University of CINCINNATI

UNIVERSITY OF CINCINNATI

DEPARTMENT OF

INTERNAL MEDICINE

Annual Research Report

ACADEMIC YEAR 2016-2017

MISSION STATEMENT

Through collaboration and innovation, we will be the leader in improving the health of our local and global community.

Our mission is to improve health for all through:

- Personalized care embracing best clinical practices
- Innovative interdisciplinary research
- Premier clinical and scientific training
- Creative community partnerships

Front cover: Immunofluorescence microscopy image from Dr. Soleimani laboratory showing the localization of the chloride channel/transporter Slc26a11 (also known as Kidney Brain Anion Transporter or KBAT) in the kidney. This protein was identified and characterized in Soleimani laboratory. This image depicts a section from kidney labeled for the water channel AQP-2 (marker of principal cells, green) and KBAT (red). KBAT (or Slc26a11) is located on the apical membrane of intercalated cells in the collecting duct (adjacent to principal cells which are stained green) and in connecting tubules and terminal portion of distal convoluted tubules (only red with no green stain). This channel/transporter is also expressed in Purkinje cells in cerebellum and in hippocampus.
To learn more about these studies and this channel/transporter, please refer to Kidney Int. 80:926-37, 2011; Kidney Int. 84:657-66, 2013; Pflugers Arch. 465:1583-97, 2013; and eNeuro. 15;3, 2016.

DEPARTMENT OF **INTERNAL MEDICINE**

Annual Research Report

ACADEMIC YEAR 2016-2017

University of CINCINNATI

TABLE OF CONTENTS

Message from the Chair

LEADING IMPROVEMENTS IN HEALTH THROUGH COLLABORATION AND INNOVATION

WE APPRECIATE THE COMMITMENT, WORK AND SERVICE OF ALL the faculty, investigators, researchers, trainees and staff of the nine divisions of the Department of Internal Medicine (DOIM).

The Associate Chair of Research, Manoocher Soleimani, MD and Associate Chair of Translational Research Carl Fichtenbaum, MD and other faculty and staff on the Research Governance Committee deserve a great deal of credit for coordinating and preparing our Annual Research Symposium, monthly Research Conferences, intramural Research Awards and Annual Research Report.

A great deal has been accomplished in each area of our tripartite mission over this past year and research is no exception. Such has occurred by tactically implementing our strategic plan. Specifically, we currently hold 133 total grants in the department 21% of which are held by primary investigators with R0-1 awards. The total award amount is $80,941,905. Of these, $13,147,754 were new grants awarded in FY17. This total award amount does not include approximately $4.8 million in clinical trial revenue DOIM investigators have brought in through University of Cincinnati Physicians, nor the nearly $4 million in research funding held by our investigators at the Cincinnati Department of Veterans Affairs Medical Center this past year.

Most importantly, we continue to support our investigators with distinguished research achievement awards, junior and senior pilot awards, challenge awards, bridge funding and others. We plan to continue these very successful initiatives.

You will be hearing groundbreaking news about many of these investigators research in the months to come. Their discoveries will be used to improve the health of our community on many levels. Their work focuses on anti-thrombotic aptamers antidotes; graft integrity in heart transplantation mediated by micro RNAs; molecular vaccines for type I diabetes; and molecular and biochemical basis of LAM, to name a few.

Sincerely,

Gregory Rouan, MD

Gordon and Helen Hughes Taylor
Professor of Medicine
and Chair, Department of Internal Medicine

Creating a Stronger Future Through Innovation and Research

The success of our department is measured by how effectively it is reshaping health care delivery, education, and research in the Cincinnati community, State of Ohio and beyond. The quality of research created by our investigators is therefore critical to our mission and success. Thus, seeking motivated faculty, as well as nurturing, educating and supporting our existing investigators are crucial steps toward achieving our goals, specifically as they pertain to translating new discoveries into improved healthcare outcomes.

Carl Fichtenbaum, MD

Manoocher Soleimani, MD

With a vision to create an environment that encourages, stimulates and promotes research, the leadership of the DOIM will continue to provide the resources and tools needed to support our research mission. These include promoting collaborative multidisciplinary research and advancing an environment of creativity.

In this annual report, you will find outlines on successful translational research projects, summaries from researchers and staff in each division, engaging spotlights about our investigators and communications concerning the department's research awards and their recipients. Taken collectively, this report illustrates how we are cultivating a productive, innovative and growing research program that supports basic, clinical and translational research to make a difference in the health of our community.

In addition to this year's annual report, we are happy to have hosted a successful Research Symposium and another round of intramural DOIM research awards to stimulate and support innovative investigator initiated ideas. Such activities are critical to the research mission of our department and our Academic Health Center.

An important emphasis at this year's symposium was our trainees, including fellows, residents, medical students and graduate students, mentored by faculty in the department. Our trainees presented their research on basic, translational or pilot projects and were able to engage in insightful discussions with other investigators, including senior and junior faculty, fellows, staff and students regarding ongoing research, research techniques, research methods and potential collaborations and mentoring relationships.

We hope you will enjoy reading this report and it will persuade you to want to learn more about the innovative research in our department. Furthermore, we encourage you to discover how you can join with us in supporting our research efforts to create a strong, healthy community.

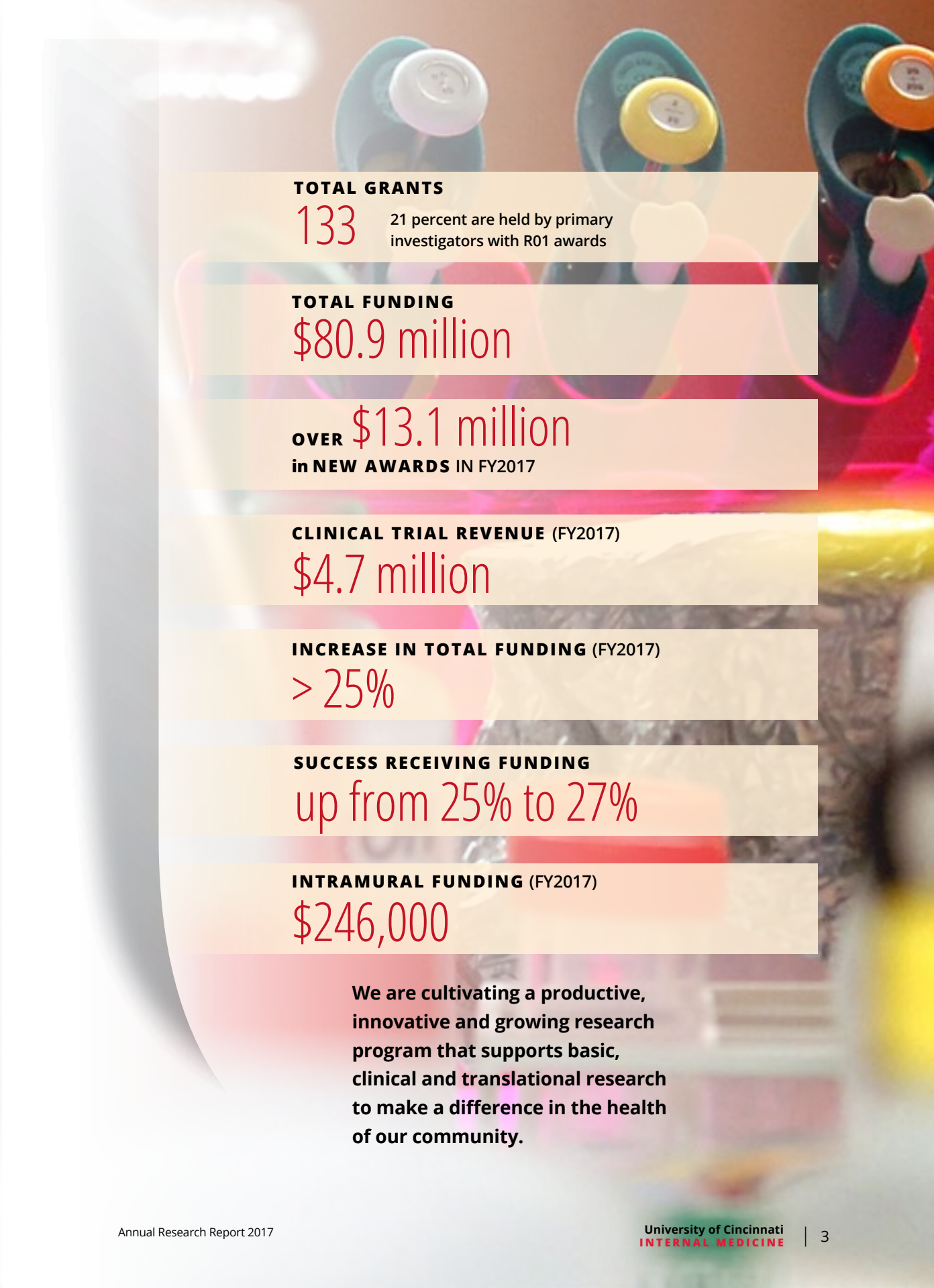
Respectfully,

Carl Fichtenbaum, MD

Associate Chair for
Translational Research
Professor of Clinical Medicine
Department of Internal
Medicine

Manoocher Soleimani, MD

Associate Chair for Research
James Heady Professor of Medicine
Department of Internal Medicine



TOTAL GRANTS

133 21 percent are held by primary investigators with R01 awards

TOTAL FUNDING

$80.9 million

OVER $13.1 million
in NEW AWARDS IN FY2017

CLINICAL TRIAL REVENUE (FY2017)

$4.7 million

INCREASE IN TOTAL FUNDING (FY2017)

> 25%

SUCCESS RECEIVING FUNDING

up from 25% to 27%

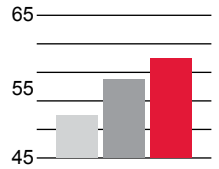
INTRAMURAL FUNDING (FY2017)

$246,000

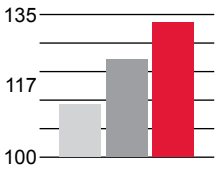
We are cultivating a productive, innovative and growing research program that supports basic, clinical and translational research to make a difference in the health of our community.

Funding Metrics

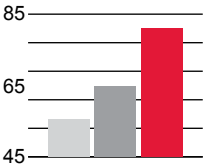
PIs Funded



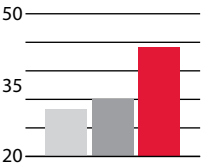
Total Awards



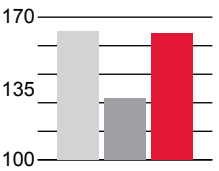
Funding *(in millions)*



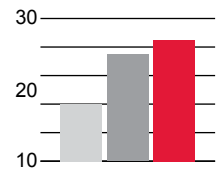
New Awards

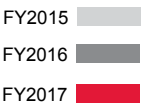


Submissions



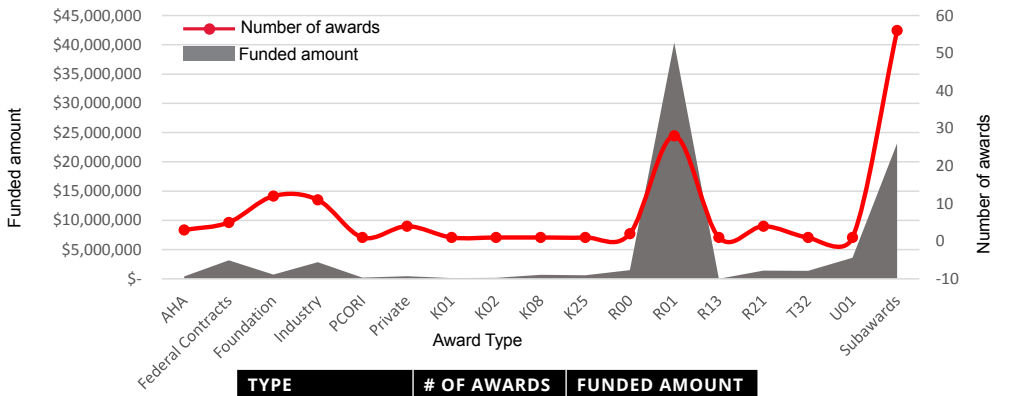
Success Rate *(%)*





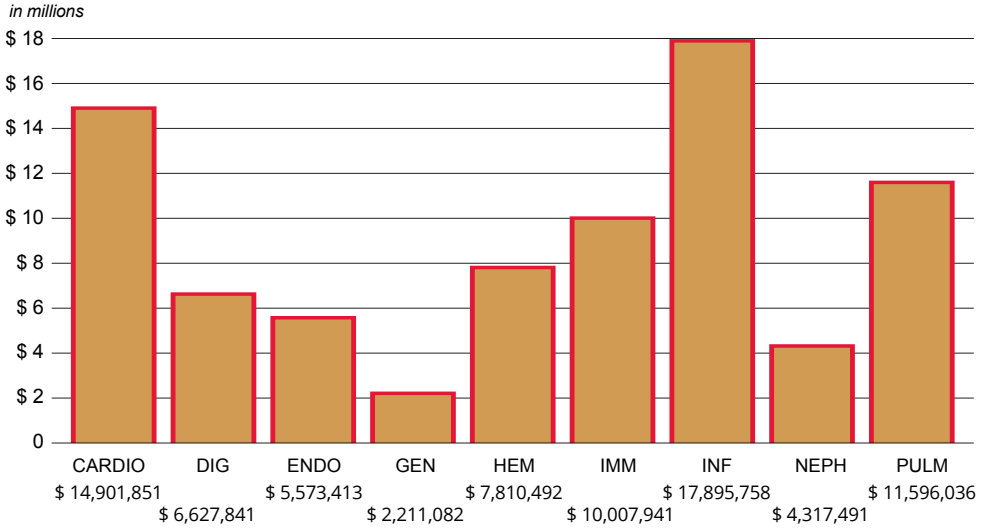
	FY15	FY16	FY17
PI's with funding	51	56	**59**
Total Awards	113	124	**133**
Funding (millions)	55.4	64.9	**80.9**
New Awards	30	32	**43**
Submissions	163	130	**162**
Success Rate (%)	18	25	**27**

Funded Awards by Type



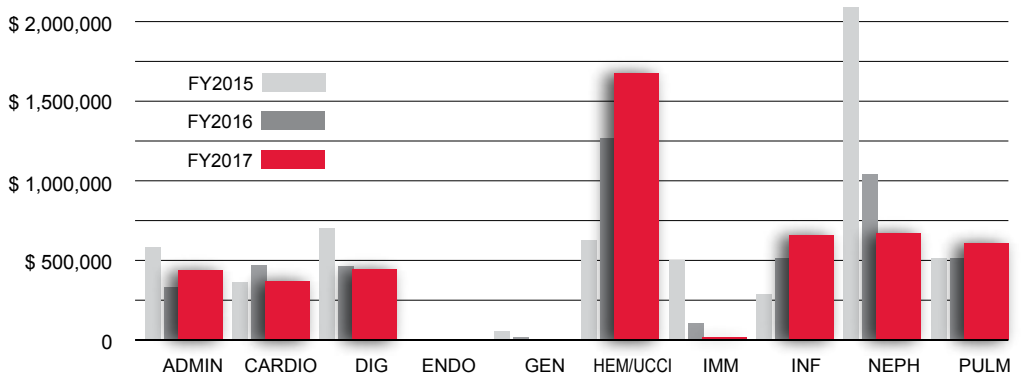
TYPE	# OF AWARDS	FUNDED AMOUNT
AHA	3	$ 420,291
Federal Contracts	5	$ 3,186,282
Foundation	12	$ 726,561
Industry	11	$ 2,839,971
PCORI	1	$ 212,364
Private	4	$ 469,352
K01	1	$ 129,319
K02	1	$ 186,361
K08	1	$ 704,232
K25	1	$ 630,964
R00	2	$ 1,482,572
R01	28	$ 40,374,243
R13	1	$ 25,000
R21	4	$ 1,412,591
T32	1	$ 1,361,995
U01	1	$ 3,606,817
Subawards	56	$ 23,172,989

Funding by Division FY2017



TOTAL FY2017 **$ 80,941,905**

Clinical Trial Revenue by Division FY2015 to FY2017



FY2015	579,172	359,263	701,323	0	55,000	625,266	497,719	285,881	2,089,361	512,325
FY2016	330,987	468,588	460,962	0	12,929	1,265,595	102,467	512,955	1,042,680	510,426
FY2017	**434,711**	**367,915**	**439,942**	**0**	**0**	**1,672,936**	**6,696**	**655,920**	**668,734**	**608,945**

TOTAL FY2017 **$ 4,855,799**

New Awards FY 2017 Department of Internal Medicine

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIRECT COSTS
CARDIO	Haworth, K	Ultrasound-mediated oxygen scavenging for inhibition	NHLBI - K25	8/1/16 - 6/30/20	$ 584,226.00
CARDIO	Wanek, A	Investigation of the Relationship Between Hemolysis and Acoustic Droplet Vaporization	Acoustical Society of America	10/1/16 - 5/31/17	$ 500.00
CARDIO	Holland, C	Diversity Supplement	NIH	8/1/16 - 7/31/18	$ 109,832.00
CARDIO	Holland, C	Echogenic Targeted Liposomes: Transfection/Drug Delivery	UTHSCH/NIH	5/1/17 - 8/31/22	$ 967,197.00
CARDIO	Tranter, M	Investigation of Human Antigen R (HuR)	NIH	7/1/16 - 3/31/21	$ 225,000.00
CARDIO	Sadayappan, S	AHA - transfer from Loyola	AHA	8/15/16 - 11/30/16	$ 75,000.00
CARDIO	Sadayappan, S	Umass sub - transfer	Umass sub R01 AR067279	8/15/16 - 6/30/17	$ 10,340.50
CARDIO	Sadayappan, S	R01 Cardiac myosin binding protein-C: Structure and Function	NHLBI	8/15/16 - 2/28/20	$ 977,759.00
CARDIO	Sadayappan, S	R01 Molecular mechanism of hypertrophic cardiomyopathy in populations of South Asian descendents	NHLBI	8/15/16 - 12/31/19	$ 866,215.00
CARDIO	Sadayappan, S	K02 Proteomic approaches to validate novel cardiac biomarkers for myocardial infarcti	NHLBI	8/15/16 - 7/31/17	$ 117,976.00
CARDIO	Sadayappan, S	A novel polymorphic MYBPC3 variant causes hypertrophic cardiomyopathy in US-South Asisan descendants	AHA	5/1/17 - 4/30/18	$ 232,532.00
CARDIO	Rubinstein, J	TRPV2 agonism for improved cardiac function in patients	AHA	1/1/17 - 12/31/18	$ 114,000.00
DIGEST	Bari, K	Pilot Study to Evaluate the Safety and Efficacy of Budesonide	Amer. College of Gastroenterology	7/1/16 - 6/30/17	$ 10,000.00
DIGEST	Kaiser, T	Novel Medication Adherence Monitoring Strategies	Amer. Society of Transplantation	7/1/16 - 6/30/17	$ 14,000.00
DIGEST	Sherman, K	R13 A1071925		9/2/16 - 8/31/17	$ 40,000.00
DIGEST	Sherman, K	Timing of Treatment for Chronic Hepatitis C Infection in Patients	MERCK	4/15/17 - 4/15/19	$ 73,961.00
DIGEST	Yacyshyn, B	Open Label, Randomized, Multicenter, Comparative Effectiveness	U. Penn / PCORI	3/20/17 - 3/19/20	$ 20,476.00
DIGEST	Yacyshyn, B	Gene discoveries in subjects with Crohn's disease of African Descent (GENESIS)	Emory/NIH	9/1/16 - 7/31/21	$ 18,780.00
ENDOCR	Patel, S	Identifying novel drug targets for obesity and metabolic diseases	Greater Cincinnati Foundation	7/1/16 - 6/30/17	$ 44,000.00
ENDOCR	Wortman, M	Targeting brain metabolism to improve congnitive impairment	L.I.F.E	9/1/16 - 8/31/17	$ 50,000.00
ENDOCR	Perez-Tilve, D	Novel peptide-based therapies for the treatment of diabetes	Novo Nordisk	1/1/17 - 12/31/17	$ 629,889.00
ENDOCR	Perez-Tilve, D	CohBAR agreement 2017	CohBar Inc	1/1/17 - 12/31/17	$ 238,344.00
ENDOCR	Winnick, J	Effect of liver glycogen content on hypoglycemic counterregulation	NIDDK	9/1/16 - 5/31/21	$ 1,370,990.00

NEW AWARDS FY 2016 *CONTINUED*

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIRECT COSTS
HEM	Sasaki, A	Synthetic Lethal Combination of KRP203/Fingolimod w/ P13k	NIH - R21NS100077	9/1/16 - 8/31/07	$ 161,104.00
IMM	Finkelman, F	Suppression of IgE-Mediated Disease by Polyclonal Rapid Desensitization	NIH - supplement to R01AI113162	7/1/16 - 6/30/17	$ 86,461.00
IMM	Finkelman, F	Wimpy antibody isotypes protect against antibody-mediated disease	NIAID	1/25/17 - 12/31/21	$ 1,676,740.00
IMM	Finkelman, F	IL-9-Producing Mast Cell Precursors and Food Allergy	CCHMC / DoD	9/30/16 - 9/29/17	$ 9,233.00
IMM	Ridgway, W	Mechanistic and Therapeutic Role of the CD137-CD137L Axis	Medical College of Wisconsin (sub) - NIDDK	7/21/16 - 5/31/21	$ 823,645.00
IMM	Shao, W	A critical role of TAM receptors in autoimmune nephritis	NIH-7 K01 DK095067-05	12/1/16 - 11/30/17	$ 119,739.00
INFECT	Cushion, M	Development of a New System for Scaled Up Culture & Propagation	NIH - Task order A22	8/1/16 - 7/31/17	$ 75,840.00
INFECT	Fichtenbaum, C	RES511290-A1068501 - Equipment	Case Western	8/1/16 - 11/30/16	$ 26,000.00
NEPH	Abu Jawdeh, B	Investigating Complement-Split Products as Potentioan Biomarkers	DCI, Inc	4/1/17 - 3-31/18	$ 25,000.00
NEPH	Amlal, H	Possible Role of Glutamine Transport and Metabolism in the Develo	DCI, Inc	4/1/17 - 3/31/18	$ 25,000.00
NEPH	Conforti, L	Tumor Microenvironment and Immune Therapies	Brandon Gromada/ Head & Neck Cancer Foundation	7/1/16 - 6/30/17	$ 6,000.00
NEPH	Thakar, C	ISCHEMIA Clinical Trial - Main Study	NYU/NIH	4/1/16 - 3/31/17	$ 72,452.00
NEPH	Thakar, C	ISCHEMIA Clinical Trial - CKD Study	NYU/NIH	4/1/16 - 3/31/17	$ 60,024.00
NEPH	Thakar, C	Hyponatremia, Congestive Heart Failure, and Kidney Disease: A Vital Connection	Otsuka Pharmaceuticals	10/20/16 - 10/20/21	$ 63,636.00
NEPH	Thakar, C	Stability Study for NGAL	BioPorto Diagnostics	4/1/17 - 3/31/2019	$ 190,589.29
PULM	McCormack, F	Multicenter Interventional Lymphangioleiomyomatosis Early Disease	NIH - U01 HL131755-1A1	9/20/16 - 6/30/21	$ 2,667,804.00
PULM	McCormack, F	The Molecular and Genetic Pathogenesis of LAM	Brigham & Womens/NHLBI	9/21/16 - 8/31/19	$ 210,000.00
PULM	McCormack, F	WTI Regulation of Pulmonary Fibrosis	CCHMC/NIH	5/22/17- 4/30/22	$ 31,580.00
PULM	McCormack, F	Integrative anaylsis of multi-omics data to target fibroblast	CCHMC / NIH	7/5/16 - 6/30/17	$ 12,001.00
PULM	Jospeph, P / Indihar, MV	A CF C3N Care Model of the Future: Proposal for Piloting a Learning Health System	CCHMC/CFF	7/1/16 - 12/31/16	$ 13,889.00
	TOTAL				**$ 13,147,754.79**

Deepe Named Drake Medalist

Infectious diseases expert honored for pioneering investigations

George Deepe Jr., MD, professor in the Division of Infectious Diseases, was presented with the College of Medicine's highest honor on Saturday, May 20. He was one of four recipients of the 2017 Daniel Drake Medal. Others who were presented the honor include Kenneth Davis Jr., MD, professor of surgery and clinical anesthesiology, Shuk-Mei Ho, PhD, Jacob Schmidlapp Endowed Professor and chair of the UC Department of Environmental Health, and Elizabeth Shpall, MD, UC College of Medicine Class of 1980.

Dr. Deepe was celebrated at a dinner at the Queen City Club and his name, biography and photo has been added to the Daniel Drake Medal exhibit in the Medical Sciences Building on the UC medical campus.

Dr. Deepe was recognized for his work on the interactions between dendritic and T-cells, and how these interactions may alter the body's immunity to the fungus that causes histoplasmosis—*Histoplasma capsulatum*. Histoplasmosis is a disease that is most frequently found in the Ohio and Mississippi River Valleys. It is most often caused by breathing in fungal spores from bird and bat droppings. Symptoms can include fever, chills, headache, muscle aches, dry cough and chest discomfort, although mild cases can be free of symptoms. There is an estimated 6.1 cases per every 100,000 population in the Midwest, according to the Centers for Disease Control and Prevention.

Dr. Deepe has investigated the immune response to *Histoplasma capsulatum*, which is found worldwide but is endemic to the Mississippi River Valley. The focus of this work has been on regulators, both soluble and cellular, that dictate the fate of the organism once it has entered the lung. He demonstrated that the cytokine tumor necrosis factor-α is critically important in host defenses to this fungus. This work explains why patients who receive the newly developed tumor necrosis factor antagonists, such as infliximab, are susceptible to developing fungal diseases. Dr. Deepe has pioneered investigations into the role of zinc in host defenses to this fungus. These studies have been at the forefront of the influence of zinc in host resistance, and he has rapidly gained substantial recognition for this cutting-edge work. ●

About The Daniel Drake Medal

The Daniel Drake Medal is given annually by the College of Medicine to living faculty or alumni for their outstanding and unique contributions to medical education, scholarship and research. The award was established in 1985 to honor the 200th birthday of Daniel Drake, MD, the founder of the Medical College of Ohio, the forerunner of the UC College of Medicine. Drake was one of the most influential physicians, educators and scientists of 19th century America.

Changing our Culture

Building strong foundations for junior faculty to become independent researchers

The J-Club is a Department of Internal Medicine (DOIM) program developed in response to divisional goals to grow, develop and support our junior faculty. Associate Chair of Translational Research Carl Fichtenbaum, MD and Assistant Professor Kevin Haworth, PhD, were instrumental in starting this program with input from the Research Governance Committee, and other faculty and staff.

The mission of the J-Club is to provide a supportive academic, professional and personal environment to foster the development of junior faculty interested in a research career. The goals include providing opportunities to create a receptive environment for junior researchers to support one another and receive support from trusted senior faculty; to provide a platform to present ideas, studies, results and grant submissions; and to assist junior faculty in obtaining funding to further their careers. The J-Club complements the existing mentorships of junior faculty.

The initial organizational meeting of the J-Club was held on Tuesday, November 15, 2016 at the College of Medicine. Junior faculty accepting the invitation to participate completed an Individual Development Plan (IDP) developed by the DOIM faculty. These IDPs were reviewed by the DOIM leadership and members of the J-Club to assist in selecting the initial J-Club members. A group of 12 junior faculty attended the first meeting that was held in March 2017. The J-Club had a social gathering at local brewery in town in the fall of 2017.

The J-Club faculty members and two faculty mentors meet twice monthly. Each member is scheduled to present to the group every few months. Guest speakers and presentations on mentorship and grant writing are also a part of the club's overall design. The curriculum includes topics ranging from how to obtain funding to how to advance and develop professionally.

The expectation is that members will be working to apply for and successfully obtain external funding for their research over the course of one to two years. ● *Faculty interested in learning more about the J-Club can contact Dr. Carl Fichtenbaum, Associate Chair for Translational Research.*

- **Junior faculty accepting the invitation to participate complete an Individual Development Plan**
- **J-Club faculty members and two faculty mentors meet twice monthly**
- **Members present to the group every few months**
- **J-Club arranges speakers and presentations on relevant topics including:**
  - **mentorship**
  - **grant writing**
  - **obtaining funding**
  - **professional advancement and development**
- **Members expected to apply for and successfully obtain external funding for their research over the course of 1-2 years**

The mission of the J-Club is to provide a supportive academic, professional and personal environment to foster the development of junior faculty interested in a research career.

Paying it Forward

A transplant patient shares how joining a clinical trial helped her family—and others

TWENTY-FOUR YEARS ago, Tamiko McClure should have been enjoying one of the happiest times in her life: She had just given birth to a healthy baby boy. But instead, she found herself often feeling sick and weak and went to the doctor looking for answers.

McClure was diagnosed with lupus. The disease eventually caused her kidneys to fail, and she was placed on the list for a kidney transplant. Though not a blood relative, McClure's cousin's wife was a match; McClure received a kidney transplant on June 12, 2007. "I consider that my second birthday," McClure says.

Following the transplant, McClure, who works as a registration auditor at UC, began the anti-rejection drug carousel that often befalls transplant patients.

"Transplant patients have to take immunosuppressant medication for the rest of their life so that they don't reject their transplanted organ," says Rita Alloway, PharmD, a UC research professor who specializes in immunosuppression pharmacotherapy. Alloway explains that the U.S. government covers 80 percent of the the cost of immunosuppressive drugs for the first three years post-transplant,

"I tell my kids, it's not just about you; you also have to think about how what you're doing might have a positive effect on the next person."

Clinical trial participant Tamiko McClure

but after that, patients are responsible for their entire cost. The financial burden varies depending on a patient's insurance coverage for prescription medications. Brand-name immunosuppressive drugs, often the first choice of clinicians and patients, can cost as much as $10,000 to $20,000 per year.

Meanwhile, generic drugs often cost a fraction of the price of brand-name options, and are hence more likely to be covered by insurance companies. But while the Food and Drug Administration (FDA) requires that generic medications are tested for safety in healthy people, the drugs are not tested in post-transplant patients; this leads to concerns about their effectiveness among clinicians and patients alike. With support from the FDA, Alloway led a clinical trial in 2014 to test a generic anti-rejection drug in patients who had received liver and kidney transplants.

"I reached out to kidney and liver transplant recipients who were stable and met the criteria for the study, and willing to participate," Alloway says.

One of the patients Alloway connected with was McClure, who immediately signed on, despite her reservations. "I was nervous at first, not knowing if the generic drug would be as effective," says McClure. "But then I realized there could be a reward at the end of this, not just for me, but for other patients. Brand-name drugs are much more expensive than generics, and no one should have to choose between eating today or getting their medication."

Clinical trial participant Tamiko McClure ***(left)*** **with Rita Alloway, PharmD**

McClure has successfully used generic immunosuppressive medication since the study. Her son, who was diagnosed with kidney disease at age 14 and is also a transplant recipient, also takes a generic drug. McClure says she would definitely encourage other patients to get involved with clinical trials that have the potential to help them and others.

"I tell my kids, it's not just about you; you also have to think about how what you're doing might have a positive effect on the next person," she says. "We as human beings have to try to figure out how we can help each other." •

While generic medications are tested for safety in healthy people, the drugs are not tested in post-transplant patients; this leads to concerns among clinicians and patients alike.

Year at a Glance

2016 July

- $1.67M **NIAID award** (Fred Finkelman, MD)
- Two **Senior Pilot Awards** funded by DOIM (Laura Conforti, PhD and George Smulian, MD)
- One **Distinguished Research Achievement award** funded by DOIM (Ken Sherman, MD, PhD)
- One **Rehn Family Research Award** funded by DOIM (Phillip Owens, PhD)
- DOIM **hire of Research Associate** (Grant Writer, Eric Smith, MD) for faculty support within Academic Research Services (ARS)

September

- **Twenty-one researchers in the department**, receiving grants totaling $100,000 in direct and indirect costs per year, were highlighted as part of the **College of Medicine's Gallery of Awardees** by the College of Medicine Research Recognition Award Program
- $1.37M **NIDDK** award (Jason Winnick, PhD)
- $2.67M **NIH U01** award (Frank McCormick, MD)
- Research Governance Committee (RGC) **redesign of monthly Research Conferences** to be interactive and collaborative

October

- **Lifetime Achievement Award**, College of Medicine (Arnold Schwartz, PhD)
- DOIM transitioned to an **electronic grant competition and awards program site** (CCAPS) for submission of all intramural awards

November

- Trisha Wise-Draper, MD, PhD, appointed as **Medical Director of the UC Cancer Institute Clinical Trials Office**

2017 January

- Four **Junior Pilot Awards** funded by DOIM (Silvi Shah, MD; Moises Huaman, MD; Phillip Owens III, PhD; Dylan Steen, MD)

February

- Atsuo Sasaki, PhD, wins **Innovator Award** at Health Care Heroes Banquet
- Jack Rubinstein, MD, named **Director of the Department of Veterans Affairs Medical Center Clinical Research Unit** in Cincinnati
- Michael Tranter, PhD, chosen as the 2017 **Research Rising Star in the College of Medicine**.
- DOIM releases **2015-2016 Annual Research Report**

March

- DOIM **J-Club** (Research Faculty Career Development Group for Junior Faculty) met for the first time
- Melanie Cushion, PhD, named recipient of the **Antimicrobial Research Award** presented by the American Society for Microbiology (ASM), at the 2017 ASM Microbe meeting

April

- Jack Rubinstein, MD, received the **Emerging Entrepreneurial Achievement Award**, presented at the 2017 University of Cincinnati Faculty Awards Ceremony

May

- **George Deepe Jr., MD**, professor in the Division of Infectious Diseases, honored as one of four recipients of the College of Medicine Daniel Drake Medal

June

- Sixth Annual **DOIM Research Symposium and Trainee Grand Rounds** expanded to 2 day format with 46 mentored trainee posters and 50 judges
- DOIM **Academic Research Services (ARS)** staff moved to new office space in MSB 6111
- **IMSTAR graduates (first class of trainees)**: Dana Sall, MD; Matt Kelleher, MD; Ahsan Zafar, MD; and Kiran Afshan, MD

Research Education and Mentoring

RESEARCH SYMPOSIUM 2017

DOIM Creating Opportunities to Meet and Learn about Research

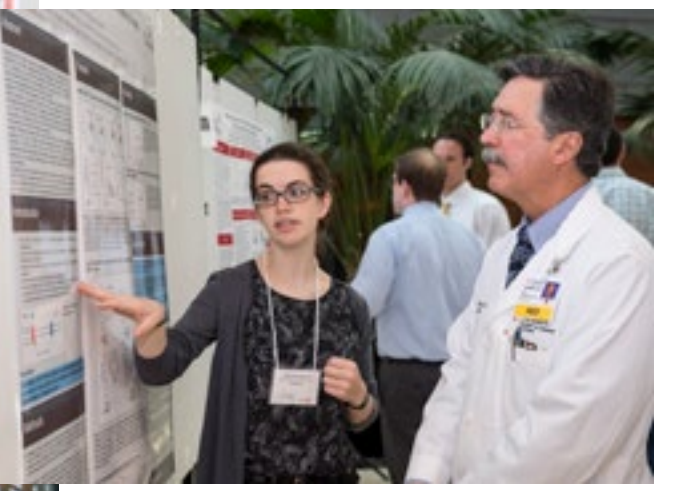
The Department of Internal Medicine's (DOIM) Annual Research Symposium is one of the department's largest events, showcasing the work of faculty, fellows, medical residents/students and graduate students. In addition, the event offers an excellent opportunity to meet and learn from internationally renowned leaders in basic and translational research.

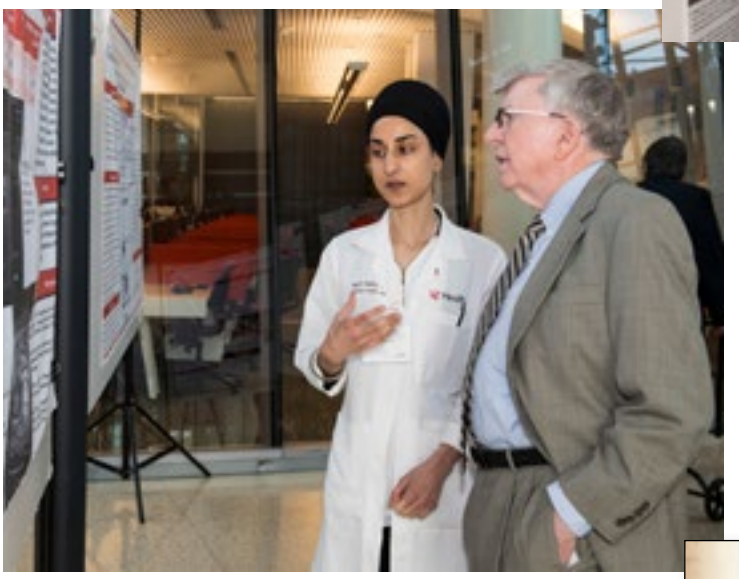
The Annual Research Symposium schedule includes engaging presentations by invited speakers from both the University of Cincinnati as well as other institutions, and panel/group discussions on the latest clinical trials and bench-to-bedside translational research. These activities create an important venue for building an environment that promotes scientific interactions with students and researchers from our Academic Health Center, and the larger research community at the University of Cincinnati.

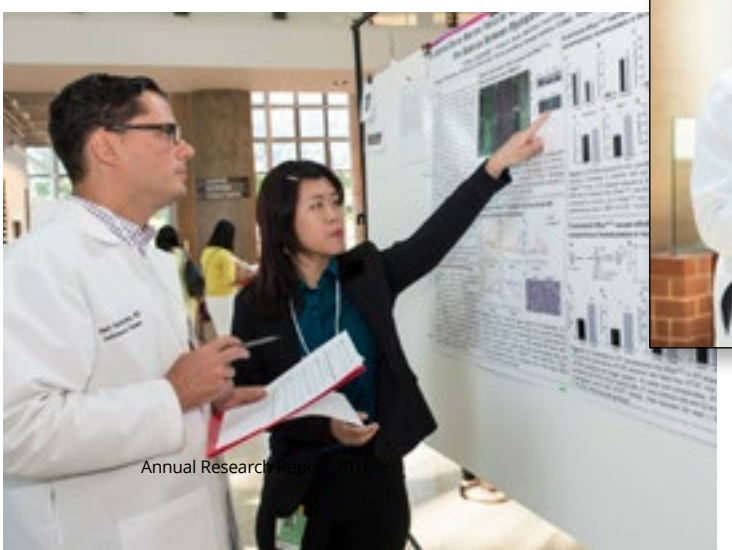
An important emphasis of the Research Symposium is to disseminate and promote the research conducted by DOIM trainees. The event, called "Trainees Grand Rounds," includes research posters presented by graduate, undergraduate, medical and MD/PhD students, as well as postdoctoral fellows and clinical residents and fellows that are mentored by faculty of the Department of Internal Medicine. The posters are judged by expert faculty members from a variety of departments at the College of Medicine. Each poster is evaluated based on its clarity, the question or hypothesis to be answered or tested, appropriateness of the methods, quality of the results and the discussion and innovation impact of the research. Monetary awards are given to the highest-scoring posters in both clinical and basic science research sections.

Themed around gene therapy research, the DOIM sixth Annual Research Symposium was held on June 9 and 10, 2017. Trainees presented 36 unique posters to be judged by 48 COM faculty. Keynote speakers from both Duke and Temple University presented to attendees.

We would like to thank all the participants and judges of this year's trainee grand rounds and research symposium. We invite all of the faculty and staff to join us in the future for this annual event. •







RESEARCH SYMPOSIUM 2017

Mentoring Moments:

Experts Sharing Ideas and Expertise on Pursuit of a Career in Research

The Department of Internal Medicine (DOIM) held its sixth Annual Research Symposium on the weekend of June 10, 2017. Kicking off the conference, Steven Houser, PhD, Professor of Medicine, Senior Associate Dean and Cardiovascular Research Chair at Temple University, spoke at an early breakfast session. This small group session sparked an unforgettable momentum among postdocs and graduate students who were eager to ask questions about challenges and opportunities for those embarking on an early career in the cardiovascular sciences.

In response, Dr. Houser shared his own personal experiences starting out as a graduate student at Temple University up to his present position at Temple University. He further commented that opportunities are out there for everyone. It's all about how you handle tasks and push harder to make your own success. He suggested that one needs to dream a lot, and then work a lot to realize those dreams. He stated that the past was the past, and it's over, but that today's accomplishments will make a bright tomorrow. He supplied many examples of this in his own career. This session was organized by Ronald Vagnozzi, PhD (Cincinnati Children's Hospital Medical Center), and James McNamara, PhD (University of Cincinnati), both postdocs.

The theme of this year's symposium focused on the practice of precision medicine. Sakthivel Sadayappan, PhD, MBA, Professor of Internal Medicine and Director of the Heart Branch of the Heart, Lung and Vascular Institute, introduced the keynote speaker, Dr. Houser. Dr. Houser's presentation was entitled "Repairing the heart after myocardial infraction". He presented some exciting and interesting unpublished studies on establishing myocardial infarction animal models and performing preclinical studies using pig models. The session was well attended by faculty, postdocs and students from both the University of Cincinnati and Cincinnati Children's. Staff from the local American Heart Association also attended. Following a breakout session, the remaining symposium events were held throughout the day with sessions on breakout topics such as basic, translational and clinical aspects of precision medicine. Moderators and speakers were from UC, Cincinnati Children's, Ohio State University, the University of Pennsylvania and Cincinnati VA Medical Center. •

RESEARCH SYMPOSIUM 2017

Department Honors Trainees' Research

Jonathan Stefely, PhD, and Christine James, MD, were awarded first place honors in the basic science and clinical research categories, respectively, for the Trainees' Research Grand Rounds Poster Session as part of the Department of Internal Medicine's sixth Annual Research Symposium. Thirty-six posters were submitted for the session held on Friday, June 9, 2017, in the CARE/Crawley Atrium.

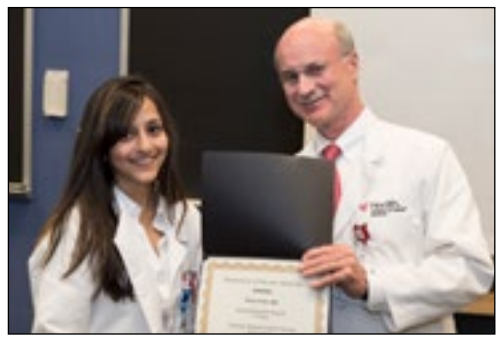
The poster session launched the research symposium which included a keynote address on Friday by Bruce Sullenger, PhD, Joseph W. and Dorothy W. Beard Professor of Experimental Surgery and associate professor in molecular genetics and microbiology, Department of Surgery, Duke University Medical Center. Sullenger's topic was, "Forward and Reverse Translation with RNA Aptamers to Control Coagulation and Inflammation."

The symposium continued on Saturday, June 10, in Kingsgate Marriott, with a keynote address by Steven Houser, PhD, president of the American Heart Association, and professor and senior associate dean at Temple University. Houser's topic was "The Future of Precision Medicine: Cardiac Repair and Injury." Breakout sessions highlighting basic science and clinical research continued throughout Saturday.

During the trainees' poster session, Stefely took top honors in the basic science category for the research poster titled, "New Anti-Cancer Candidates in the mTOR-Autophagy Pathway Revealed by Mass Spectrometry Proteomics." Stefely's mentor is Carol Mercer, PhD, Division of Hematology Oncology. He received a $500 prize.

James took the top award in the clinical research category for the research titled, "The Effect of HEPA Air Purification on Asthmatic Children Exposed to Traffic-Related Airborne Particles." Her mentor was David Bernstein, MD, Division of Immunology, Allergy and Rheumatology. James received a $500 prize.

Second place in the basic science category went to Keith Saum for the research titled "Design and Performance of a Flow-Conditioning Endovascular Implant for Improving Arteriovenous Fistula Maturation." Saum's mentor is Begonia Campos, PhD, Division of Nephrology, Kidney



CARE Program. Saum received a $250 prize.

Second place in the clinical research category went to Sulsal Hague, MD, for the research titled, "Outcomes in Patients With Head and Neck Squamous Cell Carcinoma (HNSCC) Requiring Salvage Resection After Definitive Therapy." Hague received a $250 prize.

Donatien Kamden Toukam, PhD, received honorable mention in the basic science category for the research titled "Vaccine Derived from Cancer Stem Cells Engineered to Express Interleukin-15 and its Receptor Inhibits Tumor Growth." Toukam's mentor was John Morris, MD, Division of Hematology Oncology. Toukam received a $150 prize.

Richa Patel, MD, received honorable mention in the clinical research category for the research titled "Minocycline-Induced Thyroiditis in an Adult Male with Confluent and Reticulated Papillomatosis (CRP)." Her mentor is Michael Canos, MD, Division of Endocrinology, Diabetes and Metabolism. Patel received a $150 prize.

Gregory Rouan, MD, chair of the Department of Internal Medicine, along with Manoocher Soleimani, MD, associate chair for basic research, and Carl Fichtenbaum, MD, associate chair for translational research, offered thanks to 48 faculty who served as judges.

Faculty serving as judges included the following: Enass Abdel-Hameed, MD, PhD; Bassam Abu Jawdeh, MD; Manish Anand, MD; Richard Becker, MD; Ruchi Bhabhra, MD, PhD; Michael Binder, MD; Barry Brook, MD; George Deepe, MD; Zhongyun Dong, MD, PhD; Heather Duncan, PhD; Mark Eckman, MD; Hala Elnakat Thomas, PhD; Fred Finkelman, MD; Jennifer Forrester, MD; Jason Gardner, PhD; Nishant Gupta, MD; Kevin Haworth, PhD; Aliecia Hochhausler, MD; Kristin Hudock, MD; Donetta Jackson; Zana Lummus, PhD and Rajat Madan, MD, PhD.

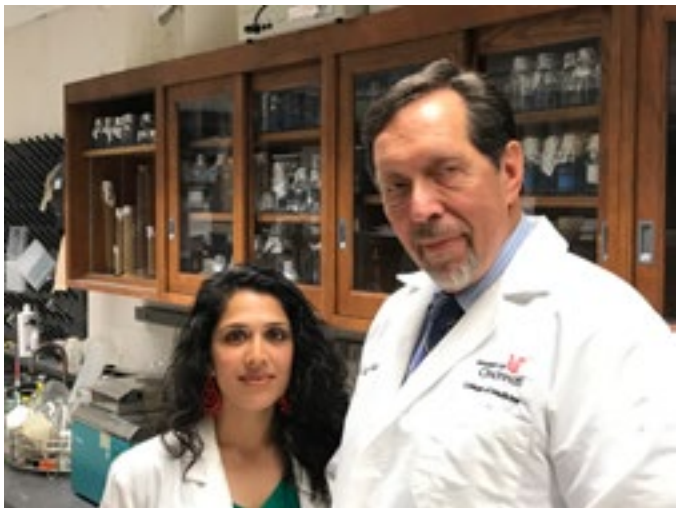
Other judges assisting during the symposium include the following: Carol Mercer, PhD; Anum Minhas, MD; John Morris, MD; Kim Nguyen, MD; Nik Nikolaidis, PhD; Phillip Owens III, PhD; Shailendra Patel, MD, PhD; Xiaoyang Qi PhD; Adam Rose, MD; Gregory Rouan, MD; Jack Rubinstein MD; Sharmeela Saha, MD; Daniel Schauer, MD; Silvi Shah, MD; Mohamed Tarek Shata, MD, PhD; Kenneth Sherman, MD, PhD; Eric Smith, MD; George Smulian, MD; Dylan Steen, MD; Michael Tranter, PhD; Houman Varghai, MD; Juliane Vierecke, MD; Abid Yaqub, MD; Jane Yu, PhD; Eric Warm, MD; and Muhammad Ahsan Zafar, MD. •

Key to Successful Mentorship: A Multidisciplinary Team Approach

According to an award-winning mentorship team, the key to a successful mentorship is a team approach. The mentoring program is one aspect of the Immunology/ Allergy Fellowship Training Grant, centered on taking highly qualified physicians early in their careers, fostering their interest in research, and creating physician scientists. That is exactly what is happening with Dr. Christine James, a Louisville, Kentucky native who is currently in the final year of her fellowship with the Department of Internal Medicine. James' research, "The Effect of HEPA Air Purification on Asthmatic Children Exposed to Traffic-Related Airborne Particles" was awarded the first place honor in the clinical research category in the Department of Internal Medicine sixth Annual Research Symposium, earning her academic recognition and a cash prize. James is matched with Dr. David Bernstein in the Division of Immunology, Allergy and Rheumatology.

Both mentor and mentee shared thoughts on the creation of their award winning poster. Bernstein noted that "less is more." This strategy includes making the poster easy to read, demonstrating novel findings with clinical implications, practicing presentation of a summary of the key findings, and narrowing the content to what is most pertinent. James noted that enthusiasm was key during the poster rounds. Her research population was pediatric while her judges were all from adult backgrounds. Engaging her audience encouraged questions and stimulated conversation. James' enthusiasm shone through during the interview when she spoke of her research and how the findings from the child population have adult implications.

When discussing the success of their mentorship, James and Bernstein agreed that a multidisciplinary team approach has been instrumental to its success. James' team of mentors is comprised of a statistician, an epidemiologist, environmental health physicians, and an allergist—Dr. Bernstein. Throughout the fellowship, the team meets together and separately and are highly collaborative for the duration of the program. One thing James particularly appreciated was her mentors' candor and constructive feedback. James noted that a contributing factor to the team's success is the recognition of their individual limitations: when a member of the team is outside their area of expertise, they know how to direct her effectively to an appropriate resource. She is also



grateful for the team's honest assessment of her progress and welcomes the open lines of communication.

From the perspective of a successful mentor, Bernstein says he strives to guide his mentees towards unanswered questions worthy of exploration. He added that the field of Allergy is one that is constantly changing, and he encourages his mentees to find their niche. One of the biggest challenges facing any mentor is time; this is mitigated to some extent by their team approach. Dr. Bernstein emphasizes that the mentoring team, to be effective, must establish a clear schedule of regular meetings at which time goals are clearly delineated and tracked.

Fellows match into the program and when asked why she chose this particular fellowship, James stated, "UC has the resources to help me achieve my research goals and is known for excellence in clinical training." The program is on its third five-year funding cycle and in its thirteenth year and is unique because it offers fellows the opportunity to interact with many internationally recognized and well-established faculty mentors in the Cincinnati Children's Hospital Medical Center, UC Health network, Environmental Protection Agency, the National Institute for Occupational Safety and Health, regional and local health departments, and more.

Through the fellowship, James has gained insight into what a physician can be outside of clinical care. From her perspective, residents are frequently not exposed to the world of possibilities associated with research and, therefore, can be unaware of the rewarding option of a research-oriented career. One way James feels she will have an advantage moving forward is her comfort with analyzing data and understanding data languages such as SAS. These skills will separate James from other fellows as she progresses in her career. Additionally, as a component of the research fellowship curriculum, James is completing a master's degree in clinical and translational research through the Department of Environmental Health. •

One of the biggest challenges facing any mentor is time; this is mitigated to some extent by their team approach.

Mentoring in Science: Training Our Next Generation of Scientists

A professor in the Division of Cardiovascular Health and Disease and the UC Department of Biomedical Engineering, Christy Holland, PhD, teaches actively in the biomedical engineering (BME) undergraduate and graduate curriculum, mentoring and advising students in the BME and Medical Scientist Training programs. She has mentored over 80 trainees ranging from high school students to fellows and has received numerous awards for her teaching such as the Student Council Mentoring Award and Richard Akeson Excellence in Teaching Award to name a few. Of significant importance is her ability to inspire and lead while expecting the most from her mentees and colleagues, all the while holding herself to the highest standards and being emblematic as a role model. Dr. Holland says, "Mentoring young scientists is one of the most enjoyable aspects of my job and one of the most important things that can be accomplished, as the impact is wide reaching and the legacy is long term."

All of the individuals that Dr. Holland has mentored have pursued biomedical engineering research projects in the Image-guided Ultrasound Therapeutics Laboratories. Her efforts as a mentor have helped students develop not only their research skills, but their professional skills as well.

Shenwen Huang, PhD, and M3 in the Medical Scientist Training Program wrote this about Dr. Holland, "I am extremely thankful … for her mentorship during my time in her lab. Her guidance has allowed me to hone my research abilities and her meticulous attention to detail has helped me develop significantly as a scientific writer. She is dedicated to her students and has often had more faith in my abilities than I have had. Her willingness to write grants in support of student-proposed projects has allowed me to expand my research abilities greatly."

Dr. Holland relies on a pedagogical model in which the typical lecture and homework elements of a course are reversed. Reading assignments are extensive, lectures in class are limited, and much of the class time is devoted to exercises, projects, or discussions, and tours of the clinical environment. A shortage exists in this country of people who choose to study biomedical sciences and engineering and this creates great opportunities for our graduates. Dr. Holland suggests that faculty who advise trainees should encourage each graduate student, resident, or fellow to write an individual development plan that identifies career goals, objectives necessary for achieving career goals, professional development needs, and progress toward achieving specific career goals.

Dr. Holland has also served as an external examiner of several PhD dissertations at other universities, including Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada; Oxford University, Oxford, England; and Erasmus University, Rotterdam, The Netherlands. Dr. Holland recently completed a fellowship in the Executive Leadership in Academic Medicine (ELAM) program, an intensive one-year fellowship of leadership training offered at Drexel University. As part of the ELAM program requirements, she completed an institutional action project designed to develop a long-term strategy to improve interdisciplinary educational and research programs at the UC College of Medicine, Cincinnati Children's Hospital Medical Center, and the UC College of Engineering and Applied Sciences, and to support faculty development in the Department of Internal Medicine by drafting an individual development plan template for the department. ●

A Personal Mission

A daughter's diagnosis motivates post-doc fellow Xiaolei Liu's research on new treatments for rare diseases

WHEN XIAOLEI LIU'S daughter was born last year, his research as a post-doctoral fellow in the College of Medicine's Division of Pulmonary, Critical Care and Sleep Medicine became personal. Liu's daughter was born with nemaline myopathy, a rare disease characterized with low muscle tone, and breathing and swallowing difficulties.

"Medical research on rare diseases is very important to my daughter's future," Liu says. "That's why I want to contribute my life's work to this field."

Liu has found that his unique background makes him particularly suited to finding potential answers for those living with another rare disease, lymphangioleiomyomatosis (LAM), which is characterized by an abnormal growth of smooth muscle cells, especially in the lungs, lymphatic system and kidneys. It can lead to loss of lung function, accumulation of lymph-rich fluid in the chest and abdomen, and growth of tumors in the kidneys.

Liu earned his bachelor's and master's degrees in pharmacy in his native China, focusing on safe drug design and clinical trials. Liu then came to Penn State to study for his PhD project in physiology, and in 2016, was recruited to UC. Today, his studies focus on metabolomics and estrogen signaling in the progression of LAM disease—examining a novel therapeutic strategy for patients with LAM and TSC2 protein deficiency.

