Dr. Olga Jonasson, chair of The Ohio State University Department of Surgery from 1987 to 1993 and the first woman in the United States to head an academic surgery department, died on Aug. 30 in Chicago.

“This is a significant loss for American surgery,” says Dr. E. Christopher Ellison, the Robert M. Zollinger professor and chair of surgery, associate vice president for health sciences, and vice dean of clinical affairs at The Ohio State University College of Medicine. “Dr. Jonasson was a leader in education and, in particular, resident training. She made significant and noteworthy contributions to surgical resident education at The Ohio State University.”

A native of Peoria, Illinois, Jonasson was an undergraduate at Northwestern University and received her medical degree with honors at the University of Illinois College of Medicine. She completed her residency in surgery at the University of Illinois Research and Education Hospital. She then served two postgraduate fellowships, the first in immunochemistry at Walter Reed Army Institute of Research, and the second in transplantation immunobiology at the Massachusetts General Hospital of Harvard Medical School.

Following her training, Jonasson joined the surgical faculty at the University of Illinois, in Chicago. A pioneer in organ transplantation, she developed one of the first clinical transplantation services in Illinois, and established a statewide histocompatibility-testing laboratory for donor-recipient matching. She was named chief of surgery at Cook County Hospital, in Chicago, in 1977.

In 1987, Jonasson became the first woman in the United States to head an academic surgery department, when she was appointed the Robert M. Zollinger professor and chair of the Department of Surgery at Ohio State. Under her leadership, the department experienced substantial growth.

In 1987, Jonasson became the first woman in the United States to head an academic surgery department.

Jonasson returned to Chicago in 1993 to take a senior position with the American College of Surgeons, where she led educational programs.

She was a member of numerous surgical societies and served on the board of directors of the American Board of Surgery and the Accreditation Council for Graduate Medical Education. The recipient of a number of honors and awards, she was named an honorary fellow of England’s Royal College of Surgeons, was appointed the Markle Scholar in Academic Medicine, and received the Elizabeth Blackwell Award of the American Medical Women’s Association.

A memorial service was held on Sept. 22 at the Church of the Ascension in Chicago.
drug that targets a particular type of breast cancer might be more effective if patients are also given a substance made by the body that stimulates certain immune cells, according to a preliminary study.

The laboratory and animal study suggests that the substance interleukin 21 (IL-21) might improve the effectiveness of the drug Herceptin. The findings suggest that this happens because the IL-21 boosts the cancer-killing activity of immune cells called natural killer (NK) cells, which attack the tumor.

The findings indicate that IL-21 stimulates NK cells to attack and destroy the Herceptin-coated cells.

"Only 25 to 35 percent of patients with this form of breast cancer respond to Herceptin," says principal investigator Dr. William E. Carson, III, associate professor of surgery in the Division of Surgical Oncology and associate director for clinical research at the OSUCCC.

"Our results suggest that giving IL-21 along with the Herceptin might increase the patient’s immune response to the tumor and perhaps boost the drug’s effectiveness."

Many researchers believe that Herceptin works because it stops tumor cells from growing and causes them to self-destruct through a natural process called programmed cell death, explains first author Julie M. Roda, a graduate research associate in Carson’s laboratory.

But, Roda says, “our findings provide new evidence that Herceptin works at least in part by stimulating NK cell activity, and that IL-21 enhances that action.”

Carson, Roda, and their collaborators chose to study IL-21 because the substance is known to activate NK cells and cause them to release substances that attract other immune cells to a tumor site.

The study’s findings came from several experiments. First, the scientists exposed NK cells in Petri dishes to both Herceptin and IL-21. This caused the cells to release three to 10 times more of a substance called interferon gamma than would cells exposed to either agent alone.

Interferon gamma is an immune-system signaling agent that causes the NK cells to become more active. It also increases the activity of other immune cells and forces tumor cells to self-destruct.

