

# Kids Connection

a monthly newsletter from MUSC Children's Hospital



February 2007

## Letter from the Chair

*Dear faculty, Children's Hospital staff and friends,*

Dr. Paul Darden will be heading our effort to obtain a Child Health Research Career Development Award (K12) grant. This is an educational grant that will provide training for basic science-oriented clinicians. It will function similarly to the program developed in the Academic Generalist Program through our clinical masters that helps to develop clinical trialists.

In recent years, we have put together a team of scientists in the Darby Children's Research Institute (DCRI) who do basic science research and train our fellows and junior faculty how to develop funded programs. Our success has been greatly enhanced by the recruitment and expansion of several programs.

We have a number of superb mentors who have helped us to develop the research careers of our faculty. The two premier groups who have provided help in mentoring junior faculty over the years have been Dr. Inderjit Singh and Dr. Bruce Hollis.

Inderjit Singh, PhD, began his pediatric research career at Johns Hopkins under the mentorship of Dr. Hugo Moser, the preeminent clinician working on understanding Adrenoleukodystrophy. During his work with Dr. Moser, Dr. Singh discovered that rather than a mitochondrial defect, this severe debilitating illness was the result of a peroxisomal enzyme defect. Dr. Singh has been working in our department of pediatrics since 1984 and has built a nationally recognized program in neuroprotection and metabolism. He is a winner of the Javitz Award, an award given to honor an investigator who has had continuous R01 funding and who has the best grant that year in neuroscience.

Dr. Bruce Hollis attended Ohio State University, received his PhD from University of Guelph in Ontario, Canada. He completed a postdoctoral fellowship at Case Western Reserve. Dr. Hollis has been a leader in the development of assays to measure hormones that regulate bone formation and turnover. In recent years, he has developed a strong collaboration with Dr. Carol Wagner, allowing them to define the needs of vitamin D in neonates and pregnant mothers. These studies have provided about \$5 million in grant funding.

Dr. Singh has been actively working with faculty to develop programs of tissue protection. He worked with neonatologist Doe Jenkins, MD, to develop a program of neuroprotection of the brain in the fetuses of mothers with chorioamnionitis. This work builds upon Dr. Singh's work in neuroinflammation in Adrenoleukodystrophy and multiple sclerosis treatment. In both of these conditions, improved function was demonstrated in patients receiving statins (usually used for lowering cholesterol, but now are being used to reduce inflammation).



**L. Lyndon Key, MD**  
Professor and Chairman  
Department of Pediatrics

You may have heard commercials from Pfizer suggesting that their statin reduces inflammation. The beginning of this understanding was developed in the neuroscience program at MUSC. MUSC has used this information in developing an RO1 grant from the FDA with Steven Willi, MD, of the Children's Hospital of Philadelphia (CHOP). Dr. Willi was a faculty member at MUSC until 2004 and is now the director of the diabetes program at CHOP.

Dr. Singh is also helping Dr. Maryellen Cavalier to develop a new strategy for reducing vascular disease by blocking adhesion proteins in Sickle Cell Disease for which South Carolina has one of the highest rates of disease per capita in the nation.

Dr. Sakamuri Reddy was our first major recruit to the DCRI and is an accomplished mentor, working with Dr. Rimon Youssef, a fellow in pediatric endocrinology. He has multiple R01s and will be a strong part of mentoring individuals who are working with me, Dr. William Ries, and Dr. Madyastha in developing laboratory skills to investigate questions of basic bone biology.

In putting together the Child Health Research Career Development Award, we will need to commit resources to develop and augment the number of trainees. To this end, we will commit in year one of the program, a position that will be funded by our department. This departmental commitment will guarantee two years of funding for the first scholar and an additional position for our program while we are building up to the maximum number of trainees that will be slated for grants under the K12 program. If funded this would allow us to have two trainees in year one of the grant, providing up to a total of three trainees.

