University of Cincinnati Department of INTERNAL MEDICINE



# Annual Research Report Academic Year 2019-2020

**DEPARTMENT OF INTERNAL MEDICINE** 

# **TOTAL GRANTS**



155 17 percent are held by primary investigators with R01 awards

# **TOTAL RESEARCH FUNDING** \$93.9 million

VETERANS AFFAIRS INVESTIGATORS FUNDING \$10.5 million



CLINICAL TRIAL REVENUE (FY2020) \$5.9 million

**INCREASE IN TOTAL FUNDING** (from FY2019 to FY2020) 5.5%

# SUCCESS RECEIVING FUNDING (FY2020) **29%**

#### IMAGE, FRONT COVER:

#### I'd Like to Place a Long Distance Call

Human induced pluripotent stem cells (iPSC) give researchers a powerful opportunity to investigate novel cellular dynamics and to apply fundamental knowledge gained towards translational science. Our brains are derived from a complex network of neuronal and glial cells. Cells that when they weave together in just the right manner can create one of the most powerful entities in the world, the mind. Depicted here is a collection of iPSC derived ectoderm showing Nestin (red), F-actin (cyan) and MAP2+ (green) cells constructing telecommunication lines between neighbors. 2020 Image Gallery awardee, Basic Research

CREDIT: Andrew Dunn, PhD, Research Fellow, Gastroenterology

# Annual Research Report ACADEMIC YEAR 2019-2020

Welcome From the Chair	2
Since 2011, our strategic plan in the Department of Internal	
Medicine has prioritized our research mission.	

# Impact

Year at a Glance	10
Drake Medalist	15
Funding	16
RISE-UC: Academic Research Services	20

# **Discover and Innovate**

Cardiovascular Health and Disease Division	25
Digestive Diseases Division	33
Endocrinology, Diabetes and Metabolism Division	39
General Internal Medicine Division	43
Hematology Oncology Division	49
Immunology, Allergy and Rheumatology Division	55
Infectious Diseases Division	65
Nephrology, Kidney CARE Program Division	71
Pulmonary, Critical Care and Sleep Medicine Division	77

# **Mentor and Support**

Emerging Researchers	
Office of the Chair	
RGC, ARS and UCRRL	

# Reports

Active Awards	
New Awards FY 2019-20	
Acknowledgements	

# Welcome from the Chair



We are privileged to provide the 2019–2020 edition of the Department of Internal Medicine Annual Research Report. In keeping with the strategic plan implemented in 2011, we are most pleased with the past and ongoing successes of our department and especially the accomplishments of our clinician scientists, basic scientists and clinical outcomes researchers over this past year. We continue to develop, mentor and support our residents, fellows, doctoral and post-doctoral students, junior and unquestionably our senior faculty to allow them to succeed. Those individuals recruited over the past year are maturing with support from department infrastructure and are showing evidence of successful academic research career development with impactful publication and major external awards. Our department's supportive offerings and constructs are not only carefully aligned with our UC College of Medicine initiatives and offerings and the UC Health system, but also the Cincinnati Veterans Administration Medical Center (VAMC) and the Cincinnati Children's Hospital Medical Center.

Since 2011 our research programs have grown annually by 6 - 14%. Our current research holdings at the end of June 2020 were over \$93 million. At the time of this printing (mid-FY21), the department's research holdings are now in the range of \$110 million. Our Academic Research Services (ARS) program is led by Kelly Niederhausen, Yolanda Wess and Eric Smith, MD. These individuals and others in the ARS program directly contributed to the successes of many of our research faculty this year, and in years past. Our departmental intramural awards system led by the Research Associate Chairs, Peter Clayton and his team supports bridge funding, junior and senior investigator awards. The success of

Annual Resear

our Internal Medicine Scholarly Training for Academic Research (IMSTAR) program has been unprecedented. We have just learned that our department is one of 19 in the nation now funded by the R38 training initiative called Stimulating Access to Research in Residency (StARR) to even further enhance and support internal medicine residents in their research-oriented academic careers. Other institutions receiving this designation include Duke, Columbia, Emory, University of California-San Francisco, Vanderbilt, University of Pennsylvania, Stanford University and Massachusetts General Hospital to name a few. This new initiative will build upon our Physician Scientist Training Program (PSTP) and the categorical training program that focuses on training in the translational sciences and scholarly, peer-reviewed publications during the second year of residency.

In June, 2020 the department held 155 total grants. This does not include \$5.9 million in clinical trial revenue nor the over \$10.5 million dollars awarded to our investigators at the Cincinnati VAMC. Forty-four of these were new grants with \$14.5 million in direct awards. Approximately 17% of those where R01 awards to PIs in the department. These significant outcomes reflect our successes since 2011 and have resulted in unprecedented yearly growth in the department's research holdings.

It has indeed been most rewarding for me to see the successes of our research faculty and how our strategic departmental research infrastructure has supported them. We will soon be transitioning to new departmental chair leadership. This transition will allow us to succeed even further over the next 3-5 years based upon additional resources to recruit established physician scientists. We are most grateful to our associate chairs for basic and translational research Sakthi Sadayappan, PhD, MBA and Carl Fichtenbaum, MD, respectively. Our new chair will very much benefit from the expertise of the two of them and our ARS personnel during this transition. With their support, this new leadership will be well served in continuing our discovery mission in the upcoming years.

### **GREGORY ROUAN, MD**

CHAIR, DEPARTMENT OF INTERNAL MEDICINE

It has indeed been most rewarding for me to see the successes of our research faculty and how our strategic departmental research infrastructure has supported them. We will soon be transitioning to new departmental chair leadership. This new leadership will be well served in continuing our discovery mission in the upcoming years.

# From the Associate Chair for Translational Research

University of Cincinnati

Annual Research Report 2020

# Preparing for Transition: Building the Research Mission

Life has many moments of transition and renewal. These are times when one can reflect and consider new ideas. As we move in 2021, our Department will have a transition of leadership. This will present opportunities and challenges. It is a time when we can ask ourselves what should we be doing to build our research mission?

This past year has been very challenging for our research mission and researchers. We have endured closing many aspects of our research and trying to navigate through a devastating pandemic. Despite many challenges, our resilience has prevailed, and our researchers continue to contribute to the emerging body of knowledge. There are many examples but just to highlight a few our faculty have obtained new grants including several career development awards. Drs. Apewokin, Lynch and Shah received K23 awards in the past year. Recently, we learned that Drs. Jose and Gulati earned a CT2 and KL2 awards, respectively. New awards came to Drs. Blackard, Cohen, DeMazumder, and Sadayappan. And, Drs. Rubinstein, Sadayappan and Schauer received an R38 training award. These recent successes highlight the talent within our Department.

This past year has also presented some opportunities in Covid research with members of our Department leading the way in building a Biorepository for Covid Research, Epidemiologic Research Studies, Treatment studies and Vaccine studies. Some of the investigators leading the way in our Department include Drs. Fichtenbaum, Huaman, Hudock, Hite and Powers. And we'd be remiss not to thank the staff, particularly in the Pulmonary and Infectious Diseases Divisions, that have given countless hours in making these new studies possible and bringing hope to our community. These efforts have increased the prominence of our institution within the community and the nation.

The Research Leadership and Research Governance Committee is spearheading an effort to review our strategic research planning. This moment is a time for us to build consensus on research priorities and share our ideas with the incoming Chair of the Department in 2021. This will aid a new leader to better understand our strengths and weaknesses.

Our strategic research plan should aim to propel our Department to the next level. Over the next 3-5 years we need to increase the number of funded researchers, build, and prepare new research mentors and enhance our training for the next generation of researchers. We must build on our strengths and look for new areas that demand research and scholarship. We must also improve our diversity and leadership in research by women and underrepresented populations. We have created the conditions for research success within our Department. Now we must think big and chart a course that will help aid discovery and build our Department's research portfolio. Together, this is a goal we can achieve.

CARL FICHTENBAUM, MD

ASSOCIATE CHAIR FOR TRANSLATIONAL RESEARCH

Despite many challenges, our resilience has prevailed, and our researchers continue to contribute to the emerging body of knowledge.

# From the Associate Chair for Basic Research

University of Cincinnati

Annual Research Report 2020

# **Building the Research Mission: New Opportunities**

How did DOIM support researchers during the pandemic crisis? By February and March of 2020, COVID-19 had become a worldwide threat to human health and the economy. Even before the state of Ohio announced a lockdown, the UC College of Medicine (COM) was working with Department of Internal Medicine (DOIM) Co-Chairs to develop COVID-19 lab disaster plans. Faculty and staff were asked to work from home beginning March 16, 2020, and all in-person activities were cancelled. In close collaboration with the COM, researchers were eventually allowed to perform critical studies. Labs and clinical researchers were able to slowly reopen research capacity, going from 25%, 50% and then 100%, by strictly following CDC COVID-19 guidelines. During this time, the Academic Research Services Office and the department Co-Chairs worked together tirelessly to review and approve lab reopening forms in a timely manner, guiding researchers through new COVID-19 policies. Although the entire country was under a state of emergency, the research mission of DOIM was never abandoned. Animal facilities continued to be monitored, and shipments and core facilities were allowed to provide full support to researchers. Critical clinical research continued and Grand Rounds, Research Conferences and meetings were moved to virtual mode and managed very effectively during this time. The first duty of DOIM was protection of researchers and participants engaged in research during the early phase of the pandemic.

What are new opportunities for research in DOIM in the FY 2020-21? The DOIM is undergoing a rapid transition with the hiring of a new department chair in the upcoming year. The addition of more resources and facilities and the hiring of more basic and clinical researchers will be priorities. The role of the Academic Research Service has expanded with the addition of Research Financial Services (RFS). RFS will provide clinical research study oversight and budget review to facilitate and grow clinical research in the department. The Research Governance Committee has formed several subcommittees, including Strategic Research, Mentoring, and Gender Equity subcommittees. These subcommittees will be fully active in the new year and will improve workflows and communication, as well as increase knowledge of and compliance with regulations and policies. Lastly, we expect that a vaccination program, combined with continuing attention to CDC guidelines, will allow us to resume our regular research routines next year. Thus, the future looks bright with new opportunities for basic and translational research in DOIM, so please stay tuned.

As DOIM Vice Chair of Basic Research, my responsibilities are to strengthen basic and translational research through advanced facilities, state-of-theart technologies, active collaborations between basic and clinical scientists, teamwork to foster innovation and discovery, in addition to advancing our understanding of human biology with the aim of treating deadly diseases, developing therapeutic strategies, and performing preclinical studies.

> SAKTHIVEL SADAYAPPAN, PHD, MBA ASSOCIATE CHAIR FOR BASIC RESEARCH

Although the entire country was under a state of emergency, the research mission of DOIM was never abandoned. Critical clinical research continued and Grand Rounds, Research Conferences and meetings were moved to virtual mode and managed very effectively during this time.



8 | University of Cincinnati

# Impact

incil

# Year at a Glance **Research Events Timeline 2019-2020**



Donald Lynch Jr., MD was accepted into the 2019 **PRIDE-Functional and** Translation Genomics of Blood Disorder Program, a research career advancing training opportunity funded by the National Heart, Lung, and Blood Institute (NHLBI).



Oversight of the **Pathobiology Molecular** Medicine (PMM) PhD program transitioned to the Department of Internal Medicine from the Department of Pathology and Laboratory Medicine.

Jane Yu, PhD was granted a Department of Defense Idea Development Award entitled, "Dysregulation of sphingolipid metabolism and actions in TSC." The award totals \$722,000 over three years.



**Centralization of IM's** regulatory clinical trials transitioned from the Heart, Lung and Vascular Institute to IM Academic **Research Services**.



Xiaoyang Qi, PhD, was honored as a senior member of the National Academy of Inventors for his contributions to the field in the discovery of a molecule found to kill many forms of cancer while leaving healthy cells unaffected.





Kevin Haworth, PhD and A. Phillip Owens, III, PhD, were awarded an R01 Supplement of \$396,621 to a current R01 to study the role of Alzheimer's Disease in PAR2.







Trisha Wise-Draper, MD, PhD, was named the "2019 **Clinical Trialist of the Year**" at the College of Medicine, she was recognized as the investigator with the greatest revenue from industry-funded clinical trial during the 2019 fiscal year





Bette Young was hired as the Program Coordinator for Pathobiology Molecular Medicine PhD program.





Department of Internal Medicine Fall Intramural Awards Competition: Junior Faculty Pilot Project Awardees: Arjan Flora, **MD**, funded in the amount of \$30,000 and Rajat Madan, MD, PhD, funded in the amount of \$30,000. Collaborative Challenge Awardee: Laura Conforti, **PhD**, funded in the amount of \$30,000. Outcomes Research Awardee:

funded in the amount of \$3,000. Post Doctorate Travel Awardee: Hani Alrefai, PhD, funded in the amount of \$1,250.













Margaret Powers, PhD.





## IMPACT Year at a Glance

## **Helen Gina Shelton**

was hired as the Clinical Regulatory Manager to lead the effort to centralize regulatory services within the department.





For four years now, the UC Office of Research annually recognizes the top externally sponsored researchers. Those IM faculty honored for each of the four years are: Vladimir Bogdanov, PhD; Robert Cohen, MD; Laura Conforti, PhD: Melanie Cushion, PhD; George Deepe, MD; Carl Fichtenbaum, MD; Fred Finkelman, MD; **Christy Holland, PhD**; Francis McCormack, MD Diego Perez-Tilve, PhD; Atsuo Sasaki, PhD: Kenneth Sherman, MD, PhD and Michael Tranter, PhD.

IM faculty honored three of the four years are: David Bernstein, MD Jason Blackard, PhD; Michael Borchers, PhD Nishant Gupta, MD;

Jamie Robertson, MD Sakthivel Sadayappan, PhD: Jason Winnick, PhD and Jane Yu, PhD.





## March 11, 2020 **Coronavirus (COVID-19)** reached Ohio with confirmed cases reported as of March 9, 2020. Contact limitations and other safety precautions were instituted for study participants, research laboratories, clinical research operations, staff, students, and faculty. Travel restrictions, remote instruction, restrictions on gathering size, remote operations and other health and safety precautions were instituted. Only critical research functions were permitted on campus through May 1, 2020.

**9th Annual Internal Medicine Research** Symposium cancelled due to COVID 19 pandemic.































11

# Silvi Shah, MD, MS.

received a CT2 Research **Career Development** Award from the CCTST.





The COVID 19 **Innovation Task Force** was established by the College of Medicine and UC Health to maximize COVID 19 research success

and minimize burden to patients and families by prioritizing and evaluating all requests for COVID-19 research funding and support.











Donald Lynch, MD, received a career

development award (K23) from the National Institutes of Health, providing \$831,500 for his project.



Sakthivel Sadayappan, PhD, MBA was named Associate Chief for Basic Research, Cardiovascular Health and Disease Division.



Xiaoyang Qi, PhD. received a Pancreatic Cancer Network Grant of \$500,000.





Laura Wexler, MD, professor in the Division of Cardiovascular Health and Disease, was named a recipient of the College of Medicine Daniel Drake Medal for 2020. (See story, page 17)

# Sakthivel Sadayappan, PhD, MBA, was awarded

a new R01 entitled, "Slow myosin binding protein-C in skeletal muscle physiology." The total funding was ~\$453,000/year over 5 years.





Senu Apewokin, MD, received a career development award (K08) from the National Cancer Institute. The grant provides \$1,108,910 for a duration of five years.



Nishant Gupta, MD, was awarded funding in the amount of \$30,000 from the College of Medicine **Research Innovation/Pilot** Grant Program.





## Richard Becker, MD,

was appointed to the National Heart, Lung, and Blood Institute (NHLBI) COVID-19 protocol Review Committee.



## Charuhas Thakar, MD,

was invited to be part of a **national expert panel discussion on AKI and Renal Replacement Therapies in hospitalized COVID patients** convened by the department of Health and Human Services and FDA.



A. Phillip Owens III, PhD, was awarded a new R01

entitled, "Role of the gut microbiota in abdominal aneurysm." The total award amount was ~648,000/year over 4 years.





## Research Reopen Phase 1 began with restart of research activities in the lab and clinical research programs in the College of Medicine. Over 60 plans from Internal Medicine researchers were reviewed by faculty researchers Rita Alloway, PharmD, Marat Khodoun, PhD and Suzanne Morris, PhD.







Robert M. Cohen, MD, was awarded a new R01 entitled, "Towards optimizing diabetes management and diagnosis by personalizing HbA1c targets." The total award amount was ~\$730,000/ year over 5 years.



## Jane Yu, PhD, was awarded

a new R01 as Co-PI with Dr. Yan Xu, Cincinnati Children's Hospital Medical Center, for the project entitled "Uterine signaling networks in the pathogenesis of pulmonary lymphangioleiomyomatosis." The total award amount was ~\$790,000/year over 4 years.



The IM Department provided Intramural funding to six faculty, staff and trainees. **Clayton Lewis, PhD** received the Trainee Award in the amount of \$1,750, Cristina Andreani, PhD, received the Trainee award in the amount of \$1,750, Dylan Steen, PhD, received the Rehn Award funded in the amount of \$16,000, Laura Conforti, PhD, received the Senior Faculty Pilot Project Award in the amount of \$30,000. Richard Becker, MD, PhD, received the Senior Faculty Pilot Project Award in the amount of \$30,000 and Caterina Bartolacci, PhD. received the Post Doctorate Travel Award funded in the amount of \$1,250.















# JUNE 2020

The DOIM was awarded an NIH-sponsored R38 training program grant entitled, "Stimulating Access to Research in the University of Cincinnati Internal Medicine Residency Program." The Co-PIs are Jack Rubinstein, MD, Sakthivel Sadayappan, PhD, MBA and Dan

Schauer, MD. Total funding amount was \$1,217,279 over 4 years. The funds will be primarily directed towards salary support for a select group of DOIM residents to complete an additional year of residency devoted to research. The goal is to increase the pipeline of physician-scientists.









Through support of the **COVID 19 Innovation Task Force**, over nine different coronavirus-related trials were activated and enrolling at UC by this date.

Under the leadership of Carl Fichtenbaum, MD, professor in the Department of Internal Medicine, UC was selected as a study site for the Moderna vaccine as it entered Phase 3 clinical trials.



Recognized by the **CoM** Office of Research in the Gallery of Awardees for receiving external research grants of \$100,000 per year or more are:

Jason T. Blackard, PhD, Robert Cohen, MD, Pamposh Kaul, PhD, and Trisha Wise-Draper, MD, PhD.









Deeptankar DeMazumder, MD,

PhD was awarded the prestigious NIH Director's New Innovator Award, total funding amount, \$2,407,500 over 5 years. •



IMPACT Drake Medalist

# Wexler named 2020 Daniel Drake Medalist

Laura Wexler, MD, professor in the Division of Cardiovascular Health and Disease, has been named one of two recipients of the Daniel Drake Medal for 2020. The award, established in 1985, is given annually to living faculty or alumni for their outstanding and unique contributions to medical education, scholarship and research. Daniel Drake, MD, was the founder of the Medical College of Ohio, the forerunner of the College of Medicine, and one of the most influential physicians, educators and scientists of his time.

Wexler served from 2001 until 2011 as senior associate dean of student affairs and admissions at the UC College of Medicine making numerous significant changes to student services and the admissions process. She instituted a new and innovative program for student mental health services and academic assistance for students. In 2008, she led UC to becoming the first U.S. medical school to adopt the Multiple Mini Interview system, a holistic approach for medical student selection that emphasizes humanistic skills and qualities. Wexler also served for 11 years as Cardiology Section chief at the Cincinnati Veterans Affairs Medical Center instituting many changes to improve access to specialty care and enhancing the cardiology fellowship and residency training programs. She received her medical degree from Washington University School of Medicine in St. Louis, completed residency training with Harvard Medical School at Boston City Hospital and a cardiology fellowship at the Massachusetts General Hospital. Wexler joined the UC College of Medicine faculty in 1987.

Annual Research Report 2020

University of Cincinnati INTERNAL MEDICINE | 15

# Research Funding FY20: **\$93,912,064**

We currently hold 155 total grants in the department, 19% of which are held by primary investigators with R0-1 awards. The total award amount is \$93,912,064. \$14.5 million of these were new grants awarded in FY20. •





					FY 2020
FY 2015				FY 2019	
<b>\$2,089,361</b> NEP	FY 2016	FY 2017	FY 2018	\$2,309,672	<b>\$3,150,471</b> HEM/UCCI
	<b>\$1,265,595</b> HEM/UCCI	<b>\$1,690,891</b> HEM/UCCI	\$1,491,820 HEM/UCCI	iiliin occi	
\$701 222					
DIG	\$1,042,680	\$668,734	¢1 110 07/	\$798,711	
\$625,266 HEM/UCCI	NEF	NEP	DIG		\$795.982
\$579,172	<b>\$512,955</b> INF	<b>\$655,920</b> INF		<b>\$680,031</b> NEP	CARD
ADMIN \$512,325	\$510,426 PUL	\$608,945	<b>\$849,773</b> NEP	\$601,957	<b>\$618,652</b> NEP
PUL	\$468,588	10E	\$479,734	PUL	\$424,930
\$497,719	CAR	\$439,942 DIG	INF	<b>\$587,215</b> CARD	PUL
\$359,263 CARD	\$460,962 DIG	<b>\$434,711</b> ADMIN	<b>\$453,430</b> PUL	\$438,503	5286 235 INF
\$285,881 INF	\$330,987 ADMIN	\$367,915	\$232,516 CARD \$159 094 ADMIN	\$234,569 ADMIN	\$212,424 ADMIN
<b>\$55,000</b> GEN MED	\$102,467 IMM \$12,929 GEM	\$6,696 IMM		\$22,083 ENDO	\$ <b>54,899</b> IMM
<b>\$0</b> ENDO	<b>\$0</b> ENDO	<b>\$0</b> END GEN MED	<b>\$0</b> ENDO GEN MED IMM	<b>\$0</b> GEN MED IMM	<b>\$0</b> ENDO GEN MED

# Clinical Trial Revenue FY20: \$5,960,741

<b>Clinical Trial</b>	Revenue	By Division	

		FY15	FY16	FY17	FY18		FY19	FY20
ADMIN	ADMIN	\$ 579,172	\$ 330,987	\$ 434,711	\$ 159,094	\$	234,569	\$ 212,424
CARD	CARD	359,263	468,588	367,915	232,516		587,215	795,982
DIG	DIG	701,323	460,962	439,942	1,118,824		798,711	416,581
ENDO	ENDO	0	0	0	0		22,083	0
GEN MED	GEN MED	55,000	12,929	0	0		0	0
HEMONC/UCCI	HEM/UCC	625,266	1,265,595	1,690,891	1,491,820	2	2,309,672	3,150,471
IMM	ІММ	497,719	102,467	6,696	0		0	54,899
INF	INF	285,881	512,955	655,920	479,734		438,503	286,235
NEP	NEP	2,089,361	1,042,680	668,734	849,773		680,031	618,652
PUL	PUL	512,325	510,426	608,945	453,430		601,957	424,930
	TOTAL	\$ 5,705,312	4,707,589	4,873,754	4,785,191	\$ !	5,672,741	\$ 5,960,174



# Six Year Trend of Research Funding

# **Research Initiative Supporting Excellence-UC (RISE-UC)** Three Initiatives Represent Impact of Academic Research Services (ARS)

The Department of Internal Medicine (DOIM) created the Research Initiative Supporting Excellence-UC (RISE-UC) in 2012 to foster the development and success of our researchers. By listening to faculty needs, we created a platform of people and programs to support researchers and trainees and to assist them in reaching their research career goals. RISE-UC heralded the development of the Academic Research Services (ARS) in 2016.

The scope of ARS continued to expand in Academic Year 2019-2020. From a service initially focused on providing grant writing assistance and administrative functions related to governance of the research mission, ARS, by the conclusion of July 2020, also provided services such as comprehensive regulatory assistance for both industry-sponsored and investigator-initiated research studies, expert biostatistics assistance through a DOIM funded position and administrative support of the Pathobiology and Molecular Medicine graduate program. A core mission, however, remained to assist DOIM researchers in the entire pre-award process for obtaining external funding, the life blood of any research-focused academic department. Three representative and interrelated initiatives during this time provide a sense of the scope of the activities.

# Timely Submission Of The Highest Quality Proposals

A chronic challenge to optimizing the grant submission process that frequently plagues any institution is ensuring timely submission of the highest quality proposals. In the competitive arena of the awarding of grants, success hinges on not only the submission of the best effort but also on a system, regardless of the outcomes, that minimizes the stress to the large team of people involved in the submission, whether they be the principal investigator, the laboratory worker generating preliminary data or the administrative staff responsible for preparing the online documents for electronic submission with all the necessary institutional checks having been completed. A chronic specific challenge in DOIM has been proposals that are not complete with the five working day internal deadline. In AY 2019-2020, the DOIM grants administration office surveyed the process for 12 months and determined that over 25% of grants were late by this standard.

In the first two quarters of AY 2019, 43 grants were submitted with ARS assistance; 53% of the grants were funded, comparing well to the overall success rate for the DOIM of 30%.

University of Cincinnati

20

Annual Research Report 2020

In order to document the status of submissions while intervening to assist investigators within the DOIM, the first two guarters of AY 2019 were tracked by ARS. A total of 43 grants were submitted with ARS assistance, ~20% were deemed late of which only one was so overdue and, therefore, not allowed to be submitted. Ultimately, ~53% of the grants were funded, comparing well to the overall success rate for the DOIM of ~30%. However, the ideal timeline for submission in which a specific aim page is in a mature form at ~6 months was not achieved in any grant. And, for example, although the College of Medicine provides an internal mechanism for formally reviewing grants if a version is advanced enough to be evaluated 60 days prior to the internal deadline, no grant was submitted taking advantage of this service. Importantly, 3 of 14 R01 NIH grants were awarded; this percentage (~20) is in line with the extreme competitiveness of these awards. The general conclusion was that ARS was having a positive impact on the proposal submission process and even the "late" grants were in the acceptable category but represented an area of needed improvement.

# Peer-Mentoring Junior Faculty Group

A junior faculty J club (J-club) organized in the fall of 2016 by Kevin Haworth, PhD, a recent K25 awardee, and Carl Fichtenbaum, MD, Associate Chair of Translational Research, with the assistance Eric Smith, MD, ARS grant writer, matured in AY2020 into a major contributor to improving research outcomes.

The J-club is a peer-mentoring group involving 10-12 of the research-oriented junior faculty. The group includes basic, translational, and clinicianscientists from most divisions within the department. The club was targeted at faculty members who had not yet received R01equivalent funding, although junior faculty with R01-equivalent funding were allowed to join. As a pre-requisite for participating, an individual development plan was required. The group meets bimonthly providing a forum for a broad variety of discussions, presentations, and training relevant to their success. One faculty member is assigned for each meeting (~45 out of 60 min) to present whatever proposal for which they wish to receive feedback. Most of the meeting

As of the end of AY2021, over 90% of the J-club participants had received significant funding.

involves feedback on a grant document, often a specific aims page, with time for other issues including a general presentation of current research activities, practice presentation for a national conference, or a didactic session provided by the Associate Chair for Translational Research. As of the end of AY2021, over 90% of the J club participants had received significant funding including a VAMC Merit Award, three American Heart Association awards. one KL2 and two CT2 career development awards sponsored by the CCTST, two NIH K career development awards, one Department of Defense, two Young Investigator awards (Entelligence and Pediatric Association), a PRIDE award, and one R01.



