PATIENT-CENTERED RESEARCH
2016 ANNUAL REPORT

Aurora Research Institute™
The information presented in this annual report is intended for general information and educational purposes. It is not intended to replace the advice of your own physician. Contact your physician if you believe you have a health problem.
President’s welcome

Aurora Research Institute has literally made a name for itself. In 2016, the Milwaukee Heart Institute moniker was retired and a new sign hoisted to the top of the building: Aurora Research Institute. This event established the institute's headquarters on the Aurora Sinai Medical Center campus, increasing exposure of the valuable research conducted throughout Aurora Health Care.

The Aurora name is not only visible from the highway, but throughout the world. Research findings are presented at major international conferences and published in renowned scientific publications. Our cardiovascular service line physician researchers have dramatically increased Aurora’s reputation through the scholarship of publication, which has helped the ranking of Aurora St. Luke’s Medical Center. One of Aurora’s distinctions includes the scientific publication Journal of Patient-Centered Research and Reviews, which continues to expand its reach with 22,500 article downloads in 2016 and readers from all 50 states and more than 160 countries.

At Aurora, research doesn’t stop with publication. Strategically positioned to align with Aurora’s major clinical service lines, the institute supports more than 500 clinical trials and investigator-initiated research studies in cardiology, oncology, neurosciences and emerging areas. These studies are conducted by dedicated clinicians and focused scientists seeking to translate research findings into the latest health care innovations. To test hypotheses that improve outcomes in cancer, aging hearts and neurological disorders, Aurora researchers in 2016 received more than $2.4 million in grants from the institute and federal, state and foundation sources.

On behalf of Aurora Research Institute and its board of directors, I am pleased to provide this highlight of our 2016 outcomes. As always, I welcome your feedback.

Helping people live well through innovative research,

Randall Lambrecht, PhD
Senior Vice President, Aurora Health Care/President, Aurora Research Institute

P.S. Please join us at the Aurora Health Care Foundation 2017 Aurora Gala on Sept. 23 benefitting research. Visit www.aurorahealthcarefoundation.org/events/aurora-gala for tickets.
Aurora Research Institute is governed by an advisory board of directors consisting of Aurora Health Care leaders who help shape the institute’s future.

**Leadership team**

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  - Neurosciences (ANII)

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  - President, Aurora Research Institute

**Board of directors**

Aurora Research Institute is governed by an advisory board of directors consisting of Aurora Health Care leaders who help shape the institute’s future.

“As a physician and CEO, I understand the roles that academic medicine, research and education play in improving the well-being of individuals and populations we serve. Aurora’s innovative research is centered on helping people live well by discovering new knowledge and translating it into ‘next-generation medicine’ through joint efforts of our clinicians and scientists.”

Nick Turkal, MD
President and CEO, Aurora Health Care
READERSHIP DOUBLES

After three years of publication, Journal of Patient-Centered Research and Reviews (JPCRR) surpassed 40,000 total article downloads, making Aurora Health Care’s medical journal one of the most frequently viewed in the Digital Commons publishing network.

With 22,500 article downloads in 2016, twice as many readers visited JPCRR’s open access website than in the previous year (bar graph). The journal’s readers hailed from all 50 states and more than 160 countries.

2016 highlights

• Annual article downloads doubled for second straight year
• Expanded global readership to more than 150 countries
• Published Health Care Systems Research Network and Aurora Scientific Day conference proceedings
• Sponsored table at North American Primary Care Research Group annual conference

JPCRR Article of the Year was awarded to Kristen Reynolds for her article, “Small Intestinal Bacterial Overgrowth: A Case-Based Review” (J Patient Cent Res Rev. 2015;2:165-173).

SPECIALTY ISSUES

JPCRR released a pair of specialty issues in 2016, the first of which focused on infectious disease. Curated by the journal’s editor-in-chief, Dennis Baumgardner, MD, this issue featured a timely editorial on Wisconsin’s *Elizabethkingia* outbreak in March. The perspective, written by Angela Tonozzi, MD, was later spotlighted in a UNESCO-published international report on the merits of open access publishing.

During a contentious presidential election year, JPCRR proudly ran a nonpartisan editorial written by Aurora Health Care CEO and longtime family physician, Nick Turkal, MD, on the importance of continued and strategic reform of U.S. health care.

The journal closed its third volume with an issue dedicated to the topic of cardiovascular aging. Guest edited by physician-researcher Arshad Jahangir, MD, articles provided an in-depth look at aging-induced physiological changes to the heart and associated cardiovascular diseases.

www.aurora.org/jpcrr

Published largely due to founding sponsor Robyn Temkin Memorial Fund, JPCRR is seeking sustaining sponsors. To make a donation, contact Michelle Schuerman at michelle.schuerman@aurora.org.
BSRC

In the past decade, Aurora Research Institute’s Biorepository and Specimen Resource Center (BSRC) has streamlined collection and processing of blood products and solid tissues from throughout Aurora Health Care, allowing investigators to advance innovative research more quickly.

The center collects leftover biospecimens from consenting research participants for the study of cancer, heart disease, neurological disorders and other ailments. More than 170,000 patients have consented to donate their specimens since BSRC’s inception nine years ago.

“BSRC gives Aurora the capability to collect specimens linked to data and to provide these specimens to researchers in a very efficient manner,” said Natalie Polinske, MS, BSRC manager.

Having amassed an inventory of more than 70,000 whole blood, plasma and serum samples, BSRC shares them with researchers to study. Hundreds of specimens have been used by Aurora researchers and, using innovative technology, thousands more have been shared with investigators throughout the country.

“Many of these studies are genome-wide association studies and studies focused on pharmacogenomics, which look at patients’ genes to determine how they will respond to a treatment,” she added.

Before the specimens are provided to researchers, de-identified clinical information on each specimen is gathered from the patient’s medical record with help from the institute’s Research Analytics team.

The center also coordinates the targeted collection of solid tissues, including tumor, organ and healthy tissue, for specific research purposes. The healthy tissue allows researchers a normal frame of reference to use when comparing the genetic makeup of various tumor types. See one woman’s story about the donation of her healthy tissue on the next page.

“BSRC has been able to establish mechanisms allowing for the collection of biospecimens from generous Aurora patients and providing them to the researchers that need them most,” Polinske said. “We are playing a key role in helping to advance health care innovations.”

A biospecimen utilization committee serves an advisory role and includes community, ethics, compliance and legal perspectives.

2016 highlights

- Expanded tissue collection studies to include new surgeons and an additional site (Grafton)
- Obtained Institutional Review Board approval for the collection of “research-use-only” biospecimens
- Distributed 171 biospecimens through 15 requests
- Signed agreement with Conversant Bio to provide biospecimens to institutions, facilities and companies for research purposes

Kujana Clayton, Brittany Last and Adriana Newson at work in Aurora Research Institute’s Biorepository and Specimen Resource Center.
LIVING WELL WHILE HELPING RESEARCH

Healthy tissue removed during breast reduction surgery is often disposed of as medical waste. At Aurora Health Care, that tissue, when given for research, is a gift that could potentially change lives.

About 4 percent of women in the U.S. undergo breast augmentation. Marie Rintelman, 47, needed to take an opposite approach. With a triple D cup size, she was experiencing complications that severely compromised her well-being.

“I was seeing a masseuse on a weekly basis, sometimes twice a week,” said the Saukville resident, whose vertebrae were beginning to fail. “I was in excruciating pain from the disks moving and all the pressure on my back.”

Her family doctor referred her to plastic surgeon Andreas Doermann, MD, in Mequon.

Dr. Doermann asked Rintelman if she wanted to donate the healthy tissue that would be removed as part of the reduction surgery to Aurora Research Institute’s Biorepository and Specimen Resource Center (BSRC).

To donate the tissue, Rintelman provided consent to research coordinator Brittany Last.

“Brittany let me know how it would be used and what they would be doing,” Rintelman said. “There was nothing to think about; of course I would. If I could help in any way to further research, it was a no-brainer.”

Looking for biomarkers and drug targets, Aurora researchers and their Minnesota collaborators at Celcuity compare molecular and genetic characteristics of healthy breast tissue to breast cancer tissue. This helps them to better understand the development of cancer for potential diagnostics and better treatments.

In August 2016, Rintelman obtained relief from her back pain through the surgery.

“My back feels great now,” Rintelman said. “It’s amazing. It changed my life.”

As her life changed, she was able to help change the lives of others.

After returning to work in September, Rintelman learned about an opportunity at Aurora Cancer Center in Grafton. Coincidentally, in November, she became a patient services representative, working with some of the patients that her donated tissue may someday benefit.
Recognitions

RESEARCH RECOGNITION EVENT
Milwaukee, Wisconsin

Award Recipients
- Heidi Zellmer, Subject Hero Award
- Shamsuddin Virani, MD, Clinical Trials Research Award
- John Richards, PhD, Translational Research Award
- Richard Rovin, MD, Principal Investigator Award
- Sarah Reimer, MD, New Investigator Award
- Nasir Sulemanjee, MD, Research Champion Award
- Aurora UW Medical Group Research Support Team (Jessica Kram, MPH, Danielle Greer, PhD)
- Kujana Clayton, Research Service Award
- Denise Coley, MS, Research Service Award
- Jovana Kuridza, Research Service Award
- Kristen Reynolds, MD, Journal of Patient-Centered Research and Reviews Article-of-the-Year Award

It takes the best people to push innovations forward. To recognize outstanding contributions to research and education, events were held throughout the year in Milwaukee and Green Bay.

Above: Focus on Innovation speakers Bijoy Khandheria (left), and Charles Bomzer (right), spoke about Aurora’s new cardio-oncology program during the Research Recognition Event.

Below: Research Recognition Event award recipients.

FALL RESEARCH AND MEDICAL EDUCATION RECEPTION - Green Bay, Wisconsin

Award Recipients
- Donald Beno, MD, Medical Educator-of-the-Year Award
- Anesthesiology, Curriculum Development in Medical Education Award
- Darren Heesacker, MD, Principal Investigator Award
- Jason DeVries, DPM, Innovation Award (Focus on Innovation speaker)
- Brandon Scharer, DPM, Innovation Award (Focus on Innovation speaker)

Fall Research and Medical Education Reception award recipients.
AURORA SCIENTIFIC DAY

Award Recipients
Rieselbach Distinguished Papers
- Michael Farrell, MD – Benefit of Report Card Feedback After Point-of-Care Assessment of Communication Quality Indicators
- Kanwar Singh, MD – Predictors of Mortality in Patients With Transient Severe Left Ventricle Systolic Dysfunction

Oral Presentations
- 1ST PLACE – Judy Tjoe, MD
  Determining Effect of Surgical Primary Tumor Extirpation in De Novo Stage IV Breast Cancer in the Era of Targeted Treatment: A Matched-Pair Analysis
- 2ND PLACE – Kushal Patel, MD
  Path to Resistance: Risk Factors Associated With Carbapenem-Resistant Pseudomonas aeruginosa
- 3RD PLACE – David Krum, MS
  3D Cardiac Mapping Using Only Single Plane Fluoroscopy

Judged Posters
- 1ST PLACE – Farhan Rizvi, PhD
  Simvastatin Prevents TGFβ1 Induced SMAD2/3 Phosphorylation in Human Ventricular Fibroblasts: Involvement of Protein Phosphatase
- 2ND PLACE TIE – Milanka Petrovic, BS
  Functional and Structural Differences in Fibroblasts from Atria of Patients With and Without Atrial Fibrillation
- 2ND PLACE TIE – Yang Shi, PhD
  The Association Between Doppler Measures of Cardiac Function and Outcomes in Patients With Left Ventricular Ejection Fraction ≤40% Undergoing Non-Cardiovascular Surgeries
- 3RD PLACE TIE – Mirza Nubair Ahmad, MD
  Aortopathy in Hypertrophic Cardiomyopathy: The Association with Dilatation of Sinus of Valsalva Versus Mid Ascending Aorta, an Epidemiological Study
- 3RD PLACE TIE – Renee Koeberl, RN
  Medtronic CareLink Express Device Usage in Midsize Emergency Department

CULTIVATING FUTURE RESEARCHERS

Sixteen students in 2016 gained valuable insights about research and supported a variety of initiatives through different internship opportunities.

Mentors primarily from Aurora Research Institute provided promising future researchers opportunities that will give them an edge as they pursue careers in medicine and other health care professions.

Aurora Research Institute Summer Student Internship Program
Led by Randall Lambrecht, PhD, and David Krum, MS

Johnathan Dzurka
Senior at Milwaukee School of Engineering
Project: Predicting clinical validity of bladder cancer nomograms
Mentor: Kourosh Ravvaz, MD, PhD

Ken Hubbard
Junior at Michigan Technological University
Project: Patient-derived xenograft models
Mentor: Amber LaCrosse, PhD

Nicholas Kluge
Senior at University of Minnesota-Twin Cities
Project: Examine association between sociodemographic and geographic factors and the development of acute kidney injury (AKI) in a community hospital setting
Mentors: Han-Yang Chen, PhD, Andy Marek

Richard Krajewski
Graduate student at Marquette University
Project: Research and health care administration: archiving process audit
Mentors: Carol Tutino, BSN, MS, Sara Planton, BSN

Kahaan Patel
Sophomore at University of Wisconsin-Madison
Project: Impact of in-house interventional cardiology team for treatment of anterior wall ST-segment elevation myocardial infarction
Mentors: Suhail Allaqaband, MD, Fuad Jan, MD, Wamiq Banday, MD

Alexander Reddy
Senior at University of Wisconsin-Milwaukee
Project: Updating biorepository web application
Mentor: Andy Marek

Laura Rolfs
Junior at St. Norbert College
Project: Feasibility and clinical application of diffusion tensor imaging when visualizing white matter and muscle anatomy in neurosurgery
Mentors: Sarika Walia, MD

Jessica Sapp
Senior at Concordia University Wisconsin
Project: Internal audit
Mentor: Katie Richter

Christopher Stoming
Second-year medical student at Medical College of Wisconsin
Project: Adrenal Incidentaloma
Mentors: Ahmed Dalmar, MD, Arshad Jahangir, MD

DISTINCTIONS
Aurora Metro Medical Staff Summer Research Fellowship Program
Led by Neil Guenther, MD, and Hershel Raff, PhD
Supported by physicians who donate to Aurora Health Care Foundation’s Medical Staff Endowment Fund

Breanna Aldred
Junior at University of Miami
Project: Peroxisome proliferator-activated receptor-α, a connecting link between miR21-regulated TGFβ1 signaling and profibrotic gene transcription in cardiac fibrosis
Mentor: Farhan Rizvi, PhD

Olivia Fukui
Second-year medical student at Wake Forest School of Medicine
Project: Characterization of estrogen receptor phosphorylation pattern in malignant glioma
Mentor: Santhi Konduri, PhD

Tarun Jella
Sophomore at Case Western Reserve University
Project: Lomeguatrib MGMT inhibition enhances activity of CDK4 and CDK6 inhibitors in breast cancer
Mentor: Santhi Konduri, PhD

Emily Nelson
Senior at Hillsdale College
Project: Ranolazine protects human failing myocardium against dronedarone-induced mitochondrial dysfunction and oxidative stress
Mentor: Larisa Emeylanova, PhD

Emily Waples
Junior at Duke University
Project: Role of epigenetic changes in pancreatic islet cell function due to early-life stress on adult glucose, insulin and C-peptide response
Mentor: Hershel Raff, PhD (top photo, page 9)

Aurora BayCare Medical Center Research Internship Program
Led by Annette Paul, MAT

Alex Baek
Graduate at University of California-San Diego
Project: Supporting various research studies
Mentors: Annette Paul, MAT, and Aurora BayCare Medical Center research staff

Matt Kroll
Graduate at University of Wisconsin-Green Bay
Project: Supporting various research studies
Mentors: Annette Paul, MAT, and Aurora BayCare Medical Center research staff

University students are not the only young people who have the opportunity to learn from Aurora Health Care doctors and researchers.

