

GILL HEART INSTITUTE State of the Heart 2012



UKHealthCare. Gill Heart Institute

About UK HealthCare



Fifty years ago under the leadership of Governor Albert B. "Happy" Chandler, the University of Kentucky opened the UK College of Medicine and established the Albert B. Chandler Hospital. The medical college and the new hospital were founded to address a physician shortage and inadequate clinical services for the people of central, southern and eastern Kentucky.

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Over the years, the College of Medicine and Chandler Hospital have grown into a substantial academic medical center and now serve as a regional referral center. On the campus, five additional health care-related colleges have joined the College of Medicine in producing clinicians, teachers, researchers and health experts for the Commonwealth and the nation, while creating a nucleus of intellectual inquiry matched by few academic medical centers.

Seven years ago the UK College of Medicine, the practice plans and Chandler Hospital were organized as a clinical enterprise – UK HealthCare – under a new Executive Vice President for Health Affairs, in an effort to better support the university's responsibilities to the Commonwealth.

We are committed to a strategy emphasizing advanced subspecialty care here in Lexington, while pursuing productive, mutually supportive relationships with regional and rural providers. We recognized efficiency, quality, safety and service as critical success factors. Aggressive faculty recruitment has enabled UK HealthCare to increase its capacity to care for those who need our advanced level of care.

The initiatives we outlined in 2004 have succeeded beyond our highest expectations. Our accelerated pace of accomplishment indicates the state was ready for the university to fully assume the mantle of leadership in providing medical care to the people of the Commonwealth. Because of the breadth and quality of faculty recruited and our educational and research agenda, critical clinical programs are made available to the state, ensuring Kentuckians have access to the best of contemporary care. We are now poised to serve as a clinical destination for patients from beyond our original market boundaries. The new patient-care facility is evidence of a commitment by UK HealthCare to serve the citizens of Kentucky with the highest level of care. This new facility houses 1.2 million-square-feet of the most advanced health care space seen anywhere in the United States, designed to meet both present and future needs. It includes establishment of the Gill Imaging Center, which provides the latest in MRI and CT imaging technology. Today, improvements and expansion of our facilities continues. We recently completed the addition of eight new, state-of-the-art operating rooms and opened one of the country's largest hybrid operating rooms.

UK HealthCare has forged linkages and relationships with community providers and is poised to deploy a more integrated system of care. Our partnership with Norton Healthcare in Louisville allows us to work together to address some of Kentucky's most pressing health problems, including heart disease, stroke, and obesity. As an extension of outreach, the Gill Heart Institute is developing an affiliate network with community providers to strengthen the services available at the community level, provide patients with a seamless spectrum of care, and offer much-needed educational "wellness" programs.

While we continue to nurture and promote partnerships throughout the Commonwealth, we are also positioning ourselves as a regional provider. We continue to increase the numbers of patients who come to us for advanced specialty care such as heart and other solid organ transplants. With volume comes the ability to support the infrastructure necessary to be considered a primary medical destination for those seeking world-class care for the most complex and life-threatening conditions.

We continue to seek the talents of the highest achievers in the area of research and medicine. As always, our focus remains on quality and to be the benchmark of excellence by which others measure themselves. Paying attention to the needs of patients, improving efficiency, and engaging faculty and staff in the pursuit of excellence produces the best possible outcomes for us all.

Michael Karpf, MD Executive Vice President for Health Affairs UK HealthCare

About the University of Kentucky College of Medicine



Frederick C. de Beer, MD

At the University of Kentucky, College of Medicine we pride ourselves in educating future physicians and scientists. The College provides innovative, high-quality education to all of our learners. Our programs are fully accredited and nationally respected. From the unique Rural Physician Leadership Program to the challenging MD-PhD dual degree, we have options to meet the individual interests and passions of students and mentors.

Graduate students and postdoctoral fellows benefit from the College's strong collaborative research programs and the many exciting biomedical research projects taking place here. For house staff, our College offers more than 50 specialty and subspecialty areas of medicine. The faculty of the UK College of Medicine are excellent educators, who are dedicated to teaching in an ambiance of collegiality and respect.

We are also conducting breakthrough biomedical research. Currently, UK College of Medicine has more than 229,000-square-feet of modern research space to facilitate basic, translational, and clinical research. The productivity of the College's faculty has led to impressive gains in research funding. Grants and contracts in the College of Medicine reached \$134.8 million in fiscal year 2010, including more than \$88 million in National Institutes of Health (NIH) funding. With the UK Center for Clinical and Translational Science's recent Clinical and Translational Science Award from the NIH, we are a part of a select national biomedical research consortium and on our way to becoming a Top 20 research institution. These and other accomplishments mean more opportunities to participate in valuable research endeavors. We view research as a collaborative effort and benefit from being one of the few universities in the nation to have all six health science colleges on our campus. The College of Medicine is now well-positioned for inter-professional health care collaboration and research.

Our clinical enterprise is a standard-bearer in providing quality, complex patient care to the Commonwealth and beyond. Our clinical faculty deliver care at UK Albert B. Chandler Hospital, Kentucky Children's Hospital, UK Good Samaritan Hospital, Markey Cancer Center, Gill Heart Institute, Kentucky Neuroscience Institute and Kentucky Clinic, as well as the adjacent Lexington Veterans Affairs Medical Center. These state-of-the-art facilities provide an excellent training ground for students, researchers and house staff. Additionally, a new 1.2 million-square-foot patient care Pavilion at UK Albert B. Chandler Hospital was recently completed. This Pavilion includes the new UK Chandler Emergency Department and the Makenna David Pediatric Emergency Center, and is paramount in the plan to become a premier regional medical center concentrating on cancer, trauma, neurosciences, organ transplantation and pediatric subspecialties.

With our academic and clinical operations working together synergistically, we are on the verge of pushing the College of Medicine from very good to great. It is truly an exciting time to be a part of the University of Kentucky's College of Medicine.

Frederick C. de Beer, MD Dean, College of Medicine Vice President for Clinical Academic Affairs Professor of Internal Medicine University of Kentucky

About the Linda and Jack Gill Heart Institute

The Linda and Jack Gill Heart Institute is at the forefront in the battle against heart disease and stroke in Kentucky and is nationally recognized as a leader in advancing the treatment and prevention of cardiovascular disease. Our mission is to improve heart health by providing clinical services based on the latest evidence and technology, advancing the field with research, and educating students, physicians, health care providers and the public.

The Gill Heart Institute's comprehensive approach to heart and vascular health begins with promoting cardiovascular wellness and extends to treating life-threatening complications with the newest therapies and devices. Our greatest asset is our faculty — a multidisciplinary clinical team that includes members from six services — adult and pediatric cardiology, cardiothoracic surgery, vascular surgery, cardiac radiology, and cardiac anesthesiology. Our cutting-edge facilities are available in the Albert B. Chandler Hospital, ranked No. 1 in Kentucky in *U.S. News & World Report's* "Best Hospitals 2012 – 2013; the UK Good Samaritan Hospital, office locations at the Gill Heart Institute Building on the UK campus, at Maxwell Street in downtown Lexington, and at nearly a dozen outreach sites around the Commonwealth.

The Gill Heart Institute serves as a focal referral center for the treatment of cardiovascular diseases. We offer the only advanced heart failure and transplantation program in the region, and are one of 34 centers in the U.S. certified in the implantation of the SynCardia temporary Total Artificial Heart. The Gill Imaging Center, equipped with two 64-slice CT scanners, a 1.5 Tesla, and a 3.0 Tesla MRI scanner, performs complex adult and pediatric cases in a close collaboration between cardiology and radiology. Our complete cardiovascular care includes a cardiac rehabilitation program, cutting-edge electrophysiology and interventional cardiology procedures, minimally-invasive approaches to structural heart disease, and extensive surgical services for heart and vascular disease. Our aim is to provide every patient with exceptionally compassionate care in the safest and most appropriate manner possible based on the best evidence and latest technological advances.

The University of Kentucky is the region's top teaching and research institution, and our educational and research emphasis fosters a "bench to bedside" translational approach that ensures patients benefit from the latest scientific advances. The Saha Cardiovascular Center unites a strong group of investigators geared towards elucidating the underpinning of cardiovascular disease. Our participation in clinical studies makes available innovative treatments that would otherwise not be available in this region of the country - such as renal denervation for resistant hypertension. The University's receipt of a Clinical and Translational Science Award (CTSA) from the NIH places us in an elite group of 60 biomedical research institutions positioned "to improve human health by streamlining science, transforming training environments and improving the conduct, quality and dissemination of clinical and translational research".

We are committed to educating physicians and scientistsin-training and developing the careers of young investigators. The excellence of our training programs has been recognized by the NIH and professional organizations such as the American Heart Association and the Society for Cardiac Angiography and Interventions. Improving the cardiovascular health of Kentuckians and beyond will require educating health care providers and the public, and our faculty enthusiastically disseminates knowledge to local communities about progress and emerging issues in cardiovascular disease.

The following pages describe our history, services, and accomplishments. In them, you will learn of our commitment to the highest standards of excellence in the diagnosis and treatment of cardiovascular diseases and our dedication to scholarly pursuits that will improve the future of heart health in Kentucky and the nation.

Susan S. Smyth, MD, PhD Division of Cardiovascular Medicine





Gill Heart Institute History

In 1859 Transylvania Medical School (the first medical school west of the Appalachian Mountains) closed, leaving a void in the training of physicians in the Eastern part of Kentucky and the surrounding region. Nearly a century later, in 1956, the Kentucky General Assembly approved the construction of the University of Kentucky medical center with the call to establish "... a Medical Center, which shall include a College of Medicine, a College of Dentistry, a College of Nursing, and a University Teaching Hospital."

The hospital was named in honor of **Governor Albert B. Chandler**, because of his strong support in establishing an institution to "Serve the poor people of Eastern Kentucky." The Albert B. Chandler Medical Center was dedicated in 1960 and the college accepted its first class of 39 medical students – the future graduating class of 1964. The 454,426-square-foot hospital complex was completed in 1962 and featured 400 inpatient beds, 50 beds for newborns and premature infants, 95 beds for ambulatory care, and a 25-bed rehabilitation unit.

Dr. William R. Willard was named the first Dean of the College of Medicine, and in 1961 he recruited Dr. Edmund D. Pellegrino from Yale University to be the first Chairman of the Department of Medicine. The Division of Cardiovascular Medicine was established with the appointment of its first two faculty members, Dr. John T. Reeves (interim chief) and Dr. Alberto Mazzoleni. Dr. Reeves had an interest in pulmonary hypertension, and his research centered on high-altitude hypoxemia and right heart hemodynamics. He established the first cardiac catheterization laboratory and, with Dr. Jacqueline Noonan in Pediatrics, founded 20 Regional Heart Clinics where adult and pediatric patients were treated. Dr. Mazzoleni was recruited from Beth Israel in Boston where he worked with cardiologist Dr. Louis Wolff (of Wolff-Parkinson-White Syndrome fame). Mazzoleni served as Director of Medical Education and was a leader in cardiology education until his retirement in 2003. During his 40 years at the university, Dr. Mazzoleni trained more than 150 cardiology fellows. In 2010, the Alberto Mazzoleni Professorship in Cardiology was created as the first teaching professorship in medicine at UK. Funding

Gill Heart Institute Leadership



Mark Plunkett, MD Frank C. Spencer Associate Professor of Surgery Chief, Cardiothoracic Surgery Surgical Director, Gill Heart Institute



Susan S. Smyth, MD, PhD Jeff Gill Professor of Cardiology Chief, Cardiovascular Medicine Medical Director, Gill Heart Institute



Alan Daugherty, PhD, DSc Gill Foundation Chair in Preventive Cardiology Senior Associate Dean for Research Director, Saha Cardiovascular Research Center

for the professorship came largely from former cardiology fellows in appreciation of the unwavering commitment of "Dr. Mazz" to excellence in education. In October 2010 **Dr. Mikel D. Smith** was honored as the first Mazzoleni Professor in Cardiology.

Dr. Borys Surawicz was named the first Chief of Cardiology in 1962 and held the position until 1981. Born in Moscow and educated in Vilno, Poland, Dr. Surawicz moved to Germany after WWII to work with **Dr. Eugene Lepeschkin**, the author of a primary textbook on ECG at the time. Dr. Lepeschkin subsequently joined the faculty at the University of Vermont, and Dr. Surawicz soon joined him there. Surawicz published the first papers on how to

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measure the QRS and QT intervals, and was lead author on the original description of the effects of potassium and calcium on the ECG. Reflecting back on the decision to accept the position to direct a Division of Cardiology in the new medical school at the University of Kentucky, Dr. Surawicz recalled:

"In those times, Eastern Kentucky had been somewhat isolated geographically and culturally and the new school had a mission. For cardiology, it meant setting up traveling clinics throughout the coal-mining mountain district, and provided an opportunity for medical and surgical treatment in Lexington. Running the Division meant to develop a curriculum for medical students, to organize postgraduate education, to care for cardiac patients on the wards and in the clinic, to set up a cardiac cath lab and coronary care unit, and to compete for NIH-funded research and clinical training program grants [fellowship stipends]. Fortunately, I was able to recruit a splendid faculty working in an atmosphere of unprecedented friendship and collegiality."

The sixties and seventies were busy times for the new division. Some of the highlights during that period included:

- Admission of the first patient to the new UK hospital

 a child treated by Dr. Jacqueline Noonan for patent ductus arteriosis, a congenital heart defect that appears soon after birth. Dr. Noonan is internationally known for her description of Noonan Syndrome, a genetic disorder characterized by distinct facial traits, short stature, and congenital heart defects.
- The Cardiovascular Fellowship program was created with support from a training grant from the NIH in 1963; Drs. Leonard Gettes, John Bergland, and Warren Rucker were the first fellows. In the ensuing years, more than 200 clinical trainees have followed, and 100 research fellows have completed training at the University of Kentucky. Throughout the years, UK has been continuously recognized as providing excellence in state-of-the-art training in all aspects of clinical cardiology.
- After serving a term as the President of the Association of University Cardiologists, Dr. Surawicz became the first UK faculty to serve as the President of the American College of Cardiology, from 1978 to 1980.



- Among the notable faculty in the 1960s and 1970s was Dr. Ralph Shabetai, who directed the cardiac catheterization laboratory. Shabetai's work formed the basis for the understanding of pericardial tamponade and constriction. He left UK to become Chief of the VA Hospital at the University of California-San Diego. Dr. Leonard **Gettes,** who was the founding director of the Coronary Care Unit, established the first Code Teams, implemented biomarker testing to diagnosis of myocardial infarction, and the use of defibrillators for bedside treatment of ventricular arrhythmias. Dr. Gettes went on to become Chief of Cardiology at the University of North Carolina. Dr. Henry "Hank" Hanley, who worked with Dr. Michael DeBakey, was instrumental in the deployment of heart catheterization at UK. He later became Chief of Cardiology at LSU-Shreveport. Dr. Mauricio Rosenbaum spent a sabbatical year in Lexington that was remarkable for its educational significance to UK. Rosenbaum is credited with recognizing the importance of Chagas Disease, and revolutionized electrocardiography with the first-ever description of hemiblocks in humans. Dr. Pratap Reddy, who worked under electrophysiology notables, Drs. Mark Josephson, Mark Gallagher, and Onkar Narula, was recruited to be the founding director of electrophysiology. Dr. Reddy later became the Chief of Cardiology at LSU-Shreveport, a position he continues to hold.
- As a result of the efforts of Drs. Surawicz, Mazzoleni, Gettes, and Rosenbaum, this was the era when "ECG was King" in cardiology, and the University of Kentucky was one of the centers of excellence in this field in the country. Dr. Surawicz organized more than 20 ACCsponsored courses at UK, Louisville, and Cincinnati to teach practicing and academic cardiologists about

ECG. UK faculty were recognized as national experts in sudden cardiac death, the effects of electrolytes on the ECG, and new antiarrhythmic agents.

• During this period, the innovative valve surgeon, Dr. Frank Spencer, was appointed as founding Chief of the Division of Cardiothoracic Surgery. Dr. Spencer authored one of the primary textbooks of the era, The Clinical Practice of Surgery. He left UK to become Chief of Cardiothoracic Surgery at New York University. In 1966, Dr. Ben Eiseman (who trained at Harvard Medical School and Massachusetts General Hospital and served as Professor of Surgery and Chairman of UK's Surgical Division from 1961 to 1967), Dr. Spencer, and Dr. W.G. Malette were among the first physicians to describe mechanical assist devices: "Total replacement of the heart with a pump has captured popular fancy and undoubtedly ultimately will be feasible for the irretrievably damaged or congenitally deformed heart... The appeal is so great, however, that many investigators



are trying to land on Mars before they even reach the moon!" (Annual Review of Medicine, Volume 17, 1966).

In the early 1970s, the Echocardiography laboratory was established by the collective efforts of Dr. Jamie Jacobs (recruited from Indiana University, where M-mode technology was being pioneered by Dr. Harvey Feigenbaum) and Drs. V. Aravandakshin and Jacqueline Noonan. After a visit to Dr. Feigenbaum's laboratory, Dr. Surawicz and others at UK determined echo to be a useful test for the future, and the first M-mode study was performed in 1974 on a patient with suspected mitral stenosis.

In 1981, **Dr. Anthony DeMaria** was recruited to serve as the Director of the Division of Cardiology. During his tenure at UK, he served as President of the American College of Cardiology and President of the American Society of Echocardiography. After leaving the university, he became Professor of Medicine and Chief of Cardiology at the University of California-San Diego School of Medicine. Under Dr. DeMaria's attentive stewardship, cardiovascular medicine thrived at UK:

- Included among the notable accomplishments was the emergence of Kentucky as a pioneering center in cardiovascular imaging. Drs. Mikel Smith and DeMaria, were the first to characterize the use of the color Doppler jet in mitral regurgitation and concluded that "...maximal jet area from Doppler color flow imaging provides a simple measurement that predicts angiographic grade, but manifests a weak correlation with regurgitant volume and does not predict hemodynamic dysfunction..." (Journal of the American College of Cardiology 1989, 13:3, 585–590). The group was also instrumental in analyzing transmitral flow velocities to detect left ventricular filling patterns and diastolic function. UK imaging experts directed the Heart House course at the National Learning Center in Bethesda, MD for more than 10 years. Dr. Mikel Smith assumed direction of the Echo and Stress laboratory in 1989 and remains its leader today.
- The first thrombolytic trials for myocardial infarction in Kentucky were performed by Dr. Cindy L. Grines, an interventional cardiologist now at Detroit Medical Center, and others. Drs. Grines, David Booth, Steve Nissen, John Gurley, and DeMaria also reported on the acute effects of beta-blocker therapy after thrombolysis in humans.
- In 1991 the group published one of the first reports on the use of intravascular ultrasound to assess coronary dimensions and wall morphology. (Nissen SE, Gurley JC, Grines CL, Booth, DC, McClure R, Berk M, Fisher C, and DeMaria. "Intravascular ultrasound assessment of lumen size and wall morphology in normal subjects and patients with coronary artery disease." *Circulation* 1991; 84: 1087-1099). Dr. Steve Nissen, who completed his cardiology fellowship at UK in 1983 and currently serves as the Chair of Cardiovascular Medicine at the Cleveland Clinic, went on to champion quantitative

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coronary angiography and intravascular ultrasound to detect and manage the progression and regression of coronary atherosclerosis.

• Dr. Michael Sekala, who trained under famed heart surgeon Dr. Michael E. Debakey, founded the transplant program during this period. The first heart transplant was performed in Lexington in 1991. UK is still the only hospital east of Louisville to perform heart transplants in the Commonwealth.

In the 1990s, the medical center expanded physically. Following Dr. DeMaria's departure in 1991, and **Dr. David Booth** assumed leadership as the Chief of the Division of Cardiology. With the recruitment of **Drs. Pedro Moreno** and **Alan Daugherty**, UK established a reputation for excellence in atherosclerosis research. In collaboration with **Dr. Lisa Cassis**, Daugherty developed one of the first preclinical models of aortic aneurysm (*J Clin Invest* 2000;105:1605-12). **Dr. Frederick deBeer**, who currently serves as the Dean of the College of Medicine, together with Daugherty and Cassis, built a program that has made fundamental contributions to the understanding of the cellular and molecular underpinnings of atherosclerosis, aneurysm, and inflammation.

