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CLINICAL RESEARCH

Monograph provides comprehensive review of Zollinger-Ellison syndrome

A comprehensive review of Zollinger-Ellison syndrome, written by Dr. E. Christopher Ellison, the Robert M. Zollinger professor and chairman of surgery, associate vice president for health sciences, and vice dean of clinical affairs at The Ohio State University Medical Center, was published in the January issue of Current Problems in Surgery.

Titled “The Zollinger-Ellison Syndrome: A Comprehensive Review of Historical, Scientific, and Clinical Considerations,” the monograph updates previous studies of the condition by Dr. Ellison, particularly anniversary papers published 40 and 50 years after the landmark 1955 journal article on the disorder, written by the late Dr. Robert M. Zollinger and the late Dr. Edwin H. Ellison, Ellison’s father.

Zollinger-Ellison syndrome is a rare, complex condition characterized by the occurrence of tumors, called gastrinomas, in the pancreas or in the upper part of the small intestine. Gastrinomas secrete a large amount of the hormone gastrin, which causes the stomach to produce too much acid and usually leads to peptic ulcers.

Dr. Ellison’s principal research interests are gastrinoma and Zollinger-Ellison syndrome and pancreatic and hepatic cancer. He has authored or co-authored nearly 200 published peer-reviewed articles, abstracts, invited reviews, monographs, and book chapters on these and other topics.

In 1955, Annals of Surgery published a paper by Dr. Robert M. Zollinger and Dr. Edwin H. Ellison that first characterized the Zollinger-Ellison syndrome. Zollinger was chairman of the Department of Surgery at Ohio State from 1946 to 1974. Dr. Edwin Ellison served on the Surgery faculty at Ohio State for 12 years and later was chairman of surgery at Marquette University School of Medicine, now the Medical College of Wisconsin, in Milwaukee.

Ellison
LABORATORY RESEARCH

Two drugs kill resistant melanoma cells in preclinical study

Combining a well-known biologic agent with a new targeted anticancer drug triggers the death of melanoma cells that are resistant to therapy, according to a laboratory study led by a researcher in the Department of Surgery at The Ohio State University Medical Center.

The study shows that combining the biologic therapy interferon-alpha (IFNa) with the drug bortezomib causes melanoma cells to self-destruct by the biochemical process of apoptosis, a form of programmed cell death in multicellular organisms. The drug combination significantly increased survival in a mouse-tumor model, and it cut the growth of transplanted human tumors by half in a second model. The study marks the first time the two drugs have been used together for this disease.

The combination even killed melanoma cells that had high levels of two important survival proteins, Bcl-2 and Mcl-1, which block the process of cell self-destruction.

The findings, published in a recent issue of the journal Cancer Research, led to a phase 1 clinical trial now in progress, which is testing the safety of the drug combination in humans.

“Advanced melanoma is highly resistant to most chemotherapy drugs, so it is particularly important to investigate new combination therapies for this disease,” says Dr. William E. Carson, III, professor of surgery in the Division of Surgical Oncology and principal investigator for the study.

“Our preclinical data indicate that the antitumor effects of this combination are better than either agent alone, and we observed no significant side effects, suggesting that this may be a good treatment strategy for melanoma and possibly other cancers.”

Bortezomib inhibits the action of proteosomes, complexes in cells that break down proteins. IFNa, approved by the Food and Drug Administration for the treatment of melanoma, increases the sensitivity of melanoma cells to self-destruction. Millennium Pharmaceuticals, Inc., provided the bortezomib used in the study. (See page 4)
“We found that the two drugs synergistically activate complementary cell-death pathways and overcome the usual mechanisms that make melanoma cells resistant to standard therapies,” says first author Gregory Lesinski, assistant professor of internal medicine and a researcher in the innate immunity program.

According to the National Cancer Institute, melanoma is the most deadly form of skin cancer and is becoming more common every year. The disease is highly curable when treated early, but only 10 to 15 percent of patients with advanced melanoma live more than five years. In the United States, the number of new cases in 2008 was estimated at more than 62,000, and the number of deaths, at more than 8,000.