# Enhancing Mentoring Opportunities Across the Research Experience

Another emphasis related to the above efforts was a focus on enhancing mentoring at the level of residents, fellows, graduate students and postdoctoral fellows. In July 2020, with the assistance of the ARS, the DOIM was awarded a highly competitive NIH sponsored T32 training program under the guidance of Co-PIs, Vladimir Bogdanov, PhD and Xiaoyang Qi, PhD, Division of Hematology / Oncology. The focus to provide postdoctoral level researchers with

 formal and integrated instruction on the role of intellectual property protection in drug development in the context of a complex economy that is both market-based and government-regulated;

- a comprehensive didactic and practical training in anti-cancer compound evaluation, with a primary focus on rigorous training in how to conceptualize, design, manage, and successfully carry to completion a clinical trial involving a novel drug;
- establish a collaborative structure that promotes genuinely creative and productive interactions between PhD scientists and MD-MD/PhD clinicians.

Following in the heels of this award were efforts to obtain an

R38 training program, in this case, focused on resident training. Based on the existing IMSTAR and PSTP programs already in place within the DOIM dedicated to fellow level training, the notion was that a resident-focused curriculum would complement these fellowship oriented efforts. With the assistance of ARS and the Co-Pls, Jack Rubinstein, MD, Sakthivel Sadayappan, PhD, MBA and Daniel Schauer, MD, the R38 was ultimately awarded in 2020. This provides a funded extra year of research for selected DOIM residents with the goal of fostering an academic fellowship and physician scientist career.

# Postdoctoral Focus T32 training program Ca Plat

Co-Pls: Vladimir Bogdanov, PhD Xiaoyang Qi, Ph

# • Resident Focus:

R38 training program Stimulating Access to Research in Residency (StARR) Co-PIs: Jack Rubinstein, MD Sakthivel Sadayappan, PhD, MBA Daniel Schauer, MD

## ACADEMIC RESEARCH SERVICES

Online at: med.uc.edu/depart/intmed/ research/contact-us-staff

Send a message to ARS to inquire about any of the department's programs and initiatives. IMResearch@uc.edu

22

# Discover and Innovate

# Division of Cardiovascular Health and Disease

## ENDOWED CHAIR: Mabel Stonehill Endowed Chair

The Division of Cardiovascular Health and Disease is continuing and expanding upon its history of high-quality clinical, preclinical and basic research programs. The Division's mission is to enhance collaborative clinical, basic and translational research that is broadly related to treating cardiovascular diseases. Our vision includes facilitating collaboration and synergy among investigators, integrating basic and clinical research programs, and promoting rapid translation from bench to bedside.



Charles Hattemer, MD CHIEF

Sakthivel Sadayappan, PhD, MBA ASSOCIATE CHIEF, BASIC RESEARCH

## Research Focus Areas/Types:

Our research programs are focused on understanding the basic biology of the cardiovascular system; defining mechanisms underlying the development of heart failure, myocardial and reperfusion injury, genetic cardiomyopathies and stroke; and engaging in the development and testing of novel therapies, devices and diagnostic assays to treat these diseases. To meet our research missions, we provide multi-center clinical care, perform clinical trials and utilize various animal models, including mouse, rat, guinea pig and pig, in addition to in vitro assays, artificial intelligence, and machine learning techniques.

Investigators/Trainees:

Our faculty range from early

career to established investigators with recognized excellence in the delivery of clinical practice and research, teaching, education and training. All basic researchers have multiple externally-funded research projects. Articles submitted by our investigators to peer review are regularly published in high-impact journals like Nature, PNAS, Circulation Research, and the Journal of Biological Chemistry. Our faculty is represented at many prestigious national and international conferences and meetings by participating, moderating and presenting timely and vital research studies. Faculty members routinely participate in organizing scientific sessions, like the American Heart Association. Some faculty members have multiple patents for drugs, concepts and devices to treat patients with heart failure. A few have even initiated startup companies, such as High Enroll by Dr. Dylan Steen and NobleRx Neuroprotection by Dr. Christy Holland, and licensed their inventions to various pharmaceutical companies.

## Mentoring and Teaching:

Our faculty members are fully engaged in training and mentoring the next generation of physicians, scientists by offering a variety of programs and giving priority to the training of underrepresented minorities and women scientists. In the Division, the following programs are actively carried out: Medical Scientist Training Program (MSTP), Physician Scientist Training Program (PSTP), AHA Summer Undergraduate Research Fellowship (SURF), Predoctoral and Postdoctoral training programs supported by both AHA and NIH. In addition, we have established an Early-Career Cardiovascular Researchers Network in Cincinnati, including early-career researchers from both UC and Cincinnati Children's Hospital, to boost local interaction, networking and collaboration.

#### **Collaborations:**

Collaboration and team efforts are our mantra for actively engaging the Division. The Division of Cardiovascular Health and Disease provides the opportunity to work with physicians, physician-scientists and basic scientists under one umbrella in a very collaborative manner in various programs that include clinical trials for various novel drugs, collection of human samples to perform mechanistic studies in the laboratory, nextgeneration DNA sequencing, testing biomarkers, and developing machine learning tools to decode heart-brain talk. Both clinical and basic scientists were involved in this study, alongside our trainees, serving as a model for collaboration in the Division. Overall, our faculty members are collegial by nature and ready to partner with faculty from inside and outside UC.

# Christy Holland, PhD

PROFESSOR DIVISION OF CARDIOVASCULAR HEALTH AND DISEASE hristy Holland, PhD, knows a picture is worth a thousands words — literally. The University of Cincinnati professor of internal medicine and biomedical engineering is also editorin-chief of "Ultrasound in Medicine and Biology," the official journal of the World Federation of Ultrasound in Medicine and Biology.

"Ultrasound in Medicine and Biology is the only ultrasound journal that balances basic science and clinical papers," Holland says. "As such, it is highly complementary to the purely clinical ultrasound journals, and we are very keen to further enhance its visibility to both pre-clinical and clinical researchers."

The journal has strong foundations in innovative ultrasound developments, elastography, biological effects of ultrasound and therapeutic ultrasound, and Holland says it has become the journal of choice to report innovative pre-clinical research in the field. She should know, as a Yale-educated expert in the unique possibilities ultrasound holds for treating patients. Holland's current research in UC's Image-Guided Ultrasound Therapeutics Laboratories is focused on the development of ultrasound-enhanced thrombolysis, a therapy that dissolves dangerous blood clots, and to provide new information to assist the design of targeted agents that will improve thrombolysis in acute stroke treatment. Her work will also allow clinicians to stage atherosclerosis (hardening of the arteries) and apply directed therapy to improve blood flow.

"We also hope to develop a combined ablation and targeted thrombolytic high amplitude ultrasound ("histotripsy") technique that lyses stiff thrombi in the deep veins, decreases the risk of pulmonary embolism and improves long-term prognosis," Holland says.

Holland's work isn't contained to the lab, either — and she is eager for it to make a real-world impact. In 2019, building on seven patents she holds on intellectual property and paired with Rick D'Augustine, an entrepreneur-in-residence with UC's Venture Lab at the 1819 Innovation Hub, Holland launched NobleRx Neuroprotection. The start-up aims to develop a novel neuroprotectant delivery platform to help stroke teams and emergency care personnel treat stroke victims by protecting the brain against irreversible damage caused by oxygen deprivation. The team has secured funds from Ohio Third Frontier Entrepreneurial Services Provider Program to develop Xenon-loaded microbubbles to provide neuroprotection during stroke, complete formative testing and develop an FDA regulatory strategy to enable first in human trials.

She also plans to recruit a new postdoctoral fellow and graduate student to work in the Image-Guided Ultrasound Therapeutics Laboratories.

"The excellent questions that students ask help motivate my work," Holland says. "They challenge me to have a deeper understanding of my research." • HOLLAND'S CURRENT RESEARCH IS FOCUSED ON THE DEVELOPMENT OF ULTRASOUND-ENHANCED THROMBOLYSIS. HER WORK WILL ALSO ALLOW CLINICIANS TO STAGE ATHEROSCLEROSIS AND APPLY DIRECTED THERAPY TO IMPROVE BLOOD FLOW.

#### **DISCOVER & INNOVATE**

#### Cardiovascular Health and Disease

PUBLICATIONS July 1, 2019 thru June 30, 2020

- Desai D, Stiene D, Song T, Sadayappan S. Distal Arthrogryposis and Lethal Congenital Contracture Syndrome - An Overview. Front Physiol. 2020 Jun 25;11:689. doi: 10.3389/fphys.2020.00689. PMID: 32670090; PMCID: PMC7330016.
- 2 Arif M, Nabavizadeh P, Song T, Desai D, Singh R, Bazrafshan S, Kumar M, Wang Y, Gilbert RJ, Dhandapany PS, Becker RC, Kranias EG, Sadayappan S. Genetic, clinical, molecular, and pathogenic aspects of the South Asian-specific polymorphic MYBPC3<sup>∆25bp</sup> variant. Biophys Rev. 2020 Aug;12(4):1065-1084. doi: 10.1007/s12551-020-00725-1. Epub 2020 Jul 12. PMID: 32656747; PMCID: PMC7429610.
- 3 Kumar M, Haghighi K, Kranias EG, Sadayappan S. Phosphorylation of cardiac myosin-binding protein-C contributes to calcium homeostasis. J Biol Chem. 2020 Aug 7;295(32):11275-11291. doi: 10.1074/jbc. RA120.013296. Epub 2020 Jun 18. PMID: 32554466; PMCID: PMC7415972.
- 4 Sadayappan S, Puckelwartz MJ, McNally EM. South Asian-Specific MYBPC3<sup>Δ25bp</sup> Intronic Deletion and Its Role in Cardiomyopathies and Heart Failure. Circ Genom Precis Med. 2020 Jun;13(3):e002986. doi: 10.1161/CIRCGEN.120.002986. Epub 2020 Jun 16. PMID: 32543992; PMCID: PMC7301913.
- 5 Becker RC, Phillip Owens A 3rd, Sadayappan S. The potential roles of Von Willebrand factor and neutrophil extracellular traps in the natural history of hypertrophic and hypertensive cardiomyopathy. Thromb Res. 2020 Aug;192:78-87. doi: 10.1016/j. thromres.2020.05.003. Epub 2020 May 7. PMID: 3 2 4 6 0 1 7 5 ; P M C I D : PMC7340095.
- 6 Petrany MJ, Song T, Sadayappan S, Millay DP. Myocytederived Myomaker expression is required for regenerative fusion but exacerbates membrane instability in dystrophic myofibers. JCI Insight. 2020 May 7;5(9):e136095. doi:10.1172/jci.insight.136095. PMID: 32310830; PMCID: PMC7253022.
- 7 Butts B, Ahmed MI, Bajaj NS, Cox Powell P, Pat B, Litovsky S, Gupta H, Lloyd SG, Denney TS, Zhang X, Aban I, Sadayappan S, McNamara JW, Watson MJ, Ferrario CM, Collawn JF, Lewis C, Davies JE, Dell'Italia LJ. Reduced Left Atrial Emptying Fraction and Chymase Activation in Pathophysiology of Primary Mitral Regurgitation. JACC Basic Transl Sci. 2020 Jan 22;5(2):109-122. doi: 10.1016/j.jacbts.2019.11.006. PMID: 32140620; PMCID: PMC7046515.
- Becker RC, Sadayappan S. Designing Human In Vitro Models for Drug Development. J Am Coll Cardiol. 2020 Feb 18;75(6):587-589. doi:10.1016/j.jacc.2019.12.013. PMID: 32057372.
- 9 Becker RC, Owens AP 3rd, Sadayappan S. Tissuelevel inflammation and ventricular remodeling in hypertrophic cardiomyopathy. J Thromb Thrombolysis. 2020 Feb;49(2):177-183. doi: 10.1007/s11239-019-02026-1. PMID: 31898271; PMCID: PMC7001758.

- 10 Vagnozzi RJ, Maillet M, Sargent MA, Khalil H, Johansen AKZ, Schwanekamp JA, York AJ, Huang V, Nahrendorf M, Sadayappan S, Molkentin JD. An acute immune response underlies the benefit of cardiac stem cell therapy. Nature. 2020 Jan;577(7790):405-409. doi: 10.1038/s41586-019-1802-2. Epub 2019 Nov 27. PMID: 31775156; PMCID: PMC6962570.
- 11 Vagnozzi RJ, Pfleger J, Sadayappan S. Basic Cardiovascular Sciences Scientific Sessions 2019: Integrative Approaches to Complex Cardiovascular Diseases. Circ Res. 2019 Oct 25;125(10):924-931. doi: 10.1161/CIRCRESAHA.119.315977. Epub 2019 Oct 24. PMID: 31647770; PMCID:PMC6818742.
- 12 Li A, Nelson SR, Rahmanseresht S, Braet F, Cornachione AS, Previs SB, O'Leary TS, McNamara JW, Rassier DE, Sadayappan S, Previs MJ, Warshaw DM. Skeletal MyBP-C isoforms tune the molecular contractility of divergent skeletal muscle systems. Proc Natl Acad Sci U S A. 2019 Oct 22;116(43):21882-21892. doi: 10.1073/ pnas.1910549116. Epub 2019 Oct 7. PMID: 31591218; PMCID: PMC6815179.
- **13** Song T, **Sadayappan S**. Featured characteristics and pivotal roles of satellite cells in skeletal muscle regeneration. J Muscle Res Cell Motil. 2020 Dec;41(4):341-353. doi: 10.1007/s10974-019-09553-7. Epub 2019 Sep 7. PMID:31494813.
- 14 Manoharan P, Song T, Radzyukevich TL, Sadayappan S, Lingrel JB, Heiny JA. KLF2 in Myeloid Lineage Cells Regulates the Innate Immune Response during Skeletal Muscle Injury and Regeneration. iScience. 2019 Jul 26;17:334-346. doi: 10.1016/j.isci.2019.07.009. Epub 2019 Jul 8. PMID: 31326700; PMCID: PMC6652133.
- 15 Alam P, Haile B, Arif M, Pandey R, Rokvic M, Nieman M, Maliken BD, Paul A, Wang YG, Sadayappan S, Ahmed RPH, Kanisicak O. Inhibition of Senescence-Associated Genes Rb1 and Meis2 in Adult Cardiomyocytes Results in Cell Cycle Reentry and Cardiac Repair Post-Myocardial Infarction. J Am Heart Assoc. 2019 Aug 6;8(15):e012089. doi: 10.1161/JAHA.119.012089. Epub 2019 Jul 18. PMID: 31315484; PMCID: PMC6761626.
- 16 Sadayappan S, Gilbert RJ. The potential role of neddylation in pre- and postnatal cardiac remodeling. Am J Physiol Heart Circ Physiol. 2019 Aug 1;317(2):H276-H278. doi: 10.1152/ajpheart.00260.2019. Epub 2019 Jul 5. PMID: 31274350; PMCID: PMC6732480.
- 17 Patrick H. Kee, Melanie R. Moody, Shao-Ling Huang, Hyunggun Kim, Xing Yin, Tao Peng, Susan T. Laing, Melvin E. Klegerman, Mohammad H. Rahbar, Deborah Vela, Curtis Genstler, Kevin J. Haworth, Christy K. Holland, David D. McPherson. (2020) "Stabilizing peristent restenosis using a novel therapeutic carrier." JACC: Basic to Translational Science. 5(1):1-11 doi: 10.1016/j.jacbts.2019.09.005
- 18 Viktor Bollen, Samuel A. Hendley, Jonathan D. Paul, Adam D. Maxwell, Kevin J. Haworth, Christy K. Holland, Kenneth B. Bader. (2020) "In vitro thrombolytic efficacy of single- and five-cycle histotripsy pulses and rt-PA." Ultrasound in Medicine and Biology. 46(2):336-349 doi: 10.1016/j.ultrasmedbio.2019.10.009

- Robert Kleven, Himanshu Shekhar, Kunal Karani, Nuria Salido, T. Douglas Mast, Kevin J. Haworth, Christy K. Holland. (2019) "The effect of 220 kHz insonation scheme on rt- PA thrombolytic efficacy in vitro." Physics in Medicine and Biology. 64(16):165015(1-17) doi: 10.1088/1361-6560/ab293b
- 20 Karla P. Mercado-Shekhar, Haili Su, Deepak S. Kalaikadal, John N. Lorenz, Raj M. Manglik, Christy K. Holland, Andrew N. Redington, Kevin J. Haworth. (2019) "Acoustic droplet vaporization-mediated dissolved oxygen scavenging in blood-mimicking fluids, plasma, and blood." Ultrasonics Sonochemistry. 56:114-124 doi: 10.1016/j.ultsonch.2019.03.029
- 21 Anthony SR, Guarnieri A, Lanzillotta L, Gozdiff A, Green LC, O'Grady K, Helsley RN, Owens AP, Tranter M. HuR expression in adipose tissue mediates energy expenditure and acute thermogenesis independent of UCP1 expression. Adipocyte. 2020. 9(1): 335-345.
- 22 Anthony SR, Guarnieri AR, Gozdiff A, Helsley RN, Owens AP, **Tranter M**. Mechanisms linking adipose tissue inflammation to cardiac hypertrophy and fibrosis. Clinical Science. 2019. 133(22): 2329-44.
- 23 Brown AL, Conrad K, Allende DS, Gromovsky AD, Neumann C, Owens AP, Tranter M, Helsley RN. Choline supplementation attenuates high fat diet-induced hepatocellular carcinoma (HCC) in mice. J of Nutrition. 2019. 1;150(4): 775-783.
- 24 M. Lafond, N. Salido, K. J. Haworth, A. Hannah, C. Genstler, C. K. Holland, "Cavitation emissions nucleated by Definity® infused through an EkoSonic® catheter in a flow phantom," Ultrasound Med Biol (In Press, 2020).

#### IMPACT PUBLICATION

- 25 K. Kooiman, S. Roovers, S. A. G. Langeveld, R. T. Kleven, H. Dewitte, M. A. O'Reilly, J.-M. Escoffre, A. Bouakaz, M. D. Verweij, K. Hynynen, I. Lentacker, E. Stride, C. K. Holland, "Ultrasound-responsive cavitation nuclei for therapy and drug delivery," Ultrasound Med Biol 46:1296-1325 (2020), https://doi.org/10.1016/j.ultrasmedbio.2020.01.002.
- 26 H. Shekhar, W. Panmanee, M. Lafond, A. Palaniappan, C T. McDaniel, D. J. Hassett, C. K. Holland, "Bactericidal activity of lipid-shelled nitric oxide-loaded microbubbles," Frontiers in Pharmacology 10: Article 1540 (2020), https://doi.org/10.3389/fphar.2019.01540.
- 27 K. R. Lattwein, H. Shekhar, J. J. P. Kouijzer, W. J. B. van Wamel, C. K. Holland, K. Kooiman, "Sonobactericide: An emerging treatment strategy for bacterial infections," Ultrasound Med Biol 46:193-215 (2020), https:// doi.org/10.1016/j.ultrasmedbio.2019.09.011.
- 28 P. H. Kee, M. R. Moody, S.-L. Huang, H. Kim, X. Yin, T. Peng, S. T. Laing, M. E. Klegerman, M. H Rahbar, D. Vela, C. Genstler, K. J. Haworth, C. K. Holland, D. D. McPherson, "Stabilizing peri-stent restenosis using a novel therapeutic carrier," JACC: Basic to Translational Science (Published online November 2019) https://doi.org/10.1016/j.jacbts.2019.09.005.

- 29 V. Bollen, S. A. Hendley, J. D. Paul, A. D. Maxwell, K. J. Kaworth, C. K. Holland, K. B. Bader, "In vitro thrombolytic efficacy of single- and five-cycle histotripsy pulses and rt-PA," Ultrasound Med Biol 46:336-349 (2020), https://doi.org/10.1016/j.ultrasmedbio.2019.10.009.
- 30 R. T. Kleven, H. Shekhar, K. Karani, K. J. Haworth, and C. K. Holland, "Effect of duty cycle on the thrombolytic efficacy of 220 kHz ultrasound and rt-PA in vitro", Phys Med Biol 64:165015 (2019), https://doi. org/10.1088/1361-6560/ab293b.

#### IMPACT PUBLICATION

- 31 H. Shekhar, R. T. Kleven, A. Palaniappan, T. Peng, K. B. Karani, S. Huang, D. D. McPherson, C. K. Holland "In vitro characterization of sonothrombolysis and echocontrast agents to treat ischemic stroke," Scientific Reports 9:9902 (2019), https://doi.org/10.1038/ s41598-019-46112-z.
- 32 H. Shekhar, A. Palaniappan, T. Peng, M. R. Moody, K. J. Haworth, S. Huang, D. D. McPherson, C. K. Holland, "Lipid-shelled microbubbles for ultrasound-triggered release of Xenon," Neurotherapeutics (Published online 24 April 2019), https://doi.org/10.1007/s13311-019-00733-4.
- 33 K. P. Mercado-Shekhar, H. Su, D. S. Kalaikadal, J. N. Lorenz, R. M. Manglik, C. K. Holland, A. N. Redington, K. J. Haworth, "Acoustic droplet vaporization-mediated dissolved oxygen scavenging in blood mimicking fluids, plasma, and blood," Ultrasonics Sonochemistry 56:144-124 (2019), https://doi.org/10.1016/j.ultsonch.2019.03.029.

#### IMPACT PUBLICATION

34 Bateman TM, Ananthasubramaniam K, Berman DS, Gerson M, Gropler R, Henzlova M, Mendoza F, Miyamoto M, Shah M, Weiland F. Reliability of the 123ImIBG heart/mediastinum ratio: Results of a multicenter test-retest reproducibility study. J Nucl Cardiol 2019 Oct;26:1555-

#### **IMPACT PUBLICATION**

- 35 Boyne P, Scholl V, Doren S, Carl D, Billinger SA, Reisman DS, Gerson M, Kissela B, Vannest J, Dunning K. Locomotor training intensity after stroke: Effects of interval type and mode. Topics in Stroke Rehabilitation 2020 Oct;27(7):483-493.
- 36 Boyne P, Meyrose C, Westover J, Whitesel D, Hatter K, Reisman DS, Carl D, Khoury JC, Gerson M, Kissela B, Dunning K. Effects of exercise intensity on acute circulating molecular responses poststroke. Neurorehabil Neural Repair 2020 Mar;34(3):222-234.
- 37 Athar MW, Waqar F, Dwivedi AK, Ahmad S, Sanghvi S, Scott E, Khan N, Gerson MC. Effects of gender and defect reversibility on detection of coronary disease with an upright and supine cadmium-zinc-telluride camera. J Nucl Cardiol. 2019 Sep 5. doi: 10.1007/ s12350-019-01878-7. [Epub ahead of print]
- 38 Doytchinova A, Gerson MC: 123I-meta-lodobenzylguanidine imaging in patients with cardiac resynchronization therapy: Results are intriguing, but unknowns remain. J Nucl Card 2020, Feb:27(1)291-293 (Editorial)

#### **DISCOVER & INNOVATE**

#### Cardiovascular Health and Disease

**PUBLICATIONS** CONTINUED

- **39** Laipply K, **Gerson M**: Is faster always better? What is the implication of a shorter time to imaging with tetrofosmin compared to sestamibi. J Nucl Card Published online May 13, 2020.
- 40 Kassem KM, Souka A, Harris DM, Parajuli S, Cook JL. Eosinophilic myocarditis: Classic presentation of elusive disease. Circ: Cardiovascular Imaging 2019 Sept:12(9) epub.
- 41 Cox MT, Abbass MA, Mast TD. Numerical analysis of three-dimensional echo decorrelation imaging. J Acoust Soc Am 147, EL478–483 (2020).
- 42 Abbass MA, Ahmad SA, Mahalingam N, Krothapalli KS, Masterson JA, Rao MB, Barthe PG, Mast TD. In vivo ultrasound thermal ablation control using echo decorrelation imaging in rabbit liver and VX2 tumor. PLOS One, 14, e0226001/20pp (2019).
- 43 Dugan S, Li SR, Masterson JA, Woeste HM, Mahalingam N, Spencer C, Mast TD, Riley MA, Boyce SE. Tongue part movement trajectories for /r/ using ultrasound. Perspectives of the ASHA Special Interest Groups, 4, 1644–1652 (2019).
- 44 Kleven RT, Shekhar H, Karani KB, Salido NG, Mast TD, Haworth KJ, Holland CK. The effect of 220 kHz insonation scheme on rt-PA thrombolytic efficacy in vitro. Phys Med Biol 64, 165015/17pp (2019).
- 45 Annand CT, Lamb M, Dugan S, Li SR, Woeste HM, Mast TD, Riley MA, Masterson JA, Mahalingam N, Eary KJ, Spencer C, Boyce S, Jackson S, Baxi A, Seward R. Using ultrasound imaging to create augmented visual biofeed- back for articulatory practice. Proceedings of the Annual Conference of the International Speech Communication Association, INTERSPEECH, 974–975 (2019).
- 46 Li SR, Woeste HM, Dugan S, Mast TD, Riley MA, Annand C, Masterson JA, Mahalingam N, Eary KJ, Spencer C, Boyce S. Differentiating normal vs. misarticulated tongue trajectories from ultrasound for fast automatic articulatory biofeedback. Proceedings of the 19th International Congress of Phonetic Sciences (2019).
- 47 Rubinstein J, Woo JG, Garcia AM, Alsaied T, Li J, Lunde PK, Moore RA, Laasmaa M, Sammons A, Mays WA, Miyamoto SD, Louch WE, Veldtman GR.Pediatr Cardiol. 2020 Dec;41(8):1675-1688. doi: 10.1007/s00246-020-02427-7. Epub 2020 Aug 7.PMID: 32770262
- O'Connor B, Robbins N, Koch SE, Rubinstein J.Prog Biophys Mol Biol. 2020 Jun 18:S0079-6107(20)30057 2. doi: 10.1016/j.pbiomolbio.2020.06.001. Online ahead of print.PMID: 32565182
- 49 Moseley A, Laipply K, Rubinstein J.J Am Coll Cardiol. 2020 Apr 21;75(15):1865. doi: 10.1016/j. jacc.2020.01.060.PMID: 32299601 No abstract available.
- 50 Onusko E, McDermott MR, Robbins N, Liu G, Kranias EG, Rubinstein J, Koch SE.PLoS One. 2020 Mar 27;15(3):e0230386. doi: 10.1371/journal. pone.0230386. eCollection 2020.PMID: 32218573 Free PMC article