In 1997, **Linda and Jack Gill** donated \$5 million to establish a comprehensive academic program in cardiovascular science, including establishment of the Gill Heart Institute and endowed professorships. The founding principles of the Gill Heart Institute were to unite high quality clinical heart care with leading-edge heart health research and to become one of the Top 10 public cardiovascular facilities in the nation. Accomplishments of this period include:

- Substantial commitments were made to expanding the heart failure and transplantation program that culminated with the appointment of Dr. William Abraham as Chief of the Division in 2000. During this period, Dr. Abraham, currently the Chief of Cardiovascular Medicine at Ohio State University, described the use of "Cardiac Resynchronization in Chronic Heart Failure" (*N Engl J Med* 2002; 346:1845-1853), and participated in studies of B-type natriuretic peptide in the diagnosis of heart failure (*N Engl J Med* 2002; 347:161-167), and use of nesritidie in the treatment of heart failure.
- In 2004, construction of the \$25 million Linda and Jack Gill Heart Institute Building was completed. The five-level, 108,000-square-foot structure houses clinics,



diagnostic areas, six catheterization and electrophysiology laboratories with associated support services, and numerous administrative and faculty offices. The Gill Imaging Center, the first of its kind devoted to advanced cardiovascular imaging in the region, holds next-generation CT technology (a first for Kentucky) and two MRI units for imaging the heart and vascular system. **Dr. David Moliterno** from Cleveland Clinic, and **Dr. Mark Plunkett**, from UCLA, were recruited to serve as the Medical Director and Surgical Director, respectively, of the Gill Heart Institute.

Tremendous growth in cardiovascular clinical care, research, and education took place under Dr. Moliterno's leadership as Chief of the Division. Moliterno, an interventional cardiologist widely recognized for his involvement with clinical trials, recruited Dr. Debabrata **Mukherjee** from the University of Michigan, to direct the cardiac catheterization laboratories, and Dr. Steven Steinhubl from the University of North Carolina to oversee clinical cardiology research and education. Dr. Khaled M. Ziada, from Cleveland Clinic, later joined the team and assumed direction of the catheterization laboratory upon the departure of Dr. Mukherjee (who currently serves as founding Chief of Cardiovascular Medicine at Texas Tech in El Paso). Dr. Chuck Campbell, who was enlisted to direct the cardiac care unit, led the development of an integrated, adult inpatient cardiovascular service. Basic and translational research within the division were strengthened with the addition of Drs. Susan Smyth and Andrew Morris, from the University of North Carolina.

Gill Heart Institute Accomplishments in the 2000s:

- Growth in clinical care with nearly a 70% increase in total cardiovascular visits, driven by the establishment of a dozen outreach sites overseen by **Dr. Rick McClure** and enhanced by the opening of the of UK Cardiac Rehabilitation Center in 2009, under the direction of **Dr. Alison Bailey**.
- Cardiovascular imaging advancements with faculty recruitment and infusion of novel technology was integrated under the direction of Dr. Vincent Sorrell, the imaging faculty is comprised of Drs. Anil Attili, Michael Brooks, and Michael Winkler in the Division of Cardiovascular & Thoracic Radiology, and Drs. Sorrell, Mikel Smith, Paul Anaya, and Steve Leung, in the Division of Cardiovascular Medicine. The first cardiovascular imaging fellow joined the program in 2012.
- Faculty expansion with the recruitment of section members and leaders in adult cardiac electrophysiology include: Drs. Shamik Aikat, Samy-Claude Elayi, Gustavo Morales, and Jeffrey Brumfield, who are assisted by Stephanie Lusher, ARNP. The dramatic expansion of electrophysiology services has energized research in clinical electrophysiology, and forms the foundation for the establishment of a cardiac clinical electrophysiology fellowship.
- Reinvigoration of the advanced heart failure, transplantation, and mechanical circulatory support program occurred with the recruitment of **Dr. Navin Rajagopalan**, who serves as the Medical Director of Heart Transplantation and Ventricular Assist Device Program and, more recently, with the addition of **Dr. Charles Hoopes** from the University of California at San Francisco, to serve as UK Director of Transplant.
- Revitalization of research activities led to UK achieving the status of one of the 10 highest-funded institutions by the American Heart Association. Moliterno, who was instrumental in studies of vorapaxar, a thrombin receptor antagonist and first-in-class antiplatelet therapy (*Lancet* 2009:373;919-928.), served as editor-in-chief of "CathSAP-3" for the American College of Cardiology and, with Mukherjee, authored several major textbooks and board-review publications in interventional cardiology. Under Steinhubl's direction, Phase I studies of the

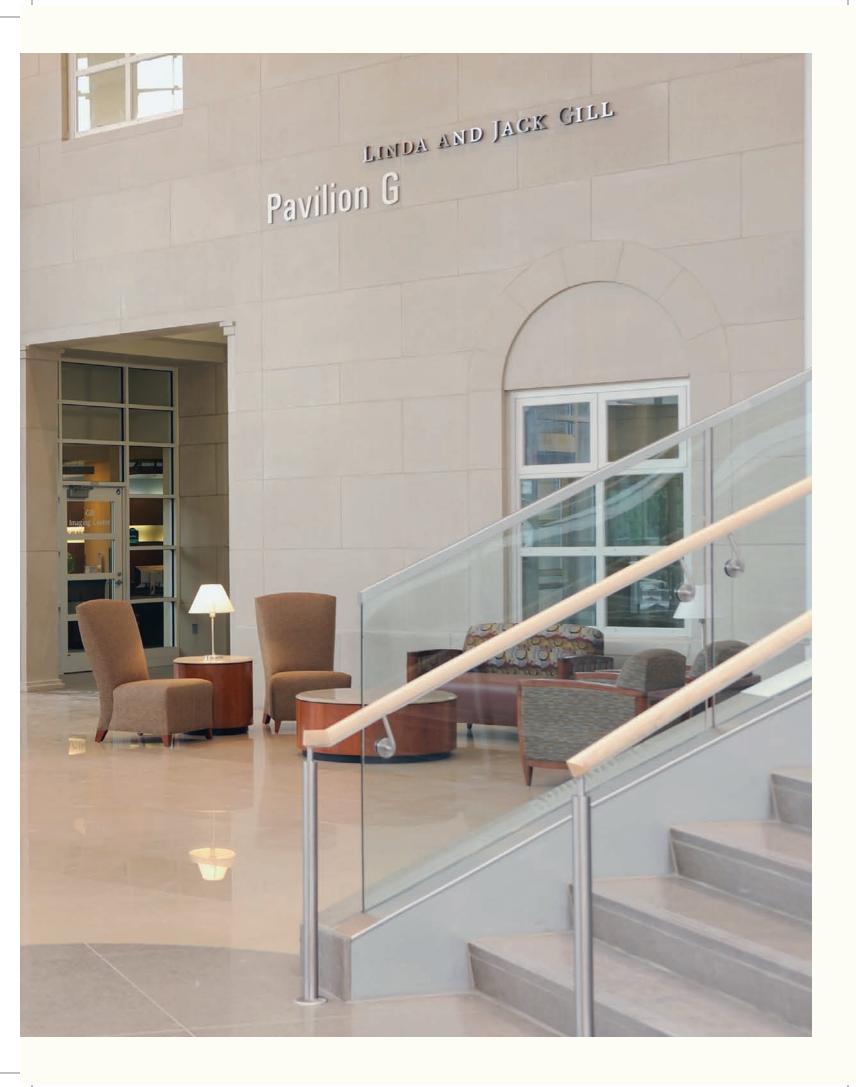
P2Y12 antagonist cangrelor (*Thromb Res.* 2008;121:527-34) and the first, in-man study of an RNA aptamer targeting FIXa (*Circulation.* 2006;114:2490-7), were performed at the University of Kentucky. Studies by Drs. Campbell, Steinhubl, and Smyth supported use of low-dose 81 mg aspirin for prevention of cardiovascular disease (*JAMA* 2007; 297:2018-24). Booth and other investigators in the COURAGE study demonstrated the benefits of medical versus revascularization for patients with stable angina. Fresh talent was added with junior physician-scientist investigators, including **Drs. Ahmed Abdel-Latif, Zhenyu Li**, and more recently, **Brandon Fornwalt**.

- The commitment to education and training remains firm as the fellowships grew to 18 general cardiology fellows, four interventional fellows, one imaging fellow, two cardiothoracic fellows, two vascular fellows, one EP fellow (joining in 2013), and four research fellows. Extramural support for training in cardiovascular medicine and science comes from the NIH with the awarding of a postdoctoral T32 training grant for fellows in cardiovascular science (Director, Smyth) and from the Society for Cardiac Angiography and Interventions for interventional fellows (Director, Ziada). Additionally, the institution houses two, NIH predoctoral T32 training grants for students – one in cardiovascular research and one in muscle biology in the cardiopulmonary system
- In 2010, the Cardiovascular Research Center was renamed in recognition of an endowment made by Dr. Sibu Saha and his wife, Becky Saha. The Saha CVRC serves as a major center for research of cardiovascular diseases, focusing on the prevention, diagnosis and treatment of diseases affecting the heart and blood vessels – including atherosclerosis, aneurysm, stroke, heart attack, obesity and hypertension.
- What was once a cornfield has been transformed into one of the South's most advanced medical centers. In 2011, the new Albert B. Chandler Hospital and Pavilion opened, connecting the Gill Heart Institute to the new hospital. In 2012, UK's Albert B. Chandler Hospital was ranked No. 1 in Kentucky in U.S. News & World Report's "Best Hospitals 2013."



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Adult Cardiovascular Services



The Gill Heart Institute offers a complete range of comprehensive cardiovascular care services and clinical treatment programs. Our physicians are experienced in the latest advances in the evaluation and treatment of heart and vascular diseases. As the only academic medical center in the region, we serve as a clinical destination for advanced cardiovascular care in this part of the country.

Inpatient adult cardiovascular services

Our physicians, scientists, nurses, and affiliated staff are committed to the highest level of care – for both simple and complex cases – and to delivering safe and appropriate treatments. Our superb clinical care is provided by approximately 150 nursing and clinical staff that manage adult and surgical cardiovascular cases in an integrated intensive care unit and in acute care beds. This patient-centered approach reduces the number of transitions experienced during the continuum of the hospital stay. Our patient-centered focus also allows us to keep the time in hospital as short as possible – indeed, our length of stay index remains below that of most other academic medical centers.

The last eight years were a period of tremendous growth in inpatient care at UK Healthcare. Hospital admissions increased 63%, from 19,000 per year to more than 32,000. This volume places UK in the 75th percentile of academic medical centers. In keeping with the growth of UK HealthCare, our inpatient adult cardiovascular admissions have also seen a significant expansion, at nearly 2,000 annually. Our total cardiovascular annual visits went from just over 15,000 in 2005 to nearly 25,000 in 2012. These gains translate into a doubling in our percentage of the area's adult hospital cardiovascular treatment volume. As we emerge as a quarternary destination site, our casemix index, a measure of the clinical complexity of the care (based on associated medical conditions) has increased. Hypothermia, EKOS ultrasound accelerated infusion, catheter-based delivery of thrombolytic drugs; percutaneous and surgically-implanted ventricular assist devices; and extracorporeal membrane oxygenation (ECMO) technology are employed daily in the intensive care unit. And, while the care that we provide has become more complex and diverse, we maintain the highest clinical standards. The UK ECMO Program has been designated as a Center of Excellence with receipt of the Excellence in Life Support Award from the Extracorporeal Life Support Organization (ELSO), in recognition of exceptional care, training and education, as well as achieving optimal levels of performance, innovation, satisfaction, and quality. In 2011, we ranked in the Top 10 of academic hospitals for in-hospital cardiology survival, according to the University Health Consortium product-line definitions. And, UK's Albert B. Chandler Hospital was designated the No. 1 hospital in Kentucky, according to the 2012-13 Best Hospitals rankings published July 17, 2012, by U.S. News & World Report. This performance is possible due to an atmosphere that promotes patient-centered care provided by a multidisciplinary team with a commitment to utilizing cutting-edge therapies with the safest and most evidencebased approaches, tailored to individual patient needs.

Outpatient and outreach sites

Our cardiologists provide the region's most comprehensive diagnostic assessment and therapeutic strategies in 10 different locations in Lexington, the Bluegrass region, and beyond. With more than 40 clinics per month in offices outside of Lexington, visits to Gill-affiliated sites topped 16,500 last year. As we implement aggressive treatment with support from revolutionary diagnostic technology, we also work closely with local providers to enhance appropriate clinical services available in rural areas of the state.

Cardiac catheterization laboratories

Operating in four, state-of-the-art catheterization laboratories situated in 20,000-square-feet dedicated to periprocedural patient care, our team of interventionalists, nurses, pharmacists, and technicians employ sophisticated technologies to approach complex cases safely and with excellent outcomes. The University of Kentucky's contributions to interventional cardiology are not new intravascular ultrasound imaging of human coronary arteries was born at UK in the late 1980s. The concept of air transport and early reperfusion for acute myocardial infarctions has been championed by UK cardiologists for more than three decades. And the interventional cardiology training program at UK was one of the first ever to be established in the U.S.

As a tertiary center, the cardiac catheterization laboratory performs complex coronary, valvular, and vascular interventions. Between the Gill Heart Institute and the Lexington VA Medical Center, our interventional cardiologists perform more than 800 interventional coronary procedures every year. In addition to standard coronary angioplasty, we have special expertise in more complex interventional approaches that provide a higher level of diagnostic accuracy and innovative therapeutic interventions to patients with complex conditions for whom standard techniques are unfeasible or inadequate. The team is highly experienced with pressure-wire assessment of coronary lesions, virtual histology intravascular ultrasound, and optical coherence tomography for arterial imaging. We have substantial experience with rotoblator atherectomy for complex, coronary lesions and in restoration of patency in chronic total occlusions, not amenable to standard angioplasty techniques. We perform high-risk coronary interventions, often with the support of assist devices, either in the catheterization laboratory or in the state-of-the-art hybrid OR suite.

In addition to coronary procedures, UK interventional cardiologists are highly experienced in peripheral and cerebrovascular interventional procedures. Hundreds of renal, iliac and femoral procedures are performed at the Gill Heart Institute every year with excellent outcomes. Many of those procedures are referred to the Gill for their complexity, and require innovative approaches such as transpopliteal access, subintimal dissection with ultrasound guided re-entry, and/or atherectomy. Our skilled operators also offer extra-cranial cerebrovascular interventions including subclavian, vertebral, and carotid angioplasty and stenting. The team has been part of the national FDA-mandated registry that examined the outcomes of

carotid stenting following approval of devices for clinical use. We are committed to the very best procedures that pay the utmost attention to patient safety—that is why all of our carotid procedures are performed using distal or proximal protection systems to guard against embolic events.

Renal denervation is another recent innovation that is available at the Gill Heart Institute catheterization laboratories; its aim is to help in the management of uncontrolled hypertension. This technology involves the use of radiofrequency catheters to ablate the sympathetic nervous plexus surrounding the renal artery using a transluminal radiofrequency catheter. It is offered by a limited number of centers across the country in the context of a Phase III clinical trial. The Gill Heart Institute is the only center in the state of Kentucky that is included in this important national study.

Pharmacy support

Four, board-certified pharmacotherapy specialists with added qualifications in cardiology, provide comprehensive and individualized review of care for Gill Heart patients. Hospitalized patients benefit from 24-hour clinical pharmacy coverage and daily medication review by pharmacy team members. Cardiology pharmacy faculty are jointly appointed to the UK College of Pharmacy, one of the Top Five Colleges of Pharmacy in the nation, according to *US News & World Report*. Our pharmacy services are one of only eighteen accredited Cardiology Pharmacy Residency training programs in the country.

Publications:

Coronary Artery Disease, Acute Coronary Syndromes & Interventional Cardiology

Anti-platelet and anti-thrombotic therapy

Rajan L, Moliterno DJ. New anticoagulants in ischemic heart disease. *Curr Cardiol Rep.* 2012 Aug;14(4):450-6.

Wiisanen ME, Moliterno DJ. Platelet protease-activated receptor antagonism in cardiovascular medicine. *Coron Artery Dis.* 2012 Jul 6.

Abdel-Latif A, Smyth SS. Preventing Platelet Thrombosis With a PAR1 Pepducin. *Circulation*. 2012 Jul 3;126(1):13-5.

Wallace, EL, Smyth SS. Spontaneous coronary thrombosis following thrombolytic therapy for acute cardiovascular accident and stroke: a case study. *J Thromb Thrombolysis.* 2012 Jun 10.

Rowley JW, Finn AV, French PA, Jennings LK, Bluestein D, Gross PL, Freedman JE, Steinhubl SR, Zimmerman GA, Becker RC, Dauerman HL, **Smyth SS**; 2011 Platelet Colloquium Participants. Cardiovascular devices and platelet interactions: understanding the role of injury, flow, and cellular responses. *Circ Cardiovasc Interv*. 2012 Apr;5(2):296-304.

Kristensen SD, Würtz M, Grove EL, De Caterina R, Huber K, **Moliterno DJ**, Neumann FJ. Contemporary use of glycoprotein IIb/IIIa inhibitors. *Thromb Haemost*. 2012 Feb;107(2):215-24.

Tricoci P, Huang Z, Held C, **Moliterno DJ**, Armstrong PW, Van de Werf F, White HD, Aylward PE, Wallentin L, Chen E, Lokhnygina Y, Pei J, Leonardi S, Rorick TL, Kilian AM, Jennings LH, Ambrosio G, Bode C, Cequier A, Cornel JH, Diaz R, Erkan A, Huber K, Hudson MP, Jiang L, Jukema JW, Lewis BS, Lincoff AM, Montalescot G, Nicolau JC, Ogawa H, Pfisterer M, Prieto JC, Ruzyllo W, Sinnaeve PR, Storey RF, Valgimigli M, Whellan DJ, Widimsky P, Strony J, Harrington RA, Mahaffey KW; TRACER investigators. Thrombin-receptor antagonist vorapaxar in acute coronary syndromes. *N Engl J Med.* 2012 Jan 5;366(1):20-33.

Granada JF, Price MJ, French PA, Steinhubl SR, Cutlip DE, Becker RC, **Smyth SS**, Dauerman HL. Platelet-mediated thrombosis and drug-eluting stents. *Circ Cardiovasc Interv*. 2011 Dec 1;4(6):629-37.

Smyth SS. Anti-platelet therapy. Curr Drug Targets. 2011 Nov;12(12):1790.

Bailey AL, Campbell CL. Oral antiplatelet therapy for acute coronary syndromes: aspirin, P2Y12 inhibition and thrombin receptor antagonists. *Curr Drug Targets*. 2011 Nov;12:1805-12.

Dunn SP, Macaulay TE. Drug-Drug Interactions Associated with Antiplatelet Therapy. *Cardiovasc Hematol Agents Med Chem*. Oct;14 2011.

Faxon DP, Eikelboom JW, Berger PB, Holmes DR Jr, Bhatt DL, **Moliterno DJ**, Becker RC, Angiolillo DJ. Antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting: a North American perspective: executive summary. *Circ Cardiovasc Interv.* 2011 Oct 1;4(5):522-34.

Faxon DP, Eikelboom JW, Berger PB, Holmes DR, Bhatt DL, **Moliterno DJ**, Becker RC, Angiolillo DJ. Consensus document: antithrombotic therapy in patients with atrial fibrillation undergoing coronary stenting. A North-American perspective. *Thromb Haemost.* 2011 Oct;106(4):572-84.

Rajan L, Moliterno DJ. Beyond aspirin and clopidogrel: is there a need for additional antiplatelet therapy in ACS? *Curr Cardiol Rep.* 2011 Aug;13(4):303-11.

Tricoci P, Newby LK, Hasselblad V, Kong DF, Giugliano RP, White HD, Théroux P, Stone GW, **Moliterno DJ**, Van de Werf F, Armstrong PW, Prabhakaran D, Rasoul S, Bolognese L, Durand E, Braunwald E, Califf RM, Harrington RA. Upstream use of small-molecule glycoprotein IIb/ Illa inhibitors in patients with non-ST-segment elevation acute coronary syndromes: a systematic overview of randomized clinical trials. *Circ Cardiovasc Qual Outcomes.* 2011 Jul;4(4):448-58.

