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Jefferson Translations

Volume 2, No. 1, Fall/Winter 2004-2005

for friends and colleagues of the Department of Medicine at Jefferson Medical College

Heart Failure Center Meets Critical Need

Jefferson's Heart Failure Center, established in 2003, came into existence at an opportune time. Paul Mather, MD, Director of the Advanced Heart Failure and Cardiac Transplant Center and Associate Professor of Medicine, notes

that "heart failure is the only disease that is growing as the population ages." Eighty percent of people over 65 have some form of heart failure, and there are 550,000 new cases a year in the U.S. As many as 287,000 die from the disease annually, and it accounts for 7 percent of all U.S. healthcare costs.

In addition to saving lives of patients who have suffered heart attacks, physicians at the new Jefferson center also seek to reduce the injury

that creates or triggers the attacks in the first place. "Heart failure treatment has changed significantly over the past 20 years," explains Dr. Mather, who joined Jefferson from Temple University in early 2004. He notes that while the approach formerly targeted patients' symptoms, it now seeks to identify the underlying causes. "We have shifted to a model that is both hemodynamic (symptom-based) and neurohormonal. We try to fool the body's compensatory mechanism to retard the progress of the disease."

While there are already four other heart transplant centers in Philadelphia, Dr. Mather emphasizes the need for another program in the region, to respond to the number of patients with heart failure, which is growing exponentially. "At present, centers must routinely turn away a majority of patients," he says. "This program fills a niche within the Jefferson medical healthcare system to address advanced heart failure, which provides a comprehensive, cutting-edge approach to the disease process."

Jefferson's program is a "fresh, aggressive new program built on a foundation of extensive experience," says Dr. Mather.

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From the Chairman



This issue of *Translations* highlights a number of individuals and teams that represent the very

best Jefferson has to offer in terms of research, clinical care, and education. The new Advanced Heart Failure Center is thriving under the leadership of Dr. Paul Mather, which makes the Jefferson Heart Institute even more comprehensive. The Center for Translational Medicine continues its cutting-edge research with the expertise of Dr. Andrea Eckhart, who runs the Eugene Feiner Laboratory for Vascular Biology and Thrombosis.

I am proud to showcase in this issue the accomplishments of our faculty, many of whom were recognized this year — some by Dean Nasca for their efforts in education and mentoring, and others by the National Institutes of Health with new R01 grants. This issue also profiles the contributions of the divisions of Gastroenterology and Hepatology; Critical Care, Pulmonary, Allergic, and Immunologic Diseases; and Clinical Pharmacology.

Finally, I would like to express my gratitude to the many individuals, foundations, and organizations who have supported the Department of Medicine during the past fiscal year. Their contributions continue to be critical as we strive to bring exceptional research and clinical care to the Philadelphia region.

Arthur M. Feldman, MD, PhD
Magee Professor of Medicine and
Chairman of the Department



Jefferson's Heart Failure Center faculty and staff (front, left to right): Kim Phillips; Patricia Gray; Sharon Rubin, MD; Lisa Wus; Michelle Munday; Sharon Millinghausen; Theresa Pondok, MD; and Paul Mather, MD; (back) Jill Reynolds; Kimberly Evans; Barbara Ebert, CRNP; Heather Miller, RN, MSN; Natalie Pierson, RN, BSN; Rebecca O'Shea; Anne Canny, RN, MSN; and David Whellan, MD, MHS

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Eckhart Contributes Cutting-Edge Research

Andrea Eckhart, PhD, Associate Professor of Medicine, was one of the original faculty members to join the department's progressive research initiative, the Center for Translational Medicine, directed by Walter Koch, PhD. She has always had an interest in understanding the cause of diseases — particularly hypertension and atherosclerosis. A move to the U.S. from her native Canada provided her with the opportunity to explore these interests.



After completing her PhD at the University of North Carolina in cardiovascular physiology, she joined Dr. Koch's lab at Duke University as a postdoctoral fellow in 1997. She was subsequently hired at Duke University as a faculty member in 2000.

Andrea Eckhart, PhD, directs the Eugene Feiner Laboratory for Vascular Biology and Thrombosis

One of the things that appealed to Dr. Eckhart about the Center for Translational Medicine is that it is very collaborative, which she sees as unique to Jefferson. "The center strives to expand research efforts by taking advantage of the expertise available within the entire community," she says. Dr. Eckhart also notes that the center's labs are not islands that operate distinctly. "This is a cooperative environment," she explains. "Our sharing encourages much more efficient use of precious government funding and donations."