Other Department of Surgery researchers involved in the study were Dr. Michael R. Go, assistant professor of surgery in the Division of Vascular Diseases and Surgery; Dr. Lloyd G. Brown, chief resident in general surgery; and Dr. Kristan D. Guenterberg, resident in general surgery.

The study was supported by funding from the Harry J. Lloyd Charitable Trust, the Melanoma Research Foundation, the Valvano Foundation for Cancer Research Award, and the National Cancer Institute.
LABORATORY RESEARCH

Blueberries may inhibit vascular tumors

Researchers in the Department of Surgery at The Ohio State University Medical Center have shown that feeding a blueberry extract to mice with tumors that are primarily found in infants and children will decrease tumor size and increase survival.

Mice that were fed the blueberry extract lived twice as long as control animals and had tumors that were 60 percent smaller, researchers found. The study also showed that the blueberry extract inhibited two important biochemical signaling pathways needed by tumor cells to grow.

The findings were published in January, in Antioxidants & Redox Signaling, the leading journal in its field.

“This work provides the first evidence demonstrating that blueberry extract can limit tumor formation by inhibiting the formation of blood vessels and inhibiting certain signaling pathways,” says principal investigator Dr. Gayle M. Gordillo, assistant professor of surgery and director of research in the Division of Plastic Surgery. “Oral administration of blueberry extract represents a potential therapeutic strategy for treating endothelial cell tumors in children.”

The study examined hemangioendotheliomas, a type of vascular tumor formed by a proliferation of endothelial cells, the cells that line the interior of blood vessels. The tumors, which usually occur within four weeks of birth, affect about three percent of children, and more frequently, premature infants.

Dr. Gordillo says that because about 90 percent of these vascular tumors resolve on their own within nine years, they are usually not treated, and families wait for them to go away naturally. However, the tumors often occur on the head or neck and produce an obvious deformity, and they can be life-threatening if they obstruct the airway.

She says current treatment options, such as high-dose steroids, can cause developmental delays and suppression of the immune system, so they are less than ideal for young children. Surgically removing the tumors is generally avoided, because a patient could potentially bleed to death or end up with a significant deformity. Many families choose to accept the deformity that these tumors create, because the risks associated with treatment are so severe.

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“Our hope is that if we feed blueberry juice to a child with this type of tumor, we can intervene and shrink the tumor before it becomes a big problem,” says Dr. Gordillo, who directs the hemangioma vascular malformation clinic at Nationwide Children’s Hospital. “Our next step is a pilot study with humans, to see if we can measure response to the treatment using imaging techniques and the monitoring of chemical changes in the urine.”

The finding that the blueberry extract inhibited two important biochemical signaling pathways needed by tumor cells could have implications for other cancers, such as breast cancer, some melanomas, and head, neck, and ovarian cancers, she says.

Gordillo collaborated on the study with Chandan K. Sen, Ph.D., professor of surgery in the Division of General and Gastrointestinal Surgery and a member of the molecular carcinogenesis and chemoprevention program in Ohio State’s Comprehensive Cancer Center. Sen is also vice chairman for research in the Department of Surgery, associate dean for translational and applied research in the College of Medicine, and director of the Comprehensive Wound Center at The Ohio State University Medical Center.

Other Ohio State researchers involved in the study were Huiqing Fang, Justin Harper, Savita Khanna, and Gary Phillips.

Funding from the National Institutes of Health/National Institute for General Medical Sciences supported the research.
INTERNATIONAL OUTREACH

Minimally invasive surgery experts serve on charitable mission to Cape Verde

Two minimally invasive surgery specialists in the Department of Surgery at The Ohio State University Medical Center recently served on a charitable mission to a hospital in Praia, Cape Verde.

Cape Verde is a developing nation located on a group of islands in the Atlantic Ocean, off the west coast of Africa. Praia, a city of 124,000, is the nation’s capital and its largest city.

Dr. Jeffrey W. Hazey, associate professor of surgery in the Division of General and Gastrointestinal Surgery, and 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 at Ohio State’s Medical Center, conducted a laparoscopic surgery course Jan. 26–30 for the surgeons and surgical staff at Praia’s Hospital Agostinho Neto.

