategy to promote positive health outcomes for both mothers and their babies," said Scott. "Despite growing data on these benefits, 25.1 percent of babies born in Tennessee in 2011 were never breastfed. We're working to foster the healthy development of children in our state by promoting and supporting breastfeeding mothers and caregivers – and in doing so, we're increasing breastfeeding rates in Tennessee. We're making a difference."

Top 10 Reasons for Calling	April	May	June	7th Quarter Total	7th Quarter Percentage
Medications and breastfeeding	54	53	49	156	13.2%
Not making enough milk	53	50	53	156	13.2%
Breast or nipple pain	27	27	56	110	9.3%
Breast engorgement	29	28	25	82	7.0%
Baby feeding too much/too little	25	27	24	76	6.4%
Sore nipples	20	18	26	64	5.4%
Appropriate feeding by age/weight	18	23	15	56	4.7%
Breastfeeding technique	20	22	14	56	4.7%
Breast pumps and rentals	15	14	25	54	4.6%
Weaning	13	15	17	45	3.8%
<b>TOTALS:</b>	<b>274</b>	<b>277</b>	<b>304</b>	<b>855</b>	<b>72.5%</b>

In the program's seventh quarter, the majority of calls (13.2 percent) were made for questions about medications and breastfeeding.

	Calls Attempted	Not Reached	Reached	Answered Question	Still Breast-feeding	Percentage Still Breast-feeding
24 hour follow-up	-	-	74	74	71	95.9%
4 week follow-up	779	549	230	221	177	80.1%
8 week follow-up	665	498	167	155	132	85.2%
12 week follow-up	632	492	140	130	101	77.7%

In the program's seventh quarter, more than 77 percent of callers were still breastfeeding at the time of their 12-week follow-up phone call.



## Briefs

### Le Bonheur Children's adds dermatology, endocrinology chiefs

Teresa Wright, MD, was recently named chief of Pediatric Dermatology for Le Bonheur Children's. Wright comes to Memphis from Texas Children's Hospital, where she served as section chief of Pediatric Dermatology, co-director of the hospital's Vascular Anomalies program and director of the Pediatric Dermatology Fellowship training program. Wright studied medicine at the University of Massachusetts Medical Center and completed fellowship training in pediatric dermatology at Children's Mercy Hospitals and Clinics. She has special interest and expertise in the diagnosis and management of hemangiomas and other vascular skin lesions.



Teresa Wright, MD

Ramin Alemzadeh, MD, joined Le Bonheur Children's as chief of Pediatric Endocrinology. He most recently served as chief for the University of Illinois-Chicago's Division of Pediatric Endocrinology and Diabetes. Alemzadeh completed a fellowship in pediatric endocrinology, metabolism and nutrition at North Shore University Hospital/Cornell University Medical College. He attended medical school at St. George's University School of Medicine in the West Indies. He specializes in the management of type 1 and type 2 diabetes, lipid disorders, metabolic bone disorders, polycystic ovary syndrome, disorders of growth and puberty and adrenal disorders.



Ramin Alemzadeh, MD

### Knott-Craig inducted to American Association for Thoracic Surgery

Christopher Knott-Craig, MD, co-director of the Le Bonheur Heart Institute, was recently inducted to the American Association for Thoracic Surgery during its 95th annual meeting in Seattle. Specific qualifications reviewed for membership include accomplishments in clinical performance, professional stature, professional conduct, leadership advancing the discipline and contributions to surgical literature in English language peer-reviewed journals. Active membership is limited to 850 members.



Christopher Knott-Craig, MD

### Boop named president-elect of the American Association of Neurological Surgeons

Semmes-Murphey Pediatric Neurosurgeon Frederick Boop, MD, has been named president-elect of the American Association of Neurological Surgeons (AANS). Boop serves as co-director of Le Bonheur's Neuroscience Institute and



Frederick Boop, MD

professor and chairman of the Department of Neurosurgery for the University of Tennessee Health Science Center. His appointment was announced during the 83rd AANS Annual Scientific Meeting, held in Washington, D.C., May 2-6, 2015.

### CHAMP receives EPA's Environmental Leadership award

Le Bonheur Children's Hospital's CHAMP program – Changing High Risk Asthma in Memphis through Partnership – recently received the 2015 National Environmental Leadership Award in Asthma Management from the Environmental Protection Agency (EPA). The award is EPA's highest recognition program, honoring health care providers and community programs for excellence and success in helping people with asthma lead healthy, active lives.



