



# SURGERY TODAY

Quarterly Newsletter of The Ohio State University Department of Surgery  
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## PLASTIC SURGERY

### Researchers identify role of protein in blood vessel tumor growth

Findings could lead to an antibody-based therapy for vascular malformations, other diseases

**R**esearchers in The Ohio State University Department of Surgery have identified a protein that plays a key role in the growth of blood vessel tumors, and they say their findings could lead to an antibody-based therapy for the tumors, which can cause facial deformities in infants and young children.

In studying the role of macrophages, a type of white blood cell, in tumor development, the researchers found that a protein known as MCP-1 (monocyte chemoattractant protein 1) recruits macrophages to the tumor site. There, they stimulate new blood vessel development, or angiogenesis, in endothelial cells that line the blood vessels, which fuels tumor growth.

This means that therapies eliminating



Gordillo

the MCP-1 protein could be important in treating or preventing vascular tumors and other tumors in which MCP-1 is expressed.

The findings were published in the Oct. 2004 issue of the *American Journal of Physiology – Cell Physiology*.

The research provides the first evidence that MCP-1 and macrophages



Sen

are needed for vascular tumors to grow, and that anti-MCP-1 therapy prevents vascular tumor development in animals with intact immune systems, says Dr. Gayle M. Gordillo, lead author of the study and assistant professor of surgery in the Division of Plastic Surgery.

Gordillo's partners in the project were Chandan K. Sen, Ph.D., professor of surgery in the Division of General Surgery, and Sashwati Roy, Ph.D.,

**A new treatment option is needed because current therapies, which include steroids and alpha interferon, have a number of high-risk side effects.**

assistant professor of surgery in the Division of General Surgery.

In the study, Gordillo, Sen, and Roy determined the role of MCP-1 in recruiting macrophages by observing the responses of hemangioendotheliomas (HEs), a type of blood vessel tumor, to an MCP-1-neutralizing antibody in mice, when varying levels of macrophages were present. Tumors treated with the antibody failed to develop.

"Our observations specifically link MCP-1 and macrophages as key contributors to the development of these tumors," says Gordillo, who is also

(See **Tumor growth** on page 2)



ENDOWMENTS

Gift to benefit surgical research

Dr. Richard King, a fourth-year resident in surgery at Penn State Hershey Medical Center, has presented a gift of \$50,000 to The Ohio State University Department of Surgery to establish an endowed grant in surgical research.

Made in honor of his father, Surgery alumnus Dr. James D. King, the grant will help to provide seed money for a young investigator engaged in research while in the master of medical science in surgery program.

King is also creating a collection of his father's papers, correspondence, and

memorabilia at the Medical Heritage Center of the Prior Health Sciences Library.

"My father's story is one I wish to tell and preserve as an inspiration to others," King says. "Ohio, Columbus, and OSU formed the center of my father's life in America for most of his formative years, and I



King

believe it would be appropriate to establish his legacy there."

Dr. James King was born in Singapore to parents of Chinese descent. A graduate of Miami University, in Oxford, Ohio, he received his medical degree at George Washington University, in Washington, D.C., and was a resident at Peiping Union Medical College, in China.

At Ohio State, King received his master of science degree in surgery in 1937, and in 1940, the first doctoral degree in surgical research ever presented by the University.

His distinguished career included service during World War II as chief surgeon in the First Chinese Army and later as a captain in the U.S. Army Medical Corps. After returning to Ohio, he was chief of thoracic surgery at the Veterans Hospital in Dayton. ❖

Tumor growth

From page 1

director of the hemangioma and vascular malformation clinic at Columbus Children's Hospital. "MCP-1's essential role in supporting proliferation of HEs indicates that accessory cells, such as macrophages, play a significant role in facilitating the growth of these tumors. Antibody-based therapy that blocks MCP-1 may be effective in substantially limiting the incidence and quality of the malformation."

A new treatment option is needed because current therapies, which include steroids and alpha interferon, have a number of high-risk side effects. Steroids suppress the immune system, stunt growth and development, and cause weight gain and irritability. Alpha interferon can cause irreversible neurologic damage in children. Surgical removal is too dangerous because of potential bleeding complications and skin loss.

Blood vessel tumors affect up to three percent of all children, typically resulting in a prominent red mass on the head and neck. Up to one in four patients with HEs dies of anemia associated with the tumors.