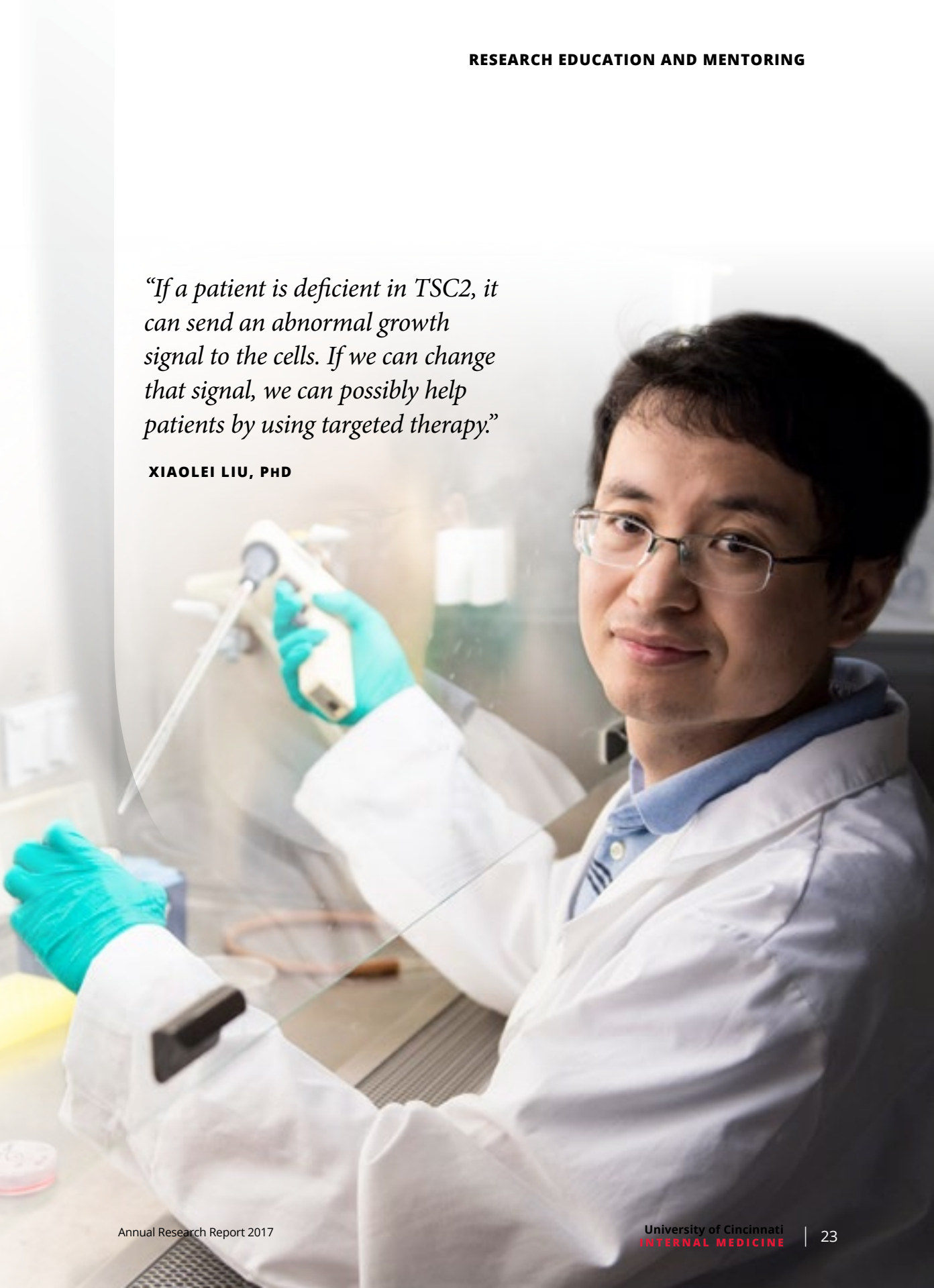
His studies focus on metabolomics and estrogen signaling in the progression of LAM disease—examining a novel therapeutic strategy for patients with LAM and TSC2 protein deficiency.

"If a patient is deficient in TSC2, it can send an abnormal growth signal to the cells," explains Liu, who is hopeful that the research will be published in more academic journals (early studies have been featured in three publications so far) and attract more funding in the future. "If we can change that signal, we can possibly help patients with LAM with targeted therapy."

Besides the research itself, Liu's other favorite aspect of his position is in overseeing and working with students in the lab. "I think training is important to encourage more young students to begin research," Liu says. "Whatever their interests, I want to share my experience and knowledge to help them be more productive, efficient, and develop faster as academic researchers." ●

"If a patient is deficient in TSC2, it can send an abnormal growth signal to the cells. If we can change that signal, we can possibly help patients by using targeted therapy."

XIAOLEI LIU, PHD



IMSTAR GRADUATE

Better Systems, Better Outcomes

Muhammad Zafar wants to optimize healthcare delivery for all patients.

Assistant Professor Muhammad Zafar, MD, has always been passionate about the details—in particular, how patient care is managed in healthcare systems. "I was interested in quality improvement," Zafar says. "Not just one happy patient, but designing a system that works for all patients, at all times, during all encounters."

Zafar, who is currently medical director of Pulmonary Rehabilitation at UC's Heart, Lung and Vascular Institute, is from Pakistan and says that completing medical school in his home country helped to sharpen his research focus. "I was able to experience a healthcare system with a lot of constraints and see poverty and suffering firsthand in a resource-constrained country," he says.

After finishing a pulmonary/critical care fellowship at UC, Zafar says the number of opportunities he saw to pursue his area of interest and the support he received from mentors and faculty advisors kept him in Cincinnati. Today, he is leading a multi-disciplinary team of practitioners that includes physicians, pharmacists, respiratory therapists and nurses with the goal of reducing remissions for patients with chronic obstructive lung disease. Chronic obstructive pulmonary disease (COPD) affects approximately one in ten American adults, and many of these patients have recurrent flare-ups that require them to come to the hospital, get admitted and discharged—with a high risk of repeating the cycle again and again.

"Our project has aimed to create a reliable, coordinated system of care delivery that keeps these patients out of the hospital and gives them the best chance to succeed," Zafar says. Since the project started in 2015, the team has been able to reduce the readmission rate among the COPD patients in its care from 22 percent to 15 percent. The project has worked so well that it has now expanded to include the UC Medical Center Emergency Department in an effort to also reduce the number of COPD patients who visit the ED and are not admitted. "In addition, we are now trying to figure out better ways of prioritizing ED patients with COPD to improve patient outcomes even further."

However, Zafar is not stopping there: He just launched a new project that will better optimize care in the Intensive Care Unit by reducing ICU complications, waste and cost.

"Medical science is generating many new interventions and therapies, but it's a huge hurdle to bring that science to patients," Zafar says. "We can close this gap if we develop healthcare systems that are more reliable; then we can deliver optimal and efficient care to all patients, without remissions and across providers." •

The department's **Internal Medicine Scholarly Training in Academic Research (IMSTAR)** program seeks to train scholars in academic medicine by providing opportunities for trainees to develop mentored research as well as offering them structured learning experiences in clinical teaching and leadership development. Dr. Zafar was a 2016 IMSTAR participant.

Office of the Chair

Research Governance Committee

Front row, left to right: Alison Kastl, Carl Fichtenbaum, Sakthivel Sadayappan, Peter Clayton, Kelly Niederhausen, Mark Eckman, Vladimir Bogdanov

Back row, left to right: Yolanda Wess, Hassane Amlal, Xiaoyang Qi, Diego Perez-Tilve, Eric Smith, Elizabeth Kopras

Not pictured: Gregory Rouan, Manoocher Soleimani, Rita Alloway, Richard Becker, David Bernstein, Christy Holland, Teresa Larkin, Francis McCormack, Dennis McGraw, John Morris, Jack Rubinstein, George Smulian, Trisha Wise-Draper, Daniel Schauer, Mercedes Falciglia, Bruce Yacyshyn, Jason Winnick, Arnold Schwartz

Academic Research Services

Yolanda Wess

Eric Smith

Angie Duke

UC Retrovirology Reference Lab

Left to right: Josette Robinson-Eaton, Molly Leibel, Chelsea Dietz

Robert Baughman, MD
Professor
Office of the Chair

Dr. Robert Baughman, along with longtime collaborator Dr. Elyse Lower, has a long standing interest in sarcoidosis and other interstitial lung diseases. Our group has established several novel agents for the treatment of sarcoidosis, including methotrexate, infliximab, aprelimast, mesenchymal stem cells, roflumilast, repository corticotropin injection, and rituximab and is developing novel agents for pulmonary and extra pulmonary disease including sarcoidosis associated pulmonary fibrosis. We currently have National Heart Lung and Blood Institute (NHLBI) funding for studying a new combination of antibiotics for advanced sarcoidosis.

We have headed a multination registry of sarcoidosis associated pulmonary hypertension, which now included over 200 patients, a quarter of whom are followed in Cincinnati. We have also led studies for treatment of sarcoidosis associated pulmonary hypertension. We are part of the Foundation for Sarcoidosis Research Clinical Studies Network, an eight-center group focused on sarcoidosis. We have recently launched a new registry to follow patients with advanced sarcoidosis. We have had visiting scholars from Netherlands, China, and Turkey and continue our collaborations with groups across the world.

In addition to the NHLBI, we also have funding from the Foundation for Sarcoidosis Research and several industry partners.

Key words: sarcoidosis, pulmonary hypertension, pulmonary fibrosis

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Mirsaeidi, M., Banoei, M. M., Nienow, C. K., Abassi, T., Hakim, A., Schraufnagel, D., Winston, B. W., Sweiss, N., **Baughman, R.**, Garcia, J. G., and Machado, R.. Plasma metabolomic profile in fibrosing pulmonary sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 2016; 33(1):29-38.

2 **Baughman, R. P.**, Judson, M. A., Lower, E. E., Drent, M., Costabel, U., Flavin, S., Lo, K. H., and Barnathan, E. S..Infliximab for chronic cutaneous sarcoidosis: a subset analysis from a double-blind randomized clinical trial. Sarcoidosis Vasc Diffuse Lung Dis 2016; 32(4):289-295.

3 **Baughman RP**, Barney JB, O'hare L, and Lower EE. A retrospective pilot study examining the use of Acthar gel in sarcoidosis patients. Respir Med 2016; 110:66-72.

4 **Baughman RP**, Field S, Costabel U, Crystal RG, Culver DA, Drent M et al. Sarcoidosis in America. Analysis Based on Health Care Use. Ann Am Thorac Soc 2016; 13(8):1244-1252.

5 Mirsaeidi M, Omar HR, **Baughman R**, Machado R, Sweiss N. The association between BNP, 6MWD test, DLCO% and pulmonary hypertension in sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis 2016; 33(4):317-320.

6 Ford HJ, **Baughman RP**, Aris R, Engel P, Donohue JF. Tadalafil therapy for sarcoidosis-associated pulmonary hypertension. Pulm Circ 2016; 6(4):557-562.

7 Zhou Y, Lower EE, LI HP, Costea A, Attari M, **Baughman RP**. Cardiac sarcoidosis: the impact of age and implanted devices on survival. Chest 2017; 151(1): 139-148.

8 Zhou Y, Lower EE, Li H, Farhey Y, **Baughman RP**. Clinical characteristics of patients with bone sarcoidosis. Semin Arthritis Rheum 2017;47: 143-148.

9 Sriprasart T, Aragaki A, **Baughman R**, Wikenheiser-Brokamp K, Khanna G, Tanase D, Kirschner M, Benzaquen S. A Single US Center Experience of Transbronchial Lung Cryobiopsy for Diagnosing Interstitial Lung Disease With a 2-Scope Technique. J Bronchology Interv Pulmonol 2017; 24(2):131-135.

PUBLICATIONS *CONTINUED*

10 Monast CS, Li K, Judson MA, **Baughman,R.P**,Wadman,E., Watt,R.; Silkoff,P.E.; Barnathan,E.S.; Brodmerkel,C. Sarcoidosis extent relates to molecular variability. Clin Exp Immunol 2017; 188(3):444-454.

11 Uzunhan Y, Nunes H, Jeny F, Lacroix,M., Brun,S.; Brillet,P.Y., Martinod,E., Carette,M.F.; Bouvry,D., Charlier,C., Lanternier,F., Planes,C., Tazi,A., Lortholary,O., **Baughman,R.P.**, Valeyre,D. Chronic pulmonary aspergillosis complicating sarcoidosis. Eur Respir J 2017; 49(6):1602396-2016.

12 Kirkil G, Lower EE, **Baughman RP**. Predictors of mortality in pulmonary sarcoidosis Chest 2017 Jul 18. pii: S0012-3692(17)31255-2. doi: 10.1016/j.chest.2017.07.008.

13 Lower EE, Khan S, Kennedy D, **Baughman RP**. Discordance of the estrogen receptor and HER-2/neu in breast cancer from primary lesion to first and second metastatic site. Breast Cancer Targets and Therapy 2017; 9: 1-6.

14 Saketkoo LA, **Baughman RP**. Biologic therapies in the treatment of sarcoidosis. Expert Rev Clin Immunol 2016;1-9.

15 Korsten, P., Strohmayer, K., **Baughman, R. P.**, and Sweiss, N. J.. Refractory pulmonary sarcoidosis - proposal of a definition and recommendations for the diagnostic and therapeutic approach. Clin Pulm Med 2016; 23(2):67-75.

16 Zhou, Y., Lower, E. E., Li, H., and **Baughman, R. P.** Clinical management of pulmonary sarcoidosis. Expert Rev Respir Med 2016; 10(5):577-591.

17 Pilar Brito-Zerón, Roberto Pérez-Alvarez, Lucio Pallarés, Soledad Retamozo, **Robert P. Baughman** & Manuel Ramos-Casals. Sarcoidosis: an update on current pharmacotherapy options and future directions. Expert Opin Pharmacother 2016; 17(18):2431-2448.

18 Khalid Al-Kofahi, Peter Korsten, Christian Ascoli, Shanti Virupannavar, Mehdi Mirsaeidi, Ian Chang, Naim Qaqish, Lesley A. Saketkoo, **Robert P. Baughman**, Nadera J. Sweiss. Management of extrapulmonary sarcoidosis: challenges and solutions. Ther Clin Risk Manag 2016; 12:1623-1634. eCollection;%2016.:1623-1634.

19 Korsten P, Strohmayer K, **Baughman RP** et al. Refractory pulmonary sarcoidosis - proposal of a definition and recommendations for the diagnostic and therapeutic approach. Clin Pulm Med 2016; 23(2):67-75.

20 Veltkamp, M., Drent, M., and **Baughman, R. P.**, Infliximab or biosimilars in sarcoidosis; to switch or not to switch? Sarcoidosis.Vasc.Diffuse.Lung Dis., Vol. 32, No. 4, 2016, pp. 280-283.

21 **Baughman, R. P.**, Engel, P. J., and Nathan, S., "Pulmonary Hypertension in Sarcoidosis," Clin.Chest Med., Vol. 36, No. 4, 2015, pp. 703-714.

22 **Baughman RP**, Papanikolaou I. Current concepts regarding calcium metabolism and bone health in sarcoidosis. Curr Opin Pulm Med 2017;10.

23 Shlobin OA, **Baughman RP**. Sarcoidosis-Associated Pulmonary Hypertension. Semin Respir Crit Care Med 2017; 38(4):450-462.

24 **Baughman RP**, Lower EE. Measuring sarcoidosis around the world: Using the same ruler. Rev Port Pneumol (2006) 2017; 23(5):247-248.

DIVISION OF

Cardiovascular Health and Disease

Cardiovascular Health and Disease

Richard C. Becker, MD
DIVISION DIRECTOR

Richard C. Becker, MD, FAHA
DIVISION DIRECTOR

The **Division of Cardiovascular Health and Disease** is actively engaged in a full range of research programs, including fundamental and translational science, clinical outcomes, population health, implementation science and artificial intelligence. Our aspiration is to positively impact the health of patients by making important advances in biomedical science, fostering a multidisciplinary environment of excellence, translating discoveries into daily clinical practice, designing clinical interventions and measuring their effectiveness, creating innovative approaches to health and wellness, pushing the boundaries of artificial intelligence and computer-based learning and addressing health disparities in our community and region.

The division employs a programmatic, theme-based approach to research that is carefully and strategically aligned with UC Health clinical services, the learning health system and UC College of Medicine in structural heart disease, adult congenital heart disease, aortopathies, heritable and acquired inflammatory coronary anomalies, advanced heart failure, vascular medicine, cardiac imaging, thrombophilias and arrhythmias, including those causing sudden cardiac death.

Our research focuses on the development of new drugs, devices, technologies and cell-based therapies and is funded by the National Institutes of Health, American Heart Association, the UC Heart, Lung and Vascular Institute, UC College of Medicine, Department of Internal Medicine, VA Medical Center, industry, public-private partnerships, philanthropy and intramural grant awards designed specifically to support discovery, collective intelligence, collaboration and training the next generation of scientific researchers and clinician-investigators.

In the coming year, new research initiatives will focus on artificial intelligence, machine-based learning, predictive modeling and simulation among patients with life-threatening cardiovascular conditions, point-of-purchase public health and prevention, genotype-phenotype relationships in heritable and acquired myocardial and coronary vascular disease, novel drug delivery systems, cell-based models of disease and “clinical trials in a dish” platform development. The Division of Cardiovascular Health and Disease is fully committed to preventing, treating and curing diseases of the heart and circulatory systems through biomedical research and scholarly undertakings at the highest levels.

Programming Perfection

Laura Hildreth keeps the work of UC's Heart, Lung and Vascular Institute pumping

LAURA HILDRETH LOVES HER JOB as program manager for UC's Heart, Lung and Vascular Institute (HLVI). However, the road that led her there wasn't exactly straight.

"I would describe my career path as wandering," says Hildreth, who started her undergraduate studies as an art and pre-med student. She then found her way to Chicago to study painting—and ended up as a photojournalist. That decision led her to Los Angeles, where she worked as a Public Information Officer for a chiropractic college; then to Bridgeport, Connecticut, where she worked at the University of Bridgeport and earned her master's degree in nutrition. It was then that a colleague from a professional organization mentioned a job in Cincinnati.

"The job required a background in art, marketing, photography and college administration," Hildreth says. "The ad might as well have had my name on it."

That was in 1999. Hildreth would spend the next 14 years recruiting students for PhD programs as part of the College of Medicine Graduate Education Office. Then, in 2014, she moved to her current position with the HLVI—and immediately found a perfect fit. Today, Hildreth manages programs that support research, education and clinical initiatives at the Institute—up to 40 projects at any given time, she says. Hildreth's current projects include developing a new arrhythmia center, managing the HVLI seminar series and creating a new scholarly video series, Scholarvision. Hildreth also helps organize HLVI teams for the American Heart Association's Heart Mini marathon each year, manages the Institute's website and works with UC Health to manage the clinical side of the site.

"I've always loved working at UC," Hildreth says. "I love working with faculty and students. It's a very positive, progressive environment. At the HLVI, I get to collaborate daily with faculty and trainees across many different divisions and disciplines."

She says the advice she gave to prospective students interested in healthcare and research during her recruiting days still rings true, too.

"I would tell them they would be well-served to study under our faculty, who rank in the top eight percent nationally for sponsored research funding," Hildreth says. "But I would also tell them that besides the College of Medicine's excellence in education, research and patient care, UC is very student centered. It was easy for me to call up a faculty member and ask them to mentor a student. And that helps them realize the fantastic opportunities that exist at UC." ●

Hildreth manages programs that support heart, lung and vascular research, education and clinical initiatives—up to 40 projects at any given time.

"I would tell prospective students that besides the College of Medicine's excellence in education, research and patient care, UC is very student centered. And that helps them realize the fantastic opportunities that exist at UC."

LAURA HILDRETH

Richard C. Becker, MD, FAHA

Stonehill Endowed Professor of Medicine
Chief, Division of Cardiovascular Health and Disease

I am currently the Stonehill Endowed Chair and Professor of Medicine, Chief of the Division of Cardiovascular Health and Disease, and Director of the Heart, Lung and Vascular Institute at the University of Cincinnati College of Medicine and UC Health. My academic career has centered on coronary heart disease, vascular biology and thrombosis and is currently funded by a NHLBI R01, an American Heart Association Strategic Focused Network Award and a NHLBI U54 grant-Translational Centers for Thrombotic and Hemostatic Disorders. The U54 has supported doctoral candidates, post-doctoral fellows and early career investigators. I have also mentored fellows during their transition to faculty through American Heart Association Fellow-to-Faculty awards, NIH K12s, T32s, K25s, F32s and other career development pathways.

Our group is actively involved in the investigation of nucleic acid aptamers that are designed to target coagulation proteins, platelet surface receptors and Von Willebrand Factor and their complementary antidotes (drug-antidote pairs for the treatment of thrombotic diseases, disorders and conditions), drug development, drug safety working with the FDA, nucleic acid scavengers for the treatment of autoimmune and other inflammatory conditions and molecular regulatory pathways in systemic hypertension and target organ injury.

My primary collaborators are at the UC Heart, Lung and Vascular Institute (Sakthivel Sadayappan, PhD, MBA), Duke University School of Medicine (Bruce Sullenger, PhD, Tom Povsic MD, PhD, Julie Layzer, PhD), Ohio State University (Shai Nimjee, MD, PhD) and Cincinnati Children's (Elaine Urbina, MD).

Andrew Crean, BSc, BM, MRCP, MSc, FRCR, MPhil

Professor, Sanghvi Endowed Chair in Cardiovascular Imaging
Division of Cardiovascular Health and Disease

Areas of research include multimodality cardiovascular imaging, which plays a central role in caring for patients with congenital heart disease (CHD). CHD clinicians and scientists are interested not only in cardiac morphology but also in the maladaptive ventricular responses and extracellular changes predisposing to adverse outcomes in this population. Expertise in the applications, strengths, and pitfalls of these cardiovascular imaging techniques as they relate to CHD is essential. Recent work includes assessment of noninvasive imaging in adult congenital heart disease, including adults with repaired tetralogy of Fallot.

Clinical interests include cardiac imaging; cardiopulmonary imaging; structural heart.

Deeptankar DeMazumder, MD, PhD

Assistant Professor
Division of Cardiovascular Health and Disease

My goal is to transform clinical observations into testable research hypotheses, translate basic research findings into medical advances, and participate in the design and evaluation of patient treatment protocols in rigorous clinical trials. My two ongoing primary projects are aimed at understanding fundamental issues in critical illness in the context of epidemiology, mechanism and prevention, as well as pathological disturbances of electromechanical coupling in failing hearts from humans and animal models:

(1) I am employing vertically integrated techniques of molecular genetic profiling, protein chemistry, and linear and nonlinear processing of physiological signals to patient-based studies. My efforts are aimed at developing novel strategies and algorithms based on dynamic predictive monitoring of time-varying physiological signals for identifying subclinical signatures of critical illness in asymptomatic community subjects and patients with critical illness.

(2) More than any physiological intricacy, I find the electrical nature and mechanical coupling of the heart to be the most exciting, sophisticated and addictively challenging to understand. Using a variety of molecular, genetic and cellular approaches, my research is focused on the mechanistic link between heart failure and sudden death and the mechanisms by which autonomic modulation therapies confer salutary effects.

Stephanie H. Dunlap, DO

Associate Professor of Clinical Medicine
Medical Director, UC Health Advanced Heart Failure Treatment Center
Division of Cardiovascular Health and Disease

I am the Principal Investigator of multiple clinical trials in the Division of Cardiovascular Health and Disease with specialization in trials for those with cardiomyopathy and heart failure. I conduct studies on persons suffering from heart failure symptoms from a variety of causes like hypertension, coronary artery disease and valvular heart disease. We are currently conducting trials with a medication that helps the body excrete fluid, thus making it easier for the patient to breathe.

During the past year, we conducted a trial with biomarkers and we are using these biomarker proteins found in the blood stream of patients with heart failure to augment their medical therapy for heart failure. We are starting a very exciting new trial that will study the effects of injecting stem cells into the hearts of patients resistant to all other therapies for heart failure.

I also work with others in the division as a co-investigator for trials using ultrafiltration machines to remove excess fluid and for implantable devices to stimulate the vagus nerve. My focus is on end-stage heart failure including placement of left ventricular assist devices and cardiac transplantation. I provide assistance to residents and fellows, faculty and staff to assist them in conducting research. Funding sources include NIH and industry contracts.

Mohamed A. Effat, MD

Professor of Clinical Medicine
Director of the Interventional Cardiology Fellowship Program
Division of Cardiovascular Health and Disease

I am an active researcher at UC Division of Cardiovascular Health and Disease. I have been involved in many investigator initiated clinical and translational research studies, as well as national and international clinical trials. My research interests are mainly to explore innovative concepts, incorporating fundamental fluid dynamics principles into the physiological evaluation of cardiovascular blood flow.

My research also explores the application of new fluid dynamics-based measures for determination of severity of aortic valve stenosis, while linking these parameters to long-term survival status. We have recently concluded a large clinical outcome study (Clinical trial.gov Identifier NCT01719016) funded by a VA Merit Review Grant. I am currently seeking a NIH multi-site clinical trial funding (Collaborative R01) for the next phase of our advanced research on the physiological assessment of coronary disease in the cardiac catheterization laboratory. I have been closely involved with the theory, design, and conduct of the research studies that produced the proof of concept, and provided the pilot data supporting the feasibility of investigating our novel parameters in this planned clinical trial. This trial will determine the clinical applicability of our proposed indices for coronary and aortic valve disease evaluation. By providing evidence for improved clinical decision-making on the basis of such novel end-points, this body of work may help improve and refine practice guidelines.

David Feldman, MD, PhD

Professor of Clinical Medicine
Division of Cardiovascular Health and Disease
Director of Clinical Services and Director of Advanced Myocardial and Circulatory Services for UC Heart, Lung and Vascular Institute

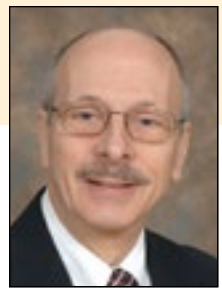
I am a heart failure (HF) clinician-scientist with a dedicated focus to translational research and a commitment to improvements in clinical care through my research efforts. Specifically, I am interested in defining mechanisms of cardiac remodeling, G protein-couple receptor (GPCR) signaling and the mechanism involved in acute heart failure.

My long-term goal is to improve heart failure management and ultimately reveal novel opportunities for novel therapeutic options brought form the "bench" to the "bedside". To accomplish these goals, I have developed a research environment that is highly organized and multi-disciplinary. I have also been fortunate to have long-term R01 in mechanisms of reverse remodeling during CRT in heart failure, as well as several additional grants from other sources. I also study mechanisms of the immunity in heart failure and mechanisms to improve heart transplant functions.

Importantly, as a translational scientist, I have also stayed active in clinical trials. I am involved in over 50 trials and have served as a national/international steering committee member on two of these. My accomplishments, recognized by my peers, have allowed me to serve on the guidelines and research committees for both the Heart Failure Society of America (HFSA) and the International Societies of Heart and Lung Transplant (ISHLT).

Myron C. Gerson MD

Emeritus Professor of Medicine
Director of Electrocardiography, Director of the UCMC Exercise Laboratory



My primary research program involves improving diagnostic accuracy for coronary artery disease detection using a novel cardiac nuclear medicine camera system involving cadmium-zinc-telluride (CZT) technology. The Exercise Laboratories of UC Medical Center and West Chester Hospital use an upright CZT camera for research and clinical studies. Our recent publications in this area are available electronically in the *Journal of Nuclear Cardiology*. A second area of investigation involves application of the anti-gravity treadmill in conjunction with myocardial perfusion imaging for patients who are unable to exercise to target heart rate on a standard treadmill.

I have a long-standing productive collaboration with the Division of Nuclear Medicine, Department of Radiology. This has produced many industry grants and extensive publications.

I am a faculty mentor for Cardiology Fellow, Dr. Fahad Waqar. Dr. Waqar has published a review article and an editorial in a major peer-reviewed journal and is a central figure in our CZT research program. I have also served as principal investigator assisting Dr. Patrick Daly in his productive investigation of new applications of the anti-gravity treadmill. Additional research projects involve Dr. Regina Kayse in a study including cardiac neural imaging and Dr. Atif Hassan in a study of renal transplant donors.

My hobbies include bicycling, travel, and classical music.

David M. Harris, MD

Associate Professor of Clinical Medicine
Division of Cardiovascular Health and Disease
Medical Director, 6 South Cardiovascular Services
Director, Cardiovascular Fellowship
Echocardiography Director

My expertise is in cardiac MRI and echocardiography. My current non-funded research projects include myocardial strain assessment in valvular heart disease (mitral regurgitation and aortic stenosis), baseline strain as a negative predictive value for cardiac stress tests, and myocardial strain before and after structural heart procedures. I continue to investigate the association between pericardial adipose and inflammation in patients with HIV and coronary artery disease, using cardiac MRI.

I am interested in the MRI evaluation and risk stratification of ischemic and non-ischemic cardiomyopathies, with a particular focus in stress-induced cardiomyopathy. The cardiovascular service provides care for thousands of patients annually with a wide variety of cardiovascular illness, severity of disease and co-morbidities. The cardiac MRI team consists of highly skilled technologists and the 3D processing laboratory.

I am currently a research mentor for internal medicine residents and cardiology fellows. I look forward to building research collaborations over the coming years.

Kevin J. Haworth, PhD

Research Assistant Professor
Division of Cardiovascular Health and Disease

I am the Principal Investigator of the Biomedical Ultrasound and Cavitation Laboratory (BUCL) within the Image-guided Ultrasound Therapeutics Laboratories. The BUCL specializes in the application of acoustic droplet vaporization, signal processing and ultrasound imaging algorithms. Acoustic droplet vaporization is the phenomena of selectively creating in situ microbubbles using focused ultrasound. Acoustic droplet vaporization is being explored for drug delivery, thermal ablation, molecular imaging, and gas scavenging. A main focus of our lab is oxygen scavenging to attenuate reperfusion injury (funded via an NIH-NHLBI K25 Grant).

Our signal processing and imaging work is centered on processing ultrasound signals to increase the information that can be garnered from them. In collaboration with Christy Holland we are funded (NIH-NHLBI R01) to develop ultrasound imaging algorithms to support ultrasound-mediated drug delivery to vascular tissue. We also have experience in applying our algorithms to non-ultrasound signals and images (such as optical microscopy). An example of a past collaboration was analysis of video microscopy of fluorescently tagged zebra fish hearts to estimate heart rate and cardiac output.

We have active collaborations with Christy Holland (Internal Medicine), John Lorenz (Physiology), Andrew Redington (CCHMC), and Doug Mast (Biomedical Engineering).

Christy K. Holland, PhD

Professor of Internal Medicine
Division of Cardiovascular Health and Disease and Biomedical Engineering Program
Director of Research, UC Heart, Lung and Vascular Institute

Having been trained as an applied physicist at Wellesley College and Yale University, but immersed in medical research and education for the past 28 years, I have come to value a multi- and interdisciplinary team approach to problem solving.

I direct the Image-Guided Ultrasound Therapeutics Laboratories in the UC Cardiovascular Center (IgUTL), which focuses on applications of biomedical ultrasound including sonothrombolysis, ultrasound-mediated drug and bioactive gas delivery, development of echogenic liposomes, early detection of cardiovascular disease, and ultrasound-image guided ablation.

I am the principal investigator of an NIH R01 grant entitled, "Ultrasound-Assisted Thrombolysis for Stroke Therapy," and an NIH Research Supplement to Promote Diversity. Collaborators include David D. McPherson, MD, who is developing echogenic liposomes for the evaluation and treatment of atherosclerosis in coronary and peripheral vascular beds and Todd Abruzzo, MD, who is using an interventional vascular porcine arterial thrombus model to test treatment efficacy. Through NIH diversity supplemental funds, Karla Mercado, PhD, Kevin Haworth, PhD, and I are developing an ultrasound elasticity imaging technique to predict rt-PA lytic susceptibility of clots in order to guide the choice of appropriate therapies for stroke patients. I am also the principal investigator of a subcontract to an NIH R01 entitled, "Echogenic targeted liposomes for transfection/drug delivery," which includes an industrial partnership with EKOS BTG Interventional Medicine.

Hina Jamali, MD

Assistant Professor
Division of Cardiovascular Health and Disease

Dr. Jamali completed her fellowship in cardiovascular diseases at the University of Cincinnati prior to joining the faculty. She specializes in diseases of the heart and blood vessels and manages complex cardiac conditions such as heart attacks and life-threatening, abnormal heartbeat rhythms. She is also a member of the Heart Lung and Vascular Institute. She recently completed the IMSTAR program, where she reported on cardiac imaging modalities that are available to diagnose cardiac autonomic dysfunction and autonomic modulation techniques, including pharmacologic and device-based therapies. She also assessed the usefulness of 123I-MIBG imaging in sepsis-induced cardiomyopathy.

Robert O'Donnell, MD, MSc

Associate Professor of Clinical Medicine and Radiology
Vice Chief of Clinical Services-Ambulatory Care
Division of Cardiovascular Health and Disease
Associate Director, Advanced Imaging and Cardiovascular Diagnostics

My research interests revolve around cardiac imaging modalities. My active research interests include ongoing investigator initiated studies. These studies evaluate the presence and severity of cardiac involvement in amyloidosis using gadolinium enhanced cardiac MRI, evaluate the ability of advanced cardiac imaging (PET, CMR) to predict obstructive multi-vessel coronary artery disease, or make an assessment of the prognostic and diagnostic value of cardiac PET/CT.

My ongoing collaborative studies focus on: use of an antigravity treadmill to improve compliance with exercise myocardial perfusion testing; assessment of the ability of statins to limit progression of coronary atherosclerosis (and prevent vascular events) in patients with HIV (a multi-institutional REPRIEVE cardiac CT sub-study and in collaboration with the UC infectious diseases division); retrospective assessment of CMR data for both research and quality control purposes; and assessment of pericardial fat metabolism/inflammation by CMR in patients with HIV (acting as mentor).

A. Phillip Owens III, PhD

Assistant Professor
Division of Cardiovascular Health and Disease

The primary focus of my research is to examine the effects of coagulation proteins, proteases, and receptors in the pathogenesis of cardiovascular disease (CVD), specifically atherosclerosis and abdominal aortic aneurysms (AAAs). We utilize genetically modified mice and mouse models of disease to generate data and attempt to verify these results in the human condition, when possible, with retrospective clinical data or human specimens. While several drug therapies exist for atherosclerosis, there are currently no pharmaceutical therapies for patients with AAA. Further, even with modern pharmaceutical regimens for patients with coronary artery disease, it is still the leading cause of mortality. Therefore, the long-term goals of my work are to increase the understanding of thrombosis in atherosclerotic and aneurysmal disease and translate these findings into effective therapeutics to improve survival and quality of life for CVD patients.

Our recent publication demonstrates platelet accumulation and activation is detrimental in a mouse model of established AAAs (Arteriosclerosis Thrombosis and Vascular Biology 2015. 35(9): 2032-41). The results indicate that platelet inhibitors are beneficial in pre-existing aneurysms. Our future studies are examining the role of platelet signaling in AAAs.

My research is supported by an NIH R00 Pathway to Independence Grant to examine the role of Tissue Factor & Clot Formation in Abdominal Aortic Aneurysms.

Florence G. Rothenberg, MD

Associate Professor of Clinical Medicine
Division of Cardiovascular Disease and Health

I am the President of the American Federation for Medical Research, a national organization whose goal is to advance academic careers of junior investigators in medical research.

Our research goal is to reduce mortality in non-acute coronary syndrome (ACS) critically-ill patients with troponin elevation. In a large retrospective study we found that troponin was an independent predictor of 30-day mortality, and beta-blocker, aspirin, and statin use was associated with 30-day mortality reductions in a troponin-dependent manner. Ours is the first study to demonstrate mortality reduction with medical intervention in a troponin-dependent fashion.

I am an investigator for the multicenter PRESERVE Trial, the largest study of contrast induced nephropathy, results to be presented August 2017. I served as site-PI for the PROMISE Trial, which yields insights into the role of CT angiography in detecting coronary disease. I investigated embryonic development of the heart and nervous system, working with biomedical engineers to create technology to understand embryonic physiology and hemodynamics. I am a member of Women in Medicine and Science, an organization at UC whose goal is to advance "the full and successful participation and inclusion of women within academic medicine by addressing gender equity, recruitment and retention, awards and recognition, and career advancement" (AAMC).

Jack Rubinstein, MD

Associate Professor of Medicine
Director of Clinician Scientist Training Program
Division of Cardiovascular Health and Disease

My research laboratory is focused on translational cardiology. We work in collaboration with many basic and clinical scientists and have our own research focus on the role of Transient Receptor Potential Channels in mediating cardiac function and structure under normal and diseased conditions.

Our research has led us to investigate novel therapeutic options for the prevention and treatment of heart failure, which are currently being developed for pre-clinical and early clinical trials. The research has been funded by multiple entities including the American Heart Association and the National Institutes of Health as well as various internal funding mechanisms.

I enjoy exercising, spending time with my family and drinking bourbon (rarely at the same time).

Sakthivel Sadayappan, PhD, MBA

Professor of Medicine
Division of Cardiovascular Health and Disease
Director of Heart Branch of the UC Heart, Lung and Vascular Institute

The long-term goal of the Sadayappan Lab involves 1) elucidating the causes of muscle-specific diseases at the molecular level and 2) identifying therapeutic targets that will lead to the development of effective cures. Therefore, the short-term goals of current research studies involve 1) identifying cardiac-specific early biomarkers of HF; 2) restoring sarcomere structure and function; and 3) screening for compounds to improve sarcomere function during ischemia-reperfusion injury. In particular, hypertrophic cardiomyopathy (HCM) is a major genetic disorder among populations of South Asian descent, leading to contractile dysfunction, heart failure, and sudden cardiac death. In an unrelated, but nonetheless pivotal, study, we are studying the differential role(s) of slow and fast myosin binding protein-C in skeletal muscles, using both in vitro culture systems and animal models.

Full-time Sadayappan Lab members are Shiv Kumar Viswanathan, PhD (AHA-funded), James McNamara (AHA-funded), Taejeong Song, PhD, Jennifer Schwanekamp, PhD, Mohit Kumar, MS (AHA-funded), Angela Taylor, MS and Lisa A. Martin, BS.

As part of our commitment to the development of young scientists, the Sadayappan Lab provides expertise and training in cell biology, molecular biology, structural biology and physiology of the muscle and encourages collaborations in various areas of muscle biology. For more information about lab activities, please visit www.sadayappanlab.org.

Arnold Schwartz, PhD, MD (H.C.), DSc (H.C.), RPh

Distinguished Research Professor, University of Cincinnati
Wendland Professor of Pharmacology and Materia Medica

Dr. Schwartz is a 2016 Drake Medal honoree as well as a recipient of a Lifetime Achievement Award from the UC College of Medicine, awarded for his outstanding and unique contributions to medical education, scholarship and research. He was the first to clone and characterize a human heart calcium channel and identify the sites for the calcium channel blocking drugs diltiazem, verapamil and amlodipine, which are widely used to treat heart failure and hypertension. Prior to that, he established the mechanism of action of digitalis.

Schwartz earned his master's at Ohio State University and PhD at SUNY Downstate, Brooklyn. Following postdoctoral fellowships in London and Aarhus, Denmark, he joined the faculty at Baylor College of Medicine.

Since 1977, Schwartz has nurtured hundreds of graduate and medical students and young faculty at the UC College of Medicine as the principal investigator of a National Heart, Lung and Blood Institute training grant for 38 years, and a Program Project grant for 28 years, and a NIH MERIT Award. He has over 500 peer-reviewed papers published.

Schwartz also received the 2012 George Rieveschl Jr. Award for Distinguished Scientific Research from the University of Cincinnati.

Yukitaka Shizukuda, MD, PhD

Professor
Division of Cardiovascular Health and Disease

I am an associate investigator of the National Heart, Lung, and Blood Institute sponsored clinical research project. I am evaluating clinical subjects at the Clinical Center of the National Institutes of Health.

I have been also assisting research projects with fellows and residents in our division and mentored numerous medical trainee-initiated IRB research protocols in the past ten years. My research areas include iron overload cardiomyopathy, utilization of echocardiography, cardiac MRI, and coronary CT for clinical practice, exercise physiology, and heart transplant. My research is in part supported by intramural funds from the National Heart, Lung, and Blood Institute.

I am collaborating with translational science researchers and clinical investigators of the National Institutes of Health. Through this interaction, I am very pleased to learn the state-of-the-art translational research and cardiac imaging technology, which helps my research mentorship role in our division.

Dylan L. Steen MD, MS
Assistant Professor of Clinical Medicine
Division of Cardiovascular Health and Disease
Director of Clinical Trials and Population Health Research
for the UC Heart, Lung and Vascular Institute

My administrative role in the Division and the HLVI is to support the development of the clinical research infrastructure.

My personal research efforts are focused on two areas:
The first is the control of modifiable, atherosclerotic risk factors including poor diet, sedentary lifestyles, tobacco use, obesity, hyperlipidemia, diabetes, and hypertension. Current projects include a study of novel dietary interventions in partnership with the grocery industry to improve nutritional intake. Other current projects include: 1) the evaluation of lipid-lowering medication utilization and cholesterol target achievement and 2) determination of real-world cardiovascular event rates and risk model development in the U.S., UK, and France using large, generalizable, country-specific datasets.

The second involves the design, development, and study of novel tools and methods to conduct clinical research. Currents projects include development of a clinical study patient recruitment technology software system towards commercialization. In this particular project, the technology has been designed to provide insights into optimal recruitment processes.

Michael Tranter, PhD
Assistant Professor
Division of Cardiovascular Health and Disease

The long-term goals of my research are to increase our understanding of the molecular mechanisms of cardiovascular disease. The ongoing work in the laboratory is broadly centered around post-transcriptional gene regulation in the setting of (1) pathological left ventricular hypertrophy and fibrosis, and (2) the mechanisms of cardioprotection against ischemia/reperfusion injury.

My laboratory has identified human antigen R (HuR) as a new player in the development of pathological cardiac hypertrophy in response to pressure overload (e.g. chronic hypertension). A recent publication from the lab shows that HuR promotes cardiomyocyte hypertrophy downstream of p38 MAP kinase in an isolated neonatal cardiomyocyte model (Slone et al, Cellular Signaling, 2016). Using a new inducible, cardiac-specific HuR knockout mouse created by our lab, we also show that deletion of HuR in the adult heart preserves cardiac function while decreasing pathological ventricular remodeling following transverse aortic constriction (TAC), a model of hypertension-induced pathological cardiac hypertrophy. Ongoing projects in the lab are designed to identify (1) the upstream signaling mediators of HuR in hypertrophic myocytes, and (2) the downstream target genes of HuR and the mechanisms by which regulation of these targets promotes pathology. This work is funded by a NIH R01 grant.

Hareeprasad Vongooru, MD
Assistant Professor of Clinical Medicine
Division of Cardiovascular Health and Disease

An example of my work includes a study to evaluate clinical outcomes after left ventricular assist device (LVAD) implantation in patients with severe pre-LVAD renal dysfunction (RD). Renal dysfunction (RD) is common among patients with advanced heart failure (HF). It is often caused by the hemodynamic perturbations and potentially could improve after restoration of normal hemodynamics. No definitive tests are available to reliably predict the reversibility of RD in HF patients. This study demonstrated that carefully selected patients can benefit from LVAD support. In the patient without severe RD at baseline, kidney function did not decline and remained similar to the pre-LVAD value during 1 year follow-up. Significant preexisting TR and advanced end organ dysfunction reflected by a MELD score ≥ 17 can identify patients at increased risk for poor kidney function after LVAD implantation.

My specialties include cardiovascular disease, cardiology, heart disease, heart failure, heart transplant, cardiac imaging, cardiac surgery.

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1 Vaduganathan M, Harrington RA, Stone GW, Deliargyris EN, Steg PG, Gibson CM, Hamm CW, Price MJ, Menozzi A, Prats J, Elkin S, Mahaffey KW, White HD, Bhatt DL; CHAMPION Investigators. **Imran A**. Cangrelor With and Without Glycoprotein IIb/IIIa Inhibitors in Patients Undergoing Percutaneous Coronary Intervention. J Am Coll Cardiol. 2017 Jan 17;69(2):176-185. doi: 10.1016/j.jacc.2016.10.055. PubMed PMID: 28081827.

2 Kolli KK, van de Hoef TP, Effat MA, Banerjee RK, Peelukhana SV, Succop P, Leesar MA, **Imran A**, Piek JJ, Helmy TA. Diagnostic cutoff for pressure drop coefficient in relation to fractional flow reserve and coronary flow reserve: A patient-level analysis. Catheter Cardiovasc Interv. 2016 Feb 1;87(2):273-82. doi: 10.1002/ccd.26063. Epub 2015 Oct 1. PubMed PMID: 26424295.

3 Chen ST, Hellkamp AS, **Becker RC**, Berkowitz SD, Breithardt G, Fox KAA, Hacke W, Halperin JL, Hankey GJ, Mahaffey KW, Nessel CC, Piccini JP, Singer DE, Patel MR. Outcome of Patients Receiving Thrombolytic Therapy While on Rivaroxaban for Nonvalvular Atrial Fibrillation (from Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation). Am J Cardiol. 2017 Aug 7. pii: S0002-9149(17)31301-2. doi: 10.1016/j.amjcard.2017.07.095. [Epub ahead of print] PubMed PMID: 28886856.

4 Jiang R, Babyak MA, Brummett BH, Hauser ER, Shah SH, **Becker RC**, Siegler IC, Singh A, Haynes C, Chryst-Ladd M, Craig DM, Williams RB. Brain-derived neurotrophic factor rs6265 (Val66Met) polymorphism is associated with disease severity and incidence of cardiovascular events in a patient cohort. Am Heart J. 2017 Aug;190:40-45. doi: 10.1016/j.ahj.2017.05.002. Epub 2017 May 18. PubMed PMID: 28760212.

5 Washam JB, Hellkamp AS, Lokhnygina Y, Piccini JP, Berkowitz SD, Nessel CC, **Becker RC**, Breithardt G, Fox KAA, Halperin JL, Hankey GJ, Mahaffey KW, Singer DE, Patel MR; ROCKET AF Steering Committee and Investigators. Efficacy and Safety of Rivaroxaban Versus Warfarin in Patients Taking Nondihydropyridine Calcium Channel Blockers for Atrial Fibrillation (from the ROCKET AF Trial). Am J Cardiol. 2017 Aug 15;120(4):588-594. doi: 10.1016/j.amjcard.2017.05.026. Epub 2017 May 29.PubMed PMID: 28645473.

6 Leef GC, Hellkamp AS, Patel MR, **Becker RC**, Berkowitz SD, Breithardt G, Halperin JL, Hankey GJ, Hacke W, Nessel CC, Singer DE, Fox KAA, Mahaffey KW, Piccini JP. Safety and Efficacy of Rivaroxaban in Patients With Cardiac Implantable Electronic Devices: Observations From the ROCKET AF Trial. J Am Heart Assoc. 2017 Jun 14;6(6). pii: e004663. doi: 10.1161/JAHA.116.004663. PubMed PMID:28615214.

7 Lowenstern A, Storey RF, Neely M, Sun JL, Angiolillo DJ, Cannon CP, Himmelmann A, Huber K, James SK, Katus HA, Morais J, Siegbahn A, Steg PG, Wallentin L, **Becker RC**; PLATO Investigators. Platelet-related biomarkers and their response to inhibition with aspirin and p2y(12)-receptor antagonists in patients with acute coronary syndrome. J Thromb Thrombolysis. 2017 Aug;44(2):145-153. doi: 10.1007/s11239-017-1516-y. PubMed PMID: 28608165.

8 Pollack CV Jr, Davoudi F, Diercks DB, **Becker RC**, James SK, Lim ST, Schulte PJ, Spinar J, Steg PG, Storey RF, Himmelmann A, Wallentin L, Cannon CP; PLATO Investigators. Relative efficacy and safety of ticagelor vs clopidogrel as a function of time to invasive management in non-ST-segment elevation acute coronary syndrome in the PLATO trial. Clin Cardiol. 2017 Jun;40(6):390-398. doi: 10.1002/clc.22733. Epub 2017 Jun 9. PubMed PMID: 28598510.

9 Balla SR, Cyr DD, Lokhnygina Y, **Becker RC**, Berkowitz SD, Breithardt G, Fox KAA, Hacke W, Halperin JL, Hankey GJ, Mahaffey KW, Nessel CC, Piccini JP, Singer DE, Patel MR. Relation of Risk of Stroke in Patients With Atrial Fibrillation to Body Mass Index (from Patients Treated With Rivaroxaban and Warfarin in the Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation Trial). Am J Cardiol. 2017 Jun 15;119(12):1989-1996. doi:10.1016/j.amjcard.2017.03.028. Epub 2017 Mar 29. PubMed PMID: 28477860.

10 Ducrocq G, Schulte PJ, Budaj A, Cornel JH, Held C, Himmelmann A, Husted S, Storey RF, Cannon CP, **Becker RC**, James SK, Katus HA, Lopes RD, Sorbets E, Wallentin L, Steg PG. Balancing the risk of spontaneous ischemic and major bleeding events in acute coronary syndromes. Am Heart J. 2017 Apr;186:91-99. doi: 10.1016/j.ahj.2017.01.010. Epub 2017 Jan 26. PubMed PMID: 28454837.

11 Sun Y, Hu D, Stevens S, Lokhnygina Y, **Becker RC**, Berkowitz SD, Breithardt G Hacke W, Halperin JL, Hankey GJ, Mahaffey KW, Nessel CC, Piccini JP, Singer DE, Fox KAA, Patel MR. Efficacy and safety of rivaroxaban versus warfarin in patients from mainland China with nonvalvular atrial fibrillation: A subgroup analysis from the ROCKET AF trial. Thromb Res. 2017 Aug;156:184-190. doi: 10.1016/j.thromres.2017.04.010. Epub 2017 Apr 13. PubMed PMID: 28433206.

12 Lindholm D, Hagström E, James SK, **Becker RC**, Cannon CP, Himmelmann A, Katus HA, Maurer G, López-Sendón JL, Steg PG, Storey RF, Siegbahn A, Wallentin L. Growth Differentiation Factor 15 at 1 Month After an Acute Coronary Syndrome Is Associated With Increased Risk of Major Bleeding. J Am Heart Assoc. 2017 Apr 14;6(4). pii: e005580. doi: 10.1161/JAHA.117.005580. PubMed PMID: 28411246;PubMed Central PMCID: PMC5533037.

13 Staudacher DL, Putz V, Heger L, Reinöhl J, Hortmann M, Zelenkofske SL, **Becker RC**, Rusconi CP, Bode C, Ahrens I. Direct factor IXa inhibition with the RNA-aptamer pegnivacogin reduces platelet reactivity in vitro and residual platelet aggregation in patients with acute coronary syndromes. Eur Heart J Acute Cardiovasc Care. 2017 Apr 1:2048872617703065. doi: 10.1177/2048872617703065.[Epub ahead of print] PubMed PMID: 28403626.

PUBLICATIONS *CONTINUED*

14 Lindner SM, Fordyce CB, Hellkamp AS, Lokhnygina Y, Piccini JP, Breithardt G, Mahaffey KW, Singer DE, Hacke W, Halperin JL, Hankey GJ, Berkowitz SD, Nessel CC, **Becker RC**, Fox KA, Patel MR; ROCKET AF Steering Committee and Investigators. Treatment Consistency Across Levels of Baseline Renal Function With Rivaroxaban or Warfarin: A ROCKET AF (Rivaroxaban Once-Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation) Analysis. Circulation. 2017 Mar 7;135(10):1001-1003. doi: 10.1161/CIRCULATIONAHA.116.024666. PubMed PMID:28264892.

15 Sun JL, Boyle SH, Samad Z, Babyak MA, Wilson JL, Kuhn C, **Becker RC**, Ortel TL, Williams RB, Rogers JG, O'Connor CM, Velazquez EJ, Jiang W. Mental stress-induced left ventricular dysfunction and adverse outcome in ischemic heart disease patients. Eur J Prev Cardiol. 2017 Apr;24(6):591-599. doi:10.1177/ 2047487316686435. Epub 2017 Jan 9. PubMed PMID: 28067532.

16 Nimjee SM, White RR, **Becker RC**, Sullenger BA. Aptamers as Therapeutics. Annu Rev Pharmacol Toxicol. 2017 Jan 6;57:61-79. doi: 10.1146/annurev-pharmtox-010716-104558. PubMed PMID: 28061688.

17 Johnson DA, Lieberman D, Inadomi JM, Ladabaum U, **Becker RC**, Gross SA, Hood KL, Kushins S, Pochapin M, Robertson DJ. Increased Post-procedural Non-gastrointestinal Adverse Events After Outpatient Colonoscopy in High-risk Patients. Clin Gastroenterol Hepatol. 2017 Jun;15(6):883-891.e9. doi: 10.1016/j.cgh.2016.12.015. Epub 2016 Dec 23. PubMed PMID: 28017846.

18 Lindholm D, James SK, Bertilsson M, **Becker RC**, Cannon CP, Giannitsis E, Harrington RA, Himmelmann A, Kontny F, Siegbahn A, Steg PG, Storey RF, Velders MA, Weaver WD, Wallentin L; PLATO Investigators. Biomarkers and Coronary Lesions Predict Outcomes after Revascularization in Non-ST-Elevation Acute Coronary Syndrome. Clin Chem. 2017 Feb;63(2):573-584. doi: 10.1373/clinchem.2016.261271. Epub 2016 Dec 8. PubMed PMID: 27932413.

19 Kayse R, **Becker RC**. The case for preoperative aspirin administration in patients undergoing elective CABG: is it open or closed? Ann Transl Med. 2016 Oct;4(Suppl 1):S26. PubMed PMID: 27867994; PubMed Central PMCID: PMC5104638.

20 Shah R, Hellkamp A, Lokhnygina Y, **Becker RC**, Berkowitz SD, Breithardt G, Hacke W, Halperin JL, Hankey GJ, Fox KA, Nessel CC, Mahaffey KW, Piccini JP, Singer DE, Patel MR; ROCKET AF Steering Committee Investigators. Use of concomitant aspirin in patients with atrial fibrillation: Findings from the ROCKET AF trial. Am Heart J. 2016 Sep;179:77-86. doi: 10.1016/j.ahj.2016.05.019. Epub 2016 Jun 22. PubMed PMID: 27595682.

21 Sherwood MW, Cyr DD, Jones WS, **Becker RC**, Berkowitz SD, Washam JB, Breithardt G, Fox KA, Halperin JL, Hankey GJ, Singer DE, Piccini JP, Nessel CC, Mahaffey KW, Patel MR. Use of Dual Antiplatelet Therapy and Patient Outcomes in Those Undergoing Percutaneous Coronary Intervention: The ROCKET AF Trial. JACC Cardiovasc Interv. 2016 Aug 22;9(16):1694-702. doi: 10.1016/j.jcin.2016.05.039.PubMed PMID: 27539689.

22 Povsic TJ, Lawrence MG, Lincoff AM, Mehran R, Rusconi CP, Zelenkofske SL, Huang Z, Sailstad J, Armstrong PW, Steg PG, Bode C, **Becker RC**, Alexander JH, Adkinson NF, Levinson AI; REGULATE-PCI Investigators. Pre-existing anti-PEG antibodies are associated with severe immediate allergic reactions to pegnivacogin, a PEGylated aptamer. J Allergy Clin Immunol. 2016 Dec;138(6):1712-1715. doi: 10.1016/j.jaci.2016.04.058. Epub 2016 Jul 14. PubMed PMID: 27522158.

23 Vemulapalli S, Hellkamp AS, Jones WS, Piccini JP, Mahaffey KW, **Becker RC**, Hankey GJ, Berkowitz SD, Nessel CC, Breithardt G, Singer DE, Fox KA, Patel MR. Blood pressure control and stroke or bleeding risk in anticoagulated patients with atrial fibrillation: Results from the ROCKET AF Trial. Am Heart J. 2016 Aug;178:74-84. doi: 10.1016/j.ahj.2016.05.001. Epub 2016 May 6. PubMed PMID: 27502854.

24 Piccini JP, Hellkamp AS, Washam JB, **Becker RC**, Breithardt G, Berkowitz SD, Halperin JL, Hankey GJ, Hacke W, Mahaffey KW, Nessel CC, Singer DE, Fox KA, Patel MR. Response by Piccini et al to Letters Regarding Article, "Polypharmacy and the Efficacy and Safety of Rivaroxaban Versus Warfarin in the Prevention of Stroke in Patients With Nonvalvular Atrial Fibrillation". Circulation. 2016 Jul 12;134(2):e7-8. doi: 10.1161/CIRCULATIONAHA.116.022737. PubMed PMID: 27400902.

25 Fordyce CB, Hellkamp AS, Lokhnygina Y, Lindner SM, Piccini JP, **Becker RC**, Berkowitz SD, Breithardt G, Fox KA, Mahaffey KW, Nessel CC, Singer DE, Patel MR; ROCKET AF Steering Committee and Investigators. On-Treatment Outcomes in Patients With Worsening Renal Function With Rivaroxaban Compared With Warfarin: Insights From ROCKET AF. Circulation. 2016 Jul 5;134(1):37-47. doi: 10.1161/CIRCULATIONAHA.116.021890. Erratum in: Circulation. 2016 Aug 23;134(8):e114. PubMed PMID: 27358435.

26 Shimada YJ, Bansilal S, Wiviott SD, **Becker RC**, Harrington RA, Himmelmann A, Neely B, Husted S, James SK, Katus HA, Lopes RD, Steg PG, Storey RF, Wallentin L, Cannon CP; PLATO Investigators. Impact of glycoprotein IIb/IIIa inhibitors on the efficacy and safety of ticagrelor compared with clopidogrel in patients with acute coronary syndromes: Analysis from the Platelet Inhibition and Patient Outcomes (PLATO) Trial. Am Heart J. 2016 Jul;177:1-8. doi: 10.1016/j.ahj.2016.03.015. Epub 2016 Apr 13. PubMed PMID: 27297843.