Sixth- through eighth-graders from the Discovery World “Inside the Human Body” summer camp toured Aurora St. Luke’s Medical Center. The students watched a simulated brain surgery. They also learned how vessels work and about what tools surgeons use to remove tumors.

“The children saw our brand new operating room for our neurosciences program,” said Nina Garlie, PhD, an Aurora Research Institute patient-centered research director. “They were in the gallery interacting with the surgeons.”

Local media coverage of the tour included WTMJ4 and WISN12, and ABC affiliates in Madison, Wausau and Joplin, Mo., picked up the story.

WTMJ4 reported on fifth-graders from Milwaukee College Preparatory School and FOX6 on high-schoolers from Brookfield East High School who visited Aurora St. Luke’s to see a live brain surgery from the gallery. Both groups had hands-on experience with the robot in the anatomy laboratory. Srikant Chakravarthi, MD (below), led one of the groups.
GIVING MORE

Institute caregivers surpassed the previous year’s giving during Aurora Health Care Foundation’s 2016 Aurora Partnership Campaign. Available during October and November, the campaign provides a way for Aurora caregivers to support internal and external charitable funds. At the conclusion of the two-month campaign, institute caregivers pledged about $18,300, a 5 percent increase over 2015, with more than $13,000 going to Aurora funds.

The institute’s ongoing partnership with Aurora’s foundation also benefitted the Sexual Assault Treatment Center at Aurora Sinai Medical Center with a Tradition of Caring event sponsorship.

TAking strides

Through Lombardi walks in Green Bay and Milwaukee, three teams of institute caregivers, family and friends raised $12,075 for the Vince Lombardi Cancer Foundation. In partnership with Aurora Health Care Foundation, the Lombardi walks raise funds that will directly impact Aurora patients in their fight for freedom from cancer. The institute also helped sponsor the Vince Lombardi Award of Excellence Dinner Ball in April.

More than a dozen caregivers supported the institute’s team and booth at the American Heart Association 2016 Milwaukee Heart and Stroke Walk/Fun Run in Milwaukee, raising $275 to help fight heart disease and stroke. Booth visitors learned heart anatomy with animal hearts and tried their hand at pipetting, a research activity.

fulfilling wishes

Forty institute caregivers fulfilled wishes for warm clothes, action figures, dolls and more for 31 economically disadvantaged students who attend Hawthorne Elementary School through Aurora Sinai Medical Center’s Adopt-A-Student program. Institute support for the program nearly doubled from 2015 when 24 institute caregivers adopted 16 students. In total, Aurora Sinai adopted 306 Hawthorne students in 2016, donating more than 2,000 gifts.
CARDIOVASCULAR
RESEARCH

176 cardiovascular research studies as of Dec. 31, 2016

585 new subjects enrolled in cardiovascular clinical trials in 2016

141 cardiovascular publications and abstracts in 2016

DANIEL O’HAIR, MD JASBIR SRA, MD
Co-Vice Presidents, Aurora Cardiovascular Services
Aurora Health Care hosts one of the few research centers in the world devoted entirely to study the effect of aging on the cardiovascular system. The Center for Integrative Research on Cardiovascular Aging (CIRCA) is led by renowned cardiologist Arshad Jahangir, MD.

With the support of a generous $2 million donation from the late Sheikh Khalifa bin Hamad Al Thani in 2014, CIRCA’s mission is to conduct basic, translational and clinical research on the biology of cardiac aging, and to develop new ways to predict, diagnose and treat age-related cardiovascular dysfunction to preserve wellness and improve the quality of life of older people.

In Discovery Laboratory at Aurora Sinai Medical Center and the cardiovascular research laboratory at Aurora St. Luke’s Medical Center, Dr. Jahangir and the CIRCA team are studying the molecular basis for the aging heart’s decreased ability to tolerate stress and increased susceptibility to injury and heart rhythm disorders.

The CIRCA team has presented their original research at national and international conferences.

2016 CIRCA publication highlights

CIRCA researchers published original clinical, translational and bench research in several peer-reviewed journals.

**TARGETING MITOCHONDRIA TO PREVENT ATRIAL FIBRILLATION**

Atrial fibrillation (AFib) is the most common abnormal heart rhythm and increases risk for stroke, heart failure and death. Research scientist Larisa Emelyanova, PhD, and colleagues published findings in American Journal of Physiology-Heart Circulation Physiology defining changes in the function of mitochondria, which produce energy in cells, associated with AFib.

This translational research study compared atrial tissue from middle-aged and elderly patients with a history of AFib to a matched group of patients without AFib. The researchers found an association between AFib and a reduction in specific mitochondrial activity.

This study may help identify targets for therapies that prevent atrial fibrillation.

**DISCOVERING CHAMBER-SPECIFIC DIFFERENCES IN HUMANS**

Research scientist Farhan Rizvi, PhD, and colleagues published a paper in American Journal of Physiology-Cell Physiology identifying differences in responsiveness between cardiac fibroblasts from the upper and lower heart chambers. Cardiac fibroblasts, which help repair injured heart tissue by forming scar tissue, have become an intense research focus in aging-associated disease. Excessive or patchy scar tissue buildup increases risk for heart failure and AFib. No therapies effectively prevent such scar formation or progression.

The study results highlight the complexity of atrial and ventricular tissue function and their responsiveness to injury. The study provides support for development of therapies targeting atrial fibroblasts to reduce excessive scar formation after injury without significantly altering ventricular fibroblast function.

**FINDING A POTENTIAL NEW CAUSE FOR SCAR BUILDUP**

Research scientist Gracious Ross, PhD, and colleagues published a study in Biology Open comparing cardiac fibroblasts from ventricular tissue of patients with advanced heart failure to that of healthy patients. The team discovered a new cause for excessive scar buildup.

This study is an important contribution to medicine as it provides a potential new target for development of therapies to reduce fibrosis and progression of heart failure and arrhythmia in diseased hearts.
Growing beating heart cells in a dish

Research scientist Rosy Joshi-Mukherjee, PhD, and research technologist Stacie Edwards are building a cell-based program at CIRCA using induced pluripotent stem (iPS) cell technology. This revolutionary technology takes Aurora researchers closer to growing miniature beating heart tissue on which new therapies for treating cardiovascular disease can be tested in a dish. Use of this technology may reduce or eliminate the need for experimental animal models and the controversial use of embryonic stem cells in the search for new therapies to prevent and treat heart failure.

After launching the cell-based program in late 2015, the team has made progress implementing the iPS cell technology and establishing techniques to successfully grow heart cells derived from reprogrammed iPS cells. The research was presented by Dr. Joshi-Mukherjee at Gordon Research Conference on Cardiac Arrhythmia Mechanisms in Ventura, Calif., in February 2017.

After testing iPS cells for specific markers to ensure the reprogramming had been successful, Dr. Joshi-Mukherjee and her team initiated a cardiac differentiation protocol to transform the iPS cells into beating heart cells that expressed specific cardiac markers and with electrophysiological characteristics of beating cells from various chambers of the heart.

To continue this work, Dr. Joshi-Mukherjee received a $50,000 Cardiovascular Surgery Research Award. In the future, researchers plan to generate iPS cells directly from blood or skin tissues from Aurora patients, potentially leading to a precision medicine approach.
Translating care

The TAVR success story

The journey to bring a new major medical treatment to patients requires cooperation from a dedicated team of researchers, coordinators, doctors, nurses and clinical trial participants. The transcatheter aortic valve replacement (TAVR) procedure represents one success story that continues as Aurora Health Care physician researchers have become national experts on this latest advancement.

WHAT’S TAVR?

TAVR provides a less invasive alternative to open-heart surgery for patients with severe narrowing of the aortic valve who are unable to safely undergo surgery because of age or other medical conditions. Left untreated, these patients have a 50 percent risk of dying at one year.

During the procedure, the physician inserts a new valve to the heart through an artery using a catheter. Patients spend less time in the hospital because the chest cavity does not need to be opened.

AURORA’S ROLE

Aurora Research Institute played a key role in Medtronic Inc.’s CoreValve™ device being used for the TAVR procedure, participating in clinical trials that led to U.S. Food and Drug Administration (FDA) approvals in 2014 through 2016.

Aurora has been the only site in the state to participate in the clinical trials contributing to CoreValve’s approvals and the first site in the state to commercially offer the CoreValve™ device to patients after each approval.

In October 2016, the FDA approved the Evolut™ R 34-mm aortic valve in the CoreValve family, and it is currently the largest-sized TAVR system available in the U.S. Aurora enrolled more patients in this clinical trial than any other site in the country.

This large valve expands the population that can undergo the procedure. Previously, patients with larger aortic anatomy would have had to undergo open-heart surgery.

1,000TH TAVR

Since it became available through participation in a clinical trial in 2011, Aurora St. Luke’s Medical Center celebrated its 1,000th TAVR procedure Dec. 8, 2016.

A brief ceremony began when cardiologist Tanvir Bajwa, MD, and cardiovascular and thoracic surgeon Daniel O’Hair, MD, arrived just moments after completing their latest TAVR case. Drs. Bajwa and O’Hair have served as local principal investigators for the different clinical trials studying the CoreValve platform. Paul Werner, MD, and Suhail Allaqaband, MD, have assisted as subinvestigators for these trials.
CARDIOVASCULAR RESEARCH

No other health system in the country has a team that has performed as many TAVR procedures together. The team at Aurora St. Luke’s performs typically eight to 10 TAVR procedures a week with a 100 percent success rate. Physicians and government officials from around the world have visited Milwaukee to watch the Aurora St. Luke’s TAVR team in action.

1,000th TAVR event photos.

ONE MAN’S TAVR EXPERIENCE

Nonagenarian Charles Zern, volunteered to enroll in a CoreValve clinical trial in 2013.

After having hip surgery in 2010, the Wauwatosa resident developed atrial fibrillation, an irregular heartbeat, while in the hospital. Less than a year later, he was rushed to the hospital with heart failure.

Tests determined that Zern had severe aortic stenosis. He had no other major health concerns, and the surgeon determined that open-heart surgery presented an intermediate risk, despite his age of 88 years. His cardiologist sent him to Aurora St. Luke’s to see Dr. O’Hair and learn more about the TAVR clinical trial.

Wendy Dunaj, RN, manager of cardiovascular clinical trials, and Deb Waller, BSN, research coordinator, explained the clinical trial process and answered Zern’s questions regarding participation.

Zern qualified for the SURTAVI clinical trial (NCT01586910), but his treatment assignment would be comparable to flipping a coin to either open-heart surgery or TAVR. After being randomly selected, Zern underwent TAVR on July 8, 2013. Dr. Bajwa and Dr. O’Hair performed the procedure together.

Zern said that he would do it all again in a heartbeat. He is happy that his participation in this clinical trial could help others. He is about halfway through his clinical trial participation. Researchers will follow him for another two years.

“I feel fine now, but I get a little short of breath because of the heart failure,” Zern said. “The best part of the whole experience is that I am still here.”

Zern will celebrate his 92nd birthday in June 2017 and is planning a train trip across the Canadian countryside.

“I wouldn’t be here if it weren’t for Dr. Bajwa and Dr. O’Hair,” Zern said. “They are absolutely the top. They not only have an interest, they care.”

Zern’s experience should not be used to predict outcomes of the clinical trial or the procedure. Data collection continues.
For a medical device to become available for widespread use in the United States, generally it must first be cleared by the Food and Drug Administration (FDA). Clinical trial results help the FDA determine whether a device should be cleared. In addition to TAVR (see pages 15-16), Aurora Health Care participated in clinical trials that led to FDA approval of five other heart health innovations in 2016.

**Bioresorbable stent**

Aurora St. Luke’s Medical Center became one of the first sites in the nation to implant the Abbott Absorb bioresorbable stent, approved by the FDA in July 2016 for patients with coronary artery disease. Affecting 15 million people in the U.S. alone, coronary artery disease is the leading cause of death worldwide.

Aurora researchers first studied the stent through a Phase III clinical trial sponsored by Abbott (clinicaltrials.gov identifier: NCT01751906). Aurora St. Luke’s was the only site in the state to participate in the trial. Now the stent is available for widespread use.

“It [the bioresorbable stent] supports the artery for a period of time and then, in about three years, it dissolves and disappears,” said Suhail Allaqaband, MD, local principal investigator. “A game changer in the treatment of clogged arteries.”

Before the advent of the bioresorbable stent, interventional cardiologists used only metal stents that remained in place for the rest of the person’s life, all the while restricting vessel motion. Dr. Allaqaband said the lack of metal will simplify future heart surgeries. It also promotes healing and enlarges the artery.

Data collection for the clinical trial continues. Don Lobacz, RN, is site coordinator.

**Preventing stroke recurrence**

Blood clots can travel to the brain through a hole in the heart called a patent foramen ovale (PFO) and cause stroke. This hole often isn’t found until a stroke has occurred. For more than 10 years, Aurora researchers have participated in clinical trials to study PFO closure devices, including the St. Jude Medical Amplatzer PFO Occluder, hoping to reduce stroke recurrence.

In October 2016, the FDA approved the use of the occluder, a device implanted nonsurgically, and in mid-November, interventional cardiologist Tanvir Bajwa, MD, became the first in Wisconsin to implant the approved device.

“The recent FDA approval of the PFO Occluder brings new hope for patients ages 18 to 60 with cryptogenic stroke who may be seeking alternative treatment options for prevention,” Dr. Bajwa said. “Being the first hospital in the state to provide this new device to patients builds on our commitment to innovation and providing the best in patient care.”

Dr. Bajwa is the local principal investigator at Aurora St. Luke’s for the Amplatzer trial (clinicaltrials.gov identifier: NCT00465270). He and Dr. Allaqaband have served as local principal investigators at Aurora St. Luke’s for two additional PFO clinical trials. Aurora enrolled the most subjects of any site for two of the three studies. In the third trial, Aurora enrolled the second most subjects.

Data collection for the clinical trials continues. Deb Waller, BSN, is site coordinator.
Gore Excluder® Iliac Branch Endoprosthesis

With participation by Aurora St. Luke’s, W.L. Gore and Associates proved the safety and effectiveness of the Gore Excluder® Iliac Branch Endoprosthesis to the FDA, receiving approval in February 2016 to make the device commercially available. Interventional radiologist Mark Mewissen, MD, led the clinical trial at Aurora St. Luke’s to evaluate this first-of-its-kind device for endovascular treatment of aneurysms in the common iliac or aortoiliac arteries, which are located in the abdominal area (clinicaltrials.gov identifier: NCT01883999). Aneurysms are ballooning and weakening of the arteries. This device allows for preservation of flow in the internal iliac arteries, and important circulation to vital structures in the pelvis. Nicole Baecker, BSN, is site coordinator.