Le Bonheur created CHAMP in 2013, thanks to a \$2.9 million Health Care Innovations award from the Centers for Medicare and Medicaid. The program is focused on reducing asthma-related hospitalizations and emergency room visits.

### RIVUR study receives Clinical Research Forum Top 10 award

The RIVUR study's primary outcome paper, "Antimicrobial prophylaxis for children with vesicoureteral reflux," recently received a 2015 Clinical Research Forum Top 10 Clinical Research Achievement Award. This annual national competition seeks to identify major advances resulting from the nation's investment in research to benefit the health and welfare of its citizens. Late Le Bonheur Nephrologist and former Pediatrician-in-Chief Russell Chesney, MD, co-authored the study, which was published in the *New England Journal of Medicine*.

### Pershad publishes commentary on IV ketamine bolus

Jay Pershad, MD, medical director of Le Bonheur's PediFlight Transport and Transfer Center, published an expert commentary on the role of ketamine when administered as an intravenous bolus to facilitate fracture reduction in the pediatric emergency department. The editorial, "Intravenous Ketamine Bolus: Not So Fast!", was published in the May online issue of the *Annals of Emergency Medicine*.



Jay Pershad, MD

## Study finds ER stress, innate sensing of viruses cause acute lung injury

Cellular stress resulting from recognition of proteins from pandemic influenza viruses activates immune responses through a novel innate sensor, according to recent research led by Le Bonheur Children's researcher Jon McCullers, MD. The study – "Acute Lung Injury Results from Innate Sensing of Viruses by an ER Stress Pathway" – was published in the June issue of *Cell Reports*. McCullers and his team examined the molecular underpinnings of immune recognition, host responses and pathogenesis of pandemic influenza viruses. The team determined the mechanism by which addition of sugars to viral proteins during evolution in humans results in diminished pathogenicity in adapted viruses. Findings showed that infection with pandemic strains with few sugars activated a response known as endoplasmic reticulum (ER) stress – leading to

inflammation, injury of the lungs and mortality. Seasonal influenza strains or viruses engineered to mimic adapted viruses displaying excess sugars on the viral proteins did not cause ER stress, allowing preservation of the lungs and survival. McCullers says that understanding this mechanism should improve strategies for treating pneumonia caused by zoonotic viral infections including influenza. McCullers, an infectious disease specialist and world-renowned influenza researcher, serves as pediatrician in chief for Le Bonheur Children's Hospital.

*Hrincius ER, Liedmann S2, Finkelstein D3, Vogel P4, Ganseboom S1, Samarasinghe AES, You D5, Cormier SAS, McCullers JA6. Cell Rep. 2015 Jun 16;11(10):1591-603. doi: 10.1016/j.celrep.2015.05.012. Epub 2015 Jun 4. Acute Lung Injury Results from Innate Sensing of Viruses by an ER Stress Pathway.*

## Biorepository opens doors to new discoveries

**L**e Bonheur Children's Hospital is one of a handful of children's hospitals nationwide to establish a research biorepository – a place where patient DNA is collected and stored for future research studies.

The project – called the Biorepository and Integrative Genomics (BIG) initiative – provides a unique opportunity to focus on minority health issues and disparities because of Memphis' pediatric population, Children's Foundation Research Institute researcher David Hains, MD, a pediatric nephrologist said.

"We have a lot of children in the Memphis area who potentially could be overlooked by some of the bigger repositories," said Hains. "By launching this initiative in Memphis, we ensure that everyone in the United States will be represented in genetic research. Furthermore, a unique population will likely yield unique results."

All patients admitted to Le Bonheur Children's are asked if they would like to donate a DNA sample to the repository. If they agree, DNA is removed from leftover blood from the patient's physician-ordered blood draw and stored for future studies. This blood would otherwise be thrown away.

The BIG repository keeps the child's personal information in a confidential file to create a link between the DNA sample and medical record. Researchers will be able to get de-identified clinical data and DNA samples to perform DNA-based genomic studies.

"The research repository will provide opportunities for researchers to discover new treatments, correlations and focus on cures for future patients," said Hains. "We are excited to be on the frontier of identifying factors and improving health in groups of individuals."