Preceding the course, Dr. Hazey and Dr. Melvin worked to obtain donations of equipment, which they took with them. During the course, they performed some gynecological procedures.

Supported by the Go Global Initiative of the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES), Hazey and Melvin provided training in laparoscopic cholecystectomy procedures, in which the gallbladder is removed using minimally invasive surgical techniques. They also performed some gynecological procedures.

The mission of the SAGES Go Global Initiative is to provide training in laparoscopic surgery and flexible endoscopic procedures to surgeons worldwide who care for patients with limited or no access to medical care. The initiative concentrates on training in high-impact, high-volume, low-complexity procedures.

“SAGES performs a site visit ahead of time to determine whether a program can be expected to have longevity at a particular location,” Dr. Hazey says. “The organization also requests follow-up reports, to make sure that a location continues to use the techniques and technology to their full potential.”

Before the course, Dr. Hazey and Dr. Melvin worked to obtain donations of equipment, which they took with them. During the course, they performed an (See page 8)
average of three cases per day for four days. They also set up an ongoing support system for the surgeons there.

Dr. Julio Teixeira, chief of minimally invasive surgery at the St. Luke’s-Roosevelt Hospital Center, in New York, N.Y., also served as a visiting faculty member for the course.

Dr. Hazey says his most memorable impression of Cape Verde is of the chief surgeon at the hospital, Dr. Victor Manuel Mureira de Costa. “The amount of work he does is unbelievable, and he does it for very little money.

“The people have to live with very little,” Dr. Hazey says.

Cape Verde’s economy is hampered by limited natural resources and serious water shortages. About 90 percent of food must be imported, and the nation suffers from a high annual trade deficit.

Dr. Hazey says that in the future, he hopes to participate in a mission to another island in Cape Verde or in a follow-up mission to Praia. ✤
Residents recognized for research

**Dr. Mary E. Dillhoff**, a general surgery resident in the Master of Medical Science Program (MMSP), presented “MicroRNA-21 (MIR-21) Is Overexpressed in Esophageal Adenocarcinoma and a Potential Predictor of Progression in Barrett’s Esophagus” at the annual meeting of the Society of University Surgeons, Feb. 3–6, in Fort Myers, Fla. At the 20th Annual Presidential Symposium of the Columbus Surgical Society, she received the first-place Platinum Award for her presentation, “Overexpression of Micro-RNA 205 Is a Predictor of Poor Survival in Esophageal Adenocarcinoma.” The symposium was held Feb. 28 at The Ohio State University Medical Center. At the 62nd annual meeting of the Society of Surgical Oncology, March 4–8, in Phoenix, Ariz., Dr. Dillhoff presented “Overexpression of Micro-RNA 205 is a Predictor of Poor Survival in Esophageal Adenocarcinoma.” Dr. Dillhoff’s mentor is Dr. Mark Bloomston, assistant professor of surgery in the Division of Surgical Oncology.

**Dr. Kristan D. Guenterberg**, a general surgery resident in the MMSP, presented “Cetuximab-Coated Pancreatic Cancer Cells Increase Activity of IL-21-Treated NK Cells” at the annual meeting of the Society of University Surgeons. Dr. Guenterberg’s mentor is Dr. William E. Carson, III, professor of surgery in the Division of Surgical Oncology.

**Dr. Ioannis S. Hatzaras**, a general surgery resident in the Master of Public Health Program, presented “Elevated CA 19-9 Portends Poor Prognosis Despite Surgical Resection of Biliary Malignancies” at the annual meeting of the American Hepato-Pancreato-Biliary Association, March 11–15, in Miami Beach, Fla. Dr. Hatzaras’ mentor is Dr. Mark Bloomston, assistant professor of surgery in the Division of Surgical Oncology.

**Dr. Lisa M. Haubert**, a general surgery resident in the Master of Anatomy Program, presented “Surgical Clinical Correlates in Anatomy: Implementation of a First-Year Medical School Program” at the meeting of the Association of American Medical Colleges Central Group on Educational Affairs, March 26–28, in Rochester, Minn. Dr. Haubert’s mentor is Dr. Susan D. Moffatt-Bruce, assistant professor of surgery in the Division of Cardiothoracic Surgery.