Navik 3D™

With support and backing from Aurora, APN Health, LLC in February 2016 received FDA clearance to market its advanced three-dimensional cardiac mapping system, Navik 3D™. Development of the Navik 3D system was a collaborative effort led by renowned Aurora cardiac electrophysiologist Jasbir Sra, MD. The system reduces cost and complexity of electrophysiology procedures by providing real-time 3D maps that provide catheter location in the heart. Navik 3D is the first cardiac mapping system that doesn’t require specialized equipment. Instead it uses the patient monitoring and fluoroscopic imaging systems already present in electrophysiology laboratories.

Micra Transcatheter Pacing System

In April 2016, the FDA approved the Micra Transcatheter Pacing System (Medtronic Inc.), the first pacemaker that doesn’t require surgery, and reduces device pocket infections. The device, about the size of a nickel, is implanted directly in the right ventricle via a minimally invasive procedure through a vein in the leg. Serving as principal investigators at Aurora St. Luke’s, cardiac electrophysiologists Dr. Sra and Vikram Nangia, MD, were the first in Wisconsin to implant the miniature leadless pacemaker as part of a clinical trial (clinicaltrials.gov identifier: NCT02004873). Anthony Chambers, BSN, is site coordinator.

Jasbir Sra (left) collaborates during a procedure in the electrophysiology suite.
Clinical trial highlights

Researching regeneration of diseased heart muscle

Aurora St. Luke's Medical Center is the only site in Wisconsin conducting the Phase II ALLSTAR trial sponsored by biotechnology company Capricor Inc. (clinicaltrials.gov identifier: NCT01458405). Local principal investigator Tanvir Bajwa, MD, is testing the safety and effectiveness of cardiac stem cells derived from donors unrelated to the recipients, CAP-1002, in regenerating heart muscle and reducing scar size in subjects who have had a heart attack. A heart attack damages, or scars, heart muscle, which increases the risk of heart failure. Clinical trial subjects are randomly assigned to receive the investigational cardiac stem cell therapy or a placebo. Because the process is blinded to avoid scientific bias, the physician, caregiver and patient do not know whether the study therapy or placebo was used. Investigators will follow the study subjects for up to five years to determine the safety of the treatment and whether the scar, or infarct, size has decreased in those who received the stem cells compared to those who did not. Dena Burke, BSN, is coordinating the trial for Aurora.

Investigational products such as CAP-1002 have not been approved by the FDA.

Hundreds of patients enroll in cardiovascular trials at Aurora Health Care each year. Available clinical trials study treatments and devices for the spectrum of heart diseases.

Studying pulmonary arterial hypertension

Pulmonary arterial hypertension (PAH), a rare but serious condition, causes pressure in a patient’s pulmonary arteries to become critically high. Aurora St. Luke’s is the only site in Wisconsin to participate in the Multinational, Multicenter Study to Assess the Effects of Oral Sildenafil on Mortality in Adults With Pulmonary Arterial Hypertension (AFFILIATE) and was the first site in the United States to enroll a subject (clinicaltrials.gov identifier: NCT02060487). Led locally by Diane Zwicke, MD, this study will assess the effect of different dosages of oral sildenafil on mortality in adults with PAH. Pfizer Inc. is sponsoring this Phase IV international study. The trial coordinators are Linda Boehm, RN, and Kelsey Krueger.

Aurora St. Luke’s is one of 30 sites across the U.S. participating in a national registry trial conducted by the University of California-San Diego for patients with chronic thromboembolic pulmonary hypertension (CTEPH), which is high blood pressure in the pulmonary arteries that lasts six months or more (clinicaltrials.gov identifier: NCT02429284). Led locally by Dr. Zwicke, the registry will track at least 750 subjects with a new CTEPH diagnosis over the next six years. The registry will foster understanding of the disease, treatment responses and improvement of care for patients with CTEPH. Linda Boehm, RN, is the local coordinator.
Tailoring antiplatelet drug decisions to individual genetics

After receiving a stent, patients will take antiplatelet medication to prevent blood clots from forming. Studies have suggested that patients with a certain genetic liver enzyme abnormality may not respond as well to the currently approved antiplatelet medication, clopidogrel. A newer antiplatelet drug, ticagrelor, works regardless of the abnormality, but is more expensive and requires more frequent doses. As part of the TAILOR PCI trial, local principal investigator Louie Kostopoulos, MD, is studying whether or not genetic testing can identify the best antiplatelet therapy for patients who receive a coronary stent (TAILOR-PCI, clinicaltrials.gov identifier: NCT01742117). This Phase IV trial is sponsored by Mayo Clinic and National Institutes of Health. Dena Burke, BSN, is coordinating the trial at Aurora St. Luke’s.

“Wrapping-up” devices to reduce infections

Devices such as pacemakers and implantable cardioverter-defibrillators can become infected. Local principal investigator Vinay Mehta, MD, joined Medtronic Inc.’s global study evaluating the TYRX™ Absorbable Antibacterial Envelope’s effectiveness in reducing major infections following cardiovascular implantable electronic device procedures (clinicaltrials.gov identifier: NCT02277990). This postmarketing study tracks subjects’ occurrence of a major infection over one year. Alex Albers is coordinating the trial at Aurora BayCare Medical Center.

Providing expert input for latest imaging device

Aurora St. Luke’s is the only site in the nation providing clinical evaluation of GE Healthcare’s Vivid IQ, Vivid E95 and LOGIQ E9 ultrasound systems. Vivid E95 is looking at the highest resolution four-dimensional ultrasound imaging. Principal investigator Bijoy Khandheria, MD, is providing feedback on workflow, performance, user preference, image quality and device features. Research coordinator Kathy Schmidlkofer is providing site coordination. Vivid and LOGIQ are trademarks of General Electric company.

88 cardiovascular clinical trials open to accrual and follow-up as of Dec. 31, 2016

585 new subjects enrolled in cardiovascular clinical trials in 2016
Grant awards

With more than $750,000 in external and internal grant awards, Aurora Health Care researchers launched new and continued existing cardiovascular research projects.

External funding

### 2016 EXTERNAL AWARDS

<table>
<thead>
<tr>
<th>Project Description</th>
<th>Investigator(s)</th>
<th>Amount</th>
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<tbody>
<tr>
<td>Smarter management and resource use for today’s complex cardiac care (SMARTCare)</td>
<td>Kenneth Phillips, MD</td>
<td>$225,735 (continuing support)</td>
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<td>Centers for Medicare and Medicaid Services subaward from American College of Cardiology Foundation</td>
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<tr>
<td>Predictive optimal anticlotting treatment for segmented patient populations</td>
<td>Kourosh Ravvaz, MD, PhD</td>
<td>$120,221 (continuing support)</td>
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<td>National Institutes of Health subaward from Harvard University</td>
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<tr>
<td>Predicting risk of cardiotoxicity in cancer patients undergoing chemotherapy incorporating genetic signatures</td>
<td>Vinay Thohan, MD</td>
<td>$80,000</td>
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<td>Greater Milwaukee Foundation</td>
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<tr>
<td>Using systems science methods to study cardiac risk in the Somali community</td>
<td>Ahmed Dalmar, MD</td>
<td>$20,691 (continuing support)</td>
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<tr>
<td>National Heart, Lung, and Blood Institute subaward from HealthPartners Institute for Education and Research</td>
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<tr>
<td>Biomarkers to identify patients at high risk for heart failure after cardiac surgery</td>
<td>Farhan Rizvi, PhD</td>
<td>$10,000</td>
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<td>David V. Uihlein Foundation</td>
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### AWARD HIGHLIGHT

Chemotherapy drugs, such as anthracycline, though effective in combatting cancer, can cause damage to the heart that may lead to death. Advanced heart failure and transplant cardiologist Vinay Thohan, MD, hypothesized that the reason for the damage may partially lie in the patient’s genetic structure.

Dr. Thohan and his team are assessing 14 years of data to identify which patients treated with anthracyclines developed heart damage. DNA from these patients stored in Aurora’s Biorepository and Specimen Resource Center will allow the researchers to assess whether any of more than 100 gene variants associated with heart damage correlate with cardiac outcomes.

This project aims to better identify which patients are more susceptible to cardiotoxicities from chemotherapy, allowing oncologists to design patient-centered treatment plans.

This study is supported by an $80,000 grant award from Greater Milwaukee Foundation.

### TRANSFORMATIONAL GIFT

A $1 million gift by anonymous donors will help influence the next generation of cardiologists. The gift will create the Colton Scholar in Cardiology Research in honor of Dr. A Jamil Tajik, which will support the hiring of research scholars to spur cardiovascular advances.
Although many patients with congestive heart failure are treated with blood thinners, no definitive recommendation exists to minimize the risk of clotting in patients who do not have pre-existing indications.

Mentored by interventional cardiologist Tanvir Bajwa, MD, and advanced heart failure and transplant cardiologist Vinay Thohan, MD, fellow Dhruv Chawla, MD, will use echocardiography to analyze variation in the heart’s contraction to determine factors leading to the formation of clots inside the heart.

Identifying these subtle differences may help clinicians determine which patients would benefit from blood thinners.

This study is supported by a $30,000 Sullivan Cardiac Research Award for Residents and Fellows. The Sullivan research award is possible thanks to a generous $1 million gift from Vivian and Tim Sullivan to support the research of Dr. Bajwa via the fellowship program.

Funds are available because of the generosity of donors to Aurora Health Care Foundation.

Internal funding

$304,485
awarded by Aurora Research Institute in 2016 to Aurora Health Care investigators

2016 INTERNAL AWARDS

Sullivan Cardiac Research Award for Residents and Fellows
Up to $30,000 each
Echocardiographic mechanisms of left ventricular thrombus formation among patients with heart failure with reduced ejection fraction: the role of strain analysis assessed by two-dimensional speckled tracking
Investigator: Dhruv Chawla, MD
Therapeutic approach to implantable hemodynamic monitoring: A timing-based strategy
Investigator: Shankho Ganguli, MD

Cardiac Research Award
Up to $40,000 each
HeartQoL validation in patients with ischemic heart failure
Investigator: Nasir Sulemanjee, MD
Protein phosphatases PP2A and PPMIA in ventricular fibroblast as potential targets for ventricular fibrosis prevention in heart failure
Investigator: Farhan Rizvi, PhD
A novel strategy to protect against dronedarone-induced myocardial dysfunction in the failing heart (second-year continuation)
Researcher: Larisa Emelyanova, PhD

Cardiovascular Surgery Research Awards
Up to $50,000 each
Effect of age-associated epigenetic memory on human-induced pluripotent stem cell-derived cardiomyocytes differentiation and maturation
Investigator: Rosy Joshi-Mukherjee, PhD
De-differentiation of cardiac myofibroblasts to fibroblasts as a strategy to mitigate cardiac fibrosis and progression of heart failure
Investigator: Gracious Ross, PhD, DVM
Autoantibodies to angiotensin type 1 receptor in cardiac transplant candidates: Do pre-existing antibodies have a role in long-term outcomes?
Investigator: Martin Oaks, PhD

AWARD HIGHLIGHT

Aurora Cardiovascular Services Research Support Fund
Up to $2,000 each
Oral presentation – Expeditious reperfusion in non-ST segment elevation myocardial infarction: A single center 10-year experience at International Academy of Cardiology Annual Scientific Sessions
Investigator: Shetabi Kambiz, MD
Oral presentation – Drug-eluting devices in femoropopliteal disease: Trends of use and patient outcomes at Transcatheter Cardiovascular Therapeutics
Investigator: Daniel Ortiz, MD
Poster presentation – Recovery of left ventricular mechanics following transcatheter aortic valve implantation at American Heart Association Scientific Sessions
Investigator: Daniel Harland, MD
Patient feature

My best day is today

In the second half of 2012, after having a ruptured mitral valve repaired more than five years earlier and enduring one heart attack and chronic heart failure, Greendale resident Alan Sanford, then 70, was at the maximum age for heart transplant. Not considered high enough risk to be placed on the waiting list, he seemed to be out of options. Or was he?

BEGINNING THE JOURNEY

In February 2007, while his wife, Adelle Sanford, was out of town, Alan found himself panting and out of breath while taking a short walk down his driveway to take out the trash. When Adelle, a registered nurse at Aurora St. Luke’s Medical Center, returned, she encouraged him to see a cardiologist who told Alan that he had a ruptured mitral valve, the dual-flap valve that helps facilitate the flow of blood into the left ventricle of the heart.

A few weeks later, Alan had the valve repaired, but during one of the subsequent follow-up visits, it was discovered that he had also had a silent heart attack. He then received a Holter monitor, a portable device that continuously measures and records the heart’s activity.

In July 2007 while playing volleyball, a sport Alan and Adelle had enjoyed for almost 35 years, Alan passed out on the sand in cardiac arrest. Adelle lifted his chin to open his airway and was ready to begin cardiopulmonary resuscitation, when he spontaneously returned to consciousness.

“When I came to, I said, ‘I think I can finish the game,’” Alan said.

But the paramedics had arrived, and took him to the emergency department. The doctors there received information from the Holter monitor that helped them swiftly make treatment decisions.

Later in the month, Alan received a pacemaker and stent. He began cardiac rehabilitation. His health remained relatively steady for almost three years. However, in May 2010, he suffered a ventricular tachycardia, which means his heart rate became dangerously high. He then needed a stent repair in mid-June. At this point, Alan had grown tired of and from his heart problems.

Interventional cardiologist, Suhail Allaqaband, MD, suggested that Alan consider a heart transplant.

“That was second only to hearing the big C-word,” Alan said.

He then visited Nasir Sulemanjee, MD, a member of the Aurora St. Luke’s Heart Failure and Transplant team, to learn more about transplantation, but Alan was at the maximum age of 70 for a heart transplant, and his heart was not considered a high enough risk to put him on the waiting list for a transplant.

Clinical trial subject shares decade-long experience with heart disease.
TAKING A CHANCE

Then Dr. Sulemanjee suggested a clinical trial using stem cells for heart failure that was being conducted at Aurora. DREAM HF-1 is a double-blind, placebo-controlled, Phase III study designed to test the safety and effectiveness of a new stem cell therapy known as rexlemestrocel-L in people with chronic heart failure compared with subjects who do not receive the stem cells (clinicaltrials.gov identifier: NCT02032004). Dr. Sulemanjee is the local principal investigator.

Stem cells may be capable of repairing damaged tissues due to their regenerative abilities. The stem cells in the DREAM HF-1 study are manufactured from the bone marrow of healthy donors and injected into damaged heart tissue.

Alan decided to pursue the study, but did not initially qualify for enrollment because his heart failure was not severe enough. However, seven months later in August 2015, Alan developed a case of pulmonary edema and went to the emergency department. Pulmonary edema is caused by extra fluid in the lungs and can make it difficult to breathe.

Alan called the Aurora research coordinator for the study, Don Lobacz, RN, who determined that Alan qualified for the DREAM HF-1 study. On October 14, 2015, Sanford received his injection.

“This is a double-blind study, so you don’t know if you are going to get the stem cells or not,” Alan said. “I was told that when I went through the procedure, I would go to the operating room, they would insert the catheter, and the doctor will go through the whole routine that he would go through whether or not I received the stem cells.”