Moliterno DJ; TENACITY Steering Committee and Investigators. A randomized two-by-two comparison of high-dose bolus tirofiban versus abciximab and unfractionated heparin versus bivalirudin during percutaneous coronary revascularization and stent placement: the tirofiban evaluation of novel dosing versus abciximab with clopidogrel and inhibition of thrombin (TENACITY) study trial. *Catheter Cardiovasc Interv.* 2011 Jun 1;77(7):1001-9.

Williams MS, Weiss EJ, Sabatine MS, Simon DI, Bahou WF, Becker LC, Parise LV, Dauerman HL, French PA, **Smyth SS**, Becker RC; 2010 Platelet Colloquium Participants. Genetic regulation of platelet receptor expression and function: application in clinical practice and drug development. *Arterioscler Thromb Vasc Biol.* 2010 Dec;30(12):2372-84.

Abdel-Latif A, Mukherjee D, Mesgarzadeh P, Ziada KM. Drug-

eluting stents in patients with end-stage renal disease: meta-analysis and systematic review of the literature. *Catheter Cardiovasc Interv.* 2010 Dec 1;76(7):942-8.

- This study examined the use of drug eluting (DES) and bare metal stents (BMS) in patients with end-stage renal disease (ESRD) in seven eligible studies (n = 869 patients).
- Compared with BMS-treated patients, DES-treated patients had significantly lower target lesion/vessel revascularization (OR 0.55 CI: 0.39-0.79) and major adverse cardiac events (MACE) (OR 0.54; CI: 0.40-0.73).
- The study concluded that use of DES in patients with ESRD is safe and yields significant reduction in the risk of revascularization and MACE.

Dauerman HL, Bhatt DL, Gretler DD, French PA, **Smyth SS**, Becker RC. Bridging the gap between clinical trials of antiplatelet therapies and applications among elderly patients. *Am Heart J.* 2010 Apr;159(4):508-517.

Macaulay TE, Allen C, Ziada KM. Thrombin receptor antagonism -the potential of antiplatelet medication SCH 530348. *Expert Opin Pharmacother.* 2010 Apr;11(6):1015-22.

Revascularization strategies

Wallace EL, Abdel-Latif A, Charnigo R, Moliterno DJ, Brodie B, Matnani R, Ziada KM. Meta-analysis of long-term outcomes for drugeluting stents versus bare-metal stents in primary percutaneous coronary interventions for ST-segment elevation myocardial infarction. *Am J Cardiol.* 2012 Apr 1;109(7):932-40.

- This study examined outcomes associated with the use of drug-eluting stents (DES) and bare-metal stents (BMS) in primary percutaneous coronary intervention (PPCI) in eight randomized clinical trials and five observational studies.
- Patients receiving DESs had a significantly lower risk of target lesion revascularization (OR 0.48, Cl 0.37 to 0.61), target vessel revascularization (OR 0.53, Cl 0.42 to 0.66), and accordingly major adverse cardiac events (OR 0.69; Cl 0.56 to 0.84).

- Those receiving DESs had a significantly lower mortality compared to those receiving BMSs (OR, 0.65, 95% CI 0.53 to 0.80, p <0.001).
- The study concluded that first-generation DES use in PPCI resulted in decreased repeat revascularization with no increase in ST, mortality, or recurrent myocardial infarction.

Foley JD, Moliterno DJ. Contemporary occurrence of stent thrombosis in clinical practice: Better never than late. *Catheter Cardiovasc Interv.* 2012 Mar 1;79(4):557-8.

Chan MY, Sun JL, Newby LK, Lokhnygina Y, White HD, **Moliterno DJ**, Théroux P, Ohman EM, Simoons ML, Mahaffey KW, Pieper KS, Giugliano RP, Armstrong PW, Califf RM, Van de Werf F, Harrington RA. Trends in clinical trials of non-ST-segment elevation acute coronary syndromes over 15 years. *Int J Cardiol.* 2012 Feb 16.

Abdel-Latif A, Moliterno DJ. Creating biodegradable-polymer drugeluting stents: shortening the duration of polymer and dual antiplatelet therapy while lengthening the follow-up. *Catheter Cardiovasc Interv.* 2012 Feb 1;79(2):217-8.

Wallace EL, **Moliterno DJ**. The use of drug-eluting stents versus bypass surgery for left main coronary artery disease. *Curr Cardiol Rep.* 2011 Oct;13(5):361-3.

Ziada KM, Charnigo R, Moliterno DJ. Long-term follow-up of drugeluting stents placed in the setting of ST-segment elevation myocardial infarction. *JACC Cardiovasc Interv.* 2011 Jan;4(1):39-41.

Wiisanen ME, Abdel-Latif A, Mukherjee D, Ziada KM Drug-eluting stents versus bare-metal stents in saphenous vein graft interventions: a systematic review and meta-analysis. *JACC Cardiovasc Interv.* 2010 Dec;3(12):1262-73.

- This study examined outcomes associated with the use bare-metal stents (BMS) and drug-eluting stents (DES) in saphenous vein graft (SVG) percutaneous coronary interventions (PCIs) in 4 randomized controlled trials and 19 cohort studies.
- Patients receiving DESs had a lower risk of mortality (OR: 0.75; CI: 0.59 to 0.96), target lesion revascularization (OR: 0.57; CI: 0.40 to 0.82), and MACE (OR: 0.61; CI: 0.42 to 0.79).
- There was no evidence of increased risk of myocardial infarction or stent thrombosis.

Medical therapy for coronary artery disease

Greene RS, Rangel RM, Edwards KL, Chastain LM, **Brouse SD**, Alvarez CA, Collins LJ, Brilakis ES, Banerjee S. Ranolazine for the treatment of refractory angina in a veterans population. *Cardiovasc Revasc Med.* 2012 Mar;13(2):141.e1-5.

Whayne TF Jr, Saha SP, Quevedo K, Mukherjee D. Optimal Medical Therapy for Coronary Artery Disease in 2011-Perspectives from the STICH Trial. *Cardiovasc Hematol Agents Med Chem.* 2011 Sep 9.

Chaitman BR, Hartigan PM, **Booth DC**, Teo KK, Mancini GB, Kostuk WJ, Spertus JA, Maron DJ, Dada M, O'Rourke RA, Weintraub WS, Berman DS, Shaw LJ, Boden WE; Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial investigators. Do major cardiovascular outcomes in patients with stable ischemic heart disease in the clinical outcomes utilizing revascularization and aggressive drug evaluation trial differ by healthcare system? *Circ Cardiovasc Qual Outcomes.* 2010 Sep;3(5):476-83.

Boden WE, O'Rourke RA, Teo KK, Hartigan PM, Maron DJ, Kostuk WJ, Knudtson M, Dada M, Casperson P, Harris CL, Chaitman BR, Shaw L, Gosselin G, Nawaz S, Title LM, Gau G, Blaustein AS, **Booth DC**, Bates ER, Spertus JA, Berman DS, Mancini GB, Weintraub WS; COURAGE Trial Research Group. Optimal medical therapy with or without PCI for stable coronary disease. *N Engl J Med*. 2007 Apr 12;356(15):1503-16

Novel biomarkers and targets

Foley JD, Sneed JD, Steinhubl SR, Kolasa J, Ebersole JL, Lin Y, Kryscio RJ, McDevitt JT, **Campbell CL**, Miller CS. Oral fluids that detect cardiovascular disease biomarkers. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012 Aug;114(2):207-14.

- The aim of this study was to determine the utility of oral fluids for assessment of coronary and cardiovascular health.
- Concentrations of the majority of biomarkers were higher in unstimulated whole saliva (UWS) than in sublingual swabs (LS) or gingival swabs (GS).
- The absolute numbers of circulating VSELs and hematopoietic stem cells in STEMI correlated negatively with patient age.
- Coronary and CV disease biomarkers in UWS correlated better with serum than with LS and GS.
- C-reactive protein and troponin and several other markers demonstrated time effect changes consistent with serum biomarkers.
- The authors concluded that changes in serum biomarker profiles are reflected in oral fluids suggesting that oral fluid biomarkers could aid in the assessment of cardiac ischemia/necrosis.

Becker RC, **Smyth SS**. Biomarker science: on a theme of personalized medicine. *J Thromb Thrombolysis*. 2012 Jul;34(1):141-2.

Van Diepen S, Roe MT, Lopes RD, Stebbins A, James S, Newby LK, **Moliterno DJ**, Neumann FJ, Ezekowitz JA, Mahaffey KW, Hochman JS, Hamm CW, Armstrong PW, Theroux P, Granger CB. Baseline NT-proBNP and biomarkers of inflammation and necrosis in patients with ST-segment elevation myocardial infarction: insights from the APEX-AMI trial. *J Thromb Thrombolysis*. 2012 Jul;34(1):106-13.

Selim S, Sunkara M, Salous AK, Leung SW, Berdyshev EV, Bailey A, Campbell CL, Charnigo R, Morris AJ, Smyth SS. Plasma levels of sphingosine 1-phosphate are strongly correlated with haematocrit, but variably restored by red blood cell transfusions. *Clin Sci* (Lond). 2011 Dec;121(12):565-72.

 Anemia and RBC (red blood cell) transfusion may be associated with worse clinical outcomes. The mechanisms underlying these harmful effects are unknown. RBCs have been proposed to buffer plasma S1P (sphingosine 1-phosphate), a lysophospholipid essential for the maintenance of endothelial integrity and important in the regulation of haematopoietic cell trafficking. The present study examined the effect of anemia, RBC transfusion and RBC storage duration on plasma S1P levels.

- The authors confirmed a role for RBCs in buffering plasma S1P and identified a disturbance in that capacity after transfusion.
- They suggest that changes in S1P content may contribute to an RBC storage lesion.

Anaya P, Moliterno DJ. Patient, heal thyself: the ongoing evolution of patient self-directed care and hand-held technology. *Ann Intern Med.* 2011 Apr 5;154(7):500-1.

Campbell CL, Steinhubl SR, Hooper WC, **Jozic J, Smyth SS**, Bernstein D, De Staercke C, Syros G, Negus BH, Stuckey T, Stone GW, Mehran R, Dangas G. Bleeding events are associated with an increase in markers of inflammation in acute coronary syndromes: an ACUITY trial substudy. *J Thromb Thrombolysis*. 2011 Feb;31(2):139-45.

- This study sought to identify biomarkers that predicted bleeding in 92 patients hospitalized with acute coronary syndromes (ACS).
- Patients who experienced an in-hospital major bleed had elevated C-reactive protein (hs-CRP) levels (mg/I).
- Interleukin-6 (IL-6) levels also increased from admission to hospital discharge non-significantly in those patients with a bleeding event.
- These data suggest that major bleeding is associated with development of a pro-inflammatory state.

Abdel-Latif A, Zuba-Surma EK, **Ziada KM**, Kucia M, Cohen DA, Kaplan AM, Van Zant G, **Selim S**, **Smyth SS**, Ratajczak MZ. Evidence of mobilization of pluripotent stem cells into peripheral blood of patients with myocardial ischemia. *Exp Hematol.* 2010 Dec;38(12):1131-1142.e1.

- The impact of ischemic heart disease and ST elevation myocardial infarction (STEMI) on mobilization of primitive pluripotent stem cells (PSCs) enriched in very small embryonic-like stem cells (VSELs) was examined:
- Stem cell populations such as VSELs were significantly higher in STEMI patients at presentation and declined over time.
- The absolute numbers of circulating VSELs and hematopoietic stem cells in STEMI correlated negatively with patient age
- A corresponding increase in pluripotent, cardiac, and endothelial gene expression in unfractionated blood cells was observed.
- The authors concluded that myocardial ischemia mobilizes primitive PSCs including pluripotent VSELs into the circulation. The peak of mobilization occurs within 12 hours in patients presenting with STEMI, which may represent a therapeutic window for future clinical applications.

Miller CS, **Foley JD**, **Bailey AL**, **Campell CL**, Humphries RL, Christodoulides N, Floriano PN, Simmons G, Bhagwandin B, Jacobson JW, Redding SW, Ebersole JL, McDevitt JT. Current developments in salivary diagnostics. *Biomark Med*. 2010 Feb;4(1):171-89.

Investigator Initiated Studies

Early Use of Rosuvastatin in Acute Coronary Syndromes: Targeting Platelet-Leukocyte Interactions (AVATAR)

Principal Investigator (overall): Susan Smyth, MD, PhD

Summary: This is an investigator-initiated clinical trial to test the hypothesis that early, high-dose administration of the HMG-CoA reductase inhibitor rosuvastatin in the setting of acute coronary syndrome and percutaneous coronary intervention exerts beneficial vascular effects by attenuating platelet function and reducing platelet - leukocyte interactions

Contact: Tiffany Sandlin, RN, 859-323-8516

Functional validation of lysophospholipid metabolism pathways identified by human genetics of CAD

Principal Investigator (overall): Susan Smyth, MD, PhD

Summary: A recent meta-analysis of genome-wide association studies (GWAS) of coronary artery disease (CAD) comprising 22,233 individuals with CAD (cases) and 64,762 controls of European descent identified PPAP2B as 1 of 13 loci newly associated loci for CAD. This is an NIH-sponsored study to test the hypothesis that the PPAP2B risk-associated allele predicts lower LPP3 expression and/or activity in blood cells.

Contact: Mani Panchatcharam, PhD 859-323-2274

Currently Enrolling Clinical Trials

Prevention of Cardiovascular Events in Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin (PEGASUS)

Principal Investigator (site): Khaled Ziada, MD

Summary: This study is being carried out to see if a new drug called ticagrelor given twice daily in addition to the ASA therapy, decreases the frequency of cardiovascular events.

Contact: Ruth Oremus, RN 859-323-5259

A Single Ascending Dose Study Examining the Safety and Pharmacokinetic Profile of Reconstituted High Density Lipoprotein (CSL112) Administered to Patients

Principal Investigator (site): Alison Bailey, MD

Summary: Reconstituted high density lipoprotein used in patients with acute coronary syndrome (ACS) may reduce atherosclerotic plaque burden, thereby reducing the risk of recurrent cardiovascular events.

Contact: Kay Moles, RN 859-323-8516



Ongoing and recently completed trials

Drug-Eluting Stents vs. Bare Metal Stents In Saphenous Vein Graft Angioplasty (DIVA)

Principal Investigator (site): Khaled Ziada, MD

Summary: Patients who need stenting of SVG blockages will be randomized to receive DES or BMS in a 1:1 ratio.

Contact: Kay Moles, RN 859-323-8516

International Study of Comparative Health Effectiveness with Medical and Invasive Approaches (ISCHEMIA)

Principal Investigator (site): David Booth, MD

Summary: The purpose of the trial is to determine the best management strategy for higher-risk patients with stable ischemic heart disease. This is a multicenter, randomized controlled trial with a target enrollment of ~8000 patients with at least moderate ischemia on stress imaging.

Contact: Ruth Oremus, RN 859-323-5259

The PARIS Registry: Patterns of Non-Adherence to Antiplatelet Regimens in Stented Patients – an Observational Single-Arm Study

Principal Investigator (site): David Moliterno, MD

SOLID TIMI-52 The Stabilization of pLaques Using Darapladib-Thrombolysis in Myocardial Infarction 52

Principal Investigator (site): Charles Campbell, MD

Structural and Congenital Heart Disease



Our team has tremendous experience in diagnosing and treating structural and congenital heart defects. We specialize in complex and high-risk cases, including implantation of the Sapien transcatheter heart valve by percutaneous approach for individuals with inoperable, severe aortic stenosis. We offer patients the most sophisticated diagnostic tools for early and accurate detection and a multi-disciplinary management by a team of interventional cardiologists, cardiac surgeons, technicians, and highly experienced acute-care nurses. In addition to surgical approaches, our physicians are experienced in transcutaneous aortic valve implantation, mitral balloon valvuloplasty and percutaneous treatment of congenital heart defects. We recently assembled a team dedicated to transcatheter aortic valve replacements for aortic stenosis patients at high risk for standard valve surgery.

The Gill Heart Valve Program is led by two of the 2011 "Best Doctors in America, Dr. Chandrashekhar Ramaiah", UK's director of Minimally Invasive Heart Surgery, and interventional cardiologist, Dr. John Gurley.

They will perform the new transaortic valve implantation (TAVI) procedure in the region's only hybrid OR facilities, with leading-edge imaging and industrial robotics technology. Having performed the first aortic valvuloplasty in 1984, UK's valve team has nearly 30 years of experience with transcatheter valve procedures and offers the greatest expertise in structural heart disease in the region.

Congenital Heart Disease Program

Congenital heart disease patients and their families can find state-of-the-art diagnostic services and treatment options in the Kentucky Congenital Heart Clinic. Under the medical direction of **Dr. Douglas Schneider**, the clinic specializes in perinatal, pediatric and adult congenital cardiology, cardiovascular surgery, and cardiovascular research for children and adults with congenital heart disease. The new space includes a full-service diagnostic center, advanced arrhythmia testing. and pediatric and fetal echocardiography. The team is supported by cardiothoracic surgeons who specialize in early correction or complete repair of single ventricle heart defects, and other congenital heart disease, often performed within days of birth.

Publications:

Leung SW, Elayi CS, Charnigo RJ Jr, Syed MA. Clinical significance of right ventricular dysfunction in left ventricular non-compaction cardiomyopathy. *Int J Cardiovasc Imaging*. 2012 Jun;28(5):1123-31.

Sorrell VL, Pancyzk E, Alpert JS. A new disease: bicuspid aortic valve aortopathy syndrome. *Am J Med.* 2012 Apr;125(4):322-3.

Plaisance BR, Winkler MA, Attili AK, Sorrell VL. Congenital bicuspid aortic valve first presenting as an aortic aneurysm. *Am J Med.* 2012 Apr;125(4):e5-7.

Elayi CS, Allen CL, Leung SW, Lusher S, Morales GX, Wiisanen M, Aikat S, Kakavand B, Shah JS, Moliterno DJ, Gurley JC. Inside-out access: a new method of lead placement for patients with central venous occlusions. *Heart Rhythm.* 2011 Jun;8(6):851-7. Garabedian MJ, Hansen WF, Gianferrari EA, Lain KY, Fragneto RY, **Campbell CL, Booth DC.** Epoprostenol treatment for idiopathic pulmonary arterial hypertension in pregnancy. *J Perinatol.* 2010 Sep;30(9):628-31.

Lax D, Bhatt RD, Klewer SE, **Sorrell VL**. Are all ventricular septal defects created equal? *J Am Soc Echocardiogr*. 2010 Jul;23(7):791.e5-7.

Kalra N, Klewer SE, Raasch H, **Sorrell VL**. Update on tetralogy of Fallot for the adult cardiologist including a brief historical and surgical perspective. *Congenit Heart Dis.* 2010 May-Jun;5(3):208-19.

Abdy NA, Valdes SO, **Sorrell VL**, Klewer SE, Barber BJ. Apical hypertrophic cardiomyopathy in an adolescent. *Congenit Heart Dis.* 2010 Mar-Apr;5(2):182-7.

Marcus F, Basso C, Gear K, **Sorrell VL**. Pitfalls in the diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia. *Am J Cardiol*. 2010 Apr 1;105(7):1036-9.

Wilson J, Reda H, Gurley JC. Anomalous right coronary artery originating from the left anterior descending artery: case report and review of the literature. *Int J Cardiol.* 2009 Nov 12;137(3):195-8.

Currently Enrolling Clinical Trials

PREMIUM Migraine Trial

Principal Investigator: John Gurley, MD

Summary: The Purpose of this study is to evaluate the impact of percutaneous closure of a patent foramen ovale (a hole in the heart), using the AMPLATZER PFO Occluder, on the incidence of migraine headaches.