"Most of these tumors show up in the first month of life," Gordillo says. "About 90 percent go away by themselves over time, but until they do, children are forced to accept a period of deformity, sometimes up to age 9."

Sen, director of the laboratory of molecular medicine at the Davis Heart and Lung Research Institute, says the study lays the foundation for clinical trials testing the effectiveness of antibody-based therapies and, even sooner, an experimental nutritional intervention for vascular malformations.

"Previous work in our lab has shown that a certain form of berry extract significantly regulates MCP-1 function," says Sen, who served as a mentor to Gordillo on the study.

The challenge lies in regulating MCP-

1 levels safely, because the protein is also active in the wound-healing process, when macrophages make free radicals and promote angiogenesis, both of which are beneficial in wound healing.

"There are times when you want to promote angiogenesis, but not with tumors, because it contributes to tumor growth," Gordillo says. "MCP-1 can be brought in as a repair response to help people with wounds, but it can make negative contributions to the health and well-being of people with tumors."

Because angiogenesis is implicated in the development of other kinds of tumors and chronic inflammatory conditions, the researchers say the findings of the study suggest anti-MCP-1 therapy may be a useful approach for other diseases.

"This study's identification of the role of MCP-1 expression has obvious potential for other tumors," Gordillo says. "The concept could be applicable to a broad variety of tumors in which we know MCP-1 is expressed." ❖



## SURGICAL ONCOLOGY

# Study shows how immune system responds to various levels of IFN-a

Findings suggest new definitions of optimal dosing to decrease toxicity of immunotherapy

Researchers in The Ohio State University Comprehensive Cancer Center (OSUCCC) have devised a new way to understand how the immune system responds to interferon alfa (IFN-a), a common treatment for malignant melanoma that sometimes produces debilitating side effects.

The findings, reported in the Sept. 1, 2004 issue of the *Journal of the National Cancer Institute*, describe how various components of the immune system react to immunotherapy, and suggest new definitions of optimal dosing to decrease its toxicity.

“We’ve known for years that interferon alfa can boost a patient’s immune system, but we really haven’t understood some of its molecular targets until now,” says Dr. William E. Carson III, senior author of the study, associate professor of surgery in the Division of Surgical Oncology, and director of clinical research at OSUCCC.

Interferon alfa slows tumor growth and blocks the formation of new blood vessels that tumors need to grow and spread. When IFN-a enters the body at the cellular level, one of the first gatekeepers it activates is a protein called



Carson

STAT1 (signal transducer and activator of transcription 1). Interferon causes STAT1 to go through a chemical change called phosphorylation, a process that leads to widespread gene expression throughout the cell that regulates immune response.

Carson and Dr. Gregory Lesinski, a postdoctoral fellow in his lab and lead investigator of the project, were interested in discovering which cellular subsets of the immune system — T cells, B cells, monocytes or natural killer (NK) cells — were most responsive to IFN-a therapy.

Researchers drew blood from healthy subjects and patients with melanoma, and exposed the samples to different levels of IFN-a. Using specially-designed antibodies coupled with fluorescent tags, the research team sorted and tracked STAT1 phosphorylation throughout the immune system.

They found that phosphorylated STAT1 levels increased in all immune system subsets as the concentration of IFN-a rose, but that relatively low levels of IFN-a seemed to be enough to generate maximal STAT1 activation. They also discovered that compared with melanoma patients, healthy people had higher resting levels of phosphorylated STAT1 in T cells and NK cells.

Carson says the study is important

**“Patients appear to differ widely on how much interferon they may need to spark the best response. Interestingly, our findings show that more may not be better.”**

for patients and researchers alike. “For patients, it means that we now have a way to measure how the individual immune system is responding to IFN-a therapy,” he says. “Patients appear to differ widely on how much interferon they may need to spark the best response. Interestingly, our findings show that more may not be better.”

The possible side effects of treatment with interferon alfa are flu-like symptoms, fatigue, digestive problems, mood disturbances, hair loss, and blood disorders.