CELEBRATING TODAY

Alan will not know whether he received a placebo or the stem cells until the study has completed, but he has had no cardiac-related incidents since the infusion.

“Fairly quickly, I started feeling much, much better,” Alan said “I was also aware that there could be a placebo effect.”

Before receiving the infusion, Alan’s heart ejection fraction, a test that measures the amount of blood leaving the heart as it contracts, was 20 percent. Three months afterward, his ejection fraction had improved to 30 percent. Normal ranges from 55 to 70 percent.

Alan turned 75 in May 2017. He and Adelle celebrated 50 years of marriage in January 2016. They enjoy traveling around the United States to visit their three children and seven grandchildren.

“I am very lucky,” Alan said. “Before the procedure, tomorrow was always my best day. I will do that tomorrow, I would say. Now my best day is today.”

Sponsored by Mesoblast Inc., the clinical trial is ongoing. Alan’s experience should not be used to predict outcomes of the clinical trial. Rexlemestrocel-L is an investigational agent and is being evaluated in clinical trials.
**Physician highlight**

**Research that never skips a beat**

When David Kress, MD, came to Aurora St. Luke’s Medical Center in the early 1990s he fell into a rhythm of day in and day out heart surgery. But a heart condition he’d studied in his residency kept needling him ... atrial fibrillation.

His persistence in pursuing ways to address the disease has led to a career dedicated to cardiovascular research and innovation development.

**IN FROM THE START**

Atrial fibrillation (AFib) is an irregular heartbeat that can lead to stroke and heart failure. More than 5 million people in the U.S. have the condition.

Early in his career, Dr. Kress served as principal investigator for several major clinical trials to study AFib. As a result, he experienced a series of clinical milestones that include being one of the first in the state and, in some cases, the nation to perform increasingly complex ablation techniques to eliminate AFib.

“I was in at the very beginning of the surgical ablation era, and that has matured into something that almost every surgeon does. At the time, only a handful of surgeons in the world were doing it. To me, that has been the most fulfilling part of being involved with research,” said Dr. Kress, who is director of the Surgical Arrhythmia Program at Aurora St. Luke’s.

Today, Aurora St. Luke’s is the only hospital in Wisconsin and one of only a few in the nation to offer the hybrid ablation technique pioneered by electrophysiologist Jasbir Sra, MD, and Dr. Kress. To perform the hybrid technique, an electrophysiologist and cardiothoracic surgeon work together to ablate the heart to restore its normal rhythm. The surgeon’s ablations occur outside of the heart, while the electrophysiologist uses a catheter inside of the heart to create scar tissue. The two ablations block the electrical pathways that are causing the irregular heartbeat.

**NOT JUST AFIB**

To date, Dr. Kress has participated in over 50 clinical trials and has lectured on surgical innovations in cardiac electrophysiology at major scientific meetings throughout the U.S., Canada, Europe and Asia. He has authored and reviewed numerous papers and continues to conduct research, perform surgeries and serve on scientific committees and advisory boards.

Over the years, Dr. Kress has encountered patients with acute kidney injury, an uncommon but serious complication after heart surgery. At Aurora St. Luke’s, he is participating in a Phase II clinical trial to study whether a gene-inhibiting drug prevents this complication.

The sponsor, Quark Pharmaceuticals, has developed an experimental compound, QPI-1002, to temporarily stop a natural genetic response to the trauma of cardiac surgery, allowing time for repair of cellular damage and prevention of kidney injury. The trial’s purpose is to determine the drug’s safety and effectiveness (clinicaltrials.gov identifier: NCT02610283).

Dr. Kress’ research interests also include surgically implanted devices. In the PERIGON Pivotal Trial, researchers are studying the Medtronic Model 400 aortic valve bioprosthesis in patients with aortic valve disease (clinicaltrials.gov identifier: NCT02088554).

The elimination of AFib will always be a primary area of research for Dr. Kress. As he explores new surgical innovations in cardiac electrophysiology, he continues to ensure that hearts don’t skip a beat and neither has he in his over 25 years at Aurora.
Living big data

Precision medicine puts the patient at the center of care. It encompasses individual genetic and molecular profiles and comprehensive longitudinal information stored within massive databases and electronic health records to advance tailored disease prevention and treatment. It means thinking big data.

In the past two years at Aurora Research Institute, physician-researcher Kourosh Ravvaz, MD, PhD, has been living big data, devising ways to improve survival rates, accelerate innovation and lower costs.

“As a physician with several years of experience in clinical practice, I have always had a vision to develop translational research approaches that would improve health outcomes and delivery of high-quality care,” Dr. Ravvaz said.

His team has been investigating use of patients’ genotype to optimize anticoagulation therapy. Anticoagulants are used to thin the blood, which helps prevent clot formation, a cause of stroke. Warfarin, a common anticoagulant, has been challenging for providers because the effective amount varies greatly between individuals and because many foods and drugs adversely interact with the medicine.

Newer drugs, called novel oral anticoagulants (NOACs), are costly in comparison to warfarin and have not been shown to be universally more effective, but are likely better than warfarin for some people.

“It has been shown that because of a difference in a few genes, one person’s dose could be 20 times that of someone with otherwise similar clinical characteristics,” Dr. Ravvaz said.

With the help of Aurora Health Care’s electronic health records and the institute’s Biorepository and Specimen Resource Center and Research Analytics team, the researchers are investigating whether a scoring schema incorporating a patient’s clinical and genotypic information can help clinicians decide between NOACS or warfarin at the start of treatment.

To develop the schema, a database with medical records of 350,000 patients with more than 20 million patient encounters from a 15-year period was created. That’s a lot of data. Big data.

“This effort will help keep patients out of the emergency room while preventing the consequences of stroke,” Dr. Ravvaz said.

This research is being conducted in collaboration with Harvard Medical School and University of Minnesota.

After committing to first-year funding in 2015, National Institutes of Health renewed its support for the project with Aurora receiving an additional $120,000 from Harvard. The work also is supported by Aurora Research Institute’s intramural award program.

BIG DATA EXPLORATION REQUIRES BIG COLLABORATION

Dr. Ravvaz’s team and senior research programmer analyst Jon Cook worked closely to identify patient records and ensure the quality of the cohort-associated data within a de-identified anticoagulation research database. Cook worked continuously with the study team to implement an algorithm based on previously published work regarding a complex exposure period and time in therapeutic range. He cross-referenced biorepository databases to collect available blood specimens.

Medical records of 350,000 patients
## Cardiovascular Research Committees

### CARDIOVASCULAR RESEARCH ADVISORY COMMITTEE
- Suhail Allaqaband, MD
- Khawaja Ammar, MD
- Tanvir Bajwa, MD
- Indrajit Choudhuri, MD
- Anthony DeFranco, MD
- Wendy Dunaj, RN
- Nina Garie, PhD
- Tracy Hammonds, PhD
- Arshad Jahangir, MD (chair)
- Renuka Jain, MD
- M. Fuad Jan, MD
- Bijoy Khandheria, MD
- Ryan Cooley, MD
- Anthony DeFranco, MD
- Tracy Hammonds, PhD
- Arshad Jahangir, MD
- Renuka Jain, MD (co-chair)
- Jayant Khitha, MD
- Dave Krum, MS

### CARDIOVASCULAR INVESTIGATOR-INITIATED RESEARCH COMMITTEE
- Suhail Allaqaband, MD
- Khawaja Ammar, MD
- Indrajit Choudhuri, MD
- Ryan Cooley, MD
- Anthony DeFranco, MD
- Tracy Hammonds, PhD
- Arshad Jahangir, MD
- Renuka Jain, MD (co-chair)
- Jayant Khitha, MD
- Dave Krum, MS

### Cardiovascular volumes (systemwide)

#### CARDIOVASCULAR SURGERY

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<thead>
<tr>
<th>Procedure</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery bypass graft (CABG), total</td>
<td>926</td>
<td>922</td>
<td>941</td>
</tr>
<tr>
<td>CABG on pump</td>
<td>768</td>
<td>793</td>
<td>816</td>
</tr>
<tr>
<td>Valve procedures</td>
<td></td>
<td></td>
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<tr>
<td>Aortic valve replacement</td>
<td>446</td>
<td>358</td>
<td>385</td>
</tr>
<tr>
<td>Mitral valve replacement</td>
<td>107</td>
<td>105</td>
<td>110</td>
</tr>
<tr>
<td>Other valve replacement</td>
<td>19</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>Aortic valve repair</td>
<td>7</td>
<td>9</td>
<td>15</td>
</tr>
<tr>
<td>Mitral valve repair</td>
<td>61</td>
<td>70</td>
<td>39</td>
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<tr>
<td>Other valve repair</td>
<td>8</td>
<td>16</td>
<td>23</td>
</tr>
<tr>
<td>Cardiac ablation-open</td>
<td>95</td>
<td>123</td>
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#### INTERVENTIONAL CARDIOLOGY

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<td>8,919</td>
<td>9,049</td>
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<td>Catheterization w/ pressures</td>
<td>7,087</td>
<td>6,583</td>
<td>6,529</td>
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<td>Angiography w/o pressures</td>
<td>2,359</td>
<td>2,336</td>
<td>2,520</td>
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<tr>
<td>Coronary intervention</td>
<td>2,571</td>
<td>2,402</td>
<td>2,361</td>
</tr>
<tr>
<td>With stent</td>
<td>2,443</td>
<td>2,254</td>
<td>2,206</td>
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<tr>
<td>Drug-eluting stent only</td>
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<td>2,031</td>
<td>2,066</td>
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<tr>
<td>Non-drug-eluting stent only</td>
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<td>209</td>
<td>132</td>
</tr>
<tr>
<td>Both</td>
<td>12</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>Percutaneous coronary intervention without stent</td>
<td>127</td>
<td>146</td>
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#### HEART FAILURE AND TRANSPLANT

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<tr>
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<td>443</td>
<td>426</td>
</tr>
<tr>
<td>Patent foramen/atrial septal defect closure, total</td>
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<td>98</td>
<td>112</td>
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<tr>
<td>Open</td>
<td>75</td>
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<tr>
<td>Closed</td>
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<td>Transcatheter aortic valve replacement (TAVR)</td>
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<td>272</td>
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<tr>
<td>Transcatheter mitral valve replacement (TMVR)</td>
<td>17</td>
<td>14</td>
<td>26</td>
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<tr>
<td>Balloon valvuloplasty (percutaneous)</td>
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### VASCULAR MEDICINE

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<td>Peripheral vascular intervention</td>
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<tr>
<td>With stent</td>
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<td>2,140</td>
<td>2,186</td>
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<tr>
<td>Without stent</td>
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<td>1,000</td>
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<tr>
<td>Non-coronary atherectomy</td>
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<td>37</td>
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</tr>
<tr>
<td>Endarterectomy</td>
<td>504</td>
<td>487</td>
<td>459</td>
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<tr>
<td>Carotid endarterectomy</td>
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<td>327</td>
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#### ELECTROPHYSIOLOGY

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**CARDIOVASCULAR CLINICAL TRIALS SUBCOMMITTEE**

Indrajit Choudhuri, MD (co-chair)
Anthony DeFranco, MD
Wendy Dunaj, RN
Tracy Hammonds, PhD
Arshad Jahangir, MD
M. Fuad Jan, MD
Jayant Khitha, MD
David Kress, MD

Andrey Marek
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Katie Richter
Nasir Sulemanjee, MD (co-chair)
Eric Weiss, MD

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Ryan Cooley, MD
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Renuka Jain, MD

M. Fuad Jan, MD (co-chair)
Jayant Khitha, MD
Andrey Marek
Tonga Nfоr, MD
Susan Olet, PhD
Sara Walczak

---

**Journal articles/Book chapters**


**Abstracts**


This is the most Aurora has ever had accepted.
Failing heart. The FASEB Journal 2016;30(Suppl). 

Statin therapy reduces differentiation of cardiac fibroblasts to serum-induced proliferation and inhibits human atrial fibroblast proliferation through cell-cycle regulating cyclins by inhibiting the activity of cyclin-dependent kinases. Eur J Pharmacol 2016;744. 


According to the American Cancer Society, there are more than 3.1 million breast cancer survivors in the United States, including women still being treated and those who have completed treatment.

Surgeon Judy A. Tjoe, MD, FACS, aims to change the face of breast cancer care and survivorship through Aurora Research Institute’s breast cancer research program, Translational Oncology Research: Quest for Understanding & Exploration, or TORQUE. Serving as medical research director of TORQUE, Dr. Tjoe leads clinical- and lab-based research, including studies of

Clinical research

Studies have found that women who are overweight or obese when their breast cancers are diagnosed have a greater risk of having their cancers recur compared to women who were of a healthier weight. Through a Phase III multicenter trial sponsored by Alliance for Clinical Trials in Oncology, researchers seek to determine the effect of a supervised weight loss program plus education materials versus education materials alone on preventing invasive breast cancer from coming back (clinicaltrials.gov identifier: NCT02750826). They will test whether overweight or obese women who take part in this supervised weight loss program after being diagnosed with breast cancer have a lower rate of cancer recurrence than women who do not participate in the program.

In another trial, Aurora Health Care researchers are studying whether magnetic resonance imaging (MRI) and genetic testing may help determine if removal of the breast containing the precancerous lesion is necessary for patients with ductal carcinoma in situ. The National Cancer Institute Phase II clinical trial sponsored by ECOG-ACRIN Cancer Research Group will track candidates deemed eligible for breast conservation, based on standard imaging and physical exam, who undergo mastectomy after MRI (clinicaltrials.gov identifier: NCT02352883). Tissue from consenting subjects who have surgery will be analyzed for genetic characteristics to guide therapy.

Laboratory research

Employing a bedside-to-bench approach, TORQUE scientists leverage clinical questions and patient data in the electronic health record against tissue and blood samples stored in Aurora’s Biorepository and Specimen Resource Center to conduct longitudinal studies in search of indicators for breast cancer.

Based at Aurora Sinai Medical Center, Dr. Tjoe collaborates internally with researchers in Discovery Laboratory. Senior research scientist John Richards, PhD, has focused some of his efforts on understanding the immune response using breast cancer cell lines. One study focused on using the chemotherapy drug tamoxifen to increase expression of human epidermal growth factor (HER2),...
making it more susceptible to the chemotherapy drug trastuzumab. This led to enhanced immunity to more effectively kill tumor cells. However, in already functioning HER2 breast cancer cells, tamoxifen further activated HER2, but failed to enhance immune function, which did not make them more susceptible to trastuzumab. This suggested that although the immune system responds to HER2 activated cells, there would be little benefit to increasing this activation in patients whose HER2 cells are currently functioning. The results of this study were published in August 2016 in Cancer Immunology and Immunotherapy. The study was funded in part by an Aurora Cancer Care Research Award, available because of donations to the Vince Lombardi Cancer Foundation.

Survivorship

Through the Team Phoenix cancer survivorship program, led by Dr. Tjoe and cancer rehabilitation specialist Leslie J. Waltke, DPT, researchers seek to better understand the mechanisms of how exercise improves survival after breast cancer. In collaboration with Marquette University’s Department of Exercise Science and College of Nursing, researchers are studying the effects of high and moderate exercise on aerobic capacity, strength and psychological well-being after breast cancer treatment.