Contact: Miranda Hatfield, CRA 859-323-1082

Ongoing and recently completed trials

WATCHMEN Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation Fibrillation

Principal Investigator (site): John Gurley, MD

GORE HELEX Septal Occluder and Antiplatelet Medical Management for Reduction of Recurrent Stroke or Imaging-Confirmed TIA in Patients Foramen Ovale (PFO) (the REDUCE Study)

Principal Investigator (site): John Gurley, MD

AMPLATZER Cardiac Plug (ACP) Clinical Study – Feasibility Study

Principal Investigator (site): John Gurley, MD

Closure of Muscular Ventricular Septal Defects with the Amplatzer Muscular VSD Occluder--Post Approval Study (Muscular VPA)

Principal Investigator (site): John Gurley, MD

Closure of Atrial Septal Defects with the Amplatzer Septal Occluder - Post Market Study II (ASD PMS II)

Principal Investigator (site): John Gurley, MD

Prospective Randomized Investigation to Evaluate Incidence of Headache Reduction in Subjects with Migraine and PFO Using the AMPLATZER PFO Occluder Compared to Medical Management

Principal Investigator (site): John Gurley, MD

Electrophysiology: Heart Rhythm Program



The Gill Heart Institute's Heart Rhythm Program brings together a team of certified cardiac electrophysiologists, cardiovascular surgeons, cardiologists and cardiac anesthesiologists for the management and treatment of cardiac rhythm disorders. This collaborative approach enables the development of patientcentered, combination treatment therapies including medical management, cardiac resynchronization therapy (CRT), and both catheter-based and minimally invasive surgical solutions. Our electrophysiology services include implantation of MRI-compatible pacemakers, implantable cardioverter defibrillators (ICDs) including biventricular devices, and advanced ablation procedures for rhythm disturbances such as atrial fibrillation (AF), atrial flutter, supraventricular tachycardia or ventricular tachycardia. Our highly skilled surgical teams utilize robotic systems,

magnetic catheter guidance and the latest 3-D mapping technology to perform procedures with a very high success rate.

Publications:

Elayi CS, Di Biase L, **Morales GX**, **Thompson J**, Natale A. Persistent Atrial Fibrillation Cardiac Mapping; How Many Lines, How Many Sites? Chapter 34, 4th edition. Edited by Josephson M, Blackwell Publishing Ltd 2012 (in press).

Di Biase L, Santangeli P, Burkhardt DJ, Bai R, Mohanty P, Carbucicchio C, Dello Russo A, Casella M, Mohanty S, Pump A, Hongo R, Beheiry S, Pelargonio G, Santarelli P, Zucchetti M, Horton R, Sanchez JE, **Elayi CS**, Lakkireddy D, Tondo C, Natale A. Endo-epicardial homogenization of the scar versus limited substrate ablation for the treatment of electrical storms in patients with ischemic cardiomyopathy. *J Am Coll Cardiol.* 2012 Jul 10;60(2):132-41.

Elayi CS, DI Biase L, Bai R, Burkhardt JD, Mohanty P, Sanchez J, Santangeli P, Hongo R, Gallinghouse GJ, Horton R, Bailey S, Zagrodzky J, Beheiry S, Natale A. Identifying the relationship between the non-PV triggers and the critical CFAE sites post-PVAI to curtail the extent of atrial ablation in longstanding persistent AF. *J Cardiovasc Electrophysiol*. 2011 Nov;22(11):1199-205.

Allen C, Kuo B, Morales GX, Elayi CS. Carotid sinus hypersensitivity induced syncope: A phenomenon unmasked during carotid sonography. JVU. Vol. 35, Number 3, Sep 2011, pp.162-163(2).

Morales GX, Elayi CS, Reddy VY. Extracardiac osteophytic deformation of the left atrium: an unusual anatomic finding during atrial fibrillation ablation. *Heart Rhythm.* 2011 Aug;8(8):1305.

Elayi CS, Whitbeck MG, Charnigo R, Shah J, Macaulay TE,

Morales GX, Gurley JC, Kakavand B, Thal S, Ching CK, Khaykin Y, Verma A, Barrett C, Bai R, Di Biase L, Patwardhan A, **Moliterno DJ**, Natale A; AFFIRM Study Investigators. Is there an association between external cardioversions and long-term mortality and morbidity? Insights from the Atrial Fibrillation Follow-up Investigation of Rhythm Management study. *Circ Arrhythm Electrophysiol.* 2011 Aug;4(4):465-9.

- The study investigated the association between implantable cardioverter-defibrillator shocks and increase in long-term mortality in 4060 patients from the AFFIRM (Atrial Fibrillation Follow-up Investigation of Rhythm Management) trial.
- There was no significant association between external cardioversion episodes and mortality.
- ECVe were associated with increased hospitalizations from cardiac causes.
- Digoxin, myocardial infarction, and coronary artery bypass graft were significantly associated with mortality.

Elayi CS, Gurley JC, Di Sessa TG, Kakavand B.Surgical electrocautery facilitated transseptal puncture in children. *Pacing Clin Electrophysiol.* 2011 Jul;34(7):827-31.

Elayi CS, Allen CL, Leung S, Lusher S, Morales G, Wiisanen M,

Aikat S, Kakavand B, Shah JS, **Moliterno DJ, Gurley JC**. Inside-out access: A new method of lead placement for patients with central venous occlusions. *Heart Rhythm* 2011. Jun;8(6):851-7.

Bekker JG, **Macaulay TE**. Strategies for the management of postoperative atrial fibrillation. *Orthopedics*. 2011 May;34(5):379.

Morales GX, Bodiwala K, Elayi CS. Giant J-wave (Osborn wave) unrelated to hypothermia. *Europace*. 2011 Feb;13(2):283.

Elayi CS, Whitbeck MG, Morales G, Gurley JC. Balloon-Facilitated Delivery of a Left Ventricular Pacing Lead. *Pacing Clin Electrophysiol*. 2011 Jan 28.

Elayi CS, Morales GX, Kakavand B, Shah JS. Tachycardia Initiated by One to Two Response and Terminated by ICD Shocks. *Indian Pacing Electrophysiol J.* 2010 Dec 26;10(11):522-5.

Elayi CS, Di Biase L, Barrett C, Ching CK, al Aly M, Lucciola M, Bai R, Horton R, Fahmy TS, Verma A, Khaykin Y, Shah J, **Morales GX**, Hongo R, Hao S, Beheiry S, Arruda M, Schweikert RA, Cummings J, Burkhardt JD, Wang P, Al-Ahmad A, Cauchemez B, Gaita F, Natale A. Atrial fibrillation termination as a procedural endpoint during ablation in long-standing persistent atrial fibrillation. *Heart Rhythm*. 2010 Sep;7(9):1216-23.

Aktas MK, Khan MN, Di Biase L, **Elayi C**, Martin D, Saliba W, Cummings J, Schweikert R, Natale A. Higher rate of recurrent atrial flutter and atrial fibrillation following atrial flutter ablation after cardiac surgery. *J Cardiovasc Electrophysiol.* 2010 Jul;21(7):760-5.

Roedig JJ, **Shah J, Elayi CS**, Miller CS. Interference of cardiac pacemaker and implantable cardioverter-defibrillator activity during electronic dental device use. *J Am Dent Assoc.* 2010 May;141(5):521-6.

Currently Enrolling Clinical Trials

Vest Prevention of Early Sudden Death Trial and VEST Registry

Principal Investigator: Samy-Claude Elayi, MD

Summary: This study explores the hypothesis that wearable defibrillators can impact mortality by reducing sudden death during the first three months after a heart attack in persons with high risk for life-threatening arrhythmias.

Contact: Miranda Hatfield, MA 859-323-1082

Position of Leads in Advanced Heart Failure: the POLAR Study

Principal Investigator: Samy-Claude Elayi, MD

Summary: The primary objective is to determine if lead positioning in the lateral wall of the left ventricle in patients meeting criteria for cardiac resynchronization therapy plays a role in determining myocardial function and affects the severity of mitral regurgitation.

Contact: Kay Moles, RN 859-323-8516

Cardiovascular Imaging



UK's Advanced Cardiovascular Imaging Program provides Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) of the heart and great vessels for adult and pediatric patients. The Gill Imaging Center has two, state-of-the-art, 64-slice CT scanners, one of which represents the first dual-source CT scanner in Kentucky. Two new MRI scanners, the 1.5 Tesla and 3.0 Tesla, expand UK HealthCare's advanced imaging capabilities.

Clinical 3D volumetric and functional examinations and contrast viability studies are performed daily. Real-time, 3D time-resolved MRA and pharmacologic stress MRI is regularly performed.

The Gill Heart Institute Adult Echo Lab has been accredited by the Intersocietal Accreditation Commission for Echocardiography (ICAEL), continuously since 1999. All of our interpreting cardiologists are certified by the National Board of Echocardiography. We have 129 combined years of cardiac sonographer experience in Adult Echocardiography. The Adult Echo Lab faculty has played a major role in the research and development of Doppler, color flow imaging and 3D-echo. In addition, the echo lab faculty and cardiac sonographers have been leaders in the state for ultrasound imaging, teaching national and regional courses, and providing hands-on training to physicians and sonographers in the region. The cardiologists in our Adult Echo Lab are committed to providing excellent care and education to the people of Kentucky, now and in the future.

The Gill Heart Institute Adult Nuclear Lab utilizes a stateof-the-art, upright, Dual-head SPECT camera with attenuation correction and off-line workstations using advanced Cedars-Sinai Quantitative Perfusion and Gated SPECT software. 3D regional perfusion, global and regional function at rest and after stress, and quantitative summed stress scores are measured in all patients. Our Cardiovascular Imaging Fellowship program is unique in that there is a close collaboration between cardiology and radiology, offering the opportunity to learn sophisticated tomographic anatomy as well as advanced cardiovascular physiology. Fellows develop in-depth knowledge of cardiac imaging techniques, appropriate applications, and research applications, as part of a multi-disciplinary team imaging ventricular mechanics, ischemic heart disease, hypertrophic cardiomyopathy, congenital heart disease, and valvular disease.

Publications:

Hansen AJ, **Sorrell VL**, Cooper AD, Moulton MJ. Postpartum rupture of the posteromedial papillary muscle. *J Card Surg.* 2012 May;27(3):313-6.

Hayes D Jr, **Winkler MA**, Kirkby S, Capasso P, Mansour HM, **Attili AK**. Pre-procedural planning with prospectively triggered multidetector row CT angiography prior to bronchial artery embolization in cystic fibrosis patients with massive hemoptysis. *Lung*. 2012 Apr;190(2):221-5.

Attili AK, Parish V, Valverde I, Greil G, Baker E, Beerbaum P. Cardiovascular MRI in childhood. *Arch Dis Child*. 2011 Dec;96(12):1147-55.

Pelberg R, Budoff M, Goraya T, Keevil J, Lesser J, Litwin S, Newton C, Ridner M, Rumberger J, Teague S, **Winkler M**. Training, competency, and certification in cardiac CT:A summary statement from the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr.* 2011 Sep-Oct;5(5):279-85.

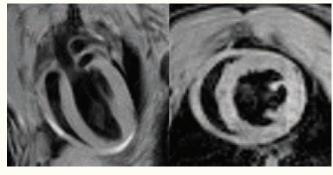
Sorrell VL, Ross WD, Kumar S, **Kalra N**. Left ventricular endocardial and epicardial border length delineation with perflutren contrast during transthoracic echocardiography. *Echocardiography*. 2011 Aug;28(7):761-6.

Kuo BT, Whitbeck MG, Gurley JC, Smith MD. Double atrial septal defect: diagnosis and closure guidance with 3D transesophageal echocardiography. *Echocardiography*. 2011 Jul;28(6):E115-7.

Hayes D Jr, Kesler MV, Skinner SC, **Attili AK**. A 19-year-old woman with progressive dyspnea and multiple pulmonary nodules. *Chest.* 2011 Jul;140(1):253-7.

Marcus FI, Bluemke DA, Calkins H, **Sorrell VL**. Cardiac magnetic resonance for risk stratification of patients with frequent premature ventricular contractions. *J Am Coll Cardiol*. 2011 Apr 12;57(15):1636-7.

Sorrell VL, Paleru V, Altbach MI, Hilwig RW, Kern KB, Gaballa M, Ewy GA, Berg RA. Mild hypothermia delays the development of stone heart from untreated sustained ventricular fibrillation--a cardiovascular magnetic resonance study. *J Cardiovasc Magn Reson*. 2011 Mar 6;13:17.



Advancing the understanding of heart disease through imaging

The University of Kentucky is one of seven institutions in the country to have the state-of-the-art 7-Tesla Clinscan MRI for imaging in preclinical, animal models. Working with world leaders at the University of Virginia (**Dr. Frederick Epstein's** laboratory), UK investigators have established advanced mouse cardiac MRI sequences that allow direct quantification of sub-millimeter motion from mouse hearts beating over 500 times per minute. Our Clinscan MRI has a Siemens control system identical to the MRIs used in our cardiology clinic, which facilitates direct translation of our findings in mice into a greater understanding of the human heart.

Currently Enrolling Clinical Trials

Prospective Multicenter Imaging Study for Evaluation of Chest Pain (PROMISE)

Principal Investigator: Vincent Sorrel, MD

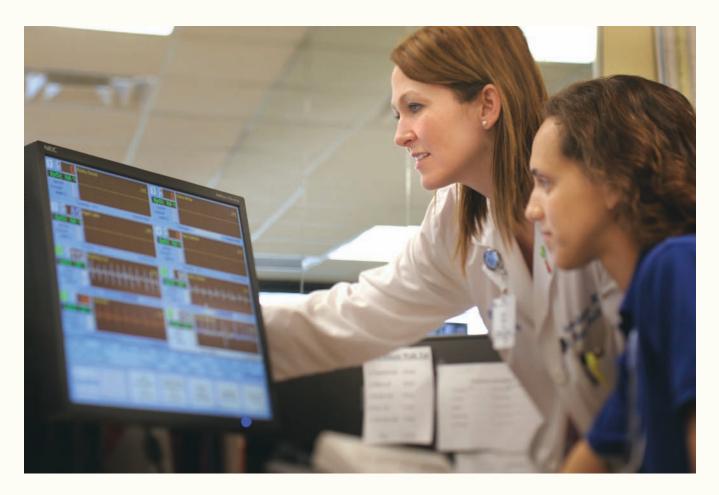
Summary: A prospective multicenter imaging study for evaluation of chest pain. Objective is to determine whether an initial non-invasive anatomic imaging strategy with coronary CT angiography (CTA) will improve clinical outcomes in subjects with symptoms concerning for coronary artery disease relative to an initial functional testing strategy (usual care).

Contact: Ruth Oremus, RN 859-323-5259

Attili AK, Schuster A, Nagel E, Reiber JH, van der Geest RJ. Quantification in cardiac MRI: advances in image acquisition and processing. *Int J Cardiovasc Imaging.* 2010 Feb;26 Suppl 1:27-40.

Fornwalt BK. The dyssynchrony in predicting response to cardiac resynchronization therapy: a call for change. *J Am Soc Echocardiogr.* 2011 Feb;24(2):180-4.

Cardiovascular Wellness and Rehabilitation



UK Cardiac Rehabilitation offers a comprehensive program of medical evaluation, supervised exercise, risk factor modification, and medication optimization to improve the chance of survival and lower the risk of another cardiac event. Headed by Alison Bailey, MD, the team includes cardiologists, a cardiac nurse specialist, exercise physiologists, and registered dieticians. Working with the team, each patient learns how to lower his or her own risk of future cardiac events and become more educated about heart disease while increasing physical activity levels and improving their quality of life. Once structured cardiac rehabilitation is completed, individuals may enroll in the "OH" program for Optimal Health, an ongoing cardiovascular risk reduction plan. The Gill Heart Institute's cardiologist Alison Bailey, MD, is the state team leader for the CDC Million Hearts[™] campaign. The goal of this national initiative is to prevent 1 million heart attacks and strokes over the next five years. Million Hearts brings together communities, health systems, nonprofit organizations, federal agencies, and private-sector partners from across the country to fight heart disease and stroke. Says Bailey: "In Kentucky, we have very high rates of smoking, and when adults smoke their children are exposed to the dangerous effects of second-hand smoke, and they're much more likely to smoke as adults themselves. In addition, Kentucky also has high rates of diabetes, obesity and hypertension and some of the lowest rates of physical activity in the nation."

Publications:

Whayne TF Jr, Maulik N. Nutrition and the healthy heart with an exercise boost. *Can J Physiol Pharmacol.* 2012 Aug;90(8):967-76.

Whayne TF Jr. Assessment of Low-Density Lipoprotein Targets. *Angiology*. 2012 Jun 25. [Epub ahead of print].

Finks SW, Airee A, Chow SL, **Macaulay TE**, Moranville MP, Rogers KC, Trujillo TC. Key articles of dietary interventions that influence cardiovascular mortality. *Pharmacotherapy*. 2012 Apr;32(4):e54-87.

Lu H, Balakrishnan A, Howatt DA, Wu C, Charnigo R, Liau G, Cassis LA, Daugherty A. Comparative effects of different modes of renin angiotensin system inhibition on hypercholesterolaemia-induced atherosclerosis. *Br J Pharmacol.* 2011 2012 Mar;165(6):2000-8.

Bruemmer D. Targeting angiogenesis as treatment for obesity. Arterioscler *Thromb Vasc Biol.* 2012 Feb;32(2):161-2.

Tannock LR. Ursolic acid effect on atherosclerosis: Apples and apples, or apples and oranges? *Atherosclerosis*. 2011 Sep 28.

Kehl KG, Findeisen HM, Fardo DW, **Bruemmer D**, Mannino DM, Sanderson WT. Race-ethnicity as an effect modifier of the association between HbAlc and mortality in U.S. adults without diagnosed diabetes. *Eur J Endocrinol.* 2011 Aug;165(2):275-81.

Whayne TF Jr. Vitamin D: popular cardiovascular supplement but benefit must be evaluated. *Int J Angiol.* 2011 Jun;20(2):63-72.

Bailey AL, Smyth SS, Campbell CL. The case against routine aspirin use for primary prevention in low-risk adults. *Am Fam Physician*. 2011 Jun 15;83(12):1387-90.

Whayne TF Jr. Statin myopathy: significant problem with minimal awareness by clinicians and no emphasis by clinical investigators. *Angiology*. 2011 Jul;62(5):415-21.

Dailey AM, **Tannock LR**. Extreme insulin resistance: indications and approaches to the use of U-500 insulin in type 2 diabetes mellitus. *Curr Diab Rep.* 2011 Apr;11(2):77-82. Review.

Beavers CJ, Dunn SP, Macaulay TE. The role of angiotensin receptor blockers in patients with angiotensin-converting enzyme inhibitor-induced angioedema. *Ann Pharmacother*. 2011 Apr;45(4):520-4.

Whayne TF Jr. What should medical practitioners know about the role of alternative medicines in cardiovascular disease management? *Cardiovasc Ther.* 2010 Apr;28(2):106-23.

Allen C, Dunn SP, Macaulay TE, Mukherjee D. Clopidogrel-proton pump inhibitor interaction: a primer for clinicians. *Cardiovasc Hematol Disord Drug Targets*. 2010 Mar;10(1):66-72.

Whayne TF Jr. Concerns about heparin therapy for hypertriglyceridemia. *Arch Intern Med.* 2010 Jan 11;170(1):108-9.

Rugg SS, Bailey AL, Browning SR. Preventing cardiovascular disease in Kentucky: epidemiology, trends, and strategies for the future. *J KY Med Assoc.* 2008 Apr;106(4):149-61.

- Despite dramatic improvements in the treatment of heart disease in recent years, Kentucky leads the nation in the prevalence of several individual risk factors for cardiovascular disease, the prevalence of multiple risk factors, and in cardiovascular mortality.
- While trends in the prevalence of some of these cardiac risk factors have shown improvement, others have remained unchanged or have worsened. The increased prevalence of obesity and diabetes, especially among young persons, is one of the most worrisome trends.
- Public health initiatives and interventions directed toward the prevention of CVD in Kentucky must address Kentucky's unique challenges if progress is to be made.