**Dr. Natalie A. Jones**, a general surgery resident and graduate of the MMSP, had her paper, “Contralateral Prophylactic Mastectomy for Unilateral Breast Cancer: An Increasing Trend,” accepted for presentation at the 62nd annual meeting of the Society of Surgical Oncology. At the 20th Annual Presidential Symposium of the Columbus Surgical Society, she received the third-place

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Silver Award for her presentation, “Cytokines Enhance the Anti-Tumor Effects of Folate-Conjugated Immunoglobulin.” Dr. Jones’ mentor is Dr. Doreen M. Agnese, assistant professor of surgery in the Division of Surgical Oncology.

Dr. Peter N. Nau, a general surgery resident in the MMSP, presented “Laparoscopic Distal Pancreatectomy with and without Splenectomy: A Retrospective Review” at the annual meeting of the Society of University Surgeons. At the 20th Annual Presidential Symposium of the Columbus Surgical Society, he received the fourth-place Bronze Award for his presentation, “Diagnostic Transgastric Endoscopic Peritoneoscopy: Extension of Initial Human Trial for Staging of Pancreatic Head Masses.” At the annual meeting of the American Hepato-Pancreato-Biliary Association, Dr. Nau received the association’s Surgical Technology Assessment and Outcomes Research Grant. His project, titled “Development of a Novel Repair Technique for Iatrogenic Common Bile Duct Injuries with a Biosynthetic Absorbable Graft,” seeks to identify a new and less invasive approach to this common surgical disease. Next year, Dr. Nau will travel to Buenos Aires, Argentina, to present the results of his research at the international AHPBA meeting. Dr. Nau’s mentor is 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.

Dr. Thomas A. Pham, a resident in general surgery, has been awarded the 2009 American Society of Transplant Surgeons-National Kidney Foundation Folkert Belzer MD Research Fellowship Award. The two-year award will support his full-time research in transplantation and transplant immunobiology, as he pursues a master of medical science degree under the mentorship of Dr. Ginny L. Bumgardner, professor of surgery in the Division of Transplantation.

Dr. Ricardo O. Quarrie, a general surgery resident, received a university fellowship from The Ohio State University Graduate School, in support of a project titled “The Role of Mitochondrial Oxygen Free Radical Production on Ischemic Preconditioning.” Awarded in a university-wide competition on the basis of academic achievement and potential for scholarly work and to support the advanced degree training of physicians in biomedical research, the fellowship provides stipend and tuition support. Dr. Quarrie will pursue a master of medical science degree under the mentorship of Dr. Juan A. Crescentanello, assistant professor of surgery in the Division of Cardiothoracic Surgery.
IN BRIEF

Publications


Presentations

**Besner G.** Burned kids. Fire and Ice, State Fire Marshal’s Office, Ohio Fire Academy, Reynoldsburg, Ohio, Nov. 8, 2008.

**Besner G.** Pediatric burn management. Columbus Fire House, Columbus, Ohio, Nov. 19, 2008.

**Caniano DA (Visiting Professor).** Surgical neonatology: quest for quality. Surgical ethics: progress and challenge. Washington University School of Medicine, St. Louis, Mo., March 17–18, 2009.


**Eakin J.** Comparison outcomes for burn patients cared for in trauma centers, based on two national registries. American Burn Association, 41st Annual Meeting, San Antonio, Texas, March 27, 2009. (See page 12)
Groner JI. Building a trauma program: the Nationwide Children’s Hospital model. Brenner Children’s Hospital, Wake Forest University Baptist Medical Center, Winston-Salem, N.C., Feb. 4, 2009.

Groner JI. (Visiting Professor). The good, the bad, and the ugly: recognition of shock in pediatric trauma. Brenner Children’s Hospital, Wake Forest University Baptist Medical Center, Winston-Salem, N.C., Feb. 4, 2009.