Lesinski says the new flow cytometry system used in the study is fast, highly quantitative, and extremely sensitive. “Using older methods, we would have had to conduct studies on each cellular subset individually,” he says. “But now we can do it all with just one blood draw. This is easier, more efficient, and less burdensome for the patient.” ❖



UNIVERSITY MEDICAL CENTER

# Ferguson named head of new Comprehensive Transplant Center

**D**r. Ronald M. Ferguson, professor of surgery and previously chief of the Division of Transplantation, has been appointed executive director of a new Comprehensive Transplantation Center at The Ohio State University Medical Center.

With the appointment, Dr. Mitchell L. Henry, professor of surgery, has replaced Ferguson as chief of the Division of Transplantation and has been appointed deputy director for surgical services in the new center.

An interdisciplinary collaboration, the new transplantation center encompasses all solid organ and cellular transplantation at Ohio State. The center will draw together a large, integrated team of specialists at University Medical Center to pursue important areas of common interest in transplantation, including immunopharmacology, immune assessment monitoring and engineering, information systems and biostatistics, clinical trials, communications and marketing, and public policy and ethics.

Expected to establish a broad national leadership role in transplantation, the center will focus initially on development of an islet cell transplantation program and expansion of the lung and liver transplantation programs.

“A basic premise of the transplant

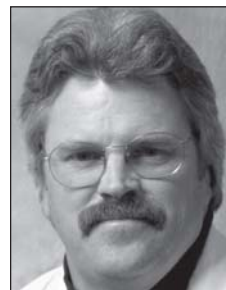


Ferguson

center is that the commonalities among the organ-specific transplant programs are far greater than those facets that make them individually unique.”

Ferguson says.

Ferguson has been a faculty member in the Department of Surgery for more than 21 years. Head of the transplantation program since its inception in 1985, he has brought the program to national prominence with one of the largest and most successful renal transplant programs in the country and outstanding kidney-pancreas and liver transplant programs. The kidney-pancreas program has been identified as the leading such program in the United States, and the clinical transplant program as a whole is a national leader in volume and outcomes. The program has performed more than 4,000 abdominal



Henry

transplants and continues to perform nearly 300 transplants each year.

Ferguson received his medical degree at Washington University, in St. Louis. He obtained a Ph.D. and completed his specialty training at the University of Minnesota, in Minneapolis. He was

**“A basic premise of the transplant center is that the commonalities among the organ-specific transplant programs are far greater than those facets that make them individually unique.”**

chairman of The Ohio State University Department of Surgery from 1993 to 1999.

Henry, the first fellow to complete the transplantation program in the Department of Surgery, has been a faculty member at Ohio State for nearly 20 years. He received his medical degree at the University of Nebraska, in Omaha, and completed his general surgery residency at Ohio State. Prior to his appointment as chief of the Division of Transplantation, he was divisional chief of clinical transplantation.

In addition to Henry, three other deputy directors of the center have been appointed. Charles G. Orosz, Ph.D., professor of surgery and director of the transplantation sciences program, has been named deputy director for research; Dr. Todd E. Pesavento, assistant professor of clinical internal medicine, has been appointed deputy director for clinical services; and Dr. Amy L. Pope-Harman, assistant professor of clinical internal medicine, has been named deputy director for education. ❖



**AMERICAN COLLEGE OF SURGEONS**

**Department well-represented at 90th Annual Clinical Congress**

Ohio State staff members participate as presenters, moderators, instructors at influential meeting

**T**he Ohio State University Department of Surgery was well-represented at the 90th Annual Clinical Congress of the American College of Surgeons, with five faculty members and one fellow from the department participating as presenters, moderators, or instructors at the Oct. 2004 meeting, in New Orleans.

**Dr. Shahab F. Abdessalam**, surgical critical care fellow in the Division of Pediatric Surgery, presented “An Analysis of Children Receiving Cardiopulmonary Resuscitation following Cardiac Arrest with Blunt Trauma.” Co-authors of the study included



*Abdessalam*

**Dr. Jonathan I. Groner**, associate professor of clinical surgery in Pediatric Surgery; **Dr. Sanjay Krishnaswami**, fellow and administrative chief in Pediatric Surgery; and **Dr. Benedict C. Nwomeh**, assistant professor of clinical surgery in Pediatric Surgery.



*Arnold*

**Dr. Mark W. Arnold**, professor of clinical surgery in the Division of General Surgery, served as moderator of a specialty session titled “New Diagnostic Techniques in Colon and Rectal Surgery.”