Investigator Initiated Studies

NIH: Rural Health Outreach Special Initiative: Heart Health in Rural Kentucky Phase II

Co-Investigator: Alison Bailey, MD

Currently Enrolling Clinical Trials

IMPROVE-IT: Improved Reduction of Outcomes: Vytorin Efficacy International Trial

Principal Investigator (site): Charles Campbell, MD

A Multicenter, Controlled, Open-label Extension (OLE) Study to Assess the Long-term Safety and Efficacy of AMG 145.

Principal Investigator (site): Alison Bailey, MD

LAPLACE: TIMI 57 - A Double-Blind, Randomized, Placebo-controlled, Multicenter, Dose- ranging Study to Evaluate Tolerability and Efficacy of AMG 145 on LDL-C in Combination with HMG-CoA Reductase Inhibitors in Hypercholesterolemic Subjects

Principal Investigator (site): Alison Bailey, MD

Women's Heart Health



Cardiovascular disease is the leading cause of death in women in the United States with nearly half a million women dying from coronary heart disease, heart failure and stroke every year. Indeed, more women will die from these causes than from the top five forms of cancer combined. Women in Kentucky die from heart disease at a rate 23 percent higher than the national average. Nearly 80 percent of all cardiac events in women could be prevented if women made the right choices for their hearts involving diet, exercise and abstinence from smoking. Recent studies show that women with suspected CVD are less likely than men to be referred for diagnostic testing and less likely to undergo invasive testing or aggressive early treatment. This gender bias alone is reason enough for women to take a proactive role in understanding their risk of CVD. For these reasons, the Gill Heart Institute's Women's Heart Health Program was created to serve the needs of women by providing a comprehensive approach to their cardiac care.

The Women's Heart Health Program is dedicated to offering support, education and clinical services to help women prevent and live with heart disease. The program is lead by a team of female cardiologists and nurse practitioners with advanced training in cardiovascular medicine. Our faculty is actively engaged in understanding why heart disease is different in men and women and optimizing strategies for the treatment of women patients.

Kentucky Women's Health Registry

- Why do some diseases affect women more than men?
- Why do women respond to some drugs and treatment therapies differently than men?
- What environmental factors and behaviors most influence women's health?

The Kentucky Women's Health Registry is finding answers to these and other important questions. Led by Dr. Leslie Crofford, the Kentucky Women's Heath Registry is the first statewide women's health registry and is open to any Kentucky women age 18 to 89. With more than 15,000 participants, the Registry serves as a tremendous resource for investigations that will enhance the quality of women's lives.

Recently, Drs. Rabab Mohsin, Dawn Scantlebury and Alison Bailey used the Kentucky Women's Health Registry to identify women with atrial fibrillation, who were then surveyed to evaluate the rates of anticoagulation use. Their findings revealed substantial underutilization of guideline-based therapy in women – 18% of women with a high-risk CHADS² score were not on any antithrombotic therapy despite evidence that women are at increased risk of thromboembolic events and gain more benefit from anticoagulation for atrial fibrillation than do men. Made possible by access to the Kentucky Women's Health Registry, their findings indicate an educational need that is being met by disseminating appropriate information to healthcare providers and patients on appropriate treatments for atrial fibrillation.

Publications:

Bailey AL, Smyth SS. Invasive coronary vasoreactivity testing to diagnose microvascular dysfunction in women. *JACC Cardiovasc Interv.* 2012 Jun;5(6):654-5.

Wang TY, Angiolillo DJ, Cushman M, Sabatine MS, Bray PF, **Smyth SS**, Dauerman HL, French PA, Becker RC. Platelet biology and response to antiplatelet therapy in women: implications for the development and use of antiplatelet pharmacotherapies for cardiovascular disease. *J Am Coll Cardiol.* 2012 Mar 6;59(10):891-900.



Lea B, Bailey AL, Wiisanen ME, Attili A, Rajagopalan N. Left ventricular noncompaction presenting as peripartum cardiomyopathy. *Int J Cardiol.* 2012 Feb 9;154(3):e65-6.

Tackett AH, Bailey AL, Foody JM, Miller JM, Apperson-Hansen C, Ohman EM, Hochman JS, Karnash SL, Califf RM, Topol EJ, **Moliterno DJ**. Hormone replacement therapy among postmenopausal women presenting with acute myocardial infarction: insights from the GUSTO-III trial. *Am Heart J*. 2010 Oct;160(4):678-84.

Bailey AL, Scantlebury DC, Smyth SS. Thrombosis and antithrombotic therapy in women. *Arterioscler Thromb Vasc Biol.* 2009 Mar;29(3):284-8.

- Sex-based differences in the prevalence and presentation of arterial and venous thrombosis exist, and emerging data indicate that men and women do not accrue equal benefit from antithrombotic therapy.
- Sex hormones alter procoagulant protein expression and the function of blood and vascular cells.
- Sex-based differences in platelet function have been reported, and in animal models, sex-based differences in thrombosis have been noted.

Peripheral Arterial and Aortic Disease



UK's Gill Heart Institute has vascular disease specialists devoted to treating blood vessel conditions. Our team includes vascular and endovascular surgeons, cardiologists with extensive endovascular experience, and imaging experts trained in vascular diseases. UK houses an advanced and nationally certified vascular laboratory dedicated to ultrasound and imaging tests and state-ofthe-art computerized tomography and magnetic resonance imaging technology, that allows diagnosis of the presence and severity of peripheral arterial disease (PAD) before any invasive procedure is undertaken.

Our interventional cardiologists and vascular surgeons operate in state-of-the-art hybrid operating rooms and catheterization laboratories equipped with all the tools needed for treating the most complex vascular conditions. Both teams offer standard vascular and endovascular services, but have also developed subspecialty expertise in areas of higher complexity that fits with the tertiary and quaternary



nature of UK's medical center. The vascular surgery team has nationally recognized expertise in endovascular treatment of abdominal aortic aneurysms. Our interventional cardiologists' capabilities include endovascular treatment of renal, iliac and femoral occlusions, use of atherectomy devices, and use of specialized intravascular ultrasoundguided techniques for crossing totally occluded segments. The group also offers endovascular treatment of carotid and subclavian disease using the latest technologies for cerebral protection, and was part of the largest FDA-mandated national registry for carotid stenting, which ensured both the appropriateness and the high quality of carotid procedures across the country.

Both our surgery and interventional cardiology specialists have a long track record in successful treatment of renovascular disease. Recently, UK was chosen as one of a select group of centers that will participate in renal denervation research, which offers a unique and novel therapy for patients with resistant hypertension. UK is the only center that offers this opportunity in the state. In addition to complex procedures, our team of experts focuses on secondary prevention efforts to avoid disease progression. Extensive efforts are directed towards smoking cessation, lipid lowering, and walking programs for those patients after successful surgical or endovascular therapy.

Our researchers are at the forefront of developing non-surgical therapy for abdominal aortic aneurysm. Anticipating a surge in diagnosed cases of abdominal aortic aneurysm (a condition for which Medicare just approved a onetime free screening for men), UK researchers have been awarded \$8.5 million in NIH funding to understand the condition and how it can be treated. Led by Alan Daugherty, PhD, UK researchers developed a preclinical model for studying the development of aortic aneurysms, and have led investigations into the role of inflammation in the disease process.

Publications:

Lu H, Rateri DL, Bruemmer D, Cassis LA, Daugherty A. Involvement of the renin-angiotensin system in abdominal and thoracic aortic aneurysms. *Clin Sci (Lond).* 2012 Nov 1;123(9):531-43.

Reijnen MM, **Minion DJ**, Lardenoye JW. Treatment of a type IIIb endoleak in a Talent endograft using telescoping cuffs and two parallel upside-down excluder contralateral legs. *J Vasc Surg.* 2012 Jun 13.

Davenport DL, Shivazad A, **Endean ED**. Short-term outcomes for open revascularization of chronic mesenteric ischemia. *Ann Vasc Surg.* 2012 May;26(4):447-53.

- This study examined the effect of conduit type (vein versus prosthetic graft) on outcomes of surgical bypass for chronic mesenteric ischemia.
- Data from the American College of Surgeons National Surgical Quality Improvement Program Participant Use File between 2005 and 2009 was analyzed.
- 156 patients (76% female) underwent surgical revascularization for mesenteric ischemia. Veins were used as conduits in 28% of cases and prosthetic grafts in 72%.
- Patients receiving a vein graft were more likely to have bowel resection and preoperative sepsis or systemic inflammatory response syndrome, had a higher likelihood of a contaminated surgical site and more often had emergent surgery.
- Mortality was higher in patients in whom a vein graft was used (16% vs. 5%, P = 0.039). There were no differences noted between the two groups

in length of stay or postoperative. complications, including infectious complications, renal insufficiency, myocardial infarction, and stroke.

Xenos ES, Vargas HD, Davenport DL. Association of blood transfusion and venous thromboembolism after colorectal cancer resection. *Thromb Res.* 2012 May;129(5):568-72.

Minion DJ, Xenos ES. The femoral-based endowedge technique to increase juxtarenal seal and correct graft tilt. *J Vasc Surg.* 2012 May;55(5):1522-5.

Davenport DL, Ritchie JD, **Xenos ES**. Incidence and risk factors for 30-day post discharge mortality in patients with vascular disease undergoing major lower extremity amputation. *Ann Vasc Surg.* 2012 Feb;26(2):219-24.

- This study examined the effect of intraoperative blood transfusion on morbidity and mortality as reported in the American College of Surgeons National Surgical Quality Improvement Program.
- Data was queried on a total of 8,799 who underwent lower extremity revascularization between 2005 and 2007.
- Transfusion of 1 or 2 units predicted 30-day mortality, (OR: 1.92; CI: 1.36-2.70); and greater volume of transfused blood was associated with higher mortality.
- Transfusion also predicted composite morbidity, sepsis/shock, pulmonary occurrences, and return to the operating room.

Davenport DL, Vargas HD, Kasten MW, **Xenos ES**. Timing and perioperative risk factors for in-hospital and post-discharge venous thromboembolism after colorectal cancer resection. *Clin Appl Thromb Hemost*. 2012 Feb 16.

Saha SP, Whayne TF Jr, Mukherjee D. Current evidence for antithrombotic therapy after peripheral vascular interventions. *Curr Vasc Pharmacol.* 2012 Jan 20.

Rubinstein C, **Endean ED, Minion DJ, Sorial EE**, **O'Keeffe SD**, **Xenos ES**. Thrombin injection for the treatment of mycotic gluteal aneurysm. *Vasc Endovascular Surg.* 2012 Jan;46(1):77-9.

Cummings MS, Kuo BT, Ziada KM. A rare anomaly of the aortic arch: aberrant right subclavian artery associated with common carotid trunk. *J Invasive Cardiol.* 2011 Oct;23(10):E241-3.

Xenos ES, Bietz GJ, Davenport DL. Endoluminal versus open repair of descending thoracic aortic rupture: a review of the National Trauma Databank. *Ther Adv Cardiovasc Dis.* 2011 Oct;5(5):221-5.

- This study profiled emergency repair with endovascular stent grafting of descending thoracic rupture from blunt trauma injury.
- A total of 997 patients (72% male) of whom 121 underwent endoluminal repair and 875 open repair for 'injury to the thoracic aorta' due to motor vehicle accident, fall or other transport.
- In comparison to those patients who underwent open repair, those undergoing endovascular repair were similar in terms of age,

demographics, associated injuries and hemodynamic status on presentation. Neither method of repair conferred significant advantage of survival, length of stay or ventilator days.

- Furthermore, no significant difference of pulmonary, renal, cardiac, infectious and neurologic complications was observed between open and endovascular repair.
- Long-term data for endoluminal repair and its durability are lacking, especially in young patients.

Davenport DL, **Xenos ES**. Early outcomes and risk factors in venous thrombectomy: an analysis of the American College of Surgeons NSQIP dataset. *Vasc Endovascular Surg.* 2011 May;45(4):325-8.

Carter R, **O'Keeffe SD**, **Minion DJ**, **Sorial EE**, **Endean ED**, **Xenos ES**. Spontaneous superior mesenteric artery dissection: report of 2 patients and review of management recommendations. *Vasc Endovascular Surg.* 2011 Apr;45(3):295-8.

Saha SP, Whayne TF Jr, Mukherjee DP.Current management of peripheral vascular disease: where is the evidence? *Cardiovasc Hematol Agents Med Chem.* 2011 Apr 1;9(2):128-36.

Martin JT, O'Connor WN, **Ramaiah C**. Isolated necrotizing aortitis presenting as incidental thoracoabdominal aortic aneurysm: a case report. *Int J Angiol.* 2011 Mar;20(1):59-62.

Carter RR, Orr NT, **Minion DJ, Xenos ES**. Aortic injury from posterior rib fracture. Eur J Cardiothorac Surg. 2011 Jan;39(1):138.

Whayne TF Jr. Metabolic syndrome, peripheral vascular disease and coronary artery disease: A concise review. *Int J Angiol.* 2010 Fall;19(3):e96-9.

Endean ED, Cavatassi W, Hansler J, **Sorial E**. Deglutition syncope: a manifestation of vagal hyperactivity following carotid endarterectomy. *J Vasc Surg.* 2010 Sep;52(3):720-2.

Saha SP, Whayne TF Jr, Mukherjee D. Evidence-based management of carotid artery disease. *Int J Angiol.* 2010 Spring; 19(1):e21-4.

O'Keeffe SD, Davenport DL, **Minion DJ, Sorial EE, Endean ED, Xenos ES**. Blood transfusion is associated with increased morbidity and mortality after lower extremity revascularization. *J Vasc Surg.* 2010 Mar;51(3):616-21, 621.e1-3.

- This study examined the effect of intraoperative blood transfusion on morbidity and mortality as reported in the American College of Surgeons National Surgical Quality Improvement Program.
- Data was queried on a total of 8,799 who underwent lower extremity revascularization between 2005 and 2007.
- Transfusion of 1 or 2 units predicted 30-day mortality, (OR: 1.92; CI: 1.36-2.70); and greater volume of transfused blood was associated with higher mortality.

 Transfusion also predicted composite morbidity, sepsis/shock, pulmonary occurrences, and return to the operating room.

Davenport DL, **O'Keeffe SD**, **Minion DJ**, **Sorial EE**, **Endean ED**, **Xenos ES**. Thirty-day NSQIP database outcomes of open versus endoluminal repair of ruptured abdominal aortic aneurysms. *J Vasc Surg*. 2010 Feb;51(2):305-9. e1.

O'Keeffe SD, Davenport D, **Endean ED**, **Xenos ES**, **Sorial EE**, **Minion DJ**. Variations in early outcomes of endovascular aneurysm repair with alternate endograft configurations. *Ann Vasc Surg.* 2010 Jan;24(1):28-33.

Currently Enrolling Clinical Trials

SEATTLE II: A Prospective, Single-arm, Multi-center Trial of EkoSonic[®] Endovascular System and Activase for Treatment of Acute Pulmonary Embolism (PE)

Principal Investigator (site): John Gurley, MD

Summary: The purpose of this study is to determine if the EKOS EkoSonic[®] Endovascular Device when used in conjunction with recombinant t-PA as a treatment for acute pulmonary embolism (PE) will decrease the ratio of RV to LV diameter within 48 ± 6 hours in patients with massive or submassive PE.

Contact: Miranda Hatfield, MA 859-323-1082

Renal Denervation in Patients with Uncontrolled Hypertension (SYMPLICITY HTN-3)

Principal Investigator (site): Khaled Ziada, MD; John Gurley, MD; Peter Sawaya, MD

Summary: The SYMPLICITY HTN-3 study is a multi-center, prospective, single-blind, randomized study of the safety and effectiveness of renal denervation in subjects with uncontrolled hypertension. Bilateral renal denervation will be performed using the Symplicity Catheter – a percutaneous system that delivers radiofrequency energy through the luminal surface of the renal artery.

Contact: Ruth Oremus, RN 859-323-5259

Ongoing and recently completed trials

Carotid Stenting for High Surgical Risk Patients; Evaluating Outcomes Through the Collection of Clinical Evidence (CHOICE)

Principal Investigator (site): Khaled Ziada, MD

Heart Failure, Transplant and Mechanical Circulatory Support



UK is at the forefront of clinical technology in heart failure care, heart transplant, and VAD services. The UK Transplant Center is the only full-service transplant center serving central and eastern Kentucky, northeast Tennessee, and areas of West Virginia. Patients benefit from our expert, multidisciplinary approach to the evaluation, treatment, and follow-up of patients with advanced heart failure. Our heart failure/transplant inpatient unit is staffed by a team of skilled caregivers made up of board-certified cardiologists and cardiovascular surgeons, advanced practice nurses, mechanical circulatory system (MCS) coordinators and technicians, as well as pharmacists, physical rehab and occupational rehab therapists, nutritionists, and social workers who help patients navigate the options available to them and help manage their long-term health. A 6,000-square-foot outpatient transplant clinic offers a centralized location for the multidisciplinary group.

Established in 1991, the heart transplant program is currently led by **Dr. Charles Hoopes,** who was recruited from the University of California at San Francisco to be the director of the UK Transplant program. **Dr. Navin Rajagopalan** serves as the Medical Director of Heart Transplantation and Ventricular Assist Device Program. **Roh Yanagida, MD, PhD**, was recently recruited from Cedars-Sinai Medical Center in Los Angeles, after completing a fellowship in cardiopulmonary transplantation.

In 1997, UK celebrated the 100th transplant and has transplanted more than 200 hearts. UK was the first heath care provider in the state to implant Syncardia's Total Artificial Heart[™] and one of only about 30 centers in the country approved to use the device. UK's transplant program has also successfully performed combined heart-kidney transplants, and is the only active combined heart-lung transplant program in the Kentucky region.

The Gill Heart Institute at UK is one of only a few centers in the U.S. to offer "Walking ECMO," utilizing a doublelumen cannula (DLC). The Chairman of Surgery, **Joseph B. Zwischenberger, MD**, teamed up with Avalon Laboratories Inc. (California), to create the Avalon Elite[™] Bi-Caval Double Lumen Catheter. The high performance device accomplishes total gas exchange for patients of all sizes with lung disease. Dr. Hoopes has capitalized on the advances in ECMO technology to promote the ambulatory approach and use of the Walking ECMO.

Pulmonary Hypertension Program

UK also provides the region's only expertise in the management of pulmonary hypertension. The pulmonary hypertension program has a multidisciplinary team of cardiologists, pulmonologists, and nurse practitioners who work together to help patients who suffer from this condition. For those patients who do not respond to treatment, referral to our lung transplant program is available.

Publications:

Malik A, Hsu JC, **Hoopes CW**, Itinarelli G, Marcus GM. Elevated Pulmonary artery systolic pressures are associated with a lower risk of atrial fibrillation following lung transplantation. *J Electrocardial* (in press).

Urisman A, Leard LE, Nathan M, Elicker BM, **Hoopes CW**, Kukreja J, Jones KD. Rapidly progressive pumonary veno-occlusive disease. *J Heart Lung Transplant*. 2012 Sep;31(9):1031-6.

Hoopes CW, Diaz-Guzman E, Gurley J, and **Zwischenberger JW**. Mechanical support for pulmonary veno-occlusive disease: hybrid atrial septostomy and VV ECMO. *Sem Thorac Cardiovasc Surg* (in press).

Hayes D Jr, Schell RM, Plunkett MD, Gurley JC, Hoopes CW. AngioJet Rheolytic Thrombectomy for Thrombotic Myocardial Injury in a 15-Year-Old Cystic Fibrosis Patient During Lung Transplantation. *Ann Thorac Surg.* 2012 Aug;94(2):626-8.

Diaz-Guzman E, Davenport DL, **Zwischenberger JB, Hoopes CW.** Lung Function and ECMO After Lung Transplantation. *Ann Thorac Surg.* 2012 Aug;94(2):686-7.

Rajagopalan N, Hoopes CW. Ventricular assist devices: Bridge to continued employment. *Int J Cardiol*. 2012 Jul 26;158(3):468.

Rajagopalan N, Hoopes CW. Renal failure following ventricular assist device placement. J Am *Coll Cardiol.* 2012 Jun 12;59(24):2220.

Diaz-Guzman E, Neltner JM, **Hoopes CW**. Organ donation and Moyamoya disease. *Am J Transplant*. 2012 May;12(5):1353-5.