- 51 Li Y, Deng S, Wang X, Huang W, Chen J, Robbins N, Mu X, Essandoh K, Peng T, Jegga AG, **Rubinstein J**, Adams DE, Wang Y, Peng J, Fan GC.Cardiovasc Res. 2020 Mar 14:cvaa067. doi: 10.1093/cvr/cvaa067. Online ahead of print.PMID: 32170929
- 52 Rubinstein J, Sanford D.Cardiol Clin. 2019 Aug;37(3):267-273. doi: 10.1016/j.ccl.2019.04.002. Epub 2019 May 15.PMID: 31279420 Review.
- 53 Cox MT, Abbass MA, Mast TD. Numerical analysis of three-dimensional echo decorrelation imaging. J Acoust Soc Am 147, EL478–483 (2020).
- 54 Abbass MA, Ahmad SA, Mahalingam N, Krothapalli KS, Masterson JA, Rao MB, Barthe PG, Mast TD. In vivo ultrasound thermal ablation control using echo decorrelation imaging in rabbit liver and VX2 tumor. PLOS One, 14, e0226001/20pp (2019).
- 55 Dugan S, Li SR, Masterson JA, Woeste HM, Mahalingam N, Spencer C, Mast TD, Riley MA, Boyce SE. Tongue part movement trajectories for /r/ using ultrasound. Perspectives of the ASHA Special Interest Groups, 4, 1644–1652 (2019).
- 56 Kleven RT, Shekhar H, Karani KB, Salido NG, Mast TD, Haworth KJ, Holland CK. The effect of 220 kHz insonation scheme on rt-PA thrombolytic efficacy in vitro. Phys Med Biol 64, 165015/17pp (2019).
- 57 Annand CT, Lamb M, Dugan S, Li SR, Woeste HM, Mast TD, Riley MA, Masterson JA, Mahalingam N, Eary KJ, Spencer C, Boyce S, Jackson S, Baxi A, Seward R. Using ultrasound imaging to create augmented visual biofeed- back for articulatory practice. Proceedings of the Annual Conference of the International Speech Communication Association, INTERSPEECH, 974–975 (2019).
- 58 Li SR, Woeste HM, Dugan S, Mast TD, Riley MA, Annand C, Masterson JA, Mahalingam N, Eary KJ, Spencer C, Boyce S. Differentiating normal vs. misarticulated tongue trajectories from ultrasound for fast automatic articulatory biofeedback. Proceedings of the 19th International Congress of Phonetic Sciences (2019).
- 59 Costea A. Pacing Clin Electrophysiol. 2020 Jan;43(1):12-18. doi: 10.1111/pace.13841. Epub 2019 Dec 23.
- 60 Urbina EM, Mendozaba B, Becker RC, Daniels ST, Falkmer BK, Hamdani G, Hanevold C, Hooper SR, Ingelfimnger JR, Lanade M, Martin LJ, Meyers K, Mitsnefes M, Rosner B, Samuels J, Flynn J. Association of Blood Pressure Level with Left Ventricular Mass in Adolescents SHIP AHOV. Hypertension 2019; 74:00-00. DOI: 10.1161/HYPERTENSIONAHA.119.13027
- 61 Ungar L, Rodriguez F, Hellkamp AS, Becker RC, Berkowitz SD, Breidhardt G, Fox KAA, Hacke W, Halperin JL, Hankey GJ, Nessel CC< Singer DE, Patel MR, Piccini JP, Mahaffey KW. Patient-Related Satisfaction and Study Drug Discontinuation: Post-Hoc Analysis of Findings from ROCKET AF. Cardiol Ther. 2019 Dec;8(2)283-295.doi: 10.1007/s40119-019-00146-6. Epub 2019 Aug 2

- 62 Andersen T, Ueland TT, Akerblom A, Bertilsson M, Aukrust P, Michelsen AE, James SK, Becker RC, Storey RF, Wallentin L, Siegahn A, Kontny F. C-X-C Ligand 16 ils an Independent Predictor of Cardiovascular Death and Morbidity in Acute Coronary Syndrome. Arteriosclre Throm Vasc Biol. 2019 Nov;39(11):2402-2410. doi: 10.116/ATVBAHA. 119.3162633. Epub 2019 Sep 26.
- 63 Akerblom A, James SK, Lakic TG, Becker RC, Canon CP, Steg PG, Himmelmann A, Katus HA, Storey RF, Wallentin L, Weaver WD, Siegbahn A, PLATO Investigators. Clin Cardiol. 2019 Dec;42(12):1202-1209. doi: 10.1002/clc.23274. Epub 2019 Oct 9.
- 64 Ueland T, Akerblom A, Ghukasyan T, Michelsen AE, Becker RC, Bertilsson M, Budaj A, Cornel JH, Himmelmann A, James SK, Siegbahn A, Storey RF, Kontny F, Aukrust P, Wallentin L; PLATO Investigators. Atherosclerosis. 2019 Nov 29;293:35-41. doi: 10.1016/j. atherosclerosis.2019.11.031. [Epub ahead of print]
- 65 Akerblom A, Wojdyla D, Steg PG, Wallentin L, James SK, Budaj A, Katus HA, Himmelmann A, Huber K, Siegbahn A, Storey RF, Becker RC, PLATO Investigators. Prevalence and relevance of abnormal glucose metabolism in acute coronary syndromes: insights from the PLATelet inhibition and patient Outcomes (PLATO) trial. J Thromb Thrombolysis. 2019 Nov; 48(4):563-569. doi: 10.007/s11239-019-01938-2.
- 66 Thomas MR, James SK, Becker RC, Himmelmann A, Katus HA, Cannon CP, Steg PG, Siegbahm A, Lakic T, Storey RF, Wallentin L. Prognostic Imapct of Baseline Inflammatory Markers in patients with acute Coronary Syndromes treated with Ticagrelor and Clopidogrel. European Heart Jouran: AcuteCardiovascular Care sagepub.com/jouranls-permissions DOI: 10.1177/2048872619878075
- 67 Tran AH, Flynn JT, Becker RC, Daniels SR, Falkner BE, Ferguson M, Hanevold CD, Hooper SR, Ingelfinger JR, Lande MB, Martin LJ, Meyers K, Mitsnefes M, Rosner B, Samuels JA, Urbina EM. Subclinical Systolic and Diastolic Dysfunction is Evident in Youth With Elevated Blood Pressure. Hypertension. 2020 June;75(6):1551-1556. doi: 10.1161/HYPERTENSIO-NAHA.119..14682. Epub 2020 May 4. PMID: 32362230
- 68 Becker KC, Coulter Kwee L, Neely ML, Grass E, Jakubowski JA, Fox KAA, White HD, Gregory SG, Gurbel PA, de Pinto Caralho L, Becker RC, Magnus Ohman E, Roe MT, Shah SH, Chan MY. Circulationg MocroRNA Profiling in Non-ST Elevated Coronary Artery Syndrome Highlights Genomic Associates with Serial Platelet Reactivity Measurements. Sci Rep 10, 6169 (2020). https://doi.org/10.1038/s41598-020-63263-6
- **69 Becker RC**. Antithrombotic Therapy in Atrial Fibrillation and Coronary Artery Disease. The New England Journal of Medicine. DOI: 10.1056/NEJMe1910560 September 2, 2019
- 70 Becker RC, Owens AP, Sadayappan S. Tissue-level Inflammation and Ventricular Remodeling in Hypertrophic Cardiomyopathy. J Thromb & Thrombolysis. 49, 177-183(2020)doi: 10.1007/s11239-019-02026-1. January 20, 2020 [Epub ahead of prin

- 71 Becker RC, Sadayappan S. Designing Human In Vitro Models for Drug Development. J Am Coll Cardiol. 2020 Feb 18;75(6):587-589. doi: 10.106/j.jacc.2019-12-013.
- 72 Becker RC. Toward Understanding the 2019 Coronavirus and its impact on the heart. Journal of Thrombosis and Thrombolysis. Online 15 April 2020. https:// doi.org/10.1007/s11239-020-02107-6
- 73 Becker RC. COVID-19 Treatment Update: Follow the Science. Journal of Thrombosis and Thrombolysis. Online 28 April 2020. http://link.springer.com/article/10.1007/s11239-020-02120-9
- 74 Becker RC, Owens AP, Sadayappan S. The Potential Roles of Von Willebrand factor ad neutrophil extracellular traps in the natural history of hypertrophic and hypertensive cardiomyopathy. Thrombosis Research. 192 (2020) 78-87. https://doi.org/10.1016/j. thromres.2020.05.003 Available online 7 May 2020.



# Division of Digestive Diseases

## ENDOWED CHAIR: Robert and Helen Gould Endowed Professorship in Internal Medicine

The Digestive Disease Division has an active research agenda across the spectrum of gastrointestinal disorders. This includes basic, and clinical/translational 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.



Kenneth E. Sherman, MD, PhD DIVISION DIRECTOR

#### **Research Focus Areas/Types:**

Currently, the division has five active research laboratories/ groups. These investigators are nationally recognized for their contributions to the understanding of:

- New treatments of hepatitis C, and interaction of HIV and hepatitis C viruses
- Viral host immunology and hepatic fibrosis
- Pharmacoeconomics
- Hepatitis B Clearance
  Mechanisms
- SARS CoV-2 replication and injury in the liver
- Effects of Cocaine on Liver Disease Progression
- Hepatitis E in Immunosuppressed Hosts
- Opioids and Viral Infections
- Drug Induced Liver Disease
- Inflammatory bowel diseases and C difficile infection
- Eosinophilic esophagitis
- Liver Transplantation Immunosuppression and use of hepatitis virus infected organs

#### Investigators/Trainees:

We have seven MD investigators engaged in clinical and translational research, three PhD investigators engaged in basic/translational research and one PharmD focused on liver transplantation. The Division has one endowed Chair (Gould) that is currently filled.

#### **Funding types:**

- National Institutes of Health
- Foundations (e.g. AASLD Foundation)
- UC College of Medicine and Department of Internal Medicine
- Industry and public-private partnerships

#### **Mentoring:**

All division laboratories are available to medical residents interested in an elective experience in a basic/translational 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.

## **Collaborations:**

A joint GI training grant with pediatric gastroenterology has recently been renewed and funded. This grant provides stipends for fellows interested in basic and translational laboratory research. The divisional faculty have active international collaborations in South Africa, Botswana, Ghana, Rwanda and India and work with leading investigators at UCSF, University of Maryland, Florida International University, University of Florida, University of North Carolina, Duke University and Harvard University.

# **DISCOVER & INNOVATE** Digestive Diseases SPOTLIGHT

# Elizabeth Stambrook, BSN, RN

SENIOR CLINICAL RESEARCH PROFESSIONAL DIGESTIVE DISEASES



College of Medid
t first, Elizabeth Stambrook was resistant to a career in research. Her father was a professor emeritus in the University of Cincinnati's Department of Molecular Genetics, and her mother was an associate senior librarian in the UC Health Sciences Library.

"I grew up in the throes of academic medicine and saw the reality of competing for funding and the amount of commitment it took to have a successful career," Stambrook says. But while attending Rutgers University, Stambrook was surprised to find that the classes she enjoyed most were biology-based psychology courses. "I ended up working in a neuroscience lab as a student, and it felt like coming home."

It was during her undergraduate years that Stambrook also realized the importance of research support staff. "They not only manage a portion of actual research activities but the scope of their responsibilities can be as broad as their Pl or credentialing will allow," she says. "These roles also develop knowledge and skills that are applicable to multiple fields within biological sciences, allowing easy transition if desired."

So after earning her bachelor's degree, Stambrook found a position managing a neuroscience lab. Then, intrigued by exposure to translational research, she transitioned into clinical research. Knowing that she would be limited by having a BA, Stambrook decided to return to school and earn her BSN and RN license.

"Completing my nursing degree was an accomplishment that has opened many pathways forward for me," says Stambrook. "The degree helped me find my current position as a clinical research nurse and paved the way towards an eventual master's degree in nursing."

Today, Stambrook is a senior clinical research professional in UC's Department of Internal Medicine's Digestive Diseases Division. Her research group focuses on liver diseases, with most projects sharing a common goal to either halt advancement of liver disease (a common pathway despite the etiology) or attenuate the effects of cirrhosis and portal hypertension.

In 2021, Stambrook's team will undertake multiple new clinical trials for NASH, or nonalcoholic steatohepatitis — liver inflammation and damage caused by a buildup of fat in the liver. NASH is a form of the condition called nonalcoholic fatty liver disease. The group will also begin their first monoclonal antibody study for treatment of eosinophilic esophagitis, (EoE), a chronic immune system disease in which eosinophils (a type of white blood cell), builds up in the lining of the esophagus. This buildup, which is caused by an immune-mediated response, can inflame or injure the esophageal tissue, leading to swallowing and eating difficulties for patients.

"If we can limit the amount of liver damage caused by NASH, then we can halt the progression of liver disease and potentially reverse it," Stambrook says.

With her nursing background, Stambrook helps move these important clinical trials forward while keeping the patients' best interests at heart — and finds herself in a role that feels just right.

"I grew up in academic medicine and swore that I would never end up doing research at a university," says Stambrook. "Despite this, all of my post-graduate jobs have been with universities or academic medical centers. I find it interesting that the things you fight against when young can ultimately end up being the right fit." •

AFTER EARNING HER BACHELOR'S DEGREE, STAMBROOK FOUND A POSITION MANAGING A NEUROSCIENCE LAB. THEN, INTRIGUED BY EXPOSURE TO TRANSLATIONAL RESEARCH, SHE TRANSITIONED INTO CLINICAL RESEARCH.

**Digestive Diseases** 

#### PUBLICATIONS July 1, 2019 thru June 30, 2020

- Relation of Magnetic Resonance Elastography to Fontan Failure and Portal Hypertension. Alsaied T, Possner M, Lubert AM, Trout AT, Szugye C, Palermo JJ, Lorts A, Goldstein BH, Veldtman GR, Anwar N, Dillman JR.Am J Cardiol. 2019 Nov 1;124(9):1454-1459. doi: 10.1016/j. amjcard.2019.07.052. Epub 2019 Aug 7. PMID: 31474329
- 2 Use, Safety, and Effectiveness of Viremic Hepatitis B Virus Donor Livers: A Potential Opportunity to Expand the Donor Pool. Lee TC, Kaiser TE, Luckett K, Wima K, Winer LK, Morris MC, Kassam AF, Safdar K, Bari K, Anwar N, Quillin RC 3rd, Shah SA.Liver Transpl. 2019 Oct;25(10):1581-1584. doi: 10.1002/lt.25595. Epub 2019 Aug 6.PMID: 31273919
- 3 Use of Hepatitis C Nucleic Acid Test-Positive Liver Allografts in Hepatitis C Virus Seronegative Recipients. Anwar N, Kaiser TE, Bari K, Schoech M, Diwan TS, Cuffy MC, Silski L, Quillin RC 3rd, Safdar K, Shah SA. Liver Transpl. 2020 May;26(5):673-680. doi: 10.1002/ lt.25741.PMID: 32125753
- Safety and Efficacy of Budesonide for Liver Transplant Immune Suppression: Results of a Pilot Phase 2a trial. Bari K, Shah SA, Kaiser TE, Cohen RM, Anwar N, Kleesattel D, Sherman KE.Liver Transpl. 2020 Jun 30. doi: 10.1002/lt.25837. Online ahead of print. PMID: 32602616
- 5 Sarcoidosis Involving the Gastrointestinal Tract: Diagnostic and Therapeutic Management.Brito-Zerón P, Bari K, Baughman RP, Ramos-Casals M.Am J Gastroenterol. 2019 Aug;114(8):1238-1247. doi: 10.14309/ajg.00000000000171.PMID: 30865014
- 6 Use of Hepatitis C Virus Antibody-Positive Donor Livers in Hepatitis C Nonviremic Liver Transplant Recipients. Luckett K, Kaiser TE, Bari K, Safdar K, Schoech MR, Apewokin S, Diwan TS, Cuffy MC, Anwar N, Shah SA.J Am Coll Surg. 2019 Apr;228(4):560-567. doi: 10.1016/j.jamcollsurg.2018.12.004. Epub 2018 Dec 23.PMID: 30586641
- 7 Delayed Sleeve Gastrectomy Following Liver Transplantation: A 5-Year Experience. Morris MC, Jung AD, Kim Y, Lee TC, Kaiser TE, Thompson JR, Bari K, Shah SA, Cohen RM, Schauer DP, Smith EP, Diwan TS.Liver Transpl. 2019 Nov;25(11):1673-1681. doi: 10.1002/ lt.25637. Epub 2019 Oct 15.PMID: 31518478
- 8 Synthetic Opioid Use and Common Injection-associated Viruses: Expanding the Translational Research Agenda. Blackard JT, Brown JL, Lyons MS.Curr HIV Res. 2019;17(2):94-101. doi: 10.2174/1570162X1766 6190618154534.PMID: 31210115
- 9 Blackard JT, Davies SM, Laskin BL.Rev Med Virol. 2020 Mar 3:e2102. doi: 10.1002/rmv.2102. Online ahead of print.PMID: 32128960
- BK polyomavirus diversity-Why viral variation matters. Sherman KE, Rouster SD, Kong LX, Aliota MT, Blackard JT, Dean GE.PLoS One. 2019 Mar 20;14(3):e0214016. doi: 10.1371/journal.pone.0214016. eCollection 2019. PMID: 30893357

- 11 Zika virus replication and cytopathic effects in liver cells. Choga WT, Anderson M, Zumbika E, Moyo S, Mbangiwa T, Phinius BB, Melamu P, Kayembe MK, Kasvosve I, Sebunya TK, **Blackard JT**, Essex M, Musonda RM, Gaseitsiwe S.Virus Genes. 2019 Feb;55(1):33-42. doi: 10.1007/s11262-018-1610-z. Epub 2018 Oct 31.PMID: 30382563
- 12 Molecular characterization of hepatitis B virus in blood donors in Botswana. Choga WT, Anderson M, Zumbika E, Moyo S, Mbangiwa T, Phinius BB, Melamu P, Kayembe MK, Kasvosve I, Sebunya TK, Blackard JT, Essex M, Musonda RM, Gaseitsiwe S.Virus Genes. 2019 Feb;55(1):33-42. doi: 10.1007/s11262-018-1610-z. Epub 2018 Oct 31.PMID: 30382563
- 13 Frequency of Hepatitis B Virus Resistance Mutations in Women Using Tenofovir Gel as Pre-Exposure Prophylaxis. Baxter C, Ngcapu S, Blackard JT, Powell EA, Penton PK, Abdool Karim SS.Viruses. 2019 Jun 19;11(6):569. doi: 10.3390/v11060569.PMID: 31248149
- 14 Addressing the Disease Burden of Vertically Acquired Hepatitis C Virus Infection Among Opioid-Exposed Infants. Protopapas S, Murrison LB, Wexelblatt SL, Blackard JT, Hall ES.Open Forum Infect Dis. 2019 Oct 21;6(12):ofz448. doi: 10.1093/ofid/ofz448. eCollection 2019 Dec.PMID: 32128320
- 15 The natural history of BK polyomavirus and the host immune response after stem cell transplantation. Laskin BL, Denburg MR, Furth SL, Moatz T, Altrich M, Kleiboeker S, Lutzko C, Zhu X, Blackard JT, Jodele S, Lane A, Wallace G, Dandoy CE, Lake K, Duell A, Litts B, Seif AE, Olson T, Bunin N, Davies SM.Clin Infect Dis. 2019 Dec 18:ciz1194. doi: 10.1093/cid/ciz1194. Online ahead of print.PMID: 31851312
- 16 Identification of hepatitis B virus genotype A/E recombinants in Ghana. Boyce CL, Willis S, Archampong TNA, Lartey M, Sagoe KW, Obo-Akwa A, Kenu E, Kwara A, Blackard JT.Virus Genes. 2019 Oct;55(5):707-712. doi: 10.1007/s11262-019-01690-y. Epub 2019 Jul 25.PMID: 31346975
- 17 In response to identification of a quadruple mutation that confers tenofovir resistance in chronic hepatitis B patients. Blackard JT, Kwara A, Sherman KE.J Hepatol. 2019 Dec;71(6):1259-1260. doi: 10.1016/j. jhep.2019.07.010. Epub 2019 Sep 26.PMID: 31564447
- 18 CCR5 receptor antagonism inhibits hepatitis C virus (HCV) replication in vitro. Blackard JT, Kong L, Rouster SD, Karns R, Horn PS, Kottilil S, Shata MT, Sherman KE.PLoS One. 2019 Oct 29;14(10):e0224523. doi: 10.1371/journal.pone.0224523. eCollection 2019. PMID: 31661521
- 19 Molecular characterization of hepatitis C virus in liver disease patients in Botswana: a retrospective crosssectional study. Bhebhe L, Anderson M, Souda S, Choga WT, Zumbika E, Shaver ZM, Mbangiwa T, Phinius BB, Banda CC, Melamu P, Musonda RM, Essex M, Blackard JT, Moyo S, Gaseitsiwe S.BMC Infect Dis. 2019 Oct 22;19(1):875. doi: 10.1186/s12879-019-4514-1.PMID: 31640596

- 20 Hepatitis C Virus Infection of Human Thyrocytes: Metabolic, Hormonal, and Immunological Implications. Hammerstad SS, Blackard JT, Lombardi A, Owen RP, Concepcion E, Yi Z, Zhang W, Tomer Y.J Clin Endocrinol Metab. 2020 Apr 1;105(4):1157-68. doi: 10.1210/clinem/dgz241.PMID: 31784757
- 21 The distribution of hepatitis B virus surface antigen polymorphisms at positions associated with vaccine escape. Raheel M, Choga WT, **Blackard JT**.J Med Virol. 2020 Feb 27. doi: 10.1002/jmv.25730. Online ahead of print.PMID: 32104912
- 22 Impact of Lamivudine-Based Antiretroviral Treatment on Hepatitis B Viremia in HIV-Coinfected South Africans. Incidence of hepatitis B virus infection among human immunodeficiency virus-infected treatment naïve adults in Botswana. Phinius BB, Anderson M, Bokete R, Mbangiwa T, Choga WT, Baruti K, Makhema J, Musonda R, Blackard JT, Essex M, Moyo S, Marlink R, Gaseitsiwe S.Medicine (Baltimore). 2020 Fe b; 9 9 (9): e1 9 3 4 1. doi: 10.1097/ MD.000000000019341.PMID: 32118769
- 23 Impact of Lamivudine-Based Antiretroviral Treatment on Hepatitis B Viremia in HIV-Coinfected South Africans. Lukhwareni A, Gededzha MP, Amponsah-Dacosta E, Blackard JT, Burnett RJ, Selabe SG, Kyaw T, Mphahlele MJ.Viruses. 2020 Jun 11;12(6):E634. doi: 10.3390/v12060634.PMID: 32545313
- 24 HIV and the liver. Sherman KE, Peters MG, Thomas DL.Top Antivir Med. 2019 Sep;27(3):101-110. PMID: 31634861
- 25 Hepatitis B Vaccination and Waning Hepatitis B Immunity in Persons Living with HIV. Farooq PD, Sherman KE.Curr HIV/AIDS Rep. 2019 Oct;16(5):395-403. doi: 10.1007/s11904-019-00461-6.PMID: 31468298
- 26 Hepatitis E: What We Think We Know. Seth A, Sherman KE.Clin Liver Dis (Hoboken). 2020 Mar 2;15(Suppl 1):S37-S44. doi: 10.1002/cld.858. eCollection 2020 Feb. PMID: 32140212
- 27 Liver Fibrosis Progression and Mortality in Hepatitis B- and C-Coinfected Persons Treated With Directly Acting Antiviral Agents: Results From ERCHIVES. Butt AA, Yan P, Aslam S, Abou-Samra AB, Sherman KE, Shaikh OS.Clin Infect Dis. 2019 Dec 16:ciz1097. doi: 10.1093/cid/ciz1097. Online ahead of print. PMID: 31840746
- 28 Use of HCV Ab+/NAT- donors in HCV naïve renal transplant recipients to expand the kidney donor pool. Dao A, Cuffy M, Kaiser TE, Loethen A, Cafardi J, Luckett K, Rike AH, Cardi M, Alloway RR, Govil A, Diwan T, Sherman KE, Shah SA, Woodle ES.Clin Transplant. 2019 Jul;33(7):e13598. doi: 10.1111/ctr.13598. Epub 2019 Jun 5.PMID: 31104346
- 29 Editorial: HCV Cure is the Start of the End For Those With Advanced Fibrosis/Cirrhosis. Seth A, Sherman KE.Clin Infect Dis. 2020 May 9:ciaa509. doi: 10.1093/ cid/ciaa509. Online ahead of print.PMID: 32386202

- **30** Treatment of HCV reduces viral hepatitis-associated liver-related mortality in patients: An ERCHIVES study. Butt AA, Yan P, Shaikh OS, Lo Re V 3rd, Abou-Samra AB, **Sherman KE**J Hepatol. 2020 Mar 5:S0168-8278(20)30120-3. doi: 10.1016/j.jhep.2020.02.022. Online ahead of print.PMID: 32145260
- 31 Cost-effectiveness of Using Kidneys From HCV-Viremic Donors for Transplantation Into HCV-Uninfected Recipients. Eckman MH, Woodle ES, Thakar CV, Alloway RR, Sherman KE.Am J Kidney Dis. 2020 Jun;75(6):857-867. doi: 10.1053/j.ajkd.2019.11.005. Epub 2020 Feb 17.PMID: 32081494
- 32 Hepatitis C virologic response in hepatitis B and C coinfected persons treated with directly acting antiviral agents: Results from ERCHIVES. Butt AA, Yan P, Aslam S, Sherman KE, Siraj D, Safdar N, Hameed B. Int J Infect Dis. 2020 Mar;92:184-188. doi: 10.1016/j. ijid.2020.01.025. Epub 2020 Jan 21.PMID: 31978574
- Sex Differences, Cocaine Use, and Liver Fibrosis Among African Americans in the Miami Adult Studies on HIV Cohort. Zarini G, Sales Martinez S, Campa A, Sherman K, Tamargo J, Hernandez Boyer J, Teeman C, Johnson A, Degarege A, Greer P, Liu Q, Huang Y, Mandler R, Choi D, Baum MKJ Womens Health (Larchmt). 2020 Jan 31. doi: 10.1089/jwh.2019.7954. Online ahead of print.PMID: 32004098
- 34 Validation and Refinement of Noninvasive Methods to Assess Hepatic Fibrosis: Magnetic Resonance Elastography Versus Enhanced Liver Fibrosis Index. Sherman KE, Abdel-Hameed EA, Ehman RL, Rouster SD, Campa A, Martinez SS, Huang Y, Zarini GG, Hernandez J, Teeman C, Tamargo J, Liu Q, Mandler R, Baum MK.Dig Dis Sci. 2020 Apr;65(4):1252-1257. doi: 10.1007/ s10620-019-05815-z. Epub 2019 Aug 29. PMID: 31468264
- 35 The enhanced liver fibrosis (ELF)-Index predicts hepatic fibrosis superior to FIB4 and APRI in HIV/HCV infected patients. Abdel-Hameed EA, Rouster SD, Kottilil S, Sherman KE.Clin Infect Dis. 2020 May 27:ciaa646. doi: 10.1093/cid/ciaa646. Online ahead of print.PMID: 32459305
- 36 Liver injury is most commonly due to hepatic metastases rather than drug hepatotoxicity during pembrolizumab immunotherapy. Tsung I, Dolan R, Lao CD, Fecher L, Riggenbach K, Yeboah-Korang A, Fontana RJ.Aliment Pharmacol Ther. 2019 Oct;50(7):800-808. doi: 10.1111/apt.15413. Epub 2019 Jul 15. PMID: 31309615
- 37 Utility of a Computerized ICD-10 Algorithm to Identify Idiosyncratic Drug-Induced Liver Injury Cases in the Electronic Medical Record. Yeboah-Korang A, Louissaint J, Tsung I, Prabhu S, Fontana RJ.Drug Saf. 2020 Apr;43(4):371-377. doi: 10.1007/s40264-019-00903-5.PMID: 31916081
- 38 Use, Safety, and Effectiveness of Viremic Hepatitis B Virus Donor Livers: A Potential Opportunity to Expand the Donor Pool. Lee TC, Kaiser TE, Luckett K, Wima K, Winer LK, Morris MC, Kassam AF, Safdar K, Bari K, Anwar N, Quillin RC 3rd, Shah SA.Liver Transpl. 2019 Oct;25(10):1581-1584. doi: 10.1002/lt.25595. Epub 2019 Aug 6.PMID: 31273919