*Bahson*

**Dr. Robert R. Bahson**, professor of surgery and chief of the Division of Urology, presented “The Role of Medical Therapy for BPH.” He also served as moderator of a postgraduate course review in urology for recertification candidates, and as discussant for forums titled “Use of Fibrin Tissue Sealants during Laparoscopic Partial Nephrectomy”; Incidence, Mortality, and Survival Trends of Prostate Cancer in Divergent



*Burak*



*Rajab*

Social Classes: A Widening Gulf?”; and “Non-narcotic Robotic Radical Prostatectomy.”

**Dr. William E. Burak Jr.**, associate professor of surgery in the Division of Surgical Oncology, presented “Case Presentations and Pathologic Considerations” and served as a skills station instructor during a postgraduate course on stereotactic breast biopsy. He presented “Breast Ultrasound Interpretation: Benign vs. Malignant” during a postgraduate course on breast ultrasound. He delivered “Vacuum-Assisted Biopsy Devices” and served as a skills station instructor during a postgraduate course on advanced breast ultrasound.



*Winston*

**Dr. Amer Rajab**, assistant professor of surgery in the Division of Transplantation, gave a video presentation titled “Hand-Assisted Laparoscopic Live Donor Nephrectomy.” Collaborators on the project were **Dr. Ronald M. Ferguson**, professor of surgery and executive director of the Comprehensive Transplantation Center; **Dr. Mitchell L. Henry**, professor of surgery and chief of the Division of Transplantation; and **Dr. Ronald P. Pelletier**, associate professor of surgery in Transplantation.

**Dr. John H. Winston III**, assistant professor of surgery in the Division of General Surgery, presented “The Role of Dynamic MR Defecography in Defecatory Dysfunction.”

The 90th Annual Clinical Congress offered 41 postgraduate courses, more than 300 hours of general and specialty sessions, and 247 research-in-progress reports. ❖



## GRANTS

**VanBuskirk AM.** Animal model for the prevention of post-transplant skin cancer. National Institutes of Health/National Cancer Institute pilot study, July 1, 2004–June 30, 2006, \$149,500.

**VanBuskirk AM.** Cytokine gene polymorphisms and production in PTLD. National Institutes of Health/National Cancer Institute pilot study, Oct. 1, 2004–Sept. 30, 2006, \$149,500.

**VanBuskirk AM.** Cytokine inhibition of CTL reactivation in PTLD. Roche Organ Transplantation Research Foundation, July 1, 2004–June 30, 2005, \$69,000.

**VanBuskirk AM.** Immunomodulatory T cells in UVB-induced skin inflammation and carcinogenesis. American Cancer Society, Ohio Division, Sept. 15, 2004–Sept. 14, 2005; \$30,000. ❖

## PUBLICATIONS

**Agnese DM, Abdessalam SF, Burak WE Jr, Arnold MW, Soble D, Hinkle GH, Young D, Khazaelli MB, Martin EW Jr.** Pilot study using humanized CC49 monoclonal antibody (HuCC49DeltaCH2) to localize recurrent colorectal carcinoma. *Ann Surg Onc* 2004; 11(2):197–202.

**Agnese DM, Yusuf F, Wilson JL, Shapiro CL, Lehman A, Burak WE Jr.** Trends in breast cancer presentation and care according to age in a single institution. *Am J Surg* 2004; 188(4):437–439.

**Arca MJ, Teich S.** Fetal versus neonatal surgery. *Clin Perinatol* 2004; 31:629–648.

**Caniano DA.** Ethical issues in the management of neonatal surgical anomalies. *Semin Perinatol* 2004; 28:240–245.

**Caniano DA, Sonnino RE, Paolo AM.** Keys to career satisfaction: insights from a survey of women pediatric surgeons. *J Pediatr Surg* 2004; 39:984–990.

**Go MR, Dundon JM, Karlowicz DJ, Domingo C, Muscarella P, Melvin WS.** Delivery of radiofrequency energy to the lower esophageal sphincter (Stretta) improves symptoms of GERD. *Surgery* 2004; 136(4):786–794.