Hong TT, Smyth JW, Chu KY, Vogan JM, Fong TS, Jensen BC, Fang K, Halushka MK, Russell SD, Colecraft H, **Hoopes CW**, Ocorr K, Chi NC, Shaw RM. BIN1 is reduced and Cav1.2 trafficking is impaired in human failing cardiomyocytes. *Heart Rhythm*. 2012 May;9(5):812-20.

Diaz-Guzman E, Lynch J, **Hoopes CW**. Venovenous extracorporeal membrane oxygenation in acute respiratory failure: do we need a new configuration? *J Thorac Cardiovasc Surg.* 2012 Apr;143(4):993-4.

Hayes D Jr, Kukreja J, Tobias JD, Ballard HO, **Hoopes CW**. Ambulatory venovenous extracorporeal respiratory support as a bridge for cystic fibrosis patients to emergent lung transplantation. *J Cyst Fibros*. 2012 Jan;11(1):40-5.

Hayes D, Diaz-Guzman E, **Zwischenberger JB**, Hoopes CW. Lung transplantation in coal workers pneumoconiosis. *Chest*. 2011 Nov;140(5):1387-8.

Azadani PN, Kumar UN, Yang Y, Scheinman MM, **Hoopes CW**, Marcus GM, Rifkin C, Olgin JE, Lee BK. Frequency of atrial flutter after adult lung transplantation. *Am J Cardiol*. 2011 Mar 15;107(6):922-6.

Salters CR Jr, Bailey AL, Whayne TF Jr. Current treatment of heart failure in the USA. *Expert Rev Cardiovasc Ther*. 2010 Feb;8(2):279-90.

Chen H, Shiboski SC, Golden JA, Gould MK, Hays SR, **Hoopes CW**, De Marco T. Impact of the lung allocation score on lung transplantation for pulmonary arterial hypertension. *Am J Respir Crit Care Med.* 2009 Sep 1;180(5):468-74.

Investigator Initiated Studies

Biologic commonalities associated with degeneration in function of cardiac skeletal and respiratory muscles in patients with heart failure)

Principal Investigator: Charles Hoopes, MD

Summary: Determine the biologic commonalities associated with degeneration in function of cardiac, skeletal and respiratory muscles in patients with heart failure and likewise changes associated with recovery to a non heart failure state, or associated with mechanical unloading. **Contact:** Connie Dampier, RN

INTERMACS-VAD therapy database

Principal Investigator: Charles Hoopes, MD

Summary: Facilitate the refinement of patient selection to maximize outcomes with current and new device options. (1) Improve and expedite new device clinical trials by providing historical control data, reliable enough to serve as Objective Performance Criteria (OPC) standards for FDA. (2) Develop consensus "best practice" guidelines to improve clinical management by reducing short and long term complications of MCSD therapy. (3) Improve economic outcomes by identifying and optimizing factors affecting cost-effectiveness. (4) Utilize MCSD Registry information to guide improvements in technology, particularly as next generation devices evolve. (5) Promote research into the underlying pathophysiologic substrate of advanced heart failure in order to define and promote the conditions necessary for myocardial recovery. (6) Evaluate parameters of functional capacity and quality of life before and after device implantation.

Contact: Connie Dampier, RN

Currently Enrolling Clinical Trials

Left Atrial Pressure Monitoring to Optimize Heart Failure Therapy (LAPTOP-HF)

Principal Investigator (site): John Gurley, MD

Summary: The purpose of this clinical study is to evaluate the safety and clinical effectiveness of use of a physician-directed, patient selfmanagement system, guided by left atrial pressure measurements, for use in patients with heart failure. The system allows patients to adjust their HF medications daily based on a physician-directed prescription plan and their current HF status, similar to the manner in which diabetes patients manage their insulin therapy.

Contact: Rebekah Evans, RN 859-323-8663

Thoratec Corporation CentriMag® Ventricular Assist System (VAS) Failure-to-Wean from Cardiopulmonary Bypass Pivotal Trial (Thoratec)

Principal Investigator (site): Charles Hoopes, MD

Summary: To evaluate the safety and effectiveness of the Levitronix CentriMag VAS when used in failure-to-wean from cardiopulmonary patients until the patient can be weaned and: a) no longer requires mechanical circulatory support, b) undergoes heart transplantation or c) undergoes further treatment with a commercially available long-term heart assist system.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

SynCardia Freedom[™] Driver System Study (Syncardia)

Principal Investigator (site): Charles Hoopes, MD

Summary: (1) To confirm the *in vitro* test results that the Freedom Driver System is a suitable pneumatic driver for clinically stable TAH-t subjects in that it operates within the specifications of the CSS Console such that the TAH-t is blind to the driver providing support in this group of patients. (2) To demonstrate that the Freedom Driver in-hospital adverse event profile is clinically comparable to the CSS Console adverse event profile for PMSS patients who meet clinical stability criteria. (3) To demonstrate that patients and lay caregivers can be trained to manage the Freedom Driver System safely outside the hospital.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

SynCardia Temporary Total Artificial Heart (TAH-t) Postmarket Surveillance Study

Summary: To demonstrate that the results achieved in the original pivotal clinical investigation of 81 subjects from five clinical sites are generalizable to clinical sites that complete the staff training defined in the SynCardia Systems, Inc. Training Manual and who enroll patients who meet the intended use defined in the product Instructions for Use.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Ongoing and recently completed trials

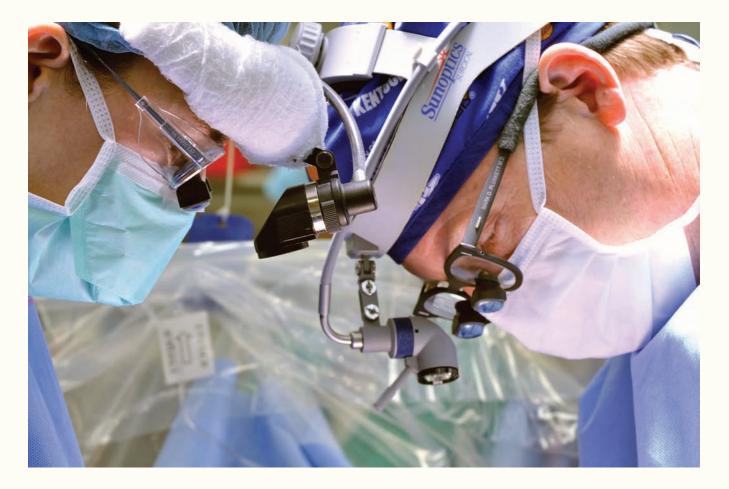
NIH: Immune Activation and Myocardial Recovery in Peripartum Cardiomyopathy

Principal Investigator: Navin Rajagopalan MD

COMPASS 2: Effects of Combination of Bosentan and Sildenafil Versus Sildenafil Monotherapy on Morbidity and Mortality in Symptomatic Pts. with Pulmonary Arterial Hypertension-A Multicenter, Double-Blind, RAndomized, Placebo-Controlled Phase IV Study

Principal Investigator (site): David Booth, MD

Cardiothoracic Surgery



The Division of Cardiothoracic Surgery is dedicated and engaged in all areas of academic practice. Our surgeons are first and foremost committed to compassionate patient care, which is reflected through excellent outcomes. Our surgeons are internationally known, active at the national level and have research support from the NIH. In addition, they are teachers passing on the art and science of medicine to medical students, residents and fellows. The Division of Cardiothoracic Surgery is under the direction of Dr. Mark D. Plunkett, Associate Professor of Surgery, Co-Director of the Gill Heart Institute, and Director of Pediatric Cardiothoracic Program at University of Kentucky Children's Hospital. With highly trained physicians and supportive staff, the division's number one mission is to provide the best care for all of our patients. We offer specific clinical programs and expertise in all areas of thoracic and cardiovascular surgery.

The cardiac surgery section provides expert care for major aortic surgery, coronary bypass, beating heart cardiac operations, arrhythmia surgery (the MAZE operation) and minimally invasive techniques including robotic surgery. We also provide specialized care for heart failure patients including cardiac assist devices, ventricular restorative procedures, and heart transplantation.

The Kentucky Children's Hospital is also housed within the UK Medical Center and provides a referral base of neonatal and pediatric patients with congenital heart diseases. The Children's Hospital offers the only pediatric cardiology and congenital cardiothoracic surgery services based in central and eastern Kentucky.

Publications:

Saha SP, Muluk S, Schenk W 3rd, Dennis JW, Ploder B, Grigorian A, Presch I, Goppelt A. A prospective randomized study comparing fibrin sealant to manual compression for the treatment of anastomotic suturehole bleeding in expanded polytetrafluoroethylene grafts. *J Vasc Surg.* 2012 Jul;56(1):134-41.

Ferraris VA. Severe Blood Conservation: Benefits and Risks: Comment on "Outcome of Patients Who Refuse Transfusion After Cardiac Surgery" *Arch Intern Med.* 2012 Jul 2:7-8.

Zhou X, Wang D, Sumpter R, Pattison G, **Ballard-Croft C**, **Zwischenberger JB**.Long-term support with an ambulatory percutaneous paracorporeal artificial lung. *J Heart Lung Transplant*. 2012 Jun;31(6):648-54.

Srinivasan R, Bhutani MS, Thosani N, S ftoiu A, Rice DC, Ioncic AM, Eapen GA, Gupta P, Jaganmohan S, Artifon EL, **Zwischenberger JB**. Clinical impact of EUS-FNA of mediastinal lymph nodes in patients with known or suspected lung cancer or mediastinal lymph nodes of unknown etiology. *J Gastrointestin Liver Dis.* 2012 Jun;21(2):145-52.

Hayes D Jr, **Zwischenberger JB**, Zhou X, Liu X, Lynch JE, **Ballard-Croft C**, Wang D.Complete respiratory support with AVCO2R and CPAP-mimic ventilation for total gas exchange in sheep. *ASAIO J.* 2012 Mar-Apr; 58(2):155-9.

Ballard-Croft C, Wang D, Sumpter LR, Zhou X, **Zwischenberger JB**. Large-animal models of acute respiratory distress syndrome. *Ann Thorac Surg.* 2012 Apr;93(4):1331-9.

Ferraris VA, Saha SP, Davenport DL, Zwischenberger JB. Thoracic surgery in the real world: does surgical specialty affect outcomes in patients having general thoracic operations? *Ann Thorac Surg.* 2012 Apr;93(4):1041-7.

Park CW, Rhee YS, Vogt FG, Hayes D Jr, **Zwischenberger JB**, DeLuca PP, Mansour HM. Advances in microscopy and complementary imaging techniques to assess the fate of drugs ex vivo in respiratory drug delivery: an invited paper. *Adv Drug Deliv Rev.* 2012 Mar 30;64(4):344-56.

Angiolillo DJ, Firstenberg MS, Price MJ, Tummala PE, Hutyra M, Welsby IJ, Voeltz MD, Chandna H, **Ramaiah C**, Brtko M, Cannon L, Dyke C, Liu T, Montalescot G, Manoukian SV, Prats J, Topol EJ; BRIDGE Investigators. Bridging antiplatelet therapy with cangrelor in patients undergoing cardiac surgery: a randomized controlled trial. *JAMA*. 2012 Jan 18;307(3):265-74.

Ferraris VA, Davenport DL, Saha SP, Austin PC, Zwischenberger JB. Thoracic surgery in the real world: does surgical specialty affect outcomes in patients having general thoracic operations? *Arch Surg.* 2012 Jan;147(1):49-55.

Ferraris VA, Davenport DL, **Saha SP**, Austin PC, **Zwischenberger JB**. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. *Arch Surg*. 2012 Jan;147(1):49-55.

- The study examined outcomes in patients entered into the American College of Surgeons National Surgical Quality Improvement Program database who received 1 or 2 units of PRBCs intraoperatively.
- Most patients (893,205 patients [94.9%]) did not receive intraoperative transfusions.
- Patients who received intraoperative infusion of 1 unit of packed red blood cells (15,186 patients [1.6%]) had higher unadjusted rates of mortality and more serious morbidity.
- The rates of adverse outcomes increased with intraoperative transfusion of more than 1 unit of packed red blood cells in a dosedependent manner.
- The authors suggest that it is likely that a small, possibly discretionary amount of intraoperative transfusion leads to increased mortality, morbidity, and resource use, and that caution should be used with intraoperative transfusions for mildly hypovolemic or anemic patients.

Skinner SC, locono JA, Ballard HO, Turner MD, Ward AN, Davenport DL, Paden ML, **Zwischenberger JB**. Improved survival in venovenous vs venoarterial extracorporeal membrane oxygenation for pediatric noncardiac sepsis patients: a study of the Extracorporeal Life Support Organization registry. *J Pediatr Surg.* 2012 Jan;47(1):63-7.

Martin JT, **Reda H**, Dority JS, **Zwischenberger JB**, Hassan ZU. Surgical resident training using real-time simulation of cardiopulmonary bypass physiology with echocardiography. *J Surg Educ.* 2011 Nov-Dec;68(6):542-6.

Javidfar J, Brodie D, Takayama H, Mongero L, **Zwischenberger J**, Sonett J, Bacchetta M. Safe transport of critically ill adult patients on extracorporeal membrane oxygenation support to a regional extracorporeal membrane oxygenation center. *ASAIO J.* 2011 Sep-Oct;57(5):421-5.

Zhou X, **Wang D**, Castro CY, Hawkins H, Lynch JE, Liu X, **Zwischenberger JB**. A pulmonary hypertension model induced by continuous pulmonary air embolization. *J Surg Res.* 2011 Sep;170(1):e11-6.

Bacchetta M, Javidfar J, Sonett J, Kim H, **Zwischenberger J, Wang D**. Ease of conversion from venovenous extracorporeal membrane oxygenation to cardiopulmonary bypass and venoarterial extracorporeal membrane oxygenation with a bicaval dual lumen catheter. *ASAIO J.* 2011 Jul-Aug;57(4):283-5.

Lynch JE, Hayes D Jr, **Zwischenberger JB**. Extracorporeal CO(2) removal in ARDS. *Crit Care Clin*. 2011 Jul;27(3):609-25.

De Bartolo C, Nigro A, Fragomeni G, Colacino FM, **Wang D**, Jones CC, **Zwischenberger J**. Numerical and experimental flow analysis of the Wang-Zwische double-lumen cannula. *ASAIO J. 2011* Jul-Aug;57(4):318-27.

Ferraris VA, Davenport DL, Saha SP, Bernard A, Austin PC, Zwischenberger JB. Intraoperative transfusion of small amounts of blood heralds worse postoperative outcome in patients having non-cardiac thoracic operations. *Ann Thorac Surg.* 2011 Jun;91(6):1674-80;

- Massive intraoperative transfusion is associated with increased morbidity and mortality in patients undergoing noncardiac thoracic operations. In this study, the outcomes after smaller transfusions (1 to 2 units) of packed red blood cells (PRBCs) during an operation was investigated.
- After propensity adjustment, transfusion of 1 or 2 units of PRBCs increased the multivariate risk of composite morbidity, pulmonary complications, systemic sepsis, wound complications, and the postoperative length of stay compared with those who did not receive transfusions.
- The authors concluded that in patients undergoing noncardiac thoracic operations, there is a dose-dependent adverse effect of intraoperative blood transfusion on outcomes, with even seemingly small amounts of blood.

Javidfar J, Brodie D, **Wang D**, Ibrahimiye AN, Yang J, **Zwischenberger JB**, Sonett J, Bacchetta M. Use of bicaval dual-lumen catheter for adult venovenous extracorporeal membrane oxygenation. *Ann Thorac Surg.* 2011 Jun;91(6):1763-8;

Wang D, Plunkett M, Lynch J, Zhou X, Ballard-Croft C,

Zwischenberger JB. Wang-Zwische double-lumen cannula leads to total cavopulmonary support in a failing Fontan sheep model. *Ann Thorac Surg.* 2011 Jun;91(6):1956-60.

- The authors tested a percutaneous Wang-Zwische double-lumen cannula (DLC) cavopulmonary support system in a sheep model of failing Fontan physiology in five sheep.
- An extracardiac conduit was anastomosed to the inferior vena cava and superior vena cava, and a graft was applied to connect the conduit and the right pulmonary artery (PA) to create total vena cava-to-PA diversion, excluding the right heart. The DLC (commercialized as AvalonElite, Avalon Laboratories LLC, Rancho Dominguez, CA) was coupled with a CentriMag pump (Levitronix Waltham, MA) to form a cavopulmonary support system.
- After total venous blood diversion from the vena cava to the right PA artery, failing Fontan physiology developed, evidenced by elevated central venous pressure and dropping mean PA pressure and systolic arterial pressure. The DLC was successfully inserted, and hemodynamics was normalized in all five sheep for the duration of the two-hour study.
- The authors concluded that in a model of failing Fontan circulation in sheep, a total cavopulmonary support system using percutaneous DLC achieved total cavopulmonary support.



Javidfar J, **Wang D**, **Zwischenberger JB**, Costa J, Mongero L, Sonett J, Bacchetta M. Insertion of bicaval dual lumen extracorporeal membrane oxygenation catheter with image guidance. *ASAIO J*. 2011 May-Jun;57(3):203-5.

Martin JT, Cibull ML, **Zwischenberger JB**, **Reda HK**. Infection of an esophageal cyst following endoscopic fine-needle aspiration. *Int J Surg Case Rep.* 2011;2(6):144-6. Epub 2011 Apr 8.

Sudharshan S, Ferraris VA, Mullett T, Ramaiah C. Effectiveness of tunneled pleural catheter placement in patients with malignant pleural effusions. *Int J Angiol.* 2011 Mar;20(1):39-42.

Ferraris VA, Ferraris SP, Saha SP. Antiplatelet drugs: mechanisms and risks of bleeding following cardiac operations. *Int J Angiol.* 2011 Mar;20(1):1-18.

Nolan H, **Wang D**, **Zwischenberger JB**. Artificial lung basics: fundamental challenges, alternative designs and future innovations. *Organogenesis.* 2011 Jan-Mar;7(1):23-7.

Luftman V, Martin CA, Guenthner G, Arnold SM, **Mullett TW**, Jhaveri M. The power of videotaped personal statements of patients with lung cancer: a recruitment strategy for smoking prevention and cessation programs. *Oncol Nurs Forum*. 2011 Jan;38(1):11-4.

Hayes D Jr, Hatton KW, Feola DJ, Murphy BS, **Mullett TW**. Airway dehiscence after lung transplantation in a patient with cystic fibrosis. *Respir Care*. 2010 Dec;55(12):1746-50.

Singhal S, **Ferraris VA**, Bridges CR, Clough ER, Mitchell JD, Fernando HC, Shrager JB. Management of alveolar air leaks after pulmonary resection. *Ann Thorac Surg.* 2010 Apr;89(4):1327-35.

Hayes D Jr, Murphy BS, **Mullett TW**, Feola DJ. Aerosolized vancomycin for the treatment of MRSA after lung transplantation. *Respirology*. 2010 Jan;15(1):184-6.