The researchers then repeated this experiment in mice. They found that animals given both IL-21 and Herceptin-coated tumor cells had nearly three times more interferon gamma in their blood than did animals injected with either of those items alone.

Still another experiment used mice with HER2-positive tumors. When the animals were treated with both the mouse version of Herceptin and IL-21, the tumors shrunk by nearly half, compared to those in mice receiving either agent alone.

Last, to test whether interferon gamma was important in causing the tumors to shrink, the researchers repeated this experiment using mice unable to make the substance.

The researchers were surprised to find that when interferon gamma was missing, the mouse drug and IL-21 combination had no effect on the tumors.

“We thought if we took out interferon gamma, the NK cells would still be able to kill the tumor cells,” Roda says.

But that didn’t happen.

“This is very interesting, because it suggests that interferon gamma production might be critical to the response to Herceptin, and I believe that we are the first to show this.”

Overall, says Carson, “Our results suggest that IL-21 might enhance the effectiveness of Herceptin and perhaps similar anticancer drugs.”

Funding from the National Cancer Institute supported the research.
A serious form of cancer that occurs in some transplant patients may develop because cells that normally serve as scouts for the immune system become weakened, a new study suggests.

The cancer is caused by Epstein-Barr virus (EBV), a herpes virus that infects more than 90 percent of Americans but is ordinarily kept under control by the immune system. That control can be lost in people whose immune system is suppressed to prevent rejection of a transplanted organ.

The cancer, called post-transplant lymphoproliferative disorder (PTLD), arises only in some transplant patients, but doctors don’t know why.

The study, led by scientists in the Department of Surgery, begins to answer that question.

The findings were published in the August issue of the American Journal of Transplantation.

“We’ve identified a mechanism that may explain why some patients develop PTLD and others don’t,” says study leader Anne M. VanBuskirk, Ph.D., assistant professor of surgery in the Division of Surgical Oncology.

“If we can understand the mechanism, perhaps we can discover how to prevent this type of cancer in transplant patients.”

Dr. William E. Carson, III, associate professor of surgery, and Dr. Lisa D. Yee, associate professor of surgery, both in the Division of Surgical Oncology, are co-authors of the study.

The incidence of the cancer varies according to the organ transplanted, ranging from 1 to 2 percent of kidney recipients and up to 20 percent of bone marrow or lung recipients. The disease usually arises within six months to one year after transplantation, and can have a 70- to 80-percent mortality rate.

The study by VanBuskirk and her colleagues examines two types of immune cells: antigen-presenting cells, which act as scouts, and memory T cells.

Scout cells detect the presence of viruses and other invaders and alert the immune system to the infection. Memory T cells are immune cells that have fought an earlier infection and remain ready to respond quickly, should the infection reoccur.

Most people are infected by EBV early in life, and the immune system brings it under control, although the virus remains hidden in some cells of the body. If the infection flares up again, scout cells alert the memory T cells, which rapidly proliferate and hunt down and kill any cells that contain growing virus or have become cancerous.

“If memory T cells are restimulated properly, they can kill the cancerous cells before PTLD develops,” VanBuskirk says. “But if that restimulation is weak or is blocked, not all of the cells are destroyed and cancer can develop. So it is critical that these two cell types work together effectively.”

The study suggests that PTLD arises because the scout cells can only weakly activate the memory T cells and stop their activation by other cells.

VanBuskirk and her team believe this happens because an immune system substance causes changes in the scout cells, inhibiting their ability to warn memory T cells about the virus. That substance is called transforming growth factor-beta (TGFb).

The researchers discovered this by exposing healthy human scout cells to TGFb. Next, they combined the scout cells with T cells and PTLD-like cancer cells.

The T cells that grew alongside the scout cells exposed to TGFb were significantly less able to kill the cancer cells than were the T cells growing with scout cells not exposed to TGFb.

In addition, when scout cells from both groups were combined, the TGFb-exposed cells were stronger and prevented the unexposed scout cells from restimulating the memory T cells.

