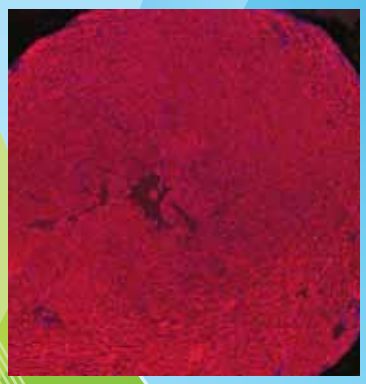
Carolinas Medical Center

Research Highlights 2011



Carolinas Medical Center

Published by Cannon Research Center, Carolinas Medical Center, Carolinas HealthCare System
Spring 2012

1542 Garden Terrace
Charlotte, NC 28203
704-355-3959

Carolinas Medical Center

Research Highlights 2011

Table of Contents

Letter from the Editor

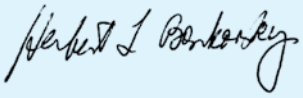
2011 has been another banner year for biomedical and translational research at Carolinas HealthCare System (CHS), and we are pleased to provide our faculty, staff and friends with this annual update.

In this issue, we highlight especially the recent initiatives and accomplishments of Blumenthal Cancer Center and our new Levine Cancer Institute, directed by Derek Raghavan, MD, PhD; our Department of General Surgery, chaired by Frederick Greene, MD; and our McColl-Lockwood Laboratory for Muscular Dystrophy Research, directed by Qi Lu, MD, PhD.

These accomplishments would not have been as numerous or robust as they are had it not been for the farsighted and generous support of donors who have made gifts large and small to support these and other research programs. We especially acknowledge with thanks major support from the Leon and Sandra Levine Foundation, which serves as the foundation for Levine Cancer Institute of CHS; from Hugh and Jane McColl, for major endowment of McColl-Lockwood Laboratory for Muscular Dystrophy Research; and for philanthropic support of general surgery research from John and Reba Shipp Minimally Invasive Surgery Endowment.

Most funding for biomedical research in the United States comes from federal governmental sources, such as the National Institutes of Health, the National Science Foundation and the Department of Defense. However, because of the recent recession and its aftermath, leading to restrictions on federal budgets, such support for research is decreasing in constant dollars. Therefore, philanthropic donations and research support from private companies have never been more important. We hope that some, upon reading this annual report, may be moved to make contributions to Carolinas HealthCare Foundation to support the ongoing patient-centered research of Carolinas HealthCare System.

Yours truly,



Herbert L. Bonkovsky, MD
Senior Advisor for Research
Director, Liver-Biliary-Pancreatic Center

Comments From Senior Leadership

Carolinas HealthCare System is proud to be playing an integral and active role in redefining the future of healthcare in the United States. Through our innovative approach to delivering the highest quality healthcare and continuing to live out our mission of serving all patients, regardless of their ability to pay, CHS works to improve the health of every community we serve. Critical to that mission, we are working tirelessly to create leading-edge, patient-focused research that will change the lives of our patients. We are proud of the accomplishments of the hundreds of investigators and research staff within the CHS family.

Michael Tarwater

Chief Executive Officer, Carolinas HealthCare System

Carolinas HealthCare System believes it can create transformational change for all of our patients by developing and deploying impactful and meaningful research efforts. By finding synergies through an integrated approach to sharing best practices and expanding on the resources available throughout our health system, we can bring groundbreaking clinical trials to our patients and change the course of healthcare. Highlighted in this report are the early and aggressive initiatives of Dr. Derek Raghavan, President of Levine Cancer Institute, and his team, which promise to serve as a model for research in the years to come.

Joe Piemont

President and Chief Operating Officer, Carolinas HealthCare System

Research is core to our mission at Carolinas HealthCare System. Despite the difficult funding climate for biomedical research in the U.S., the dedication of our team allowed us, in 2011, to achieve new records for numbers of federally funded programs and amounts of external support. Recently, CHS received its first-ever program project (P50) award from the NIH, to support multi-disciplinary bench and bedside research on muscular dystrophy. We are committed to supporting and growing this type of unique and valuable research.

James T. McDeavitt, MD

Chief Academic Officer, Carolinas HealthCare System

We are proud of the hundreds of dedicated and diligent investigators who call the University of North Carolina home. This includes our partners based at the Charlotte campus of the UNC School of Medicine, located at Carolinas Medical Center. We share the common goal of improving lives and communities across the Carolinas; and we look forward to continued and increased collaboration between our campuses.

William L. Roper, MD, MPH

Dean of the School of Medicine, Vice Chancellor for Medical Affairs and Chief Executive Officer of the UNC Health Care System at the University of North Carolina at Chapel Hill

Feature Articles

Blumenthal Cancer Center/Levine Cancer Institute

Steven A. Limentani, MD
Associate Medical Director

Richard L. White, Jr., MD, FACS
Surgical Oncology

Asim Amin, MD, PhD
Medical Oncology

The story of one of our patients, Sierra Smith (not actual name), underscores the clear advantages of receiving care in a facility that is able to enroll its patients into innovative clinical trials. Sierra, a high school algebra teacher, was in the prime of her life at the age of 35 when a routine annual exam just before Christmas in 2008 revealed a mass in her right breast. The mass was biopsied and revealed "triple negative" breast cancer. For a woman with no known risk factors for breast cancer, an educated non-smoker who eats well and does not drink alcohol, hearing the words, "you have breast cancer" came as a complete shock.

Following diagnosis, Sierra was referred for genetic testing, which revealed a mutation of the BRCA1 gene known to increase the risk of cancer of the breast, ovaries and uterus. She underwent neoadjuvant chemotherapy in January 2009 in a national clinical trial designed to compare the efficacy of current treatments. The therapy produced a significant reduction of the size of the mass. In July 2009, Sierra underwent a bilateral mastectomy, followed by radiation to the chest wall.

Sadly, the following spring, she was found to have lung metastases. In July, she entered a second clinical trial that involves the investigational drug iniparib in combination with gemcitabine and carboplatin. For the past year, she has steadfastly followed the protocol's regimen and has responded well. She is able to live a full, active life, and she is able to participate in all the activities she enjoys. She feels great and continues to teach full time. Sierra recently participated in a walk for breast cancer survivors and is currently planning next year's walk with her team.

An active, independent woman, Sierra has declined reconstructive breast surgery, but the option remains open to her. A single woman with no children, she is an outspoken breast cancer awareness advocate, and remains close to her family. She faced another significant emotional hurdle when her mother died recently. However, Sierra is determined to live each day to the fullest and celebrate survivorship. Everyone in the clinic looks forward to seeing Sierra sporting the latest in her wardrobe of humorous T-shirts including the chemo-friendly, "No Hair Day" logo.

The clinical trials team at Levine Cancer Institute consists of more than 70 dedicated clinical trials professionals across the metro-Charlotte area, home of Blumenthal Cancer Center. More than half of our team of research nurses, data coordinators, regulatory coordinators and support personnel are professionally certified. In partnering with physician-investigators across CHS, the Institute offers cutting-edge research options to cancer patients in the region. We are delighted that Derek Raghavan, MD, PhD, has come to CHS as founding president of the Institute.

Over the past year, we have built relationships with pharmaceutical companies and contract research organizations (CROs) to refine our research portfolio and focus on scientifically important clinical trials. In 2011, we launched clinical trials at Edwards Cancer Center at

Derek Raghavan, MD, PhD, FACP, FRACP
Levine Cancer Institute

Dr. Raghavan is an internationally-renowned cancer researcher and medical oncologist and President of Levine Cancer Institute. Dr. Raghavan's vision for the Institute is to bring cancer research and clinical innovations closer to home for patients across the 33-hospital Carolinas HealthCare System by redefining the role of a traditional cancer center. Since he began in April 2011, Dr. Raghavan has led efforts to eliminate barriers to top-quality care, such as distance to clinical and research sites and cultural barriers of patients and families.

Dr. Raghavan's personal, clinical and research interests are focused on genitourinary cancer, cancer in the elderly, anticancer drug discovery and development, and comparative human oncology. He currently serves on the external advisory boards of four cancer centers and on the editorial boards of numerous medical journals; has been a principal investigator for more than a dozen major research grants; has published more than 300 papers in peer-reviewed professional journals; and edited nine textbooks.

Prior to coming to Levine Cancer Institute, Dr. Raghavan served concurrent appointments as chairman and director of the Taussig Cancer Center and as the M. Frank and Margaret Domiter Rudy Institute Distinguished Chair in Translational Cancer Research at Cleveland Clinic. He also previously led cancer programs and research efforts in New York, California and Australia. Trained in medicine and oncology at the University of Sydney, Australia, Dr. Raghavan received a PhD in experimental pathology from the University of London/Ludwig Institute for Cancer Research and completed post-doctoral studies at the University of Minnesota.

Carolinas Medical Center-Union in Monroe, NC, where cancer research was not previously offered, and integrated clinical trial operations of Batte Cancer Center at Carolinas Medical Center-NorthEast in Concord, NC, into the Levine Cancer Institute clinical trials program.

A team of Levine Cancer Institute physicians and laboratory, pharmacy, information technology and architecture experts visited the nation's leading Phase I cancer centers to assess facility and process requirements for the design and operation of the Institute's new Phase I/Developmental Therapeutics Clinic currently under construction on the campus of Carolinas Medical Center in Charlotte. This clinic will serve as a nidus to obtain novel and cutting-edge pharmaceuticals for our patients close to home. During this time of expansion, the Institute clinical trials team remains focused on the quality of care for our patients, as well as the stringent regulatory requirements of our trial sponsors.

Physician-investigators at Blumenthal Cancer Center have been recognized nationally for outstanding clinical trial contributions. The gynecologic oncology team was named a provisional member of the National Cancer Institute's (NCI's) Gynecologic Oncology Group. Steven A. Limentani, MD, Associate Medical Director, was named to NCI's NSABP board. Richard White, MD, was also named to the ACOSOG/ALLIANCE board. Asim Amin, MD, PhD, enrolled 89 patients in an Expanded Access Program (EAP) trial of ipilimumab for late stage melanoma and enrolled the first patient in the United States, second worldwide, to a trial of masitinib for those with late stage melanoma.

During this exciting time of Levine Cancer Institute development, the clinical trials team continues to exemplify CHS hallmarks of caring, commitment, teamwork and integrity by giving each trial patient the highest level of personalized care. While Sierra may have lost her breasts and her hair, Sierra has the indefatigable spirit of a valorous fighter – and Blumenthal Cancer Center has her back, every single step of the way. Like so many others in the region, Sierra has seen firsthand how Levine Cancer Institute is changing the course of cancer care in the Carolinas.

For more information, visit www.levinecancerinstitute.org.

Department of General Surgery

The clinical, research and education programs of the Department of General Surgery are many and varied, including clinical and translational research in improved surgical techniques and materials, new methods for the therapy of tumors of abdominal organs, and pre-clinical studies of new candidate drugs and drug delivery systems for therapy of hepatocellular carcinoma. Due to the breadth and scope of these efforts, three related research programs have been featured in this report: Carolinas Laparoscopic and Advanced Surgery Program (CLASP) headed by B. Todd Heniford, MD; pre-clinical (bench) research programs of the department, headed by Iain H. McKillop, PhD; and clinical research programs of the section of hepato-pancreatico-biliary surgery, headed by David Iannitti, MD.

B. Todd Heniford, MD
Chief, Division of Gastrointestinal & Minimally Invasive Surgery; Co-Director, Carolinas Laparoscopic & Advanced Surgery Program; Co-Director, Carolinas Hernia Center

Developing a Statistical Algorithm to Predict Quality of Life after Inguinal Hernia Repair

Hernia repairs represent the most common general surgical operation performed in the world, with more than 800,000 inguinal hernia repairs performed annually in the United States alone. While most patients experience an uneventful recovery, some develop or continue to suffer from post-operative pain or physical limitations. The burden of chronic discomfort can be severe enough to cause permanent disability, requiring years of interventions and possible reoperation. In fact, the major reason hernia patients seek surgical repair and evaluate the efficacy of operations is to improve their health-related quality of life (QOL). In recent years, the focus of research on hernia repair shifted from minimizing recurrence of the hernia to reducing post-operative pain and expediting recovery. For these reasons, QOL has become the principal outcome measure of hernia surgery.

Chronic post-operative pain is the most common complaint reported by patients following inguinal hernia repair, with reported incidences as high as 40 percent in open, as opposed to laparoscopic repairs. Identifying and preventing such cases would dramatically reduce patient suffering, healthcare expenses and losses in productivity. Dr. Heniford and the CLASP research team have identified pre-operative and operative factors associated with chronic post-operative pain and are using this information to create an educational tool for both surgeons and patients. The proposed tool seeks to provide patients with realistic expectations regarding post-operative QOL based on individual circumstances. It helps surgeons to identify patients with an

Carolinas Laparoscopic & Advanced Surgery Program Team (CLASP): CLASP is a nationally recognized minimally invasive surgery program. The team has pioneered new surgical techniques along with groundbreaking studies and education methods.

increased risk for chronic post-operative pain in whom alternative surgical or non-surgical strategies should be considered.

Prior to the advent of disease-specific instruments, a series of 36 widely studied questions called Short Form-36 (SF-36) was the "gold standard" for measuring QOL in patients with diverse diseases and disorders, including inguinal hernia repairs. However, the general SF-36 is not an adequate measure of QOL for those with diverse chronic conditions. Thus, in 2004, Dr. Heniford and his colleagues developed Carolinas Comfort Scale™ (CCS) to address this problem as it relates specifically to chronic pain and other symptoms following hernia repair. CCS has been studied extensively and validated as a useful measure of QOL and, in a few short years, has become the international standard for evaluating QOL in patients undergoing hernia repair. Several hundred institutions utilize CCS, which has been translated into 31 languages. It is currently being used in 19 states and 42 countries throughout the world. CCS is used not only by individual surgeons and institutions, but also by large multi-center research trials and data registries, including the International Hernia Mesh Registry (IHMR). CCS is utilized in the French and British healthcare systems as a major outcome measure to evaluate hernia operations.

IHMR, the scientific committee chaired by Dr. Heniford, is a prospectively collected, multi-center, multi-national database with 40 participating sites in the United States, Europe and Canada. IHMR contains information related to patient demographics and co-morbidities, detailed description of surgical procedures, and pre- and post-surgery QOL as measured by the CCS. The registry utilizes self-reported data on QOL, recurrence and complications, enabling patients to access and complete the survey online or through the mail. These survey methods allow patients to submit forms through physician offices, which minimize outcome bias. Currently, more than 3,800 patients worldwide have enrolled, with more than 80 percent having met the one-year milestone and over 50 percent having met the two-year milestone for follow-up. The CHS contribution to this registry is substantial, and CLASP investigators have presented results at many international meetings and published results in several peer-reviewed journals.

B. Todd Heniford, MD, discusses treatment options with a team member.

Utilizing data from IHMR, Dr. Heniford, along with Amanda Walters; Amy Lincourt, PhD; Kristian Dacey; Igor Belyansky; and Victor Tsirline, has produced a statistical algorithm for predicting the incidence of chronic pain following inguinal hernia repair. Recently, the research team began to perform both cross- and independent-validation, and the results demonstrate that the incidence of post-operative chronic pain is

highly predictable and easily programmable. Thus, the algorithm can be transformed into an application, or "app", that surgeons and patients can use with iPads and smartphones. The ultimate goal is to use mobile app technology to provide surgeons and patients with a powerful prognostic tool that predicts individualized post-operative QOL outcomes and offers patients extensive educational materials concerning all types of hernias and their treatments.

Together, these applications represent data-driven, patient-centered research activities that will not only directly impact patient care, but also their QOL. These research endeavors embody the system's vision and mission.

Developing Nanoscaffold Drug Delivery Systems to Treat Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC) is diagnosed at an alarming rate in the United States, where it represents the most rapidly increasing type of cancer. On a global scale HCC is equally devastating, with more than 1 million new cases expected in 2012. The outlook for those with HCC remains bleak; our ability to cure, slow or effectively treat HCC remains poor relative to the advances made in diagnosing and treating other cancers. At present, the most effective HCC therapies are based on surgical intervention; resection, ablation or transplantation. However, surgical approaches are limited by late detection and advanced disease state, underlying pathology, tumor location, the presence of metastases and/or shortage of transplantable organs.

Similarly, advances in chemotherapy for HCC have been limited. A significant obstacle in developing pharmacological treatment options for HCC is getting sufficiently high intratumoral drug delivery in the absence of hepatic or systemic toxicity. Side effects associated with chemotherapeutic approaches to treat HCC are exacerbated by the role the liver plays in detoxification-drug metabolism, and because HCC usually arises in the setting of advanced chronic liver disease. Many cytotoxic drugs used to treat other common cancers may be equally effective in treating HCC, but only if sufficiently high doses can be achieved and retained within the tumor.

Drug delivery systems attempt to redress non-specific side effects and toxicity by delivering the drug of choice at the site of action. For HCC therapy, this has led to the development of TransArterial ChemoEmbolization (TACE) and, more recently, drug liposphere systems. While both approaches have proven to be more efficacious than conventional chemotherapy, they can also suffer from drug diffusion and, in the case of lipospheres, problems caused by migration to the lungs and toxicity associated with liposome degradation.

David A. Iannitti, MD
Chief, HepatoPancreaticoBiliary Surgery

Iain McKillop, PhD
Group Director of Research,
Department of General Surgery;
Associate Professor, University of North Carolina-Charlotte

Ahmed El-Ghannam, PhD
Associate Professor,
University of North Carolina-Charlotte

An on-going research collaboration among Drs. Iannitti and McKillop, and Ahmed El-Ghannam, PhD, Department of Mechanical Engineering, University of North Carolina-Charlotte (UNC-C), is attempting to overcome these limitations with the development of silica-calcium-phosphate-nanocomposite (SCPC) or "bio-ceramic nanoscaffolds." When formulated, SCPCs exist as solid, crystalline structures within which lie inter-connected microtubes. Each microtube is lined with nanopockets from which project drug binding chemical side chains (Figure 1). This sponge-like structure creates an enormous surface area for drug binding, and by varying the chemical properties of the side chains, it is possible for a wide range of drug types to be bound, and gradually released. The kinetics of the release process can also be regulated by changing the properties of the side chains.

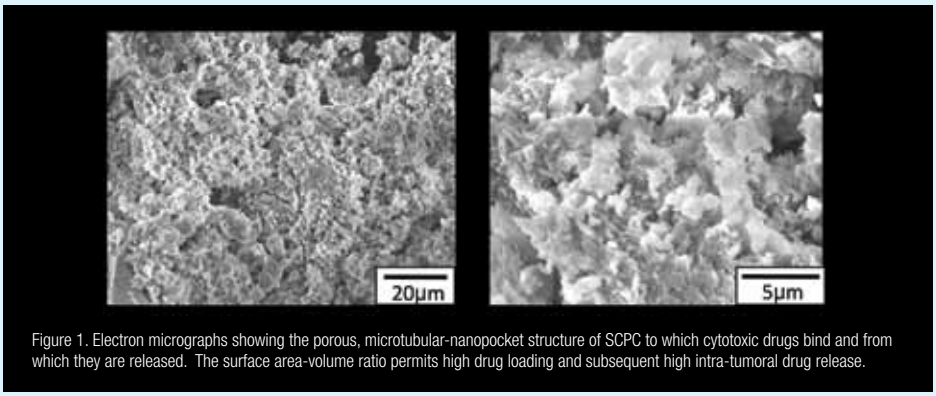


Figure 1. Electron micrographs showing the porous, microtubular-nanopocket structure of SCPC to which cytotoxic drugs bind and from which they are released. The surface area-volume ratio permits high drug loading and subsequent high intra-tumoral drug release.

Using this approach, the multidisciplinary group of researchers has demonstrated in vitro efficacy of cisplatin-SCPC hybrids against HCC cells in culture. Cisplatin was selected to test the drug delivery system. Those familiar with HCC treatment will recognize that cisplatin is not the drug of choice for clinical HCC management, due largely to systemic-renal toxicity. However, cisplatin efficiently induces death (apoptosis) in a wide range of cell types, including those of HCC, via irreversible DNA cross-linking. For these studies, the near complete absence of platinum in the body, coupled with well-established mechanisms of action, make cisplatin an ideal "reporter drug" to test for system efficacy and drug distribution studies.

Recently, the team has begun to test the efficacy of SCPC-cisplatin hybrids at treating tumor progression in vivo. Preliminary data using a subcutaneous rat model of HCC implantation demonstrated striking inhibition of tumor growth in animals in which SCPC-cisplatin hybrids were implanted adjacent to established-growing flank tumors (Figures 2A and B). Using this approach, SCPC-cisplatin hybrids revealed no detectable toxicity. In contrast, pair-matched animals treated with lower dose cisplatin administered by direct intra-peritoneal injection demonstrated no significant slowing of tumor growth, yet had marked systemic and renal toxicity. Furthermore, because the efficacy and kinetics of cisplatin release from SCPC is dependent on the three-dimensional microtube-nanopocket structure, complete drug release can be achieved without any discernable SCPC degradation.

Figure 2A

Figure 2B

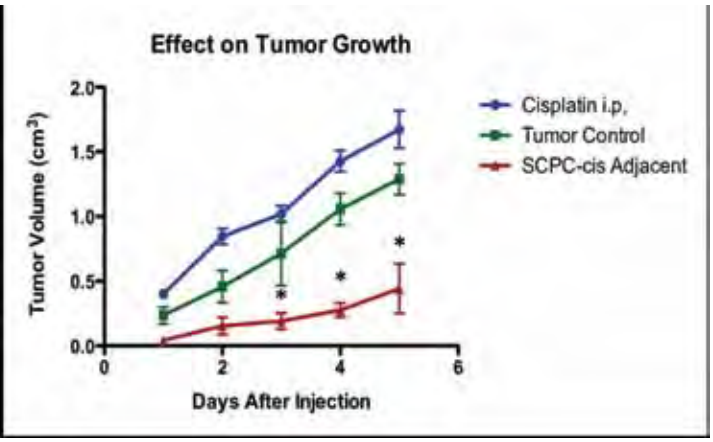
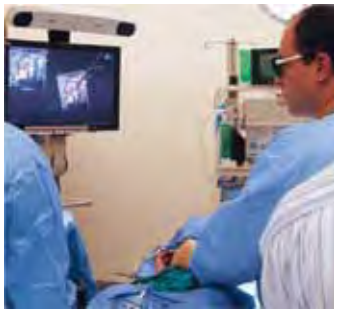


Figure 2A. X-ray demonstrating successful placement of a cisplatin-loaded SCPC bioceramic adjacent to a tumor mass created in the subcutaneous space in a rat model. **Figure 2B.** Using SCPC-cisplatin drug delivery significantly decreases rate of tumor progression as compared to control (untreated) and systemically treated (i.p.) approaches.



David Iannitti, MD, collaborates with colleague, John Martinie, MD, and InnerOptic on 3-D imaging to more accurately place microwave ablation probes within liver tissue to thermally destroy tumor targets.

Data suggest that SCPCs may represent a new drug delivery system for HCC that exhibits many potential advantages over existing approaches: drug release is localized (intratumoral), highly predictable and "programmable" based on specific SCPC formulation, and the SCPC is capable of binding and releasing a wide range of drugs, or multiple drugs from the same formulation. In moving forward with this project, the team recognizes that a major obstacle to the current approach is that HCC often present deep within the liver and, to prove successful, a means for accurate intratumoral drug delivery will be necessary.

The team has begun discussing research with InnerOptic, a start-up biotechnology company based in Hillsborough, NC. Previous studies by Dr. Iannitti, his colleague, John B. Martinie, MD, (HepatoPancreatoBiliary Surgery, CMC) and InnerOptic have worked toward using three-dimensional imaging to more accurately place microwave ablation (MWA) probes within liver tissue to thermally destroy tumor targets. This approach has proven to be highly successful in pre-clinical trials, and was recently performed as part of a landmark clinical trial at CMC. The team aims to use similar technology, together with the ability to form SCPC-drug hybrids, to accurately place novel drug delivery systems directly into hepatic tumor masses in a series of upcoming pre-clinical studies using in vitro and in vivo models.

Collectively, these approaches exemplify the synergy among diverse academic disciplines with which to address pertinent clinical problems. Translational research activities represent the cornerstone of the Department of General Surgery's research endeavors where the goal is to improve patient care and outcomes with the application of state-of-the-art bench research.

In closely related clinical research studies, Drs. Iannitti, Martinie and David Sindram, and their fellows have emerged as world leaders in the development and use of microwave energy for the therapy of HCC and other tumors of the liver, bile duct and pancreas. They partner with biotech companies to develop smaller, more powerful probes to deliver microwaves that kill cancerous cells and to develop more sophisticated means of precisely targeting microwaves only to tumors.

McColl-Lockwood Laboratory for Muscular Dystrophy Research

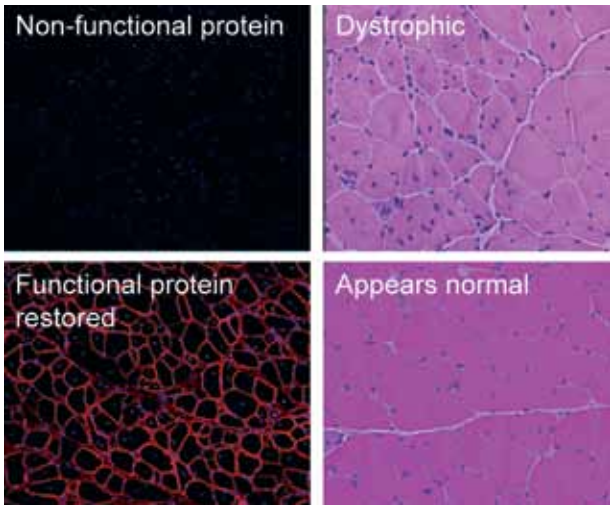
Alan Jones (not actual name) is a charming 8-year-old boy with a toothy grin because of four missing front teeth. He has a jokester personality that makes you smile when you see him. His goal is to make you laugh out loud. Alan's mobility is impaired. He waddles when he walks, which is only short distances without his bright new red wheelchair, which he shows off as soon as he comes into clinic. He was diagnosed with Duchenne muscular dystrophy (DMD) at the age of 4½, two years after his mom noticed that while he could walk, he had difficulty running and climbing and could not keep up with the other children on the playground. Mrs. Jones has become an expert on DMD and dystrophin, the gene that causes both DMD and the milder Becker muscular dystrophy (BMD), even though no one else in the family is affected. She understands that her son's dystrophin gene has a deletion within it and knows about the newer therapy called "exon-skipping," which could convert her son's out-of-frame deletion into an in-frame deletion resulting in production of functional, although abnormal, dystrophin. She hopes and prays that the exon-skipping technology, which currently is in the clinical trial phase for mutations, which are not her son's, will one day reverse his muscle disease and allow him to walk and run with his peers. She also realizes that may not happen for Alan, but believes it will for other boys affected with DMD. Alan is always first to volunteer for research studies at CMC. He has participated in comparing different muscle strength outcome measures, and was screened for a study evaluating medications to protect cardiac muscle decline, the major cause of mortality in patients with DMD. However, his heart was too "good" with no dysfunction, so he did not qualify for the research study. As much as that was a very good thing, Mrs. Jones and Alan were disappointed that he could not participate. These two studies and many others for patients with DMD, BMD and limb-girdle muscular dystrophy (LGMD) are on-going at CMC.

Qi Lu, MD, PhD
Research Group Director, Department of Neurology; Adjunct Professor, University of North Carolina-Charlotte

Muscular dystrophies are a relatively rare group of neuromuscular disorders impacting between 50,000 and 100,000 individuals in the United States. As a group, they are characterized by skeletal muscle weakness and wasting (dystrophy). The most common of these disorders, DMD, affects approximately one in 4,000 boys. In North and South Carolina and surrounding southeastern states, it is estimated that there are 28,000-30,000 individuals with muscular dystrophy. McColl-Lockwood Laboratory for Muscular Dystrophy Research, within the ALS/MD Center, Department of Neurology, was established with support from Carolinas HealthCare Foundation and private philanthropy. Its focus is on translational research for muscular dystrophy, specifically limb-girdle muscular dystrophy (LGMD 21) and DMD. These diseases are caused by mutations in FKRP and DMD genes, respectively, disrupting normal function in muscles. Currently, there is no cure or effective treatment for LGMD and DMD. The goal of McColl-Lockwood Laboratory is to develop novel treatments of these diseases.

Since opening in 2006 under the leadership of Qi Long Lu, MD, PhD, the McColl-Lockwood Laboratory has implemented groundbreaking research in several areas critical for the development of experimental therapeutics. The laboratory has established several animal models of muscular dystrophies and cell lines representing the diseased muscles from both patients and animal models. Various vectors expressing normal and mutated FKRP genes and specific antibody against the FKRP protein have been created. A drug screening protocol has been established for identifying candidate compounds to rescue glycosylation defects in some muscular dystrophies. For the first time, unique animal models with mutations in the FKRP gene have been created (Figure 1).

Figure 1. FKRP gene therapy restores expression of functional Alpha-dystroglycan(DG) and rescues muscle pathology in a mouse model of limb girdle muscular dystrophy.



Functional alpha-DG is absent in the untreated muscle (upper left), but is detected in nearly all muscle fibers (lower left, red color) in the FKRP-treated muscle. Dystrophic pathology of untreated muscle (top right) is rescued to normal histology (lower right). The panels on the left are stained with an antibody to alpha-dystroglycan containing a red chromophore, 200X; the panels on the right are stained with hematoxylin and eosin, 400X.

In collaboration with James Dollar, MD, of Carolinas Pathology Group, the laboratory has also established a program of immuno-histochemical analysis for molecular diagnosis of muscular dystrophies. A team of research scientists and technicians with specialized training and experience in drug design, pharmacology, and cell and molecular biology has been recruited. The laboratory has also organized and hosted in Charlotte a biennial international meeting in glycosylation and muscle diseases, and established widespread collaborations with internationally renowned laboratories in these research areas.

New drugs targeting critical factors involved in disease progression have already been developed; and results from initial tests indicate that these novel compounds improve disease phenotypes in models of muscular dystrophy. The drug screening program has completed its initial phase of pilot testing and entered into a large scale library screening phase involving the NIH-sponsored high throughput screening center and an in-house screening facility. The significance of such drug screening for muscular dystrophy has been boosted by support from both the Muscular Dystrophy Association (MDA) and NIH. Studies in collaboration with Xiao Xiao, PhD, in the Department of Pharmacology, UNC-Chapel Hill, have led to the creation of adeno-associated viral (AAV) vector systems for effective delivery of the normal copy of FKRP gene in both cell culture and animal models of FKRP mutations. Results of these studies demonstrated for the first time that AAV-mediated gene therapy could be an effective treatment for rescuing dystrophic phenotypes in all diseased muscles, including skeletal and cardiac muscles. Testing of existing drugs targeting muscle degeneration and inflammation has identified candidates with potential to improve muscle pathology and function. Further confirmation of the efficacy of these drugs is being conducted.

McColl-Lockwood Laboratory for Muscular Dystrophy Research Team: **First Row:** Bo Wu, PhD; Lei Xu, PhD; Kyle Madden; **Second Row:** Elizabeth Keramaris, Guqi Wang, PhD; Xiaohua Wu, PhD; **Third Row:** Pei Lu; Jason Tucker; Sujata Acharjee, PhD; Mingxing Wang, PhD; **Fourth Row:** Jeanne Maggio; Fei Guo, PhD; Qi Lu, MD, PhD

McColl-Lockwood Laboratory has consistently positioned itself at the forefront of drug development both nationally and internationally with the development of antisense oligonucleotide-mediated exon skipping technology for DMD. At the molecular level, DMD mutations disrupt the reading frame of the dystrophin mRNA, leading to a lack of dystrophin protein in DMD patients – a protein that is essential for normal muscle functioning. Exon skipping applies a short sequence of nucleic acid complementary to a specific sequence of pre-mRNA in the mutated dystrophin gene. These sequences are selected anti-sense oligonucleotides. As a result, the targeted segment (exon) of mRNA is removed (skipped) from the final mRNA product. Removal of an exon can restore the disrupted reading frame, allowing the translation of a shortened, but functional dystrophin protein. Having initially established the efficacy of an exon skipping therapy for DMD in animal models, Dr. Lu and his team have continued to make milestone achievements in the field by achieving near normal levels of dystrophin in cardiac as well as skeletal muscles in DMD models, demonstrating long-term efficacy of the therapy, identifying potential drugs for enhancing exon skipping, and identifying barriers for drug development (Figure 2).

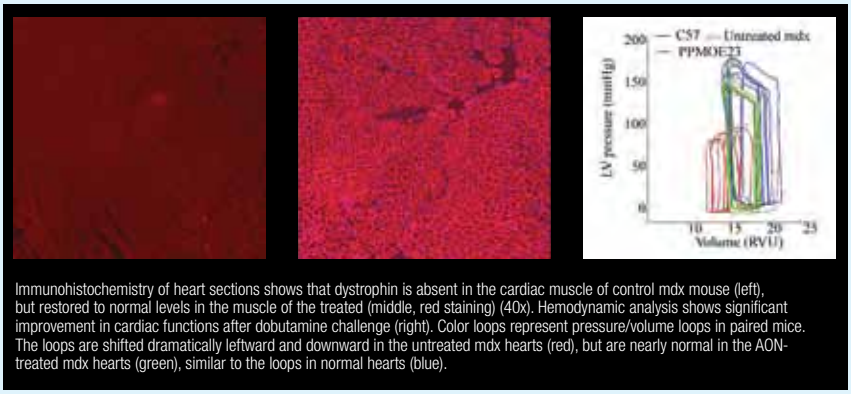
Susan Sparks, MD, PhD
Clinical Genetics, Levine Children's Hospital,
Assistant Professor of Pediatrics

Susan Sparks, MD, PhD, was one of the invited speakers for the inagural International Workshop for Glycosylation Defects in Muscular Dystrophy in 2008. Subsequently, she was recruited to the Department of Pediatrics/Clinical Genetics at Carolinas Medical Center. Dr. Sparks' clinical research focuses on glycosylation defects in muscular dystrophy and complements research being conducted in the McColl-Lockwood Laboratory.

Since joining the faculty in 2009, Dr. Sparks has established the CMC Cooperative International Neuromuscular Research Group (CINRG; www.cinrgresearch.org) clinical trial site and is principal investigator at CHS of three active clinical research trials in patients with DMD and LGMD. Through this research, a total of 40 patients locally, nationally and internationally have been evaluated at CMC. With additional grant funding from the National Children's Fund, National Greek Orthodox Ladies Philoptochos Society, the Muscular Dystrophy Association (www.mdausa.org) and Carolinas HealthCare Foundation, Dr. Sparks and her team have developed and implemented a longitudinal clinical data registry for neuromuscular disorders, continued longitudinal evaluations of patients with LGMD, and established a laboratory focused on glycosylation and muscular dystrophy. In addition, several pharmaceutical companies are interested in utilizing the CMC site for additional clinical trials, and quality initiatives have been implemented for improved clinical care of patients with muscular dystrophy. This research both complements and expands the established research of Dr. Lu.

In collaboration with Eric Hoffman, PhD, at Children's National Medical Center, Washington D.C., Drs. Lu and Sparks were awarded the first ever P50 grant from NIH to CMC in 2011. The award, from National Institute of Arthritis and Musculoskeletal and Skin Diseases, was part of a Center grant to study exon skipping in muscular dystrophy.

Figure 2. Exon skipping restores dystrophin expression and cardiac functions in a mouse model (MDx) of Duchenne Muscular Dystrophy.



Immunohistochemistry of heart sections shows that dystrophin is absent in the cardiac muscle of control mdx mouse (left), but restored to normal levels in the muscle of the treated (middle, red staining) (40x). Hemodynamic analysis shows significant improvement in cardiac functions after dobutamine challenge (right). Color loops represent pressure/volume loops in paired mice. The loops are shifted dramatically leftward and downward in the untreated mdx hearts (red), but are nearly normal in the AON-treated mdx hearts (green), similar to the loops in normal hearts (blue).

McColl-Lockwood Laboratory has developed unique testing systems both in vitro and in vivo to identify highly efficacious sequences as drug candidates for targeting each of the dystrophin exons. The laboratory also maintains a program of developing carriers for enhancing the efficiency of oligonucleotide delivery systems with the goal of reducing dosage and improving efficacy to make antisense therapy safer and economical. McColl-Lockwood Laboratory is a world leader in comprehensive studies of preclinical antisense drug development. Major research support was received from NIH, the Department of Defense, MDA, as well as many DMD-related charities. Most significant is a large U01 grant awarded to Dr. Lu by NIH National Institute of Neurological Disorders and Stroke (NINDS), for preclinical drug development targeting specific dystrophin exons.

To help speed development and clinical testing of the best drugs for exon skipping, CHS recently partnered with Children's National Medical Center (Washington, D.C.) and AVI Biopharma, a leading biotech company. This collaboration is the extension of a recent NIH P50 Center grant award to Dr. Lu and Susan Sparks, MD, PhD, together with researchers and clinicians in other centers, to apply exon skipping therapy to a wider DMD patient population.

A collaboration on translational pre-clinical experimental therapy among McColl-Lockwood Laboratory, Dr. Sparks' research and clinic trial establishment, and departments including Neurology and Physical Medicine and Rehabilitation, has made significant impact nationwide in the last five years. A Center of Muscular Dystrophy Research integrating translational and clinical trial components has been established at CHS to provide hope to muscular dystrophy patients not only in the local community, but also around the world.

Departments/Centers/Institutes

Behavioral Health Center

Lydia Stone (not actual name) is a 52-year-old woman with a history of depression. Like many Americans with mild to moderate symptoms of depression, she has received psychiatric care from a primary care physician. Despite excellent adherence to prescribed medications and a long period of treatment, her symptoms did not improve. Thus, her primary physician recommended that she see a psychiatrist. Concerned about the attached social stigma, she hesitated for many months. As a result, Lydia was on the verge of losing her employment and her marriage. Finally, under pressure from friends and co-workers, she become connected with Behavioral Health Center-Research (BHC-Research) of the Department of Psychiatry and began taking part in a clinical trial designed to help persons with inadequate response to standard treatment for symptoms of depression.

During a 52-week period, she received personalized care based on excellent psychiatric diagnostic assessments, free medications, laboratory tests, and frequent follow-up appointments. At the end of her journey, she was able to achieve her long-term goal of functional remission.

Behavioral Health Research Team:
Oleg V. Tcheremissine, MD, Research Director; Dineen Gardner, BA, Program Coordinator; Manuel A. Castro, MD, Research Psychiatrist

In 2011, BHC-Research continued its mission of providing the community with access to novel and innovative therapeutic options for psychiatric and substance abuse disorders. In the past few years, the team has been focused on the treatment of major depressive disorder (MDD). MDD is associated with increased morbidity, mortality and high healthcare costs to persons with this chronic illness, their families and society as a whole. Today, MDD is the leading cause of disability in the United States for persons ages 15 to 44. According to the World Health Organization, MDD is projected to be the second greatest burden of disease by 2020, eclipsed only by ischemic heart disease. Despite numerous advances in understanding the neurobiology of MDD, and improved therapeutic armamentarium available to providers, only 30 percent of patients achieve remission after an adequate trial of antidepressants.

The importance of conducting clinical trials in our community cannot be overestimated. Trials provide scientific rationale based on new indications for drug and other therapies. From a clinical point of view, outcomes are commonly employed to develop specific treatment guidelines and recommendations as a basis for evidence-based medicine.

BHC-Research plans to expand into other areas, including clinical outcomes measured by changes in quality of life and functioning in the community, as well as population-based research approaches.

Carolinas Rehabilitation/Department of Physical Medicine and Rehabilitation

After being involved in a motor vehicle crash and suffering a severe spinal cord injury (SCI), David Jenners (not actual name) was unable to walk. While completing intensive inpatient rehabilitation, he learned to use a wheelchair and take care of his daily needs. Upon discharge, David's life continued in a manner similar to what it was before – he worked from home as an information technologist, he maintained a regular diet and did not participate in an exercise regimen. His weight, along with abdominal girth, increased significantly over a short period of time - a condition known as central obesity. David started lifting five pound dumbbells three times a week in an effort to lose weight. However, this exercise regimen was not associated with any weight loss.

David made a follow-up appointment with his physiatrist. He learned that maintaining a balanced diet and participating in regular exercise are critical for living a healthy life, especially for patients with SCI. David was also encouraged to enroll in a study with Jesse Lieberman, MD, to learn more about his cardiovascular disease (CVD) risks, and possible diet modifications that would help him maintain a more healthy and balanced lifestyle.

Jesse A. Lieberman, MD
Physical Medicine and Rehabilitation
Junior Faculty Physician

Individuals with chronic SCI are known to have increased prevalence of dyslipidemia, glucose intolerance, insulin resistance, diabetes mellitus, obesity and markers of inflammation compared to matched able-bodied controls. Prior studies in subjects with SCI have shown that physical activity can positively affect risk factors. Some dietary patterns, specifically whole grain and dietary fiber intake, have demonstrated inverse relationships with these risk factors in the general population. However, the relationship of dietary patterns to CVD risk factors has not been studied in persons with SCI. Jesse Lieberman, MD, is interested in education and prevention of CVD in patients with SCI. Qualified candidates participate in a research study titled, "Dietary Patterns and Their Relationship to Cardiovascular Disease Risk Factors in Individuals with Chronic Spinal Cord Injury." The overall goal of this research is to determine the relationship between diet, adiposity and risk factors for CVD in persons with SCI.

The primary objectives of the study are to identify predictors of earlier development and more rapid progression of subclinical atherosclerosis, assess racial differences in severity and progression of early subclinical disease, test whether inflammation precedes subclinical disease, and evaluate the roles of genetic variation and host genetic/environment interactions in early development and progression of subclinical disease. Participants in the study come to the clinic for a one-time visit which consists of a blood draw to measure biomarkers, such as blood sugar and cholesterol, and a questionnaire covering physical activity and diet consumption.

Dr. Lieberman's work is just one example of how investigators at Carolinas Rehabilitation are improving the lives of patients with neurological disorders such as traumatic brain injury (TBI), stroke, spinal cord injury, Parkinson's disease and cancer. Carolinas Rehabilitation is one of 16 rehabilitation centers in the United States chosen by the National Institute of Disability and Rehabilitation Research (NIDRR) to participate in the prestigious TBI Model Systems Program. The comprehensive research study follows patient outcomes over a

Jesse A. Lieberman, MD, and his assistant Karen Harmen speak with a patient who has recently suffered a spinal cord injury.

long period of time and has resulted in improved rehabilitation for TBI patients. Currently in its 13th year, the study has followed more than 800 patients.

Research endeavors at Carolinas Rehabilitation also include two NIH-funded multi-site studies that collect data on interventions and care received by patients with TBI and SCI. Patients were also enrolled in several industry-sponsored clinical trials focused on improving functionality and quality of life for individuals following stroke, SCI and TBI. The expanded knowledge and innovative interventions resulting from research at Carolinas Rehabilitation translates into state-of-the-science care and improved patient outcomes for those in need of rehabilitation services.

Carolinas Simulation Center

David Jones (not actual name), a patient at CMC, was diagnosed with a precancerous polyp that required the removal of a portion of his intestines. Surgery was uneventful, but the second night following surgery he felt short of breath. David's nurse immediately examined him, placed him on oxygen to improve his breathing and contacted the on-call resident for evaluation. The resident performed a brief but focused evaluation and designed a well-outlined plan of care for Mr. Jones that he communicated effectively to his attending surgeon. A small clot was found in Mr. Jones' lungs. Following appropriate treatment, he was discharged home in excellent condition within a few days. Mr. Jones was impressed by the care he received, and particularly by the teamwork of medical and nursing staff.

Dimitrios Stefanidis, MD, PhD
Director, Surgical Simulation;
Director, Carolinas Simulation Center

Dawn Swiderski, RN, MSN
Nurse Educator, Carolinas Simulation Center

The excellent care provided to Mr. Jones did not happen by chance. Besides having well-qualified personnel taking care of him, his providers had undergone intense training at Carolinas Simulation Center (CSC). Simulation-based education is one of the newer teaching techniques being used at CHS to improve procedural and teamworking skills of healthcare providers involved in patient care. This resident had practiced the same procedure extensively on simulators and rehearsed similar scenarios with nurses using one of the sophisticated, high tech mannequins available at CSC. He had received detailed feedback on his performance by a senior mentoring surgeon, and was better prepared, more confident and more competent to care for Mr. Jones.

CSC is the only educational institute in our region accredited by both the American College of Surgeons and the Society for Simulation in Healthcare. Under the leadership of Dimitrios Stefanidis, MD, PhD, a minimally invasive surgeon, and Dawn Swiderski, MSN, RN, a nurse educator, CSC is not only improving CHS healthcare provider education but is also contributing to the advancement of simulation through research. Dr. Stefanidis has published numerous peer-reviewed manuscripts on skill acquisition using simulators and curriculum optimization and has paved the way for important and widely used curricula such as the Fundamentals of Laparoscopic Surgery Curriculum. This curriculum was developed under the auspices of The Society for American Gastrointestinal and Endoscopic Surgeons and American College of Surgeons, and is currently required by all general surgery residents before they can graduate. In 2011, Dr. Stefanidis chaired a national project to create a research agenda that highlighted the most important research questions in need of answers in the surgical simulation field, and that will provide guidance to researchers and funding agencies. Moreover, he received the first collaborative grant award of the Association for Surgical Education and the Association of Program Directors in Surgery. The goal of this multi-institutional project (seven institutions) is to establish national performance benchmarks for surgery residents in an effort to standardize surgical training across the United States.

Educational and research projects improve teaching methods for healthcare providers and are critical for improving patient care and outcomes.

Researchers from a variety of disciplines participate in simulation-based research projects conducted at CSC. Wendel Naumann, MD, has established a proficiency-based vaginal cuff closure simulator curriculum that assesses the learning curves of gynecology residents in a simulated task and the transfer of simulator-acquired skill to the operating room. Erin Stover, MD; Albert Franco, MD; and Joseph Ernest, MD, are conducting a research project that measures force applied to a neonate during vaginal delivery using the center's birthing simulator. The goal of the study is to prevent injury to neonates during delivery due to excessive force application. Practitioners learn from simulator feedback on the force they apply during delivery and can make appropriate changes during actual delivery. Under the leadership of Angela Moravek, RN, another research project demonstrated the effectiveness of simulation-based training in augmenting the knowledge and confidence of participating maternal-newborn nurses when encountering obstetrical emergencies.

Center for Nursing Research and Institute for Evidence-based Practice

Nursing research at CMC is closely linked with the Nursing Research and Evidence-based Practice Council. The council's role is to promote and advance the science and practice of nursing and facilitate education of nurses about the value and process of nursing research and evidence-based practice.

The Research and Evidence-based Practice Council has an annual Nursing Research Day that highlights a wide variety of nursing projects. Twenty CHS Nursing Services posters were selected for 2011, including: "Diabetes Education and Health Literacy in Latina Women" by Kristin Towell, RN, MSN, and Maren Coffman, RN, PhD, UNC-C faculty; "Diagnostic Accuracy of Electrocardiography and Echocardiography for Detection of Cardiovascular Abnormalities in Pre-Participation Screenings of High School Athletes" by Deborah McDougall, RN, MSN student at UNC-C; and "Determining the Impact of a Nurse-Led Telephonic Self-Management Program on Quality of Life and the Prevalence and Severity of Commonly Reported Symptoms Among Patients Newly Diagnosed with End-Stage Renal Disease" by Cyndy Rape, RN, MSN, CCTN; Trina Deaton, RN, MHA; Lisa Begeman, RN, BSN; Carol Bartlett, RN; and Shannon Jackson, MSW.

The Nursing Research and Evidence-based Practice Council: (L to R) Eddie Leonhardt, RN, MSN; Jessica Drummond, RN, BSN; Joann Riley, RN, MSN; La Quandra Feaster, RN, MSN; Kathynel Hatten, RN; Dennis Taylor, NP

Department of Emergency Medicine

It was just after dinner, and Julia Rea (not actual name) was finishing the dishes when she heard a loud thump in the living room. Walking into the room, she found her 64-year-old husband face down on the floor, unconscious. Unable to rouse him, she called 911. The 911 operator realized that Mr. Rea was likely experiencing cardiac arrest and, while dispatching first responders and paramedics, began providing Mrs. Rea instructions on how to effectively perform bystander CPR. When they arrived, the first responders and paramedics determined that Mr. Rea had ventricular fibrillation and immediately followed a highly structured resuscitation protocol aimed at increasing his chances of survival. This included performing minimally interrupted chest compressions, defibrillation, insertion of an airway device, intra-osseous vascular access, and intra-arrest therapeutic hypothermia. After 15 minutes, Mr. Rea regained a pulse and was placed into the waiting ambulance. En route to the hospital, paramedics performed post-resuscitation care and a 12-lead ECG. The ECG revealed that Mr. Rea's cardiac arrest was due to an ST-elevation myocardial infarction. The paramedics transferred care to emergency physicians who continued resuscitation and, in communication with intensivists, placed Mr. Rea into an inpatient therapeutic hypothermia treatment protocol. Mr. Rea awakened two days later. He went home with no neurological deficits seven days later.

Jonathan Studnek, PhD
Director, Pre-hospital Medicine Research

John Watts, PhD
Research Group Director, Department of Emergency Medicine

Over the past year, the Center for Pre-hospital Medicine, a part of the Department of Emergency Medicine, directed by Jonathan Studnek, PhD, Director of Pre-hospital Medicine Research, has conducted cardiac arrest resuscitation research focusing on Pre-hospital therapeutic hypothermia, the utility of a blind insertion airway device and a randomized controlled trial assessing the most efficient means of vascular access. Of note are results of a study published in *Resuscitation* concerning pre-hospital therapeutic hypothermia. The study compared patients resuscitated prior to therapeutic hypothermia with those who received cooled (4°C) saline during the intra-arrest period of resuscitation. Pre-hospital therapeutic hypothermia protocols are evolving as the new standard of care. Cooling is usually initiated only if patients experience a return of circulation. Research addressing the most appropriate sequence is limited. Analysis indicates that infusion of cooled saline during the intra-arrest period may improve the return of circulation, even at fluid volumes unlikely to change core body temperature. A randomized, controlled trial is under way within Mecklenburg County to validate these results. The best method for delivering cooled saline in the out-of-hospital setting is also being investigated.

Other important achievements within the Emergency Department in 2011 include advances in emergent cardiac and stroke care, as well as ongoing research in the appropriate utilization of imaging technologies in emergency departments.

Directed by John Watts, PhD, Emergency Medicine Research Laboratories at Cannon Research Center studies pulmonary embolism, which occurs when blood clot material breaks free in the veins and circulates through the heart to lodge in the arteries of the lung. Experimental models examine mechanisms of damage in the right ventricle, the regulation of pulmonary arterial circulation and the contribution of red blood cell rupture to the pathology of pulmonary embolism. Studies show that excessive inflammation contributes strongly to damage in the right ventricle, while dilation is hampered in non-blocked pulmonary arteries, and rupture of red blood cells release substances that reduce circulation

and gas exchange in the lungs. The team has identified treatments that minimize damage to the heart, dilate pulmonary arteries not blocked by the embolism and reduce red blood cell rupture in the experimental setting. Parallel clinical studies conducted by Jeffrey Kline, MD, director of research for the department, show that similar damage to the right ventricle, pulmonary circulation and red blood cells occurs in human pulmonary embolism. The major emphasis, therefore, is to develop therapies to reduce these detrimental processes and improve patient outcomes with pulmonary embolism.

CHS research team accomplishments were also highlighted in *Critical Care Medicine* as follows: "Watts and coworkers have elegantly demonstrated the pharmacologic effects of BAY 41-8543 in two series of experiments on a rat model of acute PE." The editorial summarizes findings that the treatment produces significant pulmonary vasodilation resulting in improved oxygenation and reduced red blood cell rupture. It concludes that the future application of this class of compounds in pulmonary embolism will depend upon developing routes of administration and chemical modifications that might give selectivity to pulmonary vascular dilation.

Department of Family Medicine

Jamal Williams (not actual name) is a 13-year-old boy with asthma, who recently lost his mother. He was unable to manage his asthma medications because his mother "helped him with that." His condition worsened, and he no longer was able to play sports – something he really enjoys doing.

Department of Family Medicine Research Team: Nichole Bayha, Susan Standridge, Mike Dulin, MD, PhD, Mark Steuerwald, Patricia Sanchez, Kendra Harris

Ivey Rice, Lindsay Kuhn and Jasmin Al-Baghdadi discuss their research findings.

Lindsay Kuhn, PA, examines a patient diagnosed with asthma.

Asthma is a chronic disease that is difficult to manage. Economically and socially disadvantaged families often have higher rates of disease, poor medical adherence and worse outcomes. This translates into higher healthcare costs. Failure to consider individual patient circumstances and goals may contribute to non-adherence with treatment programs. Patient-centered care is an innovative approach to the delivery of healthcare in which patients are encouraged and enabled to participate actively in the management of their health issues.

Shared decision-making, which involves both the patient and provider, is one approach to patient-centered care. Sharing information with each other, both express preferences and together agree upon the treatment plan.

In partnership with five community care clinics, investigators in the Department of Family Medicine and providers have used a participatory approach to plan a shared decision-making intervention for asthma. Selected clinics designed and implemented specific half-day asthma clinics, in which a shared decision-making approach is utilized in the management of asthma. Four clinics have taken part in this initiative, and more than 50 patients (including Jamal) have become involved in decision-making associated with their treatment. The participatory approach required involvement of all clinics at the planning stage, and was successful in producing an implementation plan tailored to the culture of each clinic.

The Department of Family Medicine research team is continuing its work focusing on healthcare disparities in the Hispanic community. Community-Based Participatory Approaches improve the quality of healthcare to underserved populations by identifying barriers to access, and by engaging the community to design interventions and become actively involved in improving their health outcomes.

Department of Internal Medicine

Quentin Jones (not actual name) was recently diagnosed with HIV after being admitted to the hospital this past spring. Quentin not only had to contend with the everyday realities of being a 19-year-old man, but also had to deal with a disease about which he previously had very little knowledge. Understandably, he was confused and frightened about his situation. He found out about Myers Park Infectious Disease Clinic's research program via a registry program at UNC-Chapel Hill. With the help of study coordinators, he explored available options based on his lab results and personal circumstances. He is now entering his six month of therapy and doing well. He can discuss the meaning of his lab results with doctors at a much higher level of understanding. He checks in frequently and is comfortable calling the research group to discuss his concerns and issues. Mr. Jones is just one of dozens of patients benefiting from the cutting-edge medications being offered through clinical research trials.

James M. Horton, MD
Chief of Infectious Diseases

The Division of Infectious Diseases of the Department of Internal Medicine, directed by James M. Horton, MD, continues to offer innovative research options to patients with infectious diseases. The clinical research team has grown to better serve persons with HIV/AIDS, giving them unique access to new formulations of medications (example: single tablet combinations) that are less cumbersome and elicit fewer negative side effects than standard agents currently available. The ultimate goal for all trials is to decrease pill burden and side effect profiles in the safest and most effective way, leading to increased adherence to medication regimens. Improved adherence is directly related to better disease management (viral load suppression) leading to fewer AIDS-related morbidities, mortalities, hospitalizations and complications.

Marc A. Johnson, MD, a member of the research team, is celebrating his third year as clinical trial investigator and Medical Director of Myers Park Infectious Disease Clinic. Dr. Johnson has a wealth of clinical trials experience that has added to the continued success of the CHS internal medicine research program. In addition to collaboration with UNC-Chapel Hill, Dr. Johnson is principal investigator of eight industry-sponsored trials. He is also a member of several panels exploring the next phase of HIV research, prevention and treatment modalities. Dr. Johnson is a respected advisor for several pharmaceutical companies exploring the issues of health disparities, access to care, new treatment strategies and prevention for the HIV population. He has also developed a collaboration with Liver-Biliary-Pancreatic Center faculty to improve care of persons co-infected with HIV and hepatitis C virus. Together, they are working to establish improved treatment options for these patients.

Department of Internal Medicine Team

Over the past 10 years, a number of outbreaks of skin abscesses due to community-acquired methicillin resistant *Staphylococcus aureus* (CA-MRSA) have occurred. Among the risk factors that contribute to the development of CA-MRSA is recent antibiotic use. From the moment of birth, our bodies are colonized with bacteria on the skin and in the gastrointestinal tract that provide defense against more harmful bacteria like MRSA. Antibiotics can adversely affect the delicate balance of these normal bacteria. Investigators at the Centers for Disease Control have hypothesized that destruction of normal, protective bacteria predisposes individuals to contracting skin abscesses due to MRSA. With support from Cannon Research Grants Program and the Silverman Foundation, Matthew Sullivan, MD, in Emergency Medicine and Dr. Horton have performed a pilot study examining normal skin bacteria in patients with skin abscesses. Specimens are analyzed by Martin Blaser, MD, in his laboratory at New York University. Preliminary data show a trend toward recent antibiotic use and skin abscesses. Researchers have applied for additional federal grants to continue these studies.

Marc A. Johnson, MD
Infectious Disease Clinical Director

Department of Obstetrics and Gynecology

David L. Tait, MD
Associate Director GYN Oncology

Brad S. Hurst, MD
Director of Assisted Reproduction

In 2011, research projects that received particular attention in the Department of Obstetrics and Gynecology included studies in the areas of Gynecologic Oncology, Reproductive Endocrinology and Maternal-Fetal Medicine.

The Division of Gynecologic Oncology. Ovarian cancer is the fifth leading cause of cancer death among women in the United States. More than 21,000 new cases and 15,000 deaths from ovarian cancer occur each year. Five-year survival of women diagnosed with stage I to IV disease ranges from 88 percent (stage I) to 18 percent (stage IV). The Division of Gynecologic Oncology is conducting an ovarian carcinoma biomarker discovery project with the long-term goal of developing a universal ovarian cancer screening test. Directed by David L. Tait, MD, results to date demonstrate that certain gene families are differentially expressed in malignant tumor samples, making them potential candidates for further biomarker development. In a second study comparing osteopontin expression in serous and endometrioid tumor tissue samples, osteopontin was demonstrated to express in 64 percent of endometrioid samples compared to 21 percent of serous samples. The team plans to validate and extend these results in coming years and to compare potential biomarkers with others, such as CA-125.

CMC Center for Reproductive Endocrinology and Infertility, directed by Brad S. Hurst, MD, became an ancillary study site for the Reproductive Medicine Network (RMN) in 2010. This multicenter network of seven sites throughout the United States conducts clinical studies investigating problems in reproductive medicine. In fall 2010, the fertility center began enrolling women in the Pregnancy in Polycystic Ovary Syndrome (PCOS) trial part II. This randomized, controlled, double-blind trial examines the safety and efficacy of letrozole compared to clomiphene citrate in achieving live births in infertile women with PCOS. Besides contributing to new knowledge that will help women with PCOS, patients receive the benefit of free medical care, testing and ovulation induction medications. To date, 232 women have been screened, 27 enrolled and five have conceived during the study period. Erin (not actual name) was the first woman in the study to conceive. Like many women with PCOS, she struggled with infertility and obesity. Following counseling during enrollment, Erin joined Weight Watchers, became responsive to the ovulation study drug and soon conceived. She was expected to deliver a baby girl in January 2012.

A second RMN trial began in December 2011. The Assessment of Multiple Gestation in Ovarian Stimulation (AMIGOS) trial is a study that compares three current fertility treatments in couples with unexplained infertility. In addition to bringing NIH grants to CHS and

answering important questions in the field of reproductive medicine, RMN trials enable CHS to collaborate with other institutions and to offer new treatment options to patients. No other fertility practice in the Carolinas is an RMN participant. For patients like Erin, the RMN trial improves their chances of becoming mother to a healthy infant.

Saju D. Joy, MD
Division Director, Maternal-Fetal Medicine

The Division of Maternal-Fetal Medicine, directed by Saju Joy, MD, began a study of non-invasive test for fetal aneuploidy in January 2011. For years, the hope was that fetal cells in maternal blood might be used to assess the developing fetus for fetal chromosomal abnormalities. Fetal cells, however, are rarely found in maternal blood, which limits clinical utility of such an approach. The new test, however, targets cell-free fetal DNA, which is present in maternal blood at significantly higher amounts, and has the potential to be utilized for detection of fetal chromosomal abnormalities. The division also participates in a study to evaluate the utility of novel biomarkers as an aid to diagnosis and as risk stratification tools in pregnant women. A secondary objective is to evaluate the utility of biomarkers in combination with other parameters to risk-stratify women and their unborn fetus with respect to adverse maternal or adverse fetal and neonatal outcomes. Both studies have the potential to reduce risks of invasive testing to mother and baby, offering improved diagnostic tools for obstetricians in the future.

Department of Oral Medicine

Jane Wade (not actual name) noted a persistent feeling of fatigue, muscle weakness, fever and chills for three days. She was seen in the Emergency Department and admitted to CMC. She was anemic and two blood cultures were positive for *Streptococcus oralis*. Jane had a mass on her mitral heart valve and was diagnosed with infective endocarditis. She was started on IV antibiotics and underwent cardiac surgery that replaced her mitral valve with an artificial heart valve. During her hospital stay, Jane reported chronic soreness of her gums. A dental examination revealed severe periodontal disease and multiple loose teeth. She reported that she had not seen a dentist or had a dental cleaning in more than five years. This case demonstrates the potential life-threatening impact of bacteremia (bacteria gaining entrance to the blood stream) resulting from poor dental health. Indeed, upwards of 35 percent of infective endocarditis cases arise from oral bacteria associated with poor dental health.

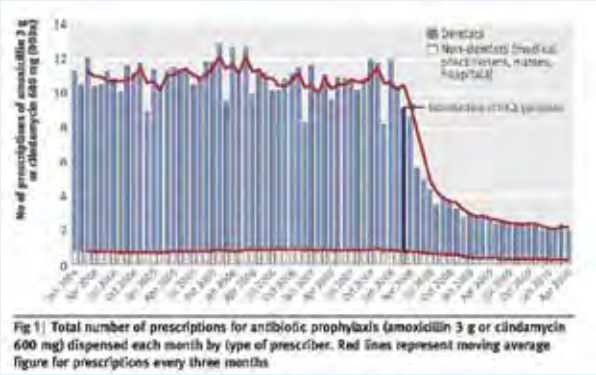


Fig 1| Total number of prescriptions for antibiotic prophylaxis (amoxicillin 3 g or clindamycin 600 mg) dispensed each month by type of prescriber. Red lines represent moving average figure for prescriptions every three months

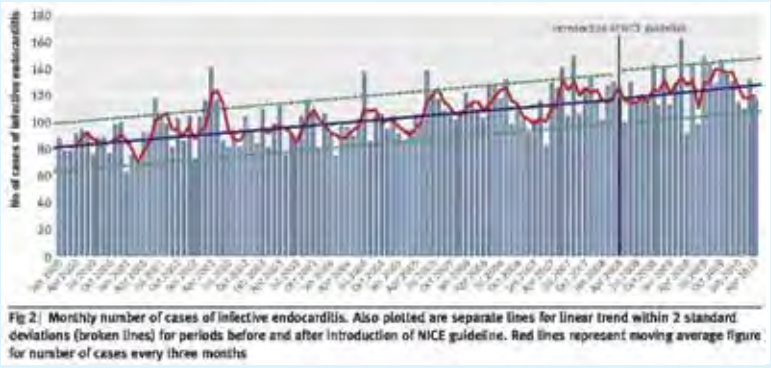


Fig 2| Monthly number of cases of infective endocarditis. Also plotted are separate lines for linear trend within 2 standard deviations (broken lines) for periods before and after introduction of NICE guideline. Red lines represent moving average figure for number of cases every three months

One of the major focus areas for the Department of Oral Medicine Research has been the association between oral disease and infections distant to the mouth, such as infective endocarditis. Peter Lockhart, DDS, Chairman of the Department of Oral Medicine, has published extensively in this field for more than 20 years. In 2011, he was senior author of a landmark paper on the topic in *British Medical Journal.** For more than 50 years, there has been a major focus on dental procedures as the underlying cause of many cases of endocarditis, and on antibiotic prophylaxis prior to dental procedures. In 2008, NIH and Clinical Excellence (NICE) in the United Kingdom (UK) produced new guidelines that recommended the elimination of antibiotic prophylaxis prior to dental procedures for all patients at risk for endocarditis. The UK was the first country to do this; the American Heart Association still recommends antibiotic prophylaxis for high-risk cardiac patients. Research by Dr. Lockhart and his colleagues addressed the issue of antibiotic prophylaxis and demonstrated that adherence to NICE guidelines did not result in increased cases of endocarditis. The results should have a major impact on future guidelines related to antibiotic prophylaxis and consequently millions of patients who will undergo future dental procedures (Figures 1 and 2).

Steering Committee for the World Workshop in Oral Medicine during a research planning committee meeting in New York in September 2011. In addition to Dr Lockhart (shown at lower left), Committee members include representatives from: University of Pennsylvania; New York University; University of Connecticut; University of Edinburgh, Scotland; Eastman Dental Center, London, England; and University of Milan, Milan, Italy.

**Thornhill MH, Dayer MJ, Forde JM, Corey GR, Chu VH, Couper DJ, Lockhart PB: Impact of NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study. BMJ 2011;342:d2392 doi:10.1136/BMJ.d2392.*

Department of Orthopaedic Surgery

Edward N. Hanley, Jr., MD
Chair, Department of
Orthopaedic Surgery

Several Orthopaedic Research Biology projects were conducted in 2011. Helen Gruber, PhD, and Edward Hanley, MD, continued exploration of cell-based changes during human disc degeneration using morphologic and molecular analyses. Recent studies have identified the presence of mitochondrial dysfunction in degenerating human discs, and discovered the constituitive expression of cathepsin K in the human intervertebral disc; a finding that has offered new insight into disc extracellular matrix remodeling via cathepsin K and receptor activator of nuclear factor-kappa beta ligand (RANKL). Variations in aggrecan localization and gene expression patterns were also found to characterize increasing stages of human intervertebral disc degeneration.

Bone research by Dr. Gruber investigated two topics: chemokine CXC receptor in knockout mice and its relationship to membranous bone healing in the adult mouse, and biomembrane formation in segmental defects in the rat. The latter research was supported by AO Foundation and AO Institute. Dr. Gruber also published a chapter on the effect of magnesium deficiency on vitamin D metabolism and action.

Orthopaedic Biology Research Team: First Row: Andrea Roberts, PhD, Synthia Bethea, Gretchen Hoelscher, Helen Gruber, PhD
Second Row: Kristina Gellar, Darla Morton, Frank Riley
Third Row: Jane Ingram, Natalia Zinchenko, Yubo Sun, PhD

Yubo Sun, PhD, David Mauerhan, MD, and Dr. Hanley continued studies on the association between calcium crystal formation and osteoarthritis (OA). They found that calcium deposition in monolayer and micromass cultures of OA fibroblast-like synoviocytes was significantly greater than those in cultures of fibroblast-like synoviocytes derived from patients with rheumatoid arthritis. Research continued for testing a phosphocitrate (PC) analogue, PCA-III, and a magnesium ion-PC complex, Mg-PC, for osteoarthritis therapy using cell and animal models. This latter research was supported by funding from the North Carolina Biotechnology Center. In 2011, Andrea Roberts, PhD, joined Dr. Sun's laboratory as a postdoctoral fellow.

Richard Peindl, PhD
Research Group Director, Orthopaedic
Engineering Research

Orthopaedic Engineering Research, directed by Richard Peindl, PhD, carried out several development and tissue engineering projects in 2011. Biomechanical studies have involved evaluation of anterior cruciate ligament allograft anchoring systems, effects of sliding hip screw placement for fixation of intertrochanteric femur fractures, and an investigation of "far cortical" screw locking techniques as applied to supracondylar fractures of the femur. Work also continues with Mark Hirsch, PhD, of Carolinas Rehabilitation on the development of a robotic Ankle Tone Measurement System (ATMS), which manipulates the ankle joint in quasi-random flexion/extension patterns of varying magnitude and frequency. The system has applications in evaluating treatments for patients with neuromuscular diseases and post-operative evaluation of patients with severe ankle trauma. Mike Ruffalo, MD, and Dr. Peindl have also recently begun a project to develop a portable ankle dorsiflexion measurement device for research studies involving the ankle joint. Ongoing tissue engineering research studies involve evaluating the effects of temperature and oscillating osmotic pressure on extending the graft storage period for joint-scale osteochondral allografts used for resurfacing osteoarthritic or traumatized joints. Dr. Peindl and James Kellam, MD, are also collaborating with Dr. Hirsch and Nigel Zheng, PhD, and Erik Wickstrom, PhD, from UNC-C in the development of a patient wearable inertial sensor device for providing motion tracking and biofeedback to individuals at high risk for falls for the purpose of physical activity modification. This research is funded by the newly awarded Carolinas Trauma Network Center of Excellence Grant.

Department of Pediatrics

Thomas A. Griffin, MD, PhD
Director of Pediatric Rheumatology

Thomas Griffin, MD, PhD, joined Levine Children's Hospital Division of Rheumatology in 2011. He previously served as Associate Professor of Pediatrics at Cincinnati Children's Hospital Medical Center. Dr. Griffin is a member of several professional organizations including the American College of Rheumatology, Pediatric Rheumatology Collaborative Study Group and the Childhood Arthritis and Rheumatology Research Alliance (CARRA). His clinical interests include identification of gene expression biomarkers to diagnose and predict outcomes in juvenile idiopathic arthritis and developing best practice guidelines and quality measures for juvenile dermatomyositis through CARRA.

Jason Dranove, MD
Pediatric Gastroenterology, Hepatology & Nutrition

The Center for Pediatric Research (CPR) at Levine Children's Hospital (LCH) continues to thrive in offering pediatric patients access to innovative therapeutics and technology. Thomas Griffin, MD, PhD, a renowned clinician and researcher, has recently joined LCH as Director of Rheumatology. With the addition of a pediatric rheumatologist, the breadth and depth of specialty expertise and research efforts at LCH continues to grow.

Division of Pediatric Rheumatology. Thomas Griffin, MD, PhD, has initiated an NIH-funded genetics repository for patients with juvenile idiopathic arthritis (JIA) at Levine Childrens Hospital. Dr. Griffin is co-investigator on an NIH P01 program project that will investigate the ability of gene expression in white blood cells to diagnose and predict outcomes in JIA.

Division of Pediatric Gastroenterology, Hepatology and Nutrition is evaluating novel agents for the treatment of gastrointestinal disorders. Ongoing clinical trials target gastroesophageal reflux, a common pediatric disorder, and hepatitis B, a less common disease in children, but one for which treatment options are limited.

Division of Pediatric Infectious Disease and Immunology is close to completion of the Congenital Cytomegalovirus (CMV) and Hearing Multicenter Screening (CHIMES) Study, an NIH-sponsored study that screens newborns for congenital infection and evaluates infected infants for hearing loss. At completion, 100,000 newborns will have been screened, and those infected will have benefitted from early intervention for hearing loss. Going forward, the division will participate in trials on antivirals for neonatal infections, including a study evaluating the role of valganciclovir in halting the progression of hearing loss in toddlers with congenital CMV infection. The division recently was awarded a 10-year CDC contract to evaluate the epidemiology of latent tuberculosis infection in Mecklenburg County.

Centers for Pediatric Intensive Care are collaborating to design studies related to the treatment of traumatic brain injury patients. Dwight Bailey, MD, Lauren Piper, MD, and William T. Tsai, MD, are completing the Cool Kids Trial, a multi-center study sponsored by NIH that evaluates the effects of cooling on traumatic brain injury. Study participants are completing neurocognitive assessments to evaluate their cognitive capability post-brain injury.

Division of Pediatric Nephrology is involved in several multicenter clinical trials through the Midwest Pediatric Nephrology Consortium, evaluating therapeutic management of nephrotic syndrome, cardiovascular complications in renal transplant recipients, transitional care in adolescents with chronic disease and genetic markers of nephrotic syndrome. Additionally, the division is involved in NIH studies related to the management of refractory nephrotic syndrome and quality of life measures in these patients.

D. Jack Weaver, MD
Pediatric Nephrology

D. Jack Weaver, MD, is investigating the role of genetic polymorphisms that predispose patients to complications of mycophenolate mofetil, an agent used to prevent rejection in renal transplant patients. Results will elucidate if screening for the polymorphism pre-transplant will lead to improved outcomes and decreased rates of rejection.

The Division of Neonatology completed a phase IIb/II multicenter trial to evaluate the safety and efficacy of Pagibaximab, an anti-staphylococcal immunoglobulin. Although the agent did not demonstrate efficacy in preventing staphylococcal infections in premature infants, results were congruent with recent studies demonstrating lack of efficacy of immunoglobulin products for improved outcomes in neonatal sepsis.

The Division of Behavior and Development. The Center for Neurodevelopmental Research (CNR) has been at the forefront of developing cutting-edge methods by which the detrimental effects of common prenatal conditions, including licit and illicit drug exposures, maternal depression and malnutrition, on early development can be assessed. Research activity at the CNR has resulted in the development of translational methods by which cry sounds of human infants and other species can be spectrum analyzed for the detection of insults to nervous system integrity among seemingly healthy infants.

Niraj C. Patel, MD
Pediatric Infectious Disease & Immunology

Dwight M. Bailey, DO
Pediatric Critical Care; Director, PICU

Philip Zeskind, PhD
Research Group Director

Lauren Piper, MD
Pediatric Cardiovascular Critical Care

Liver-Biliary-Pancreatic Center and Liver, Digestive and Metabolic Disorders Laboratory

Herbert L. Bonkovsky, MD
Senior Advisor for Research
Director, Liver-Biliary-Pancreatic Center

David A. Iannitti, MD
Chief HepatoPancreaticoBiliary Surgery

Mark W. Russo, MD
Medical Director of Liver Transplantation;
Clinical Associate Professor of Medicine

"Go home and get your affairs in order." These are the dismal words so often heard when someone is diagnosed with pancreatic cancer (PCa), the fourth leading cause of cancer death in the United States. PCa has the highest mortality rate of all major cancers: 94 percent of patients die within five years of diagnosis with only 6 percent surviving more than five years, and 75 percent of patients with PCa die within the first year of diagnosis. The bleak outcome of this disease is due to the lack of definitive warning signs or accurate detection methods in the early stages. By the time symptoms develop, PCa is usually already at advanced stages, leading to poor prognosis. Best treatment options include surgery and drug therapy; however, these options are generally inadequate, necessitating development of better early diagnostic markers and therapies.

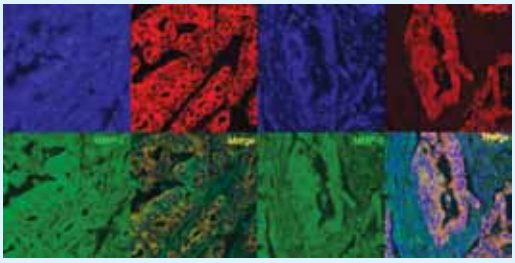


Figure 1. Expression of matrix Metalloprotease (MMP-2) and MMP-9 in human PCa tissue: blue stain shows all pancreas cells; Pan-CK has been used to differentiate tumor (red stain) vs. stroma; green stain indicates MMP expression; purple color indicates MMP expression in cancer cells.

Sriparna Ghosh, PhD, Research Scientist and Director of the Confocal Microscopy and Imaging Core at the Liver-Biliary-Pancreatic (LBP) Center of Cannon Research Center, is focused on identifying potential diagnostic biomarkers, which may lead to earlier detection and increased survival rates of PCa. Matrix metalloproteinases (MMP) 2 and 9 have been shown to play a potential role in cancer cell migration and metastasis. Dr. Ghosh's studies showed MMP-2 and -9 were expressed at varying degrees in PCa and were higher in tumors compared to stroma (non-tumor tissue) using a transgenic PCa mouse model and in human PCa patients. Higher expression of MMP-2 and -9 correlated with early stages of PCa development (Figure 1). With strong collaborations among clinicians and bench researchers, new insights into PCa pathogenesis will be revealed, leading to the identification of early diagnostic markers for PCa.

Another area of intense clinical and bench research effort is chronic hepatitis C (CHC), a disease that affects about 4 million people in the United States and 200 million worldwide. Several clinical trials of new candidate drugs for CHC are being performed at the LBP Center, directed by Herbert L. Bonkovsky, MD, David Iannitti, MD, and Mark Russo, MD. Other trials are focused on new therapies for hepatic, bile duct and pancreatic cancers.

Weihong Hou, PhD, Research Scientist, unveiled a critical role of zinc protoporphyrin (ZnPP), a normal metabolite, as a novel class of hepatitis C virus (HCV) NS3-4A protease inhibitors to modulate HCV replication and infection. ZnPP may hold promise as a novel treatment and prevention strategy against HCV infection. Additionally, Shahin Sendi, MD, a PhD candidate at UNC-C in the Department of Biology, and Marjan Mehrab-Mohseni, MS, Research Technician, are working on the role of microRNA-122 (miR122) in HCV entry into cells and HCV pathogenesis. They also are studying the therapeutic effects of Legalon-Sil (LS), a purified preparation of silibinin, a constituent of the milk thistle plant used extensively in China to treat HCV infection. Legalon-Sil down-regulated HCV proteins, and further, miR122 and

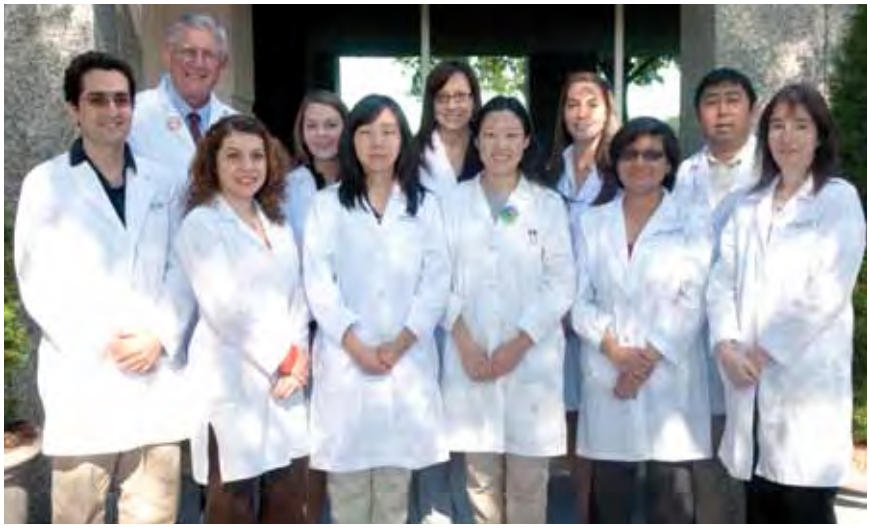
Laura W. Schrum, PhD
Group Director, Liver, Digestive and Metabolic Disorders Laboratory; Associate Professor, University of North Carolina-Charlotte

LS-modulated expression of membrane receptors necessary for HCV entry decreasing viral entry into hepatocytes.

Laura W. Schrum, PhD, Research Group Director of LDMD Laboratory, is investigating the molecular mechanisms of hepatic fibrosis/cirrhosis. HCV infection and chronic ethanol consumption are risk factors for the development of fibrosis. Hepatic stellate cell (HSC) is considered the main effector cell in liver fibrosis. Dr. Schrum's studies demonstrate that miR19b, a small non-coding microRNA (miR), regulates pro-fibrogenic signaling in the HSC controlling development and progression of liver fibrosis. These studies suggest miR19b may serve as a therapy and non-invasive diagnostic biomarker for liver fibrosis.

Heme is essential for biological processes, and abnormal heme synthesis can have severe health implications. Heme synthesis is regulated, in part, by 5-aminolevulinic acid synthase -1 (ALAS1). Ting Li, PhD, Research Scientist, and Qing Tian, Research Technician, recently uncovered a novel heme-regulatory mechanism whereby heme induces accelerated degradation of ALAS1 protein mediated by the protease LONP1.

The overarching goal of the LDMD Laboratory is to bring bench research to the bedside to unveil cellular and molecular mechanisms of liver and pancreatic diseases with the expectation of improving understanding of pathogenesis, identifying biomarkers for early detection and developing novel therapeutic strategies.



The Liver, Digestive, Metabolic Disorders Laboratory Team

R. Stuart Dickson Institute for Health Studies

Michael F. Dulin, MD, PhD
Interim Chair, Department of Family Medicine; Executive Director R. Stuart Dickson Institute for Health Studies; Director of Research, Department of Family Medicine

Under the directorship of Michael F. Dulin, MD, PhD, R. Stuart Dickson Institute for Health Studies was involved in the development of a number of innovative projects in 2011.

The Comparative Effectiveness of Asthma Interventions within a Practice Based Research Network study got off to a great start. The study, funded by the Agency for Healthcare Research and Quality (AHRQ), will bring $3 million to Carolinas HealthCare System over three years. In its first year, the study deployed an integrated approach to asthma management based on the Chronic Care Model across a multitude of primary care practices. As a result, patients from underserved populations were able to experience a shared decision making approach for their asthma care in several academic community clinics. The study has also enhanced an existing school-based asthma management program with additional resources including an electronic data collection system that will link children with their primary care providers via a school nurse. This study takes advantage of the Dickson Institute's team to provide analytics and data management while supporting personnel across CHS, including Carolinas Physicians Network, Public Health, Department of Family Medicine, Department of Pediatrics and Charlotte-Mecklenburg Schools. The following testimony by Thamara Alkhazraji, Research Coordinator, demonstrates the use of shared decision making in the treatment of asthma.

From L to R: Lauren Mowrer, Thamara Alkhazraji, MPH; Yhenneko Taylor, MS, discuss a research project

> During one of our first shared decision making sessions at a CHS ambulatory clinic, a mature 8-year-old boy named Alonso Rodriguez (not actual name) came in with his family to discuss his asthma management and treatment. Lindsay Kuhn, a physician assistant and health coach, discussed asthma with them at length and developed treatment goals that took into consideration cost, convenience, control and medication side effects. Alonso is the expert regarding his life and Lindsay's expertise lies within the realm of medicine. Because Alonso wanted fewer side effects from the medication he was currently on, he and his family were provided with therapeutic options. Together, they decided to step-down Alonso's medications because his asthma was under control and this would cause fewer side effects.

Under the leadership of Susan Christopher, Research Study Coordinator, Dickson Institute made substantial progress on the international, multi-site study Assessment of Dual Anti-platelet Therapy with Drug Eluting Stents (ADAPT-DES) in 2011. The study, aimed at examining resistance of anti-coagulant medications in patients who have received drug-eluting stents, will bring $6.4 million to CHS between 2007 and 2012. In March 2011, sites completed enrollment and data entry of 8,658 subjects. In November 2011, ADAPT-DES data were presented in a late-breaking session at the Transcatheter Cardiovascular Therapeutics conference in San Francisco, the world's largest educational meeting specializing in interventional

From L to R: Frank Gohs, MS; Susan Christopher; Richard Korn, MS, evaluate data

From L to R: Jie Zhou, MS; Kimberly Rouse, MPH; Jerry Watkins, MS; Marcy Nussbaum, MS, discuss mortality and length of stay risk model

cardiovascular medicine. The work done by Dickson Institute for this study will have a broad impact on standards of care for patients who receive drug eluting stents, and demonstrates the team's ability to coordinate large multi-site studies with complex needs for data handling and analysis.

A key innovation by the Dickson Institute team is a quality control system for monitoring adult surgical outcomes at Sanger Heart & Vascular Institute (SHVI). The system uses a risk-adjusted cumulative sum chart and National Quality Forum (NQF) report to: set performance goals relative to national benchmarks and monitor surgical outcomes to give an early alert when the surgical process performs at a rate worse than required. The Cumulative Sum Charts (CUSUM) system has played a central role in SHVI's quality program. During the last year, the reporting process has been expanded to provide CUSUM and NQF reports for CMC as well as Carolinas Medical Center-Mercy. In addition, Dickson Institute provides SHVI executive committee quality scorecards which track cardiac interventional, cardiac surgery, vascular surgery and pediatric interventional/surgery metrics.

Dickson Institute has recently implemented mortality and length of stay risk model methodology to predict expected event rates at all CHS facilities. Rates will be presented monthly on system-wide quality scorecards for each facility. Jie Zhou, Jerry Watkins, Kim Rouse, Marcy Nussbaum and John Carew, PhD, have all contributed to the success of this endeavor. Dickson Institute, with the aid of Premier, Inc., is the first site to successfully employ this methodology.

Sanger Heart & Vascular Institute Advances in Clinical Research

Michael Rinaldi, MD, FACC, FSCAI
Director, Clinical Research; Associate Professor, UNC School of Medicine

Frank R. Arko, III, MD
Vascular Surgery

Integration and growth were key themes for Sanger Heart & Vascular Institute Clinical Research in 2011 as the program continued to develop organizationally. SHVI added several new key faculty members over the past year who bring depth to the program. Charles Bridges, MD, ScD, was welcomed as Chief of Cardiac and Vascular Surgery. Frank Arko, MD, also joined SHVI in the Department of Vascular Surgery. Dr. Arko is a nationally recognized thought leader in the field of thoracic endograft therapy, and is the national PI on several clinical trials and Co-PI on another NIH/NHLBI grant.

SHVI's greatest success remains its continued strong enrollment in a large number of clinical trials with diverse participation by each of the cardiovascular disciplines. SHVI Clinical Research now has more than 2,000 patients enrolled in 45 ongoing clinical trials. Academic endeavors have not been limited to clinical trial participation. SVHI physicians serve as faculty at many major national cardiovascular conferences and in the last year generated more than 150 publications, abstracts and presentations.

Research has traditionally been conducted on the CMC and CMC-NorthEast campuses independently. Greater integration of the SHVI cardiovascular service line has created the opportunity to coordinate its research program. A three-campus enrollment mechanism leverages scope and size, making SHVI one of the largest cardiovascular clinical trials groups in the United States. Notable examples include the following:

- The CABANA trial, an NIH-funded study investigating the role of catheter ablation for atrial fibrillation. The PREVAIL trial investigates the role of the implantable "Watchman" device to reduce stroke risk associated with atrial fibrillation.

- The EXCEL trial randomizes patients with left main coronary artery disease to bypass surgery or drug eluting stents. EVEREST studies are an ongoing investigation of the MitraClip for non-surgical repair of mitral insufficiency. SHVI remains one of the leading centers in the world, and is one of only a few centers in the Southeast with experience in the exciting field of valve therapies installed percutaneously and with minimal invasion. This has led to the establishment of a coordinated Valve Center at CHS with expertise few centers can match.

- **Pediatric Cardiology and Cardiac Surgery** team is studying pulmonary valve therapies deployed percutaneously for previously failed right ventricle to pulmonary artery conduits. Pediatric Cardiac Surgery is also using innovative investigational pediatric ventricular assist devices for children with severe heart failure as a bridge to heart transplant. SHVI Pediatric Cardiology, in conjunction with Adult Cardiology, will continue its regional leadership role in the study of percutaneous devices to close atrial septal defects and patent foramina ovale.

Charles R. Bridges, MD, ScD
Chair, Department of Thoracic and Cardiovascular Surgery

Michael Katz, MD, PhD
Senior Scientist, Thoracic and Cardiovascular Surgery Research

• **The Molecular Cardiac Surgery Research Program.** Dr. Bridges, Chairman of the Department of Thoracic and Cardiovascular Surgery at SHVI, and Director of the Molecular Cardiac Surgery Research Group, joined CHS in August 2011. Dr. Bridges is a physician-investigator and a national leader in the field of gene therapy for cardiac regeneration in heart failure. His team includes Michael Katz, MD, PhD, a cardiothoracic surgeon, and Anthony Fargnoli, MS, a bio-medical engineer. Supported by a large investigator-initiated [R01] grant from NIH/NHLBI, Dr. Bridges' research group has recently developed a novel technique for closed recirculation of vectors carrying genes or of stem cells in the coronary (heart) circulation using cardiopulmonary bypass – succinctly referred to as molecular cardiac surgery with recirculating delivery (MCARD). A schematic diagram of MCARD platform technology appears in Figure 1.

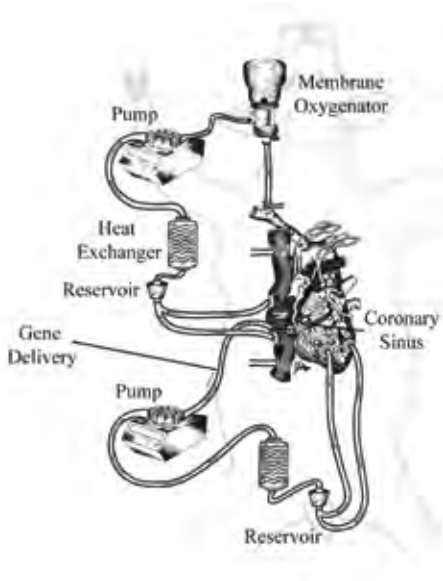


Figure 1. Gene delivery via cardiopulmonary bypass with cardioplegic arrest, using MCARD with complete cardiac isolation and closed-loop recirculation.

Key components of this approach include isolation of the heart from the systemic circulation, closed loop multiple-pass recirculation of genes to be introduced into heart muscle cells, and a component allowing for washout of the vector after gene transfer. Using a separate cardiac pump circuit, this system allows for the physical separation of arterial inflow and venous effluent from the two circuits. This technique has the advantages of increased gene-vector residence time in coronary vessels, decreased bio-distribution of gene-vector in the systemic circulation, and increased perfusion pressure and micro-vascular permeability in the heart vessels. Cumulatively, these advantages maximize uptake of vector genes into myocytes, resulting in efficient gene expression in the myocardium of large animals (Figure 2). MCARD results in a greater than100-fold increase in gene delivery, compared to intramuscular injections, resulting in transduction of up to 99 percent of cardiac myocytes with an average of 48 gene copies per cell in the anterior wall of the left ventricle. This method is superior to any previously published approach.

Currently, the most promising targets for gene therapy appear to be calcium cycling proteins and the beta-adrenergic signaling cascade. In recent experiments, enhancement of cardiac contractility and relaxation was found, as well as improvement of energy efficiency after using

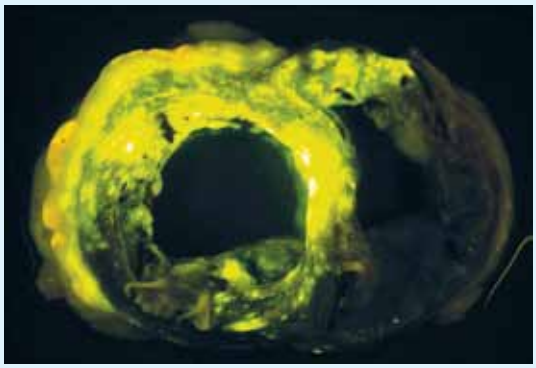


Figure 2. Green fluorescent protein (GFP) of whole mount cross-section of the ovine heart taken at mid-papillary level, including both ventricles, demonstrating robust left ventricle GFP expression after MCARD-mediated delivery of adeno-associated virus serotype 6 (scAAV6)-GFP gene.

the MCARD procedure to deliver the therapeutic gene – ARKct (carboxyl terminus of beta-adrenergic receptor kinase) into the normal ovine heart.

Further studies at Cannon Research Center will involve delivering both ARKct and SERCA2A (sarcoplasmic reticulum calcium ATPase) by MCARD. The hypothesis is that MCARD-mediated delivery of adeno-associated virus encoding ARKct or SERCA2A results in robust gene expression in the myocardium and will mediate significant functional benefits in sheep with moderate to severe heart failure. These studies will be extended into clinical trials as quickly as possible, with the ultimate goal to establish new treatments for heart failure and other cardiac disorders.

Parallel laboratory studies will evaluate cardiac regeneration using MCARD for gene or stem cell delivery and develop small animal models to assess alternative transfer methods and novel molecular constructs.

Research Administration and Operations

John Baker, MD,
Interim Vice President, Research

Research Administration is undergoing a transformative change led by John Baker, MD, Interim Vice President for Research, expanding its focus on CHS-wide clinical and translational research. The Office of Research Administration and Operations at Cannon Research Center continues to provide direction and support to investigators, physicians and staff for conducting basic, clinical and translational research committed to improving quality and cost-effectiveness of healthcare delivery based on the single unified enterprise (SUE) concept. Activities include administration and operations of research core facilities, clinical and translational research, patent and intellectual properties, research finance, safety and compliance, Cannon Grants and Cannon Summer Scholars Programs, funding opportunities and grants development.

The Poison Center, Emergency Medicine, Levine Cancer Institute, Department of Thoracic and Cardiovascular Surgery, Department of General Surgery, County Health Department, Department of Neurology (Center for ALS/Neuroscience; Muscular Dystrophy Laboratory), Nursing Research, Department of Pediatrics, Carolinas Simulation Center and community services experienced unprecedented growth in intellectual properties and federally funded grants.

Research Administration Team: L to R:
Kay Snider, Caren Anderson, Carmen Costa, Farah Bahrani-Mougeot, PhD, Melanie McDermid, Cecilia Hurtado-vaca, Herbert Bonkovsky, MD, Dhanonjoy C. Saha, PhD

To support growth in Thoracic and Cardiovascular Surgery Research, Michael Katz, MD, PhD, an experienced research cardiothoracic surgeon, and Anthony Fargnoli, MS, a biomedical engineer experienced in gene therapy, were recruited by Charles Bridges, MD, ScD, Chairman of the Department. Dr. Bridges' research focuses on adenovirus-mediated gene therapy for cardiac failure.

The Cannon Research building has been undergoing major renovations to support Dr. Bridges' research and the newly established Levine Cancer Institute headed by Derek Raghavan, MD, PhD. Dr. Raghavan's research focuses on genetic basis of cancer, genetic differences in patients' response to cancer therapies and personalized cancer treatments.

Clinical and Translational Research

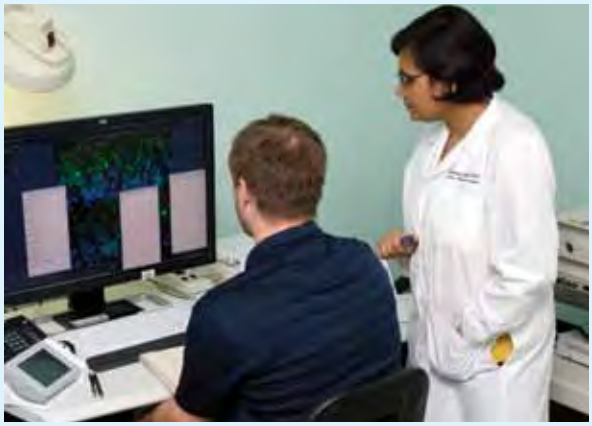
The Office of Clinical and Translational Research (OCTR) is responsible for providing programs for direction, guidance, support, education and promotion of corporate compliance, while facilitating clinical research throughout CHS. The OCTR is directed by Joan Connell, RN, and consists of the Institutional Review Board (IRB) support staff, clinical trial contract specialists, a laboratory coordinator, research monitor and educators and program coordinators.

Joan Connell, RN
Director, Office of Clinical and Translational Research

Clinical and Translational Research revised Standard Operating Procedures (SOPs), developed new educational and training programs, and participated in institution-wide quality improvement and compliance programs. Specifically, 23 OCTR SOPs for the Conduct of Clinical Trials were revised and numerous sessions to orient CHS personnel to the changes were provided.

In collaboration with Carolinas College of Health Sciences, a summer elective in clinical research for nursing students enrolled its first student in 2011. Ms. Connell developed and presented "Clinical Research Ethics: Science and Moral Protection" to CHS research personnel, a course that will continue to be offered. Other presentations include: "Clinical Research Overview" and "Challenges We Face in Clinical Trials." by Ms. Connell and William Clay, MPA, Research Monitor and Educator, respectively. These presentations are part of the one-day seminar, "Grants Development and Management: The Whole Nine Yards" developed by Research Administration and offered once a year.

The CHS IRB continued to fulfill its regulatory mandate to protect research participants through review, approval and continuing oversight of system research projects. The OCTR continues to refine IRB forms and processes to improve IRB effectiveness and efficiency. Additionally, the OCTR began implementation of a new CHS-wide electronic IRB management system.



Sriparna Ghosh, PhD, Research Scientist and Director, Carolinas Confocal Microscopy and Imaging Core Facility demonstrates how to use the microscope to produce the best results.

Core Facilities

Biostatistics Core Facility, under the directorship of Jim Norton, PhD, supports the efforts of Cannon Research Center investigators and clinical faculty, residents and staff of CMC. In addition to providing statistical analysis of clinical trials, epidemiologic studies and medical research, the facility is also involved in improving statistical education in the health sciences at CMC.

Assistance is available for research project study design, statistical analysis using SAS® and sample size calculations. The facility also participates in review of grants and manuscripts. Furthermore, Dr. Norton is available to assist residents, fellows and faculty in preparing presentations and publications. The Biostatistics Core performs analyses for the Infection Control Department and CMC Administration. In addition, Dr. Norton gives a six-hour course in biostatistics to faculty, residents and staff at CMC and takes an active role in teaching principles of biostatistics to Cannon Summer Scholars.

The mission of the ***Confocal Microscopy and Imaging Core Facility*** is to contribute to the basic, translational and clinical research community at CMC and other universities and institutes; to introduce and implement state-of-the-art cell biology and microscopic techniques; and to enhance the research capability and productivity of investigators.

The Core Facility features a state-of-the-art Zeiss LSM 710 confocal microscope system housed in a temperature-controlled room on the second floor of Cannon Research Center. Sriparna Ghosh, PhD, a trained cell and molecular biologist with advanced microscopy and image analysis background, is director of the facility. Dr. Ghosh has developed an automated quantitative image analysis method to enhance efficiency and throughput. The Core Facility performs a variety of imaging techniques including analysis of single or multiple-labeled specimens, immuno-histochemistry, immuno-fluorescence, 3-D image analysis, co-localization, time series, time lapse, FRET, FRAP, drug screening, GFP transfection efficiency, siRNA and miRNA studies and other advanced applications in both live and fixed cells and tissue.

The Core Facility also provides assistance in study design and planning, performs assays, validates antibodies and performs image analysis. Training sessions for different imaging techniques are also offered. Collaborative research opportunities are always available and encouraged. For more information, visit www.carolinasmedicalcenter.org/research.

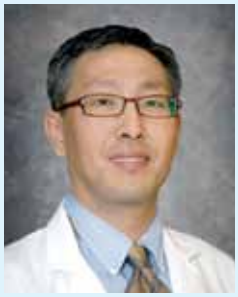
The ***Flow Cytometry Core*** is outfitted with two Becton Dickinson Flow Cytometers: a FACSCalibur and a BD FACSAria-II Flow Cytometer. The FACSCalibur has a Plus'488nm laser allowing for (up to) 3-color cell analysis. The FACSAria-II is equipped with a high-speed sorter with fixed alignment cuvette flow cell, 1 to 4 way sorting, 7-color capability and automated compensation. The FACSAria-II cell sorting capabilities allow isolation and recovery of cell populations for further study. The flow cytometers are controlled through an interface with Mac computers using Cell Quest data acquisition and FloJo analysis software. The facility employs one full-time, experienced technician and a post-doctoral fellow directed by Iain McKillop, PhD.

The mission of the ***Histology and Electron Microscopy Core Facilities*** is to provide technical histologic and morphologic support for studies developing translational links between research and patient care. The Histology Core contains instrumentation to facilitate routine paraffin tissue embedding with a programmable paraffin infiltration unit, a paraffin embedding system, autostainer and routine microtomes. This equipment includes: 2 Jung 2065 microtomes, a Jung 2050 microtome, a Jung Supercut microtome, a Hacker H/I-Flex paraffin tissue processor, an H2500 Biorad Rapid Microwave Processing system and a Jung CM3000 cryostat. Specialized non-decalcified bone histology is also performed using glycol methacrylate and methyl methacrylate with specialized hard tissue microtomes, including a large Polycut microtome. Expertise is offered in special staining, immuno-histochemistry, immuno-cytochemistry, in situ hybridization and cryo-sectioning techniques.

A microscope room houses a Zeiss Axioskop microscope and a Zeiss dual viewing microscope with brightfield, UV fluorescence and polarized light capabilities. Digital imaging is available for brightfield and UV microscopy using a Nikon/Sony system, which enables the user to capture and save digital images. This includes an automatic 35 mm camera system, a Nikon microscope interfaced with a CoolCam 2000 cooled 3-CCD color camera system for high resolution fluorescence and bright field microscopy interfaced with a Sony color video printer. Also available is Optimas and OsteoMeasure computer assisted histo-morphometric software. Two complete histo-morphometry systems and digital imaging systems are available.

The Electron Microscopy Core is completely equipped for specimen preparation and digital imaging. This Core houses two ultra-microtomes, a Phillips CM10 transmission electron microscope with digital imaging system and separate image workstation and a Lynx microwave tissue processor.

These facilities are staffed by certified histology technicians and directed by Helen Gruber, PhD, Laboratory Group Director for Orthopaedic Biology Research Laboratories.



Sunil Hwang, PhD
Research Scientist; Director
Mass Spectroscopy and
Proteomics Core Facility

The mission of ***Mass Spectrometry and Proteomics Core Facility*** is to elucidate early and specific biomarkers of human disease, especially hepatocellular carcinoma and other cancers. Research will provide molecular level insight into a number of different disease processes, which might be applied to overcome current clinical challenges. The Core is directed by Sunil Hwang, PhD, and staffed by post-doctoral fellows, students and research technologists. The facility published a variety of articles in 2011, including studies of pancreatic and hepatocellular carcinoma, iron metabolism and pulmonary embolism. Articles detail the department's innovative application of separation and proteomics techniques to the biochemical study of physiological and patho-physiological processes. Increased understanding of these diseases or disease-related events help to guide the development of new and better treatment options for affected patients. For more information, visit www.carolinasmedicalcenter.org/proteomics.

Nury Steuerwald, PhD
Senior Research Scientist;
Director, Molecular and Microarray
Core Facilities

The ***Molecular and Microarray Core Facilities*** have undergone several upgrades in the past year, including acquisition of an Affymetrix GeneAtlas Microarray system that supports a new, lower cost microarray strip format. Microarray experiments can be run on this instrument at a fraction of the cost of the Genechip system, while still obtaining comparable results.

The Core also purchased an Ion Torrent Next Generation Sequencing (NGS) instrument. NGS parallelizes the sequencing process thereby producing millions of sequences simultaneously. This technology enables one to more rapidly delve into disease mechanisms, including DNA sequence variants, RNA expression levels and promoter methylation status on a high resolution sequencing platform. High-throughput sequencing has been employed to identify unknown causative mutations in human disease and will likely impact our understanding of complex disease trait loci and pharmacogenomics. Epigenetic regulation of gene expression underlies the pathogenesis of many diseases, particularly cancer. NGS has been employed to detect and characterize DNA-protein interactions resulting in chromatin remodeling. Aberrant expression of small non-coding RNAs such as microRNAs has also been implicated in the pathogenesis of disease. An advantage of the NGS approach for transcriptome analysis is its ability to characterize all transcriptional activity, both coding and non-coding, without prior assumptions, thereby permitting the discovery of novel tissue-specific isoforms and the identification of previously undetected species.

Major upgrades are being made in the ***Vivarium,*** including the installation of a large animal bio-safety level two facility, especially to support Dr. Bridges' research. In addition, a state-of-the-art iBox Scientia, Multi-spectral Imaging System for small animal research was purchased. This macro fluorescent in vivo system non-invasively detects fluorescent markers such as green- or red- fluorescent proteins in animals for repeat observation and data generation without disturbing the animals. This imaging machine has expanded capacity to conduct studies related to tumor, cancer and metastasis, heart disease and immunology.

Angela Sanford, MBA
Assistant Vice President,
Research Finance

Research Finance, Grants and Contracts

Research expenditures continue growing as we receive increased federal funding. In 2011, expenditures increased by $1.9 million to $35.2 million. We received $8.9 million new or continuing federal awards, with aggregate total awards of $16.2 million. This represents an 86 percent increase in federal funding and a 23 percent increase in aggregate funding over 2010. In addition, we increased our indirect cost recovery by 32 percent in the same period. Overall, external funding in 2011 was 430 percent greater than that of 2008.

Dhanonjoy Saha, PhD
Assistant Vice President, Research
Administration and Operations

Patents and Intellectual Properties

We have enjoyed consistent, unprecedented growth in intellectual properties since 2008. Fifteen invention disclosures (IDEA) were received and nine patent applications were filed in 2011. However, no new patent was received from the U.S. Office of Patents and Trademarks. In 2011, we also received a record amount of revenue ($898,000) from existing patents and inventions. This amount exceeds the total amount previously received since the inception of Cannon Research Center at CHS.

We upgraded Pneumotrap®, a device for diagnosing pneumonia and other lower tract lung infections, prototype design to detect lipopolysaccharide in exhaled breath of sepsis patients, which was developed by Jeffrey Kline, MD, Department of Emergency Medicine.

A technology development licensing agreement was signed with Children's National Medical Center in Washington, D.C., and AVI Biopharma to collaborate on improved candidate drugs for therapy of muscular dystrophy. It is based upon the pioneering pre-clinical work of Qi Lu, MD, PhD, involving anti-sense oligonucleotides to achieve exon skipping and increased expression of functional dystrophin, the critical protein of muscle that is severely deficient in Duchenne muscular dystrophy.

The Exchanged Quality Data for Rehabilitation (EQUADR) team, led by Robert Larrison, President of Carolinas Rehabilitation, received the Innovate to Greatness Experimenter Award in 2011 for efforts related to the development of the CHS patented database used by rehabilitation hospitals and programs across the United States for benchmarking purposes and improving program quality.

Jean-Luc Mougeot, PhD
Senior Scientist, Cannon Motor Neuron Laboratory, Department of Neurology

Institutional Bio-safety Committee

The Institutional Bio-safety Committee (IBC) is chaired by Jean-Luc Mougeot, PhD. All policies and procedures were updated with the assistance of Carmen Costa, IACUC/IBC/RSC Coordinator. Committee members were retrained; and required bio-safety committee meetings and laboratory inspections have been held. Additionally, some members of the committee participated in the North Carolina Association for Biomedical Research Conference at Chapel Hill in September 2011. The conference provided incentives to improve coordination among the three I's (IACUC, IBC, IRB) and set forth new bio-safety/bio-ethics principles related to the oversight of dual-use research and its implications in bioterrorism. In addition, Dr. Mougeot initiated a CITI Bio-safety Course, including training on NIH guidelines for recombinant DNA research for CHS investigators and IBC members.

Research Safety and Compliance

Research safety and the well-being of all personnel continues to be a top priority at Cannon Research Center. Research Administration continues to work closely with Corporate Safety to assure a safe work environment. As in previous years, Cannon Research Center staff were given a safety refresher presentation by Laura Schrum, PhD, Director of Research Safety. Additionally, staff participated in an annual EPA RCRA/DOT Training Course organized by Corporate Safety to certify employees are compliant with safe handling of hazardous waste and material transport.

Seminars, Continuing Education and Publications

Cannon Noon Conference and special seminars at Cannon Research Center were expanded in 2011. The number of seminars presented at Cannon Research Center increased 6 percent compared with those offered in 2010. In addition, a total of 284 seminars and presentations by CHS investigators were made in 2011, a 39 percent increase compared to 2010. Video conferencing also is now available with University of North Carolina School of Medicine.

The LDMD Research Laboratory, led by Herbert L. Bonkovsky, MD, hosted the U.S. Porphyria Consortium's National Conference in July 2011 at Cannon Research Center. The conference was funded by the Rare Disease Clinical Research Network in collaboration with NIH's Office of Rare Diseases. The objectives of this consortium are to conduct longitudinal multi-disciplinary investigation of human porphyrias, including natural history, morbidity, pregnancy outcomes and mortality in people with these disorders.

For the second year, a day-long course, "Grants Development and Management: The Whole Nine Yards" was organized by Dhanonjoy C. Saha, PhD, and offered through the Area Health Education Center (AHEC). "Advanced Grant Writing" was also offered and will be available again in 2012. In 2011, Dr. Saha was invited to the Editorial Board of *Research Management Review* and to serve as co-editor of the Regional Corner (Southeast) of *National Council of University Research Administrators* (NCURA) *Magazine* – both published by NCURA. Debra Kieft serves as editorial assistant.

In 2011, speakers from a wide area of expertise and institutions presented at the CHS Research In-Progress Seminars including four from UNC-C (Valerie Grdzelishvilli, PhD, Cory Brouwer, PhD, Jun-Tao Guo, PhD, Kevin Thompson, PhD) and two from UNC School of Medicine (Lishan Su, PhD, Nicholas Shaheen, MD, MPH). Other notable speakers included Ann Bonham, PhD, Chief Scientific Officer (Association of American Medical Colleges) and Daniel Lasserson, MD (University of Oxford, UK).

John A. Watts, PhD, received the Best Basic Science Presentation Award at the 2010 Annual Meeting of the Society for Academic Emergency Medicine in Phoenix, Ariz. The award was presented at the 2011 Annual Meeting in Boston. Dr. Watts' presentation, entitled "Pulmonary vascular endothelial cell dysfunction during experimental pulmonary embolism," was co-authored by Michael Marchick, MD, Michael Gellar, BS, and Jeffrey Kline, MD.

Farah Bahrani-Mougeot, PhD, was guest speaker/visiting professor at Lanzhou International Hepatology Meeting, Lanzhou, Gansu Provence, China, in October 2011.

Mary Beth Lambert, pictured with James McDeavitt, MD, awarded first place prize for the 2011 Cannon Scholars Research Day presentation competition.

Cannon Summer Scholars Program

The 2011 Cannon Summer Scholars Program was a singular success. Among the 26 scholars were three first-year medical students, three Master's students and 20 undergraduates from 17 colleges and universities in six states. In accordance with our program goals, we successfully recruited an increased number of women and historically under-represented minorities into the program. Among the 26 scholars, 58 percent were female and 21 percent African American and other minorities, a substantial increase compared to nine percent in 2010.

James McDeavitt, MD, Chief Academic Officer of CHS, was keynote speaker at Summer Student Research Day. A distinguished member of the CHS Board of Commissioners, Thomas T. Long III, MD, also attended the Research Day event and served as a judge for the research competition. The awardees were: Mary Beth Lambert, first-year medical student, UNC School of Medicine, mentored by Michael Dulin, MD, PhD (1st place); Aimee Stone, second-year chemistry student at Wingate University, mentored by Jean-Luc Mougeot, PhD (2nd place); Shant'e Wade, physiology graduate student at North Carolina State University, mentored by Bo Wu, PhD (3rd place), and Ben Lovin, second-year chemistry student at Cornell University, mentored by Yubo Sun, PhD (3rd place).

2011 Cannon Summer Scholars Program

Scholar	University
Abrar Ahmed	UNC-Charlotte
George Alyateem	UNC-Charlotte
Ashleigh Blue	UNC-Charlotte
Joshua Bockenek	NC State University
Astrid Cerbone	UNC-Wilmington
Jaclyn Cika	Winthrop University
Tamunotonya Fiabema	UNC-Charlotte
Merischa Griffin	Johnson C. Smith University
Kathryn Harris	Massachusetts Institute of Technology
Melissa Haug	College of Wooster
Priscilla Haug	College of Wooster
Sean Holland	East Carolina University
Alec Lamb	Clemson University
Mary Beth Lambert[1]	UNC School of Medicine
Ben Lovin[3]	Cornell University
Kathryn McClure	Denison University
Michael Pettus	Medical College of South Carolina
Roland Pixley	NC State University
Soham Savani	NC State University
Aimee Stone[2]	Wingate University
Brenden Stuckey	UNC-Charlotte
Courtney Stump	Wingate University
Tam Truong	Queens University
Shant'e Wade[3]	NC State University
Sallie Wilson	Columbia University
Jingyu Zhou	Meharry Medical College

1. First place winner, Cannon Scholars Research Day Competition
2. Second place winner, Cannon Scholars Research Day Competition
3. Third place winner, Cannon Scholars Research Day Competition

Graduate Education and Training and Collaborative Grants

In addition to providing research opportunities for residents and fellows, we continue to provide graduate research training for students enrolled at UNC-C. In 2011, five UNC-C students earned degrees (three PhD and two Master's) directed by faculty of Cannon Research Center at CMC. The collaborative degree program between UNC-C and CMC enables students to complete the research portion of their degree requirements under the direction of faculty at Cannon Research Center. Students, project titles and supervising faculty members include Ashley Lakner, PhD in biology, dissertation, "Hepatic Stellate Cell Transdifferentiation," CMC mentor, Laura W. Schrum, PhD; Elizabeth Brandon-Warner, PhD in biology, dissertation, "Effects of Silibinin on Ethanol-Mediated Hepatocellular Carcinoma Progression in Male and Female Mice," CMC mentor, Iain H. McKillop, PhD; Whitney Ellefson, MS in biology, thesis "Effects of Androgenization in Alcohol-Induced Liver Injury," Co-mentors: Laura W. Schrum, PhD (CMC) and Yvette Huet, PhD (UNC-C); Jacob Swet, MS in biology, thesis "The Evaluation of Silica-calcium Phosphate Nanocomposites as a Potential Drug Delivery System for the Use in Treating Hepatocellular Carcinoma." CMC mentor: Iain H. McKillop, PhD; Timothy L. Tickle, PhD in bioinformatics, dissertation "Data Mining the Serous Ovarian Tumor Transcriptiome." Co-mentors: M. Taghi Mostafavi, PhD (UNC-C) and David Tait, MD (CMC).

The Cannon Research Grant Program awarded five grants – two to residents, one to a fellow and two to CMC faculty members.

The CMC-UNC-C Collaborative Grant Program awarded two grants in 2011 to: Laura Schrum, PhD (CMC) and Robin Coger (UNC-C), for the application entitled "Aquaporins: Targeting Water Movement for the Successful Cryopreservation of 3D Liver Systems," and Nury Steuerwald, PhD (CMC) and Mark Clemens, PhD (UNC-C), for the application entitled "Hydrogen Sulfide and miRNA interaction during experimental sepsis in vitro."

Farah Bahrani-Mougeot, PhD, continued to mentor residents, fellows and junior faculty with research projects and grantsmanship for both programs.

Community Benefit

As in years past, Cannon Research Center continued to support CHS philanthropic initiatives. Contributions to the annual CHS Giving Campaign exceeded any previous year's amounts. The success of this initiative was due to the dedication of Michelle O'Sullivan and Cecilia Hurtado-vaca. The Research Center also participated in the annual "Holiday Cheer" fundraiser. Thanks to the hard work of department fundraiser lead, Caren Anderson, collected contributions enabled Cannon Research to "adopt" and fulfill gift requests for two angels from the Salvation Army Angel Program.

Faculty and Staff Active Patents and Trademarks
Faculty and Staff Publications
Faculty and Staff Books and Book Chapters
Faculty and Staff Active Grants and Contracts

Faculty and Staff Patents and Trademarks

Banks D, Bosse M, Meyer M, Meyer R, Phieffer L, Smith K. *Use of doctylsulfocuccinate salts for cleaning petroleum contaminated surfaces.* U.S. Patent 6,140,285. 2000.

Blackwell T, Stanley K. *Mobile Medical Facility.* U.S. Patent 7,794,001. 2005.

Bonkovsky HL, Hou W. *Treating hepatitis C virus infection with metalloporphyrins.* U.S. Patent Application 12/572,651. 2009.

Bonkovsky HL, Hou W. *Treating hepatitis C virus infection with over-expression of microRNA-196.* U.S. Patent Application 12/575,884. 2009.

Bozart-Barnes B, Carl D. *The spiritual direction program.* U.S. Copyright TXu1-719-154. 2011.

Gibbs M, Bosse M, Marx J, Colucciello S, Jacobs D, Ozmar B. *Pelvic splint and associated method.* U.S. Patent 6,503,217. 2003.

Gibbs M, Bosse M, Marx J, Colucciello S, Jacobs D, Ozmar B. *Pelvic splint and associated method.* U.S. Patent 6,793,639. 2004.

Gruber H, Hanley E. *Method for producing human intervertebral disc cells.* U.S. Patent 6,080,579. 2000.

Gruber H, Hanley E. *Method for producing human intervertebral disc cells.* U.S. Patent 7,101,545. 2006.

Gruber H, Hanley E. *Method for producing human intervertebral disc cells for implantation.* U.S. Patent 7,445,776. 2008.

Halberstadt C, Peindl R. *Bioreactor for cell growth and associated methods.* U.S. Patent Application 11/957,747. 2007.

Heffner A, Pearson D. *CODE COOL.* U.S. Service Mark 4,023,801. 2011.

Heniford T, Lincourt A. *System, methods and computer program for determining an optimum hernia repair procedure.* U.S. Patent Application 11/937,837. 2007.

Heniford T, Lincourt A. *Carolinas Comfort Scale: method of evaluating the effects of a prosthetic mesh on the quality of life of a patient who has undergone a hernia repair operation.* U.S. Trademark 3,539,026. 2008.

Horton J. *Sock for the detection of pressure points on diabetic feet.* U.S. Patent 6,796,949. 2004.

Horton J. *Sock for the detection of pressure points on feet.* U.S. Patent 6,918,883. 2005.

Hurst B. *Echogenic needle for transvaginal ultrasound directed reduction of uterine fibroids and an associated method.* U.S. Patent 6,936,048. 2005.

Kline J. *A computer-based device and model for predicting probability of death from thrombosis.* U.S. Patent Application 61/532,349. 2011.

Kline J. *Device and method for collection of exhaled alveolar breath condensate.* U.S. Patent 7,547,285. 2009.

Kline J. *Disposable hand-held device for collection of exhaled breath condensate.* U.S. Patent Application 11/799,176. 2007.

Kline J. *Method and system for diagnosing post-surgical pulmonary vascular occlusions.* U.S. Patent 7,998,084. 2011.

Kline J. *Non-invasive device and method for the diagnosis of pulmonary vascular occlusions.* U.S. Patent 7,445,601. 2008.

Kline J., Hernandez J., Watts J, Albert J. *Utilizing lipopolysaccharide in exhaled breath condensate to diagnose gram negative pneumonia.* U.S. Patent 7,828,741. 2010.

Kline J, Zagorski J. *Method of using carbonic anhydrase to detect hemolysis.* U.S. Patent Application 12/951,540. 2010.

Larrison R, Chase S, Snyder S. *EQUADR.* U.S. Service Mark 4,023,805. 2011.

Lockhart P, Splinter R, Brennan M, Fox P. *Erythema measuring device.* U.S. Patent 6,862,542. 2005.

Lockhart P, Splinter R, Brennan M, Fox P. *Erythema measuring device and method.* U.S. Patent 7,477,925. 2009.

Lu Q. *Antisense oligonucleotide for modulating the expression of human dystrophin exon.* U.S. Patent Application 61/440,603. 2011.

Lu Q. *Pharmaceutical compositions comprising antisense oligonucleotides and method of using same.* U.S. Patent Application 12/800,376. 2010.

Lu Q, Lu Pei. *The use of microwave irradiation for delivery of macromolecules.* U.S. Patent Application 12/712,580. 2009.

Madjarov J. *Method and apparatus for endovascular repair of aortic pathology.* U.S. Patent Application 61/550,066. 2011.

Masters T. *Solution for the preservation of hearts.* U.S. Patent 7,288,551. 2007.

Paul R, Humphrey A, Collier K, Sarafin J, Wilson H, Garvey L. *Code Stemi.* U.S. Copyright TXu1-722-621. 2011.

Peindl R, Boatwright J. *Apparatus and method for measuring abduction strength of a patient's thumb.* U.S. Patent 5,471,996. 1995.

Peindl R, McCarthy M, MacKenzie E. *Apparatus for exercising and measuring strength of patient's limb and adjustable pivot clamp.* U.S. Patent 5,662,591. 1997.

Peindl R. Ramp WK. *Method of manufacturing a cell culture apparatus from inorganic materials.* U.S. Patent 5,635,390. 1997.
Ramp WK, Peindl R. *Bone cement compositions.* U.S. Patent 5,968,999. 1999.
Ramp WK, Peindl R. *Cell culture apparatus having smooth surface for cell growth.* U.S. Patent 5,538,887. 1996.
Raymond RM. *Cardioplegic solution for arresting an organ.* U.S. Patent 5,554,497. 1996.
Raymond RM. *Organ transplant solutions and method for transplanting an organ.* U.S. Patent 5,693,462. 1997.
Saha DC, Ahmed A. *System and method for benchmarking in a research and development environment.* U.S. Patent Application 61/556,416. 2011.
Saha DC. Domenico P. *Treatment of inflammatory conditions and diseases with metal-thiols.* U.S. Patent Application 12/920,787. 2009.
Schrum L, Lakner A. *Treatment of fibrosis using microRNA 19b.* U.S. Patent Application 61/514,764. 2011.
Sun Y, Hanley E. *Compositions and methods for the treatment of musculoskeletal related diseases and disorders using metal ion-citrate analog complexes.* U.S. Patent Application 61/453,401. 2011.
Wang G, Lu Q. *Nitrate ester analogs and their use for the treatment of muscle and muscle related diseases.* U.S. Patent Application. 61/492,650. 2011.
Wang M, Lu Q, Wu B, Lu P. *Amphiphilic cationic polymers and methods of use thereof.* U.S. Patent Application 61/535,798. 2011.

Faculty and Staff Publications

Abu Dayyeh BK, Yang M, Fuchs BC, et al. A functional polymorphism in the epidermal growth factor gene is associated with risk for hepatocellular carcinoma. Gastroenterology 2011;141:141-9.

Ahmed A. Antiviral Treatment of Cytomegalovirus Infection. Infect Disord Drug Targets 2011, June 30 [Epub ahead of print].

Anderson JL, Adams CD, Antman EM, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011;123:e426-579.

Aronow WS, Fleg JL, Pepine CJ, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. Circulation 2011;123:2434-506.

Aronow WS, Fleg JL, Pepine CJ, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. J Am Soc Hypertens 2011;5:259-352.

Belyansky I, Martin TR, Prabhu AS, et al. Poor resident-attending intraoperative communication may compromise patient safety. J Surg Res 2011;171:386-94.

Belyansky I, Tsirline VB, Klima DA, Walters AL, Lincourt AE, Heniford TB. Prospective, comparative study of postoperative quality of life in TEP, TAPP, and modified Lichtenstein repairs. Ann Surg 2011;254:709-15.

Belyansky I, Tsirline VB, Martin TR, et al. The addition of lysostaphin dramatically improves survival, protects porcine biomesh from infection, and improves graft tensile shear strength. J Surg Res 2011;171:409-15.

Belyansky I, Tsirline VB, Montero PN, et al. Lysostaphin-coated mesh prevents staphylococcal infection and significantly improves survival in a contaminated surgical field. Am Surg 2011;77:1025-31.

Besmer DM, Curry JM, Roy LD, et al. Pancreatic ductal adenocarcinoma mice lacking mucin 1 have a profound defect in tumor growth and metastasis. Cancer Res 2011;71:4432-42.

Beuhler MC, Wittler MA, Ford M, Dulaney AR. A controlled evaluation of case clinical effect coding by poison center specialists for detection of WMD scenarios. Clin Toxicol (Phila) 2011;49:684-90.

Bischoff DS, Sakamoto T, Ishida K, Makhijani NS, Gruber HE, Yamaguchi DT. CXC receptor knockout mice: characterization of skeletal features and membranous bone healing in the adult mouse. Bone 2011;48:267-74.

Boppana SB, Ross SA, Shimamura M, et al. Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns. N Engl J Med 2011;364:2111-8.

Brandon-Warner E, Walling TL, Schrum LW, McKillop IH. Chronic ethanol feeding accelerates hepatocellular carcinoma progression in a sex-dependent manner in a mouse model of hepatocarcinogenesis. Alcohol Clin Exp Res 2011, Oct. 21 [Epub ahead of print].

Burris HA, 3rd, Rugo HS, Vukelja SJ, et al. Phase II study of the antibody drug conjugate trastuzumab-DM1 for the treatment of human epidermal growth factor receptor 2 (HER2)-positive breast cancer after prior HER2-directed therapy. J Clin Oncol 2011;29:398-405.

Byrd JF, Agee N, McKillop IH, Sindram D, Martinie JB, Iannitti DA. Colour doppler ultrasonography provides real-time microwave field visualisation in an ex vivo porcine model. HPB (Oxford) 2011;13:400-3.

Byrd JF, Agee N, Nguyen PH, et al. Evaluation of composite mesh for ventral hernia repair. JSLS 2011;15:298-304.

Byrd JF, Agee N, Swan RZ, et al. Evaluation of absorbable and permanent mesh fixation devices: adhesion formation and mechanical strength. Hernia 2011;15:553-8.

Byrne JG, Rezai K, Sanchez JA, et al. Surgical management of endocarditis: the society of thoracic surgeons clinical practice guideline. Ann Thorac Surg 2011;91:2012-9.

Carew JD, Nair G, Andersen PM, et al. Presymptomatic spinal cord neurometabolic findings in SOD1-positive people at risk for familial ALS. Neurology 2011;77:1370-5.

Chan YM, Brown SC, Lu Q. Second international workshop for glycosylation defects in muscular dystrophies, 11-12 November, 2010, Charlotte, USA. Brain Pathol 2011;21:699-704.

Colabianchi N, Maslow AL, Swayampakala K. Features and amenities of school playgrounds: a direct observation study of utilization and physical activity levels outside of school time. Int J Behav Nutr Phys Act 2011;8:32.

Cole I, Glass C, Norton HJ, Tayal V. Ultrasound measurements of the saphenous vein in the pediatric emergency department population with comparison to i.v. catheter size. J Emerg Med 2011, Oct. 4 [Epub ahead of print].

Daul AM, Beuhler MC. Niacin toxicity resulting from urine drug test evasion. J Emerg Med 2011;41:e65-8.

Day SA, Lakner AM, Moore CC, et al. Opioid-like compound exerts anti-fibrotic activity via decreased hepatic stellate cell activation and inflammation. Biochem Pharmacol 2011;81:996-1003.

Di Bisceglie AM, Stoddard AM, Dienstag JL, et al. Excess mortality in patients with advanced chronic hepatitis C treated with long-term peginterferon. Hepatology 2011;53:1100-8.

Dienstag JL, Ghany MG, Morgan TR, et al. A prospective study of the rate of progression in compensated, histologically advanced chronic hepatitis C. Hepatology 2011;54:396-405.

Dulin MF, Tapp H, Smith HA, Urquieta de Hernandez B, Furuseth OJ. A community based participatory approach to improving health in a Hispanic population. Implement Sci 2011;6:38.

El Chaar M, McDeavitt K, Richardson S, Gersin KS, Kuwada TS, Stefanidis D. Does patient compliance with preoperative bariatric office visits affect postoperative excess weight loss? Surg Obes Relat Dis 2011;7:743-8.

Fargnoli AS, Katz MG, Yarnall C, et al. A pharmacokinetic analysis of molecular cardiac surgery with recirculation mediated delivery of betaARKct gene therapy: developing a quantitative definition of the therapeutic window. J Card Fail 2011;17:691-9.

Farley J, Sill MW, Birrer M, et al. Phase II study of cisplatin plus cetuximab in advanced, recurrent, and previously treated cancers of the cervix and evaluation of epidermal growth factor receptor immunohistochemical expression: a Gynecologic Oncology Group study. Gynecol Oncol 2011;121:303-8.

Faulkner MJ, Haley MW, Littmann L. Propofol infusion syndrome with severe and dynamic brugada electrocardiogram but benign clinical outcome. J Cardiovasc Electrophysiol 2011;22:827-8.

Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011;364:1395-406.

Fernandez AR, Studnek JR, Margolis GS, Mac Crawford J, Bentley MA, Marcozzi D. Disaster preparedness of nationally certified emergency medical services professionals. Acad Emerg Med 2011;18:403-12.

Fernando HC, Jaklitsch MT, Walsh GL, et al. The Society of Thoracic Surgeons practice guideline on the prophylaxis and management of atrial fibrillation associated with general thoracic surgery: executive summary. Ann Thorac Surg 2011;92:1144-52.

Fontana RJ, Sanyal AJ, Ghany MG, et al. Development and progression of portal hypertensive gastropathy in patients with chronic hepatitis C. Am J Gastroenterol 2011;106:884-93.

Foureau DM, McKillop IH, Jones CP, Amin A, White RL, Salo JC. Skin tumor responsiveness to interleukin-2 treatment and CD8 Foxp3+ T cell expansion in an immunocompetent mouse model. Cancer Immunol Immunother 2011;60:1347-56.

Freedman ND, Curto TM, Lindsay KL, Wright EC, Sinha R, Everhart JE. Coffee consumption is associated with response to peginterferon and ribavirin therapy in patients with chronic hepatitis C. Gastroenterology 2011;140:1961-9.

Friedlander M, Trimble E, Tinker A, et al. Clinical trials in recurrent ovarian cancer. Int J Gynecol Cancer 2011;21:771-5.

Garrett JS, Studnek JR, Blackwell T, et al. The association between intra-arrest therapeutic hypothermia and return of spontaneous circulation among individuals experiencing out of hospital cardiac arrest. Resuscitation 2011;82:21-5.

Ghaderi I, Vaillancourt M, Sroka G, et al. Evaluation of surgical performance during laparoscopic incisional hernia repair: a multicenter study. Surg Endosc 2011;25:2555-63.

Ghosh S, Ahrens WA, Phatak SU, Hwang S, Schrum LW, Bonkovsky HL. Association of filamin A and vimentin with hepatitis C virus proteins in infected human hepatocytes. J Viral Hepat 2011;18:e568-77.

Giles MF, Albers GW, Amarenco P, et al. Early stroke risk and ABCD2 score performance in tissue- vs time-defined TIA: a multicenter study. Neurology 2011;77:1222-8.

Glickman SW, Lytle BL, Ou FS, et al. Care processes associated with quicker door-in-door-out times for patients with ST-elevation-myocardial infarction requiring transfer: results from a statewide regionalization program. Circ Cardiovasc Qual Outcomes 2011;4:382-8.

Gruber HE, Hoelscher GL, Ingram JA, Bethea S, Zinchenko N, Hanley EN, Jr. Variations in aggrecan localization and gene expression patterns characterize increasing stages of human intervertebral disk degeneration. Exp Mol Pathol 2011;91:534-9.

Gruber HE, Hoelscher GL, Ingram JA, Hanley EN, Jr. Matrix metalloproteinase-26, a novel MMP, is constitutively expressed in the human intervertebral disc in vivo and in vitro. Exp Mol Pathol 2011;92:59-63.

Gruber HE, Ingram JA, Hoelscher GL, Zinchenko N, Norton HJ, Hanley EN, Jr. Constitutive expression of cathepsin K in the human intervertebral disc: new insight into disc extracellular matrix remodeling via cathepsin K and receptor activator of nuclear factor-kappaB ligand. Arthritis Res Ther 2011;13:R140.

Gruber HE, Norris RA, Kern MJ, et al. Periostin is expressed by cells of the human and sand rat intervertebral discs. Biotech Histochem 2011;86:199-206.

Gruber HE, Watts JA, Hoelscher GL, et al. Mitochondrial gene expression in the human annulus: in vivo data from annulus cells and selectively harvested senescent annulus cells. Spine J 2011;11:782-91.

Hammond FM, Davis CS, Whiteside OY, Philbrick P, Hirsch MA. Marital adjustment and stability following traumatic brain injury: a pilot qualitative analysis of spouse perspectives. J Head Trauma Rehabil 2011;26:69-78.

Hanna EM, Norton HJ, Reames MK, Salo JC. Minimally invasive esophagectomy in the community hospital setting. Surg Oncol Clin N Am 2011;20:521-30, ix.

Hicks-Little CA, Peindl RD, Hubbard TJ, et al. Lower extremity joint kinematics during stair climbing in knee osteoarthritis. Med Sci Sports Exerc 2011;43:516-24.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2011; 58:123-210.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: Executive Summary: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011; 124: 2610-42.

Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery. J Am Coll Cardiol 2011.

Hirsch M, Heyn P. Alzheimer disease cognitive rehabilitation: From communication to community. Top Geriatr Rehabil 2011;27:253-6.

Hirsch MA, Iyer SS, Englert D, Sanjak M. Promoting exercise in Parkinson's disease through community-based participatory research. Neurodegener Dis 2011;1:365-77.

Hope WW, Stefanidis D. The status of surgical skills training in the Carolinas: a plea for collaboration. Am Surg 2011;77:948-50.

Hope WW, von der Embse K, Mostafa G, et al. Cardiopulmonary arrest occurring in the radiology department: patient characteristics, incidence, and outcomes. Am Surg 2011;77:273-6.

Hwang SI, Lee YY, Park JO, et al. Effects of a single dose of oral iron on hepcidin concentrations in human urine and serum analyzed by a robust LC-MS/MS method. Clin Chim Acta 2011;412:2241-7.

Ito H, Nussbaum M, Hermiller JB, et al. An integer based risk score for predicting 30-day major adverse cardiac or cerebrovascular events after percutaneous coronary intervention with drug-eluting stents: results from a large prospective multicentre registry, the STENT Group. EuroIntervention 2011;6:942-8.

Jassar AS, Ford PA, Haber HL, et al. Cardiac Surgery in Jehovah's Witness Patients: Ten-Year Experience. Ann Thorac Surg 2011, Oct. 5 [Epub ahead of print].

Johnson T. Imaging in FOCUS initiative. Helping Sanger Heart & Vascular Institute change clinical practice. Cardiology 2011;40:6-7.

Johnson TV, Symanski JD, Patel SR, Rose GA. Improvement in the assessment of diastolic function in a clinical echocardiography laboratory following implementation of a quality improvement initiative. J Am Soc Echocardiogr 2011;24:1169-79.

Jones AE, Puskarich MA. Sepsis-induced tissue hypoperfusion. Crit Care Nurs Clin North Am 2011;23:115-25.

Jones AE, Troyer JL, Kline JA. Cost-effectiveness of an emergency department-based early sepsis resuscitation protocol. Crit Care Med 2011;39:1306-12.

Katz MG, Fargnoli AS, Swain JD, et al. AAV6-BARKct gene delivery mediated by molecular cardiac surgery with recirculating delivery (MCARD) in sheep results in robust gene expression and increased adrenergic reserve. J Thorac Cardiovasc Surg 2011, Dec. 3 [Epub ahead of print].

Katz MG, Fargnoli AS, Tomasulo CE, Pritchette LA, Bridges CR. Model-specific selection of molecular targets for heart failure gene therapy. J Gene Med 2011;13:573-86.

Katz MG, Swain JD, Tomasulo CE, Sumaroka M, Fargnoli A, Bridges CR. Current strategies for myocardial gene delivery. J Mol Cell Cardiol 2011;50:766-76.

Kaufman MD, Lee R, Norton HJ. Course of relapsing-remitting multiple sclerosis before, during and after natalizumab. Mult Scler 2011;17:490-4.

Keller SA, Moore CC, Clemens MG, McKillop IH, Huynh T. Activated protein C restores hepatic microcirculation during sepsis by modulating vasoregulator expression. Shock 2011;36:361-9.

Kercher KW. Adrenalectomy: is volume a surrogate for quality? Ann Surg Oncol 2011;18:2707-8.

Khan JA, Casper M, Asimos AW, et al. Geographic and sociodemographic disparities in drive times to Joint Commission-certified primary stroke centers in North Carolina, South Carolina, and Georgia. Prev Chronic Dis 2011;8:A79.

Kimberlin DW, Whitley RJ, Wan W, et al. Oral acyclovir suppression and neurodevelopment after neonatal herpes. N Engl J Med 2011;365:1284-92.

Klima DA, Brintzenhoff RA, Tsirline VB, et al. Application of subcutaneous talc in hernia repair and wide subcutaneous dissection dramatically reduces seroma formation and postoperative wound complications. Am Surg 2011;77:888-94.

Kline JA, Miller DW. Risk stratification for acute pulmonary embolism. J Natl Compr Canc Netw 2011;9:800-10.

Knowles M, Murphy EH, Dimaio JM, et al. The effects of operative indication and urgency of intervention on patient outcomes after thoracic aortic endografting. J Vasc Surg 2011;53:926-34.

Knowles M, Pellisar T, Murphy EH, et al. In vitro analysis of type II endoleaks and aneurysm sac pressurization on longitudinal stent-graft displacement. J Endovasc Ther 2011;18:601-6.

Kuwada TS, Richardson S, El Chaar M, et al. Insurance-mandated medical programs before bariatric surgery: do good things come to those who wait? Surg Obes Relat Dis 2011;7:526-30.

Lakner AM, Bonkovsky HL, Schrum LW. microRNAs: fad or future of liver disease. World J Gastroenterol 2011;17:2536-42.

Lakner AM, Walling TL, McKillop IH, Schrum LW. Altered aquaporin expression and role in apoptosis during hepatic stellate cell activation. Liver Int 2011;31:42-51.

Lambrecht RW, Sterling RK, Naishadham D, et al. Iron levels in hepatocytes and portal tract cells predict progression and outcomes of patients with advanced chronic hepatitis C. Gastroenterology 2011;140:1490-500 e3.

Lau K, Agee N, McKillop I, et al. Ex vivo evaluation of a new 1.8mm percutaneous microwave antenna using a 2.45GHz system. J Intervent Oncol 2011;3.

Lau KN, Swan RZ, Sindram D, Martinie JB, Iannitti DA. Hepatic tumor ablation: application in a community hospital setting. Surg Oncol Clin N Am 2011;20:455-66, viii.

Lavonas EJ, Ruha AM, Banner W, et al. Unified treatment algorithm for the management of crotaline snakebite in the United States: results of an evidence-informed consensus workshop. BMC Emerg Med 2011;11:2.

Lee YY, McKinney KQ, Ghosh S, et al. Subcellular tissue proteomics of hepatocellular carcinoma for molecular signature discovery. J Proteome Res 2011;10:5070-83.

Li T, Bonkovsky HL, Guo JT. Structural analysis of heme proteins: implications for design and prediction. BMC Struct Biol 2011;11:13.

Lieberman JA, Hammond FM, Barringer TA, et al. Adherence with the National Cholesterol Education Program guidelines in men with chronic spinal cord injury. J Spinal Cord Med 2011;34:28-34.

Lieberman JA, Hammond FM, Barringer TA, et al. Comparison of coronary artery calcification scores and National Cholesterol Education program guidelines for coronary heart disease risk assessment and treatment paradigms in individuals with chronic traumatic spinal cord injury. J Spinal Cord Med 2011;34:233-40.

Littmann L. Pacemaker electrocardiogram with new large negative T waves: what is the cause? J Electrocardiol 2011, June 21 [Epub ahead of print].

Littmann L, Fertman AF. Large T-wave inversion in a patient with a pacemaker. Arch Intern Med 2011;171:1314; discussion 5-6.

Littmann L, Haley MW. Double trouble. Am J Med 2011;124:1025-7.

Littmann L, Tenczer J. Widening spectrum of the J-wave syndromes. J Electrocardiol 2011, Aug. 19 [Epub ahead of print]

Lloyd DM, Lau KN, Welsh F, et al. International multicentre prospective study on microwave ablation of liver tumours: preliminary results. HPB (Oxford) 2011;13:579-85.

Lobdell KW. Value creation in cardiac surgery using the Toyota Production System. Ann Thorac Surg 2011;92:775-6.

Lockhart PB, Hong CH, van Diermen DE. The influence of systemic diseases on the diagnosis of oral diseases: a problem-based approach. Dent Clin North Am 2011;55:15-28.

Lok AS, Everhart JE, Di Bisceglie AM, Kim HY, Hussain M, Morgan TR. Occult and previous hepatitis B virus infection are not associated with hepatocellular carcinoma in United States patients with chronic hepatitis C. Hepatology 2011;54:434-42.

Lok AS, Everhart JE, Wright EC, et al. Maintenance peginterferon therapy and other factors associated with hepatocellular carcinoma in patients with advanced hepatitis C. Gastroenterology 2011;140:840-9; quiz e12.

Lu QL, Yokota T, Takeda S, Garcia L, Muntoni F, Partridge T. The status of exon skipping as a therapeutic approach to duchenne muscular dystrophy. Mol Ther 2011;19:9-15.

Maslow AL, Colabianchi N. Youth physical activity resource use and activity measured by accelerometry. American Journal of Health Behavior 2011;35:219-27.

Maslow AL, Price AE, Sui X, Lee DC, Vuori I, Blair SN. Fitness and adiposity as predictors of functional limitation in adults. J Phys Act Health 2011;8:18-26.

McGaghie WC, Draycott TJ, Dunn WF, Lopez CM, Stefanidis D. Evaluating the impact of simulation on translational patient outcomes. Simul Healthc 2011;6 Suppl:S42-7.

McKinney KQ, Lee YY, Choi HS, et al. Discovery of putative pancreatic cancer biomarkers using subcellular proteomics. J Proteomics 2011;74:79-88.

McWilliams A, Tapp H, Barker J, Dulin M. Cost analysis of the use of emergency departments for primary care services in Charlotte, North Carolina. N C Med J 2011;72:265-71.

Meadows JP, Tumlin JA, Clemens MG, McKillop IH, Evans S. Changes in neutrophil activity following cardiovascular surgery. Open Access Surg 2011;4:1-9.

Mehrab-Mohseni M, Sendi H, Steuerwald N, Ghosh S, Schrum LW, Bonkovsky HL. Legalon-SIL downregulates HCV core and NS5A in human hepatocytes expressing full-length HCV. World J Gastroenterol 2011;17:1694-700.

Mery CM, Lapar DJ, Seckeler MD, et al. Pulmonary artery and conduit reintervention rates after norwood using a right ventricle to pulmonary artery conduit. Ann Thorac Surg 2011;92:1483-9; discussion 9.

Milazi SR, Brooks BR, Mougeot J-L. Enrichment of motor neuron-like cell precursors derived from mouse embryonic stem cells by density gradient centrifugation. Acta Neuropharmacologica 2011;1:16-26.

Mita AC, Papadopoulos K, de Jonge MJ, et al. Erlotinib 'dosing-to-rash': a phase II intrapatient dose escalation and pharmacologic study of erlotinib in previously treated advanced non-small cell lung cancer. Br J Cancer 2011;105:938-44.

Mitchell AM, Jones AE, Tumlin JA, Kline JA. Immediate complications of intravenous contrast for computed tomography imaging in the outpatient setting are rare. Acad Emerg Med 2011;18:1005-9.

Modrall JG, Rosero EB, Leonard D, et al. Clinical and kidney morphologic predictors of outcome for renal artery stenting: data to inform patient selection. J Vasc Surg 2011;53:1282-89; discussion 9-90.

Modrall JG, Timaran CH, Rosero EB, et al. Predictors of outcome for renal artery stenting performed for salvage of renal function. J Vasc Surg 2011;54:1414-21 e1.

Monroe MH, Littmann L. Repetitive QRS axis shift: what is the cause? J Electrocardiol 2011;44:415, 24.

Montero PN, Acker CE, Heniford BT, Stefanidis D. Single incision laparoscopic surgery (SILS) is associated with poorer performance and increased surgeon workload compared with standard laparoscopy. Am Surg 2011;77:73-7.

Montero PN, Stefanidis D, Norton HJ, Gersin K, Kuwada T. Reported excess weight loss after bariatric surgery could vary significantly depending on calculation method: a plea for standardization. Surg Obes Relat Dis 2011;7:531-4.

Moore CC, Lakner AM, Yengo CM, Schrum LW. Nonmuscle myosin II regulates migration but not contraction in rat hepatic stellate cells. World J Hepatol 2011;3:184-97.

Mougeot JL, Bahrani-Mougeot FK, Lockhart PB, Brennan MT. Microarray analyses of oral punch biopsies from acute myeloid leukemia (AML) patients treated with chemotherapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:446-52.

Mougeot JL, Li Z, Price AE, Wright FA, Brooks BR. Microarray analysis of peripheral blood lymphocytes from ALS patients and the SAFE detection of the KEGG ALS pathway. BMC Med Genomics 2011;4:74.

Murphy CM, Hong JJ, Beuhler MC. Anaphylaxis with latrodectus antivenin resulting in cardiac arrest. J Med Toxicol 2011;7:317-21.

Murphy EH, Arko FR. Commentary: A step closer to identifying patients at risk of developing clinically significant type II endoleaks. J Endovasc Ther 2011;18:306-7.

Murphy EH, Dimaio JM, Jessen ME, Arko FR. Technique for branched thoracic stent-graft repair of a chronic type a aortic dissection in a patient with multiple prior sternotomies. J Endovasc Ther 2011;18:359-64.

Nakase-Richardson R, Sherer M, Seel RT, et al. Utility of post-traumatic amnesia in predicting 1-year productivity following traumatic brain injury: comparison of the Russell and Mississippi PTA classification intervals. J Neurol Neurosurg Psychiatry 2011;82:494-9.

Napenas JJ, Hong CH, Kempter E, Brennan MT, Furney SL, Lockhart PB. Selective serotonin reuptake inhibitors and oral bleeding complications after invasive dental treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:463-7.

Napenas JJ, Zakrzewska JM. Diagnosis and management of trigeminal neuropathic pains. Pain Manag 2011;1:353-65.

Naumann RW. The role of the phosphatidylinositol 3-kinase (PI3K) pathway in the development and treatment of uterine cancer. Gynecol Oncol 2011;123:411-20.

Naumann RW, Coleman RL. Management strategies for recurrent platinum-resistant ovarian cancer. Drugs 2011;71:1397-412.

Naunheim KS, Bridges CR, Sade RM. Should a Jehovah's Witness Patient Who Faces Imminent Exsanguination Be Transfused? Ann Thorac Surg 2011;92:1559-64.

Nelson MC, Norton HJ, Greene FL. Breast conservation therapy vs. mastectomy in the community-based setting: can this rate be used as a benchmark for cancer care? Surg Oncol Clin N Am 2011;20:427-37, vii.

Nesbit RM, Horton JM, Littmann L. Myocarditis, pericarditis, and cardiac tamponade associated with Rocky Mountain spotted fever. J Am Coll Cardiol 2011;57:2453.

Nguyen PH, Keller JE, Novitsky YW, Heniford BT, Kercher KW. Laparoscopic approach to adrenalectomy: review of perioperative outcomes in a single center. Am Surg 2011;77:592-6.

Nguyen VQC, Hirsch MA. Use of a policy debate to teach residents about health care reform. J Grad Med Ed 2011;3:376-8.
O'Brien TR, Everhart JE, Morgan TR, et al. An IL28B genotype-based clinical prediction model for treatment of chronic hepatitis C. PLoS One 2011;6:e20904.
O'Bryan JM, Potts JA, Bonkovsky HL, Mathew A, Rothman AL. Extended interferon-alpha therapy accelerates telomere length loss in human peripheral blood T lymphocytes. PLoS One 2011;6:e20922.
Oo ML, Chang SH, Thangada S, et al. Engagement of S1P-degradative mechanisms leads to vascular leak in mice. J Clin Invest 2011; 121:2290-300.
Palilonis MA, Martin TR, Jacobs D, et al. Perceptions of student-observers in the operating room. J Surg Res 2011;170:195-201.
Panov A, Kubalik N, Zinchenko N, Hemendinger R, Dikalov S, Bonkovsky HL. Respiration and ROS production in brain and spinal cord mitochondria of transgenic rats with mutant G93a Cu/Zn-superoxide dismutase gene. Neurobiol Dis 2011;44:53-62.
Panov AV, Kubalik N, Zinchenko N, et al. Metabolic and functional differences between brain and spinal cord mitochondria underlie different predisposition to pathology. Am J Physiol Regul Integr Comp Physiol 2011;300:R844-54.
Pelucio M, Roe G, Fiechtl J, et al. Assessing survey methods and firearm exposure among adolescent emergency department patients. Pediatr Emerg Care 2011;27:500-6.
Petrov M, Malik A, Mead A, Bridges CR, Stedman HH. Gene transfer to muscle from the isolated regional circulation. Methods Mol Biol 2011;709:277-86.
Pokrzywinski R, Secord AA, Havrilesky LJ, et al. Health-related quality of life outcomes of docetaxel/carboplatin combination therapy vs. sequential therapy with docetaxel then carboplatin in patients with relapsed, platinum-sensitive ovarian cancer: Results from a randomized clinical trial. Gynecol Oncol 2011;123:505-10.
Pousis C, De Giorgi C, Mylonas CC, et al. Comparative study of liver vitellogenin gene expression and oocyte yolk accumulation in wild and captive Atlantic bluefin tuna (Thunnus thynnus L.). Anim Reprod Sci 2011;123:98-105.
Puskarich MA, Trzeciak S, Shapiro NI, et al. Association between timing of antibiotic administration and mortality from septic shock in patients treated with a quantitative resuscitation protocol. Crit Care Med 2011;39:2066-71.
Puskarich MA, Trzeciak S, Shapiro NI, Heffner AC, Kline JA, Jones AE. Outcomes of patients undergoing early sepsis resuscitation for cryptic shock compared with overt shock. Resuscitation 2011;82:1289-93.
Rakoski MO, Brown MB, Fontana RJ, et al. Mallory-Denk bodies are associated with outcomes and histologic features in patients with chronic hepatitis C. Clin Gastroenterol Hepatol 2011;9:902-9.
Rashid MU, Gull S, Faisal S, et al. Identification of the deleterious 2080insA BRCA1 mutation in a male renal cell carcinoma patient from a family with multiple cancer diagnoses from Pakistan. Fam Cancer 2011;10:709-12.
Reades R, Studnek JR, Garrett JS, Vandeventer S, Blackwell T. Comparison of first-attempt success between tibial and humeral intraosseous insertions during out-of-hospital cardiac arrest. Prehosp Emerg Care 2011;15:278-81.
Robicsek F. Editorial comment: The Nuss procedure. Eur J Cardiothorac Surg 2011;40:337-8.
Robicsek F. Editorial comment: The Nuss procedure: not so fast! Eur J Cardiothorac Surg 2011;39:159.
Robicsek F. Invited commentary. Ann Thorac Surg 2011;92:641.
Robicsek F, Watts LT. Surgical correction of pectus excavatum. How did we get here? Where are we going? Thorac Cardiovasc Surg 2011; 59:5-14.
Ross SA, Novak Z, Pati S, et al. Mixed infection and strain diversity in congenital cytomegalovirus infection. J Infect Dis 2011;204:1003-7.
Rouleau T, Harrington A, Brennan M, et al. Receipt of dental care and barriers encountered by persons with disabilities. Spec Care Dentist 2011;31:63-7.
Rouleau TS, Shychuk AJ, Kayastha J, Lockhart PB, Nussbaum ML, Brennan MT. A retrospective, cohort study of the prevalence and risk factors of oral burning in patients with dry mouth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:720-5.

Roy LD, Ghosh S, Pathangey LB, Tinder TL, Gruber HE, Mukherjee P. Collagen induced arthritis increases secondary metastasis in MMTV-PyV MT mouse model of mammary cancer. BMC Cancer 2011;11:365.
Roy LD, Sahraei M, Subramani DB, et al. MUC1 enhances invasiveness of pancreatic cancer cells by inducing epithelial to mesenchymal transition. Oncogene 2011;30:1449-59.
Sade RM. Standards for relations of cardiothoracic surgical organizations with industry. Ann Thorac Surg 2011;92:3-8.
Saha DC, Ahmed A, Hanumandla S. Expectation-based efficiency and quality improvements in research administration: multi-institutional case studies. Res Manage Rev 2011;18:1-27.
Saha DC, Williams T. Letter to the Editor: Missing elements in university technology transfer offices hindering technology commercialization. Res Manage Rev 2011;18:xiii-xviii.
Sankar V, Hearnden V, Hull K, et al. Local drug delivery for oral mucosal diseases: challenges and opportunities. Oral Dis 2011;17 Suppl 1:73-84.
Satishkumar R, Sankar S, Yurko Y, et al. Evaluation of the antimicrobial activity of lysostaphin-coated hernia repair meshes. Antimicrob Agents Chemother 2011;55:4379-85.
Schwartzentruber DJ, Lawson DH, Richards JM, et al. gp100 peptide vaccine and interleukin-2 in patients with advanced melanoma. N Engl J Med 2011;364:2119-27.
Seifarth C, Littmann L, Resheq Y, et al. MCS-18, a novel natural plant product prevents autoimmune diabetes. Immunol Lett 2011;139:58-67.
Shroff R, Weaver DJ, Jr., Mitsnefes MM. Cardiovascular complications in children with chronic kidney disease. Nat Rev Nephrol 2011;7:642-9.
Siegel RJ, Biner S, Rafique AM, et al. The acute hemodynamic effects of MitraClip therapy. J Am Coll Cardiol 2011;57:1658-65.
Sindram D, Martin K, Meadows JP, et al. Collagen-elastin ratio predicts burst pressure of arterial seals created using a bipolar vessel sealing device in a porcine model. Surg Endosc 2011;25:2604-12.
Sindram D, Swan RZ, Lau KN, McKillop IH, Iannitti DA, Martinie JB. Real-time three-dimensional guided ultrasound targeting system for microwave ablation of liver tumours: a human pilot study. HPB (Oxford) 2011;13:185-91.
Smith TA, Gatens S, Andres M, Modrall JG, Clagett GP, Arko FR. Hybrid repair of thoracoabdominal aortic aneurysms involving the visceral vessels: comparative analysis between number of vessels reconstructed, conduit, and gender. Ann Vasc Surg 2011;25:64-70.
Sokolov E, Iannitti DA, Schrum LW, McKillop IH. Altered expression and function of regulator of G-protein signaling-17 (RGS17) in hepatocellular carcinoma. Cell Signal 2011;23:1603-10.
Stamou S, Lobdell K. The Obesity Paradox in Cardiac Surgery: Myth or Reality? Ann Thorac Surg 2011;92:1153-4.
Stamou SC, Kouchoukos NT, Hagberg RC, et al. Does the technique of distal anastomosis influence clinical outcomes in acute type A aortic dissection? Interact Cardiovasc Thorac Surg 2011;12:404-8.
Stamou SC, Nussbaum M, Carew JD, et al. Hypoglycemia with intensive insulin therapy after cardiac surgery: predisposing factors and association with mortality. J Thorac Cardiovasc Surg 2011;142:166-73.
Stamou SC, Nussbaum M, Stiegel RM, et al. Effect of body mass index on outcomes after cardiac surgery: is there an obesity paradox? Ann Thorac Surg 2011;91:42-7.
Stanley GA, Murphy EH, Knowles M, et al. Volumetric analysis of type B aortic dissections treated with thoracic endovascular aortic repair. J Vasc Surg 2011;54:985-92; discussion 92.
Stefanidis D, Hope WW, Scott DJ. Robotic suturing on the FLS model possesses construct validity, is less physically demanding, and is favored by more surgeons compared with laparoscopy. Surg Endosc 2011;25:2141-6.
Stefanidis D, Kuwada TS, Gersin KS. The importance of the length of the limbs for gastric bypass patients--an evidence-based review. Obes Surg 2011;21:119-24.
Stefanidis D, Richardson W, Farrell TM, Kohn GP, Augenstein V, Fanelli RD. SAGES guidelines for the surgical treatment of esophageal achalasia. Surg Endosc 2011, Nov. 2 [Epub ahead of print].
Stell LK, Stossel TP. Another dip into the muddy waters of COI. Am J Bioeth 2011;11:49-50.
Stell VH, Flippo-Morton TS, James Norton H, White RL, Jr. Sentinel lymph node biopsy after neo-adjuvant chemotherapy in breast cancer. Breast J 2011;17:71-4.

Stinchcombe TE, Peterman AH, Lee CB, et al. A randomized phase II trial of first-line treatment with gemcitabine, erlotinib, or gemcitabine and erlotinib in elderly patients (age >/=70 years) with stage IIIB/IV non-small cell lung cancer. J Thorac Oncol 2011;6:1569-77.

Stoopler ET, Shirlaw P, Arvind M, et al. An international survey of oral medicine practice: proceedings from the 5th World Workshop in Oral Medicine. Oral Dis 2011;17 Suppl 1:99-104.

Stossel TP, Stell LK. Time to 'walk the walk' about industry ties to enhance health. Nat Med 2011;17:437-8.

Swain JD, Katz MG, White JD, et al. A translatable, closed recirculation system for AAV6 vector-mediated myocardial gene delivery in the large animal. Methods Mol Biol 2011;709:331-54.

Swan RZ, Lau KN, Sindram D, Iannitti DA, Martinie JB. Pancreatic resection in a large tertiary care community-based hospital: building a successful pancreatic surgery program. Surg Oncol Clin N Am 2011;20:487-500, viii.

Tait DL, Blessing JA, Hoffman JS, et al. A phase II study of gemcitabine (gemzar, LY188011) in the treatment of recurrent or persistent endometrial carcinoma: a gynecologic oncology group study. Gynecol Oncol 2011;121:118-21.

Tapp H, Hebert L, Dulin M. Comparative effectiveness of asthma interventions within a practice based research network. BMC Health Serv Res 2011;11:188.

Thompson KJ, Lakner AM, Cross BW, et al. S-adenosyl-L-methionine inhibits collagen secretion in hepatic stellate cells via increased ubiquitination. Liver Int 2011;31:891-901.

Thompson KJ, Lau KN, Johnson S, et al. Leptin inhibits hepatocellular carcinoma proliferation via p38-MAPK-dependent signalling. HPB (Oxford) 2011;13:225-33.

Thompson KJ, McKillop IH, Schrum LW. Targeting collagen expression in alcoholic liver disease. World J Gastroenterol 2011;17:2473-81.

Thornhill MH, Dayer MJ, Forde JM, et al. Impact of the NICE guideline recommending cessation of antibiotic prophylaxis for prevention of infective endocarditis: before and after study. BMJ 2011;342:d2392.

Tian Q, Li T, Hou W, Zheng J, Schrum LW, Bonkovsky HL. Lon peptidase 1 (LONP1)-dependent breakdown of mitochondrial 5-aminolevulinic acid synthase protein by heme in human liver cells. J Biol Chem 2011;286:26424-30.

Vandeventer S, Studnek JR, Garrett JS, Ward SR, Staley K, Blackwell T. The association between ambulance hospital turnaround times and patient acuity, destination hospital, and time of day. Prehosp Emerg Care 2011;15:366-70.

Vedantham K, Swet JH, McKillop IH, El-Ghannam A. Evaluation of a bioresorbable drug delivery system for the treatment of hepatocellular carcinoma. J Biomed Mater Res A 2011, Nov. 21 [Epub ahead of print].

Watts JA, Gellar MA, Fulkerson MB, Kline JA. Pulmonary vascular reserve during experimental pulmonary embolism: Effects of a soluble guanylate cyclase stimulator, BAY 41-8543. Crit Care Med 2011;39:2700-4.

Watts JA, Gellar MA, Stuart L, Obraztsova M, Marchick MR, Kline JA. Effects of angiotensin (1-7) upon right ventricular function in experimental rat pulmonary embolism. Histol Histopathol 2011;26:1287-94.

Watts JA, Lee YY, Gellar MA, Fulkerson MB, Hwang SI, Kline JA. Proteomics of microparticles after experimental pulmonary embolism. Thromb Res 2011, Oct 17 [Epub ahead of print].

Watts JA, Marchick MR, Gellar MA, Kline JA. Up-regulation of arginase II contributes to pulmonary vascular endothelial cell dysfunction during experimental pulmonary embolism. Pulm Pharmacol Ther 2011;24:407-13.

Weekes AJ, Tassone HM, Babcock A, et al. Comparison of serial qualitative and quantitative assessments of caval index and left ventricular systolic function during early fluid resuscitation of hypotensive emergency department patients. Acad Emerg Med 2011;18:912-21.

White JD, Thesier DM, Swain JB, et al. Myocardial gene delivery using molecular cardiac surgery with recombinant adeno-associated virus vectors in vivo. Gene Ther 2011;18:546-52.

White RL, Jr., Amin A. Cancer immunotherapy. Surg Oncol Clin N Am 2011;20:531-54, ix.

White RL, Jr., Ayers GD, Stell VH, et al. Factors Predictive of the Status of Sentinel Lymph Nodes in Melanoma Patients from a Large Multicenter Database. Ann Surg Oncol 2011;18:3593-600.

Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update incorporated into the ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American Academy of Family Physicians, Society for Cardiovascular Angiography and Interventions, and the Society of Thoracic Surgeons. J Am Coll Cardiol 2011;57:e215-367.

Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA Focused Update of the Guidelines for the Management of Patients With Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 Guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation 2011;123:2022-60.

Wright RS, Anderson JL, Adams CD, et al. 2011 ACCF/AHA focused update of the Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction (Updating the 2007 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines developed in collaboration with the American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 2011;57:1920-59.

Wu B, Benrashid E, Lu P, et al. Targeted skipping of human dystrophin exons in transgenic mouse model systemically for antisense drug development. PLoS One 2011;6:e19906.

Wu B, Xiao B, Cloer C, et al. One-year treatment of morpholino antisense oligomer improves skeletal and cardiac muscle functions in dystrophic mdx mice. Mol Ther 2011;19:576-83.

Wynne J, Narveson SY, Littmann L. Cardiorenal syndrome. Heart Lung 2011, July 23 [Epub ahead of print].

Xu X, Zhang Y, Xi L, Bahrani-Mougeot F, Zhang L. Treatment of major laparoscopic bile duct injury: A long-term follow-up result Am Surgeon 2011; 77:1584-88.

Yip-Schneider MT, Doyle CJ, McKillop IH, et al. Alcohol Induces Liver Neoplasia in a Novel Alcohol-Preferring Rat Model. Alcohol Clin Exp Res 2011;35:2216-25.

Yurko Y, McDeavitt K, Martin T, et al. Antibacterial Mesh: A Novel Technique Involving Naturally Occurring Cellular Proteins. Surg Innov 2011, Aug. 25 [Epub ahead of print].

Zamor PJ, Russo MW. Liver function tests and statins. Curr Opin Cardiol 2011;26:338-41.

Zeskind PS, McMurray MS, Garber KA, et al. Development of translational methods in spectral analysis of human infant crying and rat pup ultrasonic vocalizations for early neurobehavioral assessment. Front Psychiatry 2011;2:56.

Faculty and Staff Books and Book Chapters

Belyansky I, Tsirline VB, Klima DA, Heniford BT. Surgical Approach to Umbilical Hernias: Then and Now. In: Hernias: Types, Symptoms and Treatment. Wagner JH, Ed. Hauppauge, New York; Nova Science Publishers, Inc.; 2011.

Boardman LA. Hyperthyroidism due to Graves Disease. In: Case Files: High-Risk Obstetrics. 1st Edition. Toy EET, Fonseca LLF, Ernest JJE. Eds. New York; McGraw-Hill Medical; 2011.

Englund J, Kerns W. Beta-Blockers. In Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 7th Edition; Cline D, Krone RL, Ruize E, Tintinalli JE, Eds. New York; McGraw Hill; 2011:1264-8.

Hays EP, Sullivan DM. Cutaneous Injuries. In: Trauma: A Comprehensive Emergency Medicine Approach. 1st Edition. Legome E, Shockley L, Eds.Cambridge, UK; Cambridge University Press; 2011.

Heniford BT, Martin T. Laparoscopic Staging for Gastrointestinal Cancer. In: Current Surgical Therapy. 10th Edition. Cameron J, Cameron A, Eds. Philadelphia; Elsevier; 2011.

Hong CH, Napenas JJ. Fundamental Skills: Oral Assessment and Dental Hygiene. In: Managing the Oral Effects of Cancer Treatment: Diagnosis and Survivorship. 1st Edition. Pittsburgh; Oncology Nursing Society; 2011.

Jacobs L, Sapers B. Perioperative Evaluation and Management of Neurological Disease. In: Perioperative Medicine. Cohn S, Ed. New York; Springer; 2011:343-360.

Jacobs L, Sapers B. Postoperative Stroke and Seizures. In: Perioperative Medicine. Cohn S, Ed. New York, Springer; 2011: 521-530.

Kemp JJK, Boardman LA. Abnormal Uterine Bleeding. In: 5-minute Consult Clinical Companion to Women's Health. 2nd Edition. New York; Lippincott-Williams and Wilkins; 2011.

Kerns W. Antidotes in Depth: Insulin-Euglycemia. In: Goldfrank's Toxicologic Emergencies. 9th Edition. Nelson LS, Lewin NA, Howland MA, Hoffman RS, Goldfrank LR, Flomenbaum NE, Eds. New York; McGraw Hill; 2011:893-5.

Klima DA, Belyansky I, Tsirline VB, Heniford BT: Spigelian Hernias. In: Hernias: Types, Symptoms and Treatment. Wagner JH, Ed. Hauppauge, New York; Nova Science Publishers, Inc.; 2011.

Naumann RW, Stepp KJ. Complications: Genitourinary Tract Injury During Laparoscopic Surgery. In: Nezhat's Operative Gynecologic Laparoscopy. Nezhat CA, Nezhat F, Nezhat CE, Eds. Cambridge, UK; Cambridge University Press, 2011.

Packman CH. Immune Haemolytic Anaemia. In: Encyclopedia of Life Sciences. Chichester; John Wiley & Sons, Ltd; 2011.

Panov A, Steuerwald NS, Vavilin V, Dambinova S, Bonkovsky HL. Significance of Neuronal Mitochondrial Metabolic Phenotype and Reverse Electron Transport-dependent ROS Production in Pathogenesis of ALS – Role of Neuronal Mitochondrial Metabolic Phenotype in Pathogenesis of ALS. In: Amyotrophic Lateral Sclerosis. Maurer, M, Ed. University Campus STeP Ri; Rijeka, Croatia, 2011.

Petrov M, Malik A, Mead A, Bridges CR, Stedman H. Crossing the Endothelial Barrier: Gene Transfer to Muscle from the Isolated Regional Circulation. In: Methods in Molecular Medicine: Muscle Gene Therapy-Methods and Protocols. Duan, D, Ed. Totwa, NJ: Humana Press; 2011:277-286.

Puskarich MA, Jones, AE. Mitochondrial Function in Septic Shock. In: Yearbook of Intensive Care and Emergency Medicine. Vincent, J.-L. Ed. New York; Springer; 2011.

Rude RK, Gruber HE. Effects of Magnesium Deficiency on Vitamin D Metabolism and Action. In: Vitamin D: Biochemistry, Nutrition, and Roles. 1st Edition. Stackhouse WJ, Ed. New York; Nova Science Publishers, Inc.; 2011: 147-166.

Sanchez PJ, Ahmed A. Toxoplasmosis, Syphilis, Malaria, and Tuberculosis. In: Avery's Diseases of the Newborn, 9th Edition. Taeusch HW, Ballard RA, Gleason CA, Eds. Philadelphia; Elsevier, 2011.

Segel, GB, Packman, CH. Hemolytic Anemias Resulting from Extracellular Factors. In: Nelson Textbook of Pediatrics. 19th Edition. Kliegman RM, Behrman RE, Bonita F, et al, Eds. London; Elsevier; 2011; 1680-1683.

Sparks SE, Escolar DE. Congenital Muscular Dystrophies. In: Handbook of Clinical Neurology: Muscular Dystrophies. Griggs R, Amato AA, Eds. Vol. 101, 3rd series; Philadelphia; Elsevier; 2011:47-79.

Sparks SE, Escolar DE. Congenital Muscular Dystrophies. In: Handbook of Clinical Neurology: Muscular Dystrophies. Griggs R, Amato AA, Eds. Vol. 101, 3rd series. Philadelphia; Elsevier, 2011:47-79.

Stefanidis D, Acker CE. Overview of Skills and Simulation Curricula. In: Simulation Textbook. 1st Edition. Tsuda S, Scott DJ, Jones DB, Eds. Woodbury; Cine-Med; 2011.

Tsirline VB, Belyansky I, Klima DA, Harold KL, Heniford BT. Surgical Approach to Parastomal Hernias. In: Hernias: Types, Symptoms and Treatment. Wagner JH, Ed. Hauppauge, NY; Nova Science Publishers, Inc.; 2011.

Usadi RS. Abnormal Menstrual Bleeding in Hyperandrogenic Ovulatory Dysfunction. In: Disorders of Menstruation. 1st Edition. Marshburn P, Hurst B, Eds. Oxford, UK; Blackwell Publishing; 2011:62-85.

Faculty and Staff Active Grants and Contracts

Ahmed, Amina. A Phase III Randomized, Placebo-Controlled Blinded Investigation of Six Weeks vs. Six Months of Oral Valganciclovir Therapy in Infants with Symptomatic Congenital Cytomegalovirus Infection. University of Alabama at Birmingham-NIH/NIAID.

Ahmed, Amina. A Study of the Effectiveness and Tolerability of Weekly Rifapentine/Isoniazid for Three Months vs. Daily Isoniazid for Nine Months for the Treatment of Latent Tuberculosis Infection. North Carolina Department of Health and Human Services.

Ahmed, Amina. Natural History of Novel and Seasonal Influenza. NIH/NIAID.

Ahmed, Amina. Safety and Efficacy of Varicella Zoster Immune Globulin (Human) (VariZIG™) in Patients At-Risk of Varicella Infection. Cangene Corporation, Winnipeg.

Ahmed, Amina. The Natural History of CMV-related Hearing Loss and the Feasibility of CMV Screening as Adjunct to Hearing Screening in the Newborns. University of Alabama at Birmingham-NIH.

Alden, Michael, Peindl, Richard, Hirsch, Mark, Davies, M.A. Device for dynamic measurement of muscle spasticity in the ankle. UNC Charlotte Student Research Experience for Undergraduates (SREU) Grant Program.

Asimos, Amin. Evaluation of a Statewide EMS Stroke Routing Protocol on Hospital Bypass and Thrombolytic Treatment for Acute Stroke Patients. EMF/Genentech Regionalization and Stroke Care Grant Program.

Bailey, Dwight. Pediatric Traumatic Brain Injury Consortium Hypothermia. NINDS.

Bockenek, William. Humanitarian Use Device: Synapse NeuRx Diaphragm Pacing System. Synapse Biomedical.

Bonkovsky, Herbert, Mckillop Iain. Characterization of Leucocyte Infiltrates in Liver Biopsies of Subjects with Drug-Induced Liver Injury (DILI). Duke University-NIH.

Bridges, Charles. Translational studies in Heart Failure Gene Therapy. University of Pennsylvania-NIH.

Dranove, Jason. Limited Access Protocol for the Use of Cral Cisapride in the Treatment of Pediatric Patients with Refractory Gastroesophageal Reflux Disease and other Gastrointestinal Motility Disorders. Ortho-McNeil Janssen Scientific Affairs, LLC.

Dulin, Michael. A Community Participatory Approach to Improving Health in a Hispanic Population. NIH/NCMHD.

Dulin, Michael. A Transdisiplinary Approach to the Evaluation of Social Determinants of Health. NIH-NCMHD.

Dulin, Michael. Comparative Effectiveness of Asthma Interventions within an AHRQ PBRN. AHRQ.

Fleischli, James. Tibiofemoral contact mechanics in radial meniscus tears before and after surgical repair in the human cadaveric knee. Arthrex, Inc.

Foureau, David. Rebalancing the immune system following interleukin-2 therapy against melanoma. Freedland Foundation.

Gopalareddy, Vani. A Comparative Study of the Antiviral Efficacy and Safety of Entecavir Vs. Placebo in Pediatric Subjects with Chronic Hepatitis B Virus (HBV) Infection who are HBeAg-Positive. Bristol-Myers Squibb Company.

Gruber, Helen. Biomembrane formation in the rat femur segmental defect model: Assessment of osteogenic potential, gene expression and bone formation. AO Research Institute.

Gruber, Helen. Does cytokine stimulation of PAPP-A regulate IGF Bioavailability in the Disc? AO Research Foundation.

Gruber, Helen. Expression of the osteoarthritis-associated protein asporin in severely degenerated human intervertebral disc cells. Smith Arthritis Fund, Mecklenburg County Medical Society.

Hammond, Flora. A Multi-Center, Parallel-Group, Randomized, Double-Blind, Placebo-Controlled Trial of Amantadine Hydrochloride in the Treatment of Chronic TBI Irritability and Aggression; A Replication Study . NIH/NIDRR.

Hammond, Flora. Improving Outcomes in Acute Rehabilitation for Traumatic Brain Injury through Practice Based Evidence and Individualized Planning for the First Year following Acute Rehabilitation.

Hammond, Flora. Improving Spinal Cord Injury Rehabilitation Outcomes. NIH/NIDRR.

Hammond, Flora. TBI Model Systems Project. NIDRR.

Hanna, Erin. Molecular analysis of bacterial species in an animal model of alcohol induced, infected necrotizing pancreatitis – A pilot study. Cannon Grant Program.

Heffner, Alan. Fluid Management, EM Rap Audio Discussion. NIH.

Heniford, B. Todd. A Five-Year Follow-Up, Post Implantation, Multi-Center, International Hernia Mesh Registry. Ethicon, Inc.

Heniford, B. Todd. A Multi-Year Follow-Up, Post-Implantation, Multi-Center, FlexHD, Mesh Database. MTF.

Heniford, B. Todd. Antimicrobial Coating of Synthetic Mesh for Prevention of Infections after Abdominal Wall Hernia Repairs. American Hernia Society/LifeCell.

Heniford, B. Todd. Candidate Gene Analysis of Recurrent Hernia Formation Susceptibility. W.L. Gore.

Heniford, B. Todd. Evaluation of a Novel Antibacterial Mesh in Clean and Contaminated Fields. John and Reba Shipp Endowment.

Heniford, B. Todd. Evaluation of a Novel Technique Utilizing Biologic and Synthetic Mesh. MTF.

Heniford, B. Todd. Evaluation of NG-TSM Mesh in a Chronic Pig Model. Ethicon, Inc.

Heniford, B. Todd. Evaluation of the Tensile Strength, Adhesion Profile, and Histology of (XenMatriX) in a Rodent Model. Davol.

Heniford, B. Todd. Histological Evaluation of Bio-A Mesh at Different Time Periods and Comparison to Biologic Prosthesis. W.L. Gore.

Heniford, B. Todd. MIS Fellowship Grant. Ethicon, Inc.

Heniford, B. Todd. MIS Fellowship Grant. W.L. Gore.

Heniford, BT. Surgical Fellows Fundamental Conference. W.L. Gore.

Higgins, Robert. A Phase II Evaluation of AMG 102 in the Treatment of Persistent or Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Carcinoma. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Belinostat and Carboplatin in the Treatment of Recurrent or Persistent Platinum-Resistant Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Brivanib in the Treatment of Persistent or Recurrent Carcinoma of the Cervix. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Cediranib in the Treatment of Recurrent or Persistent Endometrial Carcinoma. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Ixabepilone in the Treatment of Recurrent or Persistent Carcinosarcoma of the Uterus. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Pazopanib In the Treatment of Recurrent or Persistent Carcinosarcoma of the Uterus. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of SU11248 Sunitinib Malate in the Treatment of Persistent or Recurrent Clear Cell Ovarian Carcinoma. NCI, GOG.

Higgins, Robert. A Phase II Evaluation of Temsirolimus in Combination with Carboplatin and Paclitaxel Followed by Temsirolimus Consolidation as First-Line Therapy in the Treatment of Stage III-IV Clear Cell Carcinoma of the Ovary. NCI, GOG.

Higgins, Robert. A Phase II Randomized, Double-Blinded Evaluation of Oral Everolimus Plus Bevacizumab Vs. Oral Placebo Plus Bevacizumab In the Treatment of Recurrent or Persistent or Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. NCI, GOG.

Higgins, Robert. A Phase II Randomized, Double-Blind Trial of a Polyvalent Vaccine-KLH Conjugate + OPT-821 vs. OPT-821 in Patients with Epithelial Ovarian, Fallopian Tube, or Peritoneal Cancer Who Are in Second or Third Complete Remission. NCI, GOG.

Higgins, Robert. A Phase II Study of Paclitaxel for Ovarian Stromal Tumors as Second-Line Therapy. NCI, GOG.

Higgins, Robert. A Phase II trial of AMG 386, a Selective Angiopoiten ½ Neutralizing Peptibody, in Patients with Persistent or Recurrent Carcinoma of the Endometrium. NCI, GOG.

Higgins, Robert. A Phase II Trial of NCI-Supplied Agent: Bevacizumab for Recurrent Sex Cord-Stromal Tumors of the Ovary. NCI, GOG.

Higgins, Robert. A Phase II Trial of Radiation Therapy and Weekly Cisplatin Chemotherapy for the Treatment of Locally-Advanced Squamous Cell Carcinoma of the Vulva. NCI, GOG.

Higgins, Robert. A Phase III Randomized, Controlled Clinical Trial of Carboplatin and Paclitaxel Alone or in Combination with Bevacizumab followed by Bevacizumab and Secondary Cytoreductive Surgery in Platinum-Sensitive Recurrent Ovarian, Peritoneal Primary and Fallopian Tube Cancer. NCI, GOG.

Higgins, Robert. A Phase III Trial of Adjuvant Chemotherapy Following Chemoradiation as Primary Treatment for Locally Advanced Cervical Cancer Compared to Chemoradiation Alone: THE OUTBACK TRIAL. NCI, GOG.

Higgins, Robert. A Phase III Trial of Carboplatin and Paclitaxel Plus Placebo Vs. Carboplatin and Paclitaxel Plus Concurrent Bevacizumab Followed by Placebo, Vs. Carboplatin and Paclitaxel Plus Concurrent and Extended Bevacizumab, in Women with Newly Diagnosed, Previously Untreated, Stage III or IV, Epithelial Ovarian, Primary Peritoneal or Fallopian Tube Cancer NCI-Supplied Agent(S): Bevacizumab/Placebo. NCI, GOG.

Higgins, Robert. A Phase III Trial of Pelvic Radiation Therapy vs. Vaginal Cuff Brachytherapy Followed by Paclitaxel/Carboplatin Chemotherapy in Patients with High Risk, Early Stage Endometrial Carcinoma. NCI, GOG.

Higgins, Robert. A Randomized Phase II Trial of Paclitaxel and Carboplatin vs. Bleomycin, Etoposide, and Cisplatin for Newly Diagnosed Advanced Stage and Recurrent Chemonaive Sex Cord-Stromal Tumors of the Ovary. NCI, GOG.

Higgins, Robert. A Randomized Phase II Trial of Temsirolimus or the Combination of Hormonal Therapy Plus Temsirolimus in Women with Advanced, Persistent, or Recurrent Endometrial Carcinoma. NCI, GOG.

Higgins, Robert. A Randomized Phase III Evaluation of Docetaxel and Gemcitabine (NSC plus G-CSF with Bevacizumab vs. Docetaxel and Gemcitabine plus G-CSF with Placebo in the Treatment of Recurrent or Advanced Leiomyosarcoma of the Uterus, NCI-supplied Agent: Bevacizumab. NCI, GOG.

Higgins, Robert. A Randomized Phase III Trial of Cisplatin and Tumor Volume Directed Irradiation Followed by Carboplatin and Paclitaxel vs. Carboplatin and Paclitaxel for Optimally Debulked, Advanced Endometrial Carcinoma. NCI, GOG.

Higgins, Robert. A Randomized Phase III Trial of Cisplatin Plus Paclitaxel With and Without NCI-Supplied Bevacizumab Vs. the Non-Platinum Doublet, Topotecan Plus Paclitaxel, With and Without NCI-Supplied Bevacizumab, in Stage IVB, Recurrent or Persistent Carcinoma of the Cervix. NCI, GOG.

Higgins, Robert. A Randomized Phase III Trial of Every 3-Weeks Paclitaxel Vs. Dose Dense Weekly Paclitaxel in Combination with Carboplatin With or Without Concurrent and Consolidation Bevacizumab in the Treatment of Primary Stage II, III, or IV Epithelial Ovarian, Peritoneal or Fallopian Tube Cancer. NCI, GOG.

Higgins, Robert. A Randomized Phase III Trial of Paclitaxel Plus Carboplatin Vs. Ifosfamide Plus Paclitaxel in Chemotherapy-Naïve Patients with Newly Diagnosed Stage I-IV or Persistent or Recurrent Carcinosarcoma (Mixed Mesodermal Tumors) of the Uterus or Ovary. NCI, GOG.

Higgins, Robert. Chemotherapy Toxicity in Elderly Women with Ovarian, Primary Peritoneal or Fallopian Tube Cancer. NCI, GOG.

Higgins, Robert. GOG 0252: A Phase III Clinical Trial of Bevacizumab With IV Vs. IP Chemotherapy in Ovarian, Fallopian Tube, and Primary Peritoneal Carcinoma NCI-Supplied Agent(s): Bevacizumab. NCI, GOG.

Higgins, Robert. Pelvic Mass Study to Develop Serum Proteomic Profiles (Signatures) for Epithelial Ovarian Cancer Diagnosis and Prognosis. NCI, GOG.

Higgins, Robert. Phase II Evaluation of Paclitaxel and Carboplatin in the Treatment of Carcinosarcoma of the Uterus. NCI, GOG.

Higgins, Robert. Phase III Randomized Study of Concurrent Chemotherapy and Pelvic Radiation Therapy with or Without Adjuvant Chemotherapy in High-Risk Patients with Early-Stage Cervical Carcinoma Following Radical Hysterectomy. NCI, GOG.

Higgins, Robert. Prospective Study of Risk-Reducing Salpingo-oophorectomy and Longitudinal CA-125 Screening Among Women at Increased Genetic Risk of Ovarian Cancer. NCI, GOG.

Higgins, Robert. Prospective Study of Risk-Reducing Salpingo-oophorectomy (RRSO) and Longitudinal CA-125 Screening Among Women at Increased Genetic Risk of Ovarian Cancer: Extended Follow-up of Select GOG-0199 Study Participants. NCI, GOG.

Higgins, Robert. Quality of Life and Care Needs in Patients with Persistent or Recurrent Platinum-Resistant Ovarian, Fallopian Tube, and Peritoneal Cancer. NCI, GOG.

Higgins, Robert. Randomized Phase III Clinical Trial of Adjuvant Radiation Vs. Chemoradiation in Intermediate Risk, Stage I/IIA Cervical Cancer Treated with Initial Radical Hysterectomy and Pelvic Lymphadenectomy. NCI, GOG.

Higgins, Robert. Randomized Phase III Trial of Doxorubicin/Cisplatin/ Paclitaxel and G-CSF Vs. Carboplatin/Paclitaxel in Patients with Stage III & IV or Recurrent Endometrial Cancer. NCI, GOG.

Higgins, Robert. Utility of Preoperative FDG-PET/CT Scanning to Detect Retroperitoneal Lymph Node Metastasis in Patients with Locoregionally Advanced Carcinoma of the Cervix and High Risk Endometrial Cancer. NCI, GOG.

Higgins, RV. A Three Arm Randomized Phase II Study of Paclitaxel/Carboplatin/Bevacizumab, Paclitaxel/Carboplatin/Temsirolimus and Ixabepilone/Carboplatin/Bevacizumab as Initial therapy for Measurable Stage III or IVA, Stage IVB, or Recurrent Endometrial Cancer. NCI, GOG.

Hirsch Mark A. Carolinas ParkinsonNet Intervention: Strengthening the Infrastructure for People with Parkinson Disease to Exercise in Community-based Settings and Boosting the Quality of Expertise Among Allied Health Care Professionals. Park Foundation.

Hirsch, Mark A. Power over Parkinson's: The Experience of Participating in Exercise for Persons with Idiopathic Parkinson's Disease. Duke Foundation.

Hirsch, Mark A. Voting Empowerment Study Among Persons with TBI. Recovery Act Administrative Supplement. NIH/NICHD.

Hou, Weihong. Pilot Study of Matrine for Treatment of Chronic Hepatitis C in Murine Model. Cannon Research Grants Program.

Houchin, Lisa. IncrelexTM (meca sermin [rDNA origin] injection) Growth Forum Database - IGFD Registry: A Patient Registry for Monitoring Long-term Safety and Efficacy of IncrelexTM. Tercica, Inc.

Jackson, J.B., Sims, Stephen., Peindl, Richard, Montijo, Harvey, Scannell, Brian. Effect of Tip-Apex Distance on Screw Cutout: TFN vs DHS, Synthes USA.

Kline, Jeff. Impact of a Decision Aid on Patient Participation in Decision Making and Resource Use in Low Risk Chest Pain Patients: A Randomized Trial. Foundation for Informed Medical Decision Making.

Kline, Jeff. Outpatient Treatment of Pulmonary Embolism. NIH/NHLBI.

Kline, Jeff. Quantitative Pretest Probability to Reduce Cardiopulmonary Imaging in Low Risk Patients with Chest Pain. AHRQ.

Kline, Jeff. Randomized Trial of Tenecteplase to Treat Submassive Pulmonary Embolism. Genentech.

Kueser, Thomas. A Phase 2b/3, Multi-Center Randomized, Double-Blind, Placebo Controlled Trial to Evaluate the Safety and Efficacy of Staphylococcal Sepsis. Biosynexus, Incorporated.

Lakner, Ashley. miR 19b: Novel Regulator of HSC-mediated Hepatic Fibrosis. Cannon Research Grants Program.

Li, Ting. Heme Homeostasis and Nuclear Receptor Signaling in HSC. Cannon Research Grants Program.

Lieberman, Jesse. Dietary Patterns and Their Relationship to Cardiovascular Disease Risk Factors in Individuals with Chronic Spinal Cord Injury. NIH-NIDRR.

Lofton, La Tanya. Comparison of HP011-101 to Standard Care in the Management of Stage I-II Pressure Ulcers in Subjects with Traumatic Spinal Cord Injury. Healthpoint Biotherapeutics.

Lu, Qi. Antisense Therapy for DMD-Optimization and toxicology of AON for Exon 45 Skipping 2009-2013. NIH/NINDS.

Lu, Qi. Antisense Therapy for Duchenne Muscular Dystrophy. Morpholino Antisense Oligonucleotide and Systemic Delivery. Department of Defense.

Lu, Qi. Pediatric Toxicity and Efficacy in Long-term Systemic Treatment with Anti-sense Drug. Eunice Kennedy Shriver National Institute of Child Health & Human Development, NIH/NINDS.

Lu, Qi. Screening and Selection of Antisense Oligonucleotide for Skipping Human Dystrophin Exon in Human Myoblasts, hDMD Mice and in patient derived cells. Cure Duchenne.

Lu, Qi, Hoffman, E. Center for Research Translation of Systemic Exon-skipping in Muscular Dystrophy. NIH/NIAMS.

Massengill, Susan. Assessing and Implementing Transition to Adult Care in Children with CKD. MWPNC.

Massengill, Susan. Chronic Kidney Disease in Children. Johns Hopkins/NIH.

Massengill, Susan. Novel Therapies for Resistant FSGS. NIH-NIDDKD.

Massengill, Susan. PROMIS Pediatrics: Longitudinal Validation & Linking Pediatric & Adult Item Banks. UNC-CH.

McKillop, Iain. Development of bioceramic scaffolds for Use in Hepatocellular Carcinoma Chemotherapy. North Carolina Biotechnology Center – NCBC-MCG.

McKillop, Iain. Effect of Alcohol on Hepatocellular Carcinoma Progression in vivo. NIH/NIAAA.

Murphy, Christine, Kerns, W. The Efficacy of Methylene Blue in Treating Toxin Induced Shock. John Marx Research Foundation Award.

Nelson, Teresita. A Single-Dose, Phase 1b, Multicenter, Open-Label Study to Assess the Pharmacokinetics, Safety and Tolerability, and Pharmacodynamics of Tizanidine at 4 Different Oral Dose Levels in Pediatric Subjects 2 to 16 Years Old With Mild to Moderate Spasticity Due. Acorda Therapeutics, Inc.

Nguyen, Vu. A Prospective Multi-Center Study of the SPR System for the Treatment of Post-Stroke Shoulder Pain. NDI Medical.

Patel, Niraj. A Pharmacokinetic/Pharmacodynamic and Safety Evaluation of Investigational Intravenous Peramivir in with Influenza Disease (CASG 117). NIH-NIAID.

Patel, Niraj. Subcutaneous IgG Replacement Therapy is Effective and Safe in a Child Less Than 2 Years of Age. CSL BEHRING.

Peindl, Richard, Lee, Charles, Jacobs, David. Purchase of a Bose 3200 ElectroForce materials testing system, UNC Office of Research and Sponsored Programs Equipment Grant.

Pineiro, Victor. A Multi-Center, Double-Blind, Randomized, Placebo-controlled, Parallel Group, Withdrawal Study to Evaluate the Safety and Efficacy of Delayed- Release Rabeprazole in 1 to 11 Month Old Pediatric Subjects with Symptomatic/Erosive Gastroesophageal Reflux Disease. Johnson & Johnson Pharmaceutical Research & Dev., LLC.

Price, David E. Diagnostic Accuracy of Electrocardiography and Echocardiography for Detection of Cardiovascular Abnormalities in Pre-Participation Screenings of High School Athletes. American Medical Society for Sports Medicine.

Puskarich, Michael. L-Carnitine Administration in Early Sepsis. Post-Doctoral Fellow Grant. American Heart Association.

Raj, Vishwa. Home Compression Evaluation: At Home Evaluation of Two Pneumatic Compression Devices in the Treatment of Lower Extremity Lymphedema. Tactile Systems Technology, Inc.

Ruffolo, Michael. Construction of ankle dorsiflexion measurement devices for use in Botox Pilon study. Winkler Foundation.

Stefanidis Dimitrios. A Secondary Task for Measuring Laparoscopic Skill. AHRQ.

Schrum, Laura. Aquaporins: Targeting Water Movement for the Successful Cryopreservation of 3D liver systems. CMC-UNC-C Collaborative Grants Program.

Schrum, Laura. NFkB-mediated Collagen Regulation by SAMe in HSCs. NIH/NIAAA.

Sindram, David. McKillop, Iain. Role of Obesity and Alcohol in Hepatocellular Carcinoma Development and Progression. Society of American Gastrointestinal and Endoscopic Surgery (SAGES).

Sparks, Susan. Clinical Trial of CoEnzyme Q10 and Lisinopril in Muscular Dystrophies. University of Pittsburgh, DOD.

Sparks, Susan. CMC Pediatric Neuromuscular Clinical Data Registry. National Greek Orthodox Ladies Philoptochos Society, Inc. National Children's Medical Fund.

Sparks, Susan. Comparative Study of Clinical Endpoints in DMD: HHM vs. CQMS. Muscular Dystrophy Association, Children's National Medical Center, Washington, DC.

Sparks, Susan. Improved Diagnosis and Clinical Assessment of Limb-Girdle Muscular Dystrophy. Muscular Dystrophy Association.

Sparks, Susan. Longitudinal Assessment and Genetic Understanding of Limb-Girdle Muscular Dystrophy. Muscular Dystrophy Association.

Sparks, Susan. Lysosomal Storage Disease Registry. Genzyme.

Sparks, Susan. MPSVI Clinical Surveillance. BioMarin Pharmaceuticals.

Starman, James. A Biomechanical Comparison of Strength and Stiffness Profiles in Hybrid 4.5 mm Plating Constructs and a Far Cortical Locking Plate Construct. Winkler Foundation.

Stefanidis Dimitrios. Establishing National Performance Benchmarks for General Surgery Residents. Collaborative Grant of the Association for Surgical Education and the Association of Program Directors in Surgery.

Stefanidis Dimitrios. Feasibility and Value of a Procedural Workshop for Surgery Residents Based on Phase II of the APDS/ ACS National Skills Curriculum. Ethicon Endosurgery.

Stefanidis Dimitrios. Proving the Value of Motion Metrics for the Acquisition of Laparoscopic Skill. Society of American Gastrointestinal and Endoscopic Surgeons.

Sullivan, D. Matthew. A Pilot Study of the Indigenous Microbiota of the Skin in Patients with Methicillin Resistant Staphylococcus Aureus Skin Abscesses. Cannon Research Grant Program.

Sullivan, D. Matthew. Prevalence and Risk Factors for Community-Associated Clostridium difficil-Associated Disease Among Patients in the Emergency Department. CDC/UCLA-Olive View.

Sullivan, D. Matthew. Prevalence of Nasal and Non-Nasal Staphylococcus Aureus Colonization among Emergency Department Patients with Skin Infections and Other Presenting Complaints. CDC/UCLA-Olive View.

Sullivan, D. Matthew. Utilization of Emergency Departments for Possible Exposure to Biological Weapons. CDC/UCLA-Olive View.

Sun, Yubo. Determine and compare the calcifying potential of OA chondrocytes and meniscal cells. Smith Arthritis Fund, Mecklenburg County Medical Society.

Sun, Yubo. Develop Disease Modifying Drugs and Identify Key Disease Candidate Genes of Osteoarthritis, North Carolina Biotechnology Center.

Usadi, Rebecca. Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation. NIH/ NICHD, RMN.

Usadi, Rebecca. Pregnancy in Polycystic Ovary Syndrome II (PPCOS II): A 25-week Double-blind Randomized Trial of Clomiphene Citrate and Letrozole for the Treatment of Infertility in Women with Polycystic Ovary Syndrome. NIH/NICHD, RMN.

Usadi, Rebecca. Registry of Pregnancies Conceived following Exposure to Ovulation Stimulation Medications. NIH/NICHD, RMN.

Wang, Ming Xing. Amphiphilic Polymer Modified PMO for Treating Duchenne Muscular Dystrophy by Exon-skipping. North Carolina Biotechnology Center.

Weaver, Jack Jr. An Open-Label, Multi-Center Clinical Trial of Eculizumab in Pediatric Patients with Atypical Hemolytic-Uremic Syndrome (aHUS). Alexion Pharmaceuticals.

Weaver, Jack Jr. Genome Wide Association Study of Childhood Onset Idiopathic Nephrotic Syndrome. Duke University.

Weaver, Jack Jr. Genotype as a Predictor of Mycophenolate Mofetil Related Complications in Pediatric Transplant Recipients. No Sponsor.

White, Richard. Interleukin-2 Research at Blumenthal Cancer Center within the Melanoma and Immunotherapy Program. Purple Promise Foundation.

Wu, Xioahua. Enhancing Laminin Binding to Rat Muscular dystrophies. Muscular Dystrophy Association.

Wu, Xioahua. HTS for Enhanced Alpha Dstroglycan. NIHNIMH.

Zeskind, Philip S. Neurobiological and Behavioral Consequences of Cocaine use in Mother/infant Dyads. University of North Carolina – Chapel Hill and Yale University. NIH-NIDA.

Carolinas Medical Center

www.carolinasmedicalcenter.org

Cannon Research Center | 1000 Blythe Blvd. | Charlotte, NC 28203