#### **Digestive Diseases**

PUBLICATIONS CONTINUED

- 39 Use of HCV Ab+/NAT- donors in HCV naïve renal transplant recipients to expand the kidney donor pool. Dao A, Cuffy M, Kaiser TE, Loethen A, Cafardi J, Luckett K, Rike AH, Cardi M, Alloway RR, Govil A, Diwan T, Sherman KE, Shah SA, Woodle ES.Clin Transplant. 2019 Jul;33(7):e13598. doi: 10.1111/ctr.13598. Epub 2019 Jun 5.PMID: 31104346
- **40** Telemedicine Based Remote Home Monitoring After Liver Transplantation: Results of a Randomized Prospective Trial. Lee TC, **Kaiser TE**, Alloway R, Woodle ES, Edwards MJ, Shah SA.Ann Surg. 2019 Sep;270(3):564-572. doi: 10.1097/SLA.00000000003425. PMID: 31356267
- **41** Delayed Sleeve Gastrectomy Following Liver Transplantation: A 5-Year Experience. Morris MC, Jung AD, Kim Y, Lee TC, **Kaiser TE**, Thompson JR, Bari K, Shah SA, Cohen RM, Schauer DP, Smith EP, Diwan TS.Liver Transpl. 2019 Nov;25(11):1673-1681. doi: 10.1002/ lt.25637. Epub 2019 Oct 15.PMID: 31518478
- 42 Alternatives to immediate release tacrolimus in solid organ transplant recipients: When the gold standard is in short supply. Jorgenson MR, Descourouez JL, Brady BL, Bowman L, Hammad S, Kaiser TE, Laub MR, Melaragno JI, Park JM, Chandran MM.Clin Transplant. 2020 May 13:e13903. doi: 10.1111/ctr.13903. Online ahead of print.PMID: 32400907
- **43** Opioid Minimization after Liver Transplantation: Results of a Novel Pilot Study. Lee TC, Bittel L, **Kaiser TE**, Quillin RC 3rd, Jones C, Shah SA.Liver Transpl. 2020 Jun 23. doi: 10.1002/lt.25829. Online ahead of print. PMID: 32578334

## Division of Endocrinology, Diabetes and Metabolism

## ENDOWED CHAIR: Albert W. Vontz, Jr. Chair in Diabetes

The Division of Endocrinology, Diabetes and Metabolism is committed to improving the health of our region by translating insightful findings from innovative research into impactful outcomes for the health of patients and our community. A few examples of how the division is making a difference include the hemoglobin A1C and blood glucose research led by Robert M. Cohen, MD; Jason Winnick, PhD, study of hepatic glucose metabolism; Yufei Dai, MD, investigation of the mechanism(s) responsible for hypoglycemia after weight-loss surgery; Mercedes Falciglia, MD, outcomes research on the clinical care of patients with diabetes and Ruchi Bhabhra' s work in novel therapeutic strategies for managing pituitary disorders and the treatment of acromegaly. Basic science research includes Vincent Fong, MD, PhD, investigation of why steroids affect bone and fat cells adversely and Dr. Shailendra Patel's work on genetic disorders of cholesterol metabolism.



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

#### **Research Focus Areas/Types:**

Current research interests range from exploring the integrated pathways using animal models of diabetes and obesity, lipid disorders affecting embryonic development and atherosclerosis to diabetes and metabolic clinical research. Examples are:

- Mechanisms important in hypoglycemia responses in subjects with diabetes
- Rare lipid disorders and integrated cholesterol metabolism in animal models
- The role of cholesterol in embryonic development
- Mechanisms by which the toxic

proteins, causing Alzheimer's disease, are excreted by the brain

- The relationship between bone and metabolism
- Comparative effectiveness of various therapies for improving the durability of type 2 diabetes treatment (beta cell preservation),
- Mechanisms underlying variation between people in the hemoglobin A1c-blood glucose relationship, including racial differences
- Clinical interventions to reduce diabetes and nonalcoholic fatty liver consequences after liver transplantation
- Hematologic mechanisms contributing to the relationship between diet-induced obesity and inflammation

## Investigators/Trainees:

We have two MD PhD investigators (Patel and Fong) engaged in basic science research, two MD investigators (Cohen and Dai) and one PhD investigator (Winnick) engaged in clinical and translational research, one MD PhD (Bhabhra) engaged in clinical trials and one MD (Falciglia) in health outcomes research. We have two basic science laboratories (Patel and Fong). Additionally, all of the Endocrine fellows engage in scholarly activities and are expected to submit a manuscript as part of their training program.

#### **Funding types:**

- National Institutes of Health
- UC College of Medicine and Department of Internal Medicine)

#### Mentoring:

Jason Winnick mentors one postdoctorate fellow, Shailendra Patel hosts one undergraduate intern for laboratory-based research, and Robert Cohen mentors one internal medicine resident and one nursing PhD student for clinical and translational research. In addition, we are all qualified faculty for hosting medical students during their research rotations. Dr. Winnick is also active in the Pathobiology and Medicine Graduate program.

## **Collaborations:**

Our faculty has many collaborative research efforts with other disciplines including Adult and Pediatric Hematology; Digestive Diseases; Transplantation Surgery; Pediatric Gastroenterology, Hepatology and Nutrition; Pediatric Human Genetics; and the Department of Pathology and Laboratory Medicine.

# Robert M. Cohen, MD

PROFESSOR DIVISION OF ENDOCRINOLOGY, DIABETES AND METABOLISM



Annual Research Report 2020

edicine runs in the family for Robert Cohen, MD; his father was a physician too, as well as two of his three brothers. Still, Cohen was equally drawn to both science and medicine at first. But it was his introduction to research, through a 1969 summer program for high school students sponsored by the National Science Foundation, that helped him find his niche.

"I continued with a substantial research experience most summers throughout college at the National Institutes of Health and the Marine Biological Laboratory and spent my senior year doing research full time," Cohen says. "I saw the potential for a combined career in medicine and science. I selected endocrinology and diabetes because I thought it was an opportunity for both leading-edge science and long-term patient care relationships."

That potential for long-lasting connections has proven true over Cohen's 40-year career, in which he has focused particularly on preventing diabetes complications for patients.

"Just recently, in one afternoon I saw three of my patients who have had type 1 diabetes for more than 50 years each and another with diabetes for almost 40 years," says Cohen. "I've been their doctor for three decades."

Most recently, Cohen's research has highlighted the physiology underlying mismatches between hemoglobin A1c (HbA1c) and blood glucose that interfere with preventing diabetes complications. For decades, HbA1c has been the standard measure of glycemic control for most patients with diabetes. The test is cost-effective, easy to obtain and correlates with complication risk. However, HbA1c has limitations, including clinically significant mismatches between HbA1c and average glucose (AG).

The existence of mismatches is important as they can result in over- or under-treatment of diabetes, each of which has risks and costs. If hemoglobin A1c is erroneously thought to be too high when, in fact, the underlying AG is acceptable, the individual could be overly aggressively treated and become predisposed to both dangerous hypoglycemia and excessive induced weight gain. Conversely, patients with a "low mismatch" might not have therapy intensified to reduce their risk of diabetes complications. Significant mismatches between HbA1c and AG may occur in up to 30 percent of the population, Cohen says. His latest hypothesis suggests that red blood cell lifespan variation is the predominant cause for these mismatches, and with a new NIH-funded research grant, he plans to test the idea in larger and more diverse populations.

"We anticipate that the result of the study will have a major impact on improving diabetes care for millions of patients in both developed and developing countries around the world," says Cohen, who adds that resulting data will be shared with national and international research meetings to determine how the findings might translate into trials and clinical care.

Cohen, who came to UC as a faculty member in 1985, is proud of his research team that has worked together for more than 20 years.

"Since at UC, I have had valuable experiences with faculty members both ahead of and behind me in seniority from whom I have continued to learn and/or tried to serve as a role model," Cohen says. "Each has contributed to my career development as both clinician, investigator and teacher. •" RESEARCH HAS HIGHLIGHTED THE MISMATCHES BETWEEN HEMOGLOBIN A1C AND AVERAGE GLUCOSE. HIS LATEST HYPOTHESIS SUGGESTS THAT RED BLOOD CELL LIFESPAN VARIATION IS THE PREDOMINANT CAUSE FOR THESE MISMATCHES.

**COHEN'S RECENT** 

Endocrinology, Diabetes and Metabolism

## PUBLICATIONS July 1, 2019 thru June 30, 2020

- 1 AMERICAN ASSOCIATION OF CLINICAL ENDOCRI-NOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOL-OGY CLINICAL PRACTICE GUIDELINES FOR THE DIAG-NOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS- 2020 UPDATE EXECUTIVE SUMMARY. Camacho PM, Petak SM, Binkley N, **Diab DL**, Eldeiry LS, Farooki A, Harris ST, Hurley DL, Kelly J, Lewiecki EM, Pessah-Pollack R, McClung M, Wimalawansa SJ, Watts NB. Endocr Pract. 2020 May;26(5):564-570. doi: 10.4158/GL-2020-0524. PMID: 32427525
- 2 AMERICAN ASSOCIATION OF CLINICAL ENDOCRI-NOLOGISTS/AMERICAN COLLEGE OF ENDOCRINOL-OGY CLINICAL PRACTICE GUIDELINES FOR THE DIAG-NOSIS AND TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS-2020 UPDATE. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, Harris ST, Hurley DL, Kelly J, Lewiecki EM, Pessah-Pollack R, McClung M, Wimalawansa SJ, Watts NB. Endocr Pract. 2020 May;26(5):564-570. doi: 10.4158/GL-2020-0524. PMID: 32427525 PMID: 32427503
- 3 Optimization of Metformin in the GRADE Cohort: Effect on Glycemia and Body Weight. Sivitz WI, Phillips LS, Wexler DJ, Fortmann SP, Camp AW, Tiktin M, Perez M, Craig J, Hollander PA, Cherrington A, Aroda VR, Tan MH, Krakoff J, Rasouli N, Butera NM, Younes N; GRADE Research Group. PMID: 32139384
- 4 Simultaneous Occurrence of Germline Mutations of SDHB and TP53 in a Patient with Metastatic Pheochromocytoma. Gniado E, Carracher CP, Sharma S. J Clin Endocrinol Metab. 2020 Apr 1;105(4):dgz269. doi: 10.1210/clinem/dgz269. PMID: 31851316 Diabetes Care. 2020 May;43(5):940-947. doi: 10.2337/dc19-1769. Epub 2020 Mar 5.
- 5 Aggressive granular cell tumor of the neurohypophysis with optic tract edema and invasion into third ventricle. Dai Y, Hagen M, Andaluz N, Bhabhra R. Surg Neurol Int. 2019 Nov 15;10:217. doi: 10.25259/SNI\_356\_2019. eCollection 2019. PMID: 31819811 Free PMC article. Am J Physiol Gastrointest Liver Physiol. 2020 Feb 1;318(2):G370-G374. doi: 10.1152/ajpgi.00224.2019. Epub 2019 Nov 11. PMID: 31709832
- 6 Roux-en-Y gastric bypass surgery improves hepatic glucose metabolism and reduces plasma kisspeptin levels in morbidly obese patients with type 2 diabetes. Flynn CR, Albaugh VL, Tamboli RA, Gregory JM, Bosompem A, Sidani RM, Winnick JJ. Am J Physiol Gastrointest Liver Physiol. 2020 Feb 1;318(2):G370-G374. doi: 10.1152/ajpgi.00224.2019. Epub 2019 Nov 11. PMID: 31709832 PMID: 31689374
- PRADC1: a novel metabolic-responsive secretory protein that modulates physical activity and adiposity. Rodriguez S, Stewart AN, Lei X, Cao X, Little HC, Fong V, Sarver DC, Wong GW. FASEB J. 2019 Dec;33(12):14748-14759. doi: 10.1096/fj.201901279R. Epub 2019 Nov 5.
- 8 Delayed Sleeve Gastrectomy Following Liver Transplantation: A 5-Year Experience. Morris MC, Jung AD, Kim Y, Lee TC, Kaiser TE, Thompson JR, Bari K, Shah SA, Cohen RM, Schauer DP, Smith EP, Diwan TS. Liver Transpl. 2019 Nov;25(11):1673-1681. doi: 10.1002/ lt.25637. Epub 2019 Oct 15. PMID: 31518478

- 9 Aerobic exercise training improves hepatic and muscle insulin sensitivity, but reduces splanchnic glucose uptake in obese humans with type 2 diabetes. Gregory JM, Muldowney JA, Engelhardt BG, Tyree R, Marks-Shulman P, Silver HJ, Donahue EP, Edgerton DS, Winnick JJ. Nutr Diabetes. 2019 Sep 2;9(1):25. doi: 10.1038/s41387-019-0090-0. PMID: 31474750; PMCID: PMC6717736.
- 10 Rationale and Design for a GRADE Substudy of Continuous Glucose Monitoring. Larkin ME, Nathan DM, Bebu I, Krause-Steinrauf H, Herman WH, Higgins JM, Tiktin M, Cohen RM, Lund C, Bergenstal RM, Johnson ML, Arends V; GRADE Research Group. Diabetes Technol Ther. 2019 Dec;21(12):682-690. doi: 10.1089/ dia.2019.0202. Epub 2019 Sep 4. PMID: 31393176
- 11 Baseline Characteristics of Randomized Participants in the Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness Study (GRADE). Wexler DJ, Krause-Steinrauf H, Crandall JP, Florez HJ, Hox SH, Kuhn A, Sood A, Underkofler C, Aroda VR; GRADE Research Group. Diabetes Care. 2019 Nov;42(11):2098-2107. doi: 10.2337/dc19-0901. Epub 2019 Aug 7. PMID: 31391203; PMCID: PMC6804613.
- 12 Intensive vs Standard Treatment of Hyperglycemia and Functional Outcome in Patients With Acute Ischemic Stroke: The SHINE Randomized Clinical Trial. Johnston KC, Bruno A, Pauls Q, Hall CE, Barrett KM, Barsan W, Fansler A, Van de Bruinhorst K, Janis S, Durkalski-Mauldin VL; Neurological Emergencies Treatment Trials Network and the SHINE Trial Investigators. JAMA. 2019 Jul 23;322(4):326-335. doi: 10.1001/ jama.2019.9346. Erratum in: JAMA. 2019 Nov 5;322(17):1718. PMID: 31334795; PMCID: PMC6652154.
- 13 New-Onset Post-Transplant Diabetes Mellitus after Allogeneic Hematopoietic Cell Transplant Is Initiated by Insulin Resistance, Not Immunosuppressive Medications.Engelhardt BG, Savani U, Jung DK, Powers AC, Jagasia M, Chen H, Winnick JJ, Tamboli RA, Crowe JE Jr, Abumrad NN. Biol Blood Marrow Transplant. 2019 Jun;25(6):1225-1231. doi: 10.1016/j.bbmt.2019.02.001. Epub 2019 Feb 7. PMID: 30738170; PMCID: PMC6559863.

## Division of General Internal Medicine

## ENDOWED CHAIRS: Posey Chair and Richard W. and Sue P. Vilter Chair

Research in our Division impacts numerous stakeholders ranging from patients in our own health care system to national policy. Examples of impactful work include work funded by the Centers for Disease Control and Prevention that has contributed to updated national guidelines on screening recommendations for hepatitis C infection; NIH-funded research helping to elucidate associations between morbid obesity and the incidence of certain cancers and the impact of bariatric surgery on reducing these risks, and another study examining genetic risk factor profiles for future cardiovascular disease in children; PCORIfunded research to determine optimal treatment for migraine headache patients with medication overuse; and another PCORI-funded project to improve treatment for pediatric patients with mood disorders.



Mark H. Eckman, MD DIVISION DIRECTOR

## Research Focus Areas/Types:

Primary areas of interest include the Decision Sciences, Outcomes Research, Health Services Research, Clinical Informatics, Performance Improvement and Innovations in Medical Education, and system redesign.

#### **Impactful Publications:**

Recent high impact publications include an examination of the cost-effectiveness of transplanting kidneys from donors infected with the hepatitis C virus (HCV) into HCV-infected patients with end stage kidney disease and in another article, the effect of variations in published stroke rates on the net clinical benefit of anticoagulation for patients with atrial fibrillation in the *Annals of Internal Medicine*. An analysis of costs and outcomes of transplanting HCV-infected kidneys in HCV-uninfected recipients was selected as one of 4 Editors' Choices for 2020 in the *American Journal of Kidney Diseases*. The assessment of bariatric surgery and the risk of cancer in a large multisite cohort and in another article was published in the *Annals of Surgery*.

## Investigators/Trainees:

We have nine MD investigators engaged in clinical and translational research; Six senior faculty (Eckman, Schauer, Martin, Warm, Burrows, Diers) and three promising junior faculty; (Wood, Kinnear, Kelleher) and two endowed chairs, the Posey Chair and the Vilter Chair. Dr. Kinnear received the Macy Faculty Scholar's Award in 2020. Our faculty have received R01, UL1, Ryan White Foundation, other investigatorinitiated industry and foundation, and Anthem Blue Cross Blue Shield Foundation award funding.

### **Funding types:**

- National Institutes of Health
- Centers for Disease Control and Prevention
- PCORI
- UC College of Medicine and Department of Internal Medicine
- Industry and public-private partnerships

## **Mentoring:**

Our researchers are currently mentoring 2 PhD candidates, 7 junior faculty researchers, and 15 internal medicine residents. We also are mentoring junior faculty in other institutions, including one K-award recipient at the Cleveland Clinic, and faculty at UCSF.

## **Collaborations:**

Beyond a rich network of collaborations within the University of Cincinnati, our faculty collaborate on academic activities and research with colleagues at a number of institutions, including the Harvard Medical School, the Massachusetts General Hospital, UCSF, Kaiser Permanente, McMaster University (Ontario), the Cleveland Clinic, and the University of Birmingham (UK), among others.

# Sharice N. Wood, MD, MPH

ASSISTANT PROFESSOR OF MEDICINE, ATTENDING PHYSICIAN

20

s a primary care physician in the University of Cincinnati Medical Center's Hoxworth Center, Sharice Wood, MD, applies the training from her combined internal medicine and pediatrics residency every day.

"My goal has always been to care for underserved and underrepresented populations and ideally empower people to improve their health," Wood says. "Working in the Hoxworth clinic allows me to do this daily. At the same time, I am privileged to work with residents and medical students and continue to be a part of the academic medicine process."

During her time at Hoxworth, Wood has explored a diverse array of interests—all with the common theme of serving the underserved. In 2017-18, Wood participated in a MATEC Clinician Scholar Program aimed at helping primary care physicians provide high quality HIV/AIDS care. In 2019, she obtained board certification in Obesity Medicine to enable her to work closely with patients in their weight loss efforts. And most recently, in the fall of 2020, Wood joined with the eMERGE IV project with Cincinnati Children's Hospital Medical Center, part of a national effort to evaluate the utility of polygenic risk scores in predicting several common conditions that affect the African American community. Her role in the project will have her review and return the scores to families, along with counseling and education on disease prevention.

"This aspect of research is new for me, and we are still in the early stages, but I am looking forward to learning and growth during this process," says Wood.

This past year also saw Wood moving to the other side of bench — from researcher to subject. Wood and her husband chose to be participants in a COVID-19 vaccine trial. She decided on participation for personal reasons — Wood lost a loved one to COVID-19 — and professional, recognizing the importance of research in informing physicians' daily decisions regarding evidence-based patient care, and the need for data derived from people of color or those who lack resources so that findings can be applied to more diverse populations.

"As an African-American, I recognize that historically, people of color have been treated negatively in science and medicine, so there is often an element of distrust of the health care system. Many of my patients often express concern for these things," Wood says. In the pandemic, people of color have also been disproportionately affected by COVID-19, with higher rates of morbidity and mortality so the cycle seemed to be continuing. "In some ways, I saw my participation in the study as an opportunity to lead by example and try to build a bridge from the African American community to reconnect to the science of medicine."

As vaccines now roll out to the public, Wood, a mom of three, is proud to be an example for her patients and community. "Patients seem to listen a little differently when I speak of my participation in the survey, and even early on, I was able to have some interesting conversations with patients," Wood says. "My hope is that people will gather factual information, then make an informed decision about whether the vaccine is appropriate for their family. I hope that in most cases, the choice is 'yes.'" • "IN SOME WAYS, I SAW MY PARTICIPATION IN THE STUDY AS AN OPPORTUNITY TO LEAD BY EXAMPLE AND TRY TO BUILD A BRIDGE FROM THE AFRICAN AMERICAN COMMUNITY TO RECONNECT TO THE SCIENCE OF MEDICINE."

General Internal Medicine

## PUBLICATIONS July 1, 2019 thru June 30, 2020

## IMPACT PUBLICATION

 A Feasibility Study to Attribute Patients to Primary Interns on Inpatient Ward Teams Using Electronic Health Record Data. Schumacher DJ, Wu DTY, Meganathan K, Li L, Kinnear B, Sall DR, Holmboe E, Carraccio C, van der Vleuten C, Busari J, Kelleher M, Schauer D, Warm E. Acad Med. 2019 Sep;94(9):1376-1383. doi: 10.1097/ACM.000000000002748. PMID: 31460936

#### IMPACT PUBLICATION

- 2 A Reliability Analysis of Entrustment-Derived Workplace-Based Assessments. Kelleher M, Kinnear B, Sall D, Schumacher D, Schauer DP, Warm EJ, Kelcey B. Acad Med. 2019 Sep 17. doi: 10.1097/ ACM.00000000002997. [Epub ahead of print] PMID: 31567170
- 3 Anticoagulation in Pulmonary Arterial Hypertension: A Decision Analysis. Jose A, Eckman MH, Elwing JM. Pulm Circ. 2019 Dec 23;9(4):2045894019895451. doi: 10.1177/2045894019895451. eCollection 2019 Oct-Dec. PMID: 31903185 Free PMC article.
- 4 Automated Tool for Health Utility Assessments: The Gambler II. Adejare AA Jr, Eckman MH. MDM Policy Pract. 2020 Jan-Jun;5(1):2381468320914307. doi: 10.1177/2381468320914307. eCollection 2020 Jan-Jun. PubMed PMID: 32215320; PubMed Central PMCID: PMC7081474.
- 5 Best Predictor of Multimodal Performance in an Internal Medicine Residency. Sharma A, Schauer DP, Kelleher M, Kinnear B, Sall D, Warm E. USMLE Step 2 CK: J Grad Med Educ. 2019 Aug;11(4):412-419. doi: 10.4300/JGME-D-19-00099.1. PMID: 31440335

#### IMPACT PUBLICATION

- 6 Building the Bridge to Quality: An Urgent Call to Integrate Quality Improvement and Patient Safety Education with Clinical Care. Wong BM, Baum KD, Headric LA, Holmboe ES, Moss F, Ogrinc G, Shojania KG, Vaux E, Warm EJ, Frank JR. Acad. Med. 2019 Aug 6. doi: 10.1097/ACM.00000000002937 [Epub ahead of print]
- 7 Cancer Risk After Bariatric Surgery: Does Weight Loss Matter? Schauer DP. Surg Obes Relat Dis. 2020 May 12:S1550-7289(20)30257-4. doi: 10.1016/j. soard.2020.04.052. Online ahead of print. PMID: 32576509
- Cervical Spine Evaluation in Pediatric Trauma: A Costeffectiveness Analysis. Overmann KM, Robinson BRH,
   Eckman MH. Am J Emerg Med. 2019 Dec 9:S0735-6757(19)30793-4. doi: 10.1016/j.ajem.2019.11.051.
   Online ahead of print. PMID: 31870674
- 9 Clinical Guideline Highlights for the Hospitalist: Initial Management of Acute Pancreatitis in the Hospitalized Adult. Jenkins A, Shapiro J. J Hosp Med. 2019 Oct 23; 14:E1-E2. doi: 10.12788/jhm.3324 [Epub ahead of print)
- 10 Clinical Progress Note: Point-of-Care Ultrasound for the Pediatric Hospitalist. Kinnear B, Kelleher M, Chorny V. J Hosp Med. 2019 Nov 20;14:E1-E3. doi: 10.12788/jhm.3325. [Epub ahead of print] No abstract available. PMID: 31891559

- 11 Clinical Progress Note: Point-of-Care Ultrasound in the Evaluation of the Dyspneic Adult. Kelleher M, Kinnear B, Olson A. J Hosp Med. 2019 Dec 23;14:E1-E3. doi: 10.12788/jhm.3340. [Epub ahead of print] No abstract available PMID: 31869295
- 12 Conditions Influencing Collaboration Among the Primary Care Disciplines as They Prepare the Future Primary Care Physician Workforce. Carney PA, Thayer EK, Green LA, Warm EJ, Holmboe ES, Carraccio C, Eiff MP. Fam Med. 2020 Mar 16. doi: 10.22454/ FamMed.2020.741660. [Epub ahead of print] PubMed PMID: 32196119.
- 13 Communication with Diverse Patients: Addressing Culture and Language. O'Toole JK, Alvarado-Little W, Ledford CJW. Pediatr Clin North Am. 2019 Aug;66(4):791-804. doi: 10.1016/j.pcl.2019.03.006. Epub 2019 May 23. Review. PMID: 31230623