27 DeVore AD, Hellkamp AS, **Becker RC**, Berkowitz SD, Breithardt G, Hacke W, Halperin JL, Hankey GJ, Mahaffey KW, Nessel CC, Singer DE, Fox KA, Patel MR, Piccini JP; ROCKET AF Steering Committee and Investigators. Hospitalizations in patients with atrial fibrillation: an analysis from ROCKET AF. Europace. 2016 Aug;18(8):1135-42. doi: 10.1093/europace/euv404. Epub 2016 May 12. PubMed PMID: 27174904; PubMed Central PMCID: PMC4974633.

28 Breithardt G, Baumgartner H, Berkowitz SD, Hellkamp AS, Piccini JP, Lokhnygina Y, Halperin JL, Singer DE, Hankey GJ, Hacke W, **Becker RC**, Nessel CC, Mahaffey KW, Califf RM, Fox KA, Patel MR; ROCKET AF Steering Committee & Investigators. Native valve disease in patients with non-valvular atrial fibrillation on warfarin or rivaroxaban. Heart. 2016 Jul 1;102(13):1036-43. doi: 10.1136/heartjnl-2015-308120. Epub 2016 Feb 17. PubMed PMID: 26888572; PubMed Central PMCID: PMC4941167.

PUBLICATIONS *CONTINUED*

29 **Costea A**. Ventricular Tachycardia Ablation: Are We as Successful as We Believe We Are? J Cardiovasc Electrophysiol. 2016 Oct 6. doi: 10.1111/jce.13097. [Epub ahead of print] PubMed PMID: 27624981.

30 Zhou Y, Lower EE, Li HP, **Costea A**, **Attari M**, Baughman RP. Cardiac Sarcoidosis: The Impact of Age and Implanted Devices on Survival. Chest. 2017 Jan;151(1):139-148. doi: 10.1016/j.chest.2016.08.1457. Epub 2016 Sep 8. PubMed PMID: 27614001.

31 Burchill LJ, Huang J, Tretter JT, Khan AM, **Crean AM**, Veldtman GR, Kaul S, Broberg CS. Noninvasive Imaging in Adult Congenital Heart Disease. Circ Res. 2017 Mar 17;120(6):995-1014. doi: 10.1161/CIRCRESAHA.116.308983. Review. PubMed PMID: 28302744.

32 Tita C, Gilbert EM, Van Bakel AB, Grzybowski J, Haas GJ, Jarrah M, **Dunlap SH**, Gottlieb SS, Klapholz M, Patel PC, Pfister R, Seidler T, Shah KB, Zieliński T, Venuti RP, Cowart D, Foo SY, Vishnevsky A, Mitrovic V. A Phase 2a dose-escalation study of the safety, tolerability, pharmacokinetics and haemodynamic effects of BMS-986231 in hospitalized patients with heart failure with reduced ejection fraction. Eur J Heart Fail. 2017 Jul 5. doi: 10.1002/ejhf.897. [Epub ahead of print] PubMed PMID: 28677877.

33 Vierecke J, Schweiger M, **Feldman D**, Potapov E, Kaufmann F, Germinario L, Hetzer R, Falk V, Krabatsch T. Emergency procedures for patients with a continuous flow left ventricular assist device. Emerg Med J. 2016 Nov 15. pii: emermed-2015-204912. doi: 10.1136/emermed-2015-204912. [Epub ahead of print] PubMed PMID: 27852651.

34 Ahmad SS, **Gerson MC**. Sympathetic drive stimulating diastolic dysfunction? J Nucl Cardiol. 2017 Feb 9. doi: 10.1007/s12350-017-0809-z. [Epub ahead of print] PubMed PMID: 28185233.

35 Carl DL, Boyne P, Rockwell B, **Gerson M**, Khoury J, Kissela B, Dunning K. Preliminary safety analysis of high-intensity interval training (HIIT) in persons with chronic stroke. Appl Physiol Nutr Metab. 2017 Mar;42(3):311-318. doi: 10.1139/apnm-2016-0369. Epub 2016 Nov 21. PubMed PMID: 28177746.

36 Jameria ZA, **Abdallah M**, Fernandez-Ulloa M, **O'Donnell R**, Dwivedi AK, Washburn E, Khan N, Khaleghi M, Kalakota N, **Gerson MC**. Analysis of stress-only imaging, comparing upright and supine CZT camera acquisition to conventional gamma camera images with and without attenuation correction, with coronary angiography as a reference. J Nucl Cardiol. 2017 Jan 20. doi: 10.1007/s12350-017-0781-7. [Epub ahead of print] PubMed PMID: 28108979.

37 Jamali HK, Waqar F, **Gerson MC**. Cardiac autonomic innervation. J Nucl Cardiol. 2016 Nov 14. [Epub ahead of print] PubMed PMID: 27844333.

38 Waqar F, Jamali HK, **Gerson MC**. Role of I-123 MIBG in sepsis-induced cardiomyopathy. J Nucl Cardiol. 2016 Sep 8. [Epub ahead of print] PubMed PMID: 27638742.

39 Kim J, Kwon M, Chang J, **Harris D**, **Gerson MC**, Hwang SS, Oh SW. Meta-Analysis of Prognostic Implications of Exercise-Induced Ventricular Premature Complexes in the General Population. Am J Cardiol. 2016 Sep 1;118(5):725-32. doi: 10.1016/j.amjcard.2016.06.007. Epub 2016 Jun 14. PubMed PMID: 27394411.

40 Jameria ZA, **Abdallah M**, Dwivedi A, Washburn E, Khan N, Khaleghi M, Kalakota N, **Gerson MC**. Computer derived transient ischemic dilation ratio for identifying extensive coronary artery disease using a CZT camera and imaging in the upright position. J Nucl Cardiol. 2016 Jun 16. [Epub ahead of print] PubMed PMID: 27311453.

41 Boyne P, Dunning K, Carl D, **Gerson M**, Khoury J, Rockwell B, Keeton G, Westover J, Williams A, McCarthy M, Kissela B. High-Intensity Interval Training and Moderate-Intensity Continuous Training in Ambulatory Chronic Stroke: Feasibility Study. Phys Ther. 2016 Oct;96(10):1533-1544. Epub 2016 Apr 21. PubMed PMID: 27103222; PubMed Central PMCID: PMC5046191.

42 Lopez-Candales A, Hernández Burgos PM, Hernandez-Suarez DF, **Harris D**. Linking Chronic Inflammation with Cardiovascular Disease: From Normal Aging to the Metabolic Syndrome. J Nat Sci. 2017 Apr;3(4). pii: e341. PubMed PMID: 28670620; PubMed Central PMCID: PMC5488800.

43 Redin C, Brand H, Collins RL, Kammin T, Mitchell E, Hodge JC, Hanscom C, Pillalamarri V, Seabra CM, Abbott MA, Abdul-Rahman OA, Aberg E, Adley R, Alcaraz-Estrada SL, Alkuraya FS, An Y, Anderson MA, Antolik C, Anyane-Yeboa K, Atkin JF, Bartell T, Bernstein JA, Beyer E, Blumenthal I, Bongers EM, Brilstra EH, Brown CW, Brüggenwirth HT, Callewaert B, Chiang C, Corning K, Cox H, Cuppen E, Currall BB, Cushing T, David D, Deardorff MA, Dheedene A, D'Hooghe M, de Vries BB, Earl DL, Ferguson HL, Fisher H, FitzPatrick DR, Gerrol P, Giachino D, Glessner JT, Gliem T, Grady M, Graham BH, Griffis C, Gripp KW, Gropman AL, Hanson-Kahn A, **Harris DJ,** Hayden MA, Hill R, Hochstenbach R, Hoffman JD, Hopkin RJ, Hubshman MW, Innes AM, Irons M, Irving M, Jacobsen JC, Janssens S, Jewett T, Johnson JP, Jongmans MC, Kahler SG, Koolen DA, Korzelius J, Kroisel PM, Lacassie Y, Lawless W, Lemyre E, Leppig K, Levin AV, Li H, Li H, Liao EC, Lim C, Lose EJ, Lucente D, Macera MJ, Manavalan P, Mandrile G, Marcelis CL, Margolin L, Mason T, Masser-Frye D, McClellan MW, Mendoza CJ, Menten B, Middelkamp S, Mikami LR, Moe E, Mohammed S, Mononen T, Mortenson ME, Moya G, Nieuwint AW, Ordulu Z, Parkash S, Pauker SP, Pereira S, Perrin D, Phelan K, Aguilar RE, Poddighe PJ, Pregno G, Raskin S, Reis L, Rhead W, Rita D, Renkens I, Roelens F, Ruliera J, Rump P, Schilit SL, Shaheen R, Sparkes R, Spiegel E, Stevens B, Stone MR, Tagoe J, Thakuria JV, van Bon BW, van de Kamp J, van Der Burgt I, van Essen T, van Ravenswaaij-Arts CM, van Roosmalen MJ, Vergult S, Volker-Touw CM, Warburton DP, Waterman MJ, Wiley S, Wilson A, Yerena-de Vega MC, Zori RT, Levy B, Brunner HG, de Leeuw N, Kloosterman WP, Thorland EC, Morton CC, Gusella JF, Talkowski ME. The genomic landscape of balanced cytogenetic abnormalities associated with human congenital anomalies. Nat Genet. 2017 Jan;49(1):36-45. doi: 10.1038/ng.3720. Epub 2016 Nov 14. PubMed PMID: 27841880; PubMed Central PMCID: PMC5307971.

PUBLICATIONS *CONTINUED*

44 Sutton JT, **Haworth KJ**, Shanmukhappa SK, Moody MR, Klegerman ME, Griffin JK, Patton DM, McPherson DD, Holland CK. Delivery of bevacizumab to atheromatous porcine carotid tissue using echogenic liposomes. Drug Deliv. 2016 Nov;23(9):3594-3605. Epub 2016 Sep 30. PubMed PMID: 27689451; PubMed Central PMCID: PMC5166432.

45 Bader KB, **Haworth KJ**, Shekhar H, Maxwell AD, Peng T, McPherson DD, Holland CK. Efficacy of histotripsy combined with rt-PA in vitro. Phys Med Biol. 2016 Jul 21;61(14):5253-74. doi: 10.1088/0031-9155/61/14/5253. Epub 2016 Jun 29. PubMed PMID: 27353199; PubMed Central PMCID: PMC5563443.

46 **Kevin J. Haworth**, Kenneth B. Bader, Kyle T. Rich, **Christy K. Holland**, T. Douglas Mast. (2017). Quantitative Frequency-Domain Passive Cavitation Imaging. IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control. 64(1):177-191 doi: 10.1109/TUFFC.2016.2620492

47 Radhakrishnan K, **Holland CK**, **Haworth KJ**. Scavenging dissolved oxygen via acoustic droplet vaporization. Ultrason Sonochem. 2016 Jul;31:394-403. doi: 10.1016/j.ultsonch.2016.01.019. Epub 2016 Jan 19. PubMed PMID: 26964964; PubMed Central PMCID: PMC4788814.

48 Huang S, Shekhar H, **Holland CK**. Comparative lytic efficacy of rt-PA and ultrasound in porcine versus human clots. PLoS One. 2017 May 17;12(5):e0177786. doi: 10.1371/journal.pone.0177786. eCollection 2017. PubMed PMID: 28545055; PubMed Central PMCID: PMC5435301.

49 Shekhar H, Bader KB, Huang S, Peng T, Huang S, McPherson DD, **Holland CK**. In vitro thrombolytic efficacy of echogenic liposomes loaded with tissue plasminogen activator and octafluoropropane gas. Phys Med Biol. 2017 Jan 21;62(2):517-538. doi: 10.1088/1361-6560/62/2/517. Epub 2016 Dec 21. PubMed PMID: 28002053.

50 Raymond JL, Luan Y, Peng T, Huang SL, McPherson DD, Versluis M, de Jong N, **Holland CK**. Loss of gas from echogenic liposomes exposed to pulsed ultrasound. Phys Med Biol. 2016 Dec 7;61(23):8321-8339. Epub 2016 Nov 3. PubMed PMID: 27811382; PubMed Central PMCID: PMC5345111.

51 Bader KB, Crowe MJ, Raymond JL, **Holland CK**. Effect of Frequency-Dependent Attenuation on Predicted Histotripsy Waveforms in Tissue-Mimicking Phantoms. Ultrasound Med Biol. 2016 Jul;42(7):1701-5. doi: 10.1016/j.ultrasmedbio.2016.02.010. Epub 2016 Apr 20. PubMed PMID: 27108036; PubMed Central PMCID: PMC4899262.

52 **Holland CK**. Ultrasonic Enhance Targeted Drug Delivery – Patent # 9,669,203 issued on 6/06/2017

53 **Holland CK**. Nucleation and Detection of Stable Cavitation for Ultrasound-Enhanced Thrombolysis and Drug Delivery – Patent # 9,675,820 issued on 6/13/2017

54 Kopec AK, Abrahams SR, Thornton S, Palumbo JS, Mullins ES, Divanovic S, Weiler H, **Owens AP 3rd**, Mackman N, Goss A, van Ryn J, Luyendyk JP, Flick MJ. Thrombin promotes diet-induced obesity through fibrin-driven inflammation. J Clin Invest. 2017 Aug 1;127(8):3152-3166. doi: 10.1172/JCI92744. Epub 2017 Jul 24. PubMed PMID: 28737512; PubMed Central PMCID: PMC5531415.

55 **Rothenberg FG**, Clay MB, Jamali H, Vandivier-Pletsch RH.Systematic review of β blocker, aspirin, and statin in critically ill patients: importance of severity of illness and cardiac troponin. J Investig Med. 2017 Apr;65(4):747-753. doi: 10.1136/jim-2016-000374. Epub 2017 Jan 30.

56 Alshahrani S, Rapoport RM, Zahedi K, Jiang M, Nieman M, Barone S, Meredith AL, Lorenz JN, **Rubinstein J**, Soleimani M. The non-diuretic hypotensive effects of thiazides are enhanced during volume depletion states. PLoS One. 2017 Jul 18;12(7):e0181376. doi: 10.1371/journal.pone.0181376. eCollection 2017. PubMed PMID: 28719636; PubMed Central PMCID: PMC5515454.

57 Pandey R, Velasquez S, Durrani S, Jiang M, Neiman M, Crocker JS, Benoit JB, **Rubinstein J**, Paul A, Ahmed RP. MicroRNA-1825 induces proliferation of adult cardiomyocytes and promotes cardiac regeneration post ischemic injury. Am J Transl Res. 2017 Jun 15;9(6):3120-3137. eCollection 2017. PubMed PMID: 28670398; PubMed Central PMCID: PMC5489910.

58 Koch SE, Mann A, Jones S, Robbins N, Alkhattabi A, Worley MC, Gao X, Lasko-Roiniotis VM, Karani R, Fulford L, Jiang M, Nieman M, Lorenz JN, **Rubinstein J**. Transient receptor potential vanilloid 2 function regulates cardiac hypertrophy via stretch-induced activation. J Hypertens. 2017 Mar;35(3):602-611. doi: 10.1097/HJH.0000000000001213. PubMed PMID: 28009703.

59 Jones S, Mann A, Worley MC, Fulford L, Hall D, Karani R, Jiang M, Robbins N, **Rubinstein J**, Koch SE. The role of transient receptor potential vanilloid 2 channel in cardiac aging. Aging Clin Exp Res. 2016 Nov 1. [Epub ahead of print] PubMed PMID: 27804106.

60 **Sadayappan S**. The Myofilament Field Revisited in the Age of Cellular and Molecular Biology. Circ Res. 2017 Sep 1;121(6):601-603. doi: 10.1161/CIRCRESAHA.117.311629. PMID: 28860317

61 Grimes KM, Barefield DY, Kumar M, McNamara JW, Weintraub ST, de Tombe PP, **Sadayappan S,** Buffenstein R. The naked mole-rat exhibits an unusual cardiac myofilament protein profile providing new insights into heart function of this naturally subterranean rodent. Pflugers Arch. 2017 Aug 5. doi: 10.1007/s00424-017-2046-3. [Epub ahead of print] PubMed PMID: 28780592.

62 Tong CW, Dusio GF, Govindan S, Johnson DW, Kidwell DT, De La Rosa LM, Rosas PC, Liu Y, Ebert E, Newell-Rogers MK, Michel JB, Trzeciakowski JP, **Sadayappan S**. Usefulness of Released Cardiac Myosin Binding Protein-C as a Predictor of Cardiovascular Events. Am J Cardiol. 2017 Jul 31. pii: S0002-9149(17)31215-8. doi: 10.1016/j.amjcard.2017.07.042.

PUBLICATIONS *CONTINUED*

63 **Sadayappan S**. Cardiovascular Early Careers: Past and Present. Circ Res. 2017Jul 7;121(2):100-102. doi: 10.1161/CIRCRESAHA.117.311330. PubMed PMID: 28684620; PubMed Central PMCID: PMC5521210.

64 Lynch TL 4th, Kuster DWD, Gonzalez B, Balasubramanian N, Nair N, Day S, Calvino JE, Tan Y, Liebetrau C, Troidl C, Hamm CW, Güçlü A, McDonough B, Marian,AJ, van der Velden J, Seidman CE, Huggins GS, **Sadayappan S**. Cardiac Myosin Binding Protein-C Autoantibodies are Potential Early Indicators of Cardiac Dysfunction and Patient Outcome in Acute Coronary Syndrome. JACC Basic TranslSci. 2017 Apr;2(2):122-131. doi: 10.1016/j.jacbts.2016.12.001. Epub 2016 Dec 19. PubMed PMID: 28596995; PubMed Central PMCID: PMC5460768.

65 Sivaguru M, Kabir MM, Gartia MR, Biggs DSC, Sivaguru BS, Sivaguru VA, Fried GA, Liu GL, **Sadayappan S**, Toussaint KC Jr. Application of an advanced maximum likelihood estimation restoration method for enhanced-resolution and contrast in second-harmonic generation microscopy. J Microsc. 2017 Jun 8. doi:10.1111/jmi.12579. [Epub ahead of print] PubMed PMID: 28594468

66 Lin BL, Song T, **Sadayappan S**. Myofilaments: Movers and Rulers of the Sarcomere. Compr Physiol. 2017 Mar 16;7(2):675-692. doi: 10.1002/cphy.c160026. PubMed PMID: 28333386

67 Barefield DY, Lynch TL 4th, Jagadeesan A, Sanagala T, **Sadayappan S**. High-Throughput Diagnostic Assay for a Highly Prevalent Cardiomyopathy-Associated MYBPC3 Variant. J Mol Biomark Diagn. 2016 Nov;7(6). pii: 303. Epub 2016 Sep 30. PubMed PMID: 27990320; PubMed Central PMCID: PMC5160998

68 Lynch TL 4th, Ismahil MA, Jegga AG, Zilliox MJ, Troidl C, Prabhu SD, **Sadayappan S**. Cardiac inflammation in genetic dilated cardiomyopathy caused by MYBPC3 mutation. J Mol Cell Cardiol. 2017 Jan;102:83-93. doi: 10.1016/j.yjmcc.2016.12.002. Epub 2016 Dec 10. PubMed PMID: 27955979; PubMed Central PMCID: PMC5316303

69 Kraker J, Viswanathan SK, Knöll R, **Sadayappan S**. Recent Advances in the Molecular Genetics of Familial Hypertrophic Cardiomyopathy in South Asian Descendants. Front Physiol. 2016 Oct 28;7:499. eCollection 2016. Review. PubMed PMID: 27840609; PubMed Central PMCID: PMC5083855

70 Hoffman MP, Taylor EN, Aninwene GE 2nd, **Sadayappan S**, Gilbert RJ. Assessing the multiscale architecture of muscular tissue with Q-space magnetic resonance imaging: Review. Microsc Res Tech. 2016 Oct 2. doi: 10.1002/jemt.22777. [Epub ahead of print] Review. PubMed PMID: 27696640

71 Lipps C, Nguyen JH, Pyttel L, Lynch TL 4th, Liebetrau C, Aleshcheva G, Voss S, Dörr O, Nef HM, Möllmann H, Hamm CW, **Sadayappan S**, Troidl C. N-terminal fragment of cardiac myosin binding protein-C triggers pro-inflammatory responses in vitro. J Mol Cell Cardiol. 2016 Oct;99:47-56. doi:10.1016/j.yjmcc.2016.09.003. Epub 2016 Sep 8. PubMed PMID: 27616755; PubMed Central PMCID: PMC5107329

72 Mastrolia V, Flucher SM, Obermair GJ, Drach M, Hofer H, Renström E, **Schwartz A**, Striessnig J, Flucher BE, Tuluc P. Loss of α(2)δ-1 Calcium Channel Subunit Function Increases the Susceptibility for Diabetes. Diabetes. 2017 Apr;66(4):897-907. doi: 10.2337/db16-0336. Epub 2017 Jan 23. PubMed PMID: 28115397.

73 Bodi I, Nakayama H, **Schwartz A.** Tetrodotoxin-sensitive Ca2+ Currents, but No T-type Currents in Normal, Hypertrophied, and Failing Mouse Cardiomyocytes. J Cardiovasc Pharmacol. 2016 Dec;68(6):452-464. PubMed PMID: 27617699; PubMed Central PMCID: PMC5145783.

74 Margas W, Ferron L, Nieto-Rostro M, **Schwartz A**, Dolphin AC. Effect of knockout of α2δ-1 on action potentials in mouse sensory neurons. Philos Trans R Soc Lond B Biol Sci. 2016 Aug 5;371(1700). pii: 20150430. doi: 10.1098/rstb.2015.0430. PubMed PMID: 27377724; PubMed Central PMCID: PMC4938030.

75 **Shizukuda Y**., Tripodi D.J., Rosing D.R. Iron Overload or Oxidative Stress? The Mechanism of Early Manifestations of Asymptomatic Hereditary Hemochromatosis Subjects with C282Y Homozygosity. J Cardiovasc Transl Res 9, 400-401, 2016.

76 **Steen DL**, Khan I, Ansell D, Sanchez RJ, Ray KK. Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK in 2014: comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. BMJ Open. 2017 Feb 17;7(2):e013255. doi: 10.1136/bmjopen-2016-013255. PubMed PMID: 28213597; PubMed Central PMCID: PMC5318572.

77 Eisen A, Cannon CP, Braunwald E, **Steen DL**, Zhou J, Goodrich EL, Im K, Dalby AJ, Spinar J, Daga S, Lukas MA, O'Donoghue ML. Predictors of Nonuse of a High-Potency Statin After an Acute Coronary Syndrome: Insights From the Stabilization of Plaques Using Darapladib-Thrombolysis in Myocardial Infarction 52 (SOLID-TIMI 52) Trial. J Am Heart Assoc. 2017 Jan 11;6(1). pii: e004332. doi: 10.1161/JAHA.116.004332. PubMed PMID: 28077384; PubMed Central PMCID: PMC5523629.

78 **Steen DL**, Khan I, Becker L, Foody JM, Gorcyca K, Sanchez RJ, Giugliano RP. Patterns and predictors of lipid-lowering therapy in patients with atherosclerotic cardiovascular disease and/or diabetes mellitus in 2014: Insights from a large US managed-care population. Clin Cardiol. 2017 Mar;40(3):155-162. doi: 10.1002/clc.22641. Epub 2016 Dec 27. PubMed PMID: 28026031.

79 Slone S, Anthony SR, Wu X, Benoit JB, Aube J, Xu L, **Tranter M**. Activation of HuR downstream of p38 MAPK promotes cardiomyocyte hypertrophy. Cell Signal. 2016 Nov;28(11):1735-41. doi: 10.1016/j.cellsig.2016.08.005. Epub 2016 Aug 10. PubMed PMID: 27521603; PubMed Central PMCID: PMC5032653.

DIVISION OF

Digestive Diseases

Digestive Diseases

Kenneth E. Sherman, MD, PhD
DIVISION DIRECTOR

Kenneth E. Sherman, MD, PhD
DIVISION DIRECTOR

The **Division of Digestive Diseases** has an active research agenda across the spectrum of gastrointestinal disorders. This includes basic, translational and research studies in esophageal disorders including eosinophilic esophagitis and GERD, upper GI bleeding, pancreatobiliary disorders, inflammatory bowel disease, intestinal infections like C. difficile and liver disorders including viral hepatitis, NAFLD/NASH, PSC, PBC and liver transplantation.

Currently, the division has five active research laboratories. These laboratories are nationally recognized for their contributions to the understanding of new treatments of hepatitis C, role of quasispecies in hepatitis C, interaction of HIV and hepatitis C viruses, viral host immunology, mechanisms of bilirubin transport and physiological roles of bilirubin, nutritional consequences of and treatment of liver diseases, inflammatory bowel diseases and C difficile infection.

These laboratories are available to medical residents interested in an elective experience in a basic research laboratory. A joint GI training grant with pediatric gastroenterology has recently been renewed and funded. This grant provides stipends for fellows interested in basic laboratory research.

We have an extensive and well-developed clinical research program. In addition to GI fellows, participation in the programs is also available to house staff. Some of these include treatment of chronic viral hepatitis, reflux esophagitis, upper GI bleeding, inflammatory bowel disease, irritable bowel syndrome and peptic ulcer disease. We anticipate even further expansion of our clinical trials program.

Improving Transplant Treatment

Khurram Bari, MD, hopes to lessen immune-suppression drug side effects for liver transplant patients

KHURRAM BARI, MD, is confronted daily with motivation for his research: The assistant professor in the Division of Digestive Diseases still spends about 60 percent of his time seeing patients in a clinical setting.

"It comes down to improving the lives of patients by discovering new things, and inspiring other doctors, residents and medical students to do the same," Bari says.

A native of Pakistan, Bari attended medical school there, but came to the United States in 2005 for more training and opportunities. He completed a research fellowship at Yale, his residency at Wright State University and two clinical fellowships—one at Yale, the other at the University of Michigan—before choosing UC as his next stop. "The liver transplant team was looking to expand, and the new surgery team seemed very welcoming and open to the clinical research aspects of liver transplant," says Bari.

Bari jumped into the division's work right away. In 2015, he enrolled in UC's master's degree program for clinical and translational research. Besides seeing his patients, Bari is involved in the liver clinical trials program, serving as a sub-investigator in trials examining Hepatitis C, fatty liver, and nonalcoholic steatohepatitis. His personal project is a pilot study focused on finding better drug treatments for the immune suppression required to avoid rejection in liver transplant patients. Current medications, such as prednisone, are effective but cause a large number of side effects. Bari says budesonide, a synthetic substitute for prednisone, has unique properties that affect how it is metabolized by the liver and limits the amount of the drug that is absorbed by the rest of the body.

"All of the side effects that we see with traditional prednisone are greatly reduced with this drug," says Bari, adding that the drug has already been used with success in patients with autoimmune-related bowel diseases, Crohn's disease and ulcerative colitis, as well as with autoimmune hepatitis.

If his pilot study deems use of the drug in liver transplant patients safe, Bari plans to begin larger studies. "There is potential for this drug to be used after transplant for autoimmune suppression. It doesn't go to the rest of the body. It goes directly to the liver and acts there. If it works well in liver transplant patients, it can become an essential part of their long-term treatment." ●

"It comes down to improving the lives of patients by discovering new things, and inspiring other doctors, residents and medical students to do the same."

Khurram Bari, MD

Assistant Professor of Clinical Medicine
Division of Digestive Diseases

I am an assistant professor in the Division of Digestive Diseases, with focus on liver transplantation. I am a co-investigator on multiple clinical trials involving treatment of viral hepatitis and non-alcoholic steatohepatitis. I am principal investigator for a pilot clinical trial aimed at evaluating the efficacy and safety of budesonide as an immune suppressing agent in place of prednisone for liver transplant recipients. Prednisone is an essential component of liver transplant immune suppression, but is also associated with many well-known adverse effects. Budesonide, on the other hand, is a synthetic corticosteroid with only 10% systemic bioavailability and thus has potential to provide liver specific immune suppression with minimal systemic toxicity. The goal is to improve long term outcomes. I have received clinical research grants from American College of Gastroenterology and Center for Clinical and Translational Research and Training for this pilot.

In addition, I am collaborating with transplant surgery and infectious diseases divisions to study the risk of hepatitis C virus (HCV) transmission from the use of HCV antibody positive but non-viremic organs to HCV negative recipients.

In my free time I like to coach my son's soccer team, take on some home improvement projects, and watch movies.

Jason T. Blackard, PhD

Associate Professor
Division of Digestive Diseases

I direct a basic and translational research laboratory that focuses on human and mechanistic studies to understand the interactions between various viral pathogens. Using a variety of cell culture, immunologic, and molecular virology techniques, as well as patient-derived samples, we are investigating the pathogenic and evolutionary mechanisms by which viruses interact with the host and cause disease. Current work in the laboratory involves studies of hepatitis B (HBV), hepatitis C virus (HCV), hepatitis E (HEV), pegiviruses, and HIV.

Funded Research Projects

- Characterizing genotypic and phenotypic diversity of the HCV RNA-dependent RNA polymerase
- Investigating HBV infection and drug resistance in the context of HIV co-infection
- Evaluating extrahepatic replication of HCV

Collaborations

Current collaborators within the Department of Internal Medicine include Ken Sherman, M. Tarek Shata, and Carl Fichtenbaum. Collaborators outside of UC include the Department of Virology at Sefako Makgatho Health Sciences University (Pretoria, South Africa), the Department of Clinical Virology at the University of Pretoria (Pretoria, South Africa), the Botswana-Harvard AIDS Partnership (Gaborone, Botswana), YRG Care (Chennai, India), the HIV Epidemiologic Research Study, the Centers for Disease Control and Prevention, and the University of Ghana Medical School (Accra, Ghana).

Tiffany E. Kaiser, PharmD

Associate Professor
Division of Digestive Diseases

I actively participate in clinical research, focused on liver disease and organ transplantation in collaboration with UC digestive diseases, nephrology, surgery, transplant services and externally with other transplant centers. I am principal investigator on a pilot trial assessing the impact of novel, technology driven adherence monitoring strategies on adherence behavior in transplant recipients. Additionally, I've been selected to serve as a member on the American Society of Transplantation Transplant Pharmacy Adherence Consortium and chair the Patient Factor subgroup. Furthermore, I am working with UC Transplant to establish an Adherence Workgroup at our center.

Additional research emphasis is on liver transplant (LTx) outcomes. I continue to collaborate with Dr. Shimul Shah. We are participating in a multi-centered, randomized controlled trial of Thymoglobulin® and calcineurin inhibitor delay post-LTx in an effort to minimize risk and severity of perioperative acute kidney injury. We are evaluating if increasing "care between visits" through the utilization of innovative health information technology improves outcomes. This randomized, non-blinded pilot trial compares our post-LTx discharge traditional model of care with one that includes a telemedicine component.

Keywords: transplantation, adherence, liver, technology, outcomes

Mohamed Tarek M. Shata, MD, MSC, PhD

Adjunct Associate Professor
Division of Digestive Diseases

My research activities have been continuously supported by extramural funding, with funds from federal, international and industry sources. I have generated interesting data on the cellular immune responses to hepatitis E (HEV), using experimentally HEV-infected chimpanzees (from NIH), sera from chronic liver disease patients, and samples from an endemic area (Egypt). These data allowed us to be awarded a R21 grant (R21 A1067868), and a R01 (1R01DK108362-01) from the NIH to evaluate the role of HEV in the U.S. I was also a co-investigator in the R01 (2R01AI065256-06A1) grant titled "Antiretroviral Therapy and Hepatic Injury". The major goals of this project were to understand the relationship between initiation and use of cART, that includes the use of CCR5 blocking and its effect on the development of hepatic fibrosis. I was also awarded two grants from the Merck Investigator-initiated studies program. The major goals of those grants being to characterize the Gut-associated lymphocytes (GALT) in HIV, HCV and coinfected patients and identify the role of the immune responses in the emergence of drug mutants during therapy. Internationally, I was awarded a grant from the (USAID)-Egypt Science and Technology. The primary goal of this project is to investigate the role of Th17 lymphocytes in the pathogenesis of Schistosoma infection in humans, in Egypt.

Keywords: viral hepatitis, immune responses to viral hepatitis, HIV, schistosomiasis, liver transplantation

Kenneth E. Sherman, MD, PhD

Gould Professor of Medicine
Division Director
Division of Digestive Diseases

My research agenda is focused on viral hepatitis, with an emphasis on liver disease in those with HIV infection. I have secondary interests in autoimmune hepatitis, drug-associated hepatotoxicity and NASH. My research group has received support for several NIH-funded studies designed to examine the relationship of viral evolution and host response to natural history and treatment response.

Current funded projects focus on the role of CCR5 mutations in the development of hepatic fibrosis in those with HIV infection, and evaluation of hepatitis E associated liver disease in HIV-infected liver transplant recipients. We also devote some effort to development and validation of new diagnostic tools. Our group is closely associated with the NIAID AIDS Clinical Trials Group (ACTG) with an emphasis on laboratory and translational studies of viral hepatitis in those with HIV infection. We have approximately 20 active clinical trials, incorporating hepatitis C treatment, therapeutic vaccination for hepatitis B and NASH treatments.

Collaborations:
UC: Jason Blackard, PhD, Tarek Shata, MD, PhD, Mario Medvedovic, PhD
Outside Institutions: Adeel Butt, MD (University of Pittsburgh), Lynn Taylor, MD (Brown University), Zachery Goodman, MD, PhD (Innova Medical Center, VCU), Shyam Kottilil, MD, PhD (University of Maryland), Norah Terrault, MD, MPH (UCSF), and multiple national/international investigators within the ACTG.

Bruce Yacyshyn, MD

Professor of Clinical Medicine
Division of Digestive Diseases

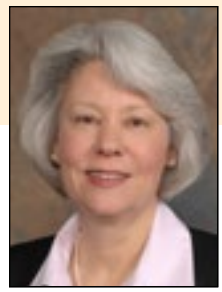
Translational research in gastroenterology (GI) is the theme of my work. Notably, research in antisense DNA was the first-in-human for systemic applications of this technology. This work is still being further developed by industry as one of the few clinically beneficial treatments for "pouchitis." In addition, adhesion molecule (Integrin) research in inflammatory bowel disease (IBD) led to several new drugs being developed including the first human description of isolated human IBD intestinal cells binding to Vedolizumab (ACT-1). While in industry, employed at P&G, my work resulted in an FDA approvable letter for Asacol HD.

I share research interests with my wife, Dr. Mary Beth Yacyshyn, an immunologist. Our work now focuses on biomarkers for IBD therapy, and Clostridium difficile pathogenesis. Our research also focuses on the inflammatory etiology of GI angioectasias.

I am a mentor to faculty, trainees and students and believe teaching and mentoring are priorities.

I am the President of the College of Medicine Faculty for 2017-18, as well as a NIH grant reviewer, and Editorial Board member for the Journal of Inflammatory Bowel Diseases. Locally, I am a local and national advisor to the CCF. Currently, I am the PI for over 21 GI clinical trials.

Mary Beth Yacyshyn, PhD
Adjunct Associate Professor
Division of Digestive Diseases



My husband, Bruce Yacyshyn, MD, and I have been involved in translational academic research for the past 25 years. Along with clinical trials, our lab focuses on various aspects of human mucosal immunology. We study innate immunity of C. difficile infection (CDI) and its recurrence. Using the human model, we examine innate immune differences with the hope of preventing recurrence and changing initial therapeutic algorithms.

Secondly, we are developing a project in the area of obscure gastrointestinal bleeding and angioectasia. We hypothesize that the development of aberrant capillaries and formation of these bleeding site maybe due to microbiome dysbiosis and host inflammatory process. Through novel targeted bioinformatics, we hope to develop guided therapeutics.

Our final focus is inflammatory bowel diseases (IBD). Using proteomics, we study early diagnosis of disease and determining the chances of success or failure of a first line therapy.

In the past 9 years at UC, with clinical trial, industry and academic funding, we have developed broad collaborations with basic scientists, clinical physicians and clinical scientists at UC Medical Center and Cincinnati Children's. Our mentorship has guided many students in the study of CDI and metabonomics, intestinal immunity and proteomics of IBD, and now intestinal angioectasia.

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 **Abdel-Hameed EA**, Rouster SD, Zhang X, Chen J, Medvedovic M, Goodman ZD, Sherman KE.Characterization of HCV NS3 Protease Variants in HCV/HIV-Coinfected Patients by Ultra-Deep Sequence Analysis: Relationship with Hepatic Fibrosis. J Acquir Immune Defic Syndr. 2017 Mar 1;74(3):353-358. doi: 10.1097/QAI.0000000000001256. PMID: 27898525

2 **Blackard JT**, Ma G, Polen C, DuBois JC, Gast J, Radens CM, Sterling RK, Sherman KE. Recombination among GB virus C (GBV-C) isolates in the United States. J Gen Virol. 2016 Jul;97(7):1537-44. doi: 10.1099/jgv.0.000477. Epub 2016 Apr 11. PMID: 27072634

3 Saha D, Pal A, Sarkar N, Das D, **Blackard JT**, Guha SK, Saha B, Chakravarty R. Occult hepatitis B virus infection in HIV positive patients at a tertiary healthcare unit in eastern India. PLoS One. 2017 Jun 7;12(6):e0179035. doi: 10.1371/journal.pone.0179035. eCollection 2017. PMID: 28591184

4 **Blackard JT**, Ma G, Welge JA, Taylor LE, Mayer KH, Klein RS, Celentano DD, Sobel JD, Jamieson DJ, King CC. Cytokine/chemokine expression associated with Human Pegivirus (HPgV) infection in women with HIV. J Med Virol. 2017 Apr 29. doi: 10.1002/jmv.24836. [Epub ahead of print] PMID: 28460153

5 Woltmann J, Burke P, Brady R,**Blackard JT**. Demographics of Hepatitis C in Southwest Ohio (2010 to 2015). Hepat Mon. 2016 Jul 20;16(8):e37904. eCollection 2016 Aug. PMID: 27799964

6 Anderson M, Gaseitsiwe S, Moyo S, Thami KP, Mohammed T, Setlhare D, Sebunya TK, Powell EA, Makhema J, **Blackard JT**, Marlink R, Essex M, Musonda RM. Slow CD4+ T-Cell Recovery in Human Immunodeficiency Virus/Hepatitis B Virus-Coinfected Patients Initiating Truvada-Based Combination Antiretroviral Therapy in Botswana. Open Forum Infect Dis. 2016 Aug 16;3(3):ofw140. eCollection 2016 Sep.PMID: 27800524

7 Archampong TN, Boyce CL, Lartey M, Sagoe KW, Obo-Akwa A, Kenu E, **Blackard JT**, Kwara A. HBV genotypes and drug resistance mutations in antiretroviral treatment-naive and treatment-experienced HBV-HIV-coinfected patients. Antivir Ther. 2017;22(1):13-20. doi: 10.3851/IMP3055. Epub 2016 May 11. PMID: 2716759

8 Amponsah-Dacosta E, Rakgole JN, Gededzha MP, Lukhwareni A, **Blackard JT**, Selabe SG, Mphahlele MJ. Evidence of susceptibility to lamivudine-based HAART and genetic stability of hepatitis B virus (HBV) in HIV co-infected patients: A South African longitudinal HBV whole genome study. Infect Genet Evol. 2016 Sep;43:232-8. doi: 10.1016/j.meegid.2016.05.035. Epub 2016 May 28. PMID: 27245151

9 Diwan TS1, Lichvar AB1, Leino AD1, Vinks AA2, Christians U3, Shields AR1,4, Cardi MA4, Fukuda T2, Mizuno T2, **Kaiser T**5, Woodle ES1, Alloway RR6. Pharmacokinetic and pharmacogenetic analysis of immunosuppressive agents after laparoscopic sleeve gastrectomy. 2017 Jun;31(6).doi: 10.1111/ctr.12975. Epub 2017 May 2.

10 Ertel AE1, **Kaiser TE2**, Abbott DE1,Shah SA3. Use of video-based education and tele-health home monitoring after liver transplantation: Results of a novel pilot study. -2016 Oct;160(4):869-76. doi: 10.1016/j.surg.2016.06.016. Epub 2016 Aug 4.

11 Paterno F1,Girnita A1,Brailey P1,Witte D1,Wang J1,Cuffy MC1, Diwan T1,Tremblay S1,Revollo JY1, Alloway RR1, **Schoech MR1**, Anwar N1,Shah SA1,Woodle SE1Successful Simultaneous Liver-Kidney Transplantation in the Presence of Multiple High-Titered Class I and II Antidonor HLA Antibodies. -2016 Nov 23;2(12):e121. eCollection 2016 Dec.

12 **Sherman KE**, Ke R, Rouster SD, Abdel-Hameed EA, Park C, Palascak J, Perelson AS. Viral dynamic modelling of Hepatitis C and resistance-associated variants in haemophiliacs. Haemophilia. 2016 Jul;22(4):543-8. doi: 10.1111/hae.12918. Epub 2016 Mar 3. PMID: 26936587

13 Hetta HF, Mekky MA, Khalil NK, Mohamed WA, El-Feky MA, Ahmed SH, Daef EA, Medhat A, Nassar MI, **Sherman KE**, Shata MT.Extra-hepatic infection of hepatitis C virus in the colon tissue and its relationship with hepatitis C virus pathogenesis. J Med Microbiol. 2016 Aug;65(8):703-12. doi: 10.1099/jmm.0.000272. Epub 2016 May 10. PMID: 27166142

14 Butt AA, Yan P, Marks K, Shaikh OS, **Sherman KE**; ERCHIVES Study Team. Adding ribavirin to newer DAA regimens does not affect SVR rates in HCV genotype 1 infected persons: results from ERCHIVES. Aliment Pharmacol Ther. 2016 Oct;44(7):728-37. doi: 10.1111/apt.13748. Epub 2016 Jul 26. PMID: 27459341

15 Judge CJ, Sandberg JK, Funderburg NT, **Sherman KE**, Butt AA, Kang M, Landay AL, Lederman MM, Anthony DD. Brief Report: CD14brightCD16- monocytes and sCD14 level negatively associate with CD4-memory T-cell frequency and predict HCV-decline on therapy.J Acquir Immune Defic Syndr. 2016 Nov 1;73(3):258-262. PMID: 27258231

16 Butt AA, Yan P, Shaikh OS, Chung RT, **Sherman KE**; ERCHIVES study. Treatment adherence and virological response rates in hepatitis C virus infected persons treated with sofosbuvir-based regimens: results from ERCHIVES. Liver Int. 2016 Sep;36(9):1275-83. doi: 10.1111/liv.13103. Epub 2016 Mar 24. PMID: 26928927

PUBLICATIONS *CONTINUED*

17 Mehta M, Hetta HF, Abdel-Hameed EA, Rouster SD, Hossain M, Mekky MA, Khalil NK, Mohamed WA, El-Feky MA, Ahmed SH, Daef EA, El-Mokhtar MA, Abdelwahab SF, Medhat A, **Sherman KE**, Shata MT. Association between IL28B rs12979860 single nucleotide polymorphism and the frequency of colonic Treg in chronically HCV-infected patients. Arch Virol. 2016 Nov;161(11):3161-9. doi: 10.1007/s00705-016-3015-4. Epub 2016 Aug 20. PMID: 27544760

18 Butt AA, Ren Y, Marks K, Shaikh OS, **Sherman KE**; ERCHIVES study. Do directly acting antiviral agents for HCV increase the risk of hepatic decompensation and decline in renal function? Results from ERCHIVES. Aliment Pharmacol Ther. 2017 Jan;45(1):150-159. doi: 10.1111/apt.13837. Epub 2016 Nov 4. PMID: 27813162

19 Ragni MV, Humar A, Stock PG, Blumberg EA, Eghtesad B, Fung JJ, Stosor V, Nissen N, Wong MT, **Sherman KE**, Stablein DM, Barin B.Hemophilia Liver Transplantation Observational Study. Liver Transpl. 2017 Jun;23(6):762-768. doi: 10.1002/lt.24688.PMID: 27935212

20 **Sherman KE**, Kang M, Sterling R, Umbleja T, Marks K, Kiser JJ, Alston-Smith B, Greaves W, Butt AA, The Actg Birth Study Team.Phase 3 trial of first generation protease inhibitor therapy for hepatitis C virus/human immunodeficiency virus coinfection. World J Hepatol. 2017 Feb 8;9(4):217-223. doi: 10.4254/wjh.v9.i4.217. PMID: 28217259 Free PMC Article

21 Soriano V, **Sherman KE**, Barreiro P. Hepatitis delta and HIV infection. AIDS. 2017 Apr 24;31(7):875-884. doi: 10.1097/QAD.0000000000001424. PMID: 28121714

22 Dhar VK1, Levinsky NC1, Xia BT1, Abbott DE1, Wilson GC1, Sussman JJ1, **Smith MT2**, Poreddy S2, Choe K3, Hanseman DJ1, Edwards MJ1, Ahmad SA4.The natural history of chronic pancreatitis after operative intervention: The need for revisional operation. -2016 Oct;160(4):977-86. doi: 10.1016/j.surg.2016.05.030. Epub 2016 Jul 20.

23 Matthis A, Zhang B, Denson L, **Yacyshyn B**, Aihara E, Denson L, Montrose M. Importance of the evaluation of N-acetyltransferase enzyme activity prior to 5-aminosalicylic acid medication for ulcerative colitis" has been reviewed and accepted for publication in Inflammatory Bowel Diseases(R). Inflamm Bowel Dis. 2016 Aug;22(8):1793-802. PMC4956520

24 Vickers RJ, Tillotson GS, Nathan R, MD, Hazan S, Pullman J, Lucasti C, Deck K, **Yacyshyn B**, Maliakkal B, Pesant Y, Tejura B, Roblin D, Gerding DN, Wilcox MH, MD for the show CoDIFy study group†. Efficacy and safety of ridinilazole (SMT19969) compared with vancomycin for the treatment of Clostridium difficile infection (CDI): A phase 2, randomised, double-blind, active-controlled, non-inferiority study. THELANCETID-D-16-01327R2. Published online April 28, 2017

25 **Yacyshyn BR**. Pathophysiology of Clostridium difficile-Associated Diarrhea. Gastroenterol Hepatol (N Y) 2016;12:558-560. PMCID: PMC5114514

26 **Yacyshyn BR**. Pathophysiology of Clostridium difficile-Associated Diarrhea. Gastroenterol Hepatol (N Y) 2016;12:558-560. PMCID: PMC5114514

27 Helmrath M, Wikenheiser-Brokamp K, **Yacyshyn MB**, Yacyshyn BR**,** Mahe M, Sundaram N, Nalapareddy KRR.Youthful levels of canonical Wnt signaling ameliorate aging of intestinal stem cells. Cell Reports. In Progress (Accepted 2017).


CORNING

DIVISION OF

Endocrinology, Diabetes and Metabolism

Endocrinology, Diabetes and Metabolism

Shailendra B. Patel, BM, ChB, DPhil
DIVISION DIRECTOR

Shailendra B. Patel, BM, ChB, DPhil
DIVISION DIRECTOR

The UC **Division of Endocrinology, Diabetes and Metabolism** is committed to improving the health of our region with the highest standard of clinical care, insights from innovative research, and education of health care providers, patients, and the community. We provide tertiary level clinical care for all endocrine disorders, ranging from diabetes, pituitary, adrenal, bone, lipid, thyroid, transgender endocrine, as well as care for adolescent patients with endocrine disorders as they transition to adulthood.

Current research interests range from exploring the neuro-humoral integrated pathways, important in diabetes and obesity, using animal models (Drs. Diego-Tilve, Winnick and Patel), to clinical research comparing effectiveness of various therapies for diabetes (Dr. Cohen) and exploring mechanisms important in hypoglycemia responses in subjects with diabetes (Dr. Winnick). We also study rare lipid disorders and integrated cholesterol metabolism in animal models (Dr. Patel) and the role of cholesterol in embryonic development (Dr. Patel).

Clinical trials in the division focus on new treatments for diabetes and pituitary disorders. For example, Dr. Cohen is a co-investigator in a National Institutes of Diabetes and Digestive and Kidney Disease sponsored multi-center trial called GRADE (Glycemia Reduction Approaches in Diabetes).

Our faculty has many collaborative research efforts with other disciplines including adult and pediatric hematology, Pediatric Gastroenterology, Hepatology and Nutrition, Pediatric Human Genetics, and the Department of Pathology and Laboratory Medicine.

Our overall goal is to build a robust, multi-disciplinary program that supports both laboratory-based and patient-based research in our clinical care, research, and education programs for endocrine disorders.

A Strong Link in the Chain

Connie Adkins has become a pivotal administrative force for the Division of Endocrinology, Diabetes and Metabolism

FOR 17 YEARS Connie Adkins has been a mainstay in the UC College of Medicine's Department of Internal Medicine. The administrative associate has spent 13 of those years in the Division of Endocrinology, Diabetes and Metabolism and really enjoys her role as the "go-to" person.

"It's a bit of a running joke that people figure I'll know the answer to their question or know how to find out the answer," Adkins says. "As corny as it may sound, having someone say, "thank you for taking the time to help find the answer" gives me a sense of accomplishment."

Adkins spends her days helping the division run smoothly by performing a variety of duties from answering phone calls, scheduling meetings, completing check and travel requests, managing the division website, putting together budgets—anything that falls under program coordination. One of her favorite aspects of her role is that every day is different. "You must be flexible in this job and have the ability to switch gears quickly to respond to interruptions and demands by others," she says.

During her tenure, Adkins completed both her bachelor's degree in information systems with a minor in business administration and her master's degree in criminal justice. She has met a variety of different people over the years and treasures some of the friendships she has forged by working for the division. "Over the years, folks have come and gone but I value the contacts I have made and the friendships that endure even though they may no longer be at UC.

"The division has faced some challenges over the years as leadership has changed but the current group is evolving into a cohesive unit." She credits the division chair, Shailendra Patel, PhD, with helping bridge the clinical and research arms of the division and reinforcing the idea that the division is a team. "At the end of the day, we're all one unit. Whatever your role is, you're endocrinology," Adkins says. •

Adkins spends her days helping the division run smoothly. One of her favorite aspects of her role is that every day is different.

"At the end of the day, we're all one unit."

CONNIE ADKINS

Robert M. Cohen, MD

Professor of Medicine
Division of Endocrinology, Diabetes and Metabolism

My primary research interest focuses on diabetes mellitus and its complications and the challenges and implications to assessment of blood glucose control resulting from physiologic variation in the relationship between hemoglobin A1c (HbA1c) and blood glucose. This interest in HbA1c has led to an additional area of focus, the measurement of variation in red blood cell (RBC) survival and mean RBC age with implications for both diabetes and for hematologic diseases and collaborations in adult and pediatric hematology. I have participated as a site principal investigator for NIH multi-center studies, currently the GRADE Trial (www.gradestudy.com), a comparative effectiveness study of the durability of second drugs for type 2 diabetes in maintaining glycemic control and by inference preservation of beta cell function. I participate in physiologic studies as outgrowths of GRADE, notably including a new sub-study which will allow extension of our interest in frequency and mechanisms of HbA1c-average glucose variability to the diverse GRADE population.

Current Funding: NIH

Collaborations: UC: Robert Franco, Khurram Bari, Hyon Kim, Ann Vuong; Cincinnati Children's: Charles Quinn; External: Lawrence Phillips, Mary Rhee, Clinton Joiner (Emory University); John Higgins, David M Nathan (Mass General, Harvard); Daniel Cox (Univ of Virginia)

Mercedes Falciglia, MD

Associate Professor of Clinical Medicine
Division of Endocrinology, Diabetes and Metabolism

My investigative focus has been primarily on the study of hyperglycemia and diabetes during acute illness. I completed a NIH career development award which supported the investigation of causes and consequences of hyperglycemia during acute illness. This body of work has included the analysis of glycemia and risk-adjusted outcomes in critically ill patients, and studying the causes of inpatient hyperglycemia, both prospectively through direct patient studies, and retrospectively through epidemiologic analyses.

Through my participation in national and local efforts, focused on systems-based diabetes management, including roles as medical director of trans-disciplinary diabetes programs at UC Medical Center and Cincinnati VAMC, I have gained experience in facilitating collaborative and interdisciplinary groups towards performance improvement practices throughout our academic health center. Among the opportunities arising from these efforts is my role as the lead endocrinologist nationally for the NIH sponsored SHINE Trial, a multicenter RCT to determine the efficacy and safety of glycemic control in patients admitted with ischemic stroke. In recent years, I have expanded the breadth of my focus to examine the implementation and processes of diabetes care during and surrounding the time of hospitalization.

Keywords: diabetes , hyperglycemia, hospitalization, transitions

Shailendra B. Patel, BM, ChB, DPhil

Albert W. Vontz Jr. Chair in Diabetes
Professor of Medicine and Division Director
Division of Endocrinology, Diabetes and Metabolism

My research interests include genetic disorders affecting cholesterol metabolism, genetic disorders of bile acid metabolism, such as cerebrotendinous xamthomatosis, genetic disorders of cholesterol synthesis, such as Smith-Lemli-Opitz-Syndrome and desmosterolosis. My interests also focus on genetic disorders of cholesterol, such as low cholesterol or high cholesterol and genetic disorders of (chole)sterol trafficking, such as sitosterolemia. These areas cover from how cholesterol is important in embryonic development to how excess cholesterol in adulthood leads to atherosclerotic diseases.

Clinical Phase II and Phase III trials

- Endocrine disorders
- Diabetes
- Lipid disorders

Pre-clinical models for obesity

- Small molecule inhibitors for obesity/ metabolic syndrome (in collaboration with David Hui, PhD, Department of Pathology and Laboratory Medicine)

Current funding is with the Greater Cincinnati Foundation: "Identifying novel drug targets for Obesity and Metabolic Disease". (Patel and Hui)

Diego Perez-Tilve, PhD

Research Assistant Professor
Metabolic Diseases Institute
Division of Endocrinology, Diabetes and Metabolism

My laboratory is focused on understanding the mechanisms involved in the neuroendocrine control of energy balance by investigating how afferent endocrine signals, such as GLP-1, ghrelin and leptin interact with neural circuits, specifically the melanocortin system, to regulate metabolism, and how those are influenced by nutrient and environmental status; and identifying the specific efferent mechanisms whereby those neural circuits in the brain control metabolism in peripheral tissues. Our technical approach is focused in the in vivo and ex-vivo analysis of glucose and lipid metabolism, food intake and energy expenditure in rodent models.
We have ongoing collaborations with pharmaceutical industry to develop new therapies to treat obesity and diabetes.

Funding and Collaborations

Our collaborators at the University of Cincinnati include Drs. James Herman, David Hui, Yve Ulrich-Lai and Charles Caldwell. External collaborators include Drs. Richard Dimarchi (Indiana University at Bloomington), David D'Alessio (Duke University), Kirk Habegger (University of Alabama-Birmingham), and Matthias Tschöp (Helmholtz Zentrum, Mucnich, Germany).
I am a member of the Digestive Health Center at Cincinnati Children's. Our research group includes five staff members and has been supported by UC start-up funds, NIH and industry partners.

Jason J. Winnick, PhD
Assistant Professor
Division of Endocrinology, Diabetes & Metabolism

My research expertise is the study of how hepatic glucose metabolism is regulated in vivo by various hormonal, substrate and metabolic cues and how these processes become dysregulated in people with type-1 and type-2 diabetes. For example, because people with type 1 diabetes are required to administer insulin to themselves after a meal, they are susceptible to overestimating their needs for the hormone, thereby resulting in debilitating hypoglycemia. One primary research focus of our lab is the study of how the hepatic and hormonal responses to fight off insulin-induced hypoglycemia become diminished in patients with type 1 diabetes as well as how they can be improved by augmenting liver glycogen stores via experimental or nutritional means. Also of interest to us is the presence of impaired hepatic insulin action in people with type 2 diabetes, which results in elevated fasting blood glucose levels and impaired glucose responses to meals. Consistent with this, we also study the ways by which hepatic glucose metabolism can be improved in this population via interventions such as exercise training, weight loss surgery and sleep.