**Groner JI.** Lethal injection: the medical charade. *Ethics Med* 2004; 20(2):25–30.

**Haut ER, Nance ML, Keller MS, Groner JI, Ford HR, Kuhn A, Tuchfarber B, Garcia V, Schwab CW, Stafford PW.** Management of penetrating colon and rectal injuries in the pediatric patient. *Dis Colon Rectum* 2004; 47(9):1526–1532.

**Hazey J, Melvin WS.** Robot-assisted general surgery. *Semin Laparoscopic Surgery* 2004; 11(2):107–112.

**Martin AE, Vollman D, Adler B, Caniano DA.** CT scans may not reduce the negative appendectomy rate in children. *J Pediatr Surg* 2004; 39:886–890.

**Wright AS, Gould JC, Melvin WS.** Computer-assisted robotic antireflux surgery. *Minerva Gastroenterol Dietol* 2004; 50: 1–8. ❖

## CHAPTERS

**Arca MJ, Caniano DA.** Breast disorders in the adolescent patient. In: Arca MJ, Hewitt G (eds). *Adolescent Medicine Clinics*. Philadelphia: W.B. Saunders Co., 2004 (Oct., Vol. 15); 473–486. ❖

## PRESENTATIONS

**Agnese DM.** Clinicopathologic variables predictive of positive nodes in melanoma in the era of sentinel nodes. Genetics and breast cancer: what the surgical oncologist should know. Society of Surgical Oncology, 57th Annual Meeting, New York, N.Y., March 18–21, 2004.

**Agnese DM.** The genetics of breast cancer. Central Ohio Case Management

Network Meeting, Worthington, Ohio, May 12, 2004.

**Agnese DM.** Surgical interventions for individuals at hereditary cancer risk. Cancer Genetics Short Course, The Ohio State University, Columbus, Ohio, April 22, 2004.

**Agnese DM.** Trends in breast cancer presentation and care according to age in a single institution. American Society of Breast Surgeons, Fifth Annual Meeting, Las Vegas, Nev., March 31–April 4, 2004.

**Caniano DA** (Visiting Professor). Surgical ethics. Hackensack University Medical Center, Hackensack, N.J., Nov. 9, 2004.

**Groner JI.** Lethal injection: a prophecy fulfilled. Second World Congress against the Death Penalty, Physicians Round Table, Montreal, Canada, Oct. 7, 2004.

**Li J, Weghorst CM, Tsutsumi M, Poi MJ, Knobloch TJ, Casto BC, Melvin WS, Tsai M, Muscarella P.** Frequent p16INK4A/CDKN2A alterations in chemically-induced Syrian golden hamster pancreatic tumors (poster). American Pancreatic Association, Annual Meeting, Chicago, Ill., Nov. 4–5, 2004.

**Melvin WS.** Clinical applications of robots in the operating room. Complications of bariatric surgery. Endoluminal treatment options for gastroesophageal reflux. Outcomes of laparoscopic Nissen fundoplication. IX Congreso de Cirugia de Centro America y Panama, San Salvador, El Salvador, Oct. 27, 2004.

**Melvin WS.** Options for the management of gastroesophageal reflux disease. Society of American Gastrointestinal Endoscopic Surgeons, Society for Surgery of the Alimentary Tract, SAGES/SSAT Joint Symposium, New Orleans, La., Oct. 13, 2004.

**Satianai B.** Business knowledge for surgeons. Baylor College of Medicine, Division of Cardiothoracic Surgery, Houston, Texas, Nov. 24, 2004.

**Satianai B.** Protocols for the evalua-



tion of acute DVT. Vascular Non-invasive Testing Symposium, General Electric Healthcare, Columbus, Ohio, Sept. 18, 2004. ❖

## RECOGNITIONS

A paper titled "Trends in Breast Cancer Presentation and Care according to Age in a Single Institution," by **Dr. Doreen M. Agnese**, assistant professor of surgery in the Division of Surgical Oncology, was summarized by the BCN News (BreastCancer.Net) on Oct. 14, 2004.

**Charles G. Orosz, Ph.D.**, professor of surgery in the Division of Transplantation and director of the Clinical Histocompatibility Laboratory, assumed the presidency of the American Society for Histocompatibility and Immunogenetics in Oct. 2004, at the society's annual meeting, in San Antonio, Texas.