Team Phoenix is a 14-week program that trains cancer survivors for a sprint distance triathlon under the direction of coaching staff and a volunteer medical team of physicians, nurses, physical therapists and nutritionists.

One study based on the Team Phoenix program was the first to describe the benefits of a clinically supported, community-based, group-/goal-oriented triathlon training program on physical function and quality of life in female breast cancer survivors. Led by Marquette associate professor Alexander Ng, PhD, the paper was published in the December 2016 issue of Supportive Care in Cancer. Drs. Tjoe and Waltke co-authored the paper.

Knee strength, maximal oxygen uptake and quality of life improved, while barriers to exercise decreased six months after the triathlon, showing that increasing aerobic capacity and consistent training may support healthier lifestyles in breast cancer survivors.

A study published in January 2016 in Journal of Clinical Nursing examined factors affecting exercise motivation, initiation and maintenance from the perspective of breast cancer survivors who participated in the highly structured and clinically supported exercise program and then a focus group. Marquette assistant professors Karen Robinson, PhD, RN, and Linda Piacentine, PhD, RN, and Drs. Tjoe, Waltke and Ng authored the paper.

The study highlighted the importance of supportive team training and was funded by the Kohl’s Cares/ American Cancer Society and through a grant from the Vince Lombardi Cancer Foundation.
Early Phase Cancer Research Program

Early phase (Phase I, I/II, II) clinical trials lay the foundation for later trials powered with more participants to determine whether a drug is safe and effective. Michael Thompson, MD, PhD, director of the Early Phase Cancer Research Program at Aurora Research Institute, believes early phase trials play an even more critical role in cancer care.

According to a statement from the American Society of Clinical Oncology (ASCO) co-authored by Dr. Thompson in January 2015, new targeted molecular therapies and immunotherapies have provided promising results in early stage trials. Also, innovative early phase trial designs that match participants with treatments based on genetic biomarkers have allowed researchers to better identify populations that may benefit from these newer drugs.

Most early phase studies are designed with therapeutic intent. Phase I trials are statistically powered to evaluate safety while Phase II trials assess how well investigational treatments work (efficacy) before they can be tested against the current standard of care (Phase III trials). Because of the concerted effort at Aurora Health Care to offer more early phase clinical trials, more participants are receiving the latest options in the fight against cancer.

The program launched in 2013, and in 2016, Aurora’s Early Phase Cancer Research Program reached a milestone with 14 available early phase cancer clinical trials, the most Aurora has offered.

![Graph showing the number of early phase clinical trials from 2009 to 2016.]

Peer-reviewed manuscripts published by Dr. Thompson

- 11 manuscripts

Abstracts published by Dr. Thompson

- 5 abstracts

Trial highlight

Researchers study second-line combination therapy for multiple myeloma

The chemotherapy drug lenalidomide is approved by the U.S. Food & Drug Administration as first-line therapy for multiple myeloma, a cancer of the white blood cells. In some patients, the first-line therapy doesn’t work or the cancer returns.

Local principal investigator Michael Thompson, MD, PhD, studied the combination of immunotherapy drugs elotuzumab and pomalidomide with a low dose of the steroid dexamethasone in a Phase II clinical trial sponsored by Bristol-Myers Squibb (clinicaltrials.gov identifier: NCT02612779).

Researchers looked at subjects in whom lenalidomide failed or the cancer returned after lenalidomide treatment.

![Image: Pam Rynes, Michael Thompson and Angi Kraut consult on a clinical trial subject.]
Clinical trial spotlight

Matching cancer therapies to genetic abnormalities

Although the dawn of targeted cancer therapies began in the early 1960s, more recent understanding of cancer cell biology has driven new treatments that have positively affected outcomes in many types of cancer.

Building on this understanding, the 2016 Precision Medicine Initiative allocated $70 million to National Cancer Institute (NCI) to help identify genetic causes of cancer and develop more effective cancer therapies. As part of the initiative, NCI sponsored a first-of-its-kind precision medicine trial: Molecular Analysis for Therapy Choice, or NCI-MATCH (clinicaltrials.gov identifier: NCT02465060).

For this multicenter, Phase II clinical trial, Aurora Health Care cancer centers are actively recruiting subjects who are 18 years and older with advanced solid tumors, lymphomas and myelomas that are no longer responding or never responded to standard therapy.

Subjects will undergo a biopsy and the tumor sample will be screened for genetic abnormalities, such as mutations, amplifications or translocations.

“Genetic tests look at the unique genetic material of patients’ tumor cells,” said Rubina Qamar, MD, local principal investigator for Aurora. “Patients with genetic abnormalities may benefit more from treatment that targets their tumor’s particular genetic abnormality. Identifying these genetic abnormalities first may help doctors plan better treatment for patients with solid tumors, lymphomas or multiple myeloma.”

Targeted treatments are based on the molecular makeup of the tumor rather than on the tumor type.

Targeted treatments are based on the molecular makeup of the tumor rather than on the tumor type. Researchers will match the subjects with a drug intended to target the specific gene abnormality.

“This trial is a type of basket trial designed with the flexibility to open and close arms for different study drugs,” Dr. Qamar said. “The trial has included many more drugs for testing than most other clinical trials and is including even more drugs as additional arms are added.”

Dr. Qamar stressed the importance of genetic screening in patients with cancer.

“Since the first validation of oncogene-targeted therapy in chronic myelogenous leukemia, it has been appreciated that treating the principal driver oncogene has a powerful impact,” Dr. Qamar said. “However, for subsequent successful applications of molecular targeted therapy, the presence of the target oncogene requires genomic prescreening of a patient’s tumor.”
Clinical trial highlights

Hundreds of patients enroll in cancer trials at Aurora Health Care each year. Available clinical trials study a variety of cancers and all stages of the cancer journey, including prevention, screening, treatment, imaging and survivorship.

Aurora’s designation as a National Cancer Institute Community Oncology Research Program (NCORP) site allows increased access to the following trials. Aurora NCORP is one of 34 NCORP sites nationwide.

Blocking effects of a mutation in non–small cell lung cancer

In some patients with non–small cell lung cancer the tumor cells have a certain mutation (EGFR). The approved chemotherapy drug afatinib is the first-line treatment for patients with EGFR-positive non–small cell lung cancer. Afatinib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. In a Phase II/III clinical trial led locally by Dhimant Patel, MD, researchers are studying whether afatinib plus cetuximab, a monoclonal antibody that triggers the immune system, may be more effective in blocking tumor growth versus afatinib alone in this population (clinicaltrials.gov identifier: NCT02438722). The study is sponsored by SWOG in collaboration with National Cancer Institute.

Exploring immunotherapies for advanced melanoma

Monoclonal antibodies that trigger the immune system, such as ipilimumab and nivolumab, may kill tumor cells by stimulating white blood cells to kill the tumor cells. Dr. Patel is the local principal investigator of a Phase II/III clinical trial exploring whether nivolumab and ipilimumab are more effective with sargramostim, which stimulates white blood cell production, in the treatment of patients with Stage 3 or 4 melanoma that cannot be removed by surgery (clinicaltrials.gov identifier: NCT02339571). The study is sponsored by ECOG-ACRIN in collaboration with National Cancer Institute.
Preventing anthracycline cardiotoxicity with statins

Some chemotherapy drugs, such as anthracyclines, may result in irreversible heart failure. Statins help lower cholesterol levels in the blood to prevent heart failure. The Preventing Anthracycline Cardiovascular Toxicity With Statins (PREVENT) clinical trial aims to discern whether the statin atorvastatin decreases the chance of developing heart problems in women receiving anthracycline-based chemotherapy for breast cancer (clinicaltrials.gov identifier: NCT01988571). Aurora offers the only sites in the state of Wisconsin for this trial. Sponsored by Wake Forest University Health Sciences, in collaboration with National Cancer Institute, the trial is being led locally by Thomas Saphner, MD.

Understanding chemo brain in lymphoma patients

Problems with memory and attention are known to occur in patients who undergo chemotherapy. It is sometimes referred to as “chemo brain.” The cognitive effects of chemotherapy can impact daily life. Led locally by Dr. Saphner, researchers seek to determine the prevalence of cognitive impairment in lymphoma patients who undergo chemotherapy (clinicaltrials.gov identifier: NCT01382082). The observational clinical trial is sponsored by Gary Morrow of the University of Rochester NCORP Research Base. Aurora NCORP sites in Two Rivers and Grafton are the only locations participating in this study in northeastern and southeastern Wisconsin.
Grant awards

With more than $1 million in external and internal grant awards, Aurora Health Care researchers launched new and continuing oncology research projects.

External funding

$996,367
received in 2016 from federal and local sources

AWARD HIGHLIGHT

The National Cancer Institute (NCI) has awarded Aurora an additional $125,000 beyond its projected $755,000 annual grant for its third year of participation in the NCI Community Oncology Research Program, or NCORP.

This is the third year in a row that the NCI has increased the grant allotment to Aurora NCORP. Aurora is projected to receive more than $4 million by the time its five-year NCORP grant cycle ends in 2019. Thomas Saphner, MD, and Michael Thompson, MD, PhD, serve as principal investigators for Aurora NCORP. Along with their team members, the principal investigators authored a paper in Wisconsin Medical Journal about establishing a new NCORP site.

Aurora is one of 34 sites nationwide participating in NCORP, which helps brings clinical cancer trials to people in their own communities. This expanded access to clinical trials, in turn, generates more broadly applicable evidence that contributes to improved patient outcomes and a reduction in cancer disparities.

Currently, Aurora NCORP has about 50 NCI clinical trials with an additional 30 studies associated with the NCI MATCH program, open to recruitment for multiple cancer types, including brain, breast, lung and prostate cancers, as well as leukemia, lymphoma and melanoma. These clinical trials are available at nearly all 19 Aurora cancer clinics. The NCI-MATCH Phase II program seeks to determine whether or not there is clinical benefit tailoring cancer treatments based on the genetic makeup of the patient’s tumor (see page 36).

Two research organizations recently recognized Aurora for its exemplary work enrolling patients to clinical trials. At its semi-annual meeting, NRG Oncology recognized Aurora as a top five accruing NCORP site, meaning that Aurora is excelling at recruiting patients to clinical trials. In addition, the Alliance for Clinical Trials in Oncology recognized Aurora as one of its top 50 highest accruing member institutions.

2016 EXTERNAL AWARDS

National Cancer Institute Community Oncology Research Program (NCORP)
Investigators: Thomas Saphner, MD; Michael Thompson, MD, PhD
$880,000 (continuing support)
National Institutes of Health/National Cancer Institute

Translational Oncology Research: Quest for Understanding & Exploration (TORQUE)
Investigator: Judy Tjoe, MD
$100,000 (first-year funding, two-year award)
Vince Lombardi Cancer Foundation

PQE3: A statewide randomized controlled trial to reduce use of ineffective or unproven breast cancer care
Investigator: Judy Tjoe, MD
$16,367
National Cancer Institute subaward from Medical College of Wisconsin
Internal funding

2016 INTERNAL AWARDS

Aurora Cancer Care Research Awards
Up to $25,000 each

Immediate and long-term health benefits of a wellness coaching app in breast cancer survivors
Investigator: Jamie Cairo, DNP

Isolation and characterization of cancer stem cells from metastatic brain tumors (continuing support)
Investigator: Richard Rovin, MD

Outpatient family conferences in advanced cancer to improve communication (continuing support)*
Investigator: Cheruppolil Santhosh-Kumar, MD

Predicting clinical validity of bladder cancer nomograms (continuing support)*
Investigator: Kourosh Ravvaz, MD, PhD

*Second-year continuation funded with 2015 foundation gift

AWARD HIGHLIGHT

As part of its generous $250,000 gift in 2016, Vince Lombardi Cancer Foundation awarded $50,000 for new and continuing projects to advance cancer research led by Aurora Health Care investigators. Facilitated by Aurora Research Institute’s Sponsored Programs Office, the Aurora Cancer Care Research Award program provides support to scientists conducting advanced research aimed to improve patient outcomes and eradicate cancer through detection, treatment, education and prevention.

With her $25,000 Aurora Cancer Care Research Award, Jamie Cairo, DNP, is studying the immediate and long-term benefits of a wellness coaching app used by survivors of breast cancer. Researchers will follow participating survivors for six months to determine whether wellness coaching provided through the app improved their outcomes. The goals are to reduce the late and long-term side effects of cancer and its treatment, improve overall quality of life and encourage the adoption of healthy lifestyle behaviors.

The foundation’s gift also provided $200,000 over two years to support the study of biomarkers through the institute’s breast cancer research program, Translation Oncology Research: Quest for Understanding and Exploration (TORQUE), led by Judy Tjoe, MD. See the list of 2016 external funding awards.

Funds are available because of the generosity of Vince Lombardi Cancer Foundation.
Patient feature

Staying strong through a whirlwind

In April of 2016, 26-year-old Port Washington resident Rachael Crane was planning her daughter Cecelia’s first birthday party. Cecelia was learning how to walk and was constantly on the move. In addition to caring for Cecelia, Crane worked full time as a warehouse coordinator, driving box trucks and fork lifts.

Then life as she knew it changed. She found a small lump in her left breast.

“I ignored it until it got to the point that it actually hurt, and I could not wear a bra anymore,” Crane said.

THE STORM ESCALATES

In June, her doctor examined it and ordered a mammogram, which led to a biopsy. The morning after the biopsy, Crane received a call.

“They told me to come in and discuss what was going on,” Crane said. “It turned out that it was actually cancer.”

Crane was diagnosed with triple-negative breast cancer, which means her tumor did not have the three receptors – estrogen, progesterone and the protein HER2 – that effective breast cancer therapies target. Although this type of cancer can respond to chemotherapy, it can also be particularly aggressive and more likely to recur than other forms of breast cancer.

“It wasn’t in our family at all,” she said. “It was completely out of nowhere.”

Within three days, she met with a surgeon, a medical oncologist, a cancer counselor and numerous nurses at Aurora Cancer Care in Grafton, who had a plethora of questions for her to answer.

Eight days after learning she had cancer, Crane underwent surgery.

“It grew really fast,” she said. “It got too big, and it was close to my heart. Everything was pushed through really quick. If we would have waited a week to two weeks, it could have been terminal.”

ENROLLING IN CLINICAL TRIALS

After the surgery, medical oncologist Corey Shamah, MD, and research coordinator Kyle Crivello, RN, received consent from Crane to participate in two clinical trials (and a substudy). The first trial, Phase III, is studying whether chemotherapy drugs doxorubicin and cyclophosphamide are more effective when followed by the investigational chemotherapy combination of paclitaxel and carboplatin or paclitaxel alone in treating triple-negative breast cancer [clinicaltrials.gov identifier: NCT02488967]. Rubina Qamar, MD, serves as the local principal investigator.

Crane also enrolled in a substudy to that trial, which involves yearly blood tests that will look for fragments of DNA from dying tumor cells, called cell-free circulating tumor DNA, or ctDNA. When found in blood samples, the ctDNA have the potential to improve early detection and predict progression of tumors.

The second trial, also led by Dr. Qamar, involves the cardiotoxic side effects sometimes associated with doxorubicin and other breast cancer therapies. This trial, exclusive to Aurora Health Care, explores biomarkers specific to early heart disease to allow for intervention...
before irreversible changes occur. In addition to blood tests, Crane will have echocardiograms every six months until two years after completing chemotherapy.