Keywords: hepatic glucose production, diabetes, liver, pancreas, glucagon, hepatic glucose metabolism, liver glycogen, hypoglycemia, surgical weight loss, exercise, gastric bypass

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Schmidt RL, Mock DM, Franco RS, **Cohen RM**, North AK, Cancelas JA, Geisen C, Strauss RG, Vlaar AP, Nalbant D, Widness JA. Antibodies to biotinylated red blood cells in adults and infants: improved detection, partial characterization, and dependence on red blood cell-biotin dose. Transfusion. 2017 Jun;57(6):1488-1496. doi: 10.1111/trf.14075. Epub 2017 Mar 5. PubMed [citation] PMID: 28261808

2 **Cohen RM**, Franco RS. Can Red Blood Cell Indices Act as Surrogate Markers for Discordance between Hemoglobin A1c and Fasting Blood Glucose? Clin Chem. 2016 Dec;62(12):1551-1553. Epub 2016 Sep 30. No abstract available. PubMed [citation] PMID: 27694390

3 Quinn CT, Smith EP, Arbabi S, Khera PK, Lindsell CJ, Niss O, Joiner CH, Franco RS, **Cohen RM**. Biochemical surrogate markers of hemolysis do not correlate with directly measured erythrocyte survival in sickle cell anemia. Am J Hematol. 2016 Dec;91(12):1195-1201. doi: 10.1002/ajh.24562. Epub 2016 Nov 8. PubMed [citation] PMID: 27648808, PMCID: PMC5118160

4 Hensler MS, **Falciglia M**, Yaqub A, Yang H, Steward DL. Elective central node dissection: Comparison of open to minimally invasive video-assisted approach. Laryngoscope. 2016 Jul;126(7):1715-8. doi: 10.1002/lary.25844. Epub 2016 Mar 1. PubMed [citation] PMID: 26928077

5 Manning AM, Yang H, **Falciglia M**, Mark JR, Steward DL. Thyroid Ultrasound-Guided Fine-Needle Aspiration Cytology Results: Observed Increase in Indeterminate Rate over the Past Decade. Otolaryngol Head Neck Surg. 2017 Apr;156(4):611-615.doi:10.1177/0194599816688190. Epub 2017 Jan 24. PubMed [citation] PMID: 28118554

6 Wang HH, Li X, **Patel SB**, Wang DQ. Evidence that the adenosine triphosphate-binding cassette G5/G8-independent pathway plays a determinant role in cholesterol gallstone formation in mice. Hepatology. 2016 Sep;64(3):853-64. doi: 10.1002/hep.28570. Epub 2016 Jun 3. PubMed [citation] PMID: 27014967

7 Nghiem-Rao TH, Dahlgren AF, Kalluri D, Cao Y, Simpson PM, **Patel SB**. Influence of gestational age and birth weight in neonatal cholesterol response to total parenteral nutrition. J Clin Lipidol. 2016 Jul-Aug;10(4):891-897.e1. doi:10.1016/j.jacl.2016.03.005. Epub 2016 Apr 28. PubMed [citation] PMID: 27578120

8 **Perez-Tilve D**. Novel Hypothalamic Mechanisms in the Pathophysiological Control of Body Weight and Metabolism. Endocrinology. 2017 May 1;158(5):1085-1094. doi:10.1210/en.2016-1944. PubMed [citation] PMID: 28200100

9 Mroz PA, **Perez-Tilve D**, Liu F, Mayer JP, DiMarchi RD. Native Design of Soluble, Aggregation-Resistant Bioactive Peptides: Chemical Evolution of Human Glucagon. ACS Chem Biol. 2016 Dec 16;11(12):3412-3420. Epub 2016 Nov 8. PubMed [citation] PMID: 27797473

10 Finan B, Clemmensen C, Zhu Z, Stemmer K, Gauthier K, Müller L, De Angelis M, Moreth K, Neff F, **Perez-Tilve D**, Fischer K, Lutter D, Sánchez-Garrido MA, Liu P, Tuckermann J, Malehmir M, Healy ME, Weber A, Heikenwalder M, Jastroch M, Kleinert M, Jall S, et al. Chemical Hybridization of Glucagon and Thyroid Hormone Optimizes Therapeutic Impact for Metabolic Disease. Cell. 2016 Oct 20;167(3):843-857.e14. doi: 10.1016/j.cell.2016.09.014. Epub 2016 Oct 6. PubMed [citation] PMID: 27720451

11 Sánchez-Garrido MA, Habegger KM, Clemmensen C, Holleman C, Müller TD, **Perez-Tilve D**, Li P, Agrawal AS, Finan B, Drucker DJ, Tschöp MH, DiMarchi RD, Kharitonenkov A. Fibroblast activation protein (FAP) as a novel metabolic target. Mol Metab. 2016 Jul 16;5(10):1015-24. doi: 10.1016/j.molmet.2016.07.003. eCollection 2016 Oct. PubMed [citation] PMID: 27689014, PMCID: PMC5034526

12 Mroz PA, **Perez-Tilve D**, Liu F, Gelfanov V, DiMarchi RD, Mayer JP. Pyridyl-alanine as a Hydrophilic, Aromatic Element in Peptide Structural Optimization. J Med Chem. 2016 Sep 8;59(17):8061-7. doi: 10.1021/acs.jmedchem.6b00840. Epub 2016 Aug 25. PubMed [citation] PMID: 27509198

13 Loyd C, Magrisso IJ, Haas M, Balusu S, Krishna R, Itoh N, Sandoval DA, **Perez-Tilve D**, Obici S, Habegger KM. Fibroblast growth factor 21 is required for beneficial effects of exercise during chronic high-fat feeding. J Appl Physiol (1985). 2016 Sep 1;121(3):687-98. doi: 10.1152/japplphysiol.00456.2016. Epub 2016 Jul 21. PubMed [citation] PMID: 27445299, PMCID: PMC5142257

14 Tschöp MH, Finan B, Clemmensen C, Gelfanov V, **Perez-Tilve D**, Müller TD, DiMarchi RD. Unimolecular Polypharmacy for Treatment of Diabetes and Obesity. Cell Metab. 2016 Jul 12;24(1):51-62. doi: 10.1016/j.cmet.2016.06.021. Review. PubMed [citation] PMID: 27411008

15 Kraft G, Coate KC, **Winnick JJ**, Dardevet D, Donahue EP, Cherrington AD, Williams PE, Moore MC. Glucagon's effect on liver protein metabolism in vivo. Am J Physiol Endocrinol Metab. 2017 May 23:ajpendo.00045.2017. doi:10.1152/ajpendo.00045.2017. [Epub ahead of print] PubMed [citation] PMID:28536182

16 Gregory JM, Rivera N, Kraft G, **Winnick JJ**, Farmer B, Allen EJ, Donahue EP, Smith MS, Edgerton DS, Williams PE, Cherrington AD. Glucose Autoregulation is the Dominant Component of the Hormone-Independent Counterregulatory Response to Hypoglycemia in the Conscious Dog. Am J Physiol Endocrinol Metab. 2017 May 16:ajpendo.00099.2017. doi: 10.1152/ajpendo.00099.2017. [Epub ahead of print] PubMed [citation] PMID: 28512154

17 Espeland MA, Probstfield J, Hire D, Redmon JB, Evans GW, Coday M, Lewis CE, Johnson KC, Wilmoth S, Bahnson J, Dulin MF, Green JB, Knowler WC, Kitabchi A, Murillo AL, Osei K, Rehman SU, Cushman WC; Look AHEAD Research Group; **ACCORD Study Group**. Systolic Blood Pressure Control Among Individuals With Type 2 Diabetes: A Comparative Effectiveness Analysis of Three Interventions. Am J Hypertens. 2015 Aug;28(8):995-1009. doi: 10.1093/ajh/hpu292. Epub 2015 Feb 9. PMID: 25666468.

DIVISION OF

General Internal Medicine

Mark H. Eckman, MD
DIVISION DIRECTOR

Research and practice activities in the **Division of General Internal Medicine** bring together investigators from a broad range of disciplines and departments. Primary areas of interest include the Decision Sciences, Outcomes Research, Health Services Research, Clinical Informatics, Performance Improvement and Innovations in Medical Education.

The focal point for research within the Division is our Center for Clinical Effectiveness. The Center provides a place for investigators from multiple divisions, departments, and professions to share ideas. Many projects have arisen through such interprofessional collaborations. A major goal has been the development of decision support tools. These tools take a variety of forms, including interactive web pages, as well as fully integrated applications in our electronic health record (EHR). In addition, these tools can incorporate patient preferences and values for health outcomes, which are of particular importance for preference sensitive decisions in which patients consider trade-offs between treatment side effects and effectiveness.

Examples of current projects include the research evaluating the impact of an Atrial Fibrillation Decision Support Tool, which is now available to clinicians throughout UC Health as a tool embedded in our Epic electronic health record. This project has involved collaborations across a diverse group including Cardiology, Neurology, Center for Health Informatics, the Center for Continuing Professional Development, the Department of English, the College of Design, Architecture, Art and Planning, UC Health Information Technology, and the UC Health Primary Care Network. Another project in collaboration with the Division of Pulmonary, Critical Care and Sleep Medicine involves the development of shared decision-making tools to assist patients with cystic fibrosis in prioritizing home therapies they must use on a daily basis. Yet another project, in collaboration with an international group of investigators, is studying the benefit of tools to support shared decision-making about antepartum thromboprophylaxis for pregnant women with a history of prior venous thromboembolism.

At a policy level, the Center conducts cost-effectiveness analyses of diagnostic, treatment and screening strategies for both adults and children. Areas of particular interest include the management of anticoagulation therapy in atrial fibrillation and venous thromboembolic disease, screening strategies for hepatitis B and C infections. A recently funded project is investigating the cost-effectiveness of using hepatitis C virus (HCV) infected kidneys for HCV-infected patients with end-stage renal disease awaiting transplantation.

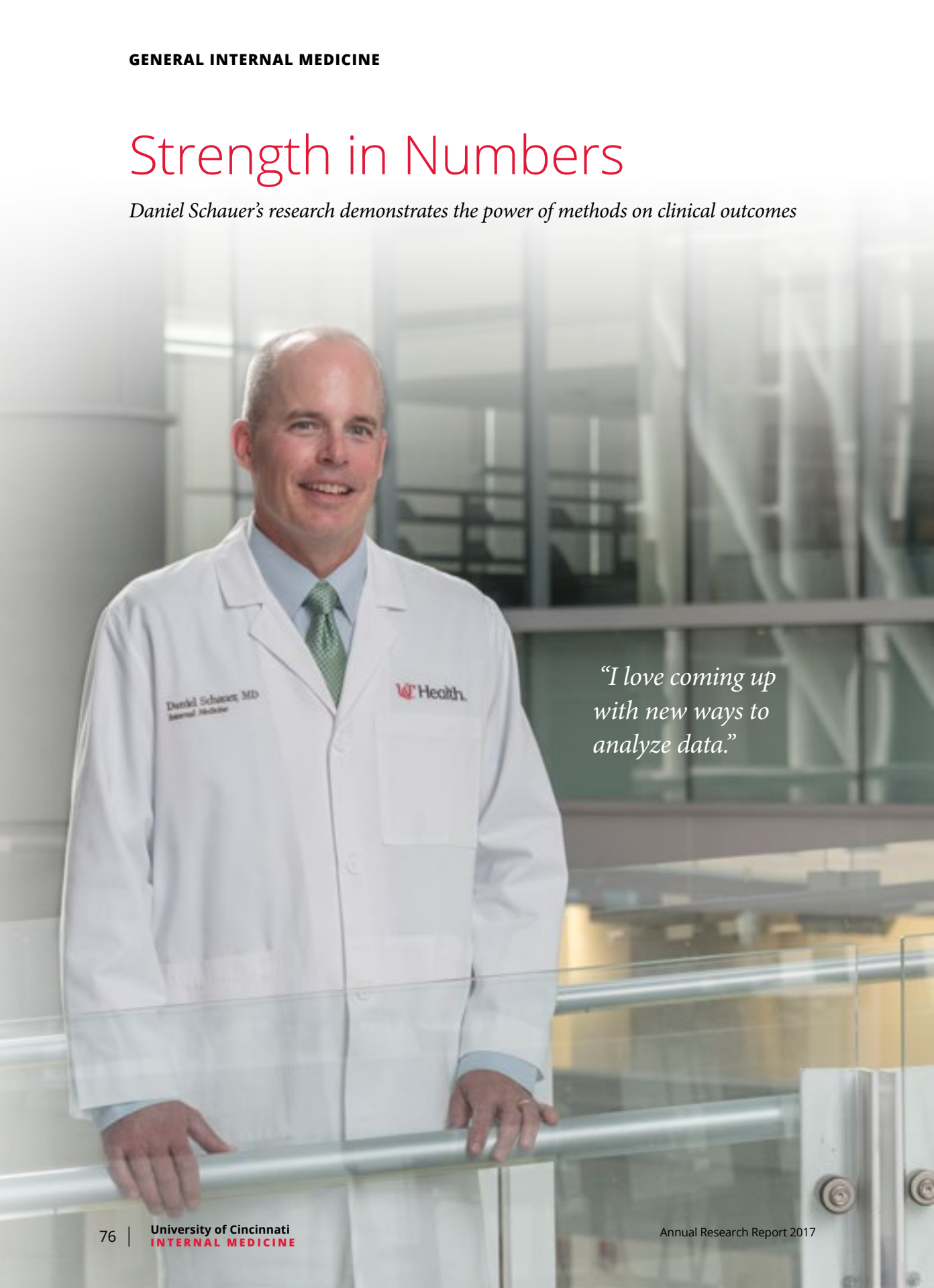
Members of the Division are involved in NIH-funded research examining bariatric surgery for patients with morbid obesity. Projects include epidemiologic studies of the impact of bariatric surgery on the incidence of a variety of cancers, issues surrounding bariatric surgery in obese patients being considered for solid organ transplantation, such as kidney transplants, and shared decision-making approaches to the consideration of bariatric surgery.

Faculty in our division have made pioneering advances in investigating the impact of hormonal fluctuations in the pathogenesis of migraine headaches. This has resulted in numerous clinical trials investigating among other topics, hormonal manipulation therapy in the control and prevention of migraine headache.

Other significant foci of research in the Division include the impact of innovations in medical education, and implementation of performance improvement and system redesign.

Strength in Numbers

Daniel Schauer's research demonstrates the power of methods on clinical outcomes



"I love coming up with new ways to analyze data."

FOR ASSOCIATE Professor Daniel Schauer, MD, the thrill of research lies not in the "why," but the "how."

"I was a math major as an undergraduate; I loved number and statistics," Schauer says. "I thought I'd left that behind when I went to medical school, but now that's where my focus is—on the methods."

After attending UC for his medical school and residency, Schauer, who is originally from Dayton, Ohio, was offered a fellowship position in Outcomes Research. "I had never done research before in my life," he says, "but once Outcomes research was described to me, I thought, 'That is a perfect fit for what I want to do with my life.'"

Today, Schauer is using his knowledge of methodology to examine a pressing problem in the United States: obesity. "There are a lot of unanswered questions around obesity that I felt I could use my methodology to address," says Schauer.

His most recent study, funded by an R01 from the National Institutes of Health, is retrospective and pulls data from five U.S. sites, comparing more than 30,000 obese patients who have had bariatric surgery with 60,000 control patients who are obese but have not had surgery. Schauer tracks their outcomes over 10 years to determine whether intentional weight loss through bariatric surgery can reduce an obese patient's risk of cancer. "Hopefully we can get down to some of the mechanisms involved in lowering cancer risk with bariatric surgery," Schauer says.

Schauer also conducts regular research with the Department of Internal Medicine's residency program, in particular examining how the program's comprehensive evaluation for residents is validated by their clinical outcomes. "This will show that our evaluations of our residents are accurate and reflects their clinical performance around patient care," he explains.

For Schauer, who has also applied his skills to transplant surgery research and decision analyses, medical education marks just one more area in which his focus on methodology is leading to potential clinical outcomes. "I love working on new methodology and coming up with new ways to analyze data," he says. "Particularly in obesity research, I hope what I do eventually influences public policy, too." •

"I had never done research before in my life but once Outcomes research was described to me, I thought, 'That is a perfect fit for what I want to do with my life.'"

Tiffiny Diers, MD

Associate Professor, Internal Medicine-Pediatrics
Division of General Internal Medicine

Dr. Diers has led implementation research in chronic pain, sickle cell disease, interprofessional collaborative practice and group visit models of care. As the PI of a HRSA-funded Sickle Cell Disease Treatment Demonstration project from 2009-2015, she worked with people living with sickle cell and community-based organizations to develop primary care capacity, a patient advocacy group, and an expanded interprofessional team at UC Medical Center.

With Dr. Jill Boone from the College of Pharmacy, Dr. Jack Kues, Amy Short and the Cincinnati Interprofessional Care Collaborative, she directed the implementation of a chronic pain group visit program. This project improved patient outcomes in pain, mood and function and is now an ongoing clinical program. Currently she is working with Dr. Shauna Acquavita in the School of Social Work on a SAMHSA-funded to project to develop an interprofessional student course on Screening Brief Intervention and Referral to Treatment, with community partners. Similarly, she is working with Dr. Pamposh Kaul from Infectious Diseases and Dr. Ruth Anne Van Loon from the School of Social Work, on a HRSA-funded project to create an interprofessional course on team-based care for HIV with a regional collaborative.

Keywords: implementation research, quality improvement, health equity, sickle cell, chronic pain

Mark H. Eckman, MD

Posey Professor of Clinical Medicine
Division Director
Division of General Internal Medicine

For the past thirty-two years, I have followed my passion as a general internist and a decision scientist, first as a member of the Division of Clinical Decision Making at the New England Medical Center (1984–1999) and more recently as Director of the Center for Clinical Effectiveness at the University of Cincinnati (1999–present). As a researcher and a clinician, this environment has supported my interests in combining clinical and theoretic applications of decision analysis to the care of individual patients and to broader issues of health policy. In particular, my methodological interests have included the development of patient-specific decision support tools, clinical informatics, cost-effectiveness analysis, and the continued study and development of new decision analytic methods.

I am deeply committed to the continued development and application of computational and information technologies to the practice of medicine and medical education. I believe that the challenges we encounter as clinicians treating individual patients and as administrators managing and leading systems of care, provide fertile soil for important research and innovative problem solving.

We have lived in Cincinnati for 18 years now and have 2 grown children. To unwind from work, I am the lead guitarist for a folk-rock band—The Creeky Knees.

Keywords: decision sciences, patient-centered outcomes research, clinical informatics, implementation science, atrial fibrillation

Vincent T. Martin, MD

Professor of Clinical Medicine
Division of General Internal Medicine
Co-director of the Headache & Facial Pain Center

Our research group has primarily focused on the identification of risk factors responsible for the triggering of attacks of migraine headache. We are best known for our studies defining the role of female ovarian hormones in the precipitation of migraine headache. We first conducted an interventional study regarding the effect of medical oophorectomy on the course of migraine headache in premenopausal women. More recently we have performed epidemiological studies to determine the effect of reproductive life events such as menarche and perimenopause on the frequency of headache in girls and women.

Another primary area of research involves the role of weather as a trigger factor for migraine. We have completed a study in which mathematical models of surface weather variables were developed to predict attacks of migraine headache. Other research areas have included how comorbid medical disorders (e.g. chronic rhinitis, asthma and Ehlers Danlos syndrome) influence the frequency of migraine headache.

We have a team of researchers that includes physician scientists, psychologists, meteorologists and biostatisticians. The epidemiological studies have been funded by the National Headache Foundation, pharmaceutical companies, and private donations. We are also a study site for a multicenter PCORI grant.

On a personal note, I have been on faculty at the University of Cincinnati since 1989 and have three grown children of which two have chosen medicine as a profession.

Keywords: migraine headache, headache, female hormones, rhinitis, asthma and Ehlers Danlos syndrome

Daniel P. Schauer, MD, MSc

Associate Professor of Clinical Medicine
Division of General Medicine

My methodological expertise is in the decision sciences, patient-centered outcomes and comparative effectiveness research. Much of my current research is focused on obesity and outcomes associated with bariatric surgery.

I am the Principal Investigator on an R01 that was funded by the NCI that examines the relationship between obesity, cancer and intentional weight loss. I have experience using many of the large publicly available datasets including the National Health Interview Survey that is linked to the National Death Index and the Nationwide Inpatient Sample in my research.

I have also collaborated with the HMO Research Network using their data sources.

Additionally, as associate program director for resident research, I oversee all of the resident research in the department of Internal Medicine.

Keywords: obesity, bariatric surgery, cancer, decision analysis, outcomes research

Eric Warm, MD
Vilter Professor of Internal Medicine
Program Director, Internal Medicine Residency
Division of General Internal Medicine

Our team has a number of ongoing projects divided into several themes. Our assessment team is studying a new system we developed based on entrustment of observable practice activities mapped to milestones. Our current work centers on validity interpretation of this data—can a system such as ours determine when a resident is ready for unsupervised practice based on competence and not simply time-based metrics (e.g., after 3 years of training)?

We have also created an educational dashboard for faculty and programmatic performance, and are studying ways to measure and improve individual, rotation level, division, and departmental performance. Our team is also working on assessment of procedural competence, attempting to determine how we know a resident is competent for a given procedure, and at what rate competence declines over time. Members of our team have collaborated with educators within our medical center, and in many other medical centers across the country, and we are participating in and leading multiple national learning and teaching collaboratives.

Keywords: graduate medical education, assessment, learning theory, learning analytics, teaching

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Provision of Recommended Chronic Pain Assessment and Management in Primary Care: Does Patient-Centered Medical Home (PCMH) Recognition Make a Difference? Elder N, Penm M, Pallerla H, Vonder Meulen MB, Short AD, **Diers T**, Imhoff RJ, Wilson B, Boone JM. J Am Board Fam Med. 2016 Jul-Aug;29(4):474-81. doi: 10.3122/jabfm.2016.04.160037. PMID: 27390379

2 Pancreas fistula risk prediction: implications for hospital costs and payments. Abbott DE, Tzeng CW, McMillan MT, Callery MP, Kent TS, Christein JD, Behrman SW, **Schauer DP**, Hanseman DJ, **Eckman MH**, Vollmer CM. HPB (Oxford). 2017 Feb;19(2):140-146. doi: 10.1016/j.hpb.2016.10.016. Epub 2016 Nov 21. PMID: 27884544

3 Cost-effectiveness of cervical spine clearance interventions with litigation and long-term-care implications in obtunded adult patients following blunt injury. Ertel AE, Robinson BR, **Eckman MH**. J Trauma Acute Care Surg. 2016 Nov;81(5):897-904. PMID: 27602907

4 Chest Computed Tomographic Image Screening for Cystic Lung Diseases in Patients with Spontaneous Pneumothorax Is Cost Effective. Gupta N, Langenderfer D, McCormack FX, **Schauer DP**, **Eckman MH**. Ann Am Thorac Soc. 2017 Jan;14(1):17-25. doi: 10.1513/AnnalsATS.201606-459OC. PMID: 27737563

5 Combined aspirin and anticoagulant therapy in patients with atrial fibrillation. So CH, **Eckman MH**. J Thromb Thrombolysis. 2017 Jan;43(1):7-17. doi: 10.1007/s11239-016-1425-5. PMID: 27665101

6 Impact of an Atrial Fibrillation Decision Support Tool on thromboprophylaxis for atrial fibrillation. **Eckman MH**, Lip GY, Wise RE, Speer B, Sullivan M, Walker N, Kissela B, Flaherty ML, Kleindorfer D, Baker P, Ireton R, Hoskins D, Harnett BM, Aguilar C, Leonard AC, Arduser L, Steen D, Costea A, Kues J. Am Heart J. 2016 Jun;176:17-27. doi: 10.1016/j.ahj.2016.02.009. Epub 2016 Feb 19. PMID: 27264216

7 Prophylactic pasireotide administration following pancreatic resection reduces cost while improving outcomes. Abbott DE, Sutton JM, Jernigan PL, Chang A, Frye P, Shah SA, Schauer DP, **Eckman MH**, Ahmad SA, Sussman JJ. J Surg Oncol. 2016 Jun;113(7):784-8. doi: 10.1002/jso.24239. Epub 2016 Apr 4. PMID: 27041733

8 Critical Deficiency Ratings in Milestone Assessment: A Review and Case Study. Kinnear B, Bensman R, Held J, O'Toole J, **Schauer D**, Warm E. Acad Med. 2017 Jun;92(6):820-826. doi: 10.1097/ACM.0000000000001383. Review. PMID: 28557948

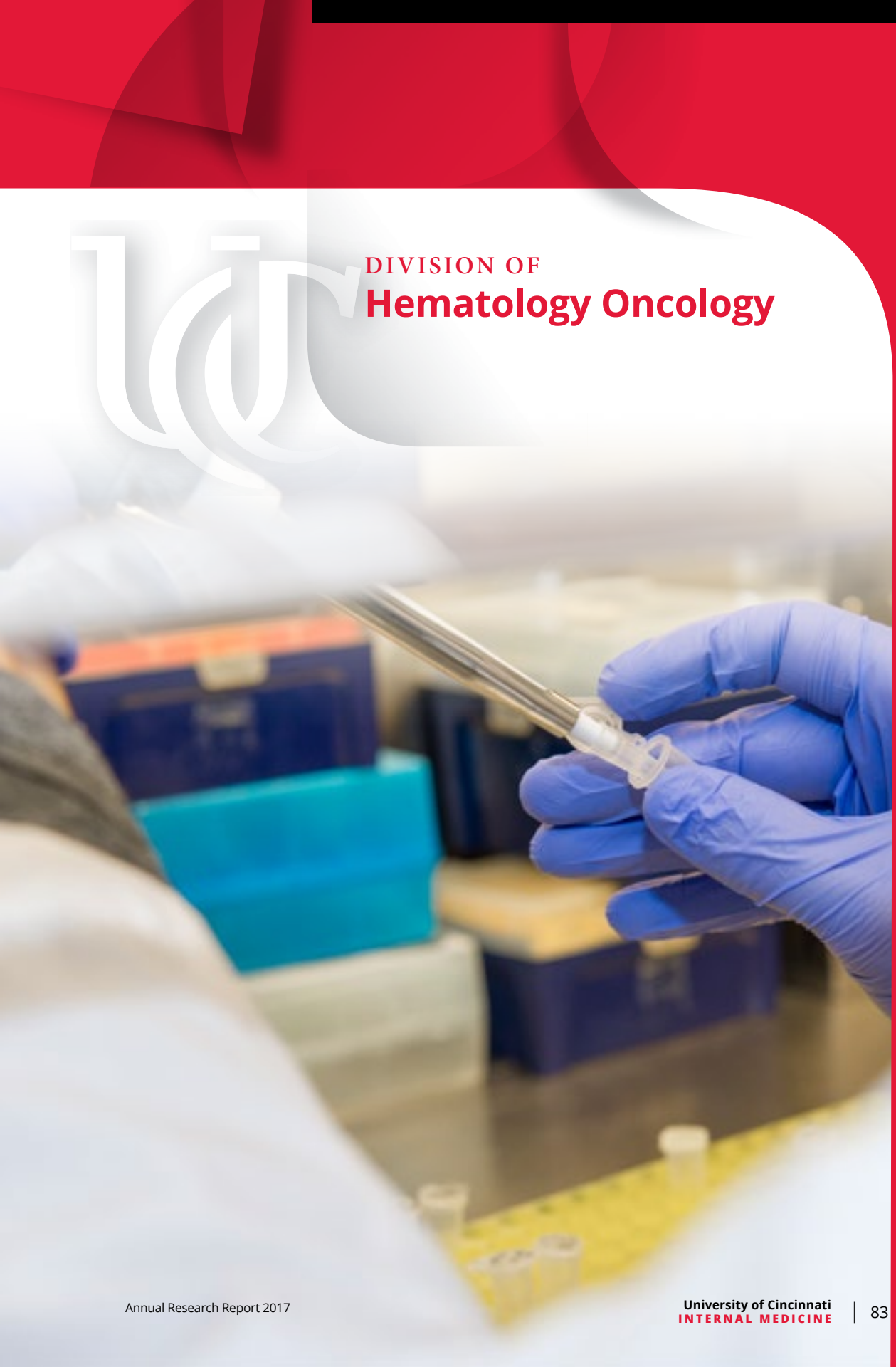
9 Metabolic syndrome in liver transplantation: A preoperative and postoperative concern. Chang AL, Cortez AR, Bondoc A, **Schauer DP**, Fitch A, Shah SA, Woodle SE, Diwan T. Surgery. 2016 Oct;160(4):1111-1117. doi: 10.1016/j.surg.2016.06.015. Epub 2016 Aug 3. PMID: 27498302

10 Entrusting Observable Practice Activities and Milestones Over the 36 Months of an Internal Medicine Residency. Warm EJ, Held JD, Hellmann M, Kelleher M, Kinnear B, Lee C, O'Toole JK, Mathis B, Mueller C, Sall D, Tolentino J, **Schauer DP**. Acad Med. 2016 Oct;91(10):1398-1405. PMID: 27355780

11 Prophylactic pasireotide administration following pancreatic resection reduces cost while improving outcomes. Abbott DE, Sutton JM, Jernigan PL, Chang A, Frye P, Shah SA, **Schauer DP**, Eckman MH, Ahmad SA, Sussman JJ. J Surg Oncol. 2016 Jun;113(7):784-8. doi: 10.1002/jso.24239. Epub 2016 Apr 4. PMID: 27041733

DIVISION OF

Hematology Oncology



Hematology Oncology

Tahir Latif, MBBS, MBA, FACP
INTERIM DIVISION DIRECTOR

Tahir Latif, MBBS, MBA, FACP
INTERIM DIVISION DIRECTOR

The **Division of Hematology Oncology** has consistently seen tremendous growth over the last few years, we currently have 32 faculty members, although many of them were recruited primarily to focus on providing state-of-the-art clinical care to patients, they are increasingly becoming involved in clinical, translational, and basic science research pursuits. All faculty members contribute to advancing the field in different ways, either through leading clinical trials, enrolling patients in clinical trials, conducting fundamental laboratory research, or educating the next generation of leaders in the field. Our division faculty work closely and collaboratively with other faculty in our UC Academic Health Center in multidisciplinary clinics, tumor boards, and academically focused, disease-based groups, as well as through outside institutions.

CLINICAL RESEARCH: Our Division currently has 78 open clinical trials that are actively enrolling patients, these trials include pharmaceutical, cooperative group, and investigator initiated trials. Over the past fiscal year, 189 patients were enrolled in these trials, which is the highest enrollment of any division in the University of Cincinnati Cancer Institute. The studies involve all types of cancer and therapies at different phases of their development. Our phase 1 studies program is one of a kind in the region providing patients, who generally had exhausted all standard treatment options, access to emerging promising therapies. We enrolled 38 patients in this program over the past year. Several of our faculty have developed investigator initiated concepts and been awarded millions of dollars from industry sponsors to conduct these trials. Two of our fellows received funding approval from pharmaceutical industry for their concepts totaling over $600,000 during the previous fiscal year. These projects will be realized in this year.

BASIC SCIENCE RESEARCH: Our Division currently has 10 independent laboratory programs that are run not only by PhD physicians, but three of these labs are also run by MD, PhD investigators. Due to the success of these investigators, our NIH funding has sharply increased over the past 5 years. Examples of the areas of basic science research focus in the Division include research on the cell cycle and DNA repair, proteasome biology in multiple myeloma, immunotherapy of lung and head and neck cancer, prostate cancer, tissue factor in blood coagulation and metabolism of cancer cells, and the biology of primary and metastatic brain tumors.

TRANSLATIONAL RESEARCH: Strong clinical and basic science research activities have provided a foundation for a very robust translational oncology research program. Almost all of our research has some correlative translational component to it. In fact, the Hematology Oncology Division offers a core for translational research, making predictive, or prognostic biomarker research affordable for our investigators.

COLLABORATIONS: Our disease specific inter-disciplinary programs in solid tumor oncology and hematologic malignancies and our research programs thrive due to active collaborations not only with other departments within the UC Academic Health Center, but from Cincinnati Children's Hospital Medical Center as well.

On the Frontline

John Morris has spent his career finding better options for battling cancer

JOHN MORRIS, MD, isn't shy about what his latest research could potentially mean for cancer patients. "Our goal is to create a vaccine to treat cancer," says Morris, professor of medicine, co-director of the Comprehensive Lung Cancer Center, associate director of the UCCI Translational Research and director of Experimental Therapeutics.

This line of research isn't new for Morris; the idea stems in part from his work at the National Institutes of Health, when he developed a phase one trial of interleukin-15—a cytokine that stimulates immune responses at the cellular level. In particular, interleukin-15 is instrumental in stimulating cytotoxic T cells and natural killer (NK) cells to attack and destroy cancer cells. But in previous studies, Morris found interleukin-15 in drug form caused unacceptable side effects in patients, such as high fevers and leaky blood vessels.

In his latest laboratory experiments, Morris has taken a different approach. He genetically engineered tumor cells using a series of lentiviruses to express interleukin-15 and its receptor, and then used those cells as a vaccine against cancer in mice. "At least in our early experiments, we've seen very powerful effects, with certain vectors suppressing the growth of lung cancer cell lines in mice," Morris says.

In addition to his laboratory studies, Morris also oversees UC's clinical trials in lung cancer and experimental therapeutics—particularly phase I trials, which are the first testing of new drugs in humans for safety and correct dosage. Overall, he says the increase in targeted cancer treatment, such as immunotherapies in lung, head and neck cancers, has improved outcomes for patients with far fewer side effects than traditional chemotherapy.

"In lung cancer, we are now seeing more patients that are living much longer, with much better quality of lives because of the new classes of drugs that target specific mutations in tumors, or immune-oncology drugs, which boost the patient's immune response against the tumor," Morris explains.

For Morris, this cutting-edge research is just the latest stop in a long career dedicated to finding better options for battling cancer. The Queens, NY, native finished his residency and fellowship at New York City's Mount Sinai Hospital before moving to the NIH and later, the National Cancer Institute. In 2010, a former colleague who had made the move to the Midwest recruited him to UC. Morris still looks forward to the potential that awaits him in the lab each day. "It's about the excitement of discovery—finding new treatments that might help people," Morris says. "It's a very exciting time in cancer research and cancer care." ●

"It's a very exciting time in cancer research and cancer care."

In his latest laboratory experiments, Morris has genetically engineered tumor cells to express interleukin-15 and its receptor, and then used those cells as a cancer vaccine for mice.

JOHN MORRIS, MD

El Mustapha Bahassi, PhD

Research Assistant Professor
Division of Hematology Oncology

Research in my laboratory is geared towards understanding the etiology of brain tumors, investigating new therapeutic strategies to treat malignant gliomas, improving adjuvant treatment decisions and enhancing early detection of relapse by developing new non-invasive biomarkers using circulating tumor DNA and circulating tumor cells.

We have developed a new mouse model to study the role of isocitrate dehydrogenase 1 (IDH1) mutations in gliomas. Up to 90% of low grade gliomas contain a mutation in one IDH1 allele that is associated with tumor initiation, maintenance and resistance to therapy. Our mouse model has helped us better understand the role of IDH1 mutation in gliomas and develop new strategies to prevent resistance to therapy.

We have also been using high throughput genomics (HTG) to develop new hypotheses on brain tumors initiation and progression. We are investigating the initiating factors of chromothripsis, a single catastrophic event that leads to massive chromosomal rearrangements that may not only contribute to cancer initiation but also possibly drive tumor progression. This new finding challenges the notion that all cancers progress as a result of the gradual acquisition of mutations over an extended period of time.

We are also using HTG to develop new biomarkers using circulating tumor DNA. We are using a combination of whole genome sequencing and long range PCR amplification to detect tumor specific mutations and follow the mutated DNA level in l blood and urine to monitor tumor dynamics.

Vladimir Bogdanov, PhD

Associate Professor of Medicine
Division of Hematology Oncology

The blood coagulation system plays many important roles in health and disease. Aside from clotting blood, coagulation proteases also contribute to such processes as angiogenesis and cellular proliferation / migration. I direct the Hemostasis Research Program in the Division of Hematology Oncology. At the present time, the Program is focused on two areas. The first is alternatively spliced Tissue Factor (asTF) as a therapeutic target in pancreatic cancer. asTF is a soluble form of Tissue Factor (TF), the trigger of blood clotting. We recently discovered that asTF is elevated in pancreatic cancer and acts as a cell agonist promoting growth and spread of pancreatic cancer cells.

Our newly developed inhibitory antibody against asTF is currently being tested in animal models. The second is red blood cells (RBC) as novel contributors to vascular dysfunction in acute and chronic inflammatory states. We recently discovered that RBC can contribute to heightened clotting and obesity-related atherosclerosis, in large part because the levels of pro-inflammatory chemokines bound to RBC become high on high-fat diet. We hope that these observations will improve our understanding of RBC biology, and help develop new diagnostic and/or therapeutic strategies aimed at ameliorating obesity-related vascular disease.

Mahmoud Charif, MD

Associate Professor of Clinical Medicine
Division of Hematology Oncology

During the academic year 2016-17, Dr. Charif published Early-Stage Mucinous Ovarian Adenocarcinoma with Extensive Clotting in a Previously Healthy Young Female Patient: An Uncommon Presentation of a Relatively Uncommon Disease. He assumed the role of hematology/oncology fellowship program director and mentors residents Dr. Connolly, Dr. Elyse Harris and fellow Dr. Phan.

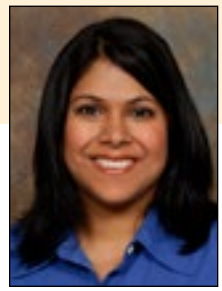
He is collaborating with the breast cancer multidisciplinary team (Drs. Lower, Zhang, Khan, and Wong) on the study MED1 estrogen receptor coactivator and breast cancer. Dr. Charif is a member of the American Society of Clinical Oncology (ASCO) and is the principal investigator on five clinical trials. He had an abstract presented at the College of American Pathologists Annual Meeting.

His interests include breast cancer, medical education, and working to improve the research quality and output of hematology and oncology fellows.

Keywords: breast cancer, hormone resistance, HER-2

Rekha Chaudhary, MD

Adjunct Associate Professor of Medicine
Division of Hematology Oncology



I have been practicing neuroncology since 2010. I am a primary investigator on multiple industry and cooperative group sponsored clinical trials. I am also Chairperson of the UC Brain Tumor Marketing Committee and the Co-Chairperson of the UC Brain Tumor Clinical Trials Committee. Since I also have an interest in integrative oncology, I am writing and have received funding for a prospective trial looking at the feasibility of ketogenic diet in glioblastoma multiforme. Ketogenic diet in conjunction with radiation therapy in mice has been shown to significantly prolong survival and decrease tumor size.

This trial is in conjunction with Dr. Robert Krikorian and Dr. Amanda Stein from the Department of Psychiatry. They will be looking at neurocognitive outcomes with the ketogenic diet and the correlation with mitochondrial respiration in platelets. Tammy Ward, registered dietitian from the UC Cancer Institute, has been trained in prescribing this diet and will be training patients on trial. This trial has been funded by the UC Brain Tumor Center, John C. Tew Endowed Chair Fund. We are also applying for funding to look at the effects of the ketogenic diet with MRIs performed with spectroscopy.

I have three children ages 13, 11 and 9, and my husband, Haleem Chaudhary, is a total joint surgeon with Beacon Orthopedics.

Zhongyun Dong, MD, PhD

Professor of Medicine
Division of Hematology Oncology

I have been active in cancer research for over 20 years. My research focuses mainly on prostate and lung cancer and attempts to better understand the molecular mechanisms underlying cancer development and progression, identify biomarkers for cancer diagnosis and prognosis, and develop novel cancer therapeutics. We have identified several novel anti-cancer small molecules, including an androgen receptor antagonist, a microtubule inhibitor, and a new class of small molecule inhibitors of proliferating cell nuclear antigen (PCNA).

With respect to biomarkers, we have found that the secretory phospholipase A2-IIa (sPLA2-IIa) is significantly elevated in the plasma of patients with advanced lung and prostate cancer. It is likely a novel master regulator of cancer stem cells and a potential target for cancer therapy. Another ongoing project is to develop magnesium alloy-based drug delivery devices for cancer therapy.

Our research is supported by grants from NIH-NCI, DOD-PCRP, American Cancer Society, NSF, several pharmaceutical companies, and our institution and currently supported by a grant from NSF.

Keywords: prostate and lung cancer, proliferating cell nuclear antigen PCNA inhibitors, secretory phospholipase A2-lia (SPLA2-lla)

James J. Driscoll, MD, PhD

Assistant Professor of Medicine
Division of Hematology Oncology

Gene microarray profiling has shown major differences between normal plasma cells and cells from monoclonal gammopathy of unclear significance (MGUS) and MM cells, with further modulations within MM cells and in cells progressing to plasma cell leukemia. Therefore, we have profiled individual patients newly diagnosed with MM in order to tailor targeted therapy for them.

My laboratory is also interested in understanding the role of the highly conserved ubiquitin+ proteasome system (UPS) that plays a pivotal role in protein homeostasis and is critical in regulating normal and cancer-related cellular processes. The hierarchical nature of the UPS provides a rich source of molecular targets for specific intervention and has therefore arisen as a promising approach to innovative anticancer therapies. Pharmacologics that inhibit the UPS have yielded unprecedented results that have doubled the survival of certain patients diagnosed with MM. However, many MM patients do not respond to proteasome inhibitors and those that do respond inevitably develop drug resistance.

In recent studies, we have demonstrated that the genetic heterogeneity strongly regulates the response of myeloma cells to proteasome inhibition. We have employed a multi-pronged approach using molecular and cellular biology tools, novel 3-D and murine models with MM cell lines and patient tumor cells to validate the role of novel small molecules and immunotherapy as a clinically relevant therapeutic strategy for MM.

Hala Elnakat Thomas, PhD

Research Assistant Professor
Division of Hematology Oncology

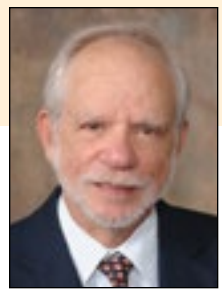
My research is primarily focused on identifying novel treatments for neuroendocrine tumors (NETs) with special emphasis on targeted therapies that inhibit mTOR signaling. My laboratory relies on biochemical, genetic and in vivo mouse preclinical studies to determine the mechanisms of response and acquired resistance to these treatments. The experimental endpoints we incorporate not only score for tolerability and anti-tumor efficacy, but also account for tumor-associated pathological manifestations such as carcinoid syndrome. We have particularly focused on the mechanism by which mTOR inhibitors delay onset of cardiac carcinoid disease and protect heart valves from fibrosis in collaboration with Dr. Jack Rubinstein.

Presently, our efforts are also aimed at identifying biomarkers that predict sensitivity to mTOR inhibitors in NETs, as well as a molecular signature to predict which patients will respond to a switch from rapalog therapy to an mTOR kinase inhibitor. We have established collaborations with researchers and oncologists both internally and nationally to develop new models for NETs including patient-derived tumor xenografts, cell lines and organoids.

My funding and laboratory funds to date have consisted of support from the Hematology and Oncology Division, the Department of Internal Medicine, the CCC, NANETS, NCI and Celgene.

Robert S. Franco, PhD

Professor Emeritus
Division of Hematology Oncology



Current interests include the mechanism of action of the therapeutic agent SAPC-DOPS in cancer, the importance of red cell life span in the interpretation of HbA1c in diabetes, and the relationship between red cell lifespan and surrogate measures of hemolysis in sickle cell disease.

Current funding consists of support through Dr. Qi's R01. There is also a pending R01 with Dr. Cohen as the co-PI that includes support.

Collaborators at UC include Dr. Xaoyang Qi, Dr. Robert Cohen, Dr. Charles Quinn, and Dr. Jose Cancelas. Outside collaborators include Dr. Jack Widness at University of Iowa, Dr. Donald Mock at University of Arkansas, and Dr. Clinton Joiner at Emory University.

In the future I intend to continue to work with outstanding collaborators at UC and nationally. My role in these research projects is to provide experience in membrane biology and red cell kinetics.

Saulius Girnius, MD

Assistant Professor of Clinical Medicine
Division of Hematology Oncology

I am involved primarily in clinical research in hematology, both benign and malignant. My primary interest in hematologic malignancies is multiple myeloma (MM), for which I am the institutional PI for a prospective, Phase 2 industry-sponsored trial.

Likewise, I am a steering committee member and site PI for the prospective observational INSIGHT-MM trial, which is an industry-sponsored, international registry with planned accrual of >5,000 patients with MM.

I have active clinical and research collaboration with the hematologists at CCHMC, focusing on hemophilia, platelet disorders, and coagulopathy of vascular malformations.

Zartash Gul, MD

Associate Professor
Division of Hematology Oncology

My interest is myeloid malignancies and allogeneic stem cell transplant. I am additionally working with a phase 1 team to expand the portfolio of studies in hematologic malignancies. I am involved in collecting bone marrow and blood samples of patients with CML and myeloproliferative diseases.

I collaborate with Dr. Mohammed Azam at Cincinnati Children's Hospital Medical Center (CCHMC), collecting bone marrow and blood samples of patients with MDS and AML. I collaborate with Dr. Dan Starczynowski at CCHMC and I collaborate with Dr. James Driscoll at University of Cincinnati, College of Medicine to evaluate the impact of NF kappa B inhibition in patients with multiple sclerosis. This is in relation to creating a hematopoietic stem cell transplant program for MS.

I am also involved in creating the transplant pathway for gvhd after transfusion for the solid organ transplant program.

I am also completing my clinical trials research certificate, and a graduate program in immunology. This will increase my capacity to write the immunotherapy based protocols in older patients with hematological malignancies in collaboration with Hoxworth.

In addition to the above activities, I am involved in industry-sponsored studies.

Nooshin Hashemi Sadraei, MD

Associate Professor of Clinical Medicine
Division of Hematology Oncology

As a clinical investigator, I focus on clinical trials, biomarker research, and outcomes studies related to head and neck malignancies and thoracic oncology. Since I joined University of Cincinnati nearly 3 years ago, I have worked on enrollment of patients on head and neck and lung clinical trials and expanding our therapeutic and translational portfolio. I am proud to be part of a team that has been among the top accruing disease sites at the UC Cancer Institute.

I am a primary investigator on several head and neck cancer clinical trials including investigator-initiated, industry funded, and cooperative group (CTEP sponsored, NCI-funded) studies. My main focus has been locally advanced or advanced (recurrent and metastatic) disease. These studies address the role of targeted therapies and/or immune therapy in treatment of cancer patients. The main goal of such studies is to improve oncologic efficacy and safety of novel treatments. I have a lot of interest in studying biomarkers that predict efficacy or toxicity. Most recently, I have focused on immune therapy and DNA repair inhibition.

Conduct and design of these studies has allowed me to interact closely with my friends and colleagues at UC, as well as leaders in the field nationally, and to collaborate with outside academic intuitions, industry, and NCI cooperative groups.

Nagla Karim, MD, PhD

Associate Professor of Clinical Medicine
Division of Hematology Oncology

My main interest since I joined the faculty at the UC Division of Hematology Oncology is in the area of experimental therapeutics/early phase clinical trials especially in the area of lung cancer. Patients with non-squamous non-small cell lung cancer tend to have a good response when treated with pemetrexed due to the low thymidylate synthase (TS) levels in their tumors (Scagliotti et al 2009, 2011). However, 30% of this group of patients have SRC overexpression in addition to the low TS making them resistant to the standard therapy with pemetrexed (Ceppi et al 2012).

Preclinical data suggests that the addition of a SRC inhibitor might improve the response to pemetrexed (Ceppi et al 2012). Moreover, there is an association between the K-ras wild type and SRC overexpression (Abdel Karim, et al IASLC-AACR 2014).

I currently collaborate with Jiang Wang, MD, PhD, from Pathobiology, and El Mustapha Bahassi, PhD and John Morris, MD, both from the Division of Hematology Oncology.

My funding source is Pfizer for drug supply only (Bosutinib; SRC inhibitor).

Tahir Latif, MBBS, MBA, FACP

Associate Professor of Clinical Medicine
Division of Hematology Oncology

As a clinician/educator, my major research interests evolve around clinical trials. Also, since I joined UC in 2010 after 6 years in private practice, I have served as the institutional PI of several clinical trials in the area of malignant hematology. I also play a major role in fostering patient enrollment in the area of solid tumor oncology for lung, head and neck and GI cancer patients. My personal focus over the last couple of years has been on the prevention and treatment of CNS involvement by diffuse large B cell lymphoma. I have been able to publish several peer-reviewed manuscripts on this topic, and I am working on developing an investigator initiated trial to incorporate monoclonal antibodies in the intrathecal prophylaxis of high risk patients.

I am currently collaborating with Imran Arif, MD from Cardiology, Mohammad Azam, PhD from Cincinnati Children's Hospital Medical Center Experimental Hematology, Steve Woodle, MD from UC Transplant Surgery and James Driscoll, MD, PhD from UC Hematology Oncology. In addition, I will also be collaborating with the Cardiology Department to define best treatment approaches of malignant pericardial effusions.

Finally, I provide mentorship in conducting clinical research for students, residents, fellows, faculty nd staff.

Carol Mercer, PhD

Research Assistant Professor
Division of Hematology Oncology

Research in the Mercer lab is focused on the mammalian target of rapamycin (mTOR) pathway and the regulation of autophagy. Our long-term goal is to understand the mechanisms that regulate autophagy and the therapeutic implications of targeting autophagy in cancer. This is important because (1) autophagy has been argued to either inhibit or promote tumor survival, depending on tumor type and tumor context; and (2) autophagy is induced by mTOR inhibitors, which are approved for some tumors, and in clinical trials for others. Our project in hepatocellular carcinoma (HCC) is based on unexpected data that phenformin inhibits both mTOR and autophagy. We are investigating the mechanistic and therapeutic implications of these data in tumor progression and survival of tumor-initiating cells.

Separately, our lab has launched a new project in breast cancer, based on the identification of a novel selective autophagy receptor, using high-resolution mass spectrometry proteomics. We are currently studying the significance of this mTOR-regulated selective autophagy receptor in the growth and survival of breast cancer cells. Future proteomic studies will determine the autophagy cargo that is selected by this receptor and the relevance to breast cancer.

John C. Morris, MD

Professor of Medicine
Division of Hematology Oncology

John C. Morris, MD, is Director of Thoracic, and Head & Neck Oncology, and Experimental Therapeutics, and Professor of Medicine in the Division of Hematology Oncology.

Dr. Morris focuses on early phase clinical trials particularly in lung cancer. Dr. Morris has authored more than 120 publications and has served as principal investigator on numerous clinical trials including Bexion's BXQ-350 (SapC-DOPS) phase I trial, an agent developed at UC, now in early clinical trials. In addition, Dr. Morris serves on numerous national committees.

Dr. Morris' laboratory research focuses on development of therapeutic cancer vaccines for lung and head and neck cancer using interleukin-15 and natural killer (NK) cell immunotherapy. IL-15 is a pleiotrophic cytokine that is a powerful stimulatior of the immune system. IL-15 stimulates the maturation and activation of tumor killing CD8+ T cells and memory T cells that impart long term immune recognition of targets as well as stimulating and activating NK cells. These immune cells all play a role in the control of cancer by recognizing and killing tumor cells. Dr. Morris wrote the first phase I clinical trial to administer recombinant human interleukin-15 (rhIL-15) as a cancer therapy while at the National Cancer Institute (NCI). Dr. Kamdem Toukam in Dr. Morris' laboratory uses a lentiviral gene transfer approach generated TC1 mouse lung cancer cells stably expressing IL-15 and its receptor (IL-15Ra).

Olugbenga O. Olowokure, MD

Associate Professor of Clinical Medicine
Division of Hematology Oncology

I specialize in gastrointestinal cancers such as malignancies of the pancreas, colon, rectum, anus, esophagus, stomach, small intestine, GIST tumors, carcinoid tumors, liver, gallbladder, and bile ducts/cholangiocarcinomas. As our most senior GI oncologist, I am the principal investigator or sub PI on all GI related malignancy protocols at the University of Cincinnati Cancer Institute.

I work with a multidisciplinary team and through these collaborations we have opened up two investigator initiated clinical trials: UC, GI 001 and 002 clinical protocols. In addition, a cholangiocarcinoma transplant protocol through collaboration with the liver transplant team was initiated.

I am collaborating with Dr. Xiaoyang Qi to put together a Phase 1 clinic team to initiate novel chemotherapy modalities including the use of SapC-DOPS – BXQ-350 in combination with chemotherapy for GI malignancies. I am a member of the Hoosier cancer GI research network and am in the early stages of working with a Mayo Clinic consortium to establish state of the art clinical trials directed at GI malignancies at UC.

I am also working on developing a series of targeted therapies and immunotherapy trials for gastrointestinal malignancies. Current projects, include assessing the role of gemcitabine plus cisplatin in advanced biliary cancers, dose reduction of Sorafenib in hepatocellular carcinoma and dose reduction of gemcitabine plus Nab-paclitaxel in pancreatic cancer.

Xiaoyang Qi, PhD

Professor of Medicine
Division of Hematology Oncology

Since I discovered Saposin C Coupled Dioleoylphosphatidylserine (SapC-DOPS) anti-cancer nanovesicles in 2002, I have devoted my efforts to translate this basic research finding from discovery stage to preclinical research. Having also identified phosphatidylserine (PS) as the unique receptor for SapC-DOPS, our central working hypothesis is that tumor cells and vessels show abnormal surface PS levels providing a portal of entry for SapC-DOPS. In preclinical studies, these stable nanovesicles have shown tumor-specific targeting activity and cancer-selective killing efficacy with significant inhibition of tumor growth in various animal tumor models. Our studies suggest that SapC-DOPS nanovesicles preferentially induce apoptotic cell death in cancerous cells via a ceramide- and caspase-mediated pathway. SapC-DOPS has striking absence of toxicity and adverse side effects in animals. In addition, these vesicles can deliver hydrophilic imaging probes, proteins, and RNA/DNA for cancer-selective targeting though specific binding of the surface exposed PS of tumor cell and vessels.

A variety of animal tumor models, including neuroblastoma, pancreas, brain, lung, skin, breast, prostate, and leukemia, have been used for efficacy and toxicity studies of this new anticancer agent. I am the exclusive inventor for nine US issued and foreign patents of SapC-DOPS technology. Our translational research with Bexion has led to the development of a first-in-human (Phase I) clinical trial approved in 2016.

Neetu Radhakrishnan, MD

Adjunct Associate Professor of Clinical Medicine
Division of Hematology Oncology

My main areas of interest are breast cancer, lymphomas, myeloproliferative disorders, aHUS, and TTP. I am also interested in assessing the response of multiple sclerosis patients to taxane and platinum containing chemotherapy. This includes assessing tolerability and outcomes at preliminary stages. I am also interested in identifying, quantifying and characterizing the prevalence of breast cancer and prostate cancer in the Asian, Southeast Asian and Middle Eastern populations as data on these ethnicities are scarce in the U.S.

I am the PI for a currently open trial: tBRE 12-158: A Phase II Randomized Controlled Trial of Genomically Directed Therapy after Preoperative Chemotherapy in Patients with Triple Negative Breast Cancer. In addition, I participate in Cooperative Group trials and facilitate tissue collection for various cancer biology programs through the UCCI.

My hobbies are badminton, dancing, and fine-tuning EPIC.

Atsuo T. Sasaki, PhD

Associate Professor
Division of Hematology Oncology

We are pioneering a new field by focusing on an energy molecule, GTP (guanine triphosphate) and its roles in primary/metastatic brain tumors. With R01 funding, we have discovered the missing GTP sensor and published the finding in *Molecular Cell* and featured in *F1000Prime, Cancer Discovery*, and *Science Signaling*. I have received nine external sources of funding totaling over $2.2 million.

Among factors for successful research, my lab most appreciates our many collaborators. We have active collaborations with local (2), national (4) and international research (6) groups. The multidisciplinary research approach has resulted in multiple funding awards including an R01 grant, manuscripts including Molecular Cell, and the application of cutting-edge research technologies, such as stable-isotope labeled metabolomics, NMR and X-ray structural analyses, and chemical library screening to identify new inhibitor/activator for the target enzyme.

As a mentor, I have assisted in the development of students, resident and post-doctoral fellows. All of my three previous post-doctoral fellows have received fellowship grants under my mentorship and have now become faculty members either in Japan or at UC. I have provided guidance to young researchers by lecturing to students and post-doctoral fellows locally, nationally and internationally.

Trisha Wise-Draper, MD, PhD

Assistant Professor of Medicine
Division of Hematology Oncology

The Takiar/Wise-Draper laboratory focuses on translational mechanisms of therapeutic resistance and biomarkers in cancer. Our main model of disease is HNC which is the 6th most common cancer worldwide. Treatment for HNC often results in significant morbidity and the outcome in high risk patients is poor. Therefore, using patient samples as well as established cell lines and patient derived xenograft (PDX) models, we are attempting to identify novel targets, potential biomarkers of resistance, and novel treatments.