#### IMPACT PUBLICATION

- 14 Cost-effectiveness of Using Kidneys From HCV-Viremic Donors for Transplantation Into HCV-Uninfected Recipients. Eckman MH, Woodle ES, Thakar CV, Alloway RR, Sherman KE. Am J Kidney Dis. 2020 Jun;75(6):857-867. doi: 10.1053/j.ajkd.2019.11.005. Epub 2020 Feb 17. PMID: 32081494
- 15 Delayed Sleeve Gastrectomy Following Liver Transplantation: A 5-Year Experience. Morris MC, Jung AD, Kim Y, Lee TC, Kaiser TE, Thompson JR, Bari K, Shah SA, Cohen RM, Schauer DP, Smith EP, Diwan TS. Liver Transpl. 2019 Nov;25(11):1673-1681. doi: 10.1002/lt.25637. Epub 2019 Oct 15. PMID: 31518478
- 16 Development and Establishment of Initial Validity Evidence for a Novel Tool for Assessing Trainee Admission Notes. Weber DE, Held JD, Jandarov RA, Kelleher M, Kinnear B, Sall D, O'Toole JK. J Gen Intern Med. 2020 Jan 28. doi: 10.1007/s11606-020-05669-6. [Epub ahead of print] PMID: 31993944
- Epigenetic Regulation of AURKA by miR-4715-3p in Upper Gastrointestinal Cancers. Gomaa,A; Peng, D; Chen, Z; Soutto,M; Abouelezz, K; Corvalan, A; El-Rifai,
   W. Sci Rep. 2019 Nov 18;9(1): 16970 PMCID: PMC6861278 DOI: 10.1038/s41598-019-53174-6
- 18 Hospitalist-Operated Compression Ultrasonography: a Point-of-Care Ultrasound Study (HOCUS-POCUS). Fischer EA, Kinnear B, Sall D, Kelleher M, Sanchesz O, Mathews B, Schnobrich D, Olson APJ. J Gen Intern Med. 2019 Aug 6. doi: 10.1007/s11606-019-05120-5. [Epub ahead of print] PMID: 31388904
- In Reply to Donato and Paladugu. Warm EJ, Kinnear
  B, Kelleher M, Sall D, Holmboe E. Acad Med. 2019
  Aug; 94(8):1064-1065. doi: 10.1097/
  ACM.00000000002800. PubMed PMID: 31361635

#### IMPACT PUBLICATION

20 Ischemic Stroke and Bleeding: Clinical Benefit of Anticoagulation in Atrial Fibrillation After Intracerebral Hemorrhage. Stanton RJ, Eckman MH, Woo D, Moomaw CJ, Haverbusch M, Flaherty ML, Kleindorfer DO. Stroke. 2020 Mar;51(3):808-814. doi: 10.1161/ STROKEAHA.119.027370. Epub 2020 Jan 31. PMID: 32000590

- 21 Leadership & Professional Development: Get to the "Both/And". Kinnear B, Warm EJ. J Hosp Med. 2019 Dec;14(12):761. doi: 10.12788/jhm.3266. PubMed PMID: 31809693
- 22 Linking Workplace-Based Assessment to ACGME Milestones: A Comparison of Mapping Strategies in Two Specialties. Kelleher M, Kinnear B, Wong SEP, O'Toole J, Warm E. Teach Learn Med. 2019 Sep 18: 1-10. doi 10.1080/10401334.2019.1653764 [Epub ahead of print] PMID: 31530183
- 23 Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy. Kassam AF, Mirza A, Kim Y, Hanseman D, Woodle ES, Quillin RC 3rd, Johnson BL, Govil A, Cardi M, Schauer DP, Smith EP, Diwan TS. Am J Transplant. 2020 Feb;20(2):422-429. doi: 10.1111/ajt.15650. Epub 2019 Nov 16. PMID: 31605562

#### IMPACT PUBLICATION

- 24 Migraine progression in subgroups of migraine based on comorbidities: Results of the CaMEO Study. Lipton RB, Fanning KM, Buse DC, Martin VT, Hohaia LB, Adams AM, Reed ML, Goadsby PJ. Neurology. 2019 Dec 10;93(24):e2224-e2236. doi: 10.1212/ WNL.00000000008589. Epub 2019 Nov 5. PMID: 31690685
- 25 Net Clinical Benefit of Oral Anticoagulation Among Older Adults With Atrial Fibrillation. Shah SJ, Singer DE, Fang MC, Reynolds K, Go AS, **Eckman MH**. Circ Cardiovasc Qual Outcomes. 2019 Nov;12(11):e006212. doi: 10.1161/CIRCOUTCOMES.119.006212. Epub 2019 Nov 11. PMID: 31707823

#### IMPACT PUBLICATION

- 26 Racial Differences and Factors Associated with Pregnancy in ESKD Patients on Dialysis in the United States. Shah S, Christianson AL, Meganathan K, Leonard AC, Schauer DP, Thakar CV. J Am Soc Nephrol. 2019 Dec;30(12):2437-2448. doi: 10.1681/ASN.2019030234. Epub 2019 Sep 25. PMID: 31554657
- 27 Racial Disparities and Factors Associated with Pregnancy in Kidney Transplant Recipients in the United States. Shah S, Christianson AL, Verma P, Meganathan K, Leonard AC, Schauer DP, Thakar CV. PLoS One. 2019 Aug 9;14(8):e0220916. doi: 10.1371/journal. pone.0220916. eCollection 2019. PMID: 31398243
- 28 Response to Comment on "Bariatric Surgery is Associated With Reduced Risk of Breast Cancer in Both Premenopausal and Postmenopausal Women". Feigelson HS, Caan B, Weinmann S, Leonard AC, Powers JD, Yenumula PR, Arterburn DE, Koebnick C, Altaye M, Schauer DP. Ann Surg. 2020 Feb;271(2):e19-e20. doi: 10.1097/SLA.00000000003603. No abstract available. PMID: 31577548
- 29 Restarting Anticoagulants after a Gastrointestinal Hemorrhage-Between Rockall and a Hard Place. Shah SJ, **Eckman MH**. J Hosp Med. 2019 Jul;14(7):448-449. doi: 10.12788/jhm.3221. No abstract available. PMID: 31251722
- **30** Seymour Diamond: A Tribute to a Giant in the Headache Field. **Martin VT**, Digre K. Headache. 2020 Jan;60(1):1-2. doi: 10.1111/head.13722. No abstract available. PMID: 31913511

- 31 The Current State of Acute Treatment for Migraine in Adults in the United States Cooper W, Doty EG, Hochstetler H, Hake A, Martin V Postgrad Med 2020 May 27; 1-9 doi: 10.1080/00325481.2020.1767402 PMID: 32459561
- 32 The Impact of Sleeve Gastrectomy on Renal Function in Patients with Chronic Kidney Disease Varies with Severity of Renal Insufficiency. Kassam AF, Taylor ME, Morris MC, Watkins BM, Thompson JR, Schauer DP, Smith EP, Diwan TS. Surg Obes Relat Dis. 2020 May;16(5):607-613. doi: 10.1016/j.soard.2020.01.021. Epub 2020 Jan 28. PMID: 32093996

#### IMPACT PUBLICATION

33 The Power of Contribution and Attribution in Assessing Educational Outcomes for Individuals, Teams, and Programs. Schumacher DJ, Dornoff E, Carraccio C, Busari J, van der Vleuten C, Kinnear B, Kelleher M, Sall DR, Warm E, Martini A, Holmboe E. Acad Med. 2019 Dec 10. doi: 10.1097/ACM.00000000003121. [Epub ahead of print] PubMed PMID: 31833856

#### IMPACT PUBLICATION

- 34 Time Allocation and Well-Being in Internal Medicine Residents: A Multi-Institutional Cross-Sectional Survey. Miller RE, Kelleher M, Duckett A, O'Rourke P, Yen MS, Call SA, Tackett S, Bishop SE. Am J Med. 2019 Dec 17. pii: S0002-9343(19)31085-X. doi: 10.1016/j.amjmed.2019.12.002. [Epub ahead of print] No abstract available. PMID: 31862330
- 35 Things We Do for No Reason: Systemic Corticosteroids for Wheezing in Preschool-Aged Children. Jones YO, Hubbell BB, thomson J, O'Toole JK. J Hosp Med 2019 Jul 24; 14:E1-E3. doi: 10.12788/jhm.3255 (Epub ahead of print] PMID:31339838
- USMLE Step 2 CK: Best Predictor of Multimodal Performance in an Internal Medicine Residency. Sharma A, Schauer DP, Kelleher M, Kinnear B, Sall D, Warm E. J Grad Med Educ. 2019 Aug; 11 (4): 412-419. doi: 10.4300/JGME-D-19-00099.1. PMID: 31440335

#### IMPACT PUBLICATION

Variation in Entrustment When Sharing a Single Assessment System Between University- and Community-Based Residency Programs: A Comparison.
 Warm EJ, Kinnear B, Kelleher M, Sall D, Schauer DP, Friedstrom S. Acad Med. 2019 Sep 3. doi: 10.1097/ACM.00000000002972 [Epub ahead of print] PMID: 31490192

#### IMPACT PUBLICATION

- 38 What Can the Giant Do? Defining the Path to Unsupervised Primary Care Practice by Competence, Not Time. Warm EJ, Kinnear B. Acad Med. 2019 Jul;94 (7):937-939. doi: 10.1097/ACM.00000000002753. PMID: 30998573
- 39 When I Say... Wisdom of Crowds. Kinnear B, Kelleher M, Sall D, Schumacher DJ, Warm EJ. Med Educ. 2020 Mar 17. doi: 10.1111/medu.14158. [Epub ahead of print] PubMed PMID: 32181514.



## Division of Hematology Oncology

## ENDOWED CHAIR: Herbert F. Koch Endowed Chair

The scientists and clinical investigators in the Division of Hematology Oncology strive to understand the molecular basis of cancer with the goal of developing novel cancer therapies. The research faculty is engaged in the design and execution of early phase clinical trials, laboratory, research and in teaching and training clinical and research trainees.



Pier Paolo Scaglioni, MD DIVISION DIRECTOR

## **Research Focus Areas/Types:**

LABORATORY RESEARCH: The Division has 7 independent laboratories pursuing the following research interests:

- Oncogene-depended intracellular signaling
- Cancer metabolism
- Cancer immunotherapy
- Role of tissue factor in cancer biology
- Identification of novel therapeutic targets
- Biology of primary and metastatic brain tumors.

CLINICAL RESEARCH: The interests of the clinical faculty span from the design and execution of early phase to later phase clinical trials clinical (phase I-III). The program has steadily increased the number and quality of clinical trials. We have a portfolio of 72 open trials for a wide array of cancer types. Our experimental therapeutic program is unique in the tristate region providing access to novel therapies that are tested in man for the first time. Several of our faculty have developed investigator-initiated trials that have attracted the financial support of government, non-profit or industry sponsors.

Over the past year, 566 patients were enrolled in interventional trials offered by the Division, which is the highest enrollment of any division in the University of Cincinnati Cancer Institute! Examples of exciting research programs are: Dr. Gulati's investigator-initiated trial aimed at assessing immune check point blockade in association with EGFR inhibition and Dr. Riaz's trial assess the effect of pan-FGFR inhibition, both in head and neck cancer.

## Investigators/Trainees:

Three clinical investigators dedicated to phase I and phase Ib trials staff the experimental therapeutic program; eight additional clinical faculty members contribute to our clinical research mission through clinical trials or outcome research. The Division has 12 Hematology and Oncology fellows, several of which are engaged in original research.

#### Funding types:

- National Institutes of Health
- UC College of Medicine and Department of Internal Medicine
- VA Medical Center
- Industry and public-private partnerships
- Department of Defense
- National Science Foundation

## **Mentoring:**

Our researchers are mentoring 4 post-doctoral fellows in addition to 4 graduate and several undergraduate students. Educational activities include research seminars and Cancer Grand rounds. Several postgraduate trainees, including Hematology and Oncology fellows, are supported by our brand-new T32 that was funded by the NCI in 2019.

## **Collaborations:**

We maintain close interactions with other clinical and basic science departments through the framework provided by the UC Cancer Institute and the Cincinnati Cancer Center within the UC Academic Health Center, Cincinnati Children's Hospital Medical Center and the Cincinnati VA Medical Center.

# Xiaoyang Qi, PhD

PROFESSOR DIVISION OF HEMATOLOGY ONCOLOGY iaoyang Qi, PhD, professor in the University of Cincinnati's Division of Hematology Oncology, is laser-focused on one objective for 2021.

"I'm striving to develop an immunotherapy for cancer," Qi says.

In 2016, Qi came one step closer to his goal. After decades of laboratory research and promising findings, the discoveries of Qi, also a Cincinnati Cancer Center researcher and scientific co-founder of Bexion Pharmaceuticals, were translated to clinical trials in humans, potentially helping thousands living with cancer.

In July 2016, Bexion Pharmaceuticals LLC announced that the U.S. Food and Drug Administration cleared their application for a first-inhuman Phase I clinical trial with the compound BXQ-350 for treatment of advanced solid tumors and glioblastoma multiforme, the most common type of brain cancer.

"It was an exciting announcement as this is the goal of every scientist — to actually make a difference in patient care," says Qi, a member of the UC Cancer Institute and the UC Gardner Neuroscience Institute and Brain Tumor Center. "Over the years when I've published new research, e-mails from patients and family members asking about a clinical trial involving my findings hit my inbox. I'm so happy when I can answer back that there is one available."

In 2013, Bexion received a \$2.9 million Small Business Innovation Research Bridge Award from the National Cancer Institute, with Qi as coprincipal investigator, to help it bring BXQ-350 into the clinical trial phase.

Qi discovered SapC-DOPS, the combination of a lysosomal protein saposin C (SapC), and a phospholipid, known as dioleoylphosphatidylserine (DOPS), that assembled into tiny cavities, or nanovesicles, can target and kill many forms of cancer cells. Lysosomes are membrane-enclosed cellular organelles that contain enzymes capable of breaking down all types of biological components; phospholipids are major components of all cell membranes and form lipid bilayers, or cell membranes.

Qi says his lab found that the combination of these two natural cellular components, or SapC-DOPS, caused cell death in human cancer cell types, including brain, lung, skin, prostate, blood, breast and pancreatic cancer, while sparing normal cells and tissues in animal models of human cancer. With numerous basic studies under his belt, Qi formed a partnership with Bexion to create the BXQ-350 compound tested in a Phase I clinical trial. Currently, several Phase 1 and 2 trials have either recently been completed, are ongoing or are scheduled for the near future.

For Qi, who was first attracted to science as a child fascinated by space exploration, the research represents a triumphant step toward seeing the real-world impact of his work.

"Having an effect or benefit on the lives of citizens and society, beyond contributions to academic research, is the ultimate win as a researcher," says Qi. • "WHEN I'VE PUBLISHED NEW RESEARCH, E-MAILS FROM PATIENTS AND FAMILY MEMBERS ASKING ABOUT A CLINICAL TRIAL INVOLVING MY FINDINGS HIT MY INBOX. I'M SO HAPPY WHEN I CAN ANSWER BACK THAT THERE IS ONE AVAILABLE."

Hematology Oncology

## PUBLICATIONS July 1, 2019 thru June 30, 2020

- Overall survival in patients with pancreatic cancer receiving matched therapies following molecular profiling: a retrospective analysis of the Know Your Tumor registry trial. Pishvaian MJ, Blais EM, Brody JR, Lyons E, DeArbeloa P, Hendifar A, Mikhail S, Chung V, Sahai V, Sohal DPS, Bellakbira S, Thach D, Rahib L, Madhavan S, Matrisian LM, Petricoin EF 3rd. Lancet Oncol. 2020 Apr;21(4):508-518. doi: 10.1016/S1470-2045(20)30074-7. Epub 2020 Mar 2. PMID: 32135080
- 2 Multi-omic molecular comparison of primary versus metastatic pancreatic tumours. Brar G, Blais EM, Joseph Bender R, Brody JR, Sohal D, Madhavan S, Picozzi VJ, Hendifar AE, Chung VM, Halverson D, Mikhail S, Matrisian LM, Rahib L, Petricoin E, Pishvaian MJ. Br J Cancer. 2019 Jul;121(3):264-270. doi: 10.1038/s41416-019-0507-5. Epub 2019 Jul 11. PMID: 31292535

#### IMPACT PUBLICATION

- 3 COVID-19 pandemic and impact on cancer clinical trials: An academic medical center perspective. Marcum M, Kurtzweil N, Vollmer C, Schmid L, Vollmer A, Kastl A, Acker K, Gulati S, Grover P, Herzog TJ, Ahmad SA, Sohal D, Wise-Draper TM. Cancer Med. 2020 Jul 10;9(17):6141-6. doi: 10.1002/cam4.3292. Online ahead of print.PMID: 32648667
- 4 Genetic Counseling and Germline Testing in the Era of Tumor Sequencing: A Cohort Study. Klek S, Heald B, Milinovich A, Ni Y, Abraham J, Mahdi H, Estfan B, Khorana AA, Bolwell BJ, Grivas P, Sohal DPS, Funchain P. JNCI Cancer Spectr. 2020 Mar 5;4(3):pkaa018. doi: 10.1093/jncics/pkaa018. eCollection 2020 Jun. PMID: 32596633
- 5 IMP dehydrogenase-2 drives aberrant nucleolar activity and promotes tumorigenesis in glioblastoma. Kofuji S, Hirayama A, Eberhardt AO, Kawaguchi R, Sugiura Y, Sampetrean O, Ikeda Y, Warren M, Sakamoto N, Kitahara S, Yoshino H, Yamashita D, Sumita K, Wolfe K, Lange L, Ikeda S, Shimada H, Minami N, Malhotra A, Morioka S, Ban Y, Asano M, Flanary VL, Ramkissoon A, Chow LML, Kiyokawa J, Mashimo T, Lucey G, Mareninov S, Ozawa T, Onishi N, Okumura K, Terakawa J, Daikoku T, Wise-Draper T, Majd N, Kofuji K, Sasaki M, Mori M, Kanemura Y, Smith EP, Anastasiou D, Wakimoto H, Holland EC, Yong WH, Horbinski C, Nakano I, DeBerardinis RJ, Bachoo RM, Mischel PS, Yasui W, Suematsu M, Saya H, Soga T, Grummt I, Bierhoff H, Sasaki AT. Nat Cell Biol. 2019 Aug;21(8):1003-1014. doi: 10.1038/s41556-019-0363-9. Epub 2019 Aug 1. PMID: 31371825
- 6 Targeting HER2 with Trastuzumab Deruxtecan: A Dose-Expansion, Phase I Study in Multiple Advanced Solid Tumors. Tsurutani J, Iwata H, Krop I, Jänne PA, Doi T, Takahashi S, Park H, Redfern C, Tamura K, Wise-Draper TM, Saito K, Sugihara M, Singh J, Jikoh T, Gallant G, Li BT. Cancer Discov. 2020 May;10(5):688-701. doi: 10.1158/2159-8290.CD-19-1014. Epub 2020 Mar 25. PMID: 32213540

- 7 Phase 1 dose-finding study of metformin in combination with concurrent cisplatin and radiotherapy in patients with locally advanced head and neck squamous cell cancer. Gulati S, Desai J, Palackdharry SM, Morris JC, Zhu Z, Jandarov R, Riaz MK, Takiar V, Mierzwa M, Gutkind JS, Molinolo A, Desai PB, Sadraei NH, Wise-Draper TM. Cancer. 2020 Jan 15;126(2):354-362. doi: 10.1002/cncr.32539. Epub 2019 Oct 18. PMID: 31626727
- 8 Phase 1b trial of pembrolizumab monotherapy for relapsed/refractory multiple myeloma: KEYNOTE-013. Ribrag V, Avigan DE, Green DJ, **Wise-Draper T**, Posada JG, Vij R, Zhu Y, Farooqui MZH, Marinello P, Siegel DS. Br J Haematol. 2019 Aug;186(3):e41-e44. doi: 10.1111/ bjh.15888. Epub 2019 Apr 1. PMID: 30937889
- 9 CD244 represents a new therapeutic target in head and neck squamous cell carcinoma. Agresta L, Lehn M, Lampe K, Cantrell R, Hennies C, Szabo S, Wise-Draper T, Conforti L, Hoebe K, Janssen EM. J Immunother Cancer. 2020 Mar;8(1):e000245. doi: 10.1136/ jitc-2019-000245. PMID: 32217758
- 10 A Compartmentalized Reduction in Membrane-Proximal Calmodulin Reduces the Immune Surveillance Capabilities of CD8+ T Cells in Head and Neck Cancer. Chimote AA, Gawali VS, Newton HS, Wise-Draper TM, Conforti L. Front Pharmacol. 2020 Feb 28;11:143. doi: 10.3389/fphar.2020.00143. eCollection 2020. PMID: 32184726
- 11 Phase 2 study of the focal adhesion kinase inhibitor defactinib (VS-6063) in previously treated advanced KRAS mutant non-small cell lung cancer. Gerber DE, Camidge DR, Morgensztern D, Cetnar J, Kelly RJ, Ramalingam SS, Spigel DR, Jeong W, Scaglioni PP, Zhang S, Li M, Weaver DT, Vaikus L, Keegan M, Horobin JC, Burns TF. Lung Cancer. 2020 Jan;139:60-67. doi: 10.1016/j.lungcan.2019.10.033. Epub 2019 Nov 4. PMID: 31739184
- Roles of Ubiquitination and SUMOylation in the Regulation of Angiogenesis. Rabellino A, Andreani C, Scaglioni PP. Curr Issues Mol Biol. 2020;35:109-126. doi: 10.21775/cimb.035.109. Epub 2019 Aug 18. PMID: 31422936
- 13 Anti-Tumor Potential of IMP Dehydrogenase Inhibitors: A Century-Long Story. Naffouje R, Grover P, Yu H, Sendilnathan A, Wolfe K, Majd N, Smith EP, Takeuchi K, Senda T, Kofuji S, Sasaki AT. Cancers (Basel). 2019 Sep 11;11(9):1346. doi: 10.3390/cancers11091346. PMID: 31514446
- 14 Depletion of phosphatidylinositol 4-phosphate at the Golgi translocates K-Ras to mitochondria. Miller TE, Henkels KM, Huddleston M, Salisbury R, Hussain SM, Sasaki AT, Cho KJ. J Cell Sci. 2019 Aug 22;132(16):jcs231886. doi: 10.1242/jcs.231886. PMID: 31331963

- 15 Structure-Activity Relationship Study of Covalent Panphosphatidylinositol 5-Phosphate 4-Kinase Inhibitors. Manz TD, Sivakumaren SC, Yasgar A, Hall MD, Davis MI, Seo HS, Card JD, Ficarro SB, Shim H, Marto JA, Dhe-Paganon S, Sasaki AT, Boxer MB, Simeonov A, Cantley LC, Shen M, Zhang T, Ferguson FM, Gray NS. ACS Med Chem Lett. 2019 Nov 3;11(3):346-352. doi: 10.1021/ acsmedchemlett.9b00402. eCollection 2020 Mar 12. PMID: 32184968
- 16 Identification of lysine methylation in the core GTPase domain by GoMADScan. Yoshino H, Yin G, Kawaguchi R, Popov KI, Temple B, Sasaki M, Kofuji S, Wolfe K, Kofuji K, Okumura K, Randhawa J, Malhotra A, Majd N, Ikeda Y, Shimada H, Kahoud ER, Haviv S, Iwase S, Asara JM, Campbell SL, Sasaki AT. PLoS One. 2019 Aug 7;14(8):e0219436. doi: 10.1371/journal.pone.0219436. eCollection 2019. PMID: 31390367
- 17 Dynamic compartmentalization of purine nucleotide metabolic enzymes at leading edge in highly motile renal cell carcinoma. Wolfe K, Kofuji S, Yoshino H, Sasaki M, Okumura K, Sasaki AT. Biochem Biophys Res Commun. 2019 Aug 13;516(1):50-56. doi: 10.1016/j. bbrc.2019.05.190. Epub 2019 Jun 10. PMID: 31196624
- 18 Long noncoding RNA HOTAIR promotes invasion of breast cancer cells through chondroitin sulfotransferase CHST15. Liu LC, Wang YL, Lin PL, Zhang X, Cheng WC, Liu SH, Chen CJ, Hung Y, Jan CI, Chang LC, Qi X, Hsieh-Wilson LC, Wang SC. Int J Cancer. 2019 Nov 1;145(9):2478-2487. doi: 10.1002/ijc.32319. Epub 2019 Apr 26. PMID: 30963568
- Systemic enzyme delivery by blood-brain barrierpenetrating SapC-DOPS nanovesicles for treatment of neuronopathic Gaucher disease. Sun Y, Liou B, Chu Z, Fannin V, Blackwood R, Peng Y, Grabowski GA, Davis HW, Qi X. EBioMedicine. 2020 May;55:102735. doi: 10.1016/j.ebiom.2020.102735. Epub 2020 Apr 10. PMID: 32279952
- 20 SapC-DOPS a Phosphatidylserine-targeted Nanovesicle for selective Cancer therapy. N'Guessan KF, Patel PH, Qi X. Cell Commun Signal. 2020 Jan 9;18(1):6. doi: 10.1186/s12964-019-0476-6. PMID: 31918715
- 21 Frequency-specific changes in the default mode network in patients with cingulate gyrus epilepsy. Leng X, Xiang J, Yang Y, Yu T, Qi X, Zhang X, Wu S, Wang Y. Hum Brain Mapp. 2020 Jun 15;41(9):2447-2459. doi: 10.1002/hbm.24956. Epub 2020 Feb 25. PMID: 32096905
- 22 Avelumab monotherapy as first-line or second-line treatment in patients with metastatic renal cell carcinoma: phase lb results from the JAVELIN Solid Tumor trial. Vaishampayan U, Schöffski P, Ravaud A, Borel C, Peguero J, Chaves J, Morris JC, Kotecki N, Smakal M, Zhou D, Guenther S, Bajars M, Gulley JL. J Immunother Cancer. 2019 Oct 24;7(1):275. doi: 10.1186/s40425-019-0746-2. PMID: 31651359