Dr. Eckhart explains that although the center is still expanding, the labs, such as the one she runs — the Eugene Feiner Laboratory for Vascular Biology and Thrombosis — are already doing research funded by the NIH. Also in her lab are three technicians, Charles Druckman, Elizabeth Mandel, and Troy Wilkins, and two post-docs, Drs. Rui-Hai Zhou, MD, and David Harris, PhD. She consults regularly with Geno Merli, MD, in Internal Medicine and Howard Weitz, MD, in Cardiology to explore possible research her lab could undertake that would directly incorporate their clinical observations.

Dr. Eckhart's research interests are in the area of hypertension. Her focus is on understanding how receptors — the proteins that help to establish blood pressure by binding hormones including epinephrine — change their signaling in vascular smooth muscle under disease conditions. "Antihypertensive therapeutic strategies are currently inadequate to decrease high blood pressure in a significant proportion of patients suffering from this disease," she says. Dr. Eckhart's lab has already developed a method to decrease blood pressure using a novel inhibitor of certain receptor pathways important in causing vasoconstriction. It is currently being studied in animal models of the disease, but it is hoped that strategies like this will soon be assessed in clinical trials. These trials will hopefully lead to the development of new antihypertensive drugs and methods of treatment for the disease.

"Here at the Center we are eager to contribute to improved patient care through the development of novel therapeutic strategies," Eckhart says. Her research, begun at the laboratory bench, will eventually transition to the bedside, providing enhanced and state-of-the-art care for patients at Jefferson.

Faculty News

Medical Faculty Garners New NIH Grants

During the first half of 2004, 12 Jefferson Department of Medicine faculty members were awarded grants from the National Institutes of Health. Awards vary in length from one to five years.

In the division of Infectious Diseases and Environmental Medicine, **Roger Pomerantz, MD**, Division Director, received a new R01 for HIV/AIDS Intraviral Reverse Transcription and Virucides. Also within the division, Associate Professor **Hui Zhang, PhD**, received a new R01 for Cytidine Deaminase and HIV-1 Replication; Assistant Professor **Phyllis Flomenberg, MD**, received a new R21 for Human T Cell Responses to Vaccinia Vaccine; and Professor **Lance Simpson, PhD**, received a

new-NIAID Contract for Pharmacokinetic Studies on Botulinum Toxin.

In the Center for Translational Medicine, **Walter Koch, PhD**, Director of the center, was awarded an R01 competitive renewal for Targeting betaARK1 in Heart Failure. **Andrea Eckhart, PhD**, Associate Professor, was awarded a new R01 for Transgenic Targeting of Vascular G Protein Signaling. (See the profile on Dr. Eckhart above.)

In the division of Hematology, **Barbara Schick, PhD**, Professor, received a new R21 for Deletion of Serglycin Proteoglycan Gene in Mice.

In Cardiology, **Paul Mather, MD**, Associate Professor of Medicine, received a subcontract for a new NIH-funded clinical trial in Genetic Modulation of Left

Ventricular Recovery. (See more about Dr. Mather's work in the cover story.)

In the division of Endocrinology, Diabetes, and Metabolic Diseases, Division Director **Barry Goldstein, MD, PhD**, received a new R01 for Adiponectin: Vascular Responses and Signaling Mechanisms.

In Rheumatology, Division Director **Sergio Jimenez, MD**, received a Competing Renewal T32 for Training in Molecular Rheumatology and Orthopedics.

Bruce Boman, MD, PhD, Director of the division of Medical Genetics, received a planning grant award for AP4 Center for Studies on Hereditary Colorectal Cancer. Also in Medical Genetics, Professor **Ronald Myers, PhD**, received a new R21 for Tailored Messaging in Colorectal Cancer Screening.

Jefferson's Hepatology and Liver Transplant Program Achieves Success

The one-year survival rate for the 24 primary patients who have had liver transplants at Jefferson since June 4, 2003, has been 100 percent. This is up from 92.5 percent for the 35 primary patients in 2003 and 2004. The standard across the country is currently 85 percent.

Victor Navarro, MD, is the Director of Jefferson's Hepatology and Liver Transplant Program, which oversees the clinical care of transplant patients. Dr. Navarro, who joined the Jefferson faculty in January of 2002, and Stephen Herrine, MD, Associate Director, were joined this July by medical hepatology fellow Simona Rossi, MD, who will become part of the full-time faculty in 2005.