The department of pediatrics has already committed a major amount of funding to creating the DCRI. The goal of this institute is to provide investigators the laboratory space and equipment to develop basic research programs that will lead to new cures in the most important disease in children. The K12 grant would allow us to begin recruiting and training young clinicians who have completed their fellowship training and who will turn basic science into clinical miracles. This will help us to recruit from a larger pool of clinical fellows whose career plans include laboratory research. This new direction will be led by Dr. Inderjit Singh and Dr. Paul Darden and as program directors. Dr. Bernie Maria, executive director of the DCRI, will be the recruiter of mentors and mentees to make this program work. This is a bold initiative, but should help every fellowship program and field of work in the department where basic science is the basis for developing cures.

We will be contacting many of you who are already involved in mentoring. In the past, space was the new frontier for pediatrics. Today, the new frontier is knowledge and accomplishment.

*Sincerely,*

L. Lyndon Key, MD  
Chair, Department of Pediatrics

## Pediatric Cardiology: Research efforts going strong

The pediatric cardiology department is pushing forward in the field, and that means strengthening and expanding its research efforts.

The program combines all aspects of taking care of and treating patients with congenital heart disease, says Dr. Philip Saul, director of the Division of Pediatric Cardiology.

"We do all patient care, and part of that is our clinical research program," says Dr. Saul. "We have a dedicated faculty who all spend at least some of their time doing research."

The clinical faculty in the division is unique. "They're all relatively young, and all have the same belief that in order to push forward in the field, more of what we do needs to be driven by evidence-based research," says Dr. Saul.

Because there are relatively few patients with each form of congenital heart disease at any one medical center, the Division actively participates in multi-center trials, studies that involve multiple hospitals. "One way we do that is through a grant funded by the NIH," says Dr. Saul.

MUSC's pediatric cardiology division is one of eight nationwide chosen to participate in the Pediatric Heart Research Network, a group of hospitals in the United States and Canada that conduct clinical research studies in children with congenital or acquired heart disease. The network sets protocol, enrolls patients and ensures that all the centers are conducting the same studies.

"We often recruit the highest number of patients, even though we're one of the smaller centers in the network," explains Dr. Saul. "We make sure all our eligible patients get into the studies, because we know it's both good for the patients and good for the field."

There are also dozens of research protocols being conducted in the Division that are focused just on patients at MUSC, including diagnostic, therapeutic and review studies. The division's basic research efforts are channeled into understanding the development of the heart.

"If we can understand how the heart is formed, we have a better idea of how to fix it using the body's own system to manipulate the heart tissue," says Dr. Saul.

"For instance, if there's a hole in a heart, we can close it by using a catheter-delivered device or surgery. But in the future, we want to determine how to turn on the gene that controls heart tissue and have the hole close on its own," suggests Dr. Saul.

This is the focus of the Division's newest investigator, Dr. Kyu-ho Lee, a researcher with a valuable combination of clinical and basic science research training (see below).

Stem cell work is an important aspect of Dr. Lee and his colleagues' research. Investigators are examining ways to use adult stem cells, rather than sutures, patches or devices, to repair heart tissue.

Investigator Dieter Haemmerich is also working on technologies to modify heart tissue using ablation, refining and developing new techniques using

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### New recruit strengthens research efforts

The unique chance to work in a pediatric cardiology department but also with a group of skilled and collaborative basic investigators focused on disease-related, developmental cardiovascular biology is what lured Dr. Kyu-Ho Lee to the Darby Children's Research Institute.

"This was a rare opportunity for me, because I'm clinically trained but also have a strong basic science training and interest," says the young recruit, who first worked with Dr. Saul at Boston Children's Hospital. He holds a joint appointment in Pediatric Cardiology and Cell Biology and Anatomy.

"It's always been my goal to be a scientific researcher; and to be involved in discovery. MUSC's resources and the Cardiovascular Biology Developmental Center (CDBC), led by Dr. Roger Markwald (also head of the Department of Cell Biology and Anatomy), were a big draw," explains Dr. Lee.

His recruitment is facilitated by the NIH's renewal of a large program project grant that provides continuing funding for the expansion of the SC Center of Biomedical Research Excellence (COBRE), and for the development of young investigators like him. This is the second, five-year renewal for the grant.

Impressed with the growth at MUSC and the focus on translational research, Dr. Lee joined DCRI and CDBC in June. "It was a good match between my training and interests, and what's being accomplished at MUSC," he says.