Specifically, I am interested in identifying mechanisms important for immunotherapy resistance. We have identified a couple of potential mediators that are under investigation. We have also identified the DEK oncogene as a possible blood biomarker and immune cell stimulator in HNC patients. We are now studying its role in cancer immune surveillance and outcome. These studies are fundamental to 1) identify patients likely to respond to particular treatment modalities, and 2) develop new therapies that can be translated into phase I clinical trials. As medical director of the Cancer Clinical Trials office I am involved in executing fundamental clinical research.

Funding includes a KL2 mentored award through the CCTST and most recently, a team science award from the DoD.

Keywords: head and neck cancer, immunotherapy, DEK, metformin, oncogenes

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Koncar RF, Feldman R, **Bahassi EM**, **Hashemi Sadraei N**.Comparative molecular profiling of HPV-induced squamous cell carcinomas. Cancer Med. 2017 6:1673-1685

2 Koncar RF., Chu Z., Romick-Rosendale LR., Wells SI, Chan TA., Qi X. and **Bahassi El M**. PLK1 inhibition enhances temozolomide efficacy in IDH1 mutant gliomas. Oncotarget. 2017 Feb 2. doi: 10.18632/oncotarget.15015.

3 Lu F, Chen Y, Zhao C, Wang H, He D, Xu L, Wang J, He X, Deng Y, Lu EE, Liu X, Verma R, Bu H, Drissi R, Fouladi M, Stemmer-Rachamimov AO, Burns D, Xin M, Rubin JB, **Bahassi EM**, Canoll P, Holland EC, Lu QR. Olig2-Dependent Reciprocal Shift in PDGF and EGF Receptor Signaling Regulates Tumor Phenotype and Mitotic Growth in Malignant Glioma.Cancer Cell. 2016 29:669-683.

4 Aljohani H, Koncar RF, Zarzour A, Park BS, Lee SH, **Bahassi El M**. ROS1 amplification mediates resistance to gefitinib in glioblastoma cells. Oncotarget. 2015 Aug 21;6(24):20388-95

5 Furgason JM, Koncar RF, Michelhaugh SK, Sarkar FH, Mittal S, Sloan AE, Barnholtz-Sloan JS, **Bahassi El M**. Whole genome sequence analysis links chromothripsis to EGFR, MDM2, MDM4, and CDK4 amplification in glioblastoma. Oncoscience. 2015 Jul 31;2(7):618-28. eCollection 2015.

6 Furgason JM, Li W, Milholland B, Cross E, Li Y, McPherson CM, Warnick RE, Rixe O, Stambrook PJ, Vijg J, **Bahassi EM**. Whole genome sequencing of glioblastoma DNAs: Overexpression of EGFR and downstream effectors is mediated by gene amplification, suppressor loss, and multiple mutational events. 2014 Mutagenesis. 29:341-50. B11

7 Salkeni MA, Zarzour A, Ansay TY, McPherson CM, Warnick RE, Rixe O, **Bahassi EM**. Detection of EGFRvIII mutant DNA in the peripheral blood of brain tumor patients. 2013 J Neurooncol. 115:27–35.

8 Li Y and **Bahassi EM**. Biofluid-based circulating tumor molecules as diagnostic tools for use in personalized medicine. 2013 J. Mol. Biomark Diagn. 5:157-163

9 Tissue factor variants induce monocyte transformation and transdifferentiation into endothelial cell-like cells. Arderiu G, Espinosa S, Peña E, Crespo J, Aledo R, **Bogdanov VY**, Badimon L. J Thromb Haemost. 2017 Jun 6. doi: 10.1111/jth.13751. [Epub ahead of print] PMID: 28585414

10 Interplay between alternatively spliced Tissue Factor and full length Tissue Factor in modulating coagulant activity of endothelial cells. Ünlü B, **Bogdanov VY**, Versteeg HH. Thromb Res. 2017 May 25;156:1-7. doi: 10.1016/j.thromres.2017.05.028. [Epub ahead of print] PMID: 28570958

11 Activation of carbonic anhydrase IX by alternatively spliced tissue factor under late-stage tumor conditions. Ramchandani D, Unruh D, Lewis CS, **Bogdanov VY**, Weber GF. Lab Invest. 2016 Dec;96(12):1234-1245. doi: 10.1038/labinvest.2016.103. Epub 2016 Oct 10. PMID: 27721473

12 A novel role of bone morphogenetic protein-7 in the regulation of adhesion and migration of human monocytic cells. Sovershaev TA, Unruh D, Sveinbjørnsson B, Fallon JT, Hansen JB, **Bogdanov VY**, Sovershaev MA. Thromb Res. 2016 Nov;147:24-31. doi: 10.1016/j.thromres.2016.09.018. Epub 2016 Sep 17. PMID: 27669124

13 **Vladimir Bogdanov** – Method Inhibiting Cell Proliferation Induced by Alternatively Spliced Tissue Factor – Patent # 9,555,109 issued on 1-31-2017

14 Zhao, D., Wang, T., Kuhlmann, J., **Dong, Z**., Chen, S., Joshi, M., Salunke, P., Shanov, V, Hong, D., Kumta, P., and W. R. Heineman. In vivo monitoring the biodegradation of magnesium alloys with an electrochemical H2 sensor. Acta Biomaterialia. 36:361-368, 2016.

15 Zhao D, Wang T, Hoagland W, Benson D, **Dong Z**, Chen S, Chou DT, Hong D, Wu J, Kumta PN, Heineman WR. Visual H2 sensor for monitoring biodegradation of magnesium implants in vivo. Acta Biomater, 45:399-409, 2016

16 Zhao D, Wang T, Nahan K, Guo X, Zhang Z, **Dong Z**, Chen S, Chou DT, Hong D, Kumta PN, Heineman WR. In vivo characterization of magnesium alloy biodegradation using electrochemical H2 monitoring, ICP-MS, and XPS. Acta Biomater, 50:556-565, 2017

17 Lu S, **Dong Z**. Overexpression of secretory phospholipase A2-IIa supports cancer stem cell phenotype via HER/ERBB-elicited signaling in lung and prostate cancer cells. Int J Oncol, 50:2113-2122, 2017

18 Woodle, ES, Tremblay S, Brailey P, Girnita A, Aronow B, Singh, H. **Driscoll JJ** (2017). Genomic and biochemical proteasomal adaptations in carfilzomib-resistant plasma cells that limit HLA-desensitization in transplantation, Science Translational Medicine (in revision).

19 Vad N, Jagannathan S, **Driscoll JJ**. (2017) Functional characterization of DT61, a novel dual PI3-kinase/mTOR inhibitor cytotoxic to glioma stem cells under hypoxia. Cell Chemistry (in revision).

20 Malek E, **Driscoll JJ**. (2017). Bone Marrow Sequestration, Tumor Unmasking and Cold Brain Detected on 18F-FDG PET/CT Imaging in Multiple Myeloma Patients. Blood Cancer Journal (in revision).

21 Malek E, Saygin C. Ye R, Covut F, Kim B-G, De Lima M, **Driscoll, JJ** (2017). Predicting Successful Regulatory Approval in Multiple Myeloma from Phase I Overall Response Rates. Journal Clinical Oncology–Clinical Cancer Informatics (in press).

22 **Driscoll, JJ**., Brailey, M. (2017) Emerging small molecule approaches to enhance the antimyeloma benefit of proteasome inhibitors. in "The Proteasome: an important player in tumor progression and a novel target for cancer therapy" Editor, Q. Ping Dou, Ph.D (in press).

23 Dosani, T, Covut F, Beck R, **Driscoll, JJ**, de Lima M, Malek E. (2017) Significance of the absolute lymphocyte/monocyte ratio as a prognostic immune biomarker in newly diagnosed multiple myeloma. Blood Cancer Journal 7:e579 doi:10.1038/bcj.2017.60.

PUBLICATIONS *CONTINUED*

24 Woodle, ES, Tremblay S, **Driscoll JJ** (2017). Targeting Plasma Cells with Proteasome Inhibitors: Principles from Primates, Jour. of the Amer. Soc. Nephrol. 28: 1951-1953.

25 Covut F., Pinto R, Dosani T, Friedman J, **Driscoll JJ** et al. (2017) Impact of Lenalidomide on Hematopoietic Myeloid and Erythroid Progenitors: Peripheral Stem Cell Collection May Not be Affected. Biol Blood Marrow Transplant 23 390–391.

26 Malek E, Abdel Malek M, Jagannathan S, Vad N, Cottini F, Anderson KC, **Driscoll JJ**. (2016) Pharmacogenomics and chemical library screens reveal a novel SCFSKP2 inhibitor that overcomes bortezomib resistance in multiple myeloma. Leukemia doi:10.1038/leu.2016.258.

27 Markeb A, El-Maali N, Sayed D, Osama A, Abdel-Malek M, Zaki A, Elwanis M, **Driscoll JJ**. (2016). Synthesis, structural characterization and preclinical efficacy of a novel paclitaxel-loaded alginate nanoparticle for breast cancer treatment, International Journal of Breast Cancer. ID 7549372 http://dx.doi.org/10.1155/2016/7549372.

28 **Driscoll JJ**, Aslam I, Malek E. (2016). High throughput Chemical Library Screens Identify a Novel Small Molecule Checkpoint Inhibitor that Activates Anti-myeloma T Cells. Clinical Lymphoma, Myeloma & Leukemia. 16 (S82) DOI: http://dx.doi.org/10.1016/j.clml.2016.07.115.

29 Malek E, Aslam I, **Driscoll JJ**. (2016) Counteracting PD-L1/PD-L2 Immune Suppression in Multiple Myeloma through Kinase Inhibition. American Society of Hematology 128 (22) 3295.

30 Tremblay S, Shields A, Alloway R, Brailey P, Abu Jawdeh B, Latif T, **Driscoll JJ**, Pando M, Girnita A, Woodle E. (2016). A Prospective Carfilzomib-Based Desensitization Trial: Phase 1 Results. Am J Transplant. 16.

31 **Driscoll JJ**, Aronow B, Tremblay S, Alloway R, Woodle E. (2016) RNAseq Transcriptome Analysis of Bone Marrow CD138+ Plasma Cell Responses to Carfilzomib Monotherapy Desensitization. Am J Transplant. 2016; 16.

32 Girnius S, **Driscoll JJ**. (2016). Proteasome Inhibitors to Treat AL Amyloidosis, in Exploring New Findings on Amyloidosis, Editor Ana-Maria Fernandez-Escamilla, ISBN 978-953-51-2619-5 1-15 DOI: 10.5772/63467.

33 Malek E, Letterrio J, Kim BG, **Driscoll JJ**, deLima M, Giralt S. (2016). Myeloid-derived Suppressor Cells: The Green Light for Myeloma Immune Escape. Blood Reviews. DOI: http://dx.doi.org/10.1016/j.blre.2016.04.002

34 Malek E, **Driscoll JJ**. (2016) High throughput chemical library screening identifies a novel p110-d inhibitor that potentiates the anti-myeloma effect of bortezomib. Oncotarget 7(25) 38523-38538. DOI: 10.18632/oncotarget.9568.

35 **Driscoll JJ**. (2016) Expression of E3 Ubiquitin Ligases in Multiple Myeloma Patients after Treatment with the Proteasome Inhibitor Bortezomib. Cancer Translational Medicine 1(5) 153-157. DOI: 10.4103/2395-3977.168577

36 Cohen, R. M., Smith, E. P., Arbabi, S., Quinn, C. T., and **Franco, R. S.**: Do Red Blood Cell Indices Explain Racial Differences in the Relationship between Hemoglobin A1c and Blood Glucose? J Pediatr, 176:7, 2016

37 Cohen, R. M., **Franco, R. S.**: Can Red Blood Cell Indices Act as Surrogate Markers for Discordance between Hemoglobin A1c and Fasting Blood Glucose? Clin Chem 62:1551, 2016.

38 Quinn, C. T., Smith, E. P., Arbabi, S., Khera, P. K., Lindsell, C. J., Niss, O., Joiner, C. H., **Franco, R. S.**, Cohen, R. M.: Biochemical surrogate markers of hemolysis do not correlate with directly measured erythrocyte survival in sickle cell anemia. Am J Hematol 91:1195, 2016

39 Mahindra A, Hari P, Fraser R, Fei M, Huang J, Berdeja J, Callander N, Costa L, Diaz MA, Freytes C, Gale RP, **Girnius S**, Holmberg L, Kharfan-Dabaja M, Kumar S, Kyle R, Lazarus H, Lee C, Maiolino A, Moreb J, Nishihori T, Pawarode A, Saad A, Savani BN, Schriber J, William B, Wirk BM, Krishnan A, Nieto Y, D;Souza A. Autologous hematopoietic cell transplantation for multiple myeloma with renal insufficiency. CIBMTR Analysis. Accepted to BBMT

40 Cytomegalovirus reactivation is associated with a lower rate of early relapse in myeloid malignancies independent of in-vivo T cell depletion strategy. Hilal T, Slone S, Peterson S, Bodine C, **Gul Z**.Leuk Res. 2017 Jun;57:37-44. doi: 10.1016/j.leukres.2017.02.009. Epub 2017 Mar 1.

41 Blinatumomab may induce graft versus host leukemia in patients with pre-B ALL relapsing after hematopoietic stem cell transplant. Khan MW, **Gul Z**. Clin Case Rep. 2016 Jun 24;4(8):743-6. doi: 10.1002/ccr3.604. eCollection 2016 Aug.

42 **Lower EE**, Khan S, Kennedy D, Baughman R. Discordance of the estrogen receptor and HER-2/neu in breast cancer from primary lesion to first and second metastatic site. IN PRESS, Breast Cancer: Targets and Therapy

43 Sasha Ruiz-Torres, Benight N, **Lower EE**, J-L Guan, Waltz S. HGFL-Mediated RON sinaling supports breast cancer stem cell phenotypes va activation of non-canonical B-catenin signaling. IN PRESS, Oncotarget

44 Shaughnessy EA, Freeman C, Lewis J, **Lower EE**, Khan S et al. Idiopathic Granulomatous Mastitis: A Diagnostic and Therapeutic Challenge, IN PRESS, Am J Surg.

45 Yang Y, Leonard M, Zhang Y.... **Lower EE**. "Critical roles for ER-interacting LxxLL motifs of MED1 in HER2-driven breast tumorigenesis." Under Revision, Cancer Research.

46 Baughman RP, Sweiss N, Keijsers R, Birring SS, Shipley R, Saketkoo LA, **Lower EE**. Repository coricotropin for Chronic Pulmonary Sarcoidosis. Lung 2017, June;195(3):313-322.

47 Zhou Y, **Lower EE**, Li H, Farhey Y, Baughman RP. Clinical characteristics of patients with bone sarcoidosis. Semin Arthritis Rheum 2017, Feb.

PUBLICATIONS *CONTINUED*

48 Zhou Y, **Lower EE**, Li HP, Costea A, Attari M, Baughman RP. Cardiac sarcoidosis: the impact of age and implanted devices on survival. Chest 2017 Janu;151(1)139-148.

49 Zhou, Y, **Lower EE**, Li H, Baughman RP. Clinical management of pulmonary sarcoidosis. Expert Rev Respir Med 2016;10(5):577-91.

50 Baughman RP, Judson MA, **Lower EE**, Drent M, Costabel U, Flavin S, Lo KH, Barnathan ES. Infliximab for chronic cutaneous sarcoidosis: a subset analysis from a double-blind randomized clinical trial. Sarcoidosis Vasc Diffuse Lung Dis 2016; 15:32(4), 289-95.

51 Baughman RP, Barney JP, O-Hare L, **Lower EE**. A retrospective pilot sutdy examining the use of Acthar gel in sarcoidosis patients. Respir Med. 2016:110:68-72.

52 Kirkil, G, **Lower EE**, Baughman RO. Predictors of mortality in pulmonary sarcoidosis. Chest IN PRESS.

53 Baughman RP, **Lower EE**. Sarcoidosis. In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Loscalzo J, editors. Harrison'e principles of internal medicine. 20 ed. New York: McGraw Hill; 2017, In press.

54 Sherrill J. Slichter, M.D., Larry J. Dumont, PhD, MBA, Jose A. Cancelas, MD, PhD, Terry Gernsheimer, MD5, Zbigniew Szczepiorkowski, MD, PhD, Nancy M. Dunbar, MD, **Stephen Medlin, DO, FACP**, MeLinh Jones, B.S., Neeta Rugg, M.S., Gautham Prakash, B.S., Greggory J. Housler, MSc, MBA, Victor W. MacDonald, Ph.D., Peter Hmel, M.S. and Janet H. Ransom, Ph.D. Treatment of Bleeding in Severely Thrombocytopenic Patients with Transfusion of Dimethyl Sulfoxide (DMSO) Cryopreserved Platelets (CPP) Is Safe – Report of a Phase 1 Dose Escalation Safety Trial. Presented at American Society of Hematology, San Diego, Ca. 12/2016

55 Agarwal R, Wang J, Wilson K, Barrett W, **Morris JC**. (2016) Response to targeted therapy in BRAF mutant anaplastic thyroid cancer. J Natl Compr Canc Netw. 14:1203-1207.

56 Sharma K, Janik J, O'Mahony D, Stewart D, Pittaluga S, Stetler-Stevenson M, Jaffe ES, Raffeld M, Fleisher T, Lee C, Steinberg SM, Waldmann TA, **Morris JC.** (2017) Phase II study of alemtuzumab (CAMPATH-1®) in patients with HTLV-1-associated adult T-cell leukemia/lymphoma. Clin Cancer Res. 23:35-42.

57 Zandvakili I, Lin Y, **Morris JC**, Yi Zheng Y. (2017) Rho GTPases: Anti- or pro-neoplastic targets? Oncogene. 36:3213-3222.

58 Sarantopoulos J, Mita AC, He A, Wade JL, Hsueh C-T, **Morris JC**, Lockhart AC, Quinn DI, Hwang J, Mier J, Zhang W, Wack C, Yin J, Clot P-F, Rixe, O. (2017) Safety and pharmacokinetics of cabazitaxel in patients with hepatic impairment: A phase I dose-escalation study. Cancer Chemother Pharmacol. 79:339-351.

59 Wise-Draper TM, Moorthy G, Salkeni MA, Abdel Karim N, Thomas HE, Mercer CA, Beg MS, O'Gara S, Olowokure O, Fathallah H, Kozma SC, Thomas G, Rixe O, Desai P, **Morris JC**. (2017) A phase Ib study of the dual PI3K/mTOR inhibitor BEZ235 combined with everolimus in patients with advanced solid malignancies. Targ Oncol. 12; 323–332.

60 Haque S, **Morris JC**. (2017). Transforming growth factor-beta: A therapeutic target for cancer. Human Vaccine Immunother.13:1741-1750.

61 Cohen EE, Nabil F. Saba NF, Gitlitz B, Haddad R, Sukari A, Neupane P, **Morris JC**, Misiukiewicz K, Manjarrez KL, Dietsch GN, Bryan JK, Hershberg RM, Ferris RL. Active8: A randomized, double-blind, placebo-controlled study of chemotherapy plus cetuximab in combination with motolimod immunotherapy in patients with recurrent or metastatic squamous cell carcinoma of the head and neck (ESMO 2016).

62 Kaplan J, Bixby D, **Morris JC**, Frankfurt O, Altman J, Wise-Draper T, Burke P, Collins S, Kannan K, Wang L, Faucetten S, Lee B, Shou Y, Levis M, Pratz K. A phase 1b/2 study of TAK-659, an investigational dual SYK and FLT-3 inhibitor, in patients (Pts) with relapsed or refractory acute myelogenous leukemia (AML) (ASH 2016).

63 Karim NA, Bahassi E, Gaber O, Hashemi-Sadraei N, **Morris J**. A phase I study of the non-receptor tyrosine kinase inhibitor (NKI) bosutinib in combination with pemetrexed in patients with advanced solid tumors. IASLC. Abstr. 4408. P2.03a-027.

64 Wood LV, Terabe M, Trepel J, Pastan I, **Morris JC**, Berzofsky JC. Translation of cancer vaccines from mice to human clinical trials. Keystone Symposia, 2017.

65 Toukam DK, Steel JC , Carwell C, Eldessouki I, **Morris JC**. A vaccine derived from cancer stem cells engineered to express interleukin-15 and its receptor enhances T cell proliferation (ASGCT, 2017, Poster 339).

66 Wood LV, Roberson BD, Agarwal PK, Apolo AB, Stroncek D, Weiner LM, **Morris JC**, Terabe M, Lee M-J, Trepel JB, Berzofsky JA. Association of autologous AdHER2 dendritic cell vaccination with antitumor activity and number of circulating tumor cells. J Clin Oncol. 35, 2017 (suppl; abstr 3089).

67 Somaiah N, Chawla SP, Block MS, **Morris JC**, Do KT, Kim JW, Druta M, Sankhala KK, Hwu P, Gnjatic S, Lu H, Kenney RT, Bohac GC, Pollack S. Immune response, safety, and survival impact from CMB305 in NY-ESO-1+ recurrent soft tissue sarcomas (STS). J Clin Oncol. 35, 2017 (suppl; abstr 11006).

68 Pollack S, Lu H, Somaiah N, Chawla SP, **Morris JC**, Do KT, Kim JW, Block MS, Vignali M, Rytlewski J, Yusko E, Hsu FJ Bohac GC, Gnjatic S, Meulen JT. Association of CMB305 or LV305-induced and baseline anti-NY-ESO-1 immunity survival in recurrent cancer patients. J Clin Oncol. 35, 2017 (suppl; abstr 3090).

PUBLICATIONS *CONTINUED*

69 Wood LV, Terabe M, Trepel J, Pastan I, **Morris JC**, Berzofsky JA. Cancer vaccine strategies: Translation from mice to human clinical trials (CITIM, 2017).

70 **Radhakrishnan N, Sacher RA**. Bone Marrow Aspiration and Biopsy. Medscape Drugs & Diseases. Updated April 18, 2017

71 **Radhakrishnan N**. Castleman Disease. Medscape Drugs & Diseases. Updated July 13, 2017.

72 Haque S., Yellu M., Randhawa J., **Hashemi Sadraei, N**. Profile of pembrolizumab in the treatment of head and neck squamous cell carcinoma: design development and place in therapy. Drug Design, Development, and Therapy. 2017: :11 2537–2549

73 **Hashemi Sadraei, N**., Feng, Y., Du, L., Fu, P., Haque, S., Dowlati, A., Gollamudi, J., Pennell, NA., Mekhail, T., Avril, S., Farver, C., Gerson, S., Sharma, N. High UDG and BRCA1 Expression is Associated with Adverse Outcome in Patients with Pemetrexed Treated Non-Small Cell Lung Cancer. Submitted to Lung Cancer . Under revision. 2017 .

74 Koncar RF, Feldman R, Bahassi EM, **Hashemi Sadraei N**. Comparative molecular profiling of HPV-induced squamous cell carcinomas. Cancer Med. 2017 6(7):1673-1685. doi: 10.1002/cam4.1108. Epub 2017 May 29. PMID: 28556593

75 **Hashemi Sadraei N**, Sikora AG, Brizel DM. Integrating immune checkpoint inhibitors and targeted agents with surgery and radiotherapy for patients with head and neck cancer. Am Soc Clin Oncol Educ Book. 2016;36: 277-282

76 Pharmacologic Targeting of S6K1 in PTEN-Deficient Neoplasia.Liu H, Feng X, Ennis KN, Behrmann CA, Sarma P, Jiang TT, Kofuji S, Niu L, Stratton Y, Thomas HE, Yoon SO, **Sasaki AT**, Plas DR. Cell Rep. 2017 Feb 28;18(9):2088-2095. doi: 10.1016/j.celrep.2017.02.022.

77 Targeting cancer metabolism by simultaneously disrupting parallel nutrient access pathways. Kim SM, Roy SG, Chen B, Nguyen TM, McMonigle RJ, McCracken AN, Zhang Y, Kofuji S, Hou J, Selwan E, Finicle BT, Nguyen TT, Ravi A, Ramirez MU, Wiher T, Guenther GG, Kono M, **Sasaki AT**, Weisman LS, Potma EO, Tromberg BJ, Edwards RA, Hanessian S, Edinger AL.J Clin Invest. 2016 Nov 1;126(11):4088-4102.

78 Structural reverse genetics study of the PI5P4Kβ-nucleotide complexes reveals the presence of the GTP bioenergetic system in mammalian cells.Takeuchi K, Senda M, Lo YH, Kofuji S, Ikeda Y, **Sasaki AT**, Senda T.FEBS J. 2016 Oct;283(19):3556-3562. doi: 10.1111/febs.13739. Review.

79 Dynamic Role of the GTP Energy Metabolism in Cancers. **Sasaki AT**. Keio J Med. 2016;65(1):21. doi: 10.2302/kjm.65-001-ABST.

80 The Lipid Kinase PI5P4Kβ Is an Intracellular GTP Sensor for Metabolism and Tumorigenesis.Sumita K, Lo YH, Takeuchi K, Senda M, Kofuji S, Ikeda Y, Terakawa J, Sasaki M, Yoshino H, Majd N, Zheng Y, Kahoud ER, Yokota T, Emerling BM, Asara JM, Ishida T, Locasale JW, Daikoku T, Anastasiou D, Senda T, **Sasaki AT**. Mol Cell. 2016 Jan 21;61(2):187-98. doi: 10.1016/j.molcel.2015.12.011. Epub 2016 Jan 7.

81 Method for Assaying the Lipid Kinase Phosphatidylinositol-5-phosphate 4-kinase α in Quantitative High-Throughput Screening (qHTS) Bioluminescent Format. Davis MI, **Sasaki AT**, Simeonov A.Methods Mol Biol. 2016;1376:1-9. doi: 10.1007/978-1-4939-3170-5_1.

82 Orr-Asman M., Chu, Z., Jiang M., Worley M., LaSance K., Koch S.E., Carreira V., Dahche H., Plas D.R., Komurov K., Qi X., Mercer C.A., Anthony L., Rubinstein J., **Thomas H.E.** mTOR kinase inhibition effectively decreases progression of a subset of neuroendocrine tumors that progress on rapalog therapy and delays cardiac impairment. Mol Cancer Ther, 2017, online ahead of print.

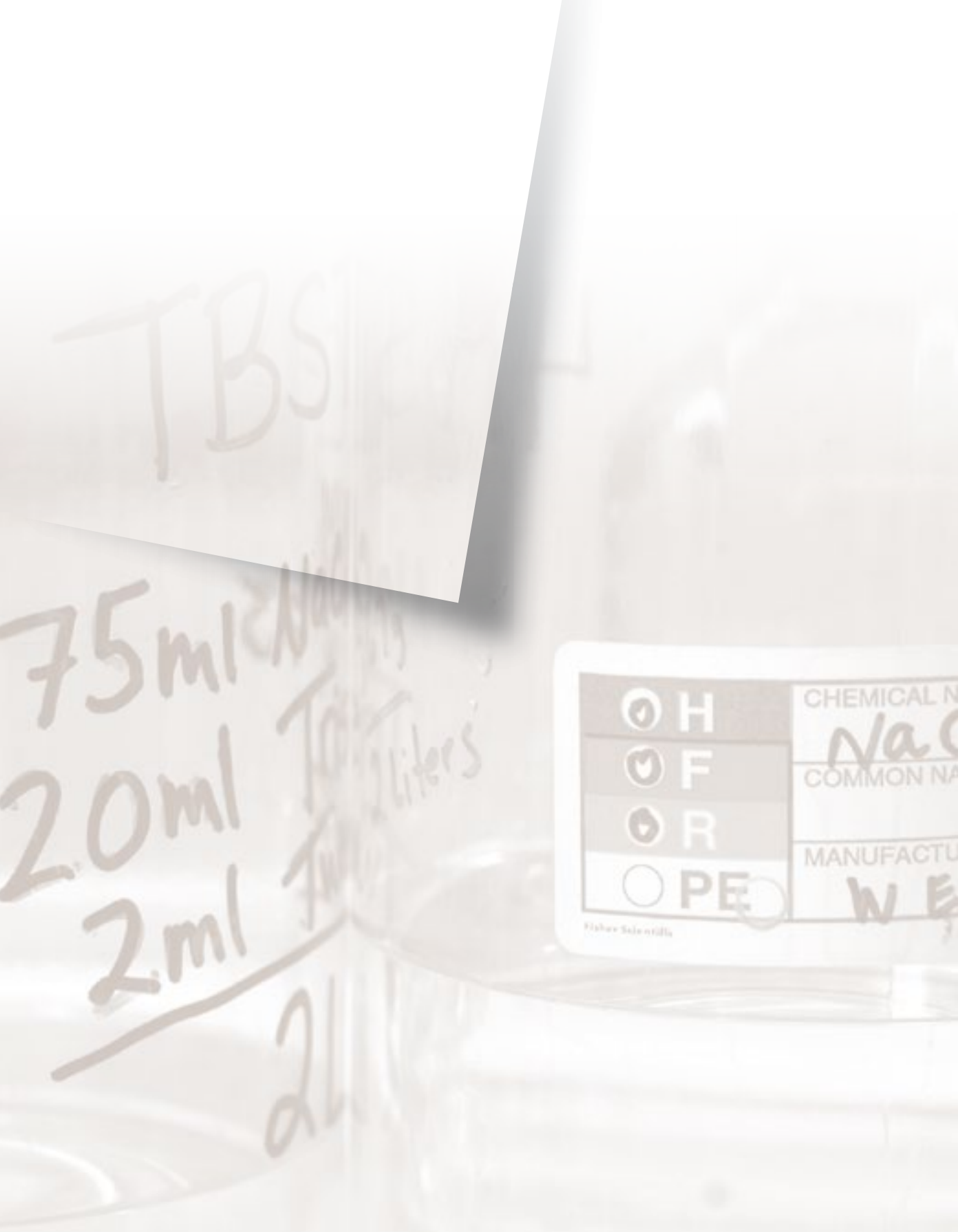
83 Liu H., Feng X., Ennis K., Gallo C., Jiang T., Kofuji S., **Thomas H.E.**, Yoo S., Sasaki A., Plas D. Pharmacologic targeting of S6K1 in PTEN-deficient neoplasia. Cell Reports, (2017), 18, 2088-95.

84 **Wise-Draper T.**, Moorthy G., Salkeni M., Abdel Karim N., Thomas H.E., Mercer C., Beg S, O'Gara S, Olowokure O., Fathallah H. Kozma S., Thomas G., Rixe O., Desai P., Morris J. A Phase Ib study of the dual PI3K/mTOR inhibitor dactolisib (BEZ235) combined with everolimus in patients with advanced solid malignancies. Targeted Oncology, (2017).

85 **Trisha Wise-Draper**, Ganesh Moorthy, Mohamad A. Salkeni, Hala Thomas, Carol A. Mercer, Sara Kozma, George Thomas, Olivier Rixe, Pankaj Desai, John C. Morris. A Dose Escalation Single Arm Phase Ib Combination Study of BEZ235 with Everolimus to Determine the Safety, Pharmacokinetics, and Pharmacodynamics in Patients with Advanced Solid Malignancies. Targeted Oncology. 2017.

86 Ameet Chimote, Peter Hajdu, Alex Syfris, Brittany Gleich, **Trisha Wise-Draper**, Keith Casper and Laura Conforti. Kv1.3 channels as markers of functionally competent CD8+ tumor infiltrating lymphocytes in head and neck cancer. Cancer Research. 2017.

87 Riaz MK, Bal S, **Wise-Draper T**. The impending financial healthcare burden and ethical dilemma of systemic therapy in metastatic cancer. J Surg Oncol. 2016 Sep;114(3):323-8. doi: 10.1002/jso.24333. Epub 2016 Jul 4. Review. PubMed PMID: 27377825.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DIVISION OF

Immunology, Allergy and Rheumatology

Immunology, Allergy and Rheumatology

William M. Ridgway, MD
DIVISION DIRECTOR

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DIVISION DIRECTOR

The **Division of Immunology, Allergy and Rheumatology** undertakes a wide range of research that is fundamentally grounded in immunology and inflammation. Rheumatic diseases often represent abnormal immune responses to self-proteins, while allergic diseases often represent abnormal immune and inflammatory responses to external (environmental) proteins.

The research in the division spans the spectrum of basic immunological research. Research projects include investigations to the pathogenesis of food allergy/hypersensitivity, anaphylaxis, new therapies for asthma and allergic diseases, mechanisms of occupational lung disease, pathogenesis of primary biliary cirrhosis and Type 1 Diabetes (organ specific autoimmunity), pathogenesis of cutaneous systemic lupus erythematosus (SLE), and novel therapies for autoimmune disease. We have a T32 in Allergy/Immunology, a participant in the CSTP program, and two separate ACGME accredited fellowship programs whose goal is to produce academic Allergists and Rheumatologists. Finally, we have hired a new PhD investigator in Immunology, Dr. Wen-hai Shao, who specializes in SLE mouse models and immune cell signaling.

Highlights of this year's research include: 1) Publication of a novel approach to reverse acute Type 1 diabetes by targeting innate immunity, published in the journal *Diabetes* by the Ridgway lab; 2) A review highlighting our work in Human IgE-independent systemic anaphylaxis, published in *Journal of Allergy and Clinical Immunology* by the Finkelman lab; 3) A collaborative study between UC Allergy and CCHMC on defects of B-cell terminal differentiation in patients with type-1 Kabuki syndrome, published in *JACI* by the J. Bernstein lab in collaboration with Dr. Lindsley; 4) A study on genetic variants in TNFα, TGFB1, PTGS1 and PTGS2 genes are associated with diisocyanate-induced asthma, published in the *Journal of Immunotoxicology* by Dr. D. Bernstein's lab. Overall, the division published over 50 articles this year.

In the coming year, a major effort will be the development of the UC Lupus Center. There is now a critical mass of SLE researchers on campus, including basic and clinical research programs. We also have re-established the UC Lupus clinic. Finally, the Evelyn Hess Chair for Lupus Research is now officially established. This year we will organize seminars to encourage cross-disciplinary research in SLE that involves both basic investigators and clinicians; and start the search for the first occupant of the Hess Chair.

Body of Research

Wen-hai Shao's work aims to turn the immune system from foe to friend in lupus patients

AS A BOY GROWING UP in a small Chinese village near the Yangtze River, Wen-hai Shao remembers seeing his neighbors suffering from disease and the impact that left on his young mind. "I always wondered what happened to them, why they got sick and how we could treat the diseases to at least make them feel better," Shao says.

That early interest led Shao to earn his master of science from the Chinese Academy of Sciences. He then went on to the United States as a research scholar in the Brown Cancer Center at the University of Louisville, where he also completed his PhD, in immunology.

"I pursued immunology because of my great interest in understanding what's going on inside the body," Shao says. "I'm particularly interested in lupus and autoimmune diseases, because those are self-attacking diseases. We are still struggling to understand how, what is supposed to be a protective function of our body, turns harmful. It's fascinating to me; we still don't know precisely how the disease develops within the body."

After finishing his doctoral studies, Shao continued studying lupus at the University of Pennsylvania as a research fellow and Temple University as a research scientist. He joined the University of Cincinnati in 2016 as an assistant professor in the Division of Immunology, Allergy and Rheumatology. Shao says the state-of-the-art lab equipment, supportive College of Medicine leadership, and availability of pilot research grants attracted him to UC. "From our division director to the dean, they all know what I'm doing here, and if I ever need anything, they are always happy to help."

Currently, Shao has a five-year K01 grant from the National Institutes of Health to study a particular aspect of lupus called lupus nephritis, in which auto-antibodies attack the kidney and eventually cause kidney failure in patients. Shao is interested in a group of receptor proteins called TAM, which are implicated in lupus nephritis. He is using animal models to determine if turning off one of the three TAM receptors could potentially slow the progression of the disease and improve patient symptoms.

"If we can inhibit one of these receptors, we could help people living with lupus nephritis to feel better," Shao says. "The more we understand, the better the treatments that we can offer." ●

"The more we understand, the better the treatments that we can offer."

WEN-HAI SHAO, PHD

David I. Bernstein, MD

Emeritus Professor of Medicine
Division of Immunology, Allergy and Rheumatology

I lead a multicenter international cooperative genotyping project conducted in collaboration with investigators from Canada and Spain. The laboratory is focused on identification of genetic markers and mechanisms of occupational asthma caused by diisocyanates. DNA samples have been collected from workers recruited in these countries who have a confirmed diagnosis of isocyanate induced occupational asthma. The work involves analyzing results of GWAS studies conducted in this cohort. Next generation sequencing has been performed on informative loci to identify functional variants associated with disease and interactions with transcription factors in human cells are currently being studied. This work is funded through an R01 renewal of grant from NIOSH-CDC.

I am also collaborating as coinvestigator in a study of the respiratory microbiome with Dr. Tiina Reponen, professor of Environmental Health. I am director of The National Surveillance Study of Immunotherapy Safety co-sponsored by the American Academy of Allergy and American College of Allergy. The purpose of this study is to identify and mitigate risk factors for severe allergic reactions following allergen injections.

I am Director and Principal Investigator of the Allergy-Immunology T32 training grant sponsored by the National Institute of Allergy and Infectious Diseases and now in its 13th year. Currently there are four trainees enrolled in this research training program. I have served as mentor and co-mentor for many of these trainees. I also serve as Co-Director of the Allergy Immunology fellowship training program.

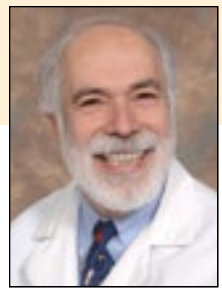
Jonathan A. Bernstein, MD

Adjunct Professor of Clinical Medicine
Division of Immunology, Allergy and Rheumatology

I have two PhD research scientists working with me in my laboratory, Dr. Deb Ghosh and Dr. Umesh Singh. Current projects include: 1) Investigation of CREON2000 Ultraviolet Air Cleaning Units Installed In the Homes of Asthmatic Children, funded by the NIAID; 2) Investigation of vascular endothelial cell biomarkers in skin biopsies obtained from patients with hereditary angioedema during and between angioedema attacks, funded by Shire; 3) Investigation of Benralizumab, an anti-IL5R Mab antagonist in the treatment of Chronic Idiopathic Urticaria, funded by Astra Zeneca. A project investigating prodromal treatment of HAE and predictive biomarkers has been approved by Pharming and will likely start first quarter 2018. We are involved in several other collaborative projects related to chronic rhinitis subtypes, mechanisms of TMA induced occupational asthma, cyanobacteria, drug hypersensitivity, food allergy and seminal plasma hypersensitivity. We are collaborating with Tesfaye Mersha, PhD, Assistant Professor, Division of Asthma Research, CCHMC, to analyze publicly accessible gene expression data to identify disease-associated genes for asthma and atopic dermatitis. This has led to intramural funding by the CEG and CPG. I am also collaborating with Anastasio Angelopoulos, Chairman of Chemical Engineering at UC, on sensor technology related to precise and selective measurement of small molecules.

Fred Finkelman, MD

Walter A. and George McDonald Foundation Professor of Medicine
Division of Immunology, Allergy and Rheumatology
Professor of Pediatrics, Department of Pediatrics



I am Co-chair of the search committee for the head of the food allergy group at Cincinnati Children's. In my research program our chief interests are anaphylaxis and food allergy, allergenicity and antibody-mediated immunopathology. We are using a rapid desensitization approach to rapidly and safely suppress IgE-mediated disease with antibodies to the high affinity IgE receptor, FceRI. We are testing the hypothesis that many allergens promote an allergic response by stimulating an unfolded protein response in epithelial cells, which stimulates production of 3 cytokines, IL-25, IL-33 and TSLP, that, in turn, promote a type 2 cytokine response. We are evaluating the ability of IgG antibody isotypes that are relatively poor in inducing effector mechanisms to suppress disease caused by antibody isotypes that are stronger inducers of these mechanisms. I have NIAID (R01) and FARE (private, non-profit foundation) funding.

Key Findings: Using live mouse models disease modes–(a) Treatment of mice with small doses of anti-FceRI monoclonal antibodies induces mast cell anergy, then removes nearly all IgE from these cells. (b) Several allergens promote the development of an epithelial cell unfolded protein response and stimulate IL-25, IL-33, and TSLP production by these cells. Agents that inhibit an unfolded protein response block expression of these cytokines. Treatment of mice that have food allergy with a combination of monoclonal antibodies to IL-25, IL-33 and TSLP abolishes this disorder.

Marat V. Khodoun, DVM, PhD

Research Assistant Professor
Division of Immunology, Allergy and Rheumatology

My research is centered on the use of molecular engineering and cellular biology methods, both in vitro cell tests and in vivo mouse models, to study the physiology and mechanisms of immunoglobulin receptor signaling in health and disease. My specific area of scientific interest has been the elucidation of the roles of FceRI, FcgRIIb, and FcgRIII receptors in allergy and anaphylaxis. More recently, I have established collaboration with Drs. Brunner, Porollo, and Kaufmann at Cincinnati Children's Hospital Medical Center where I have a laboratory space. I have broadened my focus to include systemic lupus erythematosus (SLE) and advanced lupus nephritis (ALN). I am exploring the application of multi-specific recombinant antibodies with specificity either to human FceR1 receptor or to B cell-specific receptors (CD20) and high affinity to human FcgIIRb for treatment of severe allergic and autoimmune diseases. In collaboration with Drs. Conforti and Mulloy, we have generated a mouse model of ALN using severely immune deficient NSG mice engrafted with peripheral blood mononuclear cells (PBNC) derived from either healthy individuals or patients with ALN. This mouse model demonstrates high titers of human antibodies, significant proliferation of activated T cells and other pathologies that resemble the human disease.

Christopher McKnight, MD

Adjunct Instructor of Clinical Medicine
Division of Immunology, Allergy and Rheumatology

My research is basic and translational in that I use mice to model human allergic asthma. Broadly, I have two pathways of investigation. The first pathway evaluates the significance of factors that generate inflammatory disease in the lower airways using a model that mimics the human condition more closely than the models previously reported in the literature. I have studied effectors of humoral immunity (IgE and its high affinity receptor) and effectors of cellular immunity (CD4+ T cells, CD8+ T cells, invariant NKT cells and innate lymphoid cells). This involves measuring: airway hyperresponsiveness indirectly by plethysmograph and directly by invasive forced oscillation, pulmonary eosinophilia by BAL, goblet cell metaplasia by microscopic exam, cytokine production by ELISA and cellular response by extended-panel flow cytometry involving intracellular cytokine staining.

My second pathway of investigation studies how airway epithelial cells and smooth muscle cells independently and cooperatively produce airway hyperresponsiveness after the allergic response has been established. Critically I show that airway hyperresponsiveness is extinguished when both epithelial and smooth muscle cells cannot bind interleukin-13 or interleukin-4 when potent allergen or cytokine is administered at generous doses. Importantly this work also shows that smooth muscle cell binding of IL-13 and IL-4 is superfluous in generating airway hyperresponsiveness when administering potent allergen but not when administering cytokine alone.

Suzanne C. Morris, PhD

Research Associate Professor
Division of Immunology, Allergy and Rheumatology

Research Support:

- Food Allergy Research and Education Proposal (Co-I, Fred Finkelman, PI, 6/14–9/17
- Food Allergy Research and Education. Rapid suppression of food allergy with anti-FceRIa antibody. This project uses rapid desensitization with anti-FceRIa mAb to suppress established models of food allergy in conventional and humanized mice.
- R01A1130103 (Fred Finkelman, PI), 1/1/17 – 12/31/21, NIH/NIAID, Wimpy antibody isotypes protect against antibody-mediated disease. This project tests the hypothesis that IgG isotypes that are ineffective at inducing inflammation protect against inflammatory disorders.
- 1R01AI113162-01 (Co-I, Fred Finkelman, PI), 7/15/14- 6/30/18, NIH/NIAID, Suppression of IgE-mediated disease by polyclonal rapid desensitization. This project will develop a novel approach to rapidly suppress human IgE-mediated allergy. No overlap.

William M. Ridgeway, MD

Alice W. and Mark A. Brown Professor in Internal Medicine
Division Director
Division of Immunology, Allergy and Rheumatology

My research program addresses the molecular pathogenesis of autoimmunity and the immunogenetic mechanisms of autoimmune disease, with particular attention to Primary biliary cirrhosis (PBC) and Type 1 Diabetes (T1D). The premise of this work is that autoimmune diseases are complex genetic diseases in which multiple genetic alterations of key immune system genes and their function causes autoimmunity. My lab studies two mouse models of PBC (the TGFbdnRII mouse and NOD.c3c4 mouse) and two models of T1D (the non-obese diabetic (NOD) and NOD.B10 Idd9.3 congenic mice). Recently the lab has developed novel immunotherapies for autoimmunity and published an approach whereby selective stimulation of TLR4 reversed new onset T1D (*Diabetes*, 2015).

I have collaborated with Drs. Jonathan Katz, Fred Finkelman, Claire Chougnet, Larry Dolan, Andy Herr, Jorge Bezzera, Michael Jordan, and Bruce Aronow here in Cincinnati.

Current funding includes: two R01 grants ("dnTGF Beta RII Mice and PBC", 2010-2018; and "Mechanistic and therapeutic role of the CD137-CD137L axis in Type 1 Diabetes", 2016-2021), an R21 ("Mechanism of restored immune tolerance in anti-TLR4 antibody reversal of NOD T1D", 2015-2017), and an ADA Foundation grant ("Mechanistic role and therapeutic potential of CD137 in T1D", 2016-2019).

Wen-Hai Shao, PhD

Assistant Professor
Division of Immunology, Allergy and Rheumatology

Currently, I have a five-year K01 grant from the National Institutes of Health to study a particular aspect of lupus called lupus nephritis, in which auto-antibodies attack the kidney and eventually cause kidney failure in patients. I am interested in a group of receptor proteins called TAM, which are implicated in lupus nephritis.

I am using animal models to determine if turning off one of the three TAM receptors could potentially slow the progression of the disease and improve patient symptoms.

Research Support:

K01 DK09506712/01/2016-11/30/2017. National Institute of Diabetes and Digestive and Kidney Disease. A critical role of TAM receptors in autoimmune nephritis, PI, Active.

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Creticos PS, **Bernstein DI**, Casale TB, Lockey RF, Maloney J, Nolte H. Coseasonal Initiation of Allergen Immunotherapy: A Systematic Review. J Allergy Clin Immunol Pract. J Allergy Clin Immunol Pract. 2016 Nov - Dec;4(6):1194-1204 PMID: 27349175

2 Nolte H, **Bernstein DI**, Nelson HS, Kleine-Tebbe J, Sussman GL, Seitzberg D, Rehm D, Kaur A, Li Z, Lu S.Efficacy of House Dust Mite SLIT-Tablet in North American Adolescents and Adults in a Randomized, Placebo-Controlled Trial. J Allergy Clin Immunol. 2016 Dec;138(6):1631-1638. PMID: 27521719

3 Sabbioni G, Vanimireddy LR, Lummus ZL, **Bernstein DI**. Arch Toxicol. 2017 Apr;91(4):1809-1814. Comparison of biological effects with albumin adducts of 4,4'-methylenediphenyl diisocyanate in workers. PMID: 27638504

4 Weiler JM, Brannan JD, Randolph CC, Hallstrand TS, Parsons J, Silvers W, Storms W, Zeiger J, **Bernstein DI**, Blessing-Moore J, Greenhawt M, Khan D, Lang D, Nicklas RA, Oppenheimer J, Portnoy JM, Schuller DE, Tilles SA, Wallace D. Exercise-induced bronchoconstriction update-2016. J Allergy Clin Immunol. 2016 Sep 15. PMID: 27665489

5 **Bernstein DI**, Gillespie M, Song S, Steinfeld J.Safety, efficacy, and dose response of fluticasone propionate delivered via the novel MDPI in patients with severe asthma: A randomized, controlled, dose-ranging study. J Asthma. 2016 Oct 24:1-11. PMID: 27937064

6 Zieglmayer P, Nolte H, Nelson HS, **Bernstein DI**, Kaur A, Jacobi H, Lemell P, Schmutz R, Zieglmayer R, Horak F. Long-term effects of a house dust mite sublingual immunotherapy tablet in an environmental exposure chamber trial. Ann Allergy Asthma Immunol. 2016 Dec;117(6):690-696. PMID: 27979028

7 **Bernstein DI**, Wasserman SI, Thompson WP, Freeman TM. ABAI's MOC Assessment of Knowledge Program Matures: Adding Value with Continuous Learning and Assessment. J Allergy Clin Immunol Pract. 2017 Jan - Feb;5(1):80-83. Review. PMID: 28065344

8 Golden DB, Demain J, Freeman T, Graft D, Tankersley M, Tracy J, Blessing-Moore J, **Bernstein D**, Dinakar C, Greenhawt M, Khan D, Lang D, Nicklas R, Oppenheimer J, Portnoy J, Randolph C, Schuller D, Wallace D. Ann Allergy Asthma Immunol. 2017 Jan;118(1):28-54.Stinging insect hypersensitivity: A practice parameter update 2016. PMID: 28007086

9 Johansson E, Biagini Myers JM, Martin LJ, He H, Pilipenko V, Mersha T, Weirauch M, Salomonis N, Ryan P, LeMasters GK, **Bernstein DI**, Lockey J, Khurana Hershey GK. KIF3A genetic variation is associated with pediatric asthma in the presence of eczema independent of allergic rhinitis. J Allergy Clin Immunol. 2017 Feb 23. PMID: 28238750

10 Epstein TG, Liss GM, Murphy-Berendts K, **Bernstein DI**. Evaluation of the risk of infection associated with subcutaneous allergen immunotherapy: American Academy of Allergy, Asthma, and Immunology and American College of Allergy, Asthma, and Immunology National Surveillance Study on Allergen Immunotherapy, 2014-2015. Ann Allergy Asthma Immunol. 2017 Mar 1. pii: S1081-1206(17)30016-9. PMID: 28259390.

11 Golden DB, **Bernstein DI**, Freeman TM, Tracy JM, Lang DM, Nicklas RA. AAAAI/ACAAI Joint Venom Extract Shortage Task Force Report. J Allergy Clin Immunol Pract. 2017 Mar - Apr;5(2):330-332. PMID: 28283157

12 Greenhawt M, Oppenheimer J, Nelson M, Nelson H, Lockey R, Lieberman P, Nowak-Wegrzyn A, Peters A, Collins C, **Bernstein DI**, Blessing-Moore J, Khan D, Lang D, Nicklas RA, Portnoy JM, Randolph CR, Schuller DE, Spector SL, Tilles SA, Wallace D. Sublingual immunotherapy: A focused allergen immunotherapy practice parameter update. Ann Allergy Asthma Immunol. 2017 Mar;118(3):276-282. PMID: 28284533

13 Brunton S, Nelson HS, **Bernstein DI**, Lawton S, Lu S, Nolte H. Sublingual immunotherapy tablets as a disease-modifying add-on treatment option to pharmacotherapy for allergic rhinitis and asthma. Postgrad Med. 2017 Mar 27:1-9. PMID: 28326908.

14 **Bernstein DI**, Bardelas JA Jr, Svanholm Fogh B, Kaur A, Li Z, Nolte H.A practical guide to the sublingual immunotherapy tablet adverse event profile: implications for clinical practice. Postgrad Med. 2017 Mar 22:1-8. PMID: 28326906.

15 Nelson HS, Calderon MA, **Bernstein DI**, Casale TB, Durham SR, Andersen JS, Esch R, Cox LS, Nolte H. Allergen Immunotherapy Clinical Trial Outcomes and Design: Working Toward Harmonization of Methods and Principles. Curr Allergy Asthma Rep. 2017 Mar;17(3):18. Review. PMID: 28293909.

16 Kannan JA, Brokamp C, **Bernstein DI**, LeMasters GK, Hershey GKK, Villareal MS, Lockey JE, Ryan PH.Parental Snoring and Environmental Pollutants, but Not Aeroallergen Sensitization, Are Associated with Childhood Snoring in a Birth Cohort. Pediatr Allergy Immunol Pulmonol. 2017 Mar 1;30(1):31-38PMID: 28465864

17 Ferguson GT, FitzGerald JM, Bleecker ER, Laviolette M, **Bernstein D**, LaForce C, Mansfield L, Barker P, Wu Y, Jison M, Goldman M; BISE Study Investigators. Benralizumab for patients with mild to moderate, persistent asthma (BISE): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Respir Med. 2017 May 22. 2213-2600(17) PMID: 28545978

18 Matsuoka T, **Bernstein DI**, Masuyama K, Nolte H, Okamiya K, Seitzberg D, Nelson HS. Pooled efficacy and safety data for house dust mite sublingual immunotherapy tablets in adolescents. Pediatr Allergy Immunol. 2017 Jun 29. doi: 10.1111/pai.12747. PMID: 28660739

PUBLICATIONS *CONTINUED*

19 Gupta J, Johansson E, **Bernstein JA**, Chakraborty R, Khurana Hershey GK, Rothenberg ME, Mersha TB. Resolving the etiology of atopic disorders by using genetic analysis of racial ancestry. . 2016 Jun 10. pii: S0091-6749(16)30256-1. doi: 10.1016/j.jaci.2016.02.045. [Epub ahead of print]

20 Riedl MA, Bygum A, Lumry W, Magerl M, **Bernstein JA**, Busse P, Craig T, Frank MM, Edelman J, Williams-Herman D, Feuersenger H, Rojavin M; Berinert Registry investigators. Safety and Usage of C1-Inhibitor in Hereditary Angioedema: Berinert Registry Data. . 2016 Jun 8. pii: S2213-2198(16)30128-3. doi: 10.1016/j.jaip.2016.04.018. [Epub ahead of print]

21 McLeish, A. C., Farris, S. G., Johnson, A. L., **Bernstein, J. A.**, & Zvolensky, M. J. (in press). Evaluation of Smokers with and without asthma in terms of smoking cessation outcome, nicotine withdrawal symptoms, and craving: Findings from a self-guided quit attempt. Addictive Behaviors. 2016 Dec;63:149-54.

22 Fine LM, **Bernstein JA**. Guideline of Chronic Urticaria Beyond. . 2016 Sep;8(5):396-403.

23 Beck LA, **Bernstein JA**, Maurer M. A Review of International Recommendations for the Diagnosis and Management of Chronic Urticaria.. 2016 Jun 28. doi: 10.2340/00015555-2496. [Epub ahead of print]

24 Mendelson MH, **Bernstein JA**, Gabriel S, Balp MM, Tian H, Vietri J, Lebwohl M.Patient-reported impact of chronic urticaria compared with psoriasis in the United States. . 2016 Aug 31:1-24. [Epub ahead of print]

25 Li RC, Singh U, Windom HP, Gorman S, **Bernstein JA**. Clinical associations in the diagnosis of vocal cord dysfunction. . 2016 Aug 30. pii: S1081-1206(16)30522-1. doi: 10.1016/j.anai.2016.08.002. [Epub ahead of print]

26 Banerji A, Bas M, **Bernstein JA**, Boccon-Gibod I, Bova M, Dempster J, Grumach AS, Magerl M, Poarch K, Ferreira MB. Expert perspectives on hereditary angioedema: Key areas for advancements in care across the patient journey.. 2016 Sep 22. [Epub ahead of print].

27 Greiwe J,**Bernstein JA**. Therapy of antihistamine-resistant chronic spontaneous urticaria. . 2016 Nov 3:1-8.

28 Hamelmann E, **Bernstein JA**, Vandewalker M, Moroni-Zentgraf P, Verri D, Unseld A, Engel M, Boner AL. A randomised controlled trial of tiotropium in adolescents with severe symptomatic asthma. . 2016 Nov 3. pii: ERJ-01100-2016. doi: 10.1183/13993003.01100-2016.

29 Maurer M, Sofen H, Ortiz B, Kianifard F, Gabriel S, **Bernstein JA**. Positive impact of omalizumab on angioedema and quality of life in patients with refractory chronic idiopathic/spontaneous urticaria: analyses according to the presence or absence of angioedema. 2016 Dec 2. doi: 10.1111/jdv.14075. [

30 Riedl MA, Lumry WR, Li HH, Banerji A, **Bernstein JA**, Ba M, Bjrkander J, Magerl M, Maurer M, Rockich K, Chen H, Schranz J. Subcutaneous administration of human C1 inhibitor with recombinant human hyaluronidase in patients with hereditary angioedema. . 2016 Nov;37(6):489-500.