The study follows earlier research led by VanBuskirk that suggests why only some transplant patients develop PTLD and not others.

The earlier study, published in a February 2005 issue of the journal Blood, suggested that the balance in the body of TGFb and a second immune substance called interferon gamma (IFNg) might influence development of the cancer.

“If our hypothesis proves to be true,” VanBuskirk says, “it may one day be possible to identify transplant patients who are at greater risk for PTLD and to develop new therapies that prevent or treat the disease.”

Funding from the National Cancer Institute, the National Institute of Allergy and Infectious Diseases, and the Roche Organ Transplantation Research Foundation supported the research. 

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VanBuskirk
Specialists using new minimally invasive technique to treat AF

Procedure offers alternative to several treatments

S
pecialists in the Department of Surgery are using a new minimally invasive technique to treat atrial fibrillation (AF). AF is a condition associated with stroke and heart failure, in which the heart beats out of rhythm because of disordered electrical impulses in its upper chambers, or atria.

The technique, called thoracoscopic atrial ablation with intraoperative autonomic mapping, allows surgeons to restore normal rhythm to the heart and to confirm, during the operation, successful removal of the abnormal electrical stimuli that cause AF.

The new surgical procedure provides an alternative to catheter-based radiofrequency atrial ablation, which has become a common treatment for atrial fibrillation. Unlike the surgical procedure, catheter-based atrial ablation is performed in the catheterization laboratory, and interrupts abnormal rhythm patterns using cautery inside the atria.

The catheter-based procedure has limited effectiveness in more persistent forms of AF, and requires that patients remain on coumadin, an anticoagulant, for six months following the procedure, according to Dr. John H. Sirak, assistant professor of clinical surgery in the Division of Cardiothoracic Surgery.

In contrast, the new surgical approach targets the nerve centers on the outside of the heart, from which the abnormal rhythms originate. Operating through tiny incisions in the side of the patient’s chest, the surgeon selectively stimulates key nerve centers, which allows the source of AF to be identified and ablated. The surgeon also closes the left atrial appendage, a redundant structure responsible for 90 percent of AF-associated strokes. Because the ablations are performed on the outside of the heart, the atria are not injured internally. No coumadin is needed postoperatively.

“Because this [procedure] is driven by mapping, there is no need to assume that a standard ablation has resulted in a cure. We can tell on the spot whether the treatment is working,” Sirak says. “Also, since this is a closed-chest, beating-heart operation, we can see if the patient has converted to normal rhythm from the treatment. We don’t leave the operating room without completely eliminating all of the potential sources of abnormal rhythm.”

The thoracoscopic procedure has been 100-percent successful in restoring patients to sinus rhythm, without anti-arrhythmia medications or coumadin, he says.

The new procedure also provides a minimally invasive alternative to traditional surgical treatment for AF, in which the chest is opened and the patient is placed on the heart-lung bypass machine. The thoracoscopic procedure is based on a more advanced understanding of atrial fibrillation, and is therefore significantly more effective. It also results in much faster recovery, allowing patients to leave the hospital as early as 18 hours after the operation, Sirak says.

In a normal heart, electrical impulses from the two atria at the top of the heart send electrical impulses to the ventricles, causing the ventricles to contract and pump blood to the lungs and the rest of the body.

However, in atrial fibrillation, the impulses are random and disordered, giving a “bag of snakes” appearance to the atria, Sirak says. Without the normal pumping function of the atria, cardiac output is reduced by 20 percent.

Atrial fibrillation affects about 2.5 million Americans, and its incidence doubles with each additional decade of life. AF has a strong long-term association with stroke and heart failure.
Four surgeons — including the new dean of The Ohio State University College of Medicine — and a research scientist recently joined the faculty of the Department of Surgery.