(See page 13)

Radulescu A, Yu X, Chen Y, Besner G. HB-EGF knockout mice have increased susceptibility to necrotizing enterocolitis. Columbus Surgical Society, 20th Annual Presidential Symposium, Columbus, Ohio, Feb. 28, 2009.


Zhang H-Y, Radulescu A, Besner G. HB-EGF is essential for preservation of gut barrier function after hemorrhagic shock and resuscitation in mice. The Ohio State University, Third Annual International Scholar Research Exposition, Columbus, Ohio, November 3, 2008.


Recognitions

Dr. Mark Bloomston, assistant professor of surgery in the Division of Surgical Oncology, received the Junior Faculty Award of the Society of University Surgeons at the society’s Academic Surgical Congress, Feb. 3–6, in Fort Myers, Fla. Dr. Bloomston received the one-year, $30,000 award for his project, “MicroRNA-21 Expression and Function in Pancreatic Adenocarcinoma.” (See page 14)
Dr. E. Christopher Ellison, the Robert M. Zollinger professor and chairman of surgery, associate vice president for health sciences, and vice dean of clinical affairs at The Ohio State University Medical Center, has been named to the Executive Cabinet and the Leadership Council at the Medical Center.

Under the direction of Dr. Sidney F. Miller, the Burn Center at The Ohio State University Medical Center has received verification as an adult burn center. Dr. Miller is professor of surgery in the Division of Critical Care, Trauma, and Burn and president of the American Burn Association (ABA). The verification recognizes the center’s commitment to providing outstanding burn care to its patients. The burn center, the only adult burn treatment center in Central Ohio and part of the Medical Center’s Level 1 Trauma Center, provides inpatient and outpatient care for burn wounds and serious skin conditions, complex burn management, physical and occupational therapy, speech language therapy, social work, and nutrition services. The review was conducted by the ABA and the American College of Surgeons Committee on Trauma.

Dr. Susan D. Moffatt-Bruce, assistant professor of surgery in the Division of Cardiothoracic Surgery, has been selected by the Center for Clinical and Translational Science (CCTS) at The Ohio State University Medical Center to receive a K12 award for her research project, “The Role of T Cells and Innate Immunity in Cardiac Transplantation.” The two-year award provides support for tuition and fees related to career development; research expenses; travel to research meetings, workshops, and training; and statistical services. The CCTS also offers awardees support services to further their research careers. Dr. Moffatt’s mentor for the project is Gregg A. Hadley, Ph.D., professor of surgery in the Division of Transplantation and deputy director of research for the Comprehensive Transplant Center.

Sampath Parthasarathy, Ph.D., M.B.A., the Karl P. Klassen professor of surgery and director of research in the Division of Cardiothoracic Surgery, has been awarded the Ranbaxy Science Foundation Research Award for 2007, in the field of medical sciences and medical research. Parthasarathy received the award March 19, at the foundation’s 15th Annual Symposium, which was held at the All India Institute of Medical Sciences, in Delhi, India. Parthasarathy shared the award with Ajit Varkim, distinguished professor of medicine and cellular and molecular medicine at the University of California, in San Diego.

Dr. Andrei Radulescu, a surgical research fellow in pediatric surgery, received the second-place Gold Award at the 20th Annual Presidential Symposium of the Columbus Surgical Society, for his presentation, “HB-EGF Knockout Mice Have Increased Susceptibility to Necrotizing Enterocolitis.” The symposium was held Feb. 28 at The Ohio State University Medical Center. (See page 15)
Dr. Wiley W. “Chip” Souba, Jr., professor of surgery in the Division of Surgical Oncology, dean of The Ohio State University College of Medicine, and vice president for health sciences at The Ohio State University Medical Center, met with area health care experts and advocates for health care reform on Dec. 30, 2008, to summarize their views and suggestions for a national health plan. The plan was forwarded to the transition team of then President-elect Barack Obama.

**Correction**

In the February 2009 issue of Surgery Today, Dr. William E. Carson, III, of the Division of Surgical Oncology, was incorrectly identified as associate professor of surgery. Dr. Carson’s correct title is professor of surgery.