Dr. Lee is already finding many avenues for collaboration with fellow MUSC researchers. "Heart development is complex; it's bigger than any one investigator's effort," he notes, explaining that he aims to be part of an expanding dialogue between the Pediatric Cardiology and Cell Biology departments.

"The hope is that together, between our scientific efforts and our understanding of the outcomes, we can all begin to have insight into what causes certain types of congenital heart disease, and provide new tools for its treatment."

Dr. Lee says he and his wife, Dr. Kimberly Gronsman Lee, who was recruited as associate professor in Neonatology at MUSC, fell in love with Charleston and look forward to being a part of its friendly and vibrant community.

## Letter from the Medical Director



**J. Philip Saul, MD**  
Medical Director  
Director, Pediatric Cardiology

In addition to serving as medical director, I am also the director of pediatric cardiology at the Children's Hospital. Consequently, this month's e-newsletter highlights an area near and dear to my heart – research in children's heart disease. In pediatric cardiology, as with all of our pediatric subspecialties, we recognize and value the tripartite role of an academic medical practice: patient care, teaching and research. Patient care is our first priority from both a divisional and individual standpoint. We try to ease the stress of the patients and their families by delivering timely and excellent care.

Our second priority is to educate our students and trainees. We provide excellent training programs and expect the very best from our students, the next generation of practicing physicians, educators, and scientists. Finally, that leads us to our third critical practice – research. Research is an extremely important priority for future care of our patients and for the field of pediatric cardiology. As the feature story highlights, our research goals are achieved in three different ways. One is to integrate clinical research projects into our daily patient care activities so our patients have access to exciting medical advances and new options for treatment. The second is to foster research by supporting key faculty members such as Dr. Lee, an extremely well trained pediatrician who was recruited to conduct basic research in the Darby Children's Research Institute. The final and ultimate aim of our efforts is translational research. Translational research brings advances from the laboratory to the bedside – it translates research into clinical care. Tim McQuinn, a laboratory scientist and pediatric cardiology clinician sets a wonderful standard of excellence in translational research. In conclusion, research has many components and is an integral part of the academic medical practice at MUSC. Research makes it possible to practice the very best medicine.

## Update from the Administrator



**John Sanders, MHA**  
Administrator  
MUSC Children's Hospital

### *Ronald McDonald House Expands*

The Ronald McDonald House (RMH) has become a second home for many of the families we serve at the Children's Hospital. A substantial amount of effort has been put into the expansion of the facilities of the RMH. Prior to the renovations, most of the families were those who had children in our ICUs – these were the more critical cases. In fact, more than 900 families were regrettably denied the opportunity to stay at the RMH in 2006 due to the lack of room availability.

Today, the RMH is able to accept twice the number of families with children in all of our service areas. We realize that nobody wants to have their children in the hospital but for those who do have a child with a serious illness, the RMH provides a warm and safe environment that while staying close to their loved ones. It allows families to find comfort in normal routines such as cooking dinner, doing laundry or just hanging out together like they would at home.

We are so grateful to have a strong relationship with the Ronald McDonald House and their amazing team members. The RMH faculty understands the high level of stress the families are dealing with and they do their best to be as supportive and considerate as possible. The staff and the child-friendly facility create a unique home-away-from-home environment and we appreciate all they do. RMH is an integral part of children's care in the Charleston area and we look forward to continuing our work together to better serve our patients and families.

<< *RESEARCH*, from previous page

radiofrequency energy and cryo-energy to freeze or heat small areas of the heart, destroying the tissue responsible for heart rhythm abnormalities.

“Our real goal is to translate these research findings into the clinical environment,” says Dr. Saul. “We want to make enough progress in the lab that we can then use those successes to develop new therapies that will help patients.”

That's associate professor and researcher Dr. Tim McQuinn's job. “He's bringing discoveries from the basic science lab into the clinical

environment,” explains Dr. Saul.

Currently Dr. McQuinn is examining heart inflammation that results from cardiac surgery and the use of a heart-lung bypass machine. “He's found that the inflammatory reaction of the heart muscle is severe, and an excellent target for special anti-inflammatory agents,” says Dr. Saul.

Dr. McQuinn is also developing a new heart valve with no moving parts that may be applicable to both children with congenital heart disease and adults with acquired heart valve problems.