Dr. Wiley W. “Chip” Souba, Jr., previously professor and chairman of surgery at Penn State College of Medicine and surgeon-in-chief at the Milton S. Hershey Medical Center, in Hershey, Pa., on August 9 began an appointment as professor of surgery in the Division of Surgical Oncology and dean of The Ohio State University College of Medicine.

Souba received his bachelor’s degree in chemistry at Muskingum College, in New Concord, Ohio, his medical degree at the University of Texas Medical School, in Houston, and a doctor of science degree in nutritional biochemistry at the Harvard School of Public Health, in Boston.

He was a resident at the University of Texas Medical School, in Houston, and completed fellowships at the Brigham and Women’s Hospital and the Dana-Farber Cancer Institute, in Boston, and the M.D. Anderson Hospital, in Houston.

Before joining the Penn State faculty in 1999, Souba held faculty positions at the University of Florida, in Gainesville, and Harvard.

Dr. Scott B. Armen, previously a fellow in surgical critical care and trauma at The Ohio State University Medical Center, on August 1 began an appointment as assistant professor of surgery in the Division of Critical Care, Trauma, and Burns.

Born in Mount Pleasant, Pa., Armen received his undergraduate degree at Pennsylvania State University, in University Park, Pa. He received his medical degree at Ohio State and completed a residency in general surgery at Mount Carmel Health System, in Columbus, Ohio.

Gregg A. Hadley, Ph.D., previously associate professor of surgery and microbiology and immunology at the University of Maryland, in Baltimore, on Oct. 1 began an appointment as professor of surgery in the Division of Transplantation.

Hadley received a B.S. degree in biology at Purdue University, in West Lafayette, Ind., an M.S. degree in zoology at the University of Iowa, in Iowa City, and a Ph.D. degree in microbiology at the University of Minnesota, in Minneapolis.

Dr. Susan D. Moffatt-Bruce, previously a cardiac surgeon and clinical instructor at the University of British Columbia, in Vancouver, began an appointment July 13 as assistant professor of surgery in the Division of Cardiothoracic Surgery.

Moffat-Bruce received her medical degree and completed her residency in general surgery at Dalhousie University, in Halifax, Nova Scotia. She received a doctoral degree in transplantation immunology at the University of Cambridge, in Cambridge, England, and completed a residency in cardiothoracic surgery at Stanford University, in Stanford, Calif.

Dr. Yalaunda M. Thomas, previously a fellow in surgical critical care at the University of Maryland Medical Center, in Baltimore, on Oct. 1 began an appointment as assistant professor of surgery in the Division of Critical Care, Trauma, and Burns.

Thomas received her undergraduate degree at Wake Forest University, in Winston-Salem, N.C., and her medical degree at the University of North Carolina, in Chapel Hill, N.C. She completed her residency in general surgery at the University of Illinois, in Chicago.
Division receives industry grants

The Division of General and Gastrointestinal Surgery has received two industry grants to support education and research in advanced surgical interventional and therapeutic endoscopy.

Stryker awarded the division $230,000 annually for three years to support research in, and development of, instrumentation for transluminal therapies and the endoscopic treatment of morbid obesity.

The grant will help support a new endoscopy fellow in pursuing transluminal applications of endoscopy and development of new endoscopic instruments.

Boston Scientific awarded the division $50,000 to support a surgical fellowship in advanced therapeutic endoscopy.

GRANTS

Crestanello JA. The effect of ischemic preconditioning on mitochondrial function and mitochondrial free oxygen radical production. Davis/Bremer Grant, The Ohio State University College of Medicine, July 1, 2006 – June 30, 2008, $50,000.

Horne PH. CD4-independent, CD8+ T cell-mediated alloimmunity studied through a hepatocellular allograft model. American Society of Transplantation, Physician Scientist Training Award, July 31, 2006 – July 31, 2009, $90,000.

PUBLICATIONS


RECOGNITIONS

Dr. Shahab F. Abessalam, chief resident in pediatric surgery during the 2005–06 academic year, was elected to the Alpha Omega Alpha Medical Honor Society.