Dr. Navarro's team of hepatologists is part of Jefferson's division of Gastroenterology and Hepatology, creating a multifaceted clinical and training program. His group oversees the training of a clinical nurse practitioner, fellows, and residents in liver disease.

Since Dr. Navarro's arrival, the liver research program has expanded to include a wide array of investigations, such as clinical drug trials as well as studies in transplantation, drug safety, sociological and epidemiological hepatitis C research, and new molecular approaches to the diagnosis of liver cancer. His group's

research has been presented at several recent national meetings.

Drs. Navarro and Herrine see all referrals of patients for liver transplantation, following a structured procedure that evaluates the risks and needs for surgery, as well as psychosocial and other patient issues. Working with Karen Pine, RN, the pre-transplant coordinator — named "Transplant Coordinator of the Year" by the Delaware Valley Chapter of the American Liver Foundation — and transplant social worker Joan Tannebaum, MSW, the medical staff works hand in hand with surgeons Ignazio Marino, MD, and Cataldo Doria, MD, who take a greater role following the operation. Natalie Fraser, RN, is the program's post-transplant coordinator. The program will soon expand from two to three nurse coordinators.

The transplant program has grown to over 150 patients awaiting the procedure. Jefferson receives referrals from throughout New Jersey, Delaware, and Pennsylvania. "The hospital led the way in expediting the process of patient evaluation, which was reduced from between six and nine months to as quick as one month," says Dr. Navarro. "While the number of transplants has been consistent, the outcomes have improved significantly, thanks to our procedures and Dr. Marino's team of gifted surgeons."

The program has also implemented innovative management protocols, including treatment of hepatitis C both before and after surgery as well as transplantation in HIV-positive individuals with liver failure. It has also begun a multi-disciplinary approach to liver tumors — a common complication in patients with cirrhosis. Dr. Navarro is confident that the commitment of his team will translate into continued success for the program and its patients.



Jefferson's liver transplant team, from left to right (front): Simona Rossi, MD; Joan Tannebaum, MSW; and Victor Navarro, MD; (back): Timothy Weimer, RN; Karen Pine, RN; Natalie Fraser, RN; Cataldo Doria, MD; and Carlo Ramirez, MD

Heart Failure Center

Continued from page 1

The center stresses interpersonal patient care and a multidisciplinary approach that integrates science, health, psycho-social and social work to create an optimum environment for each patient's success. New 1,200-square-foot facilities have been built at Jefferson's Heart Institute at 10th and Chestnut streets.



Paul Mather, MD, directs the Jefferson Heart Failure Center

The Advanced Heart Failure Center will work closely with another innovative program in the Department: The Center for Translational Medicine, which seeks to bring state-of-the-art research "from the bench to the bedside." Dr. Mather explains that, for cardiology research, center director Walter Koch, PhD, and his team "are the bench, and we are the bedside."

Dr. Mather himself has been involved in some 600 transplants over a decade. He is joined by two new heart failure cardiologists: Sharon Rubin, MD, who comes from Temple University, has eight years' experience, and has been involved in some 300 transplants; and David Whellan, MD, MHS, a former Duke faculty member. Heart Failure coordinators Anne Canny, RN, MSN, and Natalie

Pierson, RN, BSN, joined the program in April 2004, and transplant nurse Barbara Ebert, CRNP, came on August 1 as coordinator for the Heart Failure program, to assist with dietary issues, social work needs, and any related kidney and liver problems. For heart transplants, the Heart Failure Center teams with the surgical transplant team in the division of Cardiothoracic Surgery.

The Cardiac Transplant Center received government transplant approval on June 30, 2004. The first transplant patient was listed in November 2004, and the results of the first cardiac transplant at Jefferson will be reported shortly. "I am honored to play a role in Jefferson's ever-expanding commitment to the best in cardiac care," says Dr. Mather.

New Faculty Recruit in Endoscopic Research

Jefferson's interventional endoscopy program has expanded with the addition of David Loren, MD. Dr. Loren became Assistant Professor of Medicine in the division of Gastroenterology and Hepatology (GI) after completing an advanced endoscopy fellowship at Jefferson in June 2003. As a fellow, Dr. Loren was mentored by Thomas Kowalski, MD, Jefferson's Medical Director of Gastrointestinal Endoscopy, who is a nationally recognized leader in advanced endoscopy and pancreatic disease.

As a unit, Jefferson's is the busiest academic endoscopy program on the East Coast, and one of the top five in the country, performing more than 15,000 procedures annually. "This clinical volume allows for the opportunity to train fellows in procedures that are complex and relatively uncommon," Dr. Loren explains. During his fellowship he gained experience in all aspects of endoscopy, in literally hundreds of procedures.