Currently Enrolling Clinical Trials

An Open-Label Randomized, Multicenter, Phase IIIB Study to Assess the Efficacy, Safety, and Tolerance of Beriplex[®] P/N Compared with Plasma for Rapid Reversal of Coagulopathy Induced by Vitamin K Antagonists in Subjects Requiring an Urgent Surgical or Urgent Invasive Procedure

Primary Investigator: Sibu Saha, MD

Summary: To compare the hemostatic efficacy of Beriplex[®] P/N and plasma in preventing excessive hemorrhages during urgent surgical or urgent invasive procedures in subjects who have a deficiency of vitamin K-dependent coagulation factors II, VII, IX, X and proteins C and S acquired from oral anticoagulation.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Thoratec Corporation CentriMag[®] Ventricular Assist System (VAS) Failure-to-Wean from Cardiopulmonary Bypass Pivotal Trial

Primary Investigator: Charles Hoopes, MD

Summary: To evaluate the safety and effectiveness of the Levitronix CentriMag VAS when used in failure-to-wean from cardiopulmonary patients until the patient can be weaned and: a) no longer requires mechanical circulatory support, b) undergoes heart transplantation or c) undergoes further treatment with a commercially available long-term heart assist system.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

A Randomized, open label, parallel-group, multicenter trial to compare efficacy and safety of TachoSil[®] versus Surgicel[®] Original for the secondary hemostatic treatment of needle hole bleeding in vascular surgery

Summary: To demonstrate the superiority of TachoSil[®] as adjunct homeostatic treatment in vascular surgery compared to the standard USA licensed hemostatic agent Surgicel[®] Originial.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

SynCardia Freedom[™] Driver System Study

Primary Investigator: Charles Hoopes, MD

Summary: To confirm the *in vitro* test results that the Freedom Driver System is a suitable pneumatic driver for clinically stable TAH-t subjects in that it operates within the specifications of the CSS Console such that the TAH-t is blind to the driver providing support in this group of patients. To demonstrate that the Freedom Driver in-hospital adverse event profile is clinically comparable to the CSS Console adverse event profile for PMSS patients who meet clinical stability criteria. To demonstrate that patients and lay caregivers can be trained to manage the Freedom Driver System safely outside the hospital.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

SynCardia Temporary Total Artificial Heart (TAH-t) Postmarket Surveillance Study

Primary Investigator: Charles Hoopes, MD

Summary: To demonstrate that the results achieved in the original pivotal clinical investigation of 81 subjects from five clinical sites are generalizable to clinical sites that complete the staff training defined in the SynCardia Systems, Inc. Training Manual and who enroll patients who meet the intended use defined in the product Instructions for Use.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

A Prospective, Single-blind, Randomized, Phase III Study to Evaluate the Safety and Efficacy of Fibrin Sealant Grifols (FS Grifols) as an Adjunct to Hemostasis during Peripheral Vascular Surgery

Primary Investigator: Sibu Saha, MD

Summary: To evaluate the safety and the hemostasis efficacy of human plasma-derived fibrin sealant Grifols (FS Grifols) in peripheral vascular surgery.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Ongoing and recently completed trials

A Phase II, Randomized, Double-Blind, Multicenter, Multinational, Placebo-Controlled, Parallel-Groups Study to Evaluate the Safety and Efficacy of Intramuscular Injections of Allogeneic PLX-PAD Cells for the Treatment of Subjects with Intermittent Claudication (IC)

Primary Investigator: Sibu Saha, MD

Summary: The objectives of the study are to further establish the safety profile of local PLX-PAD injections, and to evaluate the clinical efficacy of PLX-PAD in IC subjects.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Investigator Initiated Studies

Rheos[™] Pivotal Trial. Resistant Hypertension

Primary Investigator: Sibu Saha, MD

Summary: To determine safety and effectiveness of the Rheos Systme in people with hard to treat high blood pressure.

Biologic commonalities associated with degeneration in function of cardiac skeletal and respiratory muscles in patients with heart failure

Primary Investigator: Charles Hoopes, MD

Summary: Determine the biologic commonalities associated with degeneration in function of cardiac, skeletal and respiratory muscles in patients with heart failure and likewise changes associated with recovery to a non heart failure state, or associated with mechanical unloading.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

INTERMACS-VAD therapy database

Primary Investigator: Charles Hoopes, MD

Summary: Facilitate the refinement of patient selection to maximize outcomes with current and new device options. Improve and expedite new device clinical trials by providing historical control data, reliable enough to serve as Objective Performance Criteria (OPC) standards for FDA. Develop consensus "best practice" guidelines to improve clinical management by reducing short and long term complications of MCSD therapy, improve economic outcomes by identifying and optimizing factors affecting cost-effectiveness. Utilize MCSD Registry information to guide improvements in technology, particularly as next generation devices evolve. Promote research into the underlying pathophysiologic substrate of advanced heart failure in order to define and promote the conditions necessary for myocardial recovery. Evaluate parameters of functional capacity and quality of life before and after device implantation. Disseminate registry research results through peer-reviewed journals and other publications.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Contegra Graft for pediatric congenital heart defect repairs

Primary Investigator: Dr. Mark Plunkett

Summary: The purpose of this study is to perform Humanitarian Use Device insertion in patients with congenital heart defects including Pulmonary Stenosis, Tetralogy of Fallot, Truncus Arteriosus, Transposition of the Great Vessels with Ventricular Septal Defect (VSD), Pulmonary Atresia and replacement of previously implanted but dysfunctional pulmonary homografts or valved conduits allowing flow of blood across a continuous tissue interface.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Spiration IBV valve system-Humanitarian use device

Primary Investigator: Timothy Mullett, MD

Summary: The purpose of this study is to perform Humanitarian Use Device insertion in patients with prolonged air leaks of the lung, or significant air leaks that are likely to become prolonged following lobectomy, segmentectomy or lung volume reduction surgery only.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Evaluation of perioperative Metoprolol Tartrate for atrial arrhythmis prophylaxis in patients undergoing non-cardiac thoracic surgery

Primary Investigator: Hassan Reda, MD

Summary: (1) Determine the event rate for postoperative atrial fibrillation/supraventricular arrhythmias in patients undergoing thoracic surgery who received perioperative metoprolol tartrate compared to placebo. (2) Compare the intensive care unit and total length of stay and associated health care expenditures associated with patients that develop postoperative atrial arrhythmias with those patients that do not. (3) Compare the tolerability and safety of metoprolol tartrate in this setting by comparing the incidence of stroke and incidence and treatment of hypotension, bradycardia, bronchospasm in patients who received metoprolol tartrate versus those who received placebo.

Contact: Connie Dampier, MPA, RN, CCRC, 859-323-1781

Investigator Retrospective Review Studies

- Outcomes of traumatic injuries in patients receiving warfarin therapy (Ferraris).
- Postoperative Care Tool Survey (Kozik).
- Effect of antifibrinolytic prophylaxis for on-pump cardiac surgeon transfusion rates (Ramaiah).
- A comparison of post-operative thrombotic complication for on-pump versus off-pump CABG (Ramaiah).
- Surgery for Infective Endocarditis, A Retrospective Review of Outcomes (Ramaiah).
- A retrospective review of carotid endarectomy in cardiothoracic surgery from 2002-September 2009 (Saha).
- Lobectomy/Wedge Resection for Lung Cancer: An Outcomes Analysis of 400 cases from January 2002-December 2006 (Saha).
- Retrospective review of Empyema in Cardiothoracic Surgery from 2005-2009 (Saha).

Outreach and Affiliates: World Class Care Close to Home



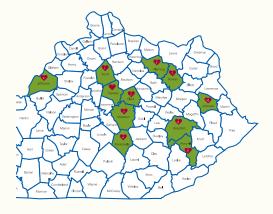
Our cardiologists provide the region's most comprehensive consultative services, diagnostic assessment and therapeutic strategies in more than 10 satellite locations in the Bluegrass Region, central and southeastern Kentucky. With more than 40 clinics per month, visits to Gill-affiliated sites topped 16,500 last year. By extending our care to these communities, patients and their families are relieved of the emotional and financial burdens associated with traveling to Lexington. These outreach activities form the basis of true partnerships between the Gill Heart Institute and communities throughout Kentucky, fulfilling the mission of UK Healthcare.

Working closely with local physicians and hospitals, we help broaden their treatment options by providing access to revolutionary diagnostic technology and the latest therapeutic advances. "Prudent partnering with communitybased physicians and regional hospitals is fundamental to our success," said Dr. Michael Karpf, UK executive vice president for health affairs. "We remain committed to responding to their needs, whether it is to provide a muchneeded specialist in the local community or to accept the transfer of a critically ill patient to UK Chandler Hospital. We want to keep patients close to home for as much of their medical care as possible, offering our specialized services and resources as needed."

Our services are tailored to the needs of each community and range from nuclear stress testing to consultative services for electrophysiology, as well as providing access to physicians certified in advanced heart failure for referral for transplantation or a ventricular assist device. We also work with regional providers to ensure that the most appropriate care is delivered, always based on the latest evidence and technological advances. Our key partnerships include:

- Collaboration with Appalachian Regional Healthcare's Heart Institute, providing comprehensive cardiovascular services that benefit the people of Eastern Kentucky. Beginning in the summer of 2011, **Dr. Edward Setser**, a UK faculty CT surgeon, began full-time practice in Hazard, Kentucky. Dr. Setser performs cardiothoracic operations at Hazard ARH Regional Medical Center. Cardiac electrophysiology was added to the program when Dr. Jeffrey Brumfield began treating patients in the Gill Heart Institute office in Hazard.
- Our partnership with Norton Healthcare allows patients in need of cardiac transplantation or ventricular assist devices to have their initial evaluation in Louisville close to home. We also offer residents of Louisville access to the most experienced structural heart and valve team in the region for minimally invasive procedures such as transcatheter aortic valve replacement. Together, Norton and UK Healthcare are developing a regional referral system and algorithm for managing ST-elevation myocardial infarction.

- 1. Georgetown
- Georgetown Community Hospital
 2. Winchester
- Clark Regional Medical Center
 3. Richmond
- John Johnstone office (Electrophysiology only)
- 4. Mount Vernon Rockcastle Regional Hospital
- 5. Flemingsburg Fleming County Hospital & Specialty Clinics
 - Louisville Norton Audubon Hospital
- Morehead St. Claire Regional Medical Center (Electrophysiology only)
- 8. Jackson Kentucky River Medical Center
- 9. Hazard ARH Regional Medical Center* (Electrophysiology and CT surgery) * Affiliate Partner
- 10. Paintsville Paul B. Hall Hospital



Saha Cardiovascular Research Center



Working in partnership with the Gill Heart Institute is the Dr. Sibu and Becky Saha Cardiovascular Research Center, where Gill physicians and scientists pursue their research interests alongside basic and translational science researchers. The Saha CVRC also teaches and trains scientists of the future.

Led by director **Alan Daugherty, PhD**, and associate director **Dennis Bruemmer, PhD**, the Saha CVRC is home to 19 core faculty, along with 75 associated faculty, four American Heart Association Fellows, 30 research staff, four administrative staff and 20 students (both preand postdoctoral). These faculty and staff work on an array of research related to the prevention, diagnosis and treatment of cardiovascular disease. The ranks of Saha CVRC faculty include physicians and scientists drawn primarily from the fields of cardiology, nutrition, endocrinology, physiology and pharmacology. Many faculty hold joint appointments with the Gill Heart Institute, the Barnstable Brown Diabetes and Obesity Research Center, the Graduate Center for Nutritional Sciences, the College of Medicine, and other areas across the healthcare campus, which exemplifies the university's commitment to interdisciplinary research.

In the most recent fiscal year, the Saha CVRC totaled \$4.1 million in NIH funding, \$321,000 in American Heart Association Awards, \$163,876 in American Diabetes Association Awards, and an additional \$150,000 from other sources, making it a powerhouse in the field of cardiovascular research.

Saha CVRC faculty serve on committees and editorial review boards for several major scientific journals. Members of the core Saha CVRC faculty have published more than 50 peer-reviewed papers in the past year, and also presented at numerous national and international conferences. Recently, the American Heart Association announced the appointment of Alan Daugherty, PhD, DSc. FAHA, as editor-in-chief of *Arteriosclerosis, Thrombosis, and Vascular Biology: Journal of the American Heart Association* (ATVB), a monthly journal devoted to the biology, prevention and impact of vascular diseases. (Daugherty A. The New ATVB Editorial Team. *Arterioscler Thromb Vasc Biol.* 2012 Jul;32(7):1545.)

In 2011, the NIH awarded UK's Center for Clinical and Translational Science \$20 million to move research discoveries to health care solutions more quickly. Awarded through the NIH's institutional Clinical and Translational Science Awards, this designation makes UK's Center for Clinical and Translational Science a part of a select national biomedical research consortium.

Goals of the University of Kentucky Saha Cardiovascular Research Center:

- To develop a nationally and internationally recognized center of excellence in cardiovascular research.
- To provide an environment for the development and retention of productive faculty.
- To facilitate the training of students, including postdoctoral fellows, graduate students, medical students and residents
- To encourage the development of translational and clinical research with funding from federal agencies and industry.

Publications:

Lipid signaling mediators

Sumanasekera C, Kelemen O, Beullens M, Aubol BE, Adams JA, Sunkara M, **Morris A**, Bollen M, Andreadis A, Stamm S. C6 pyridinium ceramide influences alternative pre-mRNA splicing by inhibiting protein phosphatase-1. *Nucleic Acids Res.* 2012 May;40(9):4025-39.

Cantrell Stanford J, **Morris AJ**, Sunkara M, Popa GJ, Larson KL, Özcan S. Sphingosine 1-phosphate (S1P) regulates glucose-stimulated insulin secretion in pancreatic beta cells. *J Biol Chem.* 2012 Apr 13;287(16): 13457-64.

Zaytseva YY, Rychahou PG, Gulhati P, Elliott VA, Mustain WC, O'Connor K, **Morris AJ**, Sunkara M, Weiss HL, Lee EY, Evers BM. Inhibition of fatty acid synthase attenuates CD44-associated signaling and reduces metastasis in colorectal cancer. *Cancer Res.* 2012 Mar 15;72(6):1504-17.

Cheng HY, Dong A, Panchatcharam M, Mueller P, Yang F, Li Z, Mills G, Chun J, **Morris AJ, Smyth SS**. Lysophosphatidic acid signaling protects pulmonary vasculature from hypoxia-induced remodeling. *Arterioscler Thromb Vasc Biol.* 2012 Jan;32(1):24-32..

Wu Z, Li X, **Sunkara M**, Spearman H, **Morris AJ**, Huang C.PIPKI regulates focal adhesion dynamics and colon cancer cell invasion. *PLoS One.* 2011;6(9):e24775. Epub 2011 Sep 12.

Shridas P, Bailey WM, Talbott KR, Oslund RC, Gelb MH, **Webb NR**. Group X Secretory Phospholipase A2 Enhances TLR4 Signaling in Macrophages. *J Immunol.* 2011 May 27.

Shridas P, Bailey WM, Boyanovsky BB, Oslund RC, Gelb MH, Webb NR. Group X secretory phospholipase A2 regulates the expression of steroidogenic acute regulatory protein (StAR) in mouse adrenal glands. *J Biol Chem.* 2010 Jun 25;285(26):20031-9.

Miriyala S, Subbramanian T, Panchatcharam M, Ren H, McDermott MI, Sunkara M, Drennan T, Smyth SS, Spielman HP, Morris AJ. Functional characterization of the atypical integral membrane lipid phosphatase PDP1/PPAPDC2 identifies a pathway for interconversion of isoprenols and isoprenoid phosphates in mammalian cells. *J Biol Chem.* 2010 Jan 28.

Lipoproteins and their receptors

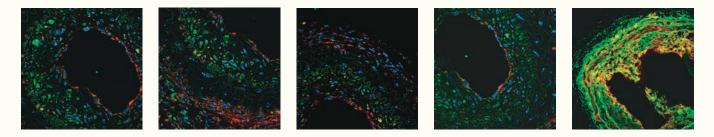
Su K, Sabeva NS, Liu J, Wang Y, Bhatnagar S, **van der Westhuyzen DR**, Graf GA. The ABCG5 ABCG8 sterol transporter opposes the development of fatty liver disease and loss of glycemic control independent of phytosterol accumulation. *J Biol Chem.* 2012 Jun 19.

Cai L, Wang Z, Ji A, **Meyer JM**, **van der Westhuyzen DR**. Macrophage SR-BI regulates pro-inflammatory signaling in mice and isolated macrophages. *J Lipid Res.* 2012 May 15.

Liu J, Liang S, Liu X, Brown JA, Newman KE, Sunkara M, **Morris AJ**, Bhatnagar S, Li X, Pujol A, Graf GA. The absence of ABCD2 sensitizes mice to disruptions in lipid metabolism by dietary erucic acid. *J Lipid Res.* 2012 Apr 6.

Ji A, Wroblewski JM, **Cai L**, de Beer MC, **Webb NR, van der Westhuyzen DR**. Nascent HDL formation in hepatocytes and role of ABCA1, ABCG1 and SR-BI. *J Lipid Res.* 2011 Dec 20.

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Wroblewski JM, Jahangiri A, Ji A, de Beer FC, van der Westhuyzen DR, Webb NR. Nascent HDL formation by hepatocytes is reduced by the concerted action of serum amyloid A and endothelial lipase. *J Lipid Res.* 2011 Dec;52(12):2255-61.

Guo L, Chen M, Song Z, **Daugherty A**, Li XA. C323 of SR-BI is required for SR-BI-mediated HDL binding and cholesteryl ester uptake. *J Lipid Res.* 2011 Dec;52(12):2272-8.

Feng H, Guo L, **Wang D**, Gao H, Hou G, Zheng Z, Ai J, Foreman O, **Daugherty A**, Li XA.Deficiency of scavenger receptor BI leads to impaired lymphocyte homeostasis and autoimmune disorders in mice. *Arterioscler Thromb Vasc Biol.* 2011 Nov;31(11):2543-51.

Zhang X, Hurng J, **Rateri DL, Daugherty A**, Schmid-Schönbein GW, Shin HY. Membrane cholesterol modulates the fluid shear stress response of polymorphonuclear leukocytes via its effects on membrane fluidity. *Am J PhysiolCell Physiol*. 2011 Aug;301(2):C451-60.

Ji A, Meyer JM, **Cai L**, Akinmusire A, **deBeer MC**, **Webb NR**, **van der Westhuyzen DR**. Scavenger Receptor SR-BI in Macrophage Lipid Metabolism. *Arterioscler Thromb Vasc Biol*. 2011 Apr 8.

De Beer MC, Ji A, **Jahangiri A**, Vaughan AM, **de Beer FC**, **van der Westhuyzen DR**, **Webb NR**.ATP binding cassette G1-dependent cholesterol efflux during inflammation. *J Lipid Res.* 2011 Feb;52(2):345-53.

Boyanovsky BB, Li X, Shridas P, Sunkara M, Morris AJ, Webb NR. Bioactive products generated by Group V sPLA(2) hydrolysis of LDL activate macrophages to secrete pro-inflammatory cytokines. *Cytokine*. 2010 Feb 5.

Shridas P, Bailey WM, Gizard F, Oslund RC, Gelb MH, **Bruemmer D, Webb NR**. Group X Secretory Phospholipase A2 Negatively Regulates ABCA1 and ABCG1 Expression and Cholesterol Efflux in Macrophages. *Arterioscler Thromb Vasc Biol.* 2010 Jul 1.

Smooth muscle cell biology

Liu S, Xie Z, Zhao Q, Pang H, Turk J, Calderon L, Su W, Zhao G, Xu H, Gong MC, Guo Z. Smooth Muscle-Specific Expression of iPLA2 Participates in the Initiation and Early Progression of Vascular Inflammation and Neointima Formation. *J Biol Chem.* 2012 May 25. **Calderon L, Liu S**, Su W, Xie Z, **Guo Z**, Eberhard W, Gong MC. iPLA2 overexpression in smooth muscle exacerbates angiotensin II-induced hypertension and vascular remodeling. *PLoS One*. 2012;7(2):e31850. Epub 2012 Feb 20.

Su W, Xie Z, **Guo Z**, Duncan MJ, Lutshumba J, Gong MC.Altered clock gene expression and vascular smooth muscle diurnal contractile variations in type 2 diabetic db/db mice. *Am J Physiol Heart Circ Physiol*. 2012 Feb;302(3):H621-33.

Subramanian V, Golledge J, Heywood EB, **Bruemmer D, Daugherty A.** Regulation of peroxisome proliferator-activated receptor- by angiotensin II via transforming growth factor- 1-activated p38 mitogen-activated protein kinase in aortic smooth muscle cells. *Arterioscler Thromb Vasc Biol.* 2012 Feb;32(2):397-405.

Xie Z, Liu D, Liu S, **Calderon L**, Zhao G, Turk J, **Guo Z**. Identification of a cAMP-response element in the regulator of G-protein signaling-2 (RGS2) promoter as a key cis-regulatory element for RGS2 transcriptional regulation by angiotensin II in cultured vascular smooth muscles. *J Biol Chem.* 2011 Dec 30;286(52):44646-58.

Gizard F, Zhao Y, Findeisen HM, Qing H, Cohn D, Heywood EB, Jones KL, Nomiyama T, **Bruemmer D.** Transcriptional regulation of S phase kinaseassociated protein 2 by NR4A orphan nuclear receptor NOR1 in vascular smooth muscle cells. *J Biol Chem.* 2011 Oct 14;286(41):35485-93.