Dr. Robert R. Bahnson, the Dave Longaberger professor of surgery and chief of the Division of Urology, was elected president of the Society of University Urologists at the society’s annual meeting March 19, in Atlanta.

Dr. Juan A. Crestanello, assistant professor of surgery in the Division of Cardiothoracic Surgery, and Dr. Benjamin Sun, associate professor of surgery and chief of Cardiothoracic Surgery, in March hosted a one-day course on temporary circulatory support for doctors from South America and Mexico. Three cardiac surgeons from Uruguay, three from Brazil, and two from Mexico attended the course, which
Dr. Ergun Kocak, a fourth-year resident in the Division of Plastic Surgery, completed the Department of Surgery’s Master of Medical Science Program (MMSP) in 2005, and he says the program was relevant to his future practice.

“As I have advanced through my residency training, I have encountered many new topics that fall outside of the scope of residency teaching, but well within the scope of my future practice,” he says.

“For example, medical statistics is a topic that comes up in nearly every scientific or clinical paper. An understanding of basic statistics is essential, not only to understand the findings presented in these papers, but also to determine the overall value and validity of a study.

“Another example is health-care management. As residents, we are consumed with learning the presentation, diagnosis, and treatment of diseases. There is little time or opportunity to focus on the larger system within which we run our practices.

“The MMSP presents an excellent opportunity to fill these gaps in our education by offering a wide range of courses in all areas of medicine, from statistics to health-care management. At the same time, the MMSP offers courses that focus heavily on the scientific aspects of diseases. During my research fellowship, I used the MMSP to learn as much as possible about the research I was engaged in, by taking courses that focused on the basic science aspects of immunology and cancer.”

Dr. J. Terrance Davis, a faculty member in the Division of Cardiothoracic Surgery for 15 years, on July 1 received an appointment as professor emeritus of surgery.

Dr. E. Christopher Ellison, the Robert M. Zollinger professor and chair of surgery, associate vice president for health sciences, and vice dean of clinical affairs, was recently recognized for his work with medical students and the Department of Family Medicine. Ellison was named “Champion of Family Medicine” at an honor reception April 26.

Dr. Jonathan I. Groner, associate professor of clinical surgery in the Division of Pediatric Surgery, recently testified as an expert witness in Federal District Court in Missouri, in Taylor v. Crawford, a case challenging the constitutionality of lethal injection in Missouri.

Philip Horne, an M.D./Ph.D. student working in the lab of Dr. Ginny L. Bumgardner, has received the 2006 Physician Scientist Award of the American Society of Transplantation. Bumgardner is professor of surgery in the Division of Transplantation.

Dr. Bodo Knudsen, assistant professor of surgery in the Division of Urology, on March 18 was elected to the board of directors of the Ohio Urological Society.

Dr. W. Scott Melvin, professor of surgery, chief of the Division of General and Gastrointestinal Surgery, and director of the Center for Minimally Invasive Surgery, was elected secretary of the Society of American Gastrointestinal and Endoscopic Surgeons at the society’s 25th annual meeting, which was held April 26–29, in Dallas. The society is the second largest surgical organization in the United States.

The islet transplant program at The Ohio State University Medical Center recently became one of only 12 academic medical centers in the United States to receive approval by the U.S. Food and Drug Administration to perform islet transplant, an innovative treatment for diabetes. Dr. Amer Rajab, assistant professor of surgery, heads the program within the Division of Transplantation.

Chandan K. Sen, Ph.D., professor of surgery in the Division of General and Gastrointestinal Surgery and vice chairman for research in the Department of Surgery, has been appointed associate editor of Physiological Genomics.
INSIDE:

1. Dr. Olga Jonasson (1934–2006)

2. Boosting killer cells might improve effectiveness of breast cancer drug

3. Failure of “scout cells” may lead to transplant cancer, study suggests

4. Specialists using new minimally invasive technique to treat AF