Dr. Loren joins the faculty as a member of the pancreaticobiliary service and has been named Director of Endoscopic Research in the Digestive Disease Division of Thomas Jefferson University Hospital. His clinical and research interests focus on endoscopic approaches to GI oncology, endoscopic management of pancreatic diseases, and endoscopic outcomes research. His collaborations with Barry Goldberg, MD, Professor of Radiology, investigate novel applications of endoscopic ultrasound in gastrointestinal cancers.

Dr. Loren is currently pursuing his master's degree in Human Investigation and Clinical Pharmacology through Jefferson's NIH K30 program (see the article on p. 5). As a clinical investigator, Dr. Loren has established a relationship with Bruce Boman, MD, PhD, Director of the division of Medical Genetics, to explore the management of patients who are at increased risk for certain kinds of hereditary cancer. Dr. Loren is also the module leader for a section on hereditary GI cancer at Jefferson Medical College.



Assistant Professor David Loren, MD, joins the Jefferson endoscopy program

"The NIH has called for a nationwide mandate to improve the quality of GI endoscopic research, and endoscopic outcomes and utilization in particular," says Dr. Loren, who notes that this effort was led by Sidney Cohen, MD, Professor of Medicine and Director of Research Programs in GI at Jefferson. "I have been reaching out to the many strengths at Jefferson to help develop an endoscopic program that will be a leader in research and clinical care, both locally and nationally," he says. "I feel extremely fortunate to be a member of such an experienced team of distinguished colleagues."

Critical Care, Pulmonary, Allergic, and Immunologic Diseases

Taking a Closer Look at Asthma



James Zangrilli, MD, does asthma research in the Pulmonary Division

"Asthma is a disease affecting 15 million Americans, it places a huge burden on our health system, and we don't know what causes it," says James Zangrilli, MD, Assistant Professor of Medicine in the division of Critical Care, Pulmonary, Allergic, and Immunologic Diseases. He is also director of the Ambulatory Care

Clinic and the Pulmonary/Critical Care Fellowship Training Program. Dr. Zangrilli's specialty is asthma and airways inflammation, and he studies the cell biology that is particular to these ailments.

Over the last two decades, research has focused on a specific kind of inflammation, caused by certain cells: T helper lymphocytes and eosinophils. While most asthma research focuses on recruitment and management of those cells, Dr. Zangrilli focuses on the resolution of the inflammation process — what physiological mechanisms the body might use to reduce the inflammation altogether. "The theory of persistent asthma is that it is caused by the failure of those mechanisms," he explains.

Research at Jefferson has established a human model in which a tiny amount of antigen (such as ragweed) is placed in a small segment of the subject's lung; this creates a localized miniature asthma

attack. "The beauty of the model," says Dr. Zangrilli, "is that we can observe the inflammation process over time; we can harvest airway cells, tissues, and secretions at baseline during periods of initiation, maintenance, and resolution." This creates a picture of asthma over a certain period — whether it is 24 hours or 2 weeks.

Dr. Zangrilli's future research will seek to characterize the cells and specific activities involved in this process over time and will include a murine model in collaboration with Angela Haczku, MD, PhD, at the University of Pennsylvania.

Another initiative of Dr. Zangrilli's this year is to establish a comprehensive outpatient asthma center at Jefferson. "We hope this will serve as an important resource for the Jefferson community and the Philadelphia area, and as a center for referrals and second opinions as well as providing an anchor for clinical research trials."

Gifts to the Department of Medicine, January 1, 2003–June 30, 2004

The department gratefully acknowledges the support of our donors.

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Education/Clinical Pharmacology

Master's Program Targets Human Investigation

In 1999 Jefferson created a training program offering a Master's of Science in Pharmacology focusing on Human Investigation, which capitalizes on Jefferson's extensive patient-oriented research programs—more than 300 each year. Scott Waldman, MD, PhD, FCP, the Samuel M. V. Hamilton Professor and Director of the division of Clinical Pharmacology, directs the program.

The program seeks to train clinicians and doctoral-level candidates in how to provide patient-based and patient-oriented research. The two-year program trains no more than 10 individuals each year, integrating coursework with practical, mentored research experience.

One of close to 50 or so programs in the United States at academic medical centers, the program was created in part due to an NIH response to the dwindling numbers of clinicians who can engage in translational and clinical research that uses humans. These include dentists, psychologists, and other healthcare providers.