Findeisen HM, Gizard F, Zhao Y, Qing H, Heywood EB, Jones KL, Cohn D, **Bruemmer D**. Epigenetic regulation of vascular smooth muscle cell proliferation and neointima formation by histone deacetylase inhibition. *Arterioscler Thromb Vasc Biol.* 2011 Apr;31(4):851-60.

Panchatcharam M, Miriyala S, **Yang F**, Leitges M, Chrzanowska-Wodnicka M, Quilliam LA, **Anaya P, Morris AJ, Smyth SS**. Enhanced proliferation and migration of vascular smooth muscle cells in response to vascular injury under hyperglycemic conditions is controlled by beta3 integrin signaling. *Int J Biochem Cell Biol*. 2010 June 22.

Xie Z, Gong MC, Su W, Xie D, Turk J, **Guo Z.** Role of calcium-independent phospholipase A2beta in high glucose-induced activation of RhoA, Rho kinase, and CPI-17 in cultured vascular smooth muscle cells and vascular smooth muscle hypercontractility in diabetic animals. *J Biol Chem.* 2010 Mar 19;285(12):8628-38.



Experimental models of atherosclerosis and aneurysm

Han SG, Howatt DA, **Daugherty A**, Gairola CG. Atherogenic and pulmonary responses of ApoE- and LDL receptor-deficient mice to sidestream cigarette smoke. *Toxicology*. 2012 Sep 28;299(2-3):133-8.

Lu H, Daugherty A. Atherosclerosis: cell biology and lipoproteins. *Curr Opin Lipidol*. 2012 Jun;23(3):263-4.

Lu H, Wu C, Howatt DA, Balakrishnan A, Charnigo RJ Jr, Cassis LA, Daugherty A. Differential effects of dietary sodium intake on blood pressure and atherosclerosis in hypercholesterolemic mice. *J Nutr Biochem.* 2012 Jun 15. [Epub ahead of print]

Zhang X, Thatcher SE, **Rateri DL, Bruemmer D, Charnigo R, Daugherty A**, Cassis LA. Transient Exposure of Neonatal Female Mice to Testosterone Abrogates the Sexual Dimorphism of Abdominal Aortic Aneurysms. *Circ Res.* 2012 Apr 26.

Wang S, Subramanian V, Lu H, Howatt DA, Moorleghen JJ, Charnigo R, Cassis LA, Daugherty A. Deficiency of receptorassociated protein attenuates angiotensin II-induced atherosclerosis in hypercholesterolemic mice without influencing abdominal aortic aneurysms. *Atherosclerosis*. 2012 Feb;220(2):375-80.

Owens AP III, Passam FH, Antoniak S, Marshall SM, McDaniel AL, Rudel L, Williams JC, Hubbard BK, Dutton JA, Wang J, Tobias PS, Curtiss LK, **Daugherty A**, Kirchhofer D, Luyendyk JP, Moriarty PM, Nagarajan S, Furie BC, Furie B, Johns DG, Temel RE, Mackman N. Monocyte tissue factor-dependent activation of coagulation in hypercholesterolemic mice and monkeys is inhibited by simvastatin. *J Clin Invest*. 2012 Feb 1;122(2).

Subramanian V, Uchida HA, Ijaz T, Moorleghen JJ, Howatt DA, Balakrishnan A. Calpain inhibition attenuates angiotensin II-induced abdominal aortic aneurysms and atherosclerosis in low-density lipoprotein receptor-deficient mice. *J Cardiovasc Pharmacol.* 2012 Jan;59(1):66-76.

Owens AP III, Rateri DL, Howatt DA, Moore KJ, Tobias PS, Curtiss LK, Lu H, Cassis LA, Daugherty A. MyD88 deficiency attenuates angiotensin Il-induced abdominal aortic aneurysm formation independent of signaling through Toll-like receptors 2 and 4. *Arterioscler Thromb Vasc Biol.* 2011 Dec;31(12):2813-9.

Uchida HA, Poduri A, **Subramanian V**, Cassis LA, **Daugherty A**. Urokinase-type plasminogen activator deficiency in bone marrow-derived cells augments rupture of angiotensin II-induced abdominal aortic aneurysms. *Arterioscler Thromb Vasc Biol.* 2011 Dec;31(12):2845-52.

Wu C, Lu H, Cassis L, **Daugherty A.** Molecular and Pathophysiological Features of Angiotensinogen: A Mini Review. *N A J Med Sci.* 2011 Oct 1;4(4):183-190.

Habegger KM, Grant E, Pfluger PT, Perez-Tilve D, **Daugherty A**, **Bruemmer D**, Tschöp MH and Hofmann SM. Ghrelin receptor deficiency does not affect diet-induced atherosclerosis in low-density lipoprotein receptor-null mice. *Front. Endocrin.* (Lausanne). 2011;2:67.

Rateri DL, Howatt DA, Moorleghen JJ, Charnigo R, Cassis LA, **Daugherty A**. Prolonged infusion of angiotensin II in apoE(-/-) mice promotes macrophage recruitment with continued expansion of abdominal aortic aneurysm. *Am J Pathol.* 2011 Sep;179(3):1542-8.

Lu H, Daugherty A. Atherosclerosis: cell biology and lipoproteins. *Curr Opin Lipidol*. 2011 Aug;22(4):322-3.

Daugherty A, Cassis LA, **Lu H**, Zhejiang J. Complex pathologies of angiotensin II-induced abdominal aortic aneurysms. *Univ Sci B*. 2011 Aug;12(8):624-8.

King VL, Thompson J, Tannock LR. Serum amyloid A in atherosclerosis. *Curr Opin Lipidol.* 2011 Aug;22(4):302-7

Thompson J, Wilson P, Brandewie K, Taneja D, Schaefer L, Mitchell B, **Tannock LR**. Accumulation of Biglycan and Lipid Retention Accelerates Diabetic Nephropathy. *Renal Am J Pathol.* 2011 Sep;179(3):1179-87.

Subramanian V, Uchida HA, Ijaz T, Moorleghen JJ, Howatt DA, Balakrishnan A. Calpain Inhibition Attenuates Angiotensin II-induced Abdominal Aortic Aneurysms and Atherosclerosis in LDL Receptor Deficient Mice. *J Cardiovasc Pharmacol.* 2011 Jul;217(1):90-6.

Wang JA, Chen WA, Wang Y, Zhang S, Bi H, Hong B, Luo Y, **Daugherty A**, Xie X. Statins exert differential effects on angiotensin II-induced atherosclerosis, but no benefit for abdominal aortic aneurysms. *Atherosclerosis*. 2011 Jul;217(1):90-6.

Rateri DL, Moorleghen JJ, Balakrishnan A, Owens AP III, Howatt DA, Subramanian V, Poduri A, Charnigo R, Cassis LA, Daugherty A. Endothelial cell-specific deficiency of Ang II type 1a receptors attenuates Ang II-induced ascending aortic aneurysms in LDL receptor-/- mice. *Circ Res.* 2011 Mar 4;108(5):574-81.

Thatcher SE, Zhang X, Howatt DA, Lu H, Gurley SB, **Daugherty A**, Cassis LA.Angiotensin-converting enzyme 2 deficiency in whole body or bone

marrow-derived cells increases atherosclerosis in low-density lipoprotein receptor-/- mice. *Arterioscler Thromb Vasc Biol.* 2011 Apr;31(4):758-65.

Gizard F, Heywood EB, Findeisen HM, Zhao Y, Jones KL, Cudejko C, Post GR, Staels B, **Bruemmer D**. Telomerase activation in atherosclerosis and induction of telomerase reverse transcriptase expression by inflammatory stimuli in macrophages. *Arterioscler Thromb Vasc Biol.* 2011 Feb;31(2).

Findeisen HM, Gizard F, Zhao Y, Cohn D, Heywood EB, Jones KL, Lovett DH, Howatt DA, Daugherty A, Bruemmer D. Telomerase deficiency in bone marrow-derived cells attenuates angiotensin II-induced abdominal aortic aneurysm formation. *Arterioscler Thromb Vasc Biol.* 2011 Feb;31(2):253-60.

Zack M, **Boyanovsky BB**, **Shridas P**, Bailey W, Forrest K, Howatt DA, Gelb MH, de Beer FC, **Daugherty A**, **Webb NR**. Group X secretory phospholipase A(2) augments angiotensin II-induced inflammatory responses and abdominal aortic aneurysm formation in apoE-deficient mice. *Atherosclerosis*. 2011 Jan;214(1):58-64.

Subramanian V, Golledge J, Ijaz T, Bruemmer D, Daugherty A. Pioglitazone-induced reductions in atherosclerosis occur via smooth muscle cell-specific interaction with PPAR{gamma}. *Circ Res.* 2010 Oct 15;107(8):953-8. **Daugherty A**. Dietary Coenzyme Q10 Does Not Protect Against Cigarette Smoke-Augmented Atherosclerosis in apoE-deficient Mice. *Radic Biol Med.* 2010 June 1.

Owens AP III, Subramanian V, Moorleghen JJ, Guo Z, McNamara CA, Cassis LA, **Daugherty A**. Angiotensin II induces a region-specific hyperplasia of the ascending aorta through regulation of inhibitor of differentiation 3. *Circ Res.* 2010 Feb 19; 109(3):611-9.

King VL, Hatch NW, Chan HW, De Beer MC, de Beer FC, Tannock LR. A murine model of obesity with accelerated atherosclerosis. *Obesity* (Silver Spring). 2010 Jan.; 18(1):35-41.

Inflammation and obesity

Federico L, Ren H, Mueller PA, Wu T, Liu S, Popovic J, Blalock EM, Sunkara M, Ovaa H, Albers HM, Mills GB, Morris AJ, Smyth SS. Autotaxin and its product lysophosphatidic acid suppress brown adipose differentiation and promote diet-induced obesity in mice. *Mol Endocrinol.* 2012 May;26(5):786-97.

Cai L, Wang Z, Ji A, Meyer JM, **van der Westhuyzen DR.** Scavenger Receptor CD36 expression contributes to adipose tissue inflammation and cell death in diet-induced obesity. *PLoS One.* 2012;7(5):e36785.

Mohammed N, Tang L, Jahangiri A, de Villiers W, **Eckhardt E**. Elevated IgG levels against specific bacterial antigens in obese patients with diabetes and in mice with diet-induced obesity and glucose intolerance. *Metabolism*. 2012 Mar 17.

Findeisen HM, Gizard F, Zhao Y, Qing H, Jones KL, Cohn D, Heywood EB, Bruemmer D. Glutathione depletion prevents diet-induced obesity and enhances insulin sensitivity. *Obesity* (Silver Spring). 2011 Dec;19(12): 2429-32.

Dailey AM, Gibert JA, **Tannock LR**. Durability of glycemic control using U-500 insulin. *Diabetes Res Clin Pract*. 2011 Nov 14.

Findeisen HM, Pearson KJ, Gizard F, Zhao Y, Qing H, Jones KL, Cohn D, Heywood EB, de Cabo R, **Bruemmer D**. Oxidative stress accumulates in adipose tissue during aging and inhibits adipogenesis. *PLoS One.* 2011 Apr 14;6(4):e18532.

Wang Y, Li J, Tang L, Wang Y, **Charnigo R**, de Villiers W, **Eckhardt E**. T-Lymphocyte responses to intestinally absorbed antigens can contribute to adipose tissue inflammation and glucose intolerance during high fat feeding. *PLoS One*. 2010 Nov 11;5 (11):e13951.

Thrombosis and inflammation

Yang F, Dong A, Abdel-Latif, A, Klyachkin YM, Mueller P, Caicedo J, Moore A, Odetunde ZJ, Barrick C, Smyth SS. Coronary artery remodeling in a model of left ventricular pressure overload is influenced by platelets and inflammatory cells. *PLoS One* (in press).

Zhang G, Xiang B, Ye S, Chrzanowska-Wodnicka M, Morris AJ, Gartner TK, Whiteheart SW, White GC II, Smyth SS, Li Z. Distinct roles for Rap1b protein in platelet secretion and integrin IIb 3 outside-in signaling. *J Biol Chem.* 2011 Nov 11;286(45):39466-77.

Zhang G, Xiang B, Dong A, Skoda RC, Daugherty A, Smyth SS, Du X, Li Z. Biphasic roles for soluble guanylyl cyclase (sGC) in platelet activation. *Blood.* 2011 Sep 29;118(13):3670-9.

Li Z and Smyth SS. Connexin 37 counteracts clotting. *Circulation*. 2011 Aug 23;124(8):873-5.

Song Z, Jin R, Yu S, Rivet JJ, **Smyth SS**, Nanda A, Granger DN, Li G. CD40 Is Essential in the Upregulation of TRAF Proteins and NF-KappaB-Dependent Proinflammatory. *PLoS One*. 2011;6(8):e23239. Epub 2011 Aug 18.

Fulkerson Z, Wu T, Sunakura M, Vander KC, **Morris AJ, Smyth SS**. Binding of autotaxin to integrins localizes lysophosphatidic acid production to platelets and mammalian cells. *J Biol Chem.* 2011 Aug 10.

Li Z, Yang F, Dunn S, Gross AK, Smyth SS. Platelets as immune mediators: their role in host defense responses and sepsis. *Thromb Res.* 2011 Mar;127(3):184-8.

Xiang B, Zhang G, Liu J, Morris AJ, Smyth SS, Gartner TK, Li Z. A G(i)-independent mechanism mediating Akt phosphorylation in platelets. *J Thromb Haemost*. 2010 Sep;8(9):2032-41.

Dong A, Caicedo J, Han SG, Mueller P, Saha S, Smyth SS, Gairola CG. Enhanced platelet reactivity and thrombosis in Apoe-/- mice exposed to cigarette smoke is attenuated by P2Y12 antagonism. *Thromb Res.* 2010 May 6.

Cardiovascular Education



The Cardiovascular Diseases Fellowship Program at the University of Kentucky is an accredited threeyear program. Fellows receive superb clinical training in an active academic medical center, the affiliated Veterans Administration Hospital, and a community experience at the UK Good Samaritan Hospital. The program is geared towards assuring an exceptional educational experience that prepares fellows to provide quality medical care in whatever arena they ultimately pursue. The fellowship provides:

- Dedicated didactic lecture series covering the core curriculum of cardiovascular diseases.
- Specialized lecture series that complement the core curriculum in electrophysiology, EKG interpretation, cardiac imaging, cardiac catheterization, research skills and statistics, and prevention.

- Exposure to state-of-the-art patient care.
- Professionalism in all aspects of patient care, education and research.
- Development of outstanding communication skills with patients, their families, and other healthcare professionals.
- Team-based approach within a multifaceted health care system to optimize patient care.
- And, most importantly, how to continue the self-learning process well beyond the completion of their fellowship training.

Annually, there are six general cardiovascular fellowship positions, two interventional fellowship positions, and an imaging fellowship position. In 2013 a clinical cardiac electrophysiology fellowship position will be offered. Our faculty has extensive and demonstrable experience in mentoring students, residents and fellows. In addition to formal training; the University of Kentucky offers weekly Cardiovascular Grand Rounds seminars that feature leaders in the field, as well as lively and interactive Cardiovascular Journal Clubs.

The university is fortunate to have secured highly competitive extramural support for trainees in the cardiovascular area:

- The University of Kentucky Interdisciplinary Cardiovascular Training Program (T32; Program Director, David Randall, PhD; Co-Director, Alan Daugherty, PhD), supports students interested in pursuing a long-term research and teaching career in the cardiovascular sciences.
- The Research Training in Muscle Biology of Cardiopulmonary Disease Program (T32: Program Director, Michael Reid, PhD), trains predoctoral and medical students for muscle research in the context of cardiopulmonary disease.
- The University of Kentucky Training Program for Clinical Scholars in Cardiovascular Science (T32 Program Director, Susan Smyth, MD, PhD; Co Director, Alison Bailey, MD), is designed to prepare exceptional clinical and postdoctoral fellows to assume leadership positions directing multidisciplinary research in the field of cardiovascular medicine.
- A Society for Cardiovascular Angiography and Interventions Interventional Cardiology Fellows-In-Training Grant Program (SCAI-FIT) grant. UK was one of only 36 institutions to receive funding for the 2012 - 2013 year through this ground-breaking opportunity (Khaled Ziada, MD, Director of the Cardiac Catheterization Laboratories).

Selected recent publications by fellows:

Foley JD III, Sneed JD, Steinhubl SR, Kolasa J, Ebersole JL, Lin Y, Kryscio RJ, McDevitt J, **Campbell CL**, Miller CS. Oral fluids that detect cardiovascular disease biomarkers. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012 Aug;114(2):207-14.

Wallace EL, Abdel-Latif A, Charnigo R, Moliterno DJ, Brodie B, Matnani R, Ziada KM. Meta-analysis of long-term outcomes for drugeluting stents versus bare-metal stents in primary percutaneous coronary interventions for ST-segment elevation myocardial infarction. *Am J Cardiol.* 2012 Apr 1;109(7):932-40. Plaisance BR, Winkler MA, Attili AK, Sorrell VL. Congenital bicuspid aortic valve first presenting as an aortic aneurysm. *Am J Med.* 2012 Apr;125(4):e5-7.

Kuo BT, Whitbeck MG, Gurley JC, Smith MD. Double atrial septal defect: diagnosis and closure guidance with 3D transesophageal echocardiography. *Echocardiography*. 2011 Jul;28(6):E115-7.

Selim S, Sunkara M, Salous AK, Leung SW, Berdyshev EV, Bailey A, Campbell CL, Charnigo R, Morris AJ, Smyth SS. Plasma levels of sphingosine 1-phosphate are strongly correlated with haematocrit, but variably restored by red blood cell transfusions. *Clin Sci* (Lond). 2011 Dec;121(12):565-72.

Salters CR Jr, Bailey AL, Whayne TF Jr. Current treatment of heart failure in the USA. *Expert Rev Cardiovasc Ther.* 2010 Feb;8(2):279-90.

Pending publications by fellows:

Kim SM, **Aikat S**, **Bailey A**, **White M**. Takotsubo cardiomyopathy as a source of cardioembolic cerebral infarction.

Foley JD III, Sneed JD, Steinhubl SR, Kolasa J, Ebersole JL, Lin Y, Kryscio RJ, McDevitt J, **Campbell CL**, Miller CS. Salivary biomarkers associated with myocardial necrosis: results from an alcohol septal ablation model.

Foley JD III, Sneed JD, Steinhubl SR, Ebersole JL, Kryscio RJ, McDevitt J, **Campbell CL**. Serum biomarker release patterns following alcohol septal ablation for treatment of hypertrophic cardiomyopathy.

Recent abstract presentations by residents and fellows:

Bradley B, **Ruiz-Rodriguez E**, **White M**, **Wiisanjen M**. Percutaneous closure of a post-myocardial infaction ventricular septal defect: a case report. Oral presentation at Kentucky ACC annual meeting, August 2012.

Kalra N. Atrial size and function post orthotopic heart transplantation – a CMR and ECHO study. Oral presentation at Kentucky ACC annual meeting, August 2012.

Kim, SM. Takotsubo cardiomyopathy as a source of cardioembolic cerebral infarction. Oral presentation at Kentucky ACC annual meeting, August 2012.

Seratnahaei A. Infective Endocarditis: A Plague for the 21st Century? Oral presentation at Kentucky ACC annual meeting August 2012.

Wallace EL. Kotter JR, Charnigo R, Kuvlieva LB, Smyth SS, Ziada KM, Campbell CL. Fibrinolytic therapy versus PPCI for ST-segment elevation myocardial infarction in Kentucky; a single center experience. Oral presentation at Kentucky ACC annual meeting, August 2012.

Wiisanen ME. Ultrasound-accelerated thrombolysis for the treatment of acute pulmonary embolism. Oral presentation at Kentucky ACC annual meeting/AHA Scientific Session, October 2012.

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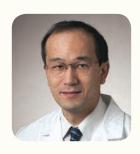
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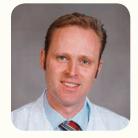
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