- 23 A Pilot Study of Sirolimus in Subjects with Cowden Syndrome or Other Syndromes Characterized by Germline Mutations in PTEN. Komiya T, Blumenthal GM, DeChowdhury R, Fioravanti S, Ballas MS, Morris J, Hornyak TJ, Wank S, Hewitt SM, Morrow B, Memmott RM, Rajan A, Dennis PA. Oncologist. 2019 Dec;24(12):1510-e1265. doi: 10.1634/theoncologist.2019-0514. Epub 2019 Jul 26. PMID: 31350329
- 24 RRx-001 followed by platinum plus etoposide in patients with previously treated small-cell lung cancer. Morgensztern D, Rose M, Waqar SN, Morris J, Ma PC, Reid T, Brzezniak CE, Zeman KG, Padmanabhan A, Hirth J, I Spira A, Trepel JB, Padda SK. Br J Cancer. 2019 Jul;121(3):211-217. doi: 10.1038/s41416-019-0504-8. Epub 2019 Jun 24. PMID: 31231122
- 25 Exosomes as a Surrogate Marker for Autophagy in Peripheral Blood, Correlative Data from Phase I Study of Chloroquine in Combination with Carboplatin/Gemcitabine in Advanced Solid Tumors. Abdel Karim N, Gaber O, Aljohani HM, Eldessouki I, Bahassi EM, Morris J. Asian Pac J Cancer Prev. 2019 Dec 1;20(12):3789-3796. doi: 10.31557/APJCP.2019.20.12.3789. PMID: 31870123
- 26 Extended treatment with MY-NEOVAX, personalized neoantigen-enhanced oncolytic viruses, for two endstage cancer patients. Bouvet M, Reid TR, Larson C, Oronsky B, Carter C, Morris JC. Oxf Med Case Reports. 2019 Dec 9;2019(11):461-463. doi: 10.1093/omcr/ omz105. eCollection 2019 Nov PMID: 31844525
- 27 Retrospective Study of the Effect of Statins on the Outcome of Lung Cancer Patients, University of Cincinnati Experience. Gaber O, Eldessouki I, Hassan R, Magdy M, Morris JC, Abdel Karim N. Asian Pac J Cancer Prev. 2019 Aug 1;20(8):2391-2396. doi: 10.31557/ APJCP.2019.20.8.2391. PMID: 31450911
- 28 A Roundtable Discussion of the Breast Cancer Therapy Expert Group (BCTEG): Clinical Developments and Practice Guidance on Human Epidermal Growth Factor Receptor 2 (HER2)-positive Breast Cancer. Mahtani R, Holmes FA, Badve S, Caldera H, Coleman R, Mamounas E, Kalinsky K, Kittaneh M, Lower E, Pegram M, Press MF, Rugo HS, Schwartzberg L, Vogel C; Breast Cancer. Therapy Expert Group (BCTEG). Clin Breast Cancer. 2020 Jun;20(3):e251-e260. doi: 10.1016/j.clbc.2019.08.001. Epub 2019 Aug 21. PMID: 32139271
- 29 Delphi consensus recommendations for a treatment algorithm in pulmonary sarcoidosis. Rahaghi FF, Baughman RP, Saketkoo LA, Sweiss NJ, Barney JB, Birring SS, Costabel U, Crouser ED, Drent M, Gerke AK, Grutters JC, Hamzeh NY, Huizar I, Ennis James W 4th, Kalra S, Kullberg S, Li H, Lower EE, Maier LA, Mirsaeidi M, Müller-Quernheim J, Carmona Porquera EM, Samavati L, Valeyre D, Scholand MB. Eur Respir Rev. 2020 Mar 20;29(155):190146. doi: 10.1183/16000617.0146-2019. Print 2020 Mar 31. PMID: 32198218

#### Hematology Oncology

PUBLICATIONS CONTINUED

- 30 Case-Based Review and Clinical Guidance on the Use of Genomic Assays for Early-Stage Breast Cancer: Breast Cancer Therapy Expert Group (BCTEG). Kittaneh M, Badve S, Caldera H, Coleman R, Goetz MP, Mahtani R, Mamounas E, Kalinsky K, Lower E, Pegram M, Press MF, Rugo HS, Schwartzberg L, Traina T, Vogel C. Clin Breast Cancer. 2020 Jun;20(3):183-193. doi: 10.1016/j.clbc.2020.01.001. Epub 2020 Jan 8. PMID: 32014370
- 31 MST1R (RON) expression is a novel prognostic biomarker for metastatic progression in breast cancer patients. Hunt BG, Wicker CA, Bourn JR, Lower EE, Takiar V, Waltz SE. Breast Cancer Res Treat. 2020 Jun;181(3):529-540. doi: 10.1007/s10549-020-05653-y. Epub 2020 Apr 27. PMID: 32342233
- 92 Physiological predictors of survival in patients with sarcoidosis-associated pulmonary hypertension: results from an international registry. Shlobin OA, Kouranos V, Barnett SD, Alhamad EH, Culver DA, Barney J, Cordova FC, Carmona EM, Scholand MB, Wijsenbeek M, Ganesh S, Lower EE, Engel PJ, Wort J, Price L, Wells AU, Nathan SD, Baughman RP. Eur Respir J. 2020 May 14;55(5):1901747. doi: 10.1183/13993003.01747-2019. Print 2020 May. PMID: 32139456
- 33 Management of repository corticotrophin injection therapy for pulmonary sarcoidosis: a Delphi study. Rahaghi FF, Sweiss NJ, Saketkoo LA, Scholand MB, Barney JB, Gerke AK, Lower EE, Mirsaeidi M, O'Hare L, Rumbak MJ, Samavati L, Baughman RP. Eur Respir Rev. 2020 Mar 20;29(155):190147. doi: 10.1183/16000617.0147-2019. Print 2020 Mar 31. PMID: 32198219
- 34 Impact of tricyclic antidepressants, selective serotonin reuptake inhibitors, and other antidepressants on overall survival of patients with advanced lung cancer from 2004 to 2014: University of Cincinnati experience. Abdel Karim NF, Hassan R, Siddiqi NI, Eldessouki I, Gaber O, Rahouma M, Kamel M, Yellu M, Gulati S, Xie C, Magdy M, Pruemer J. J Int Med Res. 2019 Dec;47(12):6016-6026. doi: 10.1177/0300060519862469. Epub 2019 Oct 23. PMID: 31640444
- 35 Current State of Systemic Therapies for Advanced Renal Cell Carcinoma. Gulati S, Vaishampayan U. Curr Oncol Rep. 2020 Feb 11;22(3):26. doi: 10.1007/s11912-020-0892-1. PMID: 32048058
- 36 Evolving treatment paradigm in metastatic non clear cell renal cell carcinoma. Gulati S, Philip E, Salgia S, Pal SK. Cancer Treat Res Commun. 2020 Mar 17;23:100172. doi: 10.1016/j.ctarc.2020.100172. Online ahead of print. PMID: 32252014
- 37 Adaptive response to inflammation contributes to sustained myelopoiesis and confers a competitive advantage in myelodysplastic syndrome HSCs. Muto T, Walker CS, Choi K, Hueneman K, Smith MA, Gul Z, Garcia-Manero G, Ma A, Zheng Y, Starczynowski DT. Nat Immunol. 2020 May;21(5):535-545. doi: 10.1038/s41590-020-0663-z. Epub 2020 Apr 20. PMID: 32313245

- 38 Noninfectious neurologic complications of hematopoietic cell transplantation: A systematic review. Sheikh MA, Toledano M, Ahmed S, Gul Z, Hashmi SK. Hematol Oncol Stem Cell Ther. 2020 May 21:S1658-3876(20)30104-7. doi: 10.1016/j.hemonc.2020.05.006. Online ahead of print. PMID: 32516577
- Additive effects of a small molecular PCNA inhibitor PCNA-I1S and DNA damaging agents on growth inhibition and DNA damage in prostate and lung cancer cells. Lu S, **Dong Z**. PLoS One. 2019 Oct 10;14(10):e0223894. doi: 10.1371/journal. pone.0223894. eCollection 2019. PMID: 31600334
- 40 Pediatric-inspired protocols in adult acute lymphoblastic leukemia: are the results bearing fruit? Muffly L, Curran E. Hematology Am Soc Hematol Educ Program. 2019 Dec 6;2019(1):17-23. doi: 10.1182/hematology.2019000009. PMID: 31808881
- Feasibility of a modified Atkins diet in glioma patients during radiation and its effect on radiation sensitization. Woodhouse C, Ward T, Gaskill-Shipley M, Chaudhary R. Curr Oncol. 2019 Aug;26(4):e433-e438. doi: 10.3747/co.26.4889. Epub 2019 Aug 1. PMID: 31548811
- 42 Complete Response to Temozolomide in Metastatic Melanoma After Failure of 5 Lines of Treatment. Magge T, Shaikh H, Chaudhary R. Am J Ther. 2020 May 14. doi: 10.1097/MJT.000000000001186. Online ahead of print. PMID: 32427619

## Division of Immunology, Allergy and Rheumatology

## ENDOWED CHAIR: Alice W. and Mark A Brown Professor

Our Division undertakes a wide range of research that is grounded in immunology and inflammation. Highlights of this year's research include: publication of a novel genetic cause of a mouse model of primary biliary cholangitis (PBC), a paper on prevention of food allergy and suppression of established food allergy by neutralization of TSLP, IL-25 and IL-33, a publication using a novel way to suppress anaphylaxis by using an Anti-Fc receptor monoclonal antibody, a paper showing that house dust-mite allergy is independent of IgE and Fc-Riα, a paper on targeted inhibition of AxI receptor tyrosine kinase in nephritis, a paper on the genetic basis of house dust-mite allergy, and a paper on targeting innate immunity to reverse Type 1 diabetes.



William M. Ridgway, MD DIVISION DIRECTOR



Avis Ware, MD DIVISION DIRECTOR (Effective January 1, 2020)

### **Research Focus Areas/Types:**

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)
- novel therapies for autoimmune disease

#### Investigators/Trainees:

We have five MD and three PhD researchers and three labs. We hired a new PhD investigator in Immunology, Dr. Wenhai Shao, who specializes in lupus mouse models and immune cell signaling. The Evelyn Hess Chair for Lupus research is now officially established and we will start the search for the first occupant of the Hess chair. Overall, the division published over 50 articles this year.

#### Funding types:

- National Institutes of Health
- VA Medical Center
- UC College of Medicine and Department of Internal Medicine
- Industry and public-private partnerships and philanthropy

## Mentoring:

We have a T32 in Allergy/ Immunology, one participant in the CSTP program, a participant in the young faculty mentored journal club, and two separate ACGME accredited fellowship programs whose goal is to produce academic Allergists and Rheumatologists.

## **Collaborations:**

In the coming years, 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. This year we will organize seminars to encourage cross-disciplinary research in SLE that involves both basic investigators and clinicians.

# David E. Adams, PhD

RESEARCH SCIENTIST DIVISION OF IMMUNOLOGY, ALLERGY AND RHEUMATOLOGY

CINCINNATI

Annual Research Report 2020

niversity of Cincinnati research scientist David Adams's passion for discovery has led him to labs around the world — but started in his Cincinnati backyard.

"I grew up in the Cincinnati area, which is world famous for its Ordovician period rocks, and I collected fossils as a kid," Adams says. Later, during his undergraduate studies at Oberlin College, he conducted a number of independent research projects in the departments of geology and chemistry. "And I caught the research bug."

It was his PhD research advisor at the University of California Berkeley, though, that determined the precise path of Adams's career in autoimmunity. "My mentor there used the Socratic method of teaching, and he taught me a lot about how to carry out basic research and to ask fundamental questions," says Adams.

Since then, Adams has spent nearly three decades in the field, including stints at the Imperial Cancer Research Fund in England, the CNRS outside of Paris and the University of Edinburgh in Scotland. Most of his research since joining UC 14 years ago has focused on the study of autoimmune diseases, including Type 1 diabetes and primary biliary cholangitis, in the laboratory of William M. Ridgway, MD; systemic lupus erythematosus (SLE) and lupus nephritis with Ram R. Singh, MD; and, most recently, with Wenhai Shao, PhD. Adams's current work in Dr. Shao's laboratory focuses on TAM receptor gene expression and signaling.

"My current work gives me the opportunity to use my molecular biology skills and training to design and synthesize novel DNA- and RNAbased reagents, which can be used to study and treat autoimmunity," Adams says.

Another example of Adams's work is on display in a paper recently published by Ridgway's group in the journal *Hepatology*, which shared findings from a mouse model of primary biliary cholangitis (PBC) that showed enoxacin offers a promising approach to treat liver disease. Enoxacin belongs to a class of molecules known as fluoroquinolones that act as potent antibiotics and are typically used to treat bacterial infections, including those of the urinary tract.

"We repurposed enoxacin to target an entirely different molecular pathway in pathogenic T cells, the biogenesis of small RNA regulators of gene expression, to suppress T cell activation," explained Adams, adding that the research harkened back to his PhD studies. "The *Hepatology* paper is a perfect example of using my pure science background to study medically relevant problems in autoimmunity."

Adams, who stays busy outside the lab with his wife of 39 years, six children and three grandchildren, says that while he enjoyed working around the globe, there's no place like home.

"UC attracts some of the best researchers in the world. My prediction is that we will continue to grow as a division and that our work will ultimately lead to cures and preventions of many diseases that plague us today," Adams says. "We address some of the most common and pervasive ailments in society. It is an honor to be a part of this community of scientists."• "WE REPURPOSED ENOXACIN TO TARGET THE BIOGENESIS OF SMALL RNA REGULATORS OF GENE EXPRESSION, TO SUPPRESS T CELL ACTIVATION ... A PERFECT EXAMPLE OF USING MY PURE SCIENCE BACKGROUND TO STUDY MEDICALLY RELEVANT PROBLEMS IN AUTOIMMUNITY."

Immunology, Allergy and Rheumatology

## PUBLICATIONS July 1, 2019 thru June 30, 2020

#### IMPACT PUBLICATION

- Schmidlin K, Sani S, Bernstein DI, Fonacier L. A Handson Approach to Contact Dermatitis and Patch Testing. Schmidlin K, Sani S, Bernstein DI, Fonacier L. A. PMID: 32112924.
- 2 Once-daily single-inhaler versus twice-daily multipleinhaler triple therapy in patients with COPD: lung function and health status results from two replicate randomized controlled trials. Ferguson GT, Brown N, Compton C, Corbridge TC, Dorais K, Fogarty C, Harvey C, Kaisermann MC, Lipson DA, Martin N, Sciurba F, Stiegler M, Zhu CQ, Bernstein DI.. PMID: 32471423; PMCID: PMC7257245.
- 3 Clinical Practice of Allergen Immunotherapy for Allergic Rhinoconjunctivitis and Asthma: An Expert Panel Report. J Allergy Clin Immunol Pract. Calderon MA, Waserman S, Bernstein DI., Demoly P, Douglass J, Gagnon R, Katelaris CH, Kim H, Nelson HS, Okamoto Y, Okubo K, Virchow JC, DuBuske L, Casale TB, Canonica GW, Nolte H. PMID: 32422372.
- 4 Efficacy and Safety of Ragweed SLIT-Tablet in Children with Allergic Rhinoconjunctivitis in a Randomized, Placebo-Controlled Trial. Nolte H, Bernstein DI, Nelson HS, Ellis AK, Kleine-Tebbe J, Lu S. PMID: 32304832.
- 5 Controversies in Allergy: Injectable Epinephrine Should Be Prescribed to All Patients on Subcutaneous Aeroallergen Immunotherapy. Bernstein DI, Tankersley M, Russell H.PMID: 32044307.

#### IMPACT PUBLICATION

- 6 Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD.Rabe KF, Martinez FJ, Ferguson GT, Wang C, Singh D, Wedzicha JA, Trivedi R, St Rose E, Ballal S, McLaren J, Darken P, Aurivillius M, Reisner C, Dorinsky P; ETHOS Investigators-Bernstein DL. PMID: 32579807.
- 7 The Effects of Air Pollution on the Development of Atopic Disease. Hassoun Y, James C, Bernstein DI. PMID: 30806950.
- 8 HEPA filtration improves asthma control in children exposed to traffic-related airborne particles. James C, Bernstein DI, Cox J, Ryan P, Wolfe C, Jandarov R, Newman N, Indugula R, Reponen T. PMID: 31743467.
- 9 NAT1 genetic variation increases asthma risk in children with secondhand smoke exposure. J Asthma. Brooks CC, Martin LJ, Pilipenko V, He H, LeMasters GK, Lockey JE, Bernstein DI, Ryan PH, Khurana Hershey GK, Biagini Myers JM. PMID: 31809667; PMCID: PMC7274907.
- 10 Decline in vaccine-type human papillomavirus prevalence in young men from a Midwest metropolitan area of the United States over the six years after vaccine introduction. Vaccine. Widdice LE, Bernstein DI, Franco EL, Ding L, Brown DR, Ermel AC, Higgins L, Kahn JA. PMID: 31582269; PMCID: PMC7293135.

11 Idiopathic postprandial diarrhea responsive to antihistamines. Hassoun Y, Stevenson MR, Bernstein DI. PMID: 31279076.

#### IMPACT PUBLICATION

- 12 Atopic dermatitis independently increases sensitization above parental atopy: The MPAACH study. Kroner JW, Baatyrbek Kyzy A, Burkle JW, Martin LJ, LeMasters GK, Bernstein DI, Lockey JE, Ryan P, Khurana Hershey GK, Biagini Myers JM. PMID: 32035158; PMCID: PMC7214219.
- 13 AAAAI/ACAAI Subcutaneous Immunotherapy Surveillance Study (2013-2017): Fatalities, Infections, Delayed Reactions, and Use of Epinephrine Autoinjectors. Epstein TG, Liss GM, Berendts KM, Bernstein DI. PMID: 30776526.
- 14 Influenza Challenge Models: Ready for Prime Time? Bernstein DI, Atmar RL, Hoft DF. PMID: 32206804.
- 15 Safety of allergen immunotherapy in North America from 2008-2017: Lessons learned from the ACAAI/ AAAAI National Surveillance Study of adverse reactions to allergen immunotherapy. Bernstein DI, Epstein TG. PMID: 32122446.
- 16 IL-4Rα expression by airway epithelium and smooth muscle accounts for nearly all airway hyperresponsiveness in murine allergic airway disease. McKnight CG, Potter C, Finkelman FD. PMID: 31745261; PMCID: PMC7641252.

### IMPACT PUBLICATION

- 17 Triple Inhaled Therapy at Two Glucocorticoid Doses in Moderate-to-Very-Severe COPD. Rabe KF, Martinez FJ, Ferguson GT, Wang C, Singh D, Wedzicha JA, Trivedi R, St Rose E, Ballal S, McLaren J, Darken P, Aurivillius M, Reisner C, Dorinsky P; ETHOS Investigators-Villareal M PMID: 32579807.
- 18 Response by Blanton et al to Letter Regarding Article, "Preimplant Phosphodiesterase-5 Inhibitor Use Is Associated With Higher Rates of Severe Early Right Heart Failure After LVAD Implantation:Blanton R, Gulati G, Kiernan M. PMID: 31514516.
- **19** Massive retroperitoneal hemorrhage after external shock wave lithotripsy in a patient with a left ventricular assist device. **Gulati G**, Kiernan M, Sabe MA.PMID: 31641612; PMCID: PMC6796679.
- 20 Heart failure management in dialysis patients: Many treatment options with no clear evidence. Roehm B, Gulati G, Weiner DE. PMID: 32282987; PMCID: PMC7597416.
- 21 Timing and Trends of Right Atrial Pressure and Risk of Right Heart Failure After Left Ventricular Assist Device Implantation. **Gulati G**, Sutaria N, Vest AR, Denofrio DD, Kawaborl M, Couper G, Kiernan MS. PMID: 31981695.
- 22 Impact of tricyclic antidepressants, selective serotonin reuptake inhibitors, and other antidepressants on overall survival of patients with advanced lung cancer from 2004 to 2014: University of Cincinnati experience. Abdel Karim NF, Hassan R, Siddiqi NI, Eldessouki I, Gaber O, Rahouma M, Kamel M, Yellu M, Gulati S, Xie C, Magdy M, Pruemer J. PMID: 31640444; PMCID: PMC7045662.

- 23 Bullous Systemic Lupus Erythematosus.Odonwodo A, Vashisht P. PMID: 32491377.
- 24 Scleroderma And Primary Myocardial Disease. Mohameden M, Vashisht P, Sharman T. PMID: 32491618.
- 25 The Diagnostic Conundrum of Felty Syndrome and T-Cell Large Granular Lymphocytic Leukemia. Onuorah N, Abraham H, Vashisht P. PMID: 32530865.

IMPACT PUBLICATION

- 26 Rapid desensitization of humanized mice with antihuman FcεRIα monoclonal antibodies. Khodoun MV, Morris SC, Angerman E, Potter C, Schuman R, Wunderlich M, Maciag JJ, Sullivan Locker KC, Mulloy JC, Herr AB, Finkelman FD. PMID: 31836406; PMCID: PMC7607676.
- 27 Asparaginase immune complexes induce Fc-yRIIIdependent hypersensitivity in naive mice. Rathod S, Ramsey M, DiGiorgio D, Berrios R, Finkelman FD, Fernandez CA. PMID: 31284767; PMCID: PMC6766650.
- 28 Ezh2-mediated epigenetic modification is required for allogeneic T cell-induced lupus disease.When Y, Smith RD, Finkelman FD, Shao WH. PMID: 32503684; PMCID: PMC7275547.
- 29 Gas6/TAM Receptors in Systemic Lupus Erythematosus. Cohen PL, Shao WH. PMID: 31360267; PMCID: PMC6652053.

#### IMPACT PUBLICATION

- 30 Ligelizumab for Chronic Spontaneous Urticaria. Maurer M, Giménez-Arnau AM, Sussman G, Metz M, Baker DR, Bauer A, Bernstein JA, Brehler R, Chu CY, Chung WH, Danilycheva I, Grattan C, Hébert J, Katelaris C, Makris M, Meshkova R, Savic S, Sinclair R, Sitz K, Staubach P, Wedi B, Löffler J, Barve A, Kobayashi K, Hua E, Severin T, Janocha R. PMID: 31577874.
- 31 Cephalosporin Allergy: Current Understanding and Future Challenges. Khan DA, Banerji A, Bernstein JA, Bilgicer B, Blumenthal K, Castells M, Ein D, Lang DM, Phillips E. PMID: 31495420; PMCID: PMC6955146.
- 32 Mutation update for the SATB2 gene. Zarate YA, Bosanko KA, Caffrey AR, Bernstein JA, Martin DM, Williams MS, Berry-Kravis EM, Mark PR, Manning MA, Bhambhani V, Vargas M, Seeley AH, Estrada-Veras JI, van Dooren MF, Schwab M, Vanderver A, Melis D, Alsadah A, Sadler L, Van Esch H, Callewaert B, Oostra A, Maclean J, Dentici ML, Orlando V, Lipson M, Sparagana SP, Maarup TJ, Alsters SI, Brautbar A, Kovitch E, Naidu S, Lees M, Smith DM, Turner L, Raggio V, Spangenberg L, Garcia-Miñaúr S, Roeder ER, Littlejohn RO, Grange D, Pfotenhauer J, Jones MC, Balasubramanian M, Martinez-Monseny A, Blok LS, Gavrilova R, Fish JL. PMID: 31021519.
- 33 Approach to the Patient with Hives. Greiwe J, Bernstein JA. PMID: 31757233.
- 34 GINA updated 2019: Landmark changes recommended for asthma management. Hogan AD, Bernstein JA. PMID: 31734328.

35 COVID-19, asthma, and biological therapies: What we need to know. Morais-Almeida M, Aguiar R, Martin B, Ansotegui IJ, Ebisawa M, Arruda LK, Caminati M, Canonica GW, Carr T, Chupp G, Corren J, Dávila I, Park HS, Hanania NA, Rosenwasser L, Sánchez-Borges M, Virchow JC, Yáñez A, Bernstein JA, Caraballo L, Chang YS, Chikhladze M, Fiocchi A, González-Diaz SN, Tanno LK, Levin M, Ortega-Martell JA, Passalacqua G, Peden DB, Rouadi PW, Sublett JL, Wong GWK, Bleecker ER. PMID: 32426090; PMCID: PMC7229954.

#### IMPACT PUBLICATION

- 36 AAAAI Mast Cell Disorders Committee Work Group Report: Mast cell activation syndrome (MCAS) diagnosis and management. Weiler CR, Austen KF, Akin C, Barkoff MS, Bernstein JA, Bonadonna P, Butterfield JH, Carter M, Fox CC, Maitland A, Pongdee T, Mustafa SS, Ravi A, Tobin MC, Vliagoftis H, Schwartz LB. PMID: 31476322.
- 37 De novo and inherited variants in ZNF292 underlie a neurodevelopmental disorder with features of autism spectrum disorder.Mirzaa GM, Chong JX, Piton A, Popp B, Foss K, Guo H, Harripaul R, Xia K, Scheck J, Aldinger KA, Sajan SA, Tang S, Bonneau D, Beck A, White J, Mahida S, Harris J, Smith-Hicks C, Hoyer J, Zweier C, Reis A, Thiel CT, Jamra RA, Zeid N, Yang A, Farach LS, Walsh L, Payne K, Rohena L, Velinov M, Ziegler A, Schaefer E, Gatinois V, Geneviève D, Simon MEH, Kohler J, Rotenberg J, Wheeler P, Larson A, Ernst ME, Akman CI, Westman R, Blanchet P, Schillaci LA, Vincent-Delorme C, Gripp KW, Mattioli F, Guyader GL, Gerard B, Mathieu-Dramard M, Morin G, Sasanfar R, Ayub M, Vasli N, Yang S, Person R, Monaghan KG, Nickerson DA, van Binsbergen E, Enns GM, Dries AM, Rowe LJ, Tsai ACH, Svihovec S, Friedman J, Agha Z, Qamar R, Rodan LH, Martinez-Agosto J, Ockeloen CW, Vincent M, Sunderland WJ, Bernstein JA; Undiagnosed Diseases Network,, Eichler EE, Vincent JB; University of Washington Center for Mendelian Genomics (UW-CMG),, Bamshad MJ. PMID: 31723249; PMCID: PMC7060121.
- **38** Occupational Rhinitis: Classification, Diagnosis, and Therapeutics. Shao Z, Bernstein JA. PMID: 31776689.

#### IMPACT PUBLICATION

39 Anaphylaxis-a 2020 practice parameter update, systematic review, and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) analysis.Shaker MS, Wallace DV, Golden DBK, Oppenheimer J, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Greenhawt M, Khan DA, Lang DM, Lang ES, Lieberman JA, Portnoy J, Rank MA, Stukus DR, Wang J; Collaborators, Riblet N, Bobrownicki AMP, Bontrager T, Dusin J, Foley J, Frederick B, Fregene E, Hellerstedt S, Hassan F, Hess K, Horner C, Huntington K, Kasireddy P, Keeler D, Kim B, Lieberman P, Lindhorst E, McEnany F, Milbank J, Murphy H, Pando O, Patel AK, Ratliff N, Rhodes R, Robertson K, Scott H, Snell A, Sullivan R, Trivedi V, Wickham A; Chief Editors, Shaker MS, Wallace DV; Workgroup Contributors, Shaker MS, Wallace DV, Bernstein JA, Campbell RL, Dinakar C, Ellis A, Golden DBK, Greenhawt M, Lieberman JA, Rank MA, Stukus DR, Wang J; Joint Task Force on Practice Parameters Reviewers, Shaker MS, Wallace DV, Golden DBK, Bernstein JA, Dinakar C, Ellis A, Greenhawt M, Horner C, Khan DA, Lieberman JA, Oppenheimer J, Rank MA, Shaker MS, Stukus DR, Wang J. PMID: 32001253.