31 Frank MM, Zuraw B, Banerji A, **Bernstein JA**, Craig T, Busse P, Christiansen S, Davis-Lorton M, Li HH, Lumry WR, Riedl M; US Hereditary Angioedema Association Medical Advisory Board.. Management of Children With Hereditary Angioedema Due to C1 Inhibitor Deficiency. . 2016 Nov;138(5). pii: e20160575.

32 Banerji A, Busse P, Shennak M, Lumry W, Davis-Lorton M, Wedner HJ, Jacobs J, Baker J, **Bernstein JA**, Lockey R, Li HH, Craig T, Cicardi M, Riedl M, Al-Ghazawi A, Soo C, Iarrobino R, Sexton DJ, TenHoor C, Kenniston JA, Faucette R, Still JG, Kushner H, Mensah R, Stevens C, Biedenkapp JC, Chyung Y, Adelman B. Inhibiting Plasma Kallikrein for Hereditary Angioedema Prophylaxis. . 2017 Feb 23;376(8):717-728.

33 Greiwe JC, **Bernstein JA**. Combination therapy in allergic rhinitis: What works and what does not work. . 2016 Nov 1;30(6):391-396.

34 James C, **Bernstein JA**. Current and future therapies for the treatment of histamine-induced angioedema. Expert Opin Pharmacother. 2017 Feb;18(3):253-262. doi: 10.1080/14656566.2017.1282461. Epub 2017 Jan 25. Review. PubMed PMID: 28081650; PubMed Central PMCID: PMC5515622.

35 **Bernstein JA**, Relan A, Harper JR, Riedl M. Sustained response of recombinant human C1 esterase inhibitor for acute treatment of hereditary angioedema attacks. Ann Allergy Asthma Immunol. 2017 Mar 8. pii: S1081-1206(17)30100-X. doi: 10.1016/j.anai.2017.01.029. [Epub ahead of print]

36 Busse P, Baker J, Martinez-Saguer I, **Bernstein JA,** Craig T, Magerl M, Riedl M, Shapiro R, Frank M, Lumry W, Rosch J, Edelman J, Williams-Herman D, Feuersenger H, Rojavin M; Berinert Registry Investigators. Safety of C1-inhibitor concentrate use for hereditary angioedema in pediatric patients. . 2017 Mar 9. pii: S2213-2198(17)30023-5. doi: 10.1016/j.jaip.2016.12.033. [Epub ahead of print]

37 Longhurst H, Cicardi M, Craig T, Bork K, Grattan C, Baker J, Li HH, Reshef A, Bonner J, **Bernstein JA**, Anderson J, Lumry WR, Farkas H, Katelaris CH, Sussman GL, Jacobs J, Riedl M, Manning ME, Hebert J, Keith PK, Kivity S, Neri S, Levy DS, Baeza ML, Nathan R, Schwartz LB, Caballero T, Yang W, Crisan I, Hernandez MD, Hussain I, Tarzi M, Ritchie B, Králícková P, Guilarte M, Rehman SM, Banerji A, Gower RG, Bensen-Kennedy D, Edelman J, Feuersenger H, Lawo JP, Machnig T, Pawaskar D, Pragst I, Zuraw BL; COMPACT Investigators. Prevention of Hereditary Angioedema Attacks with a Subcutaneous C1 Inhibitor. . 2017 Mar 23;376(12):1131-1140. doi: 10.1056/NEJMoa1613627

PUBLICATIONS *CONTINUED*

38 Craig T, Shapiro R, Vegh A, Baker JW, **Bernstein JA**, Busse P, Magerl M, Martinez-Saguer I, Riedl MA, Lumry W, Williams-Herman D, Edelman J, Feuersenger H, Machnig T, Rojavin M. Efficacy and safety of an intravenous C1-inhibitor concentrate for long-term prophylaxis in hereditary angioedema. . 2017 Mar 1;8(1):13-19.

39 **Bernstein JA**, Cremonesi P, Hoffmann TK, Hollingsworth J. Angioedema in the emergency department: a practical guide to differential diagnosis and management. Int J Emerg Med. 2017 Dec;10(1):15. doi: 10.1186/s12245-017-0141-z. Epub 2017 Apr 13.

40 Buchheit KM, **Bernstein JA**. Progestogen Hypersensitivity: Heterogeneous Manifestations with a Common Trigger. J Allergy Clin Immunol Pract. 2017 May - Jun;5(3):566-574. doi: 10.1016/j.jaip.2017.01.019.

41 Bonner N, Panter C, Kimura A, Sinert R, Moellman J, **Bernstein JA**. Development and validation of the angiotensin-converting enzyme inhibitor (ACEI) induced angioedema investigator rating scale and proposed discharge criteria. BMC Health Serv Res. 2017 May 22;17(1):366. doi: 10.1186/s12913-017-2274-4.

42 Sinert R, Levy P, **Bernstein JA**, Body R, Sivilotti MLA, Moellman J, Schranz J, Baptista J, Kimura A, Nothaft W; CAMEO study group. Randomized Trial of Icatibant for Angiotensin-Converting Enzyme Inhibitor-Induced Upper Airway Angioedema. . 2017 May 25. pii: S2213-2198(17)30172-1. doi: 10.1016/j.jaip.2017.03.003. [Epub ahead of print]

43 Farkas H, Reshef A, Aberer W, Caballero T, McCarthy L, Hao J, Nothaft W, Schranz J, **Bernstein JA**, Li HH. Treatment Effect and Safety of Icatibant in Pediatric Patients with Hereditary Angioedema. . 2017 Jun 7. pii: S2213-2198(17)30253-2. doi: 10.1016/j.jaip.2017.04.010. [Epub ahead of print]

44 Geh EN, de la Cruz AA, Ghosh D, Stelma G, **Bernstein JA**. Sensitization of a child to Cyanobacteria after recreational swimming in a lake. J Allergy Clin Immunol. 2016 June; 137(6):1902-1904. PubMed PMID: 27040373.

45 Ghosh D, Clay CD and **Bernstein JA**. The Utility of Monitoring TMA-Specific IgG to Predict IgE-meidated Sensitization in an Immunosurveillance program. Allergy. Minor revision pending.

46 Ghosh D and **Bernstein JA**. Mapping of conformational IgE epitopes on prostate specific antigen. J Allergy Clin Immunol. 2017, Volume 139, number 2 (conference abstract).

47 Strait, R. T., Thornton, S., **Finkelman, F. D.** 2016. Cg1 deficiency exacerbates collagen-induced arthritis. Arthritis Rheumatol. 68:1780-7.

48 Galand, C., Leyva-Castillo, J. M., Yoon, J., Han, A., Lee, M. S., McKenzie, A., Stassen, M., Oyoshi, M. K., **Finkelman, F. D.**, Geha, R. F. 2016. IL-33 promotes food anaphylaxis in epicutaneously-sensitized mice by targeting mast cells. J Allergy Clin Immunol. 138:1356-1366

49 Tripathi, P*., **Morris, S. C.***, Perkins, C., Sholl, A., **Finkelman, F. D.**†, Hildeman, D. A.† 2016. IL-4 and IL-15 promotion of virtual memory CD8+ T cells is determined by genetic background. Eur J Immunol. 46:2333-9.

50 Minar, P., Jackson, K., Tsai, Y. T., Rosen, M. J., Northcutt, M., **Khodoun, M.**, **Finkelman, F. D.**, Denson, L. A. 2016. A low neutrophil CD64 index is associated with sustained remission during infliximab maintenance therapy. Inflamm Bowel Dis. 22:2641-7.

51 Via, C. S., Soloviova, K., Puliaiev, M/, Puliav, R., Puliaeva, I., **Morris, S. C.**, **Finkelman, F. D.** 2017. In vivo IL-4 prevents allo-antigen driven CD8+ CTL development. Clin. Immunol. 180:11-24.

52 **Khodoun, M. V.**, Tomar, S. Tocker, J. E., Wang, Y.-H., **Finkelman, F. D.** 2017. Prevention of food allergy development and suppression of established food allergy by neutralization of TSLP, IL-25 and IL-33. J. Allergy Clin. Immunol.2017 May 26. pii: S0091-6749(17)30842-4. doi: 10.1016/j.jaci. 2017.02.046. (Epub ahead of print). PMID:28552763.

53 Clay, C. D., Strait, R. T., Mahler, A., **Khodoun, M.**, **Finkelman, F. D.** 2017. Anti-FcgRIIB monoclonal antibody suppresses murine IgG-dependent anaphylaxis by Fc domain targeting of FcgRIII. J. Allergy Clin. Immunol. In press.

54 Epp, A.*, Hobusch, J.*, Bartsch, Y. C., Petry, J., Lilienthal, G.-M., Koeleman, C. A. M., Eschweiler, S., Möbs, C., Hall, A., Morris, S. C., Petzold, D., Engellenner, C., Bitterling, J., Rahmöller, J., Leliavski, A., Thurmann, R., Collin, M., Moremen, K. W., Strait, R. T., Blanchard, V., Petersen, A., Gemoll, T., Habermann, J. K., Petersen, F., Nandy, A., Kahlert, H., Hertl, M., Wuhrer, M., Pfützner, W., Jappe, U., **Finkelman, F. D.**†, Ehlers, M.† 2017. Sialylation of IgG antibodies inhibits IgG-mediated allergic reactions. J. Allergy Clin. Immunol. In press.

55 McKnight, C. G., Jude, J. A., Zhu, Z., Panettieri, R. A. Jr., **Finkelman. F. D.** 2017. House dust mite-induced allergic airway disease is independent of IgE and FceRIa. Am. J. Respir. Cell. Mol. Biol. In press.

56 **Finkelman, F. D.** 2017. Pillars of Immunology: Identification of IgE as the allergy-associated immunoglobulin (Ig) isotype. J. Immunol. 198:3-4.

57 **Finkelman FD, Khodoun MV**, Strait R. Human IgE-independent anaphylaxis. Allergy Clin Immunol. 2016, 137:1674-80.

58 Brunner HI, Bennett MR, **Gulati G**, Abulaban K, Klein-Gitelman MS, Ardoin SP, Tucker LB, Rouster-Stevens KA, Witte D, Ying J, Devarajan P. Urine Biomarkers to Predict Response to Lupus Nephritis Therapy in Children and Young Adults. J Rheumatol. 2017 Jun 15.

59 **Gulati G,** Iffland PH 2nd, Janigro D, Zhang B, Luggen ME. Anti-NR2 antibodies, blood-brain barrier, and cognitive dysfunction. Clin Rheumatol. 2016 Dec;35(12):2989-2997.

PUBLICATIONS *CONTINUED*

60 **Gulati G,** Jones JT, Lee G, Altaye M, Beebe DW, Meyers-Eaton J, Wiley K, Brunner HI, DiFrancesco MW. Altered Blood-Brain Barrier Permeability in Patients With Systemic Lupus Erythematosus: A Novel Imaging Approach. Arthritis Care Res (Hoboken). 2017 Feb;69(2):299-305.

61 **Gulati G**, Bennett M, Abulaban K, Ma Q, Klein-Gitelman MS, Rouster-Stevens KA, Haffner C, Wiley K, Ardoin SP, Ying J, Devarajan P, Brunner HI. Renal Activity in Lupus (RAIL) Urinary Biomarkers Predict Treatment Response [abstract]. Arthritis Rheumatol. 2016; 68 (suppl 10).

62 **Gulati G**, Bennett M, Abulaban K, Song H, Zhang X, Ma Q, Brodsky SV, Nadasdy T, Haffner C, Wiley K, Ardoin SP, Devarajan P, Ying J, Rovin BH, Brunner HI. Prospective Validation Of A Novel Renal Activity Index Of Lupus Nephritis. Lupus, October 2016.

63 Brunner H, **Gulati G**, Jones JT, Altaye M, Eaton JM, Wiley K, Di Francesco M. Evidence of altered blood brain barrier permeability in systemic lupus erythematosus using magnetic resonance imaging. Clin Exp Rheumatol. 2016 Jul 1 (Vol. 34, No. 4, pp. S28-S28).

64 ang GX, Sun Y, Tsuneyama K, Zhang W, Leung PS, He XS, Ansari AA, Bowlus C, **Ridgway WM**, Gershwin ME. Endogenous interleukin-22 protects against inflammatory bowel disease but not autoimmune cholangitis in dominant negative form of transforming growth factor beta receptor type II mice. Clin Exp Immunol. 2016 Aug;185(2):154-64. doi: 10.1111/cei.12806. Epub 2016 Jun 6. (2016)

65 Hong-Di Ma, Wen-Tao Ma, Qing-Zhi Liu, Zhi-Bin Zhao, Mu-Zi-Ying Liu, Koichi Tsuneyama, Jin-Ming Gao, **William M. Ridgway**, Aftab A. Ansari M. Eric Gershwin, Yun-Yun Fei, Zhe-Xiong Lian. Chemokine Receptor CXCR3 Deficiency Exacerbates Murine Autoimmune Cholangitis by Promoting Pathogenic CD8+ T Cell Activation. Journal of Autoimmunity. 2017 Jan 24. [Epub ahead of print] (2017)

66 Matthew H. Forsberg, Ashley E. Ciecko, Kyle J. Bednar, Arata Itoh, Kritika Kachapati, **William M. Ridgway**, and Yi-Guang Chen, CD137 plays both pathogenic and protective roles in type 1 diabetes development in NOD mice, J Immunol. 2017 Mar 31. [Epub ahead of print], Journal of Immunology, (2017).

67 Targeting innate immunity to down-modulate adaptive immunity and reverse type 1 diabetes.Arata Ito and **William M Ridgway**. ImmunoTargets and Therapy Immunotargets Ther. 2017 May 19;6:31-35

68 Itoh A, Irie J, Tagawa H, Kusumoto Y, Kato M, Kobayashi N, Tanaka K, Kikuchi R, Fujita M, Nakajima Y, Wu Y, Yamada S, Kawai T, **Ridgway WM**, Itoh H. GLP-1 receptor agonist, liraglutide, ameliorates hepatosteatosis induced by anti-CD3 antibody in female mice. J Diabetes Complications. 2017 Jun 1. [Epub ahead of print]

69 **Shao, Wen-Hai**; Shu, Daniel H; Zhen, Yuxuan; Hilliard, Brendan; Priest, Stephen O; Cesaroni, Matteo; Ting, Jenny P-Y; Cohen, Philip L 20160101 Prion-like MAVS aggregation in lupus patients associates with increased interferon-I., Journal: Arthritis & rheumatology (Hoboken, N.J.) Vol(Issue): () -

70 Zhen, Yuxuan; Priest, Stephen O; **Shao, Wen-Hai** 20160101 Opposing Roles of Tyrosine Kinase Receptors Mer and Axl Determine Clinical Outcomes in Experimental Immune-Mediated Nephritis., Journal: Journal of immunology (Baltimore, Md. : 1950) Vol(Issue): () -

71 **Shao, Wen-Hai.** The role of microparticles in rheumatic diseases and their potentials as therapeutic tools. J Mol Immunol 2016, 1: 1000101

DIVISION OF

Infectious Diseases

Infectious Diseases

George Smulian, MD
DIVISION DIRECTOR

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DIVISION DIRECTOR

The **Division of Infectious Diseases** has a long standing reputation as a research focused division where the vast majority of the Division's faculty members have active roles in clinical, translational, and basic science research. The focus of the division's basic science research remains the fungal pathogens Histoplasma capsulatum and Pneumocystis spp. with additional work on host cellular response to Clostridium difficile. The clinical and translation research focus continues on HIV with expansion into diarrheal and respiratory pathogens.

The program has an international reputation as a mycology powerhouse based on the research programs of Dr. George Deepe in Histoplasma capsulatum and Dr. Melanie Cushion in Pneumocystis species. Dr. Kavitha Subramanian Vignesh has been recruited to expand the Histoplasma research activities. Close collaborations allow access to UC-based fungal research on Aspergillus and Candida and international programs in Paracocciodiodes and Cryptococcus. Young investigators such as Drs. Rajat Madan and Senu Apewokin have expanded the basic and translation focus examining the pivotal interface between host cellular, metabolism and Clostridium difficile in mouse models and in immunocompromised humans. The role of the host inflammatory response elicited by microbes in the pathogenesis of cardiovascular disease is a new area of exploration. The program of Dr. Carl Fichtenbaum focuses on HIV and cardiovascular disease, while the international program of Dr. Moises Huaman explores increased cardiovascular risk in tuberculosis infection. The clinical research program under Dr. Carl Fichtenbaum continues to conduct studies on persons with HIV infection; prevention of HIV infection; hepatitis C; influenza and appropriate antibiotic usage.

The divisional research program is committed to providing a structured mentoring environment to allow junior faculty and fellows to develop as independent investigators while sustaining the programs of the established investigators. In addition to the traditional clinical and translational research, the division has considerable expertise in hospital epidemiology, infection control, and antibiotic stewardship through its role in UC Health programs and the close collaboration with the VA National Infectious Disease Program office based here in Cincinnati.

Committed to a Cure

Sharon Kohrs has devoted her life to finding answers that fight HIV

AS SHARON KOHRS was finishing nursing school, she made a decision that was particularly brave in the late 1980s: to work as a registered nurse on the inpatient AIDS unit at UC Health Holmes Hospital.

"There was so much fear around HIV and AIDS back then," says Kohrs, who also had three young children at the time. "When I began working on the inpatient AIDS unit in 1991, almost everyone I took care of died. I prayed for the courage and strength to take care of each person to the best of my ability, right down to holding them or their loved ones as they died. I couldn't change what was happening, but I could give comfort and make sure they felt loved."

While Kohrs says she loved working directly with patients, that early experience propelled her toward HIV research. "I wanted to be part of the work to find better treatments, and hopefully one day, a cure."

After a year of working on the inpatient unit, Kohrs was asked by the director of infectious disease research to serve as a full-time research RN at UC's College of Medicine; she never left. Today, she is the clinical research director for Infectious Diseases Research. At any given time, Kohrs oversees between 35-45 clinical trials focused on HIV and other infectious diseases. She is currently particularly excited about a study into a new drug—offered both as an oral medication and a long-acting injectable—that could actually prevent HIV infection. The study is geared toward populations currently most at risk for acquiring HIV infection—in this case, those under 30, African American men who have sex with men and the transgender women's community. Currently, Cincinnati ranks fourth in this study's enrollment in the United States.

"The latter is the hardest population for us to reach," Kohrs says. "You have to first build trust. People have to know that you really are there for them, that this is about them, about bettering their lives."

For Kohrs, working to prevent—and in other studies, possibly cure—a disease that was so misunderstood and feared just a few decades ago is both her reward and motivation. She is also heading an upcoming trial with the CURE Network and has served on the global AIDS Clinical Trials Group Site Management and Clinical Care Committee since 1992.

"Being involved in cutting-edge research is really, really exciting. I come in early and leave late because I truly love what I do."

"Being involved in cutting-edge research is really, really exciting," says Kohrs. "I come in early and leave late because I truly love what I do. I'd love to see a cure for HIV in my lifetime. Our team jokes about working ourselves out of jobs; that would be more than OK." •

"Our team jokes about working ourselves out of jobs; that would be more than OK."

SHARON KOHRS

Senu Apewokin, MD

Assistant Professor of Clinical Medicine
Division of Infectious Diseases

I am the Director of the Transplant Infectious Disease Program. I have been involved in investigator-initiated and industry-sponsored studies with a focus on improving outcomes of infectious complications associated with immunosuppressive events. My recent efforts employ innovative tools such as omics and organoids to understand infections and other complications associated with chemotherapy treatment. Other efforts include evaluating outcomes of solid organ transplantation in HIV positive recipients.

Collaborators at UC include Allison Weiss, Rajat Madan, Madison Cuffy, Shimul Shah and Steve Medlin. At CCHMC collaborators are Tesfaye Mersha and David Haslam. Other collaborator is Ciaran Kelly at Harvard Medical School

Melanie T. Cushion, PhD

Senior Associate Dean for Research
University of Cincinnati College of Medicine
Research Career Scientist, VAMC
Professor, Division of Infectious Diseases

Fungi in the genus Pneumocystis cause an oftentimes lethal pneumonia (PCP) in humans and other mammals with compromised immune status. The niche of these fungi includes patients with underlying chronic diseases such as COPD or HIV and those receiving anti-inflammatory or immunosuppressive agents. PCP is not responsive to standard antifungal therapy with few treatment alternatives besides trimethoprim-sulfamethoxazole. My laboratory focuses on pre-clinical drug development that includes discovery of potential new targets by understanding the metabolism of these obligate fungi; in silico or in vitro screening of inhibitors to identify potential new drugs; evaluation of toxicity in vitro, and eventually evaluation in rodent animal models of this fungal pneumonia. Approaches used for discovery include RNA_seq, comparative genomics, and validation by qRT-PCR; high-throughput screening using yeast expression as well as new approaches such as alveolar organoids to grow these un-culturable fungi outside the lung.

My colleagues, Drs. Alexey Porollo and Mike Linke, and my lab, discovered that Pneumocystis were myo-inositol auxotrophs, meaning that these fungi cannot synthesize myo-inositol, an essential nutrient necessary for viability. We biochemically characterized the kinetics of transport and are working on a high throughput yeast system to identify potential therapies.

We also are focusing on new approaches for the ex vivo culture of Pneumocystis species and are determining what genes are necessarily up-regulated during optimal growth conditions (RNA-seq).

George Deepe, MD

Professor of Medicine
Division of Infectious Diseases

Our laboratory investigates the mechanisms by which the immune system regulates immunity to the dimorphic fungal pathogen, Histoplasma capsulatum. Infection is acquired by inhalation of airborne spores present in the soil. Upon entry into the mammalian lung, these fungal elements convert to the yeast phase that is the cause of the disease, histoplasmosis. The goals are to define the network of genes, cells, and soluble mediators that cooperate to enhance fungal elimination. We seek to identify the immune defects that permit the fungus to escape and cause severe disease. We use a number of tools including flow cytometry, imaging flow cytometry, confocal microscopy, cytokine and chemokine analysis, animal models, and inductively coupled mass spectroscopy, proteomics, and bioinformatics to achieve our goals.

Specific projects that are underway include: 1) analysis of transcription factors in macrophages and dendritic cells that regulate immunity to the fungus; 2) analysis of the role of regulatory T cells in impairing immunity; 3) utility of Histoplasma antigens as vaccine candidates, and 4) the role of zinc as a regulator of macrophage and dendritic cell function.

We are funded by a VA Merit Review, and 2 NIH R01s.

I am one of the Associate Directors of the Medical Scientist Training Program at the College of Medicine.

Carl J. Fichtenbaum, MD

Professor of Clinical Medicine
Division of Infectious Diseases
Associate Chair for Translational Research

My research interests revolve around the treatment and prevention of HIV and its associated complications. Over the past 15 years, I have focused my research on cardiovascular disease, dyslipidemia and end-organ disease in HIV infection. HIV infection elevates the cardiovascular risk two fold with events occurring at an early age. Bone disease, liver disease, kidney disease, diabetes, cancer and bacterial infections all occur at higher rates in HIV infection. The link appears to be chronic inflammation. I have been involved in the design and conduct of multi-center studies for the past two decades. For example, I am vice-chair of the REPRIEVE trial, a 6500 person trial of pitavastatin vs. placebo for prevention of cardiovascular disease and inflammatory conditions in persons with HIV infection. I am the Principal Investigator of the Clinical Trials Unit in the Division of Infectious Diseases. We have a research unit consisting of 19 staff members and 6 research clinical investigators. Funding includes multiple NIH grants and industry-supported research. In our research unit, we conduct studies on persons with HIV infection; to prevent HIV infection; hepatitis C; and influenza. We currently have 39 ongoing open clinical studies and follow ~250 participants on studies enrolling 100-150 each year on trials. We have a population of 2200 persons with HIV infection at UCMC that facilitates our research program. One of my true loves is mentoring others to succeed in research and life. Over the past 18 years at UC, I have provided mentorship to several undergraduate students, 15 medical students, 11 residents, 12 fellows, and 5 junior faculty in the Department of Medicine to assist them in conducting research.

Lisa Haglund, MD

Associate Professor of Clinical Medicine
Division of Infectious Diseases

I am the Medical Director of the Hamilton County Tuberculosis Control Clinic. My interests include treatment of HIV and of M. tuberculosis, non-tuberluous mybobacteria, and Nocardia.

I enjoy going to the local parks, hiking trails and especially bike trails in the Cincinnati area.

Moises A. Huaman, MD, MSc

Assistant Professor of Clinical Medicine
Division of Infectious Diseases

My research focus has been on tuberculosis. I am currently studying the interplay between tuberculosis and cardiovascular disease. Our data shows that persons with latent tuberculosis infection and persons with a history of active tuberculosis have increased rates of acute myocardial infarction, independent of traditional cardiovascular disease risk factors. We are now planning studies to assess subclinical atherosclerosis and immune activation in these populations.

Locally, I serve as sub-investigator for the Clinical Trials Unit in the Division of Infectious Diseases, and I am member of HIV and tuberculosis research committees. My inpatient clinical time is devoted to transplant and immunocompromised patients; therefore, I have been involved in transplant infectious diseases research as well. Internationally, I serve as adjunct investigator at Centro de Investigaciones Tecnológicas, Biomédicas y Medioambientales (CITBM) in Peru, where we are conducting a project on host-pathogen interactions in multidrug-resistant tuberculosis.

Pamposh Darbari Kaul, MD

Professor of Clinical Medicine
Division of Infectious Diseases

I am the Clinical Director of the Midwest AIDS Education and Training Center and PI of a HRSA/HIV AIDS Bureau Ryan White AIDS Education and Training Center Grant. The primary goal of the Ryan White AIDS Education and Training Grant is to enhance the capacity of HIV clinical services and to improve the quality of those services for people living with HIV.

Two projects funded by this Ryan White grant focus on expanding the number of clinicians able to provide clinical care to HIV + patients, the Clinician Scholars Program and the HIV Practice Transformation Project. The yearlong Clinician Scholars Program is designed for front-line clinicians who are interested in enhancing their skills for providing HIV care. The aim of the program is to increase the number of clinicians in Ohio providing HIV care to underserved or disproportionately affected populations. The HIV Practice Transformation Project assists clinics as they begin to provide care to their HIV+ patients and also helps them with the certification process for becoming a patient-centered medical home.

The HIV Interprofessional Education Project improves outcomes along the HIV care continuum by providing hands on learning in HIV care and treatment for UC students in medicine, nursing and pharmacy. The goal is to expand and strengthen the HIV clinical workforce.

Stephen Kralovic, MD, MPH

Professor of Clinical Medicine
Division of Infectious Diseases

My interest in infectious diseases epidemiology and quality in medical care has helped me to develop a broad interest in healthcare epidemiology in large populations, with a focus on infection prevention and control. While not "classical" research in the sense of NIH-funded or industry-sponsored research projects, there is a wealth of data and information in administrative systems that, with careful understanding of the strengths and weaknesses of the data, can be evaluated to determine success or failure for interventional programs over time, particularly infection prevention and control.

I have applied this interest to evaluating and analyzing infection prevention and control programs both locally and nationally within the Veterans Health Administration (VHA) healthcare system with respect to healthcare-associated infections. The national sustained reduction in healthcare-associated methicillin-resistant Staphylococcus aureus (MRSA) infections 10+ years into the Prevention Initiative is one such area of focus, as well as expansion into a Clostridium difficile (C diff) Prevention and Carabpenem-Resistant Enterobacteriaceae Initiatives, implementation of healthcare-associated Legionella Prevention, and VHA Antimicrobial Stewardship Programs.

Keith Luckett, MD

Assistant Professor of Clinical Medicine
Division of Infectious Diseases

My research focuses on infections in solid organ transplant recipients, specifically cytomegalovirus and hepatitis C. Currently participating in a clinical trial for high (D+/R-) and intermediate (R+) risk kidney transplant patients to assess the ability of a T-SPOT assay to diagnose and monitor CMV activity post-transplant. In addition, a separate T-SPOT assay is also being evaluated to detect allograft rejection. This is an industry sponsored trial, guided by Oxford Immunotec. In addition, we have an ongoing study looking at hepatitis C after liver transplantation.

My research is a collaboration with the Departments of Nephrology and Transplant Surgery, aided by Dr. Thakar, Woodle and Shah.

I currently also serve as the Associate Program Director for the Internal Medicine Residency as well as the Medical Director of Infectious Diseases in Solid Organ Transplant.

Rajat Madan, MD, PhD

Assistant Professor of Clinical Medicine
Division of Infectious Diseases

The overall research goal of my laboratory is to understand the cellular and molecular mechanisms by which nutrition, metabolism, and immune responses to infections are fundamentally linked. Clostridium difficile is the #1 cause of nosocomial infections and obesity is a modern-day epidemic. We are using both patient data and multiple different murine models to study how obesity alters host immune responses during Clostridium difficile infection, and in turn effects disease susceptibility, severity and outcomes. Our data shows that obesity is associated with persistent and more severe disease after C. difficile infection.

I have mentored a clinical infectious disease fellow for his research project and am currently mentoring a research post-doctoral fellow in the lab, and we have published review papers together. We have presented our exciting research data at national and international meetings. My research is currently funded by an NIH K08 grant and support from UC.

Outside of work, I like to travel and hike with my wife and son. I also enjoy gardening, biking, and reading books on evolutionary biology and physics.

Keywords: obesity, C. difficile, leptin, neutrophils, inflammation

Jaime Robertson, MD

Associate Professor of Clinical Medicine
Division of Infectious Diseases

As a post-doctoral fellow, my clinical research examined immune reconstitution as a determinant of the adverse effects of antiretroviral therapy. Since completing my fellowship, I have been an HIV care provider and an investigator with the Clinical Trials Unit in the division. We have a population of ~1800 persons with HIV infection at UCMC that facilitates our research. I have been the site principal investigator for two AIDS Clinical Trials Group studies and I am currently on the protocol development team for A5298 a Randomized, Double-Blinded, Placebo-Controlled, Phase III Trial of the Quadrivalent Human Papillomavirus (HPV) Vaccine to Prevent Anal HPV in HIV-Infected Men. I have conducted two investigator-initiated HIV clinical research studies and I am currently conducting a third K-23 funded study to determine the association between epidemiological, HPV virological, and host cellular markers and the progression of anal dysplasia in HIV.

I have expertise in performing high resolution anoscopy and infrared coagulation for the screening and treatment of HPV-related anal dysplasia and I have been a co-investigator for a phase II study evaluating the safety and tolerability of radiofrequency ablation for the treatment of anal intraepithelial neoplasia.

I am currently collaborating with a network of providers to conduct STI research in collaboration with the UCMC ED, Cincinnati Health Department and CCHMC Adolescent Clinic. I am currently providing research guidance for a fellow who is interested in HPV and viral-associated malignancies in transplant patients.

George Smulian, MD

Division Director
Ward E. Bullock Professor of Medicine
Chief, Infectious Diseases Section, Cincinnati VAMC

After many years as an investigator focused on the molecular cell biology of the fungal pathogens Pneumocystis carinii and Histoplasma capsulatum, my research focus has evolved to a more clinical nature due to my administrative and clinical roles.

My clinical research program focuses on appropriate and novel antibiotic use particularly with respect to prevention and management of Staphylococcal infections. We currently have 2 investigator-initiated clinical trials: one examining a novel agent for perioperative surgical prophylaxis for high risk surgical procedures such as joint replacement and cardiac surgery with sternotomy and a second addressing antibiotic needs in individuals with opioid use disorder. Additional clinical studies examine the use of novel agents in the prevention of health care associated pneumonia in at risk individuals. Epidemiologic studies on opioid use disorder are ongoing using data collected through involvement in the Cincinnati Exchange Project. Research funding over the years has included NIH and VA Merit Review funding, in addition to foundational, departmental and industry support.

In addition to my own program, as division director, my role is to actively and passively support the research programs and aspirations of divisional faculty, fellows and graduate students.

Kavitha Subramanian Vignesh, PhD
Research Assistant Professor
Division of Infectious Diseases

Metal regulation in the immune system is a rapidly emerging field. Immune responses modulate metals in the body and vice versa, i.e. changes in metals control immunity. As a consequence of poor dietary intake, zinc and iron deficiency are highly prevalent and impact immunological fitness in handling infection, cancer and inflammation as a whole. Zinc is crucial for the survival of all life forms. The driving purpose of our investigation is to reveal how the immune system and invading microbes evolved to battle in a "shared" zinc-environment and regulate this metal to strengthen their defenses. My scientific approach is accompanied by an open vision to incorporate new ideas and challenges.

We use diverse in vitro and in vivo techniques combining molecular, metabolic, cytometry, NMR and mass-spectrometry approaches. Our research in the recent past has shed light on intricacies of zinc regulation in frontline defenders, macrophages and dendritic cells during fungal infection. We now seek to explore the mechanisms that activate the NLRP3 inflammasome, a multiprotein complex involved in a variety of inflammatory pathologies including autoimmunity, obesity, diabetes and immune responses to microbial infection. A lot is known about inflammasome structure and consequences of activation. However, the precise molecular players and events in the activation process still remain enigmatic—this forms one focus of our ongoing work.

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 **Vargas E, Apewokin S, Madan R**. Role of the leukocyte response in normal and immunocompromised host after Clostridium difficile infection. Anaerobe. 2017 Jun;45:101-105. doi: 10.1016/j.anaerobe.2017.02.014. Epub 2017 Feb 20. PubMed PMID: 28223256; PubMed Central PMCID: PMC5531608.

2 Matin A, Sharma S, Mathur P, **Apewokin SK**. Myelosuppression-sparing treatment of central nervous system nocardiosis in a multiple myeloma patient utilizing a tedizolid-based regimen: a case report. Int J Antimicrob Agents. 2017 Apr;49(4):488-492. doi: 10.1016/j.ijantimicag.2016.11.032. Epub 2017 Feb 8. PubMed PMID: 28189735.

3 Baker FN, **Cushion MT**, Porollo A. A Quantitative Model to Estimate Drug Resistance in Pathogens. J Fungi (Basel). 2016 Dec;2(4). pii: 30. doi: 10.3390/jof2040030. Epub 2016 Dec 5. PubMed PMID: 28018911; PubMed Central PMCID: PMC5179226.

4 **Cushion MT**, Collins MS, Sesterhenn T, Porollo A, Vadukoot AK, Merino EJ. Functional Characterization of Pneumocystis carinii Inositol Transporter 1. MBio. 2016 Dec 13;7(6). pii: e01851-16. doi: 10.1128/mBio.01851-16. PubMed PMID: 27965450; PubMed Central PMCID: PMC5156303.

5 Koselny K, Green J, DiDone L, Halterman JP, Fothergill AW, Wiederhold NP, Patterson TF, **Cushion MT**, Rappelye C, Wellington M, Krysan DJ. The Celecoxib Derivative AR-12 Has Broad-Spectrum Antifungal Activity In Vitro and Improves the Activity of Fluconazole in a Murine Model of Cryptococcosis. Antimicrob Agents Chemother. 2016 Nov 21;60(12):7115-7127. Print 2016 Dec. PubMed PMID: 27645246; PubMed Central PMCID: PMC5118990.

6 Nanjappa SG, McDermott AJ, Fites JS, Galles K, Wüthrich M, **Deepe GS Jr**, Klein BS. Antifungal Tc17 cells are durable and stable, persisting as long-lasting vaccine memory without plasticity towards IFNγ cells. PLoS Pathog. 2017 May 22;13(5):e1006356. doi: 10.1371/journal.ppat.1006356. eCollection 2017 May. PubMed PMID: 28542595; PubMed Central PMCID: PMC5456400.

7 **Huaman MA, Deepe GS Jr, Fichtenbaum CJ**. Elevated Circulating Concentrations of Interferon-Gamma in Latent Tuberculosis Infection. Pathog Immun. 2016 Fall-Winter;1(2):291-303. PubMed PMID: 27853753; PubMed Central PMCID: PMC5108047.

8 Friedrich D, Fecher RA, Rupp J, **Deepe GS Jr**. Impact of HIF-1α and hypoxia on fungal growth characteristics and fungal immunity. Microbes Infect. 2017 Mar;19(3):204-209. doi: 10.1016/j.micinf.2016.10.008. Epub 2016 Oct 31. Review. PubMed PMID: 27810563.

9 **Subramanian Vignesh K**, Landero Figueroa JA, Porollo A, Divanovic S, Caruso JA, **Deepe GS Jr.** IL-4 Induces Metallothionein 3- and SLC30A4-Dependent Increase in Intracellular Zn(2+) that Promotes Pathogen Persistence in Macrophages. Cell Rep. 2016 Sep 20;16(12):3232-46. doi: 10.1016/j.celrep.2016.08.057. PubMed PMID: 27653687.

10 George MM, **Subramanian Vignesh K**, Landero Figueroa JA, Caruso JA, **Deepe GS Jr.** Zinc Induces Dendritic Cell Tolerogenic Phenotype and Skews Regulatory T Cell-Th17 Balance. J Immunol. 2016 Sep 1;197(5):1864-76. doi: 10.4049/jimmunol.1600410. Epub 2016 Jul 27. PubMed PMID: 27465530; PubMed Central PMCID: PMC4992588.

11 **Dade J, DuBois JC, Pasula R**, Donnell AM, Caruso JA, **Smulian AG, Deepe GS Jr.** HcZrt2, a zinc responsive gene, is indispensable for the survival of Histoplasma capsulatum in vivo. Med Mycol. 2016 Nov 1;54(8):865-75. doi: 10.1093/mmy/myw045. Epub 2016 Jun 22. PubMed PMID: 27335059; PubMed Central PMCID: PMC5057459.

12 Fecher RA, **Horwath MC**, Friedrich D, Rupp J, **Deepe GS Jr.** Inverse Correlation between IL-10 and HIF-1α in Macrophages Infected with Histoplasma capsulatum. J Immunol. 2016 Jul 15;197(2):565-79. doi: 10.4049/jimmunol.1600342. Epub 2016 Jun 6. PubMed PMID: 27271565; PubMed Central PMCID: PMC4935642.

13 Hsieh H, **Vignesh KS, Deepe GS Jr,** Choubey D, Shertzer HG, Genter MB. Mechanistic studies of the toxicity of zinc gluconate in the olfactory neuronal cell line Odora. Toxicol In Vitro. 2016 Sep;35:24-30. doi: 10.1016/j.tiv.2016.05.003. Epub 2016 May 12. PubMed PMID: 27179668; PubMed Central PMCID: PMC5097460.

14 Verma AH, **Bueter CL**, Rothenberg ME, **Deepe GS**. Eosinophils subvert host resistance to an intracellular pathogen by instigating non-protective IL-4 in CCR2(-/-) mice. Mucosal Immunol. 2017 Jan;10(1):194-204. doi: 10.1038/mi.2016.26. Epub 2016 Apr 6. PubMed PMID: 27049063; PubMed Central PMCID: PMC5053824.

15 **Subramanian Vignesh K, Deepe GS Jr.** Immunological orchestration of zinc homeostasis: The battle between host mechanisms and pathogen defenses. Arch Biochem Biophys. 2016 Dec 1;611:66-78. doi: 10.1016/j.abb.2016.02.020. Epub 2016 Feb 24. Review. PubMed PMID: 26921502; PubMed Central PMCID: PMC4996772.

16 Donnell, Anna M., Stephanie Lewis, Sami Abraham, **Kavitha Subramanian**, Julio Landero Figueroa, **George S. Deepe**, and Anne P. Vonderheide. "Investigation of an optimal cell lysis method for the study of the zinc metalloproteome of Histoplasma capsulatum." Analytical and Bioanalytical Chemistry (2017): 1-10.

17 Sterkel, Alana K., Jenna L. Lorenzini, J. Scott Fites, Kavitha **Subramanian Vignesh**, Thomas D. Sullivan, Marcel Wuthrich, Tristan Brandhorst, Nydiaris Hernandez-Santos, **George S. Deepe**, and Bruce S. Klein. "Fungal mimicry of a mammalian aminopeptidase disables innate immunity and promotes pathogenicity." Cell host & microbe 19, no. 3 (2016): 361-374.

18 **Huaman MA**, Kryscio RJ, **Fichtenbaum CJ**, Henson D, Salt E, Sterling TR, Garvy BA. Tuberculosis and risk of acute myocardial infarction: a propensity score-matched analysis. Epidemiol Infect. 2017 May;145(7):1363-1367. doi: 10.1017/S0950268817000279. Epub 2017 Feb 16. PubMed PMID: 28202093.

PUBLICATIONS *CONTINUED*

19 Chan ES, Landay AL, Brown TT, Ribaudo HJ, Mirmonsef P, Ofotokun I, Weitzmann MN, Martinson J, Klingman KL, Eron JJ, **Fichtenbaum CJ**, Plants J, Taiwo BO. Differential CD4+ cell count increase and CD4+: CD8+ ratio normalization with maraviroc compared with tenofovir. AIDS. 2016 Aug 24;30(13):2091-7. doi: 10.1097/QAD.0000000000001181. PubMed PMID: 27281061; PubMed Central PMCID: PMC4966543.

20 Rebeiro PF, Ivey KS, Craig KS, Hulgan T, **Huaman MA**, Nash R, Raffanti S, Equakun KA, Person AK. New Faces of HIV Infection: Age, Race, and Timing of Entry into HIV Care in the Southeastern United States. J Int Assoc Provid AIDS Care. 2017 Jul/Aug;16(4):347-352. doi: 10.1177/2325957417710719. Epub 2017 May 31. PubMed PMID: 28560901.

21 Otero L, Villegas L, **Huaman M**, Sterling T, Seas C. The need for randomised controlled trials of isoniazid monoresistant tuberculosis treatment. Lancet Infect Dis. 2017 Apr;17(4):363-364. doi: 10.1016/S1473-3099(17)30121-4. PubMed PMID: 28346171.

22 **Huaman MA**, Brawley R, Ashkin D. Multidrug-resistant tuberculosis in transplant recipients: Case report and review of the literature. Transpl Infect Dis. 2017 Apr;19(2). doi: 10.1111/tid.12672. Epub 2017 Mar 16. PubMed PMID: 28166377.

23 **Huaman MA**, Vilchez V, Mei X, Shah MB, Daily MF, Berger J, Gedaly R. Decreased graft survival in liver transplant recipients of donors with positive blood cultures: a review of the United Network for Organ Sharing dataset. Transpl Int. 2017 Jun;30(6):558-565. doi: 10.1111/tri.12900. Epub 2016 Dec 28. PubMed PMID: 27896854; PubMed Central PMCID: PMC5429188.

24 **Gamage S, Kralovic SM, Roselle GA**. Chapter 8 "Emerging Infectious Diseases: Concepts in Preparing for the Next Microbial Threat" in Disaster Medicine; Comprehensive Principles and Practices-2nd Edition, Ed. K Koenig and C Schultz, (Cambridge University Press) 2016.

25 **Kelly AA**, Jones MM, Echevarria KL, **Kralovic SM**, Samore MH, Goetz MB, Madaras-Kelly KJ, Simbartl LA, Morreale AP, Neuhauser MM, **Roselle GA**. A Report of the Efforts of the Veterans Health Administration National Antimicrobial Stewardship Initiative. Infect Control Hosp Epidemiol. 2017 May;38(5):513-520. doi: 10.1017/ice.2016.328. Epub 2017 Jan 25. PubMed PMID: 28118861.

26 Evans ME, **Kralovic SM**, Simbartl LA, Jain R, **Roselle GA**. Eight years of decreased methicillin-resistant Staphylococcus aureus health care-associated infections associated with a Veterans Affairs prevention initiative. Am J Infect Control. 2017 Jan 1;45(1):13-16. doi: 10.1016/j.ajic.2016.08.010. PubMed PMID: 28065327.

27 Khanna SR, **Kralovic SM**, Prakash R. Tuberculous Meningitis in an Immunocompetent Host: A Case Report. Am J Case Rep. 2016 Dec 23;17:977-981. PubMed PMID: 28008165; PubMed Central PMCID: PMC5214229.

28 **Gamage SD**, Ambrose M, **Kralovic SM, Roselle GA**. Water Safety and Legionella in Health Care: Priorities, Policy, and Practice. Infect Dis Clin North Am. 2016 Sep;30(3):689-712. doi: 10.1016/j.idc.2016.04.004. Review. PubMed PMID: 27515143.

29 Goto M, O'Shea AMJ, Livorsi DJ, McDanel JS, Jones MM, Richardson KK, Beck BF, Alexander B, Evans ME, **Roselle GA**, **Kralovic SM,** Perencevich EN. The Effect of a Nationwide Infection Control Program Expansion on Hospital-Onset Gram-Negative Rod Bacteremia in 130 Veterans Health Administration Medical Centers: An Interrupted Time-Series Analysis. Clin Infect Dis. 2016 Sep 1;63(5):642-650. doi:10.1093/cid/ciw423. Epub 2016 Jun 28. PubMed PMID: 27358355.

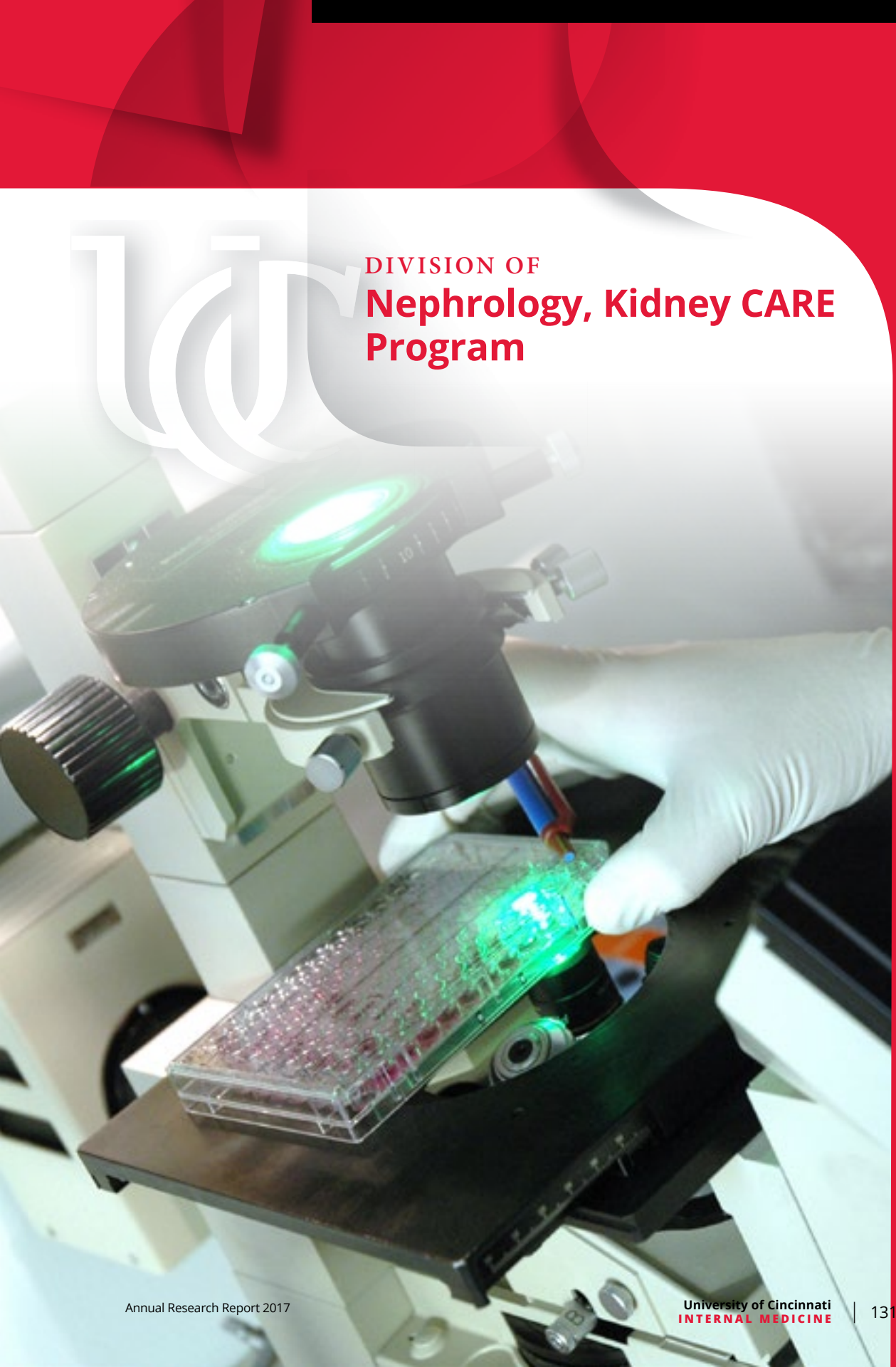
30 **Jose S**, **Madan R**. Neutrophil-mediated inflammation in the pathogenesis of Clostridium difficile infections. Anaerobe. 2016 Oct;41:85-90. doi: 10.1016/j.anaerobe.2016.04.001. Epub 2016 Apr 5. Review. PubMed PMID: 27063896; PubMed Central PMCID: PMC5050096.

31 **DuBois JC, Smulian AG**. Sterol Regulatory Element Binding Protein (Srb1) Is Required for Hypoxic Adaptation and Virulence in the Dimorphic Fungus Histoplasma capsulatum. PLoS One. 2016 Oct 6;11(10):e0163849. doi: 10.1371/journal.pone.0163849. eCollection 2016. PubMed PMID: 27711233; PubMed Central PMCID: PMC5053422.

32 **Sopirala MM**. Does CDC's Ventilator Associated Event Definition Unintentionally Contradict its Antimicrobial Stewardship Initiative? Clin Infect Dis. 2017 Jun 7. doi: 10.1093/cid/cix514. [Epub ahead of print] PubMed PMID: 28591794.

DIVISION OF

Nephrology, Kidney CARE Program



Nephrology, Kidney CARE Program

Charuhas Thakar, MD
DIVISION DIRECTOR

Charuhas Thakar, MD
DIVISION DIRECTOR

The **Division of Nephrology, Kidney CARE (Clinical Advancement, Research and Education) Program** is dedicated to the advancement in:

- Basic and applied translational research
- Clinical outcomes and implementation research
- Clinical trials
- Quality improvement and patient safety research

Currently, basic and translational research projects have a primary focus on ion-channels and immune regulation, epithelial transport, vascular biology, phosphate metabolism, acid-base physiology, and acute and chronic kidney injury. Our expanding clinical outcomes research program includes the disease areas of acute kidney injury, chronic kidney disease, dialysis, and transplantation. The division has enhanced our program through collaborations with pharmacy and nursing services to conduct implementation research in the areas of medication adherence and patient compliance. The focus on quality improvement and patient safety spans across all of our practice locations.

Realizing the importance of quality improvement research in the future of clinical medicine, the division co-directs a program at the VA to develop and train a fellow in Quality and Safety. This is a year-long training which focuses on developing QI projects, and teaches residents and students about systematic methods of incorporating quality improvement methodology within the fabric of clinical practice.

The division is at the forefront of planning or participating in national and international clinical trials of new drug development, devices, and other technology. There are over 15 active clinical trials in a variety of disease areas including polycystic kidney disease, diabetic kidney disease, anemia in kidney disease, and kidney transplantation.

The National Institutes of Health, U.S. Department of Veterans Affairs, Department of Defense, FDA, and industry, in part, support the research conducted within the division. Research publications by the Division of Nephrology investigators have appeared in the most prestigious medical journals over the past decade, including the *Journal of Clinical Investigation, PNAS, Science, Translational Medicine, Journal of American Society of Nephrology, Kidney International*, and *Critical Care Medicine and Stroke*, among others.

Moving forward, we will continue to grow our outcomes research program, basic science program, and clinical translational research through strategic recruitment to develop research programs in the areas of AKI, CKD, and ESRD/transplantation.

Critical Research

Nephrologist Charuhas Thakar leads exploration into all areas of chronic and acute kidney disease

"It's very rewarding to see the direct impact of the work we did."

PROFESSOR CHARUHAS Thakar, MD, realized early in his medical career that his interest landed on addressing some of the most difficult medical cases: nephrology in critically ill patients.

After finishing medical school in his home country of India and completing residency training in internal medicine at Yale University, Bridgeport Program in Connecticut, Thakar joined the Cleveland Clinic for his fellowship in nephrology. He stayed on as a research scholar in clinical outcomes and translational research for a few years before joining the faculty at UC and as a staff physician at the Cincinnati VA Medical Center in 2004.

Thakar is currently director of the UC College of Medicine's Division of Nephrology, Kidney CARE Program and his research resume is extensive. One of his main areas of research is in translational discoveries of biomarkers associated with acute kidney injury, and examining clinical health outcomes by utilizing strengths of large national data sets. "For example, in two separate studies we have used electronic medical records to compare clinical outcomes for patients with acute kidney injury and heart failure in the State of Washington and 45 large medical centers on the East Coast respectively," Thakar says.

He has also been involved in leading or mentoring nursing research. Nurses and nurse practitioners are a main link between primary care physicians and sub-specialists, such as nephrologists, for dialysis patients, says Thakar, who is also involved in various clinical trials. He is currently participating in a large VA cooperative study program that looks at acute kidney injury in patients undergoing cardiovascular procedures; other trials are related to diabetic nephropathy and anemia in kidney disease—both common issues in chronic kidney disease progression.

Thakar has had the satisfaction of seeing some of his work translate into real-life difference-makers for patients; for example, a bedside risk assessment score he developed at the Cleveland Clinic for patients with acute kidney injury undergoing open-heart surgery has since been utilized as both a clinical decision making tool as well as by several phase two and three clinical trials to identify and treat patients at risk of kidney failure following the procedure. "This tool allows for identifying patients to receive treatment to prevent failure within two hours of undergoing open-heart surgery," Thakar says. "It's very rewarding to see the direct impact of the work we did."

Though he deals with sometimes daunting critical questions, Thakar says positivity and perseverance have been essential for his sustained success. "I think in research you have to be an eternal optimist," he says. "You have to compartmentalize and protect your creativity from the day-to-day tasks, which can easily start eroding the enthusiasm for discovery. You have to learn to live with rejection, but not let the rejection reduce your motivation to do better. You also have to be open to the idea that if you are not getting the answers you desire, you might not be asking the right questions." •

Though he deals with sometimes daunting critical questions, Thakar says positivity and perseverance have been essential for his sustained success.

Bassam G. Abu Jawdeh, MD, FASN

Associate Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program

My research interests mainly focus on the field of kidney transplantation.

Earlier this year, I published a study on contrast-induced nephropathy in kidney transplant recipients. This study was supported by an IM department internal grant. Moreover, I have completed an industry-funded clinical trial on Sanguinate, a hemoglobin-based oxygen carrier, to prevent humoral sensitization in kidney transplant candidates and just submitted this paper for publication. I have been awarded a grant to study complement-split products as biomarkers in antibody-mediated rejection of kidney allografts—a project I am collaborating on with Cincinnati Children's.

Later this fall, I am preparing to co-direct a clinic specialized in glomerular diseases in both native as well as allograft kidneys. Data on patients seen in this clinic will be entered in a prospective REDCap database. This will be used to analyze and publish our data as well as allow us at UC to play a key role as part of the International Banff group for recurrent glomerular diseases in kidney transplantation.

Hobbies include hiking, camping and biking.

Rita R. Alloway, PharmD

Research Professor of Medicine
Division of Nephrology, Kidney CARE Program
Director, Transplant Clinical Research

I am Director of the Transplant Clinical Research Program, which spans the clinical research efforts between the Internal Medicine and Surgery Departments. Our multidisciplinary research unit maintains ≈25 studies with federal, investigator-initiated and industry funding. Our novel immunosuppression focus is to minimize toxicity and maximize efficacy with cutting-edge immunosuppressive combinations and use of chemotherapeutic agents to impair antibody formation. The BEST study is a 315 patient, 8-center study we serve as sponsor and coordinating center, which evaluates concomitant calcineurin inhibitor and steroid withdrawal with belatacept (NCT01729494). The follow-up study, BEST EVER, enrolls January 2018. We maintain complementary basic science collaborations both locally and nationally for novel approaches to desensitization and treatment of antibody mediated rejection.

My overall research goal is to incorporate the pharmacokinetic and pharmacogenetic aspects of immunosuppressants to individualize regimens, thereby improving post-transplant outcomes. I recently completed a U01 grant and FDA contract to evaluate tacrolimus generics in kidney and liver transplants. I have conducted over 30 pharmacokinetic immunosuppressant studies, also collaborating to study the impact of laparoscopic sleeve gastrectomy on immunosuppressant pharmacokinetics.

As Director, Transplant Pharmacy Specialty Residency and Fellowship, I have trained >30 candidates.