**Zeeshan A. Qureshi**, an undergraduate student working in the laboratory of **Dr. Ginny L. Bumgardner**, received a Spring 2004 Undergraduate Research Scholarship from the College of Arts and Sciences Honors Committee for a project titled "Mechanisms of CD8+ T Cell Activation by Allogeneic Liver versus Islet Parenchymal Cells." Bumgardner is associate professor of surgery in the Division of Transplantation. ❖

## IN THE NEWS

**Dr. William E. Carson III**, associate professor of surgery in the Division of Surgical Oncology, and **Dr. William B. Farrar**, professor of surgery and chief of Surgical Oncology, were interviewed on Oct. 23, 2004, by WBNS-TV, during a program titled "Breakthroughs: Conquering Cancer at the James."

On Oct. 19, 2004, Carson was quoted by the *Salt Lake Tribune*, in a story about the influence of stress on the

immune systems of breast cancer patients.

**Dr. William B. Farrar**, professor of surgery and chief of the Division of Surgical Oncology, was interviewed on Nov. 4, 2004, by WSYX-TV/6 and WBNS-TV/10, about breast cancer treatment and survival, in light of the announcement that Elizabeth Edwards, the wife of Sen. John Edwards, has breast cancer.

**Dr. Mark Galantowicz**, associate professor of surgery in the Division of Cardiothoracic Surgery and co-director of the Columbus Children's Hospital Heart Center, was featured on Oct. 25, 2004, in the *Columbus Dispatch*, in a story about a Swedish family who sought his care for a baby with hypoplastic left heart syndrome.

**Dr. Jonathan I. Groner**, associate professor of clinical surgery in the Division of Pediatric Surgery, was featured on Oct. 25, 2004, in the *American Medical News*, in a story titled "In the Execution Chamber: Do Doctors Have a Place — at All?"

**Dr. Robert E. Michler**, the John G. and Jeanne B. McCoy professor of surgery and chief of the Division of Cardiothoracic Surgery, was quoted on Oct. 15, 2004, by *Business First*, in a story titled "Local Doctors Donate Time to Save Lives."

**Dr. Patrick Ross Jr.**, associate professor of clinical surgery in the Division of Cardiothoracic Surgery, was interviewed on Sept. 3, 2004, by WBNS-TV/10 and WCMH-TV/4, about bypass surgery, in light of the news that former President Clinton was scheduled to have the surgery.

On Oct. 19, 2004, Ross was quoted by the *Mount Vernon News*, in a story about photodynamic therapy, which he and his team have been using for five years.

**Dr. Bhagwan Satiani**, professor of clinical surgery in the Division of General Vascular Surgery, was quoted on Sept. 17, 2004, by *Business First*, in a story

about the increasing treatment options for patients with cosmetic and medical conditions involving the veins.

**Elizabeth Seely**, director of pre- and post-transplantation, was quoted on Oct. 17, 2004, by the *Columbus Dispatch*, in a story about the percentage of Ohioans who agree to be organ donors. ❖

## CORRECTION

In the Nov. 2004 issue of *Surgery Today*, the research interests of Dr. Marc P. Michalsky, assistant professor of clinical surgery in the Division of Pediatric Surgery, were incorrectly identified as intestinal immunology and gut inflammatory response. As surgical director of the Columbus Children's Hospital Obesity Center, Michalsky is developing clinical and research programs focused on the surgical management of adolescent obesity. ❖

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### Editor

Darrell Peters  
Department of Surgery  
341 Means Hall  
1654 Upham Drive  
Columbus, Ohio 43210-1250  
Telephone (614) 293-8852  
Fax (614) 293-4063

### Changes of Address

Please address correspondence about changes of address to the editor.





Department of Surgery  
1654 Upham Drive  
Columbus, OH 43210-1250

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## INSIDE:

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*Dr. Richard King, a resident in surgery at Penn State Hershey Medical Center, has presented a gift of \$50,000 to the Department of Surgery to establish an endowed grant in surgical research in honor of his father, Dr. James D. King, who received the first doctoral degree in surgical research ever presented by The Ohio State University. Above, he poses with Chandan K. Sen, Ph.D. (left), professor of surgery and vice chairman for research in the Department of Surgery, and Dr. E. Christopher Ellison (right), the Robert M. Zollinger professor of surgery, chairman of the Department of Surgery, and associate vice president for health sciences and vice dean of clinical affairs in the College of Medicine and Public Health. See page 2.*