## Immunology, Allergy and Rheumatology

PUBLICATIONS CONTINUED

- 40 Long-Term Outcomes with Subcutaneous C1-Inhibitor Replacement Therapy for Prevention of Hereditary Angioedema Attacks.Craig T, Zuraw B, Longhurst H, Cicardi M, Bork K, Grattan C, Katelaris C, Sussman G, Keith PK, Yang W, Hébert J, Hanzlikova J, Staubach-Renz P, Martinez-Saguer I, Magerl M, Aygören-Pürsün E, Farkas H, Reshef A, Kivity S, Neri S, Crisan I, Caballero T, Baeza ML, Hernandez MD, Li H, Lumry W, Bernstein JA, Hussain I, Anderson J, Schwartz LB, Jacobs J, Manning M, Levy D, Riedl M, Christiansen S, Feuersenger H, Pragst I, Mycroft S, Pawaskar D, Jacobs I; COMPACT Investigators.PMID: 30772477.
- **41** Tiotropium in asthma: From bench to bedside. Mansfield L, **Bernstein JA**. PMID: 31212121.
- 42 De Novo Variants in WDR37 Are Associated with Epilepsy, Colobomas, Dysmorphism, Developmental Delay, Intellectual Disability, and Cerebellar Hypoplasia.Kanca O, Andrews JC, Lee PT, Patel C, Braddock SR, Slavotinek AM, Cohen JS, Gubbels CS, Aldinger KA, Williams J, Indaram M, Fatemi A, Yu TW, Agrawal PB, Vezina G, Simons C, Crawford J, Lau CC; Undiagnosed Diseases Network- Bernstein JA, Chung WK, Markello TC, Dobyns WB, Adams DR, Gahl WA, Wangler MF, Yamamoto S, Bellen HJ, Malicdan MCV. PMID: 31327508; PMCID: PMC6699142.
- 43 Genomics in medicine: a novel elective rotation for internal medicine residents. Geng LN, Kohler JN, Levonian P; Members of the Undiagnosed Diseases Network, Bernstein JA, Ford JM, Ahuja N, Witteles R, Hom J, Wheeler M. PMID: 31439813.
- 44 Yield of whole exome sequencing in undiagnosed patients facing insurance coverage barriers to genetic testing. Reuter CM, Kohler JN, Bonner D, Zastrow D, Fernandez L, Dries A, Marwaha S, Davidson J, Brokamp E, Herzog M, Hong J, Macnamara E, Rosenfeld JA, Schoch K, Spillmann R; Undiagnosed Diseases Network, Loscalzo J, Krier J, Stoler J, Sweetser D, Palmer CGS, Phillips JA, Shashi V, Adams DA, Yang Y, Ashley EA, Fisher PG, Mulvihill JJ, Bernstein JA, Wheeler MT. PMID: 31478310; PMCID: PMC6901723.

#### IMPACT PUBLICATION

Loss of UGP2 in brain leads to a severe epileptic encephalopathy, emphasizing that bi-allelic isoformspecific start-loss mutations of essential genes can cause genetic diseases.Perenthaler E, Nikoncuk A, Yousefi S, Berdowski WM, Alsagob M, Capo I, van der Linde HC, van den Berg P, Jacobs EH, Putar D, Ghazvini M, Aronica E, van IJcken WFJ, de Valk WG, Medicivan den Herik E, van Slegtenhorst M, Brick L, Kozenko M, Kohler JN, Bernstein JA, Monaghan KG, Begtrup A, Torene R, Al Futaisi A, Al Murshedi F, Mani R, Al Azri F, Kamsteeg EJ, Mojarrad M, Eslahi A, Khazaei Z, Darmiyan FM, Doosti M, Karimiani EG, Vandrovcova J, Zafar F, Rana N, Kandaswamy KK, Hertecant J, Bauer P, Al-Muhaizea MA, Salih MA, Aldosary M, Almass R, Al-Quait L, Qubbaj W, Coskun S, Alahmadi KO, Hamad MHA, Alwadaee S, Awartani K, Dababo AM, Almohanna F, Colak D, Dehghani M, Mehrjardi MYV, Gunel M, Ercan-Sencicek AG, Passi GR, Cheema HA, Efthymiou S, Houlden H, Bertoli-Avella AM, Brooks AS, Retterer K, Maroofian R, Kaya N, van Ham TJ, Barakat TS. PMID: 31820119; PMCID: PMC7035241.

## IMPACT PUBLICATION

Partial Loss of USP9X Function Leads to a Male Neu-46 rodevelopmental and Behavioral Disorder Converging on Transforming Growth Factor β Signaling. Johnson BV, Kumar R, Oishi S, Alexander S, Kasherman M, Vega MS, Ivancevic A, Gardner A, Domingo D, Corbett M, Parnell E, Yoon S, Oh T, Lines M, Lefroy H, Kini U, Van Allen M, Grønborg S, Mercier S, Küry S, Bézieau S, Pasquier L, Raynaud M, Afenjar A, Billette de Villemeur T, Keren B, Désir J, Van Maldergem L, Marangoni M, Dikow N, Koolen DA, VanHasselt PM, Weiss M, Zwijnenburg P, Sa J, Reis CF, López-Otín C, Santiago-Fernández O, Fernández-Jaén A, Rauch A, Steindl K, Joset P, Goldstein A, Madan-Khetarpal S, Infante E, Zackai E, Mcdougall C, Narayanan V, Ramsey K, Mercimek-Andrews S, Pena L, Shashi V; Undiagnosed Diseases Network- Bernstein JA, Schoch K, Sullivan JA, Pinto E Vairo F, Pichurin PN, Ewing SA, Barnett SS, Klee EW, Perry MS, Koenig MK, Keegan CE, Schuette JL, Asher S, Perilla-Young Y, Smith LD, Rosenfeld JA, Bhoj E, Kaplan P, Li D, Oegema R, van Binsbergen E, van der Zwaag B, Smeland MF, Cutcutache I, Page M, Armstrong M, Lin AE, Steeves MA, Hollander ND, Hoffer MJV, Reijnders MRF, Demirdas S, Koboldt DC, Bartholomew D, Mosher TM, Hickey SE, Shieh C, Sanchez-Lara PA, Graham JM Jr, Tezcan K, Schaefer GB, Danylchuk NR, Asamoah A, Jackson KE, Yachelevich N, Au M, Pérez-Jurado LA, Kleefstra T, Penzes P, Wood SA, Burne T, Pierson TM, Piper M, Gécz J, Jolly LA. PMID: 31443933; PMCID: PMC6925349.

#### IMPACT PUBLICATION

- 47 De Novo Pathogenic Variants in N-cadherin Cause a Syndromic Neurodevelopmental Disorder with Corpus Collosum, Axon, Cardiac, Ocular, and Genital Defects. Accogli A, Calabretta S, St-Onge J, Boudrahem-Addour N, Dionne-Laporte A, Joset P, Azzarello-Burri S, Rauch A, Krier J, Fieg E, Pallais JC; Undiagnosed Diseases Network- Bernstein JA, McConkie-Rosell A, McDonald M, Freedman SF, Rivière JB, Lafond-Lapalme J, Simpson BN, Hopkin RJ, Trimouille A, Van-Gils J, Begtrup A, McWalter K, Delphine H, Keren B, Genevieve D, Argilli E, Sherr EH, Severino M, Rouleau GA, Yam PT, Charron F, Srour M. PMID: 31585109; PMCID: PMC6817525.
- 48 VarSight: prioritizing clinically reported variants with binary classification algorithms. Holt JM, Wilk B, Birch CL, Brown DM, Gajapathy M, Moss AC, Sosonkina N, Wilk MA, Anderson JA, Harris JM, Kelly JM, Shaterferdosian F, Uno-Antonison AE, Weborg A; Undiagnosed Diseases Network- Bernstein JA, Worthey EA. PMID: 31615419; PMCID: PMC6792253.
- 49 Allergic and Mixed Rhinitis: Diagnosis and Natural Evolution. Greiwe JC, Bernstein JA. PMID: 31752308; PMCID: PMC6912750.
- 50 Drug-induced anaphylaxis, elicitors, risk factors, and management in Latin America.Jares EJ, Cardona Villa R, Sánchez-Borges M, de Falco A, Ensina LF, Bernstein JA, Arias-Cruz A, Cherrez-Ojeda I, Morfín Maciel B, Macías-Weinmann A, González Díaz S, Sole D, Giavina-Bianchi P, de Barayazarra S, Cuello M, Vinuesa M, Calderón JC, Zanacchi VA, Monsell S, Morelo Rocha Felix M, Serrano Reyes C, Piraino P, Jaller R, Guerzet Ayres Bastos P, Gómez M; "Latin America Drug Allergy Interest Group". PMID: 31626988.

Immunology, Allergy and Rheumatology

- 51 De novo EIF2AK1 and EIF2AK2 Variants Are Associated with Developmental Delay, Leukoencephalopathy, and Neurologic Decompensation. Mao D, Reuter CM, Ruzhnikov MRZ, Beck AE, Farrow EG, Emrick LT, Rosenfeld JA, Mackenzie KM, Robak L, Wheeler MT, Burrage LC, Jain M, Liu P, Calame D, Küry S, Sillesen M, Schmitz-Abe K, Tonduti D, Spaccini L, Iascone M, Genetti CA, Koenig MK, Graf M, Tran A, Alejandro M; Undiagnosed Diseases Network- Bernstein JA, Lee BH, Thiffault I, Agrawal PB, Bernstein JA, Bellen HJ, Chao HT. PMID: 32197074; PMCID: PMC7118694.
- 52 Modeling Cost-Effectiveness of On-Demand Treatment for Hereditary Angioedema Attacks. Bernstein JA, Tyson C, Relan A, Adams P, Magar R. PMID: 31841366.
- 53 Current and Future Treatments of Rhinitis and Sinusitis. Patel GB, Kern RC, Bernstein JA, Hae-Sim P, Peters AT. PMID: 32004747; PMCID: PMC7416524.
- 54 Heterozygous variants in MYBPC1 are associated with an expanded neuromuscular phenotype beyond arthrogryposis. Shashi V, Geist J, Lee Y, Yoo Y, Shin U, Schoch K, Sullivan J, Stong N, Smith E, Jasien J, Kranz P; Undiagnosed Diseases Network- Bernstein JA, Lee Y, Shin YB, Wright NT, Choi M, Kontrogianni-Konstantopoulos A. PMID: 31264822; PMCID: PMC6688907.
- 55 Impact of omalizumab on patient-reported outcomes in chronic idiopathic urticaria: Results from a randomized study (XTEND-CIU). Casale TB, Murphy TR, Holden M, Rajput Y, Yoo B, **Bernstein JA**. PMID: 31034999.
- 56 One Versus Two Doses of Intravenous Tranexamic Acid in Total Knee Arthroplasty.Charette RS, Bernstein JA, Sloan M, Nchako CM, Kamath AF, Nelson CL. PMID: 31731323.

#### **IMPACT PUBLICATION**

- 57 De Novo Variants in WDR37 Are Associated with Epilepsy, Colobomas, Dysmorphism, Developmental Delay, Intellectual Disability, and Cerebellar Hypoplasia. Kanca O, Andrews JC, Lee PT, Patel C, Braddock SR, Slavotinek AM, Cohen JS, Gubbels CS, Aldinger KA, Williams J, Indaram M, Fatemi A, Yu TW, Agrawal PB, Vezina G, Simons C, Crawford J, Lau CC; Undiagnosed Diseases Network- Bernstein JA, Chung WK, Markello TC, Dobyns WB, Adams DR, Gahl WA, Wangler MF, Yamamoto S, Bellen HJ, Malicdan MCV. PMID: 31491411; PMCID: PMC6732524.
- 58 Urticaria and Angioedema Across the Ages. Saini S, Shams M, Bernstein JA, Maurer M. PMID: 32298850.
- 59 AGA institute and the joint task force on allergy-immunology practice parameters clinical guidelines for the management of eosinophilic esophagitis. Hirano I, Chan ES, Rank MA, Sharaf RN, Stollman NH, Stukus DR, Wang K, Greenhawt M, Falck-Ytter YT; AGA Institute Clinical Guidelines Committee; Joint Task Force on Allergy-Immunology Practice Parameters- Bernstein JA. PMID: 32336462.

#### IMPACT PUBLICATION

- 60 AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. Gastroenterology. Hirano I, Chan ES, Rank MA, Sharaf RN, Stollman NH, Stukus DR, Wang K, Greenhawt M, Falck-Ytter YT; AGA Institute Clinical Guidelines Committee; Joint Task Force on Allergy-Immunology Practice Parameters- Bernstein JA. PMID: 32359562.
- 61 Magnetic Resonance Imaging characteristics in case of TOR1AIP1 muscular dystrophy. Bhatia A, Mobley BC, Cogan J, Koziura ME, Brokamp E, Phillips J, Newman J; Undiagnosed Diseases Network (UDN), Moore SA, Hamid R; Members of the Undiagnosed Diseases Network- Bernstein JA. PMID: 31299614 PMCID: PMC6893088.
- 62 Long-term safety outcomes of prekillikrein (Fletcher factor) deficiency: A systematic literature review of case reports. Girolami A, Rolland C, Sexton D, Vardi M, Bernstein JA. PMID: 31530337
- 63 Lanadelumab demonstrates rapid and sustained prevention of hereditary angioedema attacks. Riedl MA, Maurer M, Bernstein JA, Banerji A, Longhurst HJ, Li HH, Lu P, Hao J, Juethner S, Lumry WR; HELP Investigators. PMID: 32452549; PMCID: PMC7689768.
- 64 Development and Reporting of Prediction Models: Guidance for Authors From Editors of Respiratory, Sleep, and Critical Care Journals. Leisman DE, Harhay MO, Lederer DJ, Abramson M, Adjei AA, Bakker J, Ballas ZK, Barreiro E, Bell SC, Bellomo R, Bernstein JA, Branson RD, Brusasco V, Chalmers JD, Chokroverty S, Citerio G, Collop NA, Cooke CR, Crapo JD, Donaldson G, Fitzgerald DA, Grainger E, Hale L, Herth FJ, Kochanek PM, Marks G, Moorman JR, Ost DE, Schatz M, Sheikh A, Smyth AR, Stewart I, Stewart PW, Swenson ER, Szymusiak R, Teboul JL, Vincent JL, Wedzicha JA, Maslove DM. PMID: 32141923; PMCID: PMC7161722.
- **65** Step-up and step-down treatments for optimal asthma control in children and adolescents. **Bernstein JA**, Mansfield L. PMID: 29972079.

#### IMPACT PUBLICATION

- 66 Technical Review on the Management of Eosinophilic Esophagitis: A Report From the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters.Rank MA, Sharaf RN, Furuta GT, Aceves SS, Greenhawt M, Spergel JM, Falck-Ytter YT, Dellon ES; AGA Institute. Joint Task Force on Allergy-Immunology Practice Parameters collaborators-Bernstein JA. AGA Institute; Joint Task Force on Allergy-Immunology Practice Parameters collaborators. PMID: 32359563.
- **67** Progestogen Sensitization: a Unique Female Presentation of Anaphylaxis. **Bernstein JA**. PMID: 31993777.

#### Immunology, Allergy and Rheumatology

PUBLICATIONS CONTINUED

- 68 Definition, aims, and implementation of GA2 LEN/ HAEi Angioedema Centers of Reference and Excellence. Maurer M, Aberer W, Agondi R, Al-Ahmad M, Al-Nesf MA, Ansotegui I, Arnaout R, Arruda LK, Asero R, Aygören-Pürsün E, Banerji A, Bauer A, Ben-Shoshan M, Berardi A, Bernstein JA, Betschel S, Bindslev-Jensen C, Bizjak M, Boccon-Gibod I, Bork K, Bouillet L, Boysen HB, Brodszki N, Broesby-Olsen S, Busse P, Buttgereit T, Bygum A, Caballero T, Campos RA, Cancian M, Cherrez-Ojeda I, Cohn DM, Costa C, Craig T, Criado PR, Criado RF, Csuka D, Dissemond J, Du-Thanh A, Ensina LF, Ertaş R, Fabiani JE, Fantini C, Farkas H, Ferrucci SM, Figueras-Nart I, Fili NL, Fomina D, Fukunaga A, Gelincik A, Giménez-Arnau A, Godse K, Gompels M, Gonçalo M, Gotua M, Gower R, Grumach AS, Guidos-Fogelbach G, Hide M, Ilina N, Inomata N, Jakob T, Josviack DO, Kang HR, Kaplan A, Kasperska-Zajac A, Katelaris C, Kessel A, Kleinheinz A, Kocatürk E, Košnik M, Krasowska D, Kulthanan K, Kumaran MS, Larco Sousa JI, Longhurst HJ, Lumry W, MacGinnitie A, Magerl M, Makris MP, Malbrán A, Marsland A, Martinez-Saguer I, Medina IV, Meshkova R, Metz M, Nasr I, Nicolay J, Nishigori C, Ohsawa I, Özyurt K, Papadopoulos NG, Parisi CAS, Peter JG, Pfützner W, Popov T, Prior N, Ramon GD, Reich A, Reshef A, Riedl MA, Ritchie B, Röckmann-Helmbach H, Rudenko M, Salman A, Sanchez-Borges M, Schmid-Grendelmeier P, Serpa FS, Serra-Baldrich E, Sheikh FR, Smith W, Soria A, Staubach P, Steiner UC, Stobiecki M, Sussman G, Tagka A, Thomsen SF, Treudler R, Valle S, van Doorn M, Varga L, Vázquez DO, Wagner N, Wang L, Weber-Chrysochoou C, Ye YM, Zalewska-Janowska A, Zanichelli A, Zhao Z, Zhi Y, Zuberbier T, Zwiener RD, Castaldo A. PMID: 32248571
- **69** Tiotropium reduces airflow obstruction in asthma patients, independent of body mass index.Khurana S, Paggiaro P, Buhl R, **Bernstein JA**, Haddon J, Unseld A, Engel M, Casale TB, Dixon AE. PMID: 30898691.
- 70 Safety of recombinant human C1 esterase inhibitor for hereditary angioedema attacks during pregnancy. Moldovan D, Bernstein JA, Hakl R, Porebski G, Poarch K, Lumry WR, Relan A. PMID: 31170541.
- 71 Dupilumab improves asthma outcomes irrespective of frequency of previous asthma exacerbation history. Corren J, Castro M, Ford LB, **Bernstein JA**, Jayawardena S, Maroni J, Rowe P, Amin N, Pirozzi G, Graham NMH, Khan A, Eckert L, Teper A. PMID: 31075309.
- 72 Treatment effect of switching from intravenous to subcutaneous C1-inhibitor for prevention of hereditary angioedema attacks: COMPACT subgroup findings. Craig T, Lumry W, Cicardi M, Zuraw B, Bernstein JA, Anderson J, Jacobs J, Riedl MA, Manning ME, Banerji A, Gower RG, Caballero T, Farkas H, Feuersenger H, Jacobs I, Machnig T, Longhurst H; COMPACT Investigators- Bernstein JA. PMID: 30660873.

- 73 ClinPhen extracts and prioritizes patient phenotypes directly from medical records to expedite genetic disease diagnosis. Deisseroth CA, Birgmeier J, Bodle EE, Kohler JN, Matalon DR, Nazarenko Y, Genetti CA, Brownstein CA, Schmitz-Abe K, Schoch K, Cope H, Signer R; Undiagnosed Diseases Network, Martinez-Agosto JA, Shashi V, Beggs AH, Wheeler MT, Bernstein JA, Bejerano G. PMID: 30514889; PMCID: PMC6551315.
- 74 Tiotropium Is Efficacious in 6- to 17-Year-Olds with Asthma, Independent of T2 Phenotype. Szefler SJ, Vogelberg C, Bernstein JA, Goldstein S, Mansfield L, Zaremba-Pechmann L, Engel M, Hamelmann E. PMID: 30922990.
- 75 Resolving Clinical Phenotypes into Endotypes in Allergy: Molecular and Omics Approaches. Mersha TB, Afanador Y, Johansson E, Proper SP, Bernstein JA, Rothenberg ME, Khurana Hershey GK. PMID: 32378146.
- 76 Diffusion Tensor Imaging Abnormalities in the Uncinate Fasciculus and Inferior Longitudinal Fasciculus in Phelan-McDermid Syndrome. Bassell J, Srivastava S, Prohl AK, Scherrer B, Kapur K, Filip-Dhima R, Berry-Kravis E, Soorya L, Thurm A, Powell CM, Bernstein JA, Buxbaum JD, Kolevzon A, Warfield SK, Sahin M; Developmental Synaptopathies Consortium. PMID: 32107139; PMCID: PMC7190002.
- 77 Technical review on the management of eosinophilic esophagitis: a report from the AGA institute and the joint task force on allergy-immunology practice parameters.Rank MA, Sharaf RN, Furuta GT, Aceves SS, Greenhawt M, Spergel JM, Falck-Ytter YT, Dellon ES; AGA Institute- Bernstein JA. Joint Task Force on Allergy-Immunology Practice Parameters collaborators. AGA Institute; Joint Task Force on Allergy-Immunology Practice Parameters collaborators. PMID: 32336463.
- 78 AVADA: toward automated pathogenic variant evidence retrieval directly from the full-text literature. Birgmeier J, Deisseroth CA, Hayward LE, Galhardo LMT, Tierno AP, Jagadeesh KA, Stenson PD, Cooper DN, Bernstein JA, Haeussler M, Bejerano G. PMID: 31467448; PMCID: PMC7301356.
- 79 Making the GRADE in anaphylaxis management: Toward recommendations integrating values, preferences, context, and shared decision making. Shaker MS, Oppenheimer J, Wallace DV, Golden DBK, Lang DM; Joint Task Force for Allergy Practice Parameters; Contributors, Lang ES, Bernstein JA, Campbell RL, Chu D, Dinakar C, Ellis AK, Greenhawt M, Horner C, Lieberman JA, Rank MA, Stukus DR, Wang J. PMID: 32199979.
- 80 Interrupting the Pathway from Gestational Diabetes Mellitus to Type 2 Diabetes: The Role of Primary Care. Womens Health Issues.McCloskey L, Quinn E, Ameli O, Heeren T, Craig M, Lee-Parritz A, Iverson R, Jack B, Bernstein JA. PMID: 31562051.

- 81 Effect of fixed-dose subcutaneous reslizumab on asthma exacerbations in patients with severe uncontrolled asthma and corticosteroid sparing in patients with oral corticosteroid-dependent asthma: results from two phase 3, randomised, double-blind, placebocontrolled trials. Bernstein JA, Virchow JC, Murphy K, Maspero JF, Jacobs J, Adir Y, Humbert M, Castro M, Marsteller DA, McElhattan J, Hickey L, Garin M, Vanlandingham R, Brusselle G. PMID: 32066536.
- 82 Long-term safety and efficacy of subcutaneous C1inhibitor in older patients with hereditary angioedema. Bernstein JA, Schwartz L, Yang W, Baker J, Anderson J, Farkas H, Aygören-Pürsün E, Bygum A, Jacobs I, Feuersenger H, Pragst I, Riedl MA. PMID: 32445670.
- 83 A novel functional C1 inhibitor activity assay in dried blood spot for diagnosis of Hereditary angioedema. Lai Y, Zhang G, Zhou Z, Inhaber N, Bernstein JA, Chockalingam PS, Wu J. PMID: 32059947.
- 84 Long-term safety outcomes of prekallikrein (Fletcher factor) deficiency: A systematic literature review of case reports.Girolami A, Rolland C, Sexton D, Vardi M, Bernstein JA. PMID: 31888778.
- 85 Automated syndrome diagnosis by three-dimensional facial imaging. Hallgrímsson B, Aponte JD, Katz DC, Bannister JJ, Riccardi SL, Mahasuwan N, McInnes BL, Ferrara TM, Lipman DM, Neves AB, Spitzmacher JAJ, Larson JR, Bellus GA, Pham AM, Aboujaoude E, Benke TA, Chatfield KC, Davis SM, Elias ER, Enzenauer RW, French BM, Pickler LL, Shieh JTC, Slavotinek A, Harrop AR, Innes AM, McCandless SE, McCourt EA, Meeks NJL, Tartaglia NR, Tsai AC, Wyse JPH, Bernstein JA, Sanchez-Lara PA, Forkert ND, Bernier FP, Spritz RA, Klein OD. PMID: 32475986; PMCID: PMC7521994.
- 86 Drug-induced anaphylaxis and drug sales: Why the discordance? Jares EJ, De Falco A, Sánchez-Borges M, Bernstein JA, Zanacchi A, Monsell S, Gómez RM. PMID: 32574598.
- 87 Psychometric Study of the Social Responsiveness Scale in Phelan-McDermid Syndrome.Gergoudis K, Weinberg A, Templin J, Farmer C, Durkin A, Weissman J, Siper P, Foss-Feig J, Del Pilar Trelles M, Bernstein JA, Buxbaum JD, Berry-Kravis E, Powell CM, Sahin M, Soorya L, Thurm A, Kolevzon A; Developmental Synaptopathies Consortium. PMID: 32406614.
- 88 Emergency department evaluation of patients with angiotensin converting enzyme inhibitor associated angioedema. Mudd PA, Hooker EA, Stolz U, Hart KW, Bernstein JA, Moellman JJ. PMID: 31932133.

89 The Cost of an Episode of Care in a Total Knee Arthroplasty Patient Is More Than a Total Hip Arthroplasty Patient Within an Alternative Payment Model. Bernstein JA, Yeroushalmi D, Slover JD, Bosco JA 3rd. PMID: 32362481.

**IMPACT PUBLICATION** 

- 90 AMELIE speeds Mendelian diagnosis by matching patient phenotype and genotype to primary literature. Birgmeier J, Haeussler M, Deisseroth CA, Steinberg EH, Jagadeesh KA, Ratner AJ, Guturu H, Wenger AM, Diekhans ME, Stenson PD, Cooper DN, Ré C, Beggs AH, Bernstein JA, Bejerano G. PMID: 32434849.
- 91 Influence of alexithymia on the management of Latin American patients with asthma: A cross-sectional study. Vanegas E, Felix M, Ramon GD, López Jove O, Matos Benavides EE, Tinoco-Morán I, Bernstein JA, Cherrez-Ojeda I. PMID: 32551114; PMCID: PMC7278303.
- **92** An integrated videoconferencing intervention for chronic pain and heavy drinking among patients in HIV-care: a proof-of-concept study. Palfai TP, Saitz R, Kratzer MPL, Taylor JL, Otis JD, **Bernstein JA**. PMID: 32524827; PMCID: PMC7484138.
- **93** The Need for an Interpreter Increases Length of Stay and Influences Postoperative Disposition Following Primary Total Joint Arthroplasty **Bernstein JA**, Sharan M, Lygrisse KA, Lajam CM. PMID: 32446624.
- 94 Association Between Self-Reported Dental Hygiene Practices and Dental Procedure-Related Recurrent Angioedema Attacks in HAE Subjects: A Multicenter Survey. JSingh U, Lumry WR, Busse P, Wedner HJ, Banerji A, Craig TJ, Li HH, Tachdjian R, Jacobs JS, Riedl MA, Davis-Lorton M, Christiansen SC, Zuraw BL, Bernstein JA. PMID: 32534150.
- 95 Influence of Generational Cohorts on the Preferences for Information and Communication Technologies in Latin American Patients with Obstructive Lung Diseases. Cherrez-Ojeda I, Mata VL, Vanegas E, Felix M, Bernstein JA, Jiménez FM, Calderon JC, Chedraui P, Gavilanes AW. PMID: 32411213; PMCID: PMC7212335.

Annual Research Report 2020

1m Frid

## Division of Infectious Diseases

## ENDOWED CHAIR: Ward E. Bullock Professor of Infectious Diseases

The Division of Infectious Diseases has a long-standing reputation as a research focused division where almost 70% of the division's faculty members have active roles in clinical, translational, and basic science research. In total, the division has 11 MD investigators and 4 PhD investigators with over \$27M in research holdings.