Keywords: kidney and liver transplantation, pharmacokinetics, immunosuppression, and generic immunosuppressants

Hassane Amlal, PhD

Research Associate Professor
Division of Nephrology, Kidney CARE Program

My research interest is to study the role of renal transport physiology and understand the cellular and molecular mechanisms responsible for abnormal changes in various homeostatic functions of the kidney, including electrolytes and minerals balances, acid-base homeostasis and water metabolism.

My current research program covers three specific areas of active research in my laboratory: 1- Regulation of inorganic phosphorus (Pi) metabolism by estrogen, 2- Role of glutamine transport and metabolism in the development of diabetic nephropathy and 3- Adenine is a new signaling factor, which regulates salt and water transport in the kidney. These studies are supported by a NIH RO1, Dialysis Clinics INC. grants and Intramural funds from College of Medicine and Department of Internal Medicine.

Methodologies We use whole animal physiologic balance studies in metabolic cages using rats and mice, as well as in vitro experiments using both renal cell lines as well as freshly isolated renal tubular suspensions. We study gene and protein expression, and we measure the activity of transporters using radio-isotopes or fluorimetery. Lastly, renal function, electrolytes, minerals and acid base components are measured in both urine and blood samples.

Collaborators: Dr. Sheriff, Dr. Habeebahmed, Dr. Shull, Dr. McCormack and Dr. Cohen: Departments of Surgery, Pathology, Molecular Genetics and Internal Medicine.

Manish Anand, MD

Assistant Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program

I am a clinician educator with research interests in kidney transplantation.

I will be co-directing a glomerular disease clinic later this year. Data from the patients will be collected to define cases of recurrent or de novo GN. This will especially focus on therapeutic interventions to provide more than just anecdotal information on the treatment of recurrent glomerular diseases in the allograft. I have collaborated with researchers from leading transplant centers to study AA donors and their kidney recipients and help understand pathogenic pathways associated with APOL1 associated kidney disease. I am currently involved as a co-investigator in kidney transplant trials at UCMC. My recent publications include IgA dominant Acute Post infectious Glomerulonephritis in the kidney allograft and case series of tuberculosis post kidney transplantation.

My research areas include recurrent glomerular diseases in the kidney transplant, various aspects of living kidney donation particularly medically complex living donors, mineral bone disorders and infections after kidney transplantation.

Laura Conforti, PhD

Professor
Division of Nephrology, Kidney CARE Program

My laboratory studies cancer and autoimmunity. Our main focus areas are: (1) to understand the role that ion channels and the tumor microenvironment play in the failure of the immune system to fight cancer and the limited response of patients to immunotherapies, (2) to study how ion channels contribute to the development and persistence of the autoimmune disease systemic lupus erythematosus, and (3) to develop nanoparticles that can be used as new targeted therapies in autoimmune diseases and cancer.

I have funding from a National Institute of Health R01 renewal grant to continue to look at how lack of oxygen and adenosine in tumors can lead to their progression. In this study, we are trying to discover by which mechanisms hypoxia inhibits ion channels and ultimately T cell function to find out how we can manipulate them to maintain the T cell function and stop tumor growth. I am also the PI in a multiple PI Translation Team award from the Department of Defense to study the mechanisms of resistance to immunotherapy in cancer patients. Ultimately, my laboratory is interested in exploring how nanotechnology could be utilized for the development of targeted immunotherapies in autoimmunity and cancer.

Collaborators: Trisha Wise-Draper, MD, PhD, Edith Janssen, PhD, Marat Khodoun, DVM, PhD and Shashi Kant, MD

Heather J. Duncan, PhD

Field Service Professor
Division of Nephrology, Kidney CARE Program
Director, Clinical Trials, Nephrology

My UC career began in 1987 in Anatomy and Cell Biology, and later Otolaryngology where I published in neuroanatomy, neurophysiology, behavior and psychophysics of chemosensory systems in animals and humans. Working with patients with chemosensory disorders at the UC Taste and Smell Center I applied my experience and skills to the clinical problems of chronic kidney disease (CKD). That led to management of the clinical trials program in Nephrology in 1996.

With my Physician Investigator colleagues we have expanded this program to many indications in CKD, including anemia bone and mineral disease uremic pruritus, hemodialysis vascular access, among other indications, with over 100 completed clinical trials. Our program trains physicians to become Principal Investigators in sponsored clinical trials, and our dialysis database allows us to evaluate unique problems in chronic kidney disease with Investigator-initiated research.

Our program supports research by Nephrology faculty, Fellows and other graduate students with interdisciplinary interests and faculty from both campuses.

I have served on multiple College of Medicine committees, related to quality research and protection of human subjects.

When not working, I like oceans, Scottish music, and sewing.

Amit Govil, MD, FAST

Professor of Clinical Medicine, Division of Nephrology, Kidney CARE Program
Chief, Section of Transplantation
Medical Director, Kidney and Kidney-Pancreas Transplant Program
Director, Transplant Fellowship Program

My research interest covers all aspects of clinical transplantation. I have been a co-investigator in almost all kidney transplant related studies at UC. I have specific interest in antibody mediated injury in transplant recipients–treatment/outcomes, cardiovascular disease and outcomes in kidney and pancreas transplant, transplant failure and transition to dialysis.

As the Director of the Transplant Fellowship Program, I have trained and successfully graduated many transplant fellows.

I have collaborative research with other divisions of Internal Medicine including GI/hepatology, cardiovascular, and endocrinology besides close partnership with the transplant surgery division.

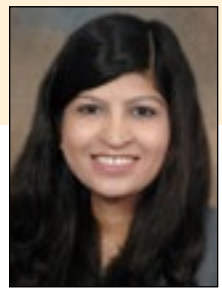
I also actively participate in clinical research with the Cincinnati Eye Institute's Corneal Stem Cell Transplant Program and have co-authored many manuscripts on outcomes in this very specialized group of patients.

I currently serve on the National Scientific Review Board of American Society of Transplantation–Transplantation and Immunology Research Network (TIRN) which funds and provides ongoing support to the most innovative research in transplantation and immunology across the country.

Keywords: antibody mediated rejection in transplant, kidney and pancreas transplant, transplant failure outcomes, living donor outcomes, corneal stem cell transplant, dual organ transplant outcomes

Silvi Shah, MD, FASN, FACP

Assistant Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program



I am a clinical investigator in the division with expertise in clinical outcome research. I am currently involved in investigator-initiated clinical and translational research studies; and industry sponsored national clinical trials. My current funding includes DOIM's Junior Faculty Pilot Award, HSL-COM Grant and university startup funds. My research interests focus on disparities in kidney disease, women's health in kidney disease including preeclampsia and pregnancy and innovative education tools in nephrology.

My ongoing study in collaboration with the Department of Family and Community Medicine is aimed to determine the racial and gender disparities that exist in nephrology care prior to initiation of dialysis. I am spearheading collaborative research efforts between investigators of the Health Sciences Library-College of Medicine. Our research team is studying the adverse fetal and maternal outcomes following pregnancy in women with kidney transplants.

My research also explores the application of innovative education tools in nephrology and involves collaboration with educators from all over the world. I currently serve as faculty member in Nephrology Social Media Collective, American Journal of Kidney Disease's NephMadness and NephJC (online nephrology journal club). I also lead the American Society of Nephrology's Women's Health and Research Community.

Manoocher Soleimani, MD

James Heady Professor of Medicine
Division of Nephrology, Kidney CARE Program
Associate Chair for Research

My research over the past 32 years has focused on understanding the mechanisms of acid base homeostasis and vascular volume and blood pressure regulation through the identification and characterization of transporters and molecules responsible for salt and/or bicarbonate absorption in the kidney and gastrointestinal tract. My laboratory was the first to clone the mammalian gene for the sodium bicarbonate cotransporter, which is an essential molecule for acid base regulation. In addition, we have identified and characterized several novel acid base or electrolyte transporters and have examined their role and regulation in the kidney and/or GI tract in pathophysiologic states. Further, we have generated over 12 genetically-engineered mouse models lacking one or more transporters in order to examine their role in blood pressure regulation or acid base homeostasis. My lab has published over 200 peer-reviewed articles in prestigious journals including *Journal of Clinical investigation* and *Journal of American Society of Nephrology*.

In addition to generating mice lacking a single gene we have been able to shed light on the role of specific molecules by generating mice with simultaneous deletion of two genes. We also identified 4 injury-activated genes that play important roles in mediating tissue damage in kidney, liver and heart. We are currently examining the effect of blocking these genes on the kidney injury caused by the anti-cancer medication cis-platinum.

Ajay Srivastava, MD

Associate Professor of Clinical Medicine
Director, Nephrology Fellowship Program
Division of Nephrology, Kidney CARE Program

I am a clinician educator with a broad range of research interests including dialysis vascular access/ interventional nephrology, trainee education, cardiovascular disease in chronic kidney disease, and critical care nephrology.

Most recently, in July 2017, I published a paper which appeared in *Advances in Chronic Kidney Disease* regarding principles of fluid therapy in the critically ill which also examined "kidney-safe" options in this population. Additionally, this year I published four chapters regarding fluid & electrolyte balance as well as chronic kidney disease in a global health textbook intended for health care providers practicing in areas with limited resources. I also have an invited manuscript that is on track for textbook publication regarding type 2 cardio-renal syndrome.

As part of the education piece as Director of the Nephrology Fellowship Program, I have also been tasked with inviting high caliber speakers to our weekly Kidney CARE Grand Rounds to further the educational endeavors of the Division.

Charuhas Thakar, MD

Arthur Russell Morgan Professor in Internal Medicine
Division Director
Division of Nephrology, Kidney CARE Program

I have led several interdisciplinary investigations related to clinical epidemiology and translational research in acute kidney injury (AKI) and progression of chronic kidney disease (CKD). My thematic interests include clinical and health outcomes research, quality improvement and patient safety research, and clinical trials. I have developed and validated local and regional patient databases, and led investigations on national registries to assess risk factors and outcomes of kidney disease in both acute care/chronic care settings.

Examples of active funded studies include: clinical outcomes in patients with kidney disease/end-stage renal disease and cardiovascular complications. My other research interest revolves around biomarkers of AKI and CKD. Examples of active funded projects include: phenotyping drug-related versus biological causes of AKI; identifying markers/mediators of dual organ ischemic injury; biomarkers of kidney injury in kidney cancer. I lead several clinical trials at UC and VAMC. Disease areas currently under investigation include diabetic nephropathy, CKD and ischemic heart disease, anemia management in CKD, glomerular disease, and AKI.

My research accomplishments have been recognized through receipt of extramural funding. I have been recognized for my research expertise by national/international institutions and organizations such as ASN.

N. Ganesh Yadlapalli, MD

Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program

I am a clinician educator interested in medical education with a special focus on global health.

My approach to improve global health is by providing educational material to health care providers in places with limited resources. I am involved in developing practical, simple and relevant information on common medical problems, incorporating the information developed by WHO and various other global organizations relevant to countries with limited resources.

I have collaborated with more than 50 authors and published a book entitled "Treatment Strategies for Common Medical Problems for Global Health". The second edition of this book has just been released.

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 **Manish Anand**, Juan Pablo Arroyo, Hassan Alhalabi, Timothy Thayer, Mark Lusco, Anthony Langone, Beatrice P. Concepcion, IgA-Dominant Acute Postinfectious Glomerulonephritis Presenting as Acute Renal Failure in a Kidney Transplant Recipient, Kidney International Reports, Volume 2, Issue 4, 2017, Pages 766-769, ISSN 2468-0249, http://dx.doi.org/10.1016/j.ekir.2017.01.011. (http://www.sciencedirect.com/science/article/pii/S246802491730013X)

2 **Abu Jawdeh BG**, Leonard AC, Sharma Y, Katipally S, Shields AR, **Alloway RR**, Woodle ES, **Thakar CV**. Contrast-Induced Nephropathy in Renal Transplant Recipients: A Single Center Experience. Front Med (Lausanne). 2017 May 26;4:64. doi: 10.3389/fmed.2017.00064. eCollection 2017. PubMed PMID: 28603715; PubMed Central PMCID: PMC5445129.

3 O'Connell PJ, Kuypers D, Mannon RR, Abecassis M, Chadban S, Gill JS, Murphy B, Nickerson PW, Schold JD, Stock P, Seron D, **Alloway R**, Bromberg J, Budde K, Jordan S, Legendre C, Lefaucheur C, Sarwall M, Segev D, Stegall MD, Tullius SG, Wong G, Woodle ES, Ascher N, Morris RE. Clinical Trials for Immunosuppression in Transplantation; The Case for Reform and Change in Direction. Transplantation. 2017 Feb 15. doi: 10.1097/TP.0000000000001648. [Epub ahead of print

4 Dember LM, Imrey PB, Duess MA, Hamburg NM, Larive B, Radeva M, Himmelfarb J, Kraiss LW, Kusek JW, Roy-Chaudhury P, Terry CM, Vazquez MA, Vongpatanasin W, Beck GJ, Vita JA; Hemodialysis Fistula Maturation StudyGroupFeldmanH.FarberA.KaufmanJ.SternL.LeSageP.KivorkC.SoaresD.MalikovaM.AllonM.YoungC.TaylorM.WoodardL.MangadiK.MundaR.LeeT.**AllowayR**.El KhatibM.CanaanT.PflumA.ThiekenL.Campos NaciffB.HuberT.BerceliS.JansenM.McCaslinG.TrahanY.DavidsonI.HwangC.LightfootT.LivingstonC.ValenciaA.DolmatchB.FenvesA.HawkinsN.CheungA.KinikiniD.TreimanG.IhnatD.SarfatiM.LavasaniI.MaloneyM.SchlotfeldtL.BuchananC.ClarkC.CrawfordC.HamlettJ.KundzinsJ.ManahanL.WiseJ.GassmanJ.GreeneT.LiL. Vascular Function at Baseline in the Hemodialysis Fistula Maturation Study.J Am Heart Assoc. 2016 Jul 22;5(7). pii: e003227. doi: 10.1161/JAHA.116.003227.

5 Diwan TS, Lichvar AB, Leino AD, Vinks AA, Christians U, Shields AR, Cardi MA, Fukuda T, Mizuno T, Kaiser T, Woodle ES, **Alloway RR**. Pharmacokinetic and pharmacogenetic analysis of immunosuppressive agents after laparoscopic sleeve gastrectomy. Clin Transplant. 2017 Jun;31(6). doi: 10.1111/ctr.12975. Epub 2017 May 2. PubMed PMID: 28342282.

6 Tremblay S, Nigro V, Woodle ES, **Alloway RR**. Reply to "Fluctuation Does Not Mean Variability: A Pharmacokinetic Point of View". Am J Transplant. 2017 Jun;17(6):1693. doi: 10.1111/ajt.14248. Epub 2017 Mar 22. PubMed PMID: 28248455.

7 Dedhia P, **Govil A, Mogilishetty G, Alloway RR**, Woodle ES, Abu Jawdeh BG. Eculizumab and Belatacept for De Novo Atypical Hemolytic Uremic Syndrome Associated With CFHR3-CFHR1 Deletion in a Kidney Transplant Recipient: A Case Report. Transplant Proc. 2017 Jan - Feb;49(1):188-192. doi: 10.1016/j.transproceed.2016.11.008. PubMed PMID: 28104134.

8 Tremblay S, Nigro V, Woodle ES, **Alloway RR**. Reply to "Fluctuation Does Not Mean Variability: A Pharmacokinetic Point of View". Am J Transplant. 2017 Jun;17(6):1693. doi: 10.1111/ajt.14248. Epub 2017 Mar 22. PubMed PMID: 28248455.

9 Paterno F, Girnita A, Brailey P, Witte D, Wang J, Cuffy MC, Diwan T, Tremblay S, Revollo JY, **Alloway RR**, Schoech MR, Anwar N, Shah SA, Woodle SE. Successful Simultaneous Liver-Kidney Transplantation in the Presence of Multiple High-Titered Class I and II Antidonor HLA Antibodies. Transplant Direct. 2016 Nov 23;2(12):e121. eCollection 2016 Dec. PubMed PMID: 27990486; PubMed Central PMCID: PMC5142368.

10 Tremblay S, Nigro V, Weinberg J, Woodle ES, **Alloway RR**. A Steady-State Head-to-Head Pharmacokinetic Comparison of All FK-506 (Tacrolimus) Formulations (ASTCOFF): An Open-Label, Prospective, Randomized, Two-Arm, Three-Period Crossover Study. Am J Transplant. 2017 Feb;17(2):432-442. doi: 10.1111/ajt.13935. Epub 2016 Aug 2. PubMed PMID: 27340950; PubMed Central PMCID: PMC5297985.

11 Webster R, Sheriff S, Faroqui R, Siddiqui F, Hawse JR, **Amlal H**. Klotho/fibroblast growth factor 23- and PTH-independent estrogen receptor-α-mediated direct downregulation of NaPi-IIa by estrogen in the mouse kidney. Am J Physiol Renal Physiol. 2016 Aug 1;311(2):F249-59. doi:10.1152/ajprenal.00542.2015. Epub 2016 May 18. PubMed PMID: 27194721; PubMed Central PMCID: PMC5008677.

12 **Conforti L**. Potassium channels of T lymphocytes take center stage in the fight against cancer. J Immunother Cancer. 2017 Jan 17;5:2. doi:10.1186/s40425-016-0202-5. eCollection 2017. PubMed PMID: 28105369; PubMed Central PMCID: PMC5240326.

13 **Chimote AA**, Hajdu P, Sfyris AM, Gleich BN, Wise-Draper T, Casper KA, **Conforti L**. Kv1.3 Channels Mark Functionally Competent CD8+ Tumor-Infiltrating Lymphocytes in Head and Neck Cancer. Cancer Res. 2017 Jan 1;77(1):53-61. doi: 10.1158/0008-5472.CAN-16-2372. Epub 2016 Nov 4. PubMed PMID: 27815390; PubMed Central PMCID: PMC5215046.

14 **Shah S**, Stevens TM, Agarwal G. Quiz: Acute Kidney Injury and Pancytopenia 5 Months After Kidney Transplantation. Am J Kidney Dis. 2017 Feb;69(2):A14-A17. doi: 10.1053/j.ajkd.2016.07.038. PubMed PMID: 28115064.

15 **Shah S**, Verma P. Overview of Pregnancy in Renal Transplant Patients. Int J Nephrol. 2016;2016:4539342. doi: 10.1155/2016/4539342. Epub 2016 Nov 30. Review. PubMed PMID: 28042483; PubMed Central PMCID: PMC5155089.

16 Alshahrani S, Rapoport RM, Zahedi K, Jiang M, Nieman M, Barone S, Meredith AL, Lorenz JN, Rubinstein J, **Soleimani M**. The non-diuretic hypotensive effects of thiazides are enhanced during volume depletion states. PLoS One. 2017 Jul 18;12(7):e0181376. doi: .1371/journal.pone.0181376. eCollection 2017. PubMed PMID: 28719636; PubMed Central PMCID: PMC5515454.

PUBLICATIONS *CONTINUED*

17 Yin K, Guo J, Lin W, Robertson SYT, **Soleimani M**, Paine ML. Deletion of Slc26a1 and Slc26a7 Delays Enamel Mineralization in Mice. Front Physiol. 2017 May 16;8:307. doi: 10.3389/fphys.2017.00307. eCollection 2017. PubMed PMID: 28559854; PubMed Central PMCID: PMC5432648.

18 Fenton RA, Poulsen SB, de la Mora Chavez S, **Soleimani M**, Dominguez Rieg JA, Rieg T. Renal tubular NHE3 is required in the maintenance of water and sodium chloride homeostasis. Kidney Int. 2017 Aug;92(2):397-414. doi: 10.1016/j.kint.2017.02.001. Epub 2017 Apr 3. PubMed PMID: 28385297; PubMed Central PMCID: PMC5511580.

19 Alshahrani S, Rapoport RM, **Soleimani M**. Vascular contractile reactivity in hypotension due to reduced renal reabsorption of Na(+) and restricted dietary Na(). Naunyn Schmiedebergs Arch Pharmacol. 2017 Mar;390(3):321-326. doi: 10.1007/s00210-017-1340-0. Epub 2017 Jan 20. PubMed PMID: 28108829.

20 **Soleimani M**, Barone S, Xu J, Alshahrani S, Brooks M, McCormack FX, Smith RD, Zahedi K. Prostaglandin-E2 Mediated Increase in Calcium and Phosphate Excretion in a Mouse Model of Distal Nephron Salt Wasting. PLoS One. 2016 Jul 21;11(7):e0159804. doi: 10.1371/journal.pone.0159804. eCollection 2016. PubMed PMID: 27442254; PubMed Central PMCID: PMC4956050.

21 Yang L, Li Y, Wang X, Mu X, Qin D, Huang W, Alshahrani S, Nieman M, Peng J, Essandoh K, Peng T, Wang Y, Lorenz J, **Soleimani M**, Zhao ZQ, Fan GC. Overexpression of miR-223 Tips the Balance of Pro- and Anti-hypertrophic Signaling Cascades toward Physiologic Cardiac Hypertrophy. J Biol Chem. 2016 Jul 22;291(30):15700-13. doi: 10.1074/jbc.M116.715805. Epub 2016 May 20. PubMed PMID: 27226563; PubMed Central PMCID: PMC4957053.

22 **Soleimani M**, Rastegar A. Pathophysiology of Renal Tubular Acidosis: Core Curriculum 2016. Am J Kidney Dis. 2016 Sep;68(3):488-98. doi: 10.1053/j.ajkd.2016.03.422. Epub 2016 May 14. PubMed PMID: 27188519.

23 **Soleimani M**. Receptor Protein Tyrosine Phosphatase γ, CO2 Sensing in Proximal Tubule and Acid Base Homeostasis. J Am Soc Nephrol. 2016 Sep;27(9):2543-5. doi: 10.1681/ASN.2016030332. Epub 2016 Apr 18. PubMed PMID: 27090266; PubMed Central PMCID: PMC5004667.

24 **Soleimani M** and Valenti G. Pendrin and Its Partners in the Kidney: Roles in Vascular Volume and Acid Base Regulation. pp-121-137, March 2017. In : The Role of Pendrin in Health and Disease. Editors: Dossena S and Paulmichi M. Publisher: Springer ISBN: 978-3-319-43285-4 (Print)

25 Walsh KB, Campos B, Hart K, **Thakar C**, Adeoye O. M2 Monocyte Microparticles Are Increased in Intracerebral Hemorrhage. J Stroke Cerebrovasc Dis. 2017 Jun 9. pii: S1052-3057(17)30257-4. doi: 10.1016/j.jstrokecerebrovasdis.2017.05.027. [Epub ahead of print] PubMed PMID: 28606659.

26 Freda BJ, Knee AB, Braden GL, Visintainer PF, **Thakar CV**. Effect of Transient and Sustained Acute Kidney Injury on Readmissions in Acute Decompensated Heart Failure. Am J Cardiol. 2017 Jun 1;119(11):1809-1814. doi: 10.1016/j.amjcard.2017.02.044. Epub 2017 Mar 16. PubMed PMID: 28395891.

27 **Thakar CV**. Long-term Outcomes of Acute Kidney Injury: The Power and Pitfalls of Observational/Population-Based Studies. Am J Kidney Dis. 2017 Jan;69(1):3-4. doi: 10.1053/j.ajkd.2016.10.004. PubMed PMID: 28007191.

28 **Thakar CV**. Vijayan A, Faubel S, Askenazi DJ, Cerda J, Fissell WH, Heung M, Humphreys BD, Koyner JL, Liu KD, Mour G, Nolin TD, Bihorac A; American Society of Nephrology Acute Kidney Injury Advisory Group. Clinical Use of the Urine Biomarker [TIMP-2] × [IGFBP7] for Acute Kidney Injury Risk Assessment. Am J Kidney Dis. 2016 Jul;68(1):19-28. doi: 10.1053/j.ajkd.2015.12.033. Epub 2016 Mar 4. PubMed PMID: 26948834; PubMed Central PMCID: PMC4921267.

29 Buszek SM, Roy-Chaudhury P, **Yadlapalli G**. Olanzapine-Induced Hypertriglyceridemia Resulting in Necrotizing Pancreatitis. ACG Case Rep J. 2016 Aug 17;3(4):e104. eCollection 2016 Aug. PubMed PMID: 27807566; PubMed Central PMCID: PMC5062670.

DIVISION OF

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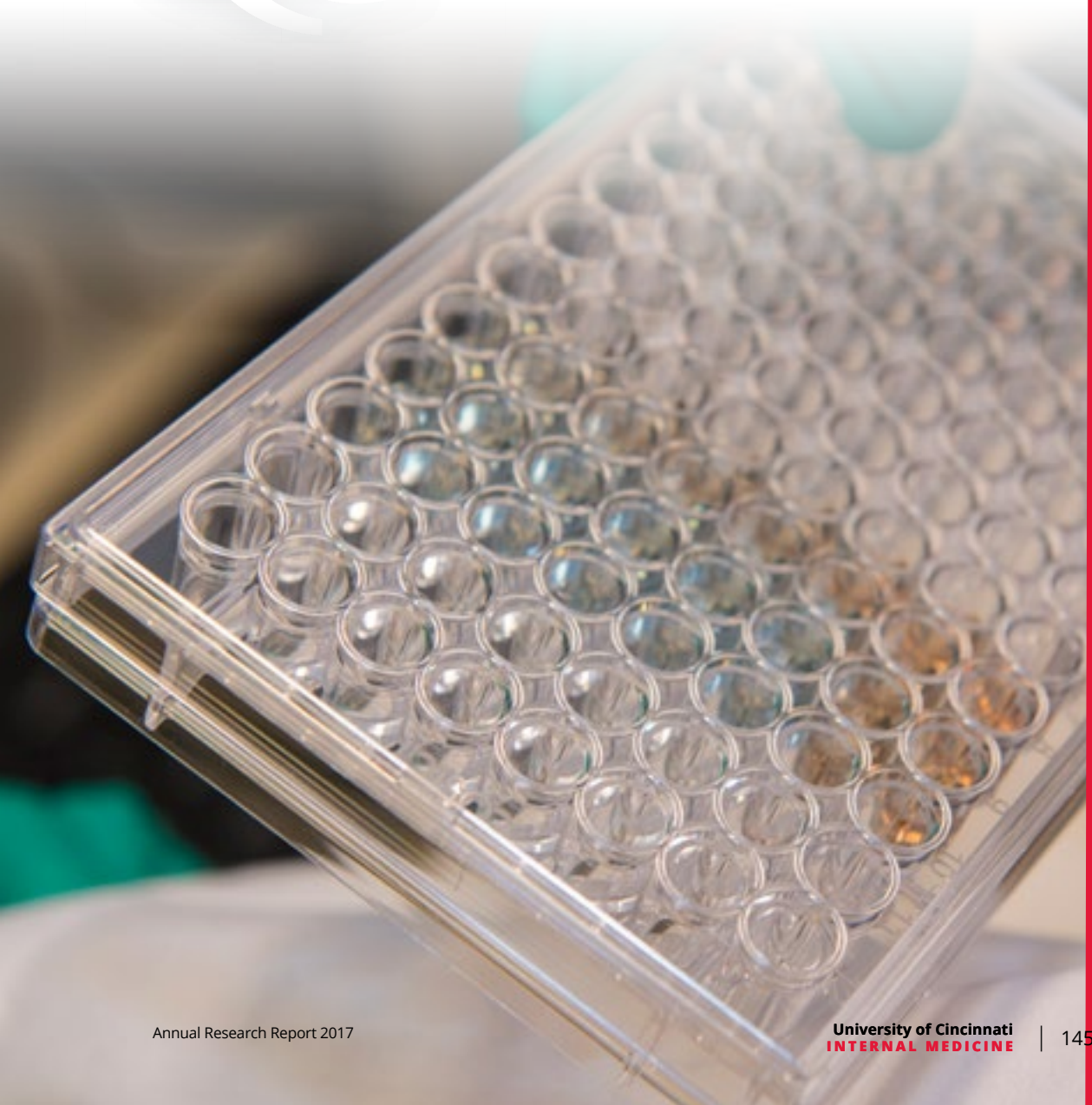

Pulmonary, Critical Care and Sleep Medicine

Frank McCormack, MD
DIVISION DIRECTOR

Frank McCormack, MD
DIVISION DIRECTOR

The **Division of Pulmonary, Critical Care and Sleep Medicine** conducts both basic and clinical research programs focused primarily on development of pathogenesis-driven molecular diagnostics and therapeutics for rare lung diseases. We are an integral part of the Translational Pulmonary Science Center, which is a collaborative project between pulmonary groups at UC and CCHMC, the Rare Lung Diseases Consortium (PIs Trapnell and McCormack), and NIH and NCATs supported platform for conducting studies in rare lung disease.

In our basic research, all projects have a human clinic trial on the horizon, at least conceptually. The laboratory has used mouse models of pulmonary Langerhans cell histiocytosis, Hermansky Pudlak syndrome, lymphangioleiomyomatosis, and pulmonary alveolar microlithiasis in preclinical studies to determine mechanisms of alveolar homeostasis in health and disease. We are also interested in the role of pulmonary airway cells, collectins and lung epithelial cells in innate immune defense against inhaled bacteria, mycobacteria, fungi and viruses, especially (and most recently) influenza.

Our clinical research is focused on investigator-initiated, multicenter, international randomized trials for lymphangioleiomyomatosis, one of which recently led to discovery of an effective treatment and to FDA approval. We are optimistic that our laboratory findings will support the design and execution of trials of phosphate restriction for pulmonary alveolar microlithiasis, BRAF inhibitors for pulmonary Langerhans cell histiocytosis, KGF treatment for pulmonary non tuberculous mycobacterial disease, and mTOR inhibitor prophylaxis and therapy for influenza.

Supportive Synergy

Researcher finds passion in fighting rare lung disease

AS A FRESHLY MINTED PhD from The City University of New York, Jane Yu was searching for a post-doc opportunity that would allow her to use her training in biochemistry to tackle cures for human disease. She was recruited by Dr. Lisa Henske at the Fox Chase Cancer Center in Philadelphia and learned of a rare lung disorder that was cutting short the lives of women.

She had never heard of lymphangioleiomyomatosis, also commonly referred to as LAM, but soon began to hear of the devastation attributed to the disease. It is fatal and affects women of childbearing age, causing progressive shortness of breath and recurrent lung collapses, or pneumothoraces. It is estimated that LAM affects five women per million worldwide.

"I never switched my direction," says Yu, who continued to research LAM when she joined the faculty of the Brigham and Women's Hospital-Harvard Medical School for a seven-year period. "I found the world of rare lung disease incredibly fascinating. There were so many supporting forces—physicians, researchers, patients and an active foundation. It was like a community of support, almost like family."

Yu says her interest in LAM brought her to Cincinnati for an annual symposium sponsored by the LAM Foundation. Sue Byrnes, the mother of a Cincinnati LAM patient, founded the LAM Foundation during the mid-1990s to organize and educate LAM patients about the importance of clinical trials. The foundation developed an $11 million research portfolio that provided the groundwork for clinical trials and nurtured a research community that could effectively compete for National Institutes of Health funding.

The synergy around this effort was attractive to Yu who found the life journey of women battling LAM inspiring but also very tragic. Two years ago she moved her entire lab from Boston to Cincinnati and is now an associate professor in the Division of Pulmonary, Critical Care and Sleep Medicine under the leadership of Dr. Frank McCormack.

"I came to the LAMposium in Cincinnati for 15 years, only skipping once because I was pregnant with my third child," says Yu. "I was able to see 100 patients during each meeting because of the foundation's support. They all walked to the podium individually and they were able to share with the audience their fight with the disease."

"What can we do to help those women with a rare and very devastating disease?" asks Yu. "I was hearing very emotional stories about when they were diagnosed and under what circumstance they figured out they had a rare disease that had very limited treatments."

Once diagnosed the women were told how many years of life they could expect.

"It's very sad. You look at the beautiful young women and some were in their early 20s. Some of them learned during pregnancy that they have this disease and that either they stop the pregnancy or risk their life to have their child," says Yu. "They didn't know that after they gave birth their lung function would deteriorate terribly. They had a lot of fear that they would not survive long, but also they might not be able to see how their children or child grows up. That is a horrifying diagnosis."

Yu says she often thinks of her own daughter, Linda, an 18-year-old undergrad at Northeastern University in Boston, whose life still holds so much promise, when listening to LAM patients. She also has two sons, Ray, a 21-year-old UC student, and Alan, a 14-year-old at Walnut Hills High School, who aspires to be a physician.

"I look at those young women and they are fighting for their lives," says Yu. "I feel like I have more of an obligation to advance my research." ●

"I found the world of rare lung disease incredibly fascinating. There were so many supporting forces—physicians, researchers, patients and an active foundation. It was almost like family."

JANE YU, PHD

Sadia Benzaquen, MD, FACP, FACCP

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Director of Interventional Pulmonology
Director of the Interventional Pulmonology Fellowship Program

I specialize in advanced diagnostic procedures such as EBUS, navigation bronchoscopy and transthoracic needle biopsy as well as advanced therapeutic procedures such as rigid bronchoscopy, endoluminal therapy (laser, APC and cryotherapy). Additional procedures that are part of my practice include endobronchial valve placement, thermoplasty, percutaneus tracheostomy, medical thorachoscopy, chest tube insertion and Pleur x catheter insertion.

I am the principal investigator at UC on the following multi-center trials.
1) The EMPROVE trial is a randomized controlled trial to evaluate the use of endobronchial valves for endoscopic volume reduction in emphysema.
2) The Navigate study is a prospective investigation of the complication rates associated with the Super Dimension Navigation system.
3) The Precepta registry is looking for specific epithelial markers for lung cancer in patients undergoing bronchoscopy for lung cancer.
4) The Brave Study is looking for specific markers for IPF using Cryo transbronchial biopsies.
5) The VAST study is a randomized controlled trial that compares endobronchial valves and conventional treatment in patients with alveolopleural fistula.

I have trained three dedicated IP fellows at UC. The first one is now the current director of the IP program at the University of Bangkok in Thailand.

My hobbies are playing soccer and basketball.

Michael Borchers, PhD

Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine

I am the Principal Investigator of multiple research grants from the NIH, the VA and private organizations. The primary focus of my laboratory is to understand alterations in the immune system (Natural killer cells, T cells, dendritic cells, macrophage) of smokers and COPD patients and how these alterations in immunity affect susceptibility to exacerbations. We utilize a mouse model of long-term cigarette smoke exposure and we have an ongoing study using low dose second-hand smoke exposures. We routinely perform immune cell isolations, flow cytometry, cell cytotoxicity assays, and adoptive transfer studies in immunodeficient mice. We have developed unique transgenic mouse models, reporter cell lines and antibodies as part of our research. I provide training to graduate and undergraduate students, Internal Medicine residents, and Pulmonary/Critical Care fellows.

I am currently collaborating with Dr. Ralph Panos in the study of immune function in COPD patients at the VA. I am collaborating with Dr. Frank McCormack and Dr. Nishant Gupta on clinical projects (lymphangiomyomatosis, LAM) and basic science projects (Pulmonary Langerhan's Cell Histiocytosis (PLCH).

I am the Associate Chair of the University Institutional Animal Care and Use Committee and serve as a member of the Department's Reappointment, Promotion and Tenure Committee.

Jean Elwing, MD

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine

I am the Principal Investigator for several clinical trials in the Division of Pulmonary, Critical Care & Sleep Medicine, evaluating existing and novel therapies for pulmonary arterial hypertension (PAH). Currently, there are 10-12 ongoing phase II and III clinical trials or registries available to PAH patients, with the main focus of examining therapeutics and treatment regimens in hopes to determine the optimal strategies. The UC PH program follows a large cohort of patients affected by PAH.

All patients seen in clinic are evaluated for possible participation in clinical trials or registries; the goal is to offer every patient an opportunity to participate in clinical research. At least 25% of patients actively participate in clinical trials at some point in their care. The UC PH Program actively collaborates with Cincinnati Children's and several other divisions at the University of Cincinnati on various research projects. The pulmonary research unit consists of five staff members and two clinical investigators who are focused on pulmonary hypertension. Funding sources include NIH and industry contracts. The program also participates in investigator initiated projects and often collaborates with trainees who are interested in clinical research.

Jason Gardner, PhD

Research Instructor
Division of Pulmonary, Critical Care and Sleep Medicine

The primary research focus of my laboratory is related to the hematopoietic response to injury. My laboratory utilizes a mouse model of injury to define the axis of cytokines, signaling pathways and cellular responses that determine post injury susceptibility to pneumonia, lung injury and anemia.

I am currently collaborating with Dr. Frank McCormack to determine the role of Keratinocyte Growth Factor (KGF) in the development of post burn pneumonia and lung injury. We are also investigating the utility of recombinant human KGF as a novel therapeutic for the treatment of Mycobacterium avium infections. I am collaborating with Dr. Frank McCormack and Dr. Jose Cancelas to determine the mechanisms responsible for the development of erythropoietin resistant anemia following injury. I am also working with Dr. Suresh Kamath and Dr. Heather Duncan to assess the relationship of G-CSF and IGF-1 in chronic kidney disease patients that require increased erythropoietin to maintain hemoglobin targets.

Nishant Gupta, MD

Adjunct Assistant Professor
Division of Pulmonary, Critical Care and Sleep Medicine

My clinical research program focuses on interstitial and rare lung diseases, especially diffuse cystic lung diseases such as lymphangioleiomyomatosis (LAM), Birt-Hogg-Dube syndrome (BHD), pulmonary Langerhans cell histiocytosis (PLCH), and Sjögren syndrome associated lung disease.

Areas of focus within these diseases include:

1. Improve our understanding of the disease epidemiology and natural history
2. Define the burden and optimal management strategies for spontaneous pneumothoraces that are frequently associated with cystic lung diseases
3. Explore novel treatment options for these diseases
4. Develop diagnostic, predictive and prognostic biomarkers
5. Disseminate knowledge about these diseases in an effort to improve detection rates and reduce the delay in diagnosis experienced by patients with rare diseases

Potential projects for students and fellows:

We have a database of the various interstitial and rare lung disease patients in the University of Cincinnati ILD clinic. Investigator-initiated proposals to answer specific questions can be performed on the database. In addition, we are a part of the NIH-sponsored Rare Lung Diseases Consortium, and can use this worldwide clinic network to conduct studies.

Kristin Hudock, MD

Assistant Professor of Medicine and Pediatrics
Division of Pulmonary, Critical Care and Sleep Medicine
Division of Pulmonary Biology, Cincinnati Children's Hospital Medical Center

My group seeks to understand how an individual's innate immune response contributes to the pathogenesis of cystic fibrosis (CF), acute respiratory distress syndrome (ARDS) and pneumonia. To accomplish this goal, we combine basic and translational approaches to discover what regulates the balance between host defense and tissue injury in human lung and inflammatory diseases.

We utilize primary human cells, murine models and patient samples to generate new knowledge regarding disease mechanisms with the goal of uncovering unique therapeutic targets. We also use our expertise in human induced pluripotent stem cells (iPSCs) to define crucial genes-to-function relationships that modify neutrophil behaviors. Our lab has specific interests in cytokine networks, neutrophil extracellular traps (NETs) and NETosis.

We also employ the aforementioned strategies to elucidate novel mechanisms in human disorders causing neutropenia, including poikiloderma with neutropenia (PN).

Our work is enriched by collaborations with, and mentorship from, investigators from both UC and CCHMC, including Dr. Bruce Trapnell, Dr. JP Clancy, Dr. Frank McCormack and Dr. Jeffrey Whitsett.

The Hudock lab is funded by the NIH, UC CCTST CT2 Scholar program, Parker B. Francis Foundation, Cystic Fibrosis Foundation, UC College of Medicine and Cincinnati Children's.

Veronica Indihar, MD

Assistant Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine

My clinical research program focuses on cystic fibrosis, with an emphasis on clinical trials and patient centered outcomes. We are working on creating a non-CF bronchiectasis clinic with special attention to airway clearance support and clinical trials given paucity of specific therapies available for this population. Clinicians with an interest in this should contact me. Our trials are generally funded by the CF-TDN network with some industry support.

We also have CF Foundation funding for a quality improvement program. We are part of the CF learning network with goal to improve CF care. I collaborate with the other CF clinicians including Drs. Patricia Joseph, Bruce Trapnell, Lisa Burns, Cheryl McCullumsmith, and Mark Eckman.

In my free time, I enjoy life with my two children and husband. Since we are from Argentina, we are looking forward to FC Cincinnati soccer games!

Patricia Joseph, MD

Professor of Clinical Medicine
Director, Adult Cystic Fibrosis Program
Division of Pulmonary, Critical Care and Sleep Medicine

I dedicate most of my clinical and research time to CF care, CF clinical trials and quality improvement. I am currently the Principal Investigator on multiple CF-related clinical trials with more planned for the near future. Our team is involved with several new investigational drugs designed to correct the defect in CF. Other studies are trials designed to improve lung function in CF, to evaluate patient methods of coping with chronic illness or to review aminoglycoside dosing and complications in CF. Our Adult CF program has a long history of involvement in quality improvement and we have recently received a grant from the CF Foundation to identify components of our CF care delivery that can be altered to increase patient engagement and improve health outcomes.

I collaborate with John P. Clancy MD, Lisa Burns MD, Veronica Indihar MD, Bruce Trapnell MD, and Christopher Droege, Pharm D on CF clinical trials; with Daniel Grossoehme on coping with chronic disease and with on Mark Eckman on patient-centered outcomes research.

Peter H. Lenz, MD, MEd

Associate Professor
Pulmonary & Critical Care Fellowship Director
Division of Pulmonary, Critical Care & Sleep Medicine

My academic investigations are focused around teaching physicians-in-training and creating appropriate programs and curricula to support aspiring clinician educators. The core components of my medical education mission are focused on audience engagement and promoting active teaching modalities. We recently surveyed program directors to assess existing teaching content and structure in US pulmonary and critical care medicine (PCCM) fellowships. We found that only one third of responders had a formal curriculum for teaching medical education skills. This appears to be discordant with a recent fellows survey that reports over 70% of fellows in training want formal instruction on teaching.

To meet this need, we have created a teaching curriculum for all of our fellows and have created a specific clinician educator track for fellows wishing to get more in depth training and experience in curriculum development, delivering effective learner feedback, and creating evaluative assessment tools. In our publication, qualitative analyses identified several barriers to implementing formal teaching skills curricula and I am interested in developing the effective strategies that are needed to design, implement, sustain, and assess teaching skills curricula for PCCM fellowships.

I mentor our fellows in the clinician educator track.

Frank McCormack, MD

Gordon and Helen Hughes Taylor Professor of Internal Medicine
Division Director
Division of Pulmonary, Critical Care and Sleep Medicine

Our group is broadly interested in translational research of rare lung diseases, which allows us to approach disease pathogenesis from the vantage point of a known molecular defect. Our goal is to develop new biomarkers and therapies with the potential to favorably impact human health in a short time frame. Many of our laboratory directions have been inspired by patients we have met, which gives our work purpose and meaning, and motivates us to ask questions that matter.

The McCormack laboratory is interested in genetic interstitial lung diseases and pulmonary innate immunity. Current projects are focused on lymphangioleiomyomatosis (LAM), pulmonary alveolar microlithiasis (PAM) and the role of the alveolar epithelium in influenza, mycobacterial and bacterial infection. We intend to conduct a trial in PAM patients through the NIH Rare Lung Disease Consortium (RLDC), a network of 55 rare lung disease clinics located around the world, with Cincinnati as the hub (PIs-Bruce Trapnell and Frank McCormack).

Other Cincinnati based RLDC projects have included developing a pathologic classification system for the pediatric interstitial lung diseases, developing diagnostic tests for pulmonary alveolar proteinosis, developing CT scanning as a biomarker of progression for alpha-1 antitrypsin deficiency, developing a longitudinal registry for LAM (MIDAS), and conducting a MILES-like trial of sirolimus in asymptomatic patients with LAM who have normal lung function (The MILED trial).

Dennis McGraw, MD

Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine

The primary focus of my laboratory is to understand how G-protein-coupled receptors (GPCR) regulate airway smooth muscle tone, with particular emphasis on the role of b2-adrenergic receptor regulation/dysregulation in asthma. We utilize cell models (including primary cultures of airway smooth muscle from genetically modified mice) to investigate multiple aspects of GPCR regulation including agonist/antagonist binding, receptor trafficking, membrane microdomain localization, dimer/oligomer formation, and second messenger signaling. We have also developed transgenic models to target GPCR signal alterations specifically to smooth muscle in order to assess the consequences of receptor and/or signal transduction alterations on physiologic responses of intact tissues and animals.

Current collaborations with Frank McCormack, MD include an investigation of pulmonary mechanics (airway hyperreactivity and compliance) in different murine models of rare human lung diseases such as pulmonary microlithiasis. I also serve as the Director of a newly created Research Bronchoscopy Core that acquires lung samples (bronchoalveolar lavage, epithelial cell brushings and endobronchial biopsies) from human subjects.

Clinically, I serve as the Section Chief for the Division of Pulmonary, Critical Care and Sleep Medicine at the Cincinnati VAMC. I also serve as a PI and co-PI for pharmaceutical studies that primarily focus on agents for treating asthma and COPD.

David Norton, MD

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Director, UCMC Medical Intensive Care Unit

I am a Principal Investigator at the University of Cincinnati College of Medicine for the National Institutes of Health (NIH)/ National Heart Lung and Blood Institute (NHLBI) sponsored Prevention and Early Treatment of Acute Lung Injury (PETAL) Trials Network. The grant was awarded in 2014 and will produce 4-6 prospective, randomized, controlled studies designed to prevent or treat severe acute respiratory distress syndrome (ARDS). The first trial (Reevaluation of Systemic Early Neuromuscular Blockade (ROSE)) began in the winter of 2016 and the University of Cincinnati has enrolled several patients. The goal of the study is to help understand whether early chemical paralysis is beneficial in the care of patients with severe acute hypoxemic respiratory failure secondary to ARDS.

The second trial (LOTUS-FRUIT) is a prospective cohort study looking at mechanical ventilation practices in the hospitals that are part of the PETAL Network. This work will help shape a low tidal volume for acute respiratory failure protocol (for patients with risk factors for subsequent ARDS development) that will be tested later this year in the LOTUS trial.

Finally, the VIOLET study will evaluate the benefit of Vitamin D supplementation as a strategy for prevention of ARDS in patients with acute respiratory failure who are at risk for this complication.

Ralph Panos, MD

Professor
Division of Pulmonary, Critical Care and Sleep Medicine

Cincinnati is the epicenter of the Chronic Obstructive Pulmonary Disease (COPD) epidemic that has made COPD the third leading cause of death in the US. Our epidemiologic studies have estimated the prevalence of COPD among Veterans at the Cincinnati VAMC to be 33-44% and two of every three Veterans with COPD are not yet diagnosed. COPD health care expenditures account for nearly 10% of the entire Cincinnati VAMC budget. Thus, COPD is a common disorder of Veterans that causes significant morbidity and mortality and its treatment is a major expense within the VHA.

Over the past 5-6 years, we have developed a multidisciplinary and multifaceted clinical research effort into many different aspects of COPD that spans the spectrum of clinical research from local investigator initiated projects, to pharmaceutical trials, to multicenter NIH and VHA sponsored trials. We obtained nearly $1M in funding from the VHA office of Specialty Care to develop a patient centered approach to the management of COPD. That program developed a VHA specific screening instrument for the detection of airflow limitation that performed as well as previously validated COPD screening tools, initiated TeleSpirometry which has now spread throughout the VHA, and led to the publication of The COPD Primer, a comprehensive book for the management of COPD.

Bruce Trapnell, MD

Professor
Director, Translational Pulmonary Science Center,
Cincinnati Children's Hospital Medical Center
Co-Director, NIH Rare Lung Diseases Clinical Research Consortium, RDCRN-3
Co-Director, Pilot Clinical and Translational Collaborative Studies Core, CTSA, UC

The Trapnell Laboratory has had a long-standing focus on the pathogenesis, diagnosis, and therapy of rare lung diseases, the role of GM-CSF in lung homeostasis and defense, and human gene therapy and focus to translational, pathway-based diagnostic and therapeutic development. Approaches involve mouse and non-human primate disease models, molecular and cell biology methodologies, natural history trials, and human treatment trials. We have contributed to the development of new diagnostics and

Recent key findings include: 1) development of a novel gene correction and cell transplantation therapy approach (pulmonary macrophage transplantation therapy) with extraordinary efficacy and potential to be the first specific therapy for children with hereditary PAP; 2) identification of a reciprocal feedback loop by which pulmonary GM-CSF regulates the size of the AM population; and 3) discovery and characterization of hereditary PAP.

Our group has been continuously funded by the NIH in lung disease research since Dr. Trapnell came to Cincinnati and has provided training in basic, clinical, and translational research at multiple levels.

Dr. Trapnell is co-Founder and current Scientific Director of the Pulmonary Alveolar Proteinosis (PAP) Foundation.

Jane Yu, PhD
Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine

I lead a research laboratory focusing on investigation of the role of tumor suppressor proteins tuberin (TSC2) and hamartin (TSC1) in steroid action, cell survival, cellular metabolism, tumorigenesis and metastasis, and signaling transduction pathways. My laboratory also develops animal models to test the efficacy of FDA-approved drugs on the progression and metastasis of mTORC1 hyperactive cells, lung inflammation and injury. Current studies include determining the role of estrogen in the progression of lymphangioleiomyomatosis (LAM), a female predominant rare lung disease, from the alteration of signaling pathways, to the integrity of alveolar epithelium and microenvironment in the lung, and to the pulmonary functions. We are also investigating the potential application of using blood-based biomarkers in LAM. Our research has been funded by NIH/ NHLBI, NIDDK, the Department of Defense, and The LAM Foundation.

My laboratory developed the first LAM-associated patient-derived primary cell line and the first metastatic model of LAM. We have also identified mTORC1-independent but mTORC2-mediated activation of prostaglandin biosynthesis in TSC and LAM, and used metabolomics profiling to identify dysregulation of glucose metabolism and pentose phosphate pathway addiction in TSC2-deficient cells.

Specialized equipment available for collaborative research includes the IVIS Spectrum Preclinical In Vivo Imaging System.

Muhammad Ahsan Zafar, MD
Assistant Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine

My interest is in improvement/ implementation science, designing micro-systems of care delivery that lead to better outcomes. Using my advanced training in this field, I have lead a multidisciplinary team to reduce readmissions and emergency department (ED) revisits for patients with COPD exacerbations who are hospitalized (project I-CARE) or seen in ED (project ExCEED). Sustaining these outcomes by increasing reliability of the processes is an ongoing endeavor. Reducing readmissions and revisits in this high risk population reduces the amassed cost and more importantly, improves quality-of-life and morbidity. We continue to find ways to improve outcomes further. In the next project we are developing better ways of patient triage in ED based on predictive risk through retrospective analysis and modeling/ simulations. This will be followed by real-time implementation of better triage methods at UCMC.

I am also leading an improvement initiative in Medical ICU. The initial projects are: 1) Situation awareness and mindfulness in patient safety (project SAVE), and 2) Waste reduction in MICU lab testing (project SMART). Mixed methods were utilized to identify these projects as high priority. We are building multidisciplinary teams of physicians, respiratory therapists, pharmacists, nurses and patients to execute these projects using improvement science methods.

PUBLICATIONS *July 1, 2016 thru June 30, 2017*

1 Benninger LA, Medepalli K, **Aragaki-Nakahodo A, Benzaquen S**, Ong PG, Gilles Debiane L, Casal RF. Sequential Bronchoscopic Cryobiopsy and Cryotherapy. Ann Am Thorac Soc. 2017 Jun;14(6):1036-1040. doi: 0.1513/AnnalsATS.201701-046CC. PubMed PMID: 28570162.

2 Sriprasart T, Aragaki A, Baughman R, Wikenheiser-Brokamp K, Khanna G, Tanase D, Kirschner M, **Benzaquen S**. A Single US Center Experience of Transbronchial Lung Cryobiopsy for Diagnosing Interstitial Lung Disease With a 2-Scope Technique. J Bronchology Interv Pulmonol. 2017 Apr;24(2):131-135. doi: 10.1097/LBR.0000000000000366. PubMed PMID: 28323726; PubMed Central PMCID:PMC5367496.

3 Roach DJ, Crémillieux Y, Serai SD, Thomen RP, Wang H, Zou Y, Szczesniak RD, **Benzaquen S**, Woods JC. Morphological and quantitative evaluation of emphysema in chronic obstructive pulmonary disease patients: A comparative study of MRI with CT. J Magn Reson Imaging. 2016 Dec;44(6):1656-1663. doi: 10.1002/jmri.25309. Epub 2016 May 17. PubMed PMID: 27185386.

4 Balestra R, **Benzaquen S**, Wang J. Sarcoidosis-like Granulomatous Lung Reaction Associated with Anti-Programmed Death Receptor-1 Ligand Therapy. Ann Am Thorac Soc. 2017 Feb;14(2):296-299. doi: 10.1513/AnnalsATS.201611-863LE. PubMed PMID: 28146383.

5 Balestra R, Selvaraju A, **Benzaquen S**, Zander DS. Pneumonic-type mucinous lung adenocarcinoma diagnosed by transbronchial cryobiopsy. Respirol Case Rep. 2017 Feb 28;5(3):e00222. doi: 10.1002/rcr2.222. eCollection 2017 May. PubMed PMID:28261482; PubMed Central PMCID: PMC5329891.

6 Liu H; Jakubzik C, Osterburg A, Nelson R, **Gupta N, McCormack F**, and **Borchers M**. Dendritic Cell Trafficking and Function in Rare Lung Diseases. Am J Respir Cell Mol Biol. 2017 Jun 6. doi: 10.1165/rcmb.2017-0051PS. [Epub ahead of print] PMID: 28586276

7 Li C, Liu X, Liu Y, Zhang E, Medepalli K, Masuda K, Li N, Kopras EJ, Kwiatkowski DJ, **Borchers MT**, Wikenheiser-Brokamp KA, Osterburg A, Mays M, Sun Y, Plas DR, Sun JL, Franz DN, Capal JK, Alayev A, Holz MK, Krueger DA, Siroky BJ, Yu JJ. Tuberin Regulates Prostaglandin Receptor-mediated Viability, via Rheb, in mTORC1-hyperactive Cells. Mol Cancer Res. 2017 Jul 14. pii: molcanres.0077.2017. doi: 10.1158/1541-7786.MCR-17-0077. [Epub ahead of print]

8 Osterburg AR, Nelson RL, Yaniv BZ, Foot R, Donica WR, Nashu MA, Liu H, Wikenheiser-Brokamp KA, Moss J, **Gupta N**, **McCormack FX**, **Borchers MT**. NK cell activating receptor ligand expression in lymphangioleiomyomatosis is associated with lung function decline. JCI Insight. 2016 Oct 6;1(16):e87270. PMID: 27734028

9 Wortham BW, Eppert BL, Flury JL, Garcia SM, Donica WR, Osterburg A, Joyce-Shaikh B, Cua DJ, **Borchers MT**. Cutting Edge: CLEC5A Mediates Macrophage Function and Chronic Obstructive Pulmonary Disease Pathologies. J Immunol. 2016 Apr 15;196(8):3227-31. PMID: 26927798

10 Kaplan HC, Thakkar SN, **Burns L**, Chini B, Dykes DM, McPhail GL, Moore E, Saeed SA, Eslick I, Margolis PA, Opipari-Arrigan L. Protocol of a Pilot Study of Technology-Enabled Coproduction in Pediatric Chronic Illness Care. JMIR Res Protoc. 2017 Apr 28;6(4):e71. doi: 10.2196/resprot.7074. PubMed PMID: 28455274; PubMed Central PMCID: PMC5429432.

11 Rahaghi FF, Feldman JP, Allen RP, Tapson V, Safdar Z, Balasubramanian VP, Shapiro S, Mathier MA, **Elwing JM**, Chakinala MM, White RJ. Recommendations for the use of oral treprostinil in clinical practice: a Delphi consensus project pulmonary circulation. Pulm Circ. 2017 Mar 21;7(1):167-174. doi: 10.1086/690109. eCollection 2017 Mar. PubMed PMID: 28680576; PubMed Central PMCID: PMC5448528.

12 Lee C, **Elwing J**. Pulse dose steroids in severe pulmonary arterial hypertension secondary to systemic lupus erythematosus. SAGE Open Med Case Rep. 2017 May 4;5:2050313X17707153. doi: 10.1177/2050313X17707153. eCollection 2017. PubMed PMID: 28515936; PubMed Central PMCID: PMC5423708.