“Standard of care dictates an echocardiogram before treatment and another six months after treatment, Crivello said.” Patients are then monitored closely for symptoms of potential heart failure, which may warrant additional studies. By participating in the study, they receive an additional three echocardiograms that are funded by the study.”

“If it may benefit me and it is going to help someone else down the line, I am all for it,” Crane said. “I am good with that. It was pretty easy to say yes.”

‘CHEMO DEFINITELY SUCKS’

As soon as Crane was fully healed from the surgery, she began six months of chemotherapy. She was randomized to receive four cycles of doxorubicin/cyclophosphamide followed by the investigational paclitaxel/carboplatin combination. It was mid-July, around her 27th birthday.

Like many chemotherapy patients, Crane lost her hair and nails. Right before Thanksgiving, she had to receive daily injections to raise her white blood count, which became low with the chemotherapy.

The day after Christmas 2016, she had her last chemotherapy infusion for the study.

“Chemo definitely sucks, don’t get me wrong,” Crane said. “At the very end of it, I was just wiped out. I would sleep all day long. But when I first started it, every third day, I would get really tired. There were some days where I could not lift an empty laundry basket. There were days when I had a lot of strength and could do almost everything, and other days when I could not even get out of bed.”

SUPPORT SYSTEM IN PLACE

Crane said that being with her daughter and husband, David, helped her endure and be strong. Her immediate family, who live nearby, rallied to help her. Family friends scheduled times to bring meals to her house while she was healing from surgery. The company she has worked for more than eight years, Molded Dimensions, adjusted her schedule so that she could heal.

The caregivers at Aurora Cancer Care in Grafton helped too.

“The nurses are amazing,” Crane said. “They make sure that you feel welcome there. It is pretty awesome. I love that place.”

After the chemotherapy, she was monitored every week and will continue to be followed every six months, with mammograms or magnetic resonance imaging yearly for 10 years. She is currently cancer free.

SETTLING INTO A NEW NORMAL

A year after finding a lump and facing a whirlwind of cancer treatments, Crane planned Cecelia's second birthday party in April.

With a prophylactic mastectomy and reconstruction surgery behind her, Crane is planning a holiday to see extended family in Portland. Her next major follow-up for the clinical trial occurs in July around her 28th birthday, a year from when her chemotherapy began. Then she is planning a camping trip in August.

This may be the eye of the storm as Crane looks to the future, but she has shown she’s determined to move forward, come rain or shine.

Sponsored by NRG Oncology, with support from National Cancer Institute, NCT02488967 is ongoing. The cardiotoxicity trial is funded by a grant from Aurora Health Care and the Vince Lombardi Cancer Foundation. Crane’s experience should not be used to predict outcomes of the clinical trials.
Physician highlight

New surgical approaches toward obliterating cancers

System Director for Surgical Oncology Aaron Chevinsky, MD, who joined Aurora Health Care in June 2016, has helped incorporate cancer-fighting technologies into Aurora’s arsenal for cancer care, while researching best practices for continuous improvement.

In December 2016, Dr. Chevinsky led a team at Aurora St. Luke’s Medical Center that became the first in the state to use NanoKnife technology on patients with otherwise inoperable pancreatic and liver cancers.

During the procedure the surgical team guides thin needles inside the patient’s body around the tumor site and electrical pulses puncture holes into the cancer cell membrane, causing them to swell and die, while preserving ducts and blood vessels.

According to a 2015 study in Annals of Surgery, this technology may double the survival rate in unresectable, locally advanced pancreatic cancers.

“We are the only site in Wisconsin to use it, and it can be used for any tumor that is surgically unresectable because of the involvement of a blood vessel,” Dr. Chevinsky said.

Dr. Chevinsky also helped introduce hyperthermic intraperitoneal chemotherapy (HIPEC) at Aurora. During HIPEC, the visible tumor is removed, then highly concentrated and heated chemotherapy is delivered to the tumor site. The heat improves absorption of the drug, potentially destroying cancer cells that remain after surgery.

With these available technologies, cancer teams need to select best treatments and the optimal timing. At the 2016 American Society for Clinical Oncology Gastrointestinal Cancers Symposium, Dr. Chevinsky presented study findings on surgical management of pancreatic cancer and the sequencing of treatments.

Researchers reviewed surgeries for presumed pancreatic cancer at Aurora to determine how many patients had chemotherapy or radiation prior to or after surgery and found that survival improved with chemotherapy before surgery.

Dr. Chevinsky stresses that a multidisciplinary team approach to sequencing therapies is crucial as state-of-the-art technologies advance from research to practice.

Oncology Research Committees

CANCER LEADERSHIP COUNCIL RESEARCH SUBCOMMITTEE
Jan DeBartolo, MSN
Carla Fuentes
Neha Glandt
Randall Lambrecht, PhD
Jennifer Mathieu
Gary Neitzel, MD
Dhimant Patel, MD
Sara Planton, BSN
Rubina Qamar, MD
Richard Rovin, MD
Thomas Saphner, MD
Michael Thompson, MD, PhD (chair)
Judy Tjoe, MD
James Weese, MD

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Corey Shamah, MD
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Judy Tjoe, MD
Shamsuddin Virani, MD
Mark Waples, MD
Joseph Weber, MD
James Weese, MD
Ellen Ziaja, MD
Frank Zuehl, MD
### Oncology volumes - new cases (systemwide)

**Source:** Cancer Registry

#### PRIMARY SITE OF DISEASE

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<th>PRIMARY SITE OF DISEASE</th>
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*Estimated. Complete data not available at time of publication.

#### PRIMARY SITE OF DISEASE

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### Oncology publications

#### 2016 AURORA-AUTHORED, PEER-REVIEWED

**Journal articles/Book chapters**


Aurora Research Institute  |  Annual Report 2016

ổnology, a prospective observational cohort study.}

Connect MDS/AML: Design of the myelodysplastic

Savona MR, Scott B; Sekeres MA, Thompson MA,

Foucar K, Garcia-Manero G, George TI, Grinblatt

E1199 phase III trial evaluating the role of taxane

from building a new National Cancer Institute

Saphner T, Thompson MA, Planton S, Singh

survivors' participation in a sprint distance

2016;65:1325-35.

neu non-amplified, but not HER2/neu-amplified,


with blastic plasmacytoid dendritic cell neoplasm

Social media and Internet resources for patients

Twitter community: #MPNSM. Curr Hematol Malig

myeloproliferative neoplasms (MPN): analysis of

JJ, Mesa R, Thompson MA. Social media and


of ER-α methylguanine DNA-methyltransferase (MGMT)

insights into estrogenic regulation of O6-


Critical role of phase I trials in cancer research and
treatment. J Clin Oncol 2017;35:139-40 (Epub

Nov 2016).


estadiol in metastatic triple-negative breast cancer:


Abstracts

Barry-Weers A, H ubregtse C, Bivjegov-

Weidman M, Weese J L. Engaging managing physicians in clinical staging prior to the initiation of cancer treatment. J Clin Oncol 2016;34(suppl:

#143).


469.


Weese JL, Citrin L, Shamah CJ, Bivjegov-


AMIN KASSAM, MD
Vice President, Aurora Neurosciences

34 neurosciences research studies as of Dec. 31, 2016
129 new subjects enrolled in neurosciences clinical trials in 2016
25 neurosciences publications and abstracts in 2016
Deep brain tumors, areas of bleeding and cysts that were once considered too risky to operate on by many are now often removed through a precise and patient-specific corridor with Aurora Neuroscience Innovation Institute (ANII)’s unique, integrated surgical techniques. Led by neurosurgeon Amin Kassam, MD, ANII includes a multidisciplinary clinic, education suite, neuroanatomical laboratory and four neurosurgical operating suites featuring first-in-the-world technology at Aurora St. Luke’s Medical Center.

SURGICAL TECHNIQUES
A bedrock of innovative research combined with collaboration among the neuro-oncology multidisciplinary team translates into increased access to innovative minimally invasive techniques. These techniques offer patients hope for better surgical results and improved long-term health outcomes. It also minimizes long-term complications as a result of their tumor or surgery.

Directed Therapy Options. Neurosurgeons collect and preserve the brain tissue they remove for pathology, molecular and genetic evaluation. These samples provide opportunities to study new treatments for patients. The ability to capture, grow and use the tumor tissue in research enables the team to study new targets for treatment that can be brought back to the patient in an individualized manner, epitomizing Aurora’s commitment to precision medicine.

All of this patient and correlated cell data is then compiled into a novel image-driven database with the goal of capturing enough data to predict outcomes. Aurora was the first institution in the world to install and implement this specific image-driven informatics system.

Mapping. An invaluable tool for Aurora’s neurosurgeons, brain mapping depicts aspects of a tumor and surrounding healthy tissue with enhanced clarity rendered in a three-dimensional space. This imaging technology allows surgeons to plan a patient-specific, real-time surgical pathway before a brain surgery procedure begins, which may translate into improved outcomes and a faster recovery.

Dynamic Navigation. Neurosurgeons use a GPS-like system that gives them real-time guidance deep within the brain. Patients can see their brain tumor removal on the same computer screen that their surgeons use to track the movements of their surgical instruments.

Safe Access. Aurora uses a specialized and innovative tool that minimizes damage to surrounding tissue by allowing neurosurgeons to safely displace the natural folds of the brain as they advance to the target site.

High-Definition Optics. This technology allows neurosurgeons to differentiate tissue types with unprecedented clarity. Being able to separate diseased tissue from healthy tissue makes it possible...
to successfully remove what would otherwise be considered inaccessible brain tumors, cysts or other difficult-to-see growths.

The robotically-operated video telescopic-microscopy system (ROVOT-m) is a novel optical tool that consists of an optical system connected to a robotic arm that has the ability to maneuver along the surgical field in a hands-free/command-prompted interface.

The culmination of these integrated technologies allows for many patients to have surgery while awake. Many patients interact on their phones or smart devices during surgery, and many go home the next morning. Having patients awake permits detailed neurocognitive evaluation throughout the procedure. This intensive monitoring provides a margin of safety difficult to achieve when the patient is asleep.

Innovative imaging techniques drive surgical strategies

Minimally invasive brain surgery requires detailed planning to avoid white matter tracts and areas of the brain that control function. Neurosurgeons and neuroradiologists at Aurora Neuroscience Innovation Institute (ANII) use advanced magnetic resonance imaging (MRI) techniques called diffusion tensor imaging (DTI) and functional MRI (fMRI) to devise patient-centered strategies.

White matter pathways connect one area of the brain to another and DTI allows those connections to be visualized (Figure 1).

Locating areas of the brain activated during language and motor tasks are possible noninvasively with fMRI. This technique relies on changes in blood flow to specific areas of the brain caused by active neurons. Changes in blood flow are elicited by having the patient conduct motor, sensory, visual, auditory and language tasks. fMRI maps of functional activation correlating with specific areas of the brain are created using statistical processing (Figure 2).

The DTI and fMRI maps are then carefully aligned so that the relationship between the tumor, for example, white matter tracts and areas of the brain that control function can be visualized simultaneously. Based on this information, a route to the tumor is designed to minimize impact of the surgery.

“The combination of DTI, fMRI and anatomic MRI provides a road map for surgery and helps determine the safety and feasibility of operating on the lesion,” said Richard Rovin, MD, medical research director.

This innovative imaging technique proved useful in a patient with a tremor and weakness in her left arm. After finding a large metastatic tumor adjacent to a part of the brain controlling motor function, the team used DTI and fMRI to identify the white matter tracts at risk with surgery (Figure 3). Functional areas at risk included the left hand, face and area that contributes to movement and sensation (Figure 4).

A precise trajectory was designed to avoid the tracts and functional areas. With this plan, the patient underwent surgery while awake to have the tumor removed. After surgery, the patient’s left arm strength improved.

The ANII team is studying the technique of fusing DTI and fMRI images. Preliminary data released in 2016 show that the technique is highly reliable in allowing to more fully remove tumors adjacent to functional areas of the brain with very low complication rates. The team is further validating the approach using technologically advanced methods of testing the patient’s speech, cognition and motor systems during the awake surgeries. Neuroradiologist Jon Jennings, MD, is the principal investigator for the study.
Clinical trial highlights

Monitoring cardiac rhythms in stroke

Development of atrial fibrillation, an abnormal heart rhythm, is a risk for people who have had an ischemic stroke. Led locally by principal investigator Rehan Sajjad, MD, researchers are comparing the incidence of atrial fibrillation documented with an implantable continuous cardiac rhythm monitoring device versus standard of care monitoring. Medtronic Inc. is sponsoring the Phase IV trial (clinicaltrials.gov identifier: NCT02700945). Kate McPolin, BSN, and Lynda Yanny, BSN, are serving as coordinators at Aurora St. Luke’s Medical Center.

Studying outcomes after stroke

Open at three Aurora sites, the Mild and Rapidly Improving Stroke Study (MaRISS) is tracking outcomes of subjects who have suffered mild and rapidly improving stroke (clinicaltrials.gov identifier: NCT02072681). Through this American Heart Association study, sponsored by the University of Miami, researchers will track the proportion of subjects not independent at 90 days after a stroke. The study is supported by investigators/coordinators at each site:
- Aurora BayCare Medical Center: James Napier, MD/Laura Thoreson and Taylor Romdenne
- Aurora Medical Center in Grafton: Rose Dotson, MD/Sue Truchan, BSN, and Stacie Bishop
- Aurora St. Luke’s Medical Center: Rehan Sajjad, MD/Carol Halliday, RN, and Lynda Yanny, BSN

Targeting MS

In multiple sclerosis, immune cells attack nerve fibers in the central nervous system, interfering with signals between the brain and the spinal cord. An approved leukemia treatment called ofatumumab reduces their ability to damage the central nervous system. Led by principal investigators Akram Dastagir, MD, at Aurora St. Luke’s Medical Center and James Napier, MD at Aurora BayCare Medical Center, researchers are comparing the effectiveness and safety of ofatumumab versus the standard treatment teriflunomide in patients with relapsing multiple sclerosis (clinicaltrials.gov identifier: NCT02792218). Sponsored by Novartis Pharmaceuticals, the Phase III study tests whether clinical trial participants treated with ofatumumab experience fewer multiple sclerosis relapses. Carol Halliday, RN, is serving as research coordinator at Aurora St. Luke’s and Alex Albers and Laura Thoreson at Aurora BayCare.

22 neurosciences clinical trials open to accrual and follow-up as of Dec. 31, 2016

129 new subjects enrolled in neurosciences clinical trials in 2016

- Neuro-Oncology (7) 32%
- Surgical (6) 27%
- Epilepsy (2) 9%
- Multiple Sclerosis (3) 14%
- Stroke (4) 18%

- Surgical (101) 78%
- Neuro-Oncology (22) 17%
- Stroke (3) 2%
- Multiple Sclerosis (2) 2%
- Interventional Radiology (1) 1%
Translational highlights

Growing tumors for testing

The spread of cancer to the brain from other primary tumors, such as breast cancer, is occurring more frequently, creating an urgent need to identify the underlying molecular factors and test drugs against those targets.