## Children's Research Institute News Brief



**Bernard L. Maria, MD, MBA**  
Executive Director  
Darby Children's  
Research Inst.



**Inderjit Singh, PhD**  
Scientific Director  
Darby Children's  
Research Inst.

### *2nd Anniversary for DCRI*

We will soon celebrate the 2nd Anniversary for the Charles P. Darby Children's Research Institute (DCRI). The DCRI and its dedicated investigators have proven to be incredibly productive over the last two years, and we are very proud of the work being done. Each day, there are new developments taking place and successful collaborations being established. The DCRI continues to attract new scientists including Dr. Bell in Renal Biology, Dr. Lee in Cardiobiology, and Dr. Swaja in Bioengineering, among others in 2006-2007.

On March 1, 2007, the DCRI invites you to learn about new discoveries in basic biology and in translational and clinical sciences that impact our children's health.

The Celebration will begin with an **Open House and Poster Session** from 2 - 4p.m., on the 2nd floor DCRI/BSB Lobby. Refreshments will be provided and investigators will be present by their posters on DCRI Floors 2 through 6. Last year, more than 150 people from several colleges, departments and the Children's Hospital attended the celebration and we expect the 2nd DCRI Birthday Celebration to attract an even large community of researchers, health professional, and trainees.

Immediately following the **Open House and Poster Session**, we will have a scientific presentation by Dr. Michael V. Johnston, an esteemed research scientist at Kennedy Krieger Institute and professor of neurology and pediatrics at the Johns Hopkins University School of Medicine. Dr. Johnston will deliver his first talk entitled Clinical Disorders of Brain Plasticity at 4 p.m. in BSB 402. The regularly scheduled MCBP Seminar Series has listed Dr. Johnston as the speaker for that day. The presentation is open to all and we encourage all staff members to attend.



**Dr. Michael V. Johnston**  
Kennedy Krieger Institute

On Friday March 2, Dr. Johnston will deliver his second talk entitled *Neonatal Encephalopathy* (8 a.m., SEI 8th Floor Auditorium). A mini-reception will follow. Please come and enjoy great celebration!

Visit [www.kennedykrieger.org/kki\\_staff\\_intro.jsp?pid=10](http://www.kennedykrieger.org/kki_staff_intro.jsp?pid=10) for more information on Dr. Mike Johnston.

## Evidence-Based Tip



**Laura Cousineau, MLS**  
MUSC Library  
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### *Diagnosis: How good is this test?*

Usually, when we use the word “diagnosis,” we are referring to the process of making a diagnosis or performing a differential diagnosis. In Evidence-Based Medicine, however, when we pose a diagnosis question, we want to know how well a particular test does in telling us if our patient does or does not have a certain condition.

Diagnostic studies give us information that tells us how well the test does, compared to “the truth,” as represented by the “gold standard.” Bandolier’s EBM Glossary defines gold

standard as “A method, procedure or measurement that is widely accepted as being the best available.” For example, a recent study at Vanderbilt University Medical Center compared the rapid flu test (influenza rapid antigen detection) to culture and reverse-transcription polymerase chain reaction. Two important percentages result from this comparison: sensitivity and specificity.

In this study, the sensitivity tells us how many of the patients who had a positive culture (the gold standard) tested positive on the rapid flu test. Out of 41 children detected by the gold standard, 26 tested positive on the rapid test. Dividing 26 by 41, we get a sensitivity of 63 percent. The specificity tells us how many of the patients who had a negative culture (the gold standard) had a negative result on the rapid flu test. Out of the 229 negatives from the gold standard, 223 children had a negative rapid test. Dividing 223 by 229, we get a specificity of 97 percent.

Sensitivity tells us how many people with the disease will have a positive diagnostic test, and specificity tells us how many people without the disease will have a negative diagnostic test. So these numbers can give us a feel for how good a test is. However, they do NOT give us the likelihood that a patient does or does not have the disease. For the rapid flu test, even though this test has a high specificity, its low sensitivity can decrease its usefulness in ruling in the disease.

To make these numbers more useful, we need to do a little more math. We need to calculate the likelihood ratio.

**Next month:** The Likelihood Ratio: what are the odds that my patient has the disease I am testing for?

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