George Smulian, MD DIVISION DIRECTOR

## **Research Focus Areas/Types:**

The focus of the division's basic science research remains fungal pathogens:

- Histoplasma capsulatum
- Pneumocystis spp.
- Host cellular response to *Clostridium difficile*

The clinical and translational research focus continues to be: • HIV

- Diarrheal pathogens
- Respiratory pathogensCOVID

## Investigators/Trainees:

The division has an international reputation as a mycology powerhouse based on the research programs of George Deepe in *Histoplasma capsulatum* and Melanie Cushion in Pneumocystis species. Kavitha Subramanian Vignesh is expanding the division's Histoplasma research activities even further. Junior investigators such as Rajat Madan and Senu Apewokin are growing the basic and translational research programs of the division by examining the pivotal interface between host cellular, metabolism and Clostridium difficile in mouse models and in immunocompromised humans. Additionally, Moises Huaman and Carl Fichtenbaum have delved into a new area of exploration for the division by investigating the role of the host inflammatory response elicited by microbes in

the pathogenesis of cardiovascular disease. The clinical research program under Dr. Fichtenbaum continues to conduct studies on persons with HIV infection; prevention of HIV infection; Hepatitis C; COVID; influenza and appropriate antibiotic usage.

## Funding types:

- National Institutes of Health
- American Heart Association
- Health Resources and Services Administration
- Department of Veterans Affairs
- UC College of Medicine and Department of Internal Medicine
- Industry, public-private partnerships and philanthropy

## **Mentoring:**

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 established investigators.

## **Collaborations:**

The division maintains close collaboration with the VA National Infectious Disease Program office based here in Cincinnati and benefits from access to the UC based fungal research on Aspergillus and Candida and international programs in Paracocciodiodes and Cryptococcus.

Infectious Diseases SPOTLIGHT

# Senu Apewokin, MD

ASSOCIATE PROFESSOR DIVISION OF INFECTIOUS DISEASES

C Health.

Semi Apewoktin, Ma Infectious Diseases Sentence of the sentence of th

It wasn't until years later that he discovered that Weiss had long held the goal of supporting a clinical researcher because of the importance of grounding basic research in clinical reality.

"She took a chance on me, supported me with her resources, and the t is history," Apewokin recalls.

Since Weiss became his primary mentor, Apewokin has focused on how microbes and host factors change to influence development of *Clostratioides difficile* infection (CDI) during immunosuppressive events, such as chemotherapy. CDI is the most common healthcare-acquired infection and increases hospital mortality and healthcare costs. Although some progress has been made in controlling rates nationwide, the current rates remain "unacceptable," Apewokin says. The most effective strategy to combat CDI starts with understanding how the disease develops. In addition to microbe-related factors, host factors play a significant role in CDI development.

"Why some patients develop CDI while others don't is not very clear," says Apewokin. "Appreciating and acknowledging that not all CDIs are the same motivates research into patient-specific factors that promote development of CDI. My research, hopefully, will emphasize this."

In addition to working with Weiss, Apewokin's UC mentoring team is consisted of David Haslam, MD, a specialist in pediatric infectious seases; Tesfaye Mersha, PhD, who studies asthma and pediatric ifectious diseases; and Pier Scaglioni, MD, who researches hematology. Fogether they have provided me with valuable resources, career guidance and advice," Apewokin says.

Looking ahead, Apewokin is hopeful that some of the limitations placed on research activities because of COVID-19 will be removed once the pandemic is under control.

"2021 follows up on a challenging year for all researchers," he says. "I look forward to a productive and exciting year."

What Apewokin knows for certain is that his work will continue to focus on a population — pharmacologically immunosuppressed hosts — that historically has been understudied. The potential impact further research could have on patients' lives drives him each day.

"The knowledge gaps in this area were very obvious during my clinical practice," Apewokin says. "There was also a glaring absence of translational researchers who studied this population. Together these needs spoke to a sense of urgency that I felt was important to make a contribution toward."

"APPRECIATING AND ACKNOWLEDGING THAT NOT ALL CDIS ARE THE SAME MOTIVATES RESEARCH INTO PATIENT-SPECIFIC FACTORS THAT PROMOTE DEVELOPMENT OF CDI. MY RESEARCH, HOPEFULLY, WILL EMPHASIZE THIS."

Infectious Diseases

#### PUBLICATIONS July 1, 2019 thru June 30, 2020

- 1 Wilson D and **Deepe**, **Jr. GS**. The Intersection of host and fungus through the zinc lens. Curr Opin Microbiol 52:35-40, 2019.
- 2 Chowdhury D, Deepe, Jr. GS, and Subramanian Vignesh K. The Metallothionein-Zinc Landscape: How It Shapes Antimicrobial Immunity in Zinc Signaling ed. by T. Fukada and T. Kambe pp. 57-77, Springer Link, 2019.
- 3 Oates JR, McKell MC, Moreno-Fernandez MA, Damen MSMA, Deepe GS, Qualls JE, Divanovic. Macrophage function in the pathogenesis of non-alcoholic fatty liver disease: The mac attack. Front. Immunol. 10:2893. doi: 10.3389, 2019.
- 4 Rossi DCP and Deepe, Jr GS. Type I interferons rule with an iron fist. Cell Host & Microbe 27: 317-319, 2020.
- 5 Shen, Q, Ray S, Evans H, Deepe, Jr. GS, and Rappleye C. Metabolism of gluconeogenic substrates by an intracellular fungal pathogen circumvents nutritional limitations within macrophages. mBio 11(2):e02712-19. doi: 10.1128, 2020
- 6 Almanan M, Raynor J, Ogunsulire I, Malyshkina A, Mukherjee S, Hummel SA, Ingram JT, et al. IL-10 producing Tfh cells accumulate with age and link inflammation with age-related immune suppression. Sci Adv . 6:eabb0806. doi: 10.1126, 2020.
- 7 A Retrospective Chart Review on the Role of Suppressive Therapy in the Management of Spinal Infections Involving Hardware. Nour Beydoun, Sonia Tandon, Sonia Krengel, Eric Johnson, Federico Palacio Bedoya, Michael Moore, Daniel Refai, Nadine Rouphael Open Forum Infectious Diseases, Volume 7, Issue 7, July 2020, ofaa253
- 8 Chagas Disease Screening Using Point of Care Testing in an At-Risk Obstetric Population. In review by The American Journal of Tropical Medicine and Hygiene
- 9 Evans ME, Kralovic SM, Roselle GA. "Contact Precautions for Methicillin-Resistant Staphylococcus aureus (MRSA) in Veterans Affairs Long-Term Care Facilities: Analysis of Policies not Practice." Clin Infect Dis 2020 Feb 14 pii: ciaa146. doi: 10.1093/cid/ciaa146 [Epub ahead of print] PMID: 32083648
- 10 Evans CT, Fitzpatrick M, Ramanathan W, Kralovic SM, Burns SP, Goldstein G, Smith B, Gerding DN, Johnson S. "Healthcare Facility-Onset, Healthcare Facility-Associated Clostridium difficile Infection in Veterans with Spinal Cord Injury and Disorder" Journal of Spinal Cord Medicine 2020;43(5): 642-652.
- 11 Ambrose M, Kralovic SM, Gamage SD, "Implementation of Legionella Prevention Policy in Healthcare Facilities: The United States Veterans Health Administration Experience" J Public Health Manag Pract 2020 Mar/Apr 26(2):E1-E11.

- 12 Talwar A, Stewart R, Althomsons S, Rinsky J, Jackson D, Galvis M, Graham P, Huaman M, Karrer J, Konda-pally K, Mitchell S, Wortham J, de Fijter S. Multidrug-Resistant Tuberculosis Among Workers at Two Food Processing Facilities Ohio, 2018–2019. MMWR Morb Mortal Wkly Rep. 2020 Aug 14;69(32):1104-1105. PMID: 32790660. PMCID:PMC7440117.
- **13 Huaman MA**, Fichtenbaum CJ. Bearing the Burden of Non-AIDS Comorbidities: This is What Women Aging with HIV Look Like. Clin Infect Dis. 2020;ciaa209. doi:10.1093/cid/ciaa209. PMID: 32115629.
- 14 Huaman MA, Sterling TR. Treatment of latent tuberculosis infection - an update. Clin Chest Med. 2019 Dec;40(4):839-848. Review. PubMed PMID:31731988. PMCID:PMC7043866.
- 15 Huaman MA. Latent Tuberculosis Infection: What is the limit between infection and disease? Diagnostico (Spanish). 2019 Dec: 57(4):205-10.
- 16 BOOK: Molecular Medical Microbiology 3rd edition CHAPTER: Clostridioides difficile: from "difficult to grow" to "difficult to treat" Authors: Shinsmon Jose, David Terrero-Salcedo and Rajat Madan
- 17 Rai MA, Hammonds J, Pujato M, Mayhew C, Roskin K, Spearman P. Comparative analysis of human microglial models for studies of HIV replication and pathogenesis. Retrovirology. 2020 Nov 19;17(1):35.
- 18 Gandhi RT, Tashima KT, Smeaton LM, Vu V, Ritz J, Andrade A, Eron JJ, Hogg E, Fichtenbaum CJ on behalf of the ACTG A5241 Study Team. Long-term Outcomes in a Large Randomized Trial of HIV-1 Salvage Therapy: 96-week Results of AIDS Clinical Trials Group A5241 (OPTIONS). J Infect Dis 2019 May 28. pii: jiz281. doi: 10.1093/infdis/jiz281. [Epub ahead of print] PMID: 31135883
- 19 Fitch KV, Kileel E, Looby S, Zanni MV, Sanchez L, Fichtenbaum CJ, Overton T, Malvestutto C, Aberg J, Klingman K, Alston-Smith B, Lavelle J, Rancourt A, Sponseller CA, Melbourne K, Ribaudo H, Umbleja T, Cooper-Arnold K, Desvigne-Nickens P, Hoffmann U, Douglas P, Grinspoon SK, on behalf of the REPRIEVE Investigators. Successful recruitment of a multi-site international randomized placebo-controlled trial in people with HIV with attention to diversity of race and ethnicity: Critical role of central coordination HIV Clinical Trials. HIV Res Clin Pract, 2020 Feb;21(1):11-23. doi: 10.1080/25787489.2020.1733794. Epub 2020 Mar 11.PMID: 32160827
- 20 Fichtenbaum CJ, Ribaudo HJ, Leon-Cruz J, Overton ET, Zanni MV, Malvestutto CD, Aberg JA, Kileel EM, Fitch KV, Van Schalkwyk M, Kumarasamy N, Martinez E, Santos BR, Joseph Y, Siminski S, Melbourne K, Sponseller CA, Desvigne-Nickens P, Bloomfield GS, Currier JS, Hoffmann U, Douglas PS, Grinspoon SK, on behalf of the REPRIEVE Investigators. Patterns of Antiretroviral Therapy Use and Immunologic Profiles at Enrollment in the REPRIEVE Trial. J Infect Dis 2020; 222 (S1): S8-19.

- 21 Grossman A, Smith M, Bonomo J, Knight W, Prestigiacomo C, Richards C, Ramser E, Adeoye O, Bertsch S, Shirani P, Vagal A, Fichtenbaum CJ, Housholder A, Khatri P, Kleindorfer D, Broderick J. Endovascular Therapy for Patients with Acute Ischemic Stroke During the COVID-19 Pandemic: A Proposed Algorithm. Stroke 2020 Stroke. 2020 Apr 30:STROKEAHA120029863. doi: 10.1161/STROKEAHA.120.029863. Online ahead of print. PMID: 32352910
- 22 Tassiopoulos K, Roberts-Toler C, Fichtenbaum CJ, Susan L Koletar, for the ACTG A5322 Study Team. Web-Based Data Collection for Older Adults Living With HIV in a Clinical Research Setting: Pilot Observational Study. J Med Internet Res 2020;22(10):e18588 URL: http://www.jmir.org/2020/10/e18588/ doi: 10.2196/18588
- 23 Gephardt A, Fichtenbaum CJ. Management of Dyslipidemia in HIV. Expert Opin Pharm, 2019 Jun 28:1-11. doi: 10.1080/14656566.2019.1636033. [Epub ahead of print] PMID: 31232617
- 24 Eron JJ, Orkin C, Cunningham D, Pulido F, Post FA, De Wit S, Lathouwers E, Hufkens V, Jezorwski J, Petrovic R, Brown K, Van Landuyt E, Opsomer M; EMERALD study group (Fichtenbaum C also included). Week 96 efficacy and safety results of the phase 3, randomized EMERALD trial to evaluate switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the once daily, single-tablet regimen of darunavir/cobicistat/emtricitabine/ tenofovir alafenamide (D/C/F/TAF) in treatment-experienced, virologically-suppressed adults living with HIV-1. Antiviral Res. 2019 Jul 4;170:104543. doi: 10.1016/j.antiviral.2019.104543. [Epub ahead of print]
- 25 Beigel JH, Aga E, Elie-Turenne MC, Cho J, Tebas P, Clark CL, Metcalf JP, Ozment C, Raviprakash K, Beeler J, Holley HP Jr, Warner S, Chorley C, Lane HC, Hughes MD, Davey RT Jr; IRC005 Study Team (Fichtenbaum C, also included). Anti-influenza immune plasma for the treatment of patients with severe influenza A: a randomised, double-blind, phase 3 trial. Lancet Respir Med. 2019 Nov;7(11):941-950. doi: 10.1016/S2213-2600(19)30199-7. Epub 2019 Sep 30.PMID: 31582360
- 26 Lathouwers E, Wong EY, Brown K, Baugh B, Ghys A, Jezorwski J, Mohsine EG, Van Landuyt E, Opsomer M, De Meyer S; AMBER and EMERALD Study Groups (Fichtenbaum C, also included). Week 96 efficacy and safety results of the phase 3, randomized EMER-ALD trial to evaluate switching from boosted-protease inhibitors plus emtricitabine/tenofovir disoproxil fumarate regimens to the once daily, single-tablet regimen of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) in treatment-experienced, virologically-suppressed adults living with HIV-1. AIDS Res Hum Retroviruses. 2020 Jan;36(1):48-57. doi: 10.1089/AID.2019.0111. Epub 2019 Oct 21. PMID: 31516033
- 27 Huaman MS, Fichtenbaum CJ. Bearing the Burden of Non-AIDS Comorbidities: This is What Women Aging with HIV Look Like. Clin Infect Dis. 2020 Mar 2:ciaa209. doi: 10.1093/cid/ciaa209. Online ahead of print.PMID: 32115629

- 28 Kozal M, Aberg J, Pialoux G, Cahn P, Thompson M, Molina JM, Grinsztejn B, Diaz R, Castagna A, Kumar P, Latiff G, DeJesus E, Gummel M, Gartland M, Pierce A, Ackerman P, Llamoso C, Lataillade M; BRIGHTE Trial Team.Fostemsavir in Adults with Multidrug-Resistant HIV-1 Infection (Fichtenbaum C, also included). N Engl J Med. 2020 Mar 26;382(13):1232-1243. doi: 10.1056/NEJMoa1902493.PMID: 32212519
- 29 Franck Boccara, Princy N. Kumar, Bruno Caramelli, Alexandra Calmy, J. Antonio G. López, Sarah Bray, Marcoli Cyrille, Robert S. Rosenson and for the BEI-JERINCK Investigators (Fichtenbaum, C also included). Evolocumab in HIV-Infected Patients With Dyslipidemia. Primary Results of the Randomized, Double-Blind BEIJERINCK Study. JACC, 2020; 75(20): 2570-2584. DOI: https://doi.org/10.1016/j.jacc.2020.03.025 PMID


# Division of Nephrology, Kidney CARE Program

# ENDOWED CHAIR: James Heady Endowed Chair

The division conducts basic and translational research alongside robust programs in clinical outcomes research and clinical trials within nephrology. First and foremost, we strive to impact the health of patients and our community through the delivery of excellent care. One of the ways we achieve this is by bringing the latest discoveries in the field of nephrology closer to the bedside. We are recognized regionally and nationally for leading and/or contributing to cutting-edge research, and advancing the knowledge about kidney diseases to patients, peers and trainees. This is achieved via a variety of mediums, including peer-reviewed publications, chapters and monographs, symposia, and focused learning sessions within the institution and the community. With our state-of-the-art laboratory facilities, we provide an academic home to our established research faculty and are committed to training graduate and post-doctoral students.



Charuhas Thakar, MD DIVISION DIRECTOR

### **Research Focus Areas/Types:**

- Acute kidney injury, chronic kidney disease, dialysis, and transplantation
- lon-channels and immune regulation
- Epithelial transport
- Vascular biology
- Phosphate metabolism, acid-base physiology

### Investigators/Trainees:

The division is at the forefront of planning or participating in

national and international clinical trials of new drug development, devices, and other technology. Promising Junior investigators are Silvi Shah, MD and Prakash Gudsoorkar, MD. More established investigators are Laura Conforti, PhD, Hassane Amlal, PhD, Rita Alloway, PharmD and Heather Duncan, PhD. Clinical trial experts include Dr. Abu Jawdeh, Dr. Anand, Dr. Govil, Dr. Kamath and Dr. Kant, among others. In total we have 5 MD investigators and 4 PhD investigators and over 15 active clinical trials. Research publications by the Division of Nephrology investigators have appeared in the most prestigious medical journals over the last decade, including the Annals of Internal Medicine, Journal of Clinical Investigation, Science, Translational Medicine, Journal of American Society of Nephrology, Kidney International, and Critical Care Medicine and Stroke.

### **Funding types:**

- National Institutes of Health (R01, U01, DOD)
- United States Department of Veteran Affairs

- Department of Defense and FDA
- UC College of Medicine and Department of Internal Medicine
- Industry and public-private partnerships and philanthropy

### **Mentoring:**

Faculty provide mentoring to eight trainees and two post doctorate fellows. Realizing the importance of quality improvement research in the future of clinical medicine, the division continues to co-direct a program at the VA to develop and train a fellow in Quality and Safety.

### **Collaborations:**

We continue to grow our outcomes research program, basic science program, and clinical translational research through strategic collaborations with the VA Medical Center, Cincinnati Children's Medical Center, UC College of Engineering, Department of Surgery, Department of Family and Community Medicine, Department of Biomedical Informatics and the Department of Emergency Medicine. All of the above collaborations have resulted in scientific productivity: either scholarly work and grant funding.

# Rita Alloway, PharmD

RESEARCH PROFESSOR DIVISION OF NEPHROLOGY, KIDNEY CARE PROGRAM

Rita Allows, PharmD



University of Cincinnati

72

Annual Research Report 2020

ephrology, Kidney CARE Program Division Research Professor Rita Alloway, PharmD, says one overarching, patient-centered objective drives her pharmaceutical research now.

**N** "Our goal is for the first kidney transplant a patient receives to be the last in a long life," Alloway says.

To that end, Alloway has focused on developing novel immunosuppressant combinations in addition to optimizing the management of current immunosuppression. As a pharmacist, Alloway has the pharmacokinetic knowledge base to develop and implement sophisticated pharmacokinetic studies addressing complex issues of drug exposure. One particularly successful example lies in the use of tacrolimus, a medicine that lowers the body's natural immune system but has a complex pharmacokinetic profile. The drug is widely used to prevent rejection of transplanted organs but its success is associated with achieving optimal tacrolimus exposure for each patient.

After years of experience with branded tacrolimus, generic tacrolimus formulations were approved. "Virtually the entire transplant community was opposed to the use of generic tacrolimus, yet the transition to generics was inevitable due to market forces," says Alloway.

Alloway and her team successfully conducted a study of the branded tacrolimus, and two different generic formulations in kidney and liver transplant recipients. The researchers determined that generics were as safe and effective as their branded counterparts.

"These data provided the transplant community with an unbiased, objective evaluation of multiple generic products in transplant recipients," Alloway says.

Always interested in better long-term outcomes for patients, today Alloway's research is focused on replacing tacrolimus altogether. Immunosuppressants offer less overall toxicity and similar efficacy, and the current average kidney graft survival is approximately 10-15 years. While kidney transplant offers a survival benefit to remaining on dialysis, there is tremendous room for improvements in long-term graft survival. Novel costimulatory blockers are commercially available to replace tacrolimus, but risks and benefits exist. While there is potential to improve adherence and reduce several risk factors negatively impacting long-term survival, a new paradigm must be adopted. A transition away from tacrolimus after almost 30 years will require a new mindset for providers and patients.

"This immunosuppression transition would be easy if it came without risks," Alloway explains, "but the increased risk of rejection and viral infections require the provider to change focus to managing these short-term risks for a potential improvement in long-term outcomes."

Alloway is confident that UC's clinical transplant team will continue addressing the unmet clinical needs of transplant patients today.

"We have an extraordinary clinical transplant team of nephrologists, hepatologists, surgeons, APPs, nurses, pharmacists, dieticians, medical assistants, social workers, leadership — without whom we couldn't succeed in our clinical research endeavors," she says.

Alloway gives ample credit to the research coordinators, who serve as patient advocates and whose "unsung, behind-the-scenes efforts" contribute to the overall success of UC's transplant program — especially during a global pandemic. "Their efforts are no less than heroic," says Alloway.

**ALLOWAY HAS THE** PHARMACOKINETIC **KNOWLEDGE BASE TO DEVELOP** AND IMPLEMENT SOPHISTICATED PHARMACOKINETIC **STUDIES ADDRESSING COMPLEX ISSUES OF** DRUG EXPOSURE, A **TRANSITION AWAY** FROM TACROLIMUS **AFTER ALMOST 30 YEARS** WILL REQUIRE A NEW MINDSET FOR PROVIDERS AND PATIENTS.

### **DISCOVER & INNOVATE**

#### Nephrology, Kidney CARE Program

### PUBLICATIONS July 1, 2019 thru June 30, 2020

- Castro-Rojas CM, Godarova A, Hummel SA, Shields AR, Tremblay S, Alloway RR, Jordan MB, Woodle ES, Hildeman DA. mTOR inhibitor therapy diminishes circulating CD8+CD28- effector memory T cells and improves allograft inflammation in belatacept-refractory renal allograft rejection. Transplantation. 2019;Aug 12. Epub ahead of print. doi: 10.1097/ TP.00000000002917
- 2 Tremblay S, Driscoll JJ, Girnita A, Brailey P, Shields AR, Hildeman DA, Alloway RR, Woodle ES. A Prospective, Iterative, Adaptive Trial of Carfilzomib-Based Desensitization. Am J Transplant. ePub ahead of print. doi:10.1111/ajt.15613.
- 3 Woodle ES, Tremblay S, Brailey P, Girnita A, Alloway RR, Aronow B, Dasgupta N, Ebstein F, Kloetzel PM, Lee MJ, Kim KB, Singh H, Driscoll JJ. Proteasomal adaptations of underlying carfilzomib resistance in human bone marrow plasma cells. Am J Transplant. ePub ahead of print. doi:10.1111/ajt.15634.
- 4 Woodle ES, Kaufman D, Shields AR, Leone J, Matas A, Wiseman A, West-Thielke P, Sa T, King EC, Alloway RR, for the BEST Study Group. Belatacept-Based Immunosuppression with Simultaneous Calcineurin Inhibitor Avoidance and Early Corticosteroid Withdrawal: A Prospective, Randomized Multicenter Trial. Am J Transplant. ePub ahead of print. doi: 10.1111/ ajt.15688.
- 5 Lichvar AB, Tremblay S, Abu Jawdeh BG, Annand M, Brailey P, Girnita A, Alloway RR, Woodle ES. Reducing Donor Specific Antibody Levels During Acute Rejection Diminishes Long Term Renal Allograft Loss: Comparison of Early and Late Rejection. Transplantation. ePub ahead of print. doi: 10.1097/ TP.00000000003145.
- 6 Woodle ES, Tremblay S, Rossy A, Castro-Rojas C, Alloway RR, Roskin K, Allman D, Hildeman D. Plasma Cell Targeting to Prevent Antibody Mediated Rejection. Am J Transplant. ePub ahead of print. doi: 10.1111/ ajt.15889
- 7 Eckman MH, Woodle ES, Thakar CV, Alloway RR, Sherman KE.Cost-effectiveness of Using Kidneys From HCV-Viremic Donors for Transplantation Into HCV-Uninfected Recipients. Am J Kidney Dis. 2020 Jun;75(6):857-867. doi: 10.1053/j.ajkd.2019.11.005. Epub 2020 Feb 17.PMID: 32081494
- 8 Castro-Rojas CM, Alloway RR, Woodle ES, Hildeman DA. High Dimensional Renal Profiling: Towards a Better Understanding of Renal Transplant Immune Suppression. Curr Transplant Rep. 2019 Mar;6(1):60-68. doi: 10.1007/s40472-019-0225-1. Epub 2019 Jan 14. PMID:
- 9 Lee TC, Kaiser TE, Alloway R, Woodle ES, Edwards MJ, Shah SA. Telemedicine Based Remote Home Monitoring After Liver Transplantation: Results of a Randomized Prospective Trial. Ann Surg. 2019 Sep;270(3):564-572. doi: 10.1097/SLA.00000000003425. PMID: 31356267

- 10 Woodle ES, Tremblay S, Rossy A, Castro-Rojas C, Alloway RR, Roskin K, Allman D, Hildeman D. Plasma Cell Targeting to Prevent Antibody Mediated Rejection. Am J Transplant. ePub ahead of print. doi: 10.1111/ ajt.15889 Special edition AJT Antibody Mediated Rejection. Invited
- 11 Shah S, Chan M, Lee T. Perspectives in individualizing solutions for dialysis access. Advances in Chronic Kidney Disease. Adv Chronic Kidney Dis. 2020 May;27(3):183-190.
- 12 Shah S, Christianson A, Thakar CV, Kramer S, Leonard A. Contraceptive use among women with end-stage kidney disease on dialysis in the United States. Kidney Medicine (in press)
- 13 Taber-Hight E, Shah S. Acute kidney injury and pregnancy. Advances in Chronic Kidney Disease. 2020 (in press).
- 14 Bajpai D, Shah S. Pregnancy and COVID-19. Adv Chronic Kidney Dis. 2020 (in press)
- **15** Shah S. Women's Health in Kidney Disease. Advances in Chronic Kidney Disease. Editorial. 2020 (in press).
- **16 Shah S**, Sparks M. COVID-19 and Kidney Disease. Advances in Chronic Kidney Disease. Editorial. 2020 (in press).
- 17 Shah S, Christianson A, Bumb S, Verma P. Contraceptive use among women with kidney transplant in the United States. Journal of Nephrology. 2020 (accepted).
- 18 Shah S, Leonard A, Harrison K, Meganathan K, Christianson A, Thakar CV. Outcomes and racial and sex differences associated with end-stage kidney disease due to acute kidney injury in the United States. 2020 June 17. Clin J Am Soc Nephrol. 2020 Jul 1;15(7):995-1006.
- 19 Shah S, Meganathan K, Harrison K, Christianson A, Leonard A, Thakar CV. Pregnancy-related acute kidney injury in the United States: clinical outcomes and health care utilization. American Journal of Nephrology. 2020 February 11: 1-11.
- 20 Shah S. Hypertensive disorders in pregnancy. Obstetric and Gynecologic Nephrology: Women's Health Issues in Patients with Kidney Disease. Editors: Mala Sachdeva, Ilene Miller. October 2019.
- 