To find these molecular targets, researchers need to understand how cancer grows and spreads. One model to test this involves growing the tumors in scientifically engineered mouse avatars from human tumor cells. This can be challenging because sometimes the tumors fail to grow.

Postdoctoral fellow Amber LaCrosse, PhD, and a team at Aurora Research Institute determined a potential new way to generate multiple tumor specimens that display patient characteristics. They implant tumor cells through the cerebral aqueduct, part of the brain’s ventricular system, rather than the traditional method that utilizes the striatum, located toward the center of the brain.

“Patient-derived tumor models are difficult to generate; however, placing the tumor cells in a region that would facilitate their spread and allow cells to choose an appropriate growth niche may facilitate successful tumorigenicity,” said Dr. LaCrosse.

Cells from the first-generation tumors were then used to grow second and third generations of tumors. Testing of the tumor masses confirmed that the third-generation cells retained key characteristics of the original patient tumor (Figure 1).

Using this unique implantation site to grow second- and third-generation tumors with distinct characteristics may help with the diagnosis and treatment of patients with brain metastases in the future.

Dr. LaCrosse’s findings were made possible by a grant from the Vince Lombardi Cancer Foundation.

Tissue collection studies

Development of genetically targeted diagnostics and therapies has increased exponentially in the past 10 years, in many ways thanks to people who are willing to donate tissue after a medical procedure (see one patient’s experience with tissue donation on page 6). To conduct neurosciences research, clinically sound and genetically diverse samples are required. Neurosciences researchers, in collaboration with Aurora Research Institute’s Biorepository and Specimen Resource Center, have focused on screening patients for viability of samples, obtaining consent and collecting these specimens for neurosciences research.

Patients are becoming more aware of the need for tissue donation to boost clinical research. A total of 82 brain tumor tissue samples were donated in 2016 by willing Aurora patients. The effort to obtain these precious samples is substantial. Over 90% of patients who are approached for consent agree to participate. Of those consenting patients, tissue collection occurs from 60% of them because sometimes the tumors are too small and must all be used for clinical purposes.
Physician highlight

Mapping a route toward wellness

A member of a collaborative multidisciplinary team at Aurora Health Care, neuroradiologist Melanie Fukui, MD, helps provide a highly detailed road map for neurosurgeons prior to brain surgery using some of the most advanced tools in imaging.

“We are fortunate at Aurora St. Luke’s to have the capital and intellectual resources to make the most of advanced imaging techniques, such as magnetic resonance (MR) perfusion, MR spectroscopy and diffusion tensor imaging,” said Dr. Fukui, who was named one of The Best Doctors in America. Dr. Fukui has been with Aurora for nearly three years and has 25 years of clinical experience.

Dr. Fukui and researchers at Aurora Neuroscience Innovation Institute are studying diffusion tensor imaging, a tool that provides detailed imaging of biological tissue (see page 48), and a three-dimensional modeling technique that can provide visualization of neural tracts when treating abnormal tissue in the brain, or lesions.

These state-of-the-art, advanced imaging techniques are routinely available to Aurora patients. This mapping technology is only one unique aspect to the patient-centered care plans that have made Aurora a national destination for brain surgery (see page 53). Multidisciplinary collaboration for each patient occurs between neuroradiologists, such as Dr. Fukui, neurosurgeons, neuro-oncologists, radiation oncologists, medical oncologists, palliative care specialists, neuropsychiatrists, advanced practice providers and care coordinators.

“We first consider the patient’s treatment goals and functional priorities, as well as whether the surgical goal is complete resection, tissue diagnosis, decompression of a critical neural structure that is producing symptoms or cyto-reduction, in order to make radiation and chemotherapy more effective options,” Dr. Fukui said. “The challenge then becomes designing a plan to achieve the surgical goal with the least disruption of normal surrounding tissue and the greatest preservation of neurological function. Sometimes it is better to take the long way, rather than the shortest route, in order to maintain critical structures.”

Dr. Fukui appreciates the face-to-face collaboration that she has experienced at Aurora. With the introduction of electronic images, such as picture archiving and communications systems, she maintains that, in other institutions, this face time has become less common. The combination of state-of-the-art imaging with true collaboration ensures that the patient obtains the best possible care.

Dr. Fukui helps map treatments for some aggressive and challenging cases, necessitating a need for a bench-to-bedside approach. Dr. Fukui says that, in the future, precision molecular imaging combined with tumor-specific agents may boost both neuroimaging and treatment.

“We are hopeful that applying new techniques to these patients’ care will translate into treatment modifications that improve outcomes,” Dr. Fukui said.
Researcher highlight

Breaking down barriers in brain cancer

With almost 20 years in the laboratory, senior research scientist Santhi Konduri, PhD, is on the cusp of translating her research into a clinical trial, providing a new investigational option in the fight against brain cancer.

Since joining Aurora Research Institute in July 2013, Dr. Konduri has focused on combining existing chemotherapy drugs with drugs approved for other indications in an attempt that may synergistically increase survival and decrease toxic effects in hard-to-treat cancers.

With Aurora Cancer Care Research Awards made possible by gifts from Vince Lombardi Cancer Foundation, Dr. Konduri and her team evaluated the drug disulfiram as part of a combination therapy for breast and pancreatic cancers. The interest in disulfiram was sparked because it is an FDA-approved drug.

The combinations significantly decreased tumor cell growth in both pancreatic and breast cancers.

Applying these initial results, Dr. Konduri is testing combinations on brain cancer, specifically glioblastoma multiforme, a rapidly growing and aggressive brain tumor.

“Some of these patients are dying within six to nine months of their diagnosis,” Dr. Konduri said. “It is too difficult for many drugs to penetrate the brain, which makes them ineffective.”

Disulfiram can cross the blood-brain barrier. But it needs help.

“These cell membranes are tougher, but when we combined copper with the disulfiram, we were more easily able to kill the primary brain tumor cells,” Dr. Konduri said. “Disulfiram combined with copper forms another compound that is able to kill the brain cancer cells effectively.”

With the addition of copper, less disulfiram is needed; high levels of disulfiram may cause neurotoxicities, which destroys normal brain cells.

“If you are able to decrease the amount of this drug, you can also reduce the side effects of the chemotherapy drugs,” Dr. Konduri said. “We want see if we can decrease side effects so that these people can lead better lives without as many complications.”

Taking the research further, Dr. Konduri added the chemotherapy drug temozolomide, which is approved for treatment of glioblastoma multiforme.

“Next we want to offer these potential therapies to consenting subjects in an ongoing clinical trial,” Dr. Konduri said.

She is currently working with other researchers at Aurora in generating a database to determine what types of patients may be eligible and most appropriate for this type of therapy. Principal biostatistician Maharaj Singh, PhD, is aiding with statistical analysis.

“Her passion for finding alternatives to current therapeutic options is evident in everything she does in the lab,” said senior research technologist Deb Donohoe, who has worked with Dr. Konduri for almost two years. “Dr. Konduri is committed to improving the future of cancer treatments at Aurora.”
Patient feature

A destination for care

As a figure competitor, Valerie Johnson was in peak physical condition, but severe headaches caused her to take a break from training. After many tests, the 36-year-old Austin, Texas resident learned she was suffering from a life-threatening brain bleed. Johnson’s local doctor referred her to the Aurora Neuroscience Innovation Institute (ANII) team at Aurora St. Luke’s Medical Center because of the leading-edge image-guided surgical techniques used there.

ANII researchers have been studying the combination of diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI) (see page 48) to avoid detrimental consequences in minimally invasive brain surgery like the one Johnson needed to control the brain bleed. This advanced imaging allows surgeons to access areas of the brain that control function while minimizing complication rates.

“I could not have done Valerie’s surgery two years ago. That’s how recent this revolutionary technology is,” said Amin Kassam, MD, vice president of neurosciences at Aurora Health Care and founder of ANII.

What started as a headache led to a trip from Texas to Wisconsin for the latest in brain surgery.

“NO SLEEPING ON THE JOB”

Neuroradiologists designed a three-dimensional map of Johnson’s brain to plan the safest route for surgeons to take during surgery.

Johnson’s bleed was located deep in the left side of her brain, surrounded by areas that control motor and memory function. At Aurora St. Luke’s, the surgery to control a bleed like that is performed while the patient is awake, a strategy used at only a handful of hospitals throughout the United States. Prior to the operation, anesthesiologists deliver a specific dose of medicine so the patient is aware of what it is going on, but cannot feel pain.

“The neurosciences team at Aurora was great. They made me feel at ease with the surgery,” Johnson said. “They assured me that being awake would be a great benefit to make sure they didn’t do something that was detrimental to me.”
At one point during the surgery Johnson appeared to be losing motor skills and she forgot who she was. At this point the doctors raised their voices to be sure Johnson could hear and respond.

“I was really sleepy from what I recall so in order to keep me awake they had to talk loudly,” Johnson said.

The team used the 3D map for information regarding the safest way to proceed to preserve memory and motor function. Not long after making adjustments, Johnson’s memory returned and she asked to call her mom.

“I do not remember most of it,” Johnson said. “I remember going to questions on an iPad and talking on the phone with my parents. Even still, all of that is pretty hazy.”

**BACK TO LIFE**

After the surgery, Johnson could speak coherently and answer questions, and her motor skills were back to normal.

The next day, she left the hospital to have lunch with her family and, a month later, she is already planning to get back into shape. She wants to start a business of her own someday, but mostly plans to spend more time with her family in the years to come.

### Neurosciences Research Committees

#### NEUROSCIENCES RESEARCH COMMITTEE

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<td>Dmitry Bosenko, MS</td>
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<td>Juanita Celix, MD</td>
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<td>Srikant Chakravarthi, MD</td>
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<td>Denise Coley, MS</td>
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<td>Martin Corsten, MD</td>
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<td>Monica Cucciare</td>
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<td>Deb Donohoe</td>
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<td>Amin Kassam, MD</td>
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<td>Timothy Heniadis</td>
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<td>Jonathan Jennings, MD</td>
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<td>Anne Kissack, MPH</td>
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<td>Nathan Kojis</td>
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<td>Santhi Konduri, PhD</td>
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<td>Amber Lacrosse, PhD</td>
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<td>Cassie Martin</td>
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<td>Paul Mintz, PhD</td>
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<td>Natalie Polinske, MS</td>
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<td>Richard Rovin, MD (co-chair)</td>
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<td>Maharaj Singh, PhD</td>
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<td>Bob Stoltz, MBA</td>
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<td>Sarika Walia, MD</td>
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<td>Thomas Wolfe, MD</td>
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#### NEUROSCIENCES CLINICAL TRIALS RESEARCH COMMITTEE

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<td>Tonya Hollirth</td>
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<td>Asadullah Khan, MD</td>
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<td>Kessarin Panichpisal, MD</td>
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<tr>
<td>Carol Tutino, BSN, MS</td>
<td></td>
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<tr>
<td>Paul Vilar</td>
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<tr>
<td>Sarika Walia, MD</td>
<td></td>
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<tr>
<td>Valerie Werner, BSN</td>
<td></td>
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<tr>
<td>Thomas Wolfe, MD</td>
<td></td>
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<tr>
<td>Lynda Yanny, BSN</td>
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</tbody>
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#### CLINICAL INNOVATION COMMITTEE

<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
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<tbody>
<tr>
<td>Juanita Celix, MD</td>
<td></td>
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<tr>
<td>Srikant Chakravarthi, MD</td>
<td></td>
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<tr>
<td>Shannon Clark, MBA</td>
<td></td>
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<tr>
<td>Martin Corsten, MD</td>
<td></td>
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<tr>
<td>Thomas Doers, MD</td>
<td></td>
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<tr>
<td>Melanie Fukui, MD</td>
<td></td>
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<tr>
<td>Nina Garlie, PhD</td>
<td></td>
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<tr>
<td>Jonathan Jennings, MD</td>
<td></td>
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<tr>
<td>Amin Kassam, MD (co-chair)</td>
<td></td>
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<td>Sammy Khalili, MD</td>
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<tr>
<td>Nathaniel Kojis</td>
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<tr>
<td>Richard Rovin, MD (co-chair)</td>
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<tr>
<td>Sarika Walia, MD</td>
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</tbody>
</table>
### Neurosciences volumes (systemwide)

#### Source: Aurora Smart Chart and Medipac

<table>
<thead>
<tr>
<th>CASES</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epilepsy</td>
<td>3,210</td>
<td>4,317</td>
<td>3,991</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>2,433</td>
<td>1,645</td>
<td>1,961</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>1,510</td>
<td>1,094</td>
<td>1,426</td>
</tr>
<tr>
<td>Hemorrhagic</td>
<td>552</td>
<td>304</td>
<td>284</td>
</tr>
<tr>
<td>Interventional radiology*</td>
<td>387</td>
<td>446</td>
<td>357</td>
</tr>
</tbody>
</table>

### Neurosciences publications

#### 2016 AURORA-AUTHORED, PEER-REVIEWED

- **Journal articles/Book chapters**
- **Abstracts**


#### Abstracts

- **Ali SI, Mallas-Serdynski L, Thomas K. Get With The Guidelines award winning hospitals are associated with decreased door to needle times in Michigan and Wisconsin. Stroke 2016;47:ATP294.**


- **Kassam AB, Corsten MJ. Reconstruction following EEA: a 0.5% CSF leak rate in 200 consecutive cases. J Neurol Surg B 2016;77:A136.**


- **Kassam A, Rovin R. EXTH-10: A novel small molecule therapy sensitizes high-grade gloma to temozolomide chemotherapy. Neuro Oncol 2016;18(suppl_6):vi5-6.**


EMERGING RESEARCH

101 emerging research studies as of Dec. 31, 2016

415 new subjects enrolled in clinical trials in emerging research in 2016

126 publications and abstracts in emerging research in 2016

WOMEN’S HEALTH
ORTHOPEDICS
FAMILY PRACTICE
POPULATION HEALTH
CRITICAL CARE
Women’s Health research

Enhancing the birth experience

Women who undergo cesarean delivery report less satisfaction with their child-birthing experience. This can be a concern as the number of cesarean deliveries increases. An alternate method of cesarean delivery at Aurora Health Care may enhance the experience for mothers.

In a family-centered cesarean delivery, the mother watches her baby being born through a clear surgical drape. Once the baby is born, immediate skin-to-skin contact allows the bonding process to begin.

This type of cesarean delivery is being compared to traditional cesarean methods in a randomized controlled trial at Aurora Sinai Medical Center and Aurora BayCare Medical Center (clinicaltrials.gov identifier: NCT02690077).

Patients are enrolled on the day of their planned cesarean delivery. All patients enrolled in the study receive descriptions of both methods and are asked their preference. An envelope containing one of the options identifies the subject’s random assignment to either the traditional or family-centered method.

“We are getting a lot of positive feedback from patients who have really enjoyed seeing their babies being born and holding their babies right after birth,” said Marie Forgie, DO, principal investigator at Aurora Sinai. “It helps the mom feel involved in the birth of her child rather than a cesarean just being an operation done on her.”

To determine the difference in patient satisfaction, researchers use an 11-item questionnaire assessed within 48 hours of delivery.

“One of the biggest patient dis-satisfiers with cesarean is the surgical atmosphere and the inability to hold their baby right away,” said Cynthia Brown-Sullivan, MD, principal investigator at Aurora BayCare. “The family-centered approach tries to mimic the natural birth experience as closely as possible.”