13 Medepalli K, Lee CM, Benninger LA, **Elwing JM**. Psychosis: call a surgeon? A rare etiology of psychosis requiring resection. SAGE Open Med Case Rep. 2016 Sep 21;4:2050313X16670084. eCollection 2016. PubMed PMID: 27708781; PubMed Central PMCID: PMC5034462.

14 Lee CM, Girnita D, Sharma A, Khanna S, **Elwing JM**. A Unique Presentation of Anti-RNA Polymerase III Positive Systemic Sclerosis Sine Scleroderma. Case Rep Rheumatol. 2016;2016:8536341. doi: 10.1155/2016/8536341. Epub 2016 Jul 31. PubMed PMID: 27559487; PubMed Central PMCID: PMC4983352.

15 Nikolaidis NM, Noel JG, Pitstick LB, **Gardner JC**, Uehara Y, Wu H, Saito A, Lewnard KE, Liu H, White MR, Hartshorn KL, **McCormack FX**. Mitogenic stimulation accelerates influenza-induced mortality by increasing susceptibility of alveolar type II cells to infection. Proceedings of the National Academy of Sciences of the United States of America. 2017. Epub 2017/07/26. doi: 10.1073/pnas.1621172114. PubMed PMID: 28739896.

16 **JC Gardner**, KS Vignesh, JG Noel, BJ Ramser, LB Pitstick, GS Deepe, FX McCormack. Keratinocyte Growth Factor-Dependent Protection From A Lethal Klebsiella Pneumoniae Pulmonary Infection. Am J Respir Crit Cate Med 2017;195:A6729 (Oral Presentation)

17 **JC Gardner**, JG Noel, BJ Ramser, JA Cancelas, FX McCormack. Thermal Injury of the Skin Induces G-CSF Dependent Attenuation of EPO Signaling and Erythroid Differentiation Arrest. Shock 2017; 47(supp1):P178. (Poster Presentation)

PUBLICATIONS *CONTINUED*

18 Papo M, Diamond EL, Cohen-Aubart F, Emile JF, Roos-Weil D, **Gupta N**, Durham BH, Ozkaya N, Dogan A, Ulaner GA, Rampal R, Kahn JE, Sené T, Charlotte F, Hervier B, Besnard C, Bernard OA, Settegrana C, Droin N, Hélias-Rodzewicz Z, Amoura Z, Abdel-Wahab O, Haroche J. High prevalence of myeloid neoplasms in adults with non-Langerhans cell histiocytosis. Blood. 2017 Aug 24;130(8):1007-1013. doi: 10.1182/blood-2017-01-761718. Epub 2017 Jul 5. PubMed PMID: 28679734; PubMedCentral PMCID: PMC5570678.

19 Cooley J, Lee YCG, **Gupta N**. Spontaneous pneumothorax in diffuse cystic lung diseases. Curr Opin Pulm Med. 2017 Jul;23(4):323-333. doi: 10.1097/MCP.0000000000000391. PubMed PMID: 28590337; PubMed Central PMCID: PMC5563542.

20 **Gupta N**, Kopras EJ, Henske EP, James LE, El-Chemaly S, Veeraraghavan S, Drake MG, **McCormack FX**. Spontaneous Pneumothoraces in Patients with Birt-Hogg-Dubé Syndrome. Ann Am Thorac Soc. 2017 May;14(5):706-713. doi: 10.1513/AnnalsATS.201611-886OC. PubMed PMID: 28248571; PubMed Central PMCID: PMC5427741.

21 **Gupta N**, Langenderfer D, **McCormack FX**, Schauer DP, Eckman MH. Chest Computed Tomographic Image Screening for Cystic Lung Diseases in Patients with Spontaneous Pneumothorax Is Cost Effective. Ann Am Thorac Soc. 2017 Jan;14(1):17-25. doi: 10.1513/AnnalsATS.201606-459OC. PubMed PMID: 27737563; PubMed Central PMCID: PMC5461992.

22 **Gupta N**, Sunwoo BY, Kotloff RM. Birt-Hogg-Dubé Syndrome. Clin Chest Med. 2016 Sep;37(3):475-86. doi: 10.1016/j.ccm.2016.04.010. Epub 2016 Jun 25. Review. PubMed PMID: 27514594.

23 Raoof S, Bondalapati P, Vydyula R, Ryu JH, **Gupta N**, Raoof S, Galvin J, Rosen MJ, Lynch D, Travis W, Mehta S, Lazzaro R, Naidich D. Cystic Lung Diseases: Algorithmic Approach. Chest. 2016 Oct;150(4):945-965. doi: 10.1016/j.chest.2016.04.026. Epub 2016 May 13. Review. PubMed PMID: 27180915.

24 Reilly JP, Anderson BJ, **Hudock KM**, Dunn TG, Kazi A, Tommasini A, Charles D, Shashaty MG, Mikkelsen ME, Christie JD, Meyer NJ. Neutropenic sepsis is associated with distinct clinical and biological characteristics: a cohort study of severe sepsis. Crit Care. 2016 Jul 18;20(1):222. doi: 10.1186/s13054-016-1398-y. PubMed PMID: 27431667; PubMed Central PMCID:PMC4950810.

25 Paris AJ, Liu Y, Mei J, Dai N, Guo L, Spruce LA, **Hudock KM**, Brenner JS, Zacharias WJ, Mei HD, Slamowitz AR, Bhamidipati K, Beers MF, Seeholzer SH, Morrisey EE, Worthen GS. Neutrophils promote alveolar epithelial regeneration by enhancing type II pneumocyte proliferation in a model of acid-induced acute lung injury. Am J Physiol Lung Cell Mol Physiol. 2016 Dec 1;311(6):L1062-L1075. doi:10.1152/ajplung.00327.2016. Epub 2016 Sep 30. PubMed PMID: 27694472; PubMed Central PMCID: PMC5206401.

26 Eckman, MH. Kopras, EJ. Montag-Leifling, K., Kirby, LP. Burns, L., I**ndihar, VM**. **Joseph, PM**. Shared Decision Making Tool for Self-Management of Home Therapies for Patients with Cystic Fibrosis. Medical Decision Making Policy & Practice. In press. 2017

27 Tangpricha V, Smith EM, Binongo J, Judd SE, Ziegler TR, Walker S, Tirouvanziam R, Zughaier SM, Lee MJ, Chesdachai S, Hermes WA, Chmiel JF, Gaggar A, Grossmann RE, **Joseph PM**, Alvarez JA. The Vitamin D for Enhancing the Immune System in Cystic Fibrosis (DISC) trial: Rationale and design of a multi-center, double-blind, placebo-controlled trial of high dose bolus administration of vitamin D3 during acute pulmonary exacerbation of cystic fibrosis. Contemp Clin Trials Commun. 2017 Jun;6:39-45. doi: 10.1016/j.conctc.2017.02.010. Epub 2017 Mar 9. PubMed PMID: 28508087; PubMed Central PMCID: PMC5427007.

28 Sriprasart T, Aragaki A, Baughman R, Wikenheiser-Brokamp K, **Khanna G**, Tanase D, Kirschner M, Benzaquen S. A Single US Center Experience of Transbronchial Lung Cryobiopsy for Diagnosing Interstitial Lung Disease With a 2-Scope Technique. J Bronchology Interv Pulmonol. 2017 Apr;24(2):131-135. doi: 10.1097/LBR.0000000000000366. PubMed PMID: 28323726; PubMed Central PMCID:PMC5367496.

29 Rynkiewicz MJ, Wu H, Cafarella TR, Nikolaidis NM, Head JF, Seaton BA, **McCormack FX**. Differential Ligand Binding Specificities of the Pulmonary Collectins Are Determined by the Conformational Freedom of a Surface Loop. Biochemistry. 2017 Aug 8;56(31):4095-4105. doi: 10.1021/acs.biochem.6b01313. Epub 2017 Jul 31. PubMed PMID: 28719181.

30 Feemster LC, Lyons PG, Chatterjee RS, Kidambi P, **McCormack FX**, Moss J, Wilson KC, Thomson CC. Summary for Clinicians: Lymphangioleiomyomatosis Diagnosis and Management Clinical Practice Guideline. Ann Am Thorac Soc. 2017 Jul;14(7):1073-1075. doi: 10.1513/AnnalsATS.201609-685CME. PubMed PMID: 28665705; PubMed Central PMCID: PMC5566288.

31 Han MK, Tyburczy ME, Darling TN, Kazerooni EA, Myers JL, **McCormack FX**, Moss J, Kwiatkowski DJ. Apparent Sporadic Lymphangioleiomyomatosis in a Man as a Result of Extreme Mosaicism for a TSC2 Mutation. Ann Am Thorac Soc. 2017 Jul;14(7):1227-1229. doi: 10.1513/AnnalsATS.201703-229LE. PubMed PMID: 28613922; PubMed Central PMCID: PMC5566294.

32 Lu C, Lee HS, Pappas GP, Dilling DF, Burger CD, Shifren A, Veeraraghavan S, Chapman JT, Parambil J, Ruoss SJ, Young LR, Hammes SR, Kopras EJ, Roads T, Krischer JP, **McCormack FX**; Trial of an Aromatase Inhibitor in Lymphangioleiomyomatosis Group. A Phase II Clinical Trial of an Aromatase Inhibitor for Postmenopausal Women with Lymphangioleiomyomatosis. Ann Am Thorac Soc. 2017 Jun;14(6):919-928. doi: 10.1513/AnnalsATS.201610-824OC. PubMed PMID: 28570161.

PUBLICATIONS *CONTINUED*

33 Sontake V, Wang Y, Kasam RK, Sinner D, Reddy GB, Naren AP, **McCormack FX**, White ES, Jegga AG, Madala SK. Hsp90 regulation of fibroblast activation in pulmonary fibrosis. JCI Insight. 2017 Feb 23;2(4):e91454. doi: 10.1172/jci.insight.91454. PubMed PMID: 28239659; PubMed Central PMCID: PMC5313067.

34 Lee LH, Gasilina A, Roychoudhury J, Clark J, **McCormack FX**, Pressey J, Grimley MS, Lorsbach R, Ali S, Bailey M, Stephens P, Ross JS, Miller VA, Nassar NN, Kumar AR. Real-time genomic profiling of histiocytoses identifies early-kinase domain BRAF alterations while improving treatment outcomes. JCI Insight. 2017 Feb

35 Krymskaya VP, **McCormack FX**. Lymphangioleiomyomatosis: A Monogenic Model of Malignancy. Annu Rev Med. 2017 Jan 14;68:69-83. doi: 10.1146/annurev-med-050715-104245. PubMed PMID: 28099079.

36 Itkin MG, **McCormack FX**, Dori Y. Diagnosis and Treatment of Lymphatic Plastic Bronchitis in Adults Using Advanced Lymphatic Imaging and Percutaneous Embolization. Ann Am Thorac Soc. 2016 Oct;13(10):1689-1696. PubMed PMID:27599255.

37 Kotloff RM, **McCormack FX**. Rare Lung Diseases: Occasionally the "Horse" Has Stripes. Clin Chest Med. 2016 Sep;37(3):xv-xvi. doi: 10.1016/j.ccm.2016.07.001. PubMed PMID: 27514604.

38 Saito A, **McCormack FX**. Pulmonary Alveolar Microlithiasis. Clin Chest Med. 2016 Sep;37(3):441-8. doi: 10.1016/j.ccm.2016.04.007. Epub 2016 Jun 24. Review. PubMed PMID: 27514591; PubMed Central PMCID: PMC4987712.

39 Itkin M, **McCormack FX**. Nonmalignant Adult Thoracic Lymphatic Disorders. Clin Chest Med. 2016 Sep;37(3):409-20. doi: 10.1016/j.ccm.2016.04.004. Review. PubMed PMID: 27514588.

40 Takada T, Mikami A, Kitamura N, Seyama K, Inoue Y, Nagai K, Suzuki M, Moriyama H, Akasaka K, Tazawa R, Hirai T, Mishima M, Hayashida M, Hirose M, Sugimoto C, Arai T, Hattori N, Watanabe K, Tamada T, Yoshizawa H, Akazawa K, Tanaka T, Yagi K, Young LR, **McCormack FX**, Nakata K. Efficacy and Safety of Long-Term Sirolimus Therapy for Asian Patients with Lymphangioleiomyomatosis. Ann Am Thorac Soc. 2016 Nov;13(11):1912-1922. PubMed PMID: 27513278.

41 Soleimani M, Barone S, Xu J, Alshahrani S, Brooks M, **McCormack FX**, Smith RD, Zahedi K. Prostaglandin-E2 Mediated Increase in Calcium and Phosphate Excretion in a Mouse Model of Distal Nephron Salt Wasting. PLoS One. 2016 Jul 21;11(7):e0159804. doi: 10.1371/journal.pone.0159804. eCollection 2016. PubMed PMID: 27442254; PubMed Central PMCID: PMC4956050.

42 Goh BC, Wu H, Rynkiewicz MJ, Schulten K, Seaton BA, **McCormack FX**. Elucidation of Lipid Binding Sites on Lung Surfactant Protein A Using X-ray Crystallography, Mutagenesis, and Molecular Dynamics Simulations. Biochemistry. 2016 Jul 5;55(26):3692-701. doi: 10.1021/acs.biochem.6b00048. Epub 2016 Jun 21. PubMed PMID: 27324153.

43 Sogbetun, F., W.L. Eschenbacher, J.A. Welge, **R.J. Panos**. Veterans Airflow Obstruction Screening Questionnaire (VAFOSQ): A Survey to Identify Veterans with Airflow Obstruction. Chronic Obstru Pulm Dis (Miami). 2016; 3(4):705-715.

44 Long-term Oxygen Treatment Trial Research Group (Richard Albert, David Au, Amanda Blackford, Richard Casaburi, J Allen Cooper, Jr, Gerard J Criner, Philip Diaz, Anne L Fuhlbrigge, Steven Gay, Richard Kanner, Neil MacIntyre, Fernando J Martinez, **Ralph J. Panos**, Steven Piantadosi, Frank Sciurba, David Shade, Thomas Stibolt, James K Stoller, Robert Wise, Roger Yusen, James Tonascia, Alice L Sternberg, and William Bailey). A Randomized Trial of Supplemental Oxygen Therapy for Chronic Obstructive Pulmonary Disease. N Engl J Med. 2016 May 29;370(22):2083-92.

45 Sogbetun, F., W.L. Eschenbacher, J.A. Welge, **R.J. Panos**. A Comparison of Five Surveys That Identify Individuals at Risk for Airflow Obstruction and Chronic Obstructive Pulmonary Disease. Respir Med. 2016 Nov; 120:1-9

46 Mulhall, AM, Zafar MA, Record S., Channell H, **Panos RJ**. A Tablet-Based Multimedia Education Tool Improves Provider and Patient Knowledge of Inhaler Use Techniques. Respir Care. 2017 Feb;62(2):163-171.

47 O'Shea AM, Vaughan Sarrazin M, Nassar B, Cram P, Johnson L, Bonello R, **Panos RJ**, Reisinger HS. Using electronic medical record notes to measure ICU telemedicine utilization. J Am Med Inform Assoc. 2017 Mar 31. doi: 10.1093/jamia/ocx029. [Epub ahead of print]

48 Zafar MA, **Panos RJ**, Gentene, A, Guido M, Ko J, Otten L, Clark K, Lee C, Robertson J, Alessandrini, E. "Reliable Adherence to a COPD Care Bundle Mitigates System-Level Failures and Reduces COPD Readmissions: A System Redesign Using Improvement Science". In press. BMJ Quality & Safety.

49 Zafar, M.A., Mulhall, A.M., Eschenbacher, W., Kaul, S., Benzaquin, S., **Panos, R.J.**, Application of Upper Airway Manometry to Measure Efficacy of Positive Expiratory Pressure Breathing Techniques in Excessive Dynamic Airway Collapse (EDAC). In revision Respir Care.

50 **Panos, R.J.**, Introduction and Definition of Chronic Obstructive Pulmonary Disease COPD. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

51 **Panos, R.J.**, Epidemiology and Economic Consequences of COPD. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

52 **Panos, R.J.**, COPD Is a Multi-Organ Disorder: Systemic Manifestations

53 **R.J. Panos** and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

PUBLICATIONS *CONTINUED*

54 **Panos, R.J.**, Sleep and COPD: The Overlap Syndrome. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

55 Panos, M.E. and **Panos, R.J.**, COPD's Effects on Psychosocial Functioning and Familial Interactions. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

56 **Panos, R.J.**, Management of Stable Chronic Obstructive Pulmonary Disease. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

57 **Panos, R.J.**, Integrating Supportive, Palliative, and End of Life Care for COPD. R.J. Panos and W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

58 Book: **Panos, R.J.** W.L. Eschenbacher, Eds. COPD Primer. February, 2016; DeGruyter. http://www.degruyter.com/view/product/468864.

59 Mulhall AM, **Rashkin MC**, **Pina EM**. Bilateral Diaphragmatic Paralysis: A Rare Complication Related to Endoscopic Ultrasound-Guided Celiac Plexus Neurolysis. Ann Am Thorac Soc. 2016 Sep;13(9):1660-2. doi: 10.1513/AnnalsATS.201603-190LE. PubMed PMID: 27627480.

60 Niehaus KL, Velasco N, **Rashkin M**, Brantly M, Hebbeler-Clark R, Trapnell BC. Alpha 1-Antitrypsin Pi MZ vs Pi ZZ: Ramifications of a Mistaken Identity. Poster presentation at the American Thoracic Society International Conference, May 2017

61 Hetzel M, Suzuki T, Hashtchin AR, Arumugam P, Carey B, Schwabbauer M, Kuhn A, Meyer J, Schambach A, Van Der Loo J, Moritz T, **Trapnell BC**, Lachmann N. Function and safety of lentivirus-mediated gene transfer for CSF2RA-deficiency. Hum Gene Ther Methods. 2017 Aug 30. doi: 10.1089/hgtb.2017.092. [Epub ahead of print] PubMed PMID: 28854814.

62 Beiko T, Janech MG, Alekseyenko AV, Atkinson C, Coxson HO, Barth JL, Stephenson SE, Wilson CL, Schnapp LM, Barker A, Brantly M, Sandhaus RA, Silverman EK, Stoller JK, **Trapnell B**, Charlie S. Serum Proteins Associated with Emphysema Progression in Severe Alpha-1 Antitrypsin Deficiency. Chronic Obstr Pulm Dis. 2017 Jul 15;4(3):204-216. doi: 10.15326/jcopdf.4.3.2016.0180. PubMed PMID: 28848932; PubMed Central PMCID: PMC5556912.

63 Mueller C, Gernoux G, Gruntman AM, Borel F, Reeves EP, Calcedo R, Rouhani FN, Yachnis A, Humphries M, Campbell-Thompson M, Messina L, Chulay JD, **Trapnell B**, Wilson JM, McElvaney NG, Flotte TR. 5 Year Expression and Neutrophil Defect Repair after Gene Therapy in Alpha-1 Antitrypsin Deficiency. Mol Ther. 2017 Jun 7;25(6):1387-1394. doi: 10.1016/j.ymthe.2017.03.029. Epub 2017 Apr 10. PubMed PMID: 28408179; PubMed Central PMCID: PMC5474959.

64 Kugathasan S, Denson LA, Walters TD, Kim MO, Marigorta UM, Schirmer M, Mondal K, Liu C, Griffiths A, Noe JD, Crandall WV, Snapper S, Rabizadeh S, Rosh JR, Shapiro JM, Guthery S, Mack DR, Kellermayer R, Kappelman MD, Steiner S, Moulton DE, Keljo D, Cohen S, Oliva-Hemker M, Heyman MB, Otley AR, Baker SS, Evans JS, Kirschner BS, Patel AS, Ziring D, **Trapnell BC**, Sylvester FA, Stephens MC, Baldassano RN, Markowitz JF, Cho J, Xavier RJ, Huttenhower C, Aronow BJ, Gibson G, Hyams JS, Dubinsky MC. Prediction of complicated disease course for children newly diagnosed with Crohn's disease: a multicentre inception cohort study. Lancet. 2017 Apr 29;389(10080):1710-1718. doi: 10.1016/S0140-6736(17)30317-3. Epub 2017 Mar 2. PubMed PMID: 28259484.

65 Young LR, **Trapnell BC**, Mandl KD, Swarr DT, Wambach JA, Blaisdell CJ. Accelerating Scientific Advancement for Pediatric Rare Lung Disease Research. Report from a National Institutes of Health-NHLBI Workshop, September 3 and 4, 2015. Ann Am Thorac Soc. 2016 Dec;13(12):385-393. PubMed PMID: 27925785; PubMed Central PMCID: PMC5291498.

66 Campo I, Luisetti M, Griese M, **Trapnell BC**, Bonella F, Grutters J, Nakata K, Van Moorsel CH, Costabel U, Cottin V, Ichiwata T, Inoue Y, Braschi A, Bonizzoni G, Iotti GA, Tinelli C, Rodi G; WLL International Study Group. Whole lung lavage therapy for pulmonary alveolar proteinosis: a global survey of current practices and procedures. Orphanet J Rare Dis. 2016 Aug 31;11(1):115. doi: 10.1186/s13023-016-0497-9. PubMed PMID: 27577926; PubMed Central PMCID: PMC5006612.

67 Suzuki T, **Trapnell BC**. Pulmonary Alveolar Proteinosis Syndrome. Clin Chest Med. 2016 Sep;37(3):431-40. doi: 10.1016/j.ccm.2016.04.006. Epub 2016 Jun 17. Review. PubMed PMID: 27514590.

68 Mucci A, Kunkiel J, Suzuki T, Brennig S, Glage S, Kühnel MP, Ackermann M, Happle C, Kuhn A, Schambach A, **Trapnell BC**, Hansen G, Moritz T, Lachmann N. Murine iPSC-Derived Macrophages as a Tool for Disease Modeling of Hereditary Pulmonary Alveolar Proteinosis due to Csf2rb Deficiency. Stem Cell Reports. 2016 Aug 9;7(2):292-305. doi: 10.1016/j.stemcr.2016.06.011. Epub 2016 Jul 21. PubMed PMID: 27453007; PubMed Central PMCID: PMC4982988.

69 Campo I, Luisetti M, Griese M, **Trapnell BC**, Bonella F, Grutters JC, Nakata K, Van Moorsel CH, Costabel U, Cottin V, Ichiwata T, Inoue Y, Braschi A, Bonizzoni G, Iotti GA, Tinelli C, Rodi G; WLL International Study Group. A Global Survey on Whole Lung Lavage in Pulmonary Alveolar Proteinosis. Chest. 2016 Jul;150(1):251-3. doi: 10.1016/j.chest.2016.04.030. PubMed PMID: 27396783.

70 Cummings KJ, Virji MA, Park JY, Stanton ML, Edwards NT, **Trapnell BC**, Carey B, Stefaniak AB, Kreiss K. Respirable indium exposures, plasma indium, and respiratory health among indium-tin oxide (ITO) workers. Am J Ind Med. 2016 Jul;59(7):522-31. doi: 10.1002/ajim.22585. Epub 2016 May 24. PubMed PMID:27219296; PubMed Central PMCID: PMC4915590.

PUBLICATIONS *CONTINUED*

71 Kleff V, Sorg UR, Bury C, Suzuki T, Rattmann I, Jerabek-Willemsen M, Poremba C, Flasshove M, Opalka B, **Trapnell B**, Dirksen U, Moritz T. Gene Therapy of βc-Deficient Pulmonary Alveolar Proteinosis (βc-PAP): Studies in a Murine in vivo Model. Mol Ther. 2008 Apr;16(4):757-764. doi: 10.1038/mt.2008.7. Epub 2016 Dec 8. PubMed PMID: 28178466.

72 Marina Holz, Adi Berman, Subrata Manna, Naomi Schwartz, Yardena Katz, Yang Sun, Catherine Behrmann, **Jane Yu**, Davis Plas, and Anya Alayev. ERRα regulates the growth of triple-negative breast cancer cells via S6K1-dependent mechanism. Signal Transduction and Targeted Therapy. Accepted [5/16/2017]

73 Xiangke Li*, Xiaolei Liu*, Linda Zhang, Chenggang Li, Erik Zhang, Wang Ma, Qingxia Fan‡ and **Jane J. Yu**.‡ Insulin growth factor binding protein 2 (IGFBP2) mediates the progression of lymphangioleiomyomatosis. Oncotarget. 2017; 8:36628-36638.

74 Na Li, Xiaolei Liu, Wang Ma, and **Jane J. Yu***, and Taiying Lu*. All-trans retinoic acid suppresses the angiopoietin-Tie2 pathway and inhibits angiogenesis and metastasis in esophageal squamous cell carcinoma. PLOS One. 2017;12(4):e0174555

75 Hilaire C. Lam, Christian V. Baglini, Alicia Llorente Lope, Andrey Parkhitko, Heng-Jia Liu, Nicola Alesi, Izabela A. Malinowska, Darius Ebrahimi-Fakhari, Afshin Saffari, **Jane J. Yu**, Ana Pereira, Damir Khabibullin, Barbara Ogorek, Julie S. Nijmeh, John M. Asara, William M. Oldham, Maria Diaz-Meco, Jorge Moscat, Carmen Priolo, Elizabeth P. Henske. p62/SQSTM1 cooperates with hyperactive mTORC1 to regulate glutathione production, maintain mitochondrial integrity and promote tumorigenesis. Cancer Res. 3/2017

76 Zhuan Lv*, **Jane J. Yu***, Wei-Jie Zhang, Li Xiong, Feng Wang, Li-Feng Li, Xue-Liang Zhou, Xin-Ya Gao, Xian-Fei Ding, Li Han, Ya-Fei Cai, Wang Ma, Liu-Xing Wang. Expression and functional regulation of stemness gene Lgr5 in esophageal squamous cell carcinoma. Oncotarget. (Online 1/29/2017) *Contribute equally.

77 Li C, Li N, Liu X, Zhang EY, Sun Y, Masuda K, Li J, Sun J, Morrison T, Li X, Chen Y, Wang J, Karim N, Zhang Y, Blenis J, Reginato M, Henske EP, and Yu JJ. Proapoptotic protein Bim attenuates estrogen-enhanced survival in lymphangioleiomyomatosis. JCI Insight. 2016;1(19):e86629. [Nov 17, 2016]

78 Goldberg AA, Joung KB, Mansouri A, Kang Y, Ecchevaria R, Baig S, Sun Y, **Yu J**, Schwertani A and Kristof AS. Oncogenic Effects of Urotensin-II in Cells Lacking Tuberous Sclerosis Complex-2. Oncotarget. 2016; 7 (38):61152-65. PMID: 27458154 [Sept 20, 2016]

79 Li J, Shin S, Sun Y, Yoon S, Li C, Zhang E, **Yu J**, Zhang J and Blenis J. mTORC1-driven tumor cells are highly sensitive to therapeutic targeting by antagonists of oxidative stress. Cancer Res. 2016;76(16):4816-27. PMID: 27197195 [Aug 15, 2016]

80 Klionsky DJ...**Yu J**... et al. Guidelines for the use and interpretation of assays for monitoring autophagy (3rd edition). Autophagy. 2016 12(1):1-222. ISSN: 1554-8627 (Print) 1554-8635 (Online) Journal homepage: http://www.tandfonline.com/loi/kaup20 PMCID: PMC4835977 [Jan 21, 2017]

81 Jiang Z, Lao T, Qiu W, Polverino F, Gupta K, Guo F, Mancini J, Cho M, Castaldi P, Sun Y, **Yu J**, Laucho-Contreras M, Kobzik L, Raby B, Choi AMK, Perrella M, Owen CA, Silverman E and Zhou X. A Chronic Obstructiove Pulmonary Disease Susceptibility gene, FAM13A, Regulates Stability of b-catenin. Am J Resp Crit Care Med. 2016; 194(2): 185-197. PMCID: PMC5003213 [July 15, 2016]

82 **Zafar MA**, Panos RJ, Ko J, Otten LC, Gentene A, Guido M, Clark K, Lee C, Robertson J, Alessandrini EA. Reliable adherence to a COPD care bundle mitigates system-level failures and reduces COPD readmissions: a system redesign using improvement science. BMJ Qual Saf. 2017 Jul 21. pii: bmjqs-2017-006529. doi:10.1136/bmjqs-2017-006529. [Epub ahead of print] PubMed PMID: 28733370.

83 Mulhall AM, **Zafar MA**, Record S, Channell H, Panos RJ. A Tablet-Based Multimedia Education Tool Improves Provider and Subject Knowledge of Inhaler Use Techniques. Respir Care. 2017 Feb;62(2):163-171. doi: 10.4187/respcare.05008.Epub 2016 Nov 15. PubMed PMID: 28108685.

84 Mastrodicasa MA, Droege CA, Mulhall AM, Ernst NE, Panos RJ, **Zafar MA**. Long acting muscarinic antagonists for the treatment of chronic obstructive pulmonary disease: a review of current and developing drugs. Expert Opin Investig Drugs. 2017 Feb;26(2):161-174. doi: 10.1080/13543784.2017.1276167. Epub 2017 Jan 9. Review. PubMed PMID: 28004591.

Reports

Active Awards June 2017 Department of Internal Medicine

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
CARDIO	Attari	1012669 / Recurrence of atrial fibrillation following non-cardio-thoracic surgery or acute medical illness	5/14/16 - 5/13/19	$ 20,000	$ 6,667
CARDIO	Becker	1012566 / 1011829 / CCHMC xxxxxx Sub AHA 15SFRN241100000 SHIP AHOY Project	4/1/2015 - 3/31/19	$ 339,658	$ 68,772
CARDIO	Becker	1012562 / 1011862-DUKE sub 5U54HL112307 Project 2	5/1/17 - 4/30/18	$ 30,788	$ 30,788
CARDIO	Becker	1012488 / 1012247 - Duke sub 2R01 HL065222-14A1-Anti-thrombotic Aptamers and Antidotes	9/1/15 - 3/31/20	$ 44,391	$ 7,078
CARDIO	DeMazumder	1013213 / Autonomic Remodeling and Modulation Therapy in Heart Failure and Sudden Death	2/1/17 - 1/31/20	$ 747,000	$ 249,000
CARDIO	Dunlap	1009098/Brigham & Women's Subaward 5R01HL091069	7/1/11 - 2/29/18	$ 26,450	$ 26,450
CARDIO	Haworth	1012816 / Ultrasound-mediated oxygen scavenging for inhibition of reperfusion injury	8/1/16 - 6/30/21	$ 630,964	$ 156,799
CARDIO	Holland	1011436/2R01NS047603-9- Ultrasound Assisted Thrombolysis	8/15/14 - 7/31/19	$ 2,764,157	$ 545,685
CARDIO	Holland	1012925 / NS047603-11S1- Mercado Diversity Supplement	8/1/16 - 7/31/19	$ 172,514	$ 86,257
CARDIO	Holland	1013431 / Echogenic Targeted Liposomes: Transfectin/Drug Delivery	9/1/17 - 8/31/22	$ 1,420,596	$ 285,513
CARDIO	Owens	1011730/4R00HL116786-03	3/15/13 - 2/28/18	$ 735,572	$ 241,397
CARDIO	Rubinstein	1011578/R01ES024744 Puga	10/11/14 - 10/31/19	$ 2,417,354	$ 110,430
CARDIO	Rubinstein	1010831/DHHS-R21 ES023319-02	8/29/13-7/31/17	$ 110,992	$ 38,485
CARDIO	Rubinstein	1012408/ Development of IV Probenocid	2/1/16 - 7/30/17	$ 117,301	$ 117,301
CARDIO	Rubinstein	1013168 / TRPV2agonism for Improved Cardiac Function in Patients with Single Ventricle Physiology	1/1/17-12/31/18	$ 125,400	$ 77,000
CARDIO	Sadayappan	1012990 / Umass Sub R01 AR067279- Sketal myosin-binding protein C	8/15/16 - 6/30/17	$ 16,337	$ 16,338
CARDIO	Sadayappan	1013068 / Molecular mechanism of hypertrophic cardiomyopathy in populations of South Asians descendants	8/15/16 - 12/31/19	$ 1,356,218	$ 405,408
CARDIO	Sadayappan	1013101 / Cardiac Mosin Binding Protein-C: Structure and Function	12/1/16 - 2/28/20	$ 1,513,006	$ 391,511
CARDIO	Sadayappan	1013065 / K02 Proteomic approaches to validate novel cardiac biomakers for myocardial infarction	8/15/16 - 7/31/17	$ 186,361	$ 186,361

***** NOA Project Period Award Amount
† NOA Current Budget Period

CONTINUED

ACTIVE AWARDS JUNE 2017 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
CARDIO	Sadayappan	1013430 / A novel polymorphic MYBPC3 variant causes hypertrophic cardiomyopathy in US0South Asian descendants	5/1/17 - 4/30/18	$ 254,136	$ 254,136
CARDIO	Sadayappan	1012970 / AHA transfer from Loyola	8/15/16 - 11/30/16	$ 75,155	$ 75,155
CARDIO	Tranter	1012547 / Investigation of Human Antigen R (HuR) as a Novel Mediator of Cardiac Hypertrophy	7/1/16 - 3/31/21	$ 1,777,500	$ 355,500
CARDIO	Tranter	1013161 / Accelerator Grant	12/1/16 - 12/1/17	$ 20,000	$ 20,000
DIGEST	Abdel-Hameed	1012373 /Evaluating changes in Host-Immune Response during HCV Therapy in Cirrhotic Patients	12/1/15 - 9/30/17	$ 25,000	$ 25,000
DIGEST	Bari	1012802 / A Pilot Study to Evaluate the Safety and Efficacy of Budesonide as an Alternative to Prednisone for Liver Transplant Immune Suppres-sion	7/1/16 - 6/30/17	$ 10,000	$ 10,000
DIGEST	Blackard	1011103 / 1010456 - R01 GM105414	5/2/13 - 4/30/18	$ 1,496,850	$ 299,434
DIGEST	Kaiser	1012910 / Novel Medication Adherence Monitoring Strategies utilizing Technology to Trigger Patient Specific Adaptive Adherence Interven-tions in Renal Transplant Recipients	7/1/16 - 6/30/17	$ 14,000	$ 14,000
DIGEST	Sherman	1012142-Ultra-deep Sequencing of NS5A Resistance Variants in HCV/HIV Coinfected Patients	9/1/15 - 5/10/18	$ 78,073	$ 78,073
DIGEST	Sherman	1012223-Hepatitis E in HIV-Infected Patients	9/23/15 - 8/31/20	$ 1,374,995	$ 274,999
DIGEST	Sherman	1012602 / 1012513-FIU 800005519-01UG/DA040381	8/1/15 - 7/31/20	$ 1,065,268	$ 161,007
DIGEST	Sherman	1012450-HIV Antiretroviral Therapy and Hepatic Injury	2/15/16 - 1/31/21	$ 1,849,870	$ 549,499
DIGEST	Sherman	1012724/ The Prioritize study: PCORI	3/1/16 - 2/28/21	$ 258,209	$ 57,402
DIGEST	Sherman	1013140 / 1012673/Prevalence of Significance of PNPLA3 Gene Polymorphisms in HCV/HIV infected Persons	6/1/16 - 11/30/17	$ 70,546	$ 38,587
DIGEST	Sherman	1012983 / Admin supplement to R01DK108362	4/1/16 - 3/31/17	$ 40,000	$ 40,000
DIGEST	Sherman	1013343/ Timing of Treatment for Chronic Hepatitis C Infection in Patients with End Stage Rengal Disease Awaiting Trans	4/15/17 - 4/14/19	$ 96,149	$ 96,149
DIGEST	Yacyshyn, Bruce	1012080 - Cubist	8/4/15 - 2/28/18	$ 193,081	$ 193,081

***** NOA Project Period Award Amount
† NOA Current Budget Period

CONTINUED

ACTIVE AWARDS JUNE 2017 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
DIGEST	Yacyshyn, Bruce	1013479 / Gene discoveries in subjects with crohn's disease of african descent	9/1/16 - 7/31/21	$ 30,000	$ 2,600
DIGEST	Yacyshyn, Bruce	1013317 / Comparative effectiveness of specific carbohydrate and mediterranean diets to induce remission in patients with crohns disease	3/20/17 - 3/19/20	$ 25,800	$ 8,600
ENDOCR	Cohen	1012844 (Yr 5)/1012028 (Yr 4)/1011388 (Yr 3) /1010749 (Yr 2) / 1010368 (Yr 1) - GRADE	1/1/12 - 7/31/20	$ 2,054,669	$ 190,186
ENDOCR	Cohen	1012554 / GWU GRADE sub R01DK104845	9/1/15 - 3/31/20	$ 221,585	$ 44,297
ENDOCR	Falciglia	1012315/1011348 - Falciglia Sub University of Virginia SHINE	8/1/14 - 7/31/18	$ 8,000	$ 2,000
ENDOCR	Patel	1012792 / Identifying novel drug targets for Obesity and Metabolic Diseases	6/1/16 - 8/31/17	$ 55,000	$ 1,000,000
ENDOCR	Perez-Tilve	1013151-Novo Nordisk	1/1/17 - 12/31/17	$ 1,000,000	$ 1,000,000
ENDOCR	Perez-Tilve	1013205 /CohBar agreement 2017	1/1/17 - 12/31/17	$ 377,215	$ 377,215
ENDOCR	Winnick	1013196 / Effect of liver glycogen content on hypoglycemic counterregulation	9/1/16 - 5/31/21	$ 1,806,944	$ 335,465
ENDOCR	Wortman	1013150 / Targeting Brain Metabolism to Improve Cognitive Impairment	9/1/16-8/31/17	$ 50,000	$ 50,000
GEN	Martin	1013209 / Determining the optimal treatment strategy for patients who have chronic migraine with medication overuse	5/1/16 - 4/30/21	$ 212,364	$ 41,721
GEN	Schauer	1010970-Impact of Bariatric Surgery on Cancer Incidence Patients	3/1/14 - 2/28/18	$ 1,998,718	$ 629,199
HEM	BOGDANOV	1012102-1011805 - 1 R01 CA190717-01Alternatively Spliced Tissue Factor and Pathobiology of Pancreatic Cancer	4/9/15 - 3/31/20	$ 1,396,170	$ 248,667
HEM	DONG	1006682 - NSF sub	09/01/08 - 8/31/18	$ 1,200,000	$ 150,000
HEM	HASHEMI	1011944-HNCF-Pharmacogenomic Profiling of Circulating Tumor Cells to Guide Head and Neck	7/1/15 - 6/30/17	$ 20,000	$ 20,000
HEM	MERCER	1011874-R21CA191814-01A1	6/1/15 - 5/31/18	$ 406,316	$ 184,663
HEM	Morris	1011153 / SWOG Purchase Service Agreement	6/9/14 - 6/30/20	$ 464,490	$ 122,821
HEM	PALASCAK	1012909 / 1012312/1011659 / 1010330/ 1011222/ 1011659-HFM/CDC	9/30/16 -9/29/17	$ 18,000	$ 18,000
HEM	PALASCAK	1012610 / 1011826/1009394/ 1011157/ 1010442-HFM	6/1/17 - 5/31/18	$ 69,161	$ 69,161

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CONTINUED

ACTIVE AWARDS JUNE 2017 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
HEM	PALASCAK	1012611 / 1011915 / 1011317-Cascade Home Svc	6/1/17 - 5/31/18	$ 10,000	$ 10,000
HEM	PALASCAK	1012612 / 1011917 / HFM Cascade Pilot Prog	6/1/17 - 5/31/18	$ 20,000	$ 20,000
HEM	QI	1009291 - R01 CA158372-03	09/27/11 - 7/31/17	$ 1,640,857	$ 325,282
HEM	QI	1012136- Intravenous Enzyme Replacement Therapy for CNS Disorders	8/31/15 - 8/30/17	$ 447,075	$ 196,625
HEM	SASAKI	1011482-1 R01NS089815-01	9/30/14 - 8/31/19	$ 1,670,215	$ 334,827
HEM	SASAKI	1012868 / Synthetic Lethal Combination of KRP203/ Fingolimod with PI3K signaling for glioblastoma multiforme death by catastrophic vacuolization	9/1/16 - 8/31/18	$ 448,208	$ 251,104
IMMUNO	BERNSTEIN, D	1012869 / 1012019/1005596/ 1010751/1011196-R01 OH 008795-04-06	9/1/06 - 8/31/17	$ 1,642,007	$ 360,717
IMMUNO	BERNSTEIN, D	1012740 / 1011860/1009656/ 1010499/ 1011351-T32 AI060515-09-11	9/1/04 -8/31/19	$ 1,361,995	$ 283,510
IMMUNO	BERNSTEIN, J	1012858/ 1011380-sub 2U44AI074918-02	7/10/14 - 7/31/17	$ 487,231	$ 59,475
IMMUNO	FINKELMAN	1011267 - FARE	7/22/14 - 09/30/17	$ 734,986	$ 246,426
IMMUNO	FINKELMAN	1011228 - 1 R01 AI113162-01	7/15/14 - 6/30/18	$ 1,334,589	$ 332,266
IMMUNO	Finkelman	1012921 / Administrative Supplement to 5R01AI113162	7/1/16 - 6/30/17	$ 100,000	$ 100,000
IMMUNO	Finkelman	1013344 / IL-9 producing Mast Cell Precursors and Food Allergy	9/30/16 - 9/29/17	$ 11,634	$ 11,634
IMMUNO	Finkelman	1013239 / Wimpy antibody isotypes protect against antibody-mediated disease	1/25/17 - 12/31/21	$ 1,833,210	$ 371,845
IMMUNO	RIDGWAY	1012836 / 1011903/1011320-UC Davis/dnTGF Beta RII Mice and PBC-COMPETITIVE RENEWAL	8/11/14 - 6/30/18	$ 916,511	$ 230,000
IMMUNO	Ridgway	1013132 / 1012461-MCW/ ADA-Mechanistic role and therapeutic potential of CD137 in T1D	1/1/16 - 12/31/17	$ 155,100	$ 51,700
IMMUNO	Ridgway	1013504 / 1012808 / Mechanistic and Therapeutic Role of the CD137-CD137L	7/21/16 - 5/31/21	$ 1,301,359	$ 280,578
IMMUNO	Shao	1013143 / A critical role of TAM receptors in autoimmune nephritis	12/1/16 - 11/30/17	$ 129,319	$ 129,319
INFECT	Cushion	1010974/1010504 Metatranscriotimics HL119190	5/22/13-2/28/18	$ 1,156,482	$ 371,622
INFECT	Cushion	1011916-St. Jude sub AI070271	7/1/12 - 6/30/17	$ 141,310	$ 51,966
INFECT	Cushion	1012453 / 1011904-3R01 HL119190 -03S1-Directed Culturing of Pneumocystis Using Metatranscriptomi.	7/1/15 - 2/28/18	$ 43,259	$ 43,259

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CONTINUED

ACTIVE AWARDS JUNE 2017 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
INFECT	Cushion	1012856 / Development of a new system for scaled up culture and propagation of Pneumocystis	7/1/16 - 6/30/18	$ 231,607	$ 119,670
INFECT	Cushion	1012928 / SUNY 73370 Sub R01	8/1/16 - 11/30/20	$ 99,815	$ 58,951
INFECT	Cushion	1013291 /Task Order A106: Therapeutics esting in Murine Model of Pneumocytosis Pneumonia	3/20/17 - 8/19/17	$ 219,205	$ 219,205
INFECT	Deepe	1011024 / 1010447 5R01AI106269-02	5/15/13-4/30/18	$ 2,334,463	$ 462,463
INFECT	Deepe	1010697 UMASS SUB	8/6/2013-7/31/2017	$ 739,938	$ 184,984
INFECT	Deepe	1012686-Dendritic cell KLF2/ Notch Axis and Th2 Responses to Eukaryotic Pathogens	6/10/16 - 5/31/21	$ 2,292,933	$ 496,000
INFECT	Fichtenbaum	1012968 / A Randomized Double-Blind, Phase 3 Study Comparing the Efficacy and Safety of High-Titer versus	6/20/16-9/30/17	$ 15,600	$ 15,600
INFECT	Fichtenbaum	1011846/1011413 Reprieve Site Selection Committee	8/8/14-4/30/2020	$ 111,045	$ 12,436
INFECT	Fichtenbaum	1011401 ACTG Protocol Funds for all "A" protocols	1/1/14-11/30/2020	$ 1,721,971	$ 267,649
INFECT	Fichtenbaum	1013188- BWH sub AI68636 Protocol Funds ACTG	12/1/14 - 11/30/2020	$ 2,349,648	$ 391,608
INFECT	Fichtenbaum	1013182-REPRIEVE Co-Chair	12/1/16 - 11/30/17	$ 15,880	$ 15,880
INFECT	Fichtenbaum	1011786-MGH 225707 1U01HL023336-02 REPRIEVE A5332 and A5333	8/8/14 - 4/30/2021	$ 627,150	$ 150,000
INFECT	Fichtenbaum	1013099-CWRU RES510456 SUB AI69501 - renewal	12/1/16 - 11/30/17	$ 380,642	$ 380,642
INFECT	Fichtenbaum	1013166-ACTG Scientific Agenda Steering Committee (SASC) Support	12/1/16 - 11/30/17	$ 12,000	$ 12,000
INFECT	Fichtenbaum	1012651 / HPTN 083: A phase 2b?3 double blind safety and efficacy study of injectable cabotegravir compared to daily oral tenofovir	12/1/16 - 11/30/17	$ 39,660	$ 39,660
INFECT	Fichtenbaum	1012586 / Randomized trial to prevent vascular events in HIV (REPRIEVE)	5/1/16 - 4/30/20	$ 50,444	$ 12,221
INFECT	Fichtenbaum	1013130 / Effect of pitavastatin on kidney function in HIV-infected person REPRIEVE kidney study	7/1/16 - 6/30/17	$ 35,425	$ 35,425
INFECT	Fichtenbaum	1013453 / HPTN 083 is a Phase 2b/3 Safety and Efficacy Study of Injectable Cabotegravir Compared to Daily Oral Tenofovir Disoproxil Fumarate/ Emtricitabine (TDF/FTC), for Pre-Exposure Prophylaxis	1/1/17 - 11/30/22	$ 3,599,441	$ 587,796

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CONTINUED

ACTIVE AWARDS JUNE 2017 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
INFECT	Kaul	1012677 / 1012148-MAETC 2015-2016	7/1/16 - 6/30/17	$ 184,741	$ 184,741
INFECT	Madan	1011574-7 K08 AI108801	8/1/14 - 7/31/19	$ 704,232	$ 176,058
INFECT	Robertson	1013322/1012460/1011782/ 1011016-CHN Ryan White 5H76HA0011-20-00	4/1/14 - 3/31/2018	$ 697,867	$ 697,867
INFECT	Subramanian	1011877-AHA 15POST25700182	7/1/15 - 6/30/17	$ 91,000	$ 45,500
NEPH	Abu Jawdeh	1013450 / Investigating Comoliment-Split Products as Potential Biomarkers for Antibody-Medicated Rejection in Renal Allografts	4/1/17 - 3/31/18	$ 25,000	$ 25,000
NEPH	Alloway	1010884/FDA HHSF223201310224	9/26/13 - 5/05/17	$ 2,250,981	$ 2,250,981
NEPH	Amlal	1013439 / Possible Role of Gluamine Transport and Metabolism in the Development	4/1/17 - 3/31/18	$ 25,000	$ 25,000
NEPH	Conforti	1011985 /2 R01CA095286-10	7/1/15 - 6/30/20	$ 1,498,123	$ 303,455
NEPH	Conforti	1013178 /Targeted Nanoparti-cle-based therapy in SLE	2/1/17 - 1/31/18	$ 60,000	$ 60,000
NEPH	Conforti	1012713 / Tumor microenviron-ment and immune therapies	7/1/16 - 6/30/17	$ 6,000	$ 6,000
NEPH	Thakar	1012777/ ISCHEMIA clinical trial-CKD study	3/1/16 - 2/28/18	$ 75,630	$ 75,630
NEPH	Thakar	1012776/ ISCHEMIA clinical trial-Main study	3/1/16 - 2/28/18	$ 91,290	$ 91,290
NEPH	Thakar	1013238 / Hyponatremia, congestive heart failure, and kidney disease: a vital connection	10/20/16 - 10/19/21	$ 70,000	$ 70,000
NEPH	Thakar	1313452 / Stability Study for NGAL	4/1/17 - 3/31/19	$ 215,467	$ 107,734
PULM	Baughman	1012755 / 1011957-VUMC 42525 1R01HL117074-03	7/1/16 - 6/30/17	$ 111,840	$ 111,840
PULM	Baughman	1011898 / fdn for Sarcoidosis Res/FSR-CSN	4/1/15 - 10/31/17	$ 60,000	$ 30,000
PULM	Borchers	1011007/R01 HL119538-01A1	4/1/14 - 3/31/18	$ 1,581,563	$ 395,000
PULM	Elwing	1012454 / CCHMC 137829 R21HL 105333-05	3/3/12 - 2/28/18	$ 95,000	$ 15,060
PULM	Gupta	1012848 / 1012472-Improving Intensive Care Patient Safety Through EHR-based Algorithms	9/1/15 - 8/31/19	$ 110,332	$ 20,301
PULM	Hudock	1012324-PBF Fellowship Hudock Uncovering Mecha-nisms of Lung Injury in CF	10/5/15 - 12/31/17	$ 131,000	$ 82,962
PULM	Hudock	1012973/ 1012443 / CFF Hudock15IO	10/1/15 - 9/30/17	$ 108,000	$ 54,000
PULM	Indihar	1013361 / 1012969 / A CF C3N Care Model of the Future: Proposal for Piloting a Learning Health System	7/1/16 - 12/31/17	$ 45,000	$ 30,000

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CONTINUED

ACTIVE AWARDS JUNE 2016 *CONTINUED*

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
PULM	Joseph	1013136 /1012329/1011765 / CFF Transforming CF Care Through Shared Decision Making (QI)	1/1/15 - 12/31/17	$ 276,488	$ 92,434
PULM	McCormack	1011731/1R01HL127455-01	4/1/15 - 3/31/19	$ 2,593,162	$ 394,535
PULM	McCormack	1012804 / 1011990 / 1011548/ HL127672 RLDC Admin Unit	9/18/14 - 7/31/19	$ 216,656	$ 40,605
PULM	McCormack	1012805 / 1011989/1011549/ HL12762 RLDC Project 1	9/18/14 - 7/31/19	$ 476,052	$ 88,339
PULM	McCormack	1012874 / 1012055/1010758/ Baylor Subaward UH2TR00961	9/1/16 - 8/31/17	$ 74,796	$ 74,796
PULM	McCormack	1013210 / 1012358 / 1011608 Shriners	1/1/13 - 12/31/17	$ 439,352	$ 111,663
PULM	McCormack	1012851 / RLDC: Multicenter International durability and safety of sirolimus in LAM trial (MIDAS)	8/1/15 - 7/31/17	$ 23,568	$ 23,568
PULM	McCormack	1013010 / Multicenter Interventional Lymphangioleio-myomatosis Early Disease Trial (MILED)-CCC	9/20/16 - 8/31/21	$ 3,606,817	$ 752,151
PULM	McCormack	1012803 / 2016 LAM Founda-tion International Lymphangi-oleiomyomatosis Research Conference	7/1/16 - 6/30/17	$ 25,000	$ 25,000
PULM	McCormack	1012879 / CCHMC-Integrative analysis of multi-omics data to target fibroblast activation in IPF	7/5/16 - 6/30/18	$ 38,371	$ 18,962
PULM	McCormack	1013112 / The molecular and genetic pathogenesis of LAM	9/21/16 - 8/31/19	$ 331,800	$ 110,600
PULM	McCormack	1013505 / CCHMC-WT1 regulation of pylmnary fibrosis	5/22/17 - 4/30/22	$ 249,481	$ 49,896
PULM	Norton	1012550 / 1011868/ 1011505/ CCLCM-CWRU/U54HL123023-01 PETAL	6/17/14 - 4/30/21	$ 181,231	$ 29,299
PULM	Norton	1012421-Reevaluation of Systemic Early neuromuscular blockade (ROSE)	11/17/15 - 4/30/18	$ 66,526	$ 66,526
PULM	Yu	1013175 / 1012306-Cornell 16050776 / R01 HL121266-03-	1/1/16- 12/31/17	$ 64,917	$ 32,704
PULM	Yu	1012220-7 R01 HL098216-06 Targeting the Estrogen Pathway Prevention & Treat of LAM-NCE	7/1/15- 3/31/18	$ 178,744	$ 178,744
PULM	Yu	1012103-7R01DK098331-02	7/1/15 - 6/30/17	$ 510,340	$ 289,140

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Annual Research Report (ARR) Committee

Top row, Left to right:
Kelly Niederhausen, Chandra DuBose

Bottom row, left to right:
Angie Duke, Leah Bischoff,
Yolanda Wess, Elizabeth Kopras

ARR Admin Team

Top, left to right:
Leah Bischoff, Melissa Dancy,
Chandra DuBose, Shakeith Lawson

Front row, left to right:
Priscilla Schmidt, Angela Duke,
Connie Adkins, Chris Salyers

Not pictured: Gayle Pollack

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COLLEGE OF MEDICINE

William S. Ball, MD
Senior Vice President for Health Affairs
Christian R. Holmes Professor and Dean,
College of Medicine

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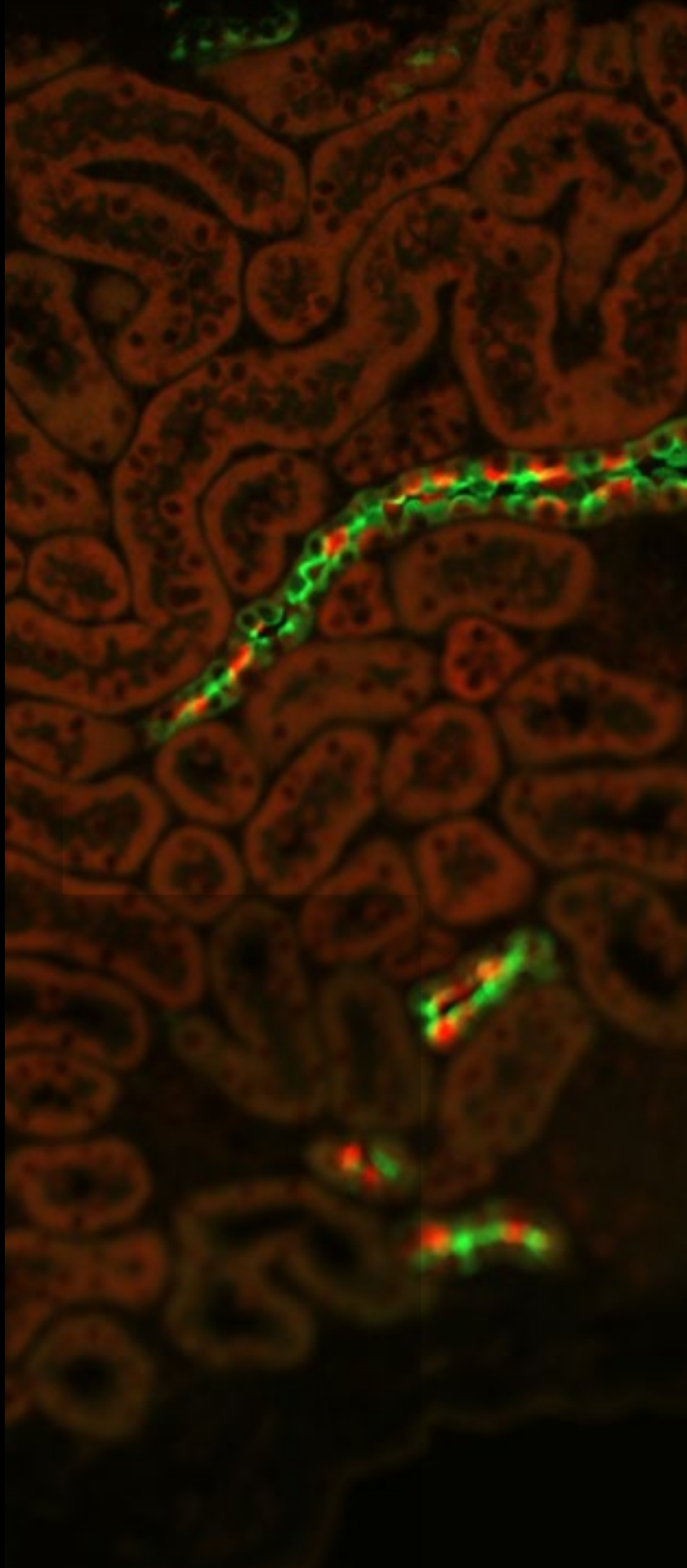

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