"The paradigms that exist for research are specialized for the examination of molecules and cells," says Dr. Waldman. "With patients, there are a number of ethical and privacy considerations, and the technique required is much more restricted than what is available to a laboratory researcher."

Within a clinic, this can require administering drugs, interacting with patients to obtain blood and/or tissue samples, or epidemiological research with a population of patients. Program trainees learn how to work with patients and how to ask answerable questions, "which can avoid wasting resources," says Dr. Waldman.

The curriculum requires both 40 hours of class time as well as participatory experiences including conferences, seminars, and rotations. Coursework explores topics such as bioethics; federal policies and regulations concerning human research; scientific writing; management and organization; and information sciences. Trainees do rotations at the Jefferson Clinical Research Unit, where they learn the nuts and bolts of how to conduct a clinical trial, from conception through the general protocol and IRB submission, recruiting subjects, budgeting, collecting data, and write-ups for publication or a pharmaceutical company.

Other rotations take place at the Cancer Clinical Review Committee, which considers the scientific merit and human protection issues, and at the *Annals of Internal Medicine*, a premier journal based nearby. Finally, the program requires a research project that each student undertakes with the help of a mentor.

The program is open not only to fellows but to interns and residents as well as faculty members. At present, one-third of the people enrolled in the program are Jefferson faculty. (Among them is Dr. David Loren, profiled on p. 4.) For more information, visit www.tju.edu/medicine/pharmacology/aca/acapostdoctoral.cfm.



Clinical Pharmacology master's program journal club in fall 2004, from left to right: (seated) Walter Kraft, MD; Mui Senh, BS; Roslyn Varki, MD; Suzanne Leis, RN; Annette Bell, MS, MT(ASCP)SH; and Howard Greenberg, MD; (standing) Amit Mittal, MD; Francisco Almeida, MD; Theresa Pondok, MD; Scott Waldman, MD, PhD, FCP; Terry Hyslop, PhD; Stephanie Schulz, PhD; Li Gong, PhD; and Constantine Daskalakis, ScD

In Memoriam: Dr. Allan J. Erslev

In 2004 Jefferson held the first Memorial Lectureship in honor and remembrance of Dr. Allan J. Erslev, the distinguished Professor of Medicine, who died in November of 2003.

Copenhagen-born Dr. Erslev trained at Harvard and Yale before becoming Director of the Cardeza Foundation in 1963. Ten years earlier, he had been the first researcher to prove the existence of the renal hormone erythropoietin, which produces red blood cells. A genetically engineered version of the hormone, called EPO, was approved by the FDA in 1989 and benefits innumerable patients with anemia, kidney dialysis, and renal disease.

Until 1985 Dr. Erslev was director of the foundation, which benefited from his work tremendously. Dr. Erslev was co-author of a standard textbook, *Hematology*, as well as the paperback *Pathophysiology of Blood*. He retired in 2002, after 43 years of teaching.



Steven McKenzie, MD (left), Director of the Cardeza Foundation and the Division of Hematology, welcomed 2004 Erslev lecturer Joseph Prchal, MD, PhD, of Baylor College of Medicine, and several Erslev family members, including (left to right) granddaughter Maia Woodbury Erslev, daughter Carole Erslev, her husband Peter Woodbury, and daughter Wendy Erslev. The portrait of Dr. Erslev now hangs on the eighth floor of the College Building at 1025 Walnut Street.

"His vigorous mind and contagious enthusiasm inspired colleagues and generations of medical students and hematology fellows," says Jaime Caro, MD, of the Cardeza Foundation.

6

Dean Recognizes Faculty with New Awards

Thomas J. Nasca, MD, Senior Vice President and Dean, Jefferson Medical College, has instituted two new awards to recognize faculty for outstanding contributions to education and mentoring at Jefferson. This year's awardees were honored at a May reception at the Union League, hosted by Dr. Nasca.

Dean's Citation for Significant Contributions to the Advancement of Education at Jefferson Medical College:

Salvatore Mangione, MD
John M. Spandorfer, MD
Serge A. Jabbour, MD
Gregory C. Kane, MD
John W. Caruso, MD
Geno J. Merli, MD
Katherine Worzala, MD
Dale D. Berg, MD
Jay Herman, MD
Joseph A. DeSimone, Jr., MD
Matthew DeCaro, MD

Dean's Citation for Faculty Mentoring:

Scott A. Waldman, MD, PhD, FCP

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