The study will assess whether differences exist in patient satisfaction between the family-centered and traditional methods, as well as whether differences occur in the time to initiation of family bonding, breast feeding rates, and neonatal and maternal outcomes.

Aurora is sponsoring the clinical trial. Jessica Kram, MPH, serves as the study coordinator at Aurora Sinai and Taylor Romdenne, at Aurora BayCare. Danielle Greer, PhD, serves as the study’s biostatistician.
Women’s Health volumes (systemwide)

Orthopedic research and volumes (systemwide)

Arthritis can cause debilitating lower back pain that may spread to one or both legs.

In June 2016, the U.S. Food and Drug Administration granted a 501(k) clearance for a claim that the iFuse Implant™, based on clinical studies that included Aurora BayCare Medical Center, demonstrated improvements in pain, patient function and quality of life.

Aurora BayCare orthopedic surgeon Robert Limoni, MD, was the local principal investigator in a trial that compared the safety and effectiveness of the device to nonsurgical management (medications, injections, physical therapy or radiofrequency ablation) in the treatment of arthritis or disruption of the sacroiliac joint. Taylor Romdenne served as the research coordinator for the study.

Source: Aurora Smart Chart

<table>
<thead>
<tr>
<th>2014</th>
<th>2015</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hand/Wrist/Forearm</td>
<td>11,770</td>
<td>13,020</td>
</tr>
<tr>
<td>Knee</td>
<td>9,447</td>
<td>13,541</td>
</tr>
<tr>
<td>Lower Leg/Foot/Ankle</td>
<td>20,640</td>
<td>24,503</td>
</tr>
<tr>
<td>Pelvis/Hip/Femur</td>
<td>7,060</td>
<td>10,883</td>
</tr>
<tr>
<td>Shoulder/Elbow/Upper Arm</td>
<td>16,460</td>
<td>20,304</td>
</tr>
<tr>
<td>Spine/Back/Neck</td>
<td>61,694</td>
<td>68,413</td>
</tr>
<tr>
<td>Other</td>
<td>25,031</td>
<td>25,030</td>
</tr>
<tr>
<td>Totals</td>
<td>152,102</td>
<td>175,694</td>
</tr>
</tbody>
</table>
The Aurora UW Medical Group (AUWMG) Research Core is responsible for supporting, growing and coordinating research and scholarly activity among AUWMG faculty and Aurora Health Care residents, students and fellows. Dennis Baumgardner, MD, directs these activities.

**IMPROVING COMMUNICATION, ONE PERSON AT A TIME**

Health care providers may need to check the clinical jargon at the patient room door and consider strategies for improving communication and quality of care, one person at a time.

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Published in Journal of Patient-Centered Research and Reviews, original research by Michael Farrell, MD, and colleagues at the Aurora Sinai Family Care Center and Center for Urban Population Health revealed how confusing medical jargon often used during patient visits can go unexplained to patients who may not feel comfortable asking for clarification.

The researchers recorded conversations between primary care physicians and their patients and provided the physicians with a previously tested report card detailing how much jargon was used and how well they assessed their patients’ understanding during the visit. The researchers found that through marrying technology and feedback, they could significantly improve physician-patient communication.

**COMBATTING OPIOID ABUSE**

Opioid drugs are the source of more overdose deaths nationwide than heroin and cocaine combined. The United States’ consumption of the world’s supply of the most common opioid painkillers, hydrocodone and oxycodone, is almost 100 percent and 81 percent, respectively, despite the rates of chronic noncancer pain being similar across developed countries.

Historically, medical literature has not supported training interventions with guidelines, recommendations and education to modify primary care providers’ behaviors for opioid prescribing, but a study led by family medicine clinician-researcher Fabiana Kotovicz, MD, found that education positively impacted primary care providers’ prescribing of appropriate opioid painkillers for chronic noncancer pain.

For this work, Dr. Kotovicz was honored at the 2016 North American Primary Care Research Group annual meeting in Colorado Springs, Colo. Her study was featured in the Pain Management Poster Walk at the conference, which is a program to introduce students, residents and fellows to experts in the field.

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The population health perspective provides a research framework for Center for Urban Population Health (CUPH) to better understand and address the health and well-being of communities. The focus of CUPH is on identifying the causes of health, disease and well-being in populations, designing and implementing preventive or treatment interventions and measuring their effectiveness against health outcomes of a community. Staff uses their expertise in partnership with providers, community leaders, organizations and residents in identifying solutions to the challenges preventing communities from realizing their full health potential.

IMPROVING RESPONSE

Ambulance transport of patients with stroke to the hospital results in faster treatment. However, one-third of stroke patients do not call 9-1-1 to get to the hospital. To address this, the Wisconsin Department of Health Services entered a five-year cooperative agreement with the Centers for Disease Control’s Paul Coverdell National Acute Stroke Program. Through the grant, the Wisconsin Coverdell Stroke Program will develop comprehensive stroke systems that increase public awareness and the use of emergency medical services for suspected stroke; improve patient care; improve rehabilitation and recovery through better clinical-community linkages; and reduce complications through improvements in secondary prevention.

CUPH is assisting with development of the program’s evaluation plan and conducting interviews with hospital partner staff and others involved in the process of transporting stroke patients to the hospitals. The resulting process maps will provide a collaboration opportunity to identify and improve systems so that more people survive and thrive after their stroke. The next model hospital and area system to be studied is Aurora Medical Center in Oshkosh.

Partners: Wisconsin Department of Health Services, MetaStar, Beloit Health System, UW Health, University of Wisconsin-Milwaukee.

LIFESTYLE PROGRAMMING

Wisconsin has been a Centers for Disease Control Well-Integrated Screening and Evaluation for Women Across the Nation (WISEWOMAN) Program grantee since 2008.

Wisconsin WISEWOMAN works with health care providers to offer cardiovascular disease risk factor screenings to low-income, under- and uninsured women between the ages of 40 and 64. This screening, medical support and risk reduction counseling is available through Aurora Health Care’s Walker’s Point Community Clinic in Milwaukee.

CUPH researchers have designed and are implementing an evaluation of the local work, recommending improvement of services and overall outcomes of the initiative.

Partners: Wisconsin Department of Health Services, Wisconsin’s Women Health Foundation, Walker’s Point Community Clinic, UW School of Medicine and Public Health.
Clinical trial highlights

ELAD study

Alcohol is a hepatotoxin. The extent and type of injury to the liver induced by alcohol is related to the amount and duration as well as individual factors such as sex, size, genetics and the presence of other liver injury, including fatty liver disease, viral hepatitis and other toxin exposure. Injury to the liver results in an intense inflammatory state, which likely contributes to more liver damage and to dysfunction and injury to other organ systems.

Medical management of acute alcoholic hepatitis is primarily supportive. Subsets of patients benefit from modulation of the inflammatory response with corticosteroids and anti-TNF agents such as pentoxifylline. Many types of liver support devices have been created but none have demonstrated an improvement in survival.

The ELAD® System, manufactured by Vital Therapies Inc., circulates a patient’s blood through the device (an extracorporeal circuit like dialysis). Plasma is separated from the blood cells and filtered across cartridges filled with live immature hepatocytes. Several pathways are being investigated as mechanisms for potential benefit. Vital Therapies is conducting an international, multicenter trial of this device in patients with acute alcoholic hepatitis. (Phase III, clinical trials.gov identifier: NCT 02612428).

Researchers at Aurora Health Care are participating in this clinical trial and actively enrolling patients with acute alcoholic hepatitis. Details of this Institutional Review Board-approved study are discussed with patients and family. Informed consent is obtained. All patients receive the current standard of care—identical to that provided patients who do not choose to participate in the study. By random assignment, half of the study patients will also be treated with ELAD. The primary endpoint is survival at 91 days after enrollment.

David J. Kramer, MD, is the principal investigator. Mary Briggs-Sedlachek, RN, Kate McPolin, BSN, and Lynda Yanny, BSN, are the study site coordinators at Aurora St. Luke’s Medical Center and Aurora Sinai Medical Center, which are the only recruitment sites in Wisconsin.

The ELAD System has not been demonstrated to be safe or effective for any indication and is not available for sale in the United States or any other country.

CAUTION: Investigational Product. Limited by United States law to investigational use.
Grant awards

With more than $600,000 in external grant awards, Aurora Health Care researchers launched new and continuing research projects in emerging research.

External funding

$608,676
received in 2016 from federal, state and foundation sources

AWARD HIGHLIGHT

Rural health care settings are less likely to have geriatric health care experts on site. To help address this gap in care, Bader Philanthropies Inc. awarded $125,000 for a second year to Aurora Health Care to fund a project geared toward prevention and early identification of clinical deterioration of older adults in these underserved areas.

The money helps fund an evidence-based Hospital Elder Life Program (HELP) at two rural Aurora medical centers with transitioned services in the home. HELP uses a model of care to maintain physical and cognitive functioning throughout hospitalization, assist with the transition from hospital to home and prevent unplanned readmission for older adults.

Michelle Simpson, PhD, RN, will continue as principal investigator for the project. Using a previously awarded grant from Bader Philanthropies Inc., Dr. Simpson developed an evidence-based risk score to quickly identify vulnerable older adults who are discharged to their homes, which is being used in conjunction with the HELP model.

Researchers will examine the impact of implementing HELP in two rural hospitals and an innovative transition-of-care model (Bundled HELP) on clinical outcomes and patient experience.

2016 EXTERNAL AWARDS

Geriatric Workforce Enhancement Program
Investigator: Michael Malone, MD
$130,389 (continuing support)
Marquette University
Year 2: Prevention and early identification of rural older adults’ clinical deterioration: implementation of the Bundled HELP at Home intervention

Investigator: Michelle Simpson, PhD, RN
$125,000 (continuing support)
Bader Philanthropies Inc.

Rural Graduate Medical Education Program
development and enhancement
Investigator: Jeff Tiemstra, MD
$125,000
Wisconsin Rural Physician Residency Assistance Program

Integrated, individualized, intelligent prescribing
Investigator: Michael Michalkiewicz, PhD
$102,908 (continuing support)
Vanderbilt University Medical Center

Wisconsin Network for Health Research
Investigator: Sara Planton, BSN
$80,000 (continuing support)
Wisconsin Partnership Program

A prospective study of newborn screening for cystic fibrosis using a novel IRT/next generation sequencing method
Investigator: Michael Farrell, MD
$31,292
The Legacy of Angels Foundation

Integrating emergency department data with law enforcement, emergency medical service and community data to reduce violence
Investigator: Andrew Marek
$14,087
Medical College of Wisconsin
EMERGING RESEARCH


Abstracts


Continued →


Reynolds KH, Simpson DE, Frederick T. SP12: Nutrition part IV maintenance of certification module is win-win for residents, faculty, and patients. 2016 Society of Teachers of Family Medicine Annual Spring Conference Abstracts. Available at: http://www.stfm.org/Conferences/AnnualSpringConference/PastConferences/2016AnnualSpringConference?m=6&s=17174.


2016 STATISTICS
AURORA RESEARCH INSTITUTE

510 total research studies as of Dec. 31, 2016*

2,678 subjects on trials Dec. 31, 2016

*Includes clinical trials and investigator-initiated studies

$25 million expenditures in 2016

341 total Aurora-authored publications in 2016
Research Business Services

26 Research Analytics requests in 2016 (>3 days effort)

34 new intellectual property disclosures and new entrepreneurial projects engaged in 2016

168 completed contracts in 2016

Sponsored Programs Office

$2.1 million extramural grants awarded in 2016

$379,485 intramural grants awarded in 2016

*Supported by an extramural grant provided by Vince Lombardi Cancer Foundation
Clinical Trials

329 clinical trials open to accrual and follow-up as of Dec. 31, 2016

1,409 new clinical trials subjects enrolled in 2016*

Open clinical trials: 3-year trend

Clinical trial enrollments: 3-year trend*

*Biorepository enrollments removed from oncology enrollments in 2016

Translational Research

181 investigator-initiated studies as of Dec. 31, 2016
Working together

Throughout Aurora Health Care a diverse network of caregivers is working toward the common goal of achieving the highest level of professional and ethical standards in research.

Collaboration among these caregivers results in the conduct of efficient, transparent and safe research.

COUNCIL FOR QUALITY ASSURANCE AND IMPROVEMENT IN RESEARCH

The Council for Quality Assurance and Improvement in Research oversees Aurora Research Institute’s Quality Management Plan, which ensures high-quality compliant research is conducted throughout Aurora.

Chaired by Nina Garlie, PhD, the council includes a broad representation of the institute, as well as members from Research Subject Protection Program and Research Compliance.

The council develops a strategic annual quality monitoring plan, assesses key performance indicators and makes recommendations to improve the quality of research. Melanie Guenther, senior research quality specialist, administers the quality assurance activities and reports findings to the council on a monthly basis.

RESEARCH SUBJECT PROTECTION PROGRAM/INSTITUTIONAL REVIEW BOARDS

Led by Michelle Maternowski, Aurora’s Research Subject Protection Program is charged with the oversight of human and animal subject research conducted at Aurora, safeguarding the rights, welfare and dignity of the human and animal subjects who participate in the research process.

Responsibilities include managing Aurora’s institutional review boards, which ensure research proposals meet the highest ethical standards.
Aurora St. Luke’s Medical Center’s cardiology and heart surgery program was the only one in the state nationally ranked by U.S. News & World Report in its 2016-17 Best Hospital rankings.

U.S. News sifted data from nearly 5,000 medical centers and survey responses from more than 30,000 physicians to rank hospitals in 16 adult specialties. Patient survival and safety data and hospital reputation helped determine the rankings.

“Aurora’s cardiovascular researchers have dramatically increased the institution’s reputation through presentation at major international conferences and publication in renowned scientific journals,” said Randall Lambrecht, PhD, president of Aurora Research Institute.

In addition to its cardiology and heart surgery program, Aurora St. Luke’s geriatrics and gastroenterology and gastrointestinal surgery programs ranked among the top 50 in the nation, contributing to the hospital ranking second in the Milwaukee metro area and third in Wisconsin. Less than 3 percent of the hospitals analyzed were nationally ranked in even one specialty.

Additionally, Aurora St. Luke’s was deemed a high performing hospital in the areas of cancer, diabetes and endocrinology, gynecology, nephrology, neurology and neurosurgery, pulmonology and urology.

Aurora BayCare Medical Center and Aurora Medical Center in Grafton tied for seventh in the state with Aurora BayCare recognized in Northeastern Wisconsin and Aurora Grafton recognized in Southeastern Wisconsin.

Meaningful and impactful research requires dedicated researchers, physicians and caregivers; generous friends and donors; and the commitment of Aurora Health Care, the Aurora Research Institute Board of Directors and leadership at sites throughout the system. But for this work to be truly patient-centered, courageous men and women must participate. Thanks to all who contributed to the patient-centered research captured in this report for helping transform innovative research into extraordinary care.
Purpose, Vision, Values

PURPOSE
We help people live well through innovative research.

VISION
Offer more treatment choices and improve patient outcomes through research and innovation

VALUES
• Every patient and community deserves the best care.
• Resources should be managed responsibly.
• A healthy workplace is built through accountability, teamwork and respect.