

# SUTURELINE

## NEWS FROM THE DEPARTMENT OF SURGERY

WINTER 2022

### **Division of Immunotherapy Engages in Groundbreaking Research**

In 2022, the Division of Immunotherapy has received notification that 5 NIH R01 grants, 2 R21 grants, and a major American Cancer Society grant have been awarded or scored in the fundable range and soon will be funded. The Department of Surgery created the Division of Immunotherapy in 2019 to lead the way in improving our understanding of the role of immunotherapy in the treatment of cancer and other diseases. Since then, the researchers in the division have engaged in pioneering research designed to trigger our bodies' own immune system to fight disease.

Here are a few of the areas where this team of researchers, led by Division Director Jun Yan, MD, PhD, have made great strides already.

#### **Training immunity to reduce tumor activity in pancreatic cancer**

Pancreatic cancer is one of the deadliest cancers, with a five-year survival rate of just 10 percent for patients diagnosed with pancreatic ductal adenocarcinoma (PDAC), the most common type. Further, one promising area of cancer treatment, immunotherapy, has not provided benefit for pancreatic cancer patients.

Division of Immunotherapy researchers led by Dr. Yan recently have shown that beta-glucan, a natural carbohydrate, can generate enhanced immune responses to cancer in the pancreas and may lead to improved efficacy of immunotherapy for pancreatic cancer.

Trained immunity is a new concept in the field of immunology and is the idea that innate immune cells possess a form of "memory," which typically only has been considered to be a feature of adaptive immune cells such as T-cells.

"Your immune cells can be trained to memorize, and then they can respond similar to a vaccine. So, you get vaccinated and then your body remembers, 'oh, this is COVID pathogen.' When you encounter those, they can greatly expand it and then eradicate these pathogens," Dr. Yan explains.

Using animal models, Division of Immunotherapy researchers found that when they injected particulate beta-glucan into the peritoneal area, it accumulated in the pancreas and promoted anti-cancer immune cell migration to the area. These immune cells were found to have a trained immunity phenotype and effectively inhibited pancreatic cancer growth.

"This research demonstrates that a natural compound can stimulate trained immunity in the pancreas," Yan said.

#### **Inducing trained immunity in pro-metastatic macrophages to control tumor metastasis**

Metastasis is the leading cause of cancer-related deaths, and myeloid cells are critical in the metastatic microenvironment. Division of Immunotherapy researchers also led by Dr. Yan have developed a method shown to reduce cancer metastasis in animal models. The researchers successfully trained immune cells to combat the cancer using whole beta glucan particles. They discovered that infusion of beta-glucan trained immune cells into tumor-bearing mice can control tumor metastasis. It shows for the first time that infusion of beta-glucan-trained innate immune cells can control and eradicate tumor metastasis.

"The approach we're taking is to see whether we can actually educate those myeloid cells and make those bad guys become good guys and help constrain the tumor growth and the metastasis," Dr. Yan says.

Since trained innate cells do not require restricted recognition as Chimeric Antigen receptor (CAR) T cells, these cells can be manufactured off the shelf. If it is successful in humans, it will substantially reduce treatment costs. This approach is considered a new player in cell-based cancer immunotherapy.

#### **Enteric VIP-producing neurons maintain gut microbiota homeostasis through regulating epithelium fucosylation**

Division of Immunotherapy researchers led by Zhong-bin Deng, PhD, are exploring the role of neutral ceramidase in intestinal fucosylation and liver steatosis and inflammation. This research is designed to garner a better understanding of the mechanisms for NcDase-induced gut fucosylation and glycosphingolipid-regulated macrophages in the development of NAFLD and may lead to the identification of novel therapeutic targets.

"Understanding the underlying mechanism and any prevention approach will be very beneficial for patients, especially for alcohol-induced liver inflammation," Dr. Yan says.

#### **Identifying and targeting a novel mechanism of chemotherapy-induced immunotherapeutic resistance in non-small cell lung cancer**

Cancer therapy with a combination of cytotoxic drugs and with immune checkpoint inhibitors (ICIs)—agents that reinvigorate the suppressed immune system to attack cancer cells (e.g., anti-PD-1 antibody)—has revolutionized the treatment of metastatic lung cancer. However, therapeutic resistance is observed in a significant proportion of patients and a critical determinant of unresponsiveness in these patients is the intra-tumoral accumulation of adenosine, a molecule that actively suppresses the effectiveness of immunotherapies.

To deplete the intra-tumoral adenosine, Division of Immunotherapy researchers led by Kavitha Yaddanapudi, PhD, have explored the use of an FDA approved drug, [PEGylated]-Adenosine Deaminase (PEG-ADA). Their proposed studies will confirm if depletion of adenosine with PEG-ADA can induce antitumor immunity and sensitize lung cancer to chemo-immunotherapy and such a therapeutic strategy can further extend the life of patient with a disease that is now a major health problem worldwide.

### Immunotherapeutic targeting of MIF-dependent chaperone activity

Despite some very encouraging improvements in response rates

and overall survival in late-stage melanoma patients receiving anti-PD-1/anti-CTLA-4 immune checkpoint blockade (ICB) immunotherapies, an unacceptably high percentage of treated patients remain unresponsive to these therapies. Division of Immunotherapy researchers led by Robert A. Mitchell, PhD, plan to investigate a unique metabolic transcriptional programming pathway that is governed by MIF-dependent chaperone activity. When therapeutically inhibited with a suicide antagonist discovered by their laboratory, highly immune suppressive myeloid lineage cells are converted to highly immune stimulatory myeloid cells in the tumor microenvironment that is sufficient to induce tumor rejection and increased survival.

"This is only the beginning—the tip of the iceberg," Dr. Yan says.

## Welcome from Dr. McMasters



Welcome to the 2022 issue of Sutureline, a newsletter about the Hiram C. Polk, Jr., MD, Department of Surgery at the University of Louisville.

The second year of the pandemic began with a surge in cases due to the omicron variant, but despite the challenges the pandemic presented, our faculty and staff adapted and overcame obstacles, and we were still able to have a productive year.

We recruited two new outstanding faculty members. Also included in this issue we recognize the outstanding research prowess of our Division of Immunotherapy and celebrate five faculty members who were recognized by the School of Medicine for their outstanding contributions to patient care, education and research. Other faculty also garnered well-deserved recognition for their dedication to their jobs, our Department and UofL.

We would like to thank all of you who have donated to the Department of Surgery this year. We truly appreciate your loyalty. We need your support more than ever this year to continue our missions in surgical education, patient care, and research so the tradition of excellence of the Department of Surgery at the University of Louisville, which dates back to 1837, can continue.

If you have not already given or have the capacity to do more, please consider [making a gift](#) to the Department of Surgery this holiday season.

Warmest wishes for the holidays and the year ahead,

Kelly M. McMasters, MD, PhD  
*Ben A. Reid, Sr., MD, Professor and Chair  
Hiram C. Polk, Jr., MD, Department of Surgery  
University of Louisville School of Medicine*

## Five Faculty Members Receive School of Medicine Excellence Awards



[Russell Farmer, MD](#), received the **2022 UofL Outstanding Educator Award**. An Associate Professor of Surgery in the section of Colon and Rectal Surgery, Dr. Farmer remains among the most lauded educators in the Department of Surgery, continually providing high-quality education to all the students, residents and fellows that come through our training programs.

Dr. Farmer has won every single possible educational award provided by the UofL Department of Surgery, some of them several times.



[Susan Galandiuk, MD](#), received the **2022 Distinguished Career of Service Award**. Director of the section of Colon and Rectal Surgery and Professor of Surgery, Dr. Galandiuk has a genuine and consistent dedication to teaching and mentoring medical students, residents and fellows at the University of Louisville and across the globe. She has been a true international

leader in the field of academic surgery and in the field of

colorectal surgery, as well as a pioneer for women in the field of surgery.

[Robert C.G. Martin, II, MD, PhD](#), received the **2022 Distinguished Service to Profession Award**. Dr. Martin is the Sam and Lolita Weakley Professor and Director of the Division of Surgical Oncology and serves as Vice-Chair of the Department of Surgery for Research. He is an energetic scholar, cancer research pioneer and a key investigator in several new approaches to cancer treatment. Dr. Martin has dedicated his career to reducing cancer patient suffering through research, education, advocacy and service.



[Gordon R. Tobin, II, MD](#), received the **2021-2022 Distinguished Service to the Profession Award**. Throughout his career, Dr. Tobin has set an example for his peers through medical excellence and humanistic leadership. This is reflected by his lifelong effort to improve: medical care and medical education for impoverished Third-World countries; human values through community and university programs; and access to medical care in the U.S. for our uninsured Americans. Dr. Tobin is a Professor in the Division of Plastic and Reconstructive Surgery.





[Jun Yan, MD, PhD](#), received the **2021-2022 Outstanding Research in Basic and Applied Sciences Award**. Dr. Yan is Director of the Division of Immunotherapy and Professor of Surgery as well as Microbiology and Immunology. Under his leadership, the Division of Immunotherapy is leading the way to improve our

understanding of the role of the immune system in the treatment of cancer and other diseases.

Congratulations to these outstanding faculty members on their well-deserved awards!

## ACADEMIC EXCELLENCE

### New Faculty

The Department of Surgery welcomed new faculty members [Mahsa Javid, MB, BChR, MA, DPhil, FRCS FRCSC](#), and [Samuel Pera, MD](#).



Dr. Javid joined the Division of Surgical Oncology. She earned her undergraduate, medical and master's degrees at Cambridge University. She completed her residency in general surgery at Oxford University and a fellowship in endocrine surgery at Yale University. She specializes in the management of benign and malignant

endocrine disease, complex cases including re-operative surgeries, conventional open and minimally invasive procedures such as surgery under local anesthesia for neck procedures and posterior retroperitoneoscopic approach for adrenal disease.

Dr. Pera joined the Division of General Surgery. He attended medical school at Rush University Medical College in Chicago. He then completed his residency in general surgery at University of Illinois - College of Medicine Peoria, which he followed with a fellowship in Surgical Critical Care, Trauma and Acute Care Surgery at the University of Louisville. His expertise includes trauma and acute care surgery, general surgery, surgical critical care and minimally invasive/robotic surgery.



### Leaving A Legacy

The UofL Hospital Trauma Center has been renamed to honor the legacy of Dr. J. David Richardson, who passed away in September of 2021. This recognition demonstrates the difference he made at UofL Hospital.

Over the years, the quadruple-boarded surgeon helped train and develop hundreds of medical students. He was board-certified in general surgery, thoracic surgery, vascular surgery and critical care surgery, served as Chief of Surgery Services and Director of Emergency Surgical Services, amongst additional leadership roles and was former President of the American College of Surgeons and many other surgical organizations.



### In the Service of Others

[Keith Miller, MD](#), UofL Health trauma surgeon and Associate Professor of Surgery, Division of General Surgery, Tara Wright, UofL Health OR Supply Coordinator and other UofL Health staff, collected and provided [Gordon R. Tobin, II, MD](#), UofL Health plastic and reconstructive surgeon and Professor, Division of Plastic and Reconstructive Surgery, much-needed items for Supplies Overseas (SOS). SOS refurbishes and recycles hospital supplies and equipment for reuse in impoverished developing countries. The hemostatic agents control life-threatening bleeding from bomb and bullet wounds. These were air-lifted to a recipient NGO humanitarian organization near Ukraine.

Dr. Tobin has been an integral part of SOS and brought the program to UofL Health many years ago. Over the past two decades, the hospitals in the downtown medical center have

been the main contributors to SOS, providing tons of supplies. Contributing hospitals now extend across the state and Southern Indiana. More than \$60 million worth of supplies have gone to hospitals in need in more than 100 countries and about 4 million pounds have been kept out of U.S. landfills.



## DEPARTMENT & ALUMNI

### News & Notes



Mary Fallat, MD, received the American Pediatric Surgical Association's Distinguished Service Award. APSA's highest honor, the Distinguished Service Award is given in recognition of a lifetime commitment to, and wide-reaching impact on, the field of pediatric surgery. It has only been awarded a handful of times in the organization's history. The frequency of this award is determined by the Board.

Dr. Fallat also received the Ladd Medal from the Section on Surgery of the American Academy of Pediatrics last fall. This is the highest award given by the American Academy of Pediatrics (AAP).

In addition, the American Academy of Pediatrics Section on Bioethics awarded Dr. Fallat with the 2022 William G. Bartholome Award for Ethical Excellence. Dr. Fallat is the current First Vice President of the American College of Surgeons, where she also serves on the Board of Regents.



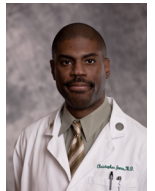
[Keith Miller, MD](#), UofL Health trauma surgeon and Associate Professor of Surgery, Division of

General Surgery, was highlighted in Louisville Business First's Health Equity Champion category for his work with the [Future Healers Program](#), which helps Louisville youth affected by violence navigate the trauma through education. Dr. Miller and University of Louisville School of Medicine student Karen Udoh were named co-recipients of the 2022 Kelsie Small Future Healer Award for exemplifying excellence, caring, compassion and commitment to education.

The inaugural episode of a new American College of Surgeons podcast series called Surgical Readings from SRGS featured the Department of Surgery's very own [Sandra Kavalukas, MD](#), colorectal surgeon and Assistant Professor of Surgery, Division of General Surgery. She discussed the management of perirectal abscess and diverticular disease, the use of fiber supplements, and the importance of engaging patients in informed decision-making.



[Christopher Jones, MD](#), Hiram C. Polk, Jr., M.D. and Lily Banerjee Chair in Surgery and Director, Division of Transplantation, was included in the KULA Gallery's "Faces of Donation," which featured portraits of local Black organ donors, donor families, recipients and physicians. The event took place Feb. 25.



### Grand Rounds Available on YouTube

The Department of Surgery's Grand Rounds are [now available](#) on YouTube. Visit our YouTube channel to view Surgery Grand Rounds presentations from May 2020 to present.

### 2022 Where Are They Now

**Elizabeth Bruenderman, MD**, MIS/Bariatrics Fellowship at Duke University, Durham, NC

**Joshua Clapp, MD**, Private Practice at Baptist Health, Madisonville, KY

**Sarah Couch, MD**, Breast Fellowship at Emory University, Atlanta, GA

**Adam Hicks, MD**, Vascular Fellowship at Indiana University, Bloomington, IN

**Jeff Howard, MD**, Private Practice at Norton Healthcare, Louisville, KY

**Nicholas Welko, MD**, Trauma Critical Care Fellowship at Washington University, St. Louis, MO

**Amy Wise, MD**, Colorectal Fellowship at University of South Florida, Tampa, FL



### Stay On The Cutting Edge

Send us your updated address so we can stay in touch!

Send your information to [radhika.bombard@louisville.edu](mailto:radhika.bombard@louisville.edu)

Join our UofL Dept. of Surgery Alumni [Facebook page](#).

Find us on Twitter [@uoflDeptofSurg](#)

### Stay In Touch

Please keep in touch and let us know what is happening with you, your practice and your family. We apologize in advance for any errors of omission. Please send your news items and updated addresses to [radhika.bombard@louisville.edu](mailto:radhika.bombard@louisville.edu).

### Make A Gift to the Department of Surgery

As you plan your year-end giving, please consider supporting to the Department of Surgery.

To make a gift by credit card, please visit [give.louisville.edu](https://give.louisville.edu). If you would like to send in a donation via mail, all gifts can be mailed to: University of Louisville Foundation, Inc., P.O. Box 772050, Chicago, IL 60677-2050. Please make checks payable to the University of Louisville Foundation. Gifts must be postmarked by December 31, 2022.

For gifts of securities or information on estate planning, please contact Denise Nuehring, Senior Director of Development: [denise.nuehring@louisville.edu](mailto:denise.nuehring@louisville.edu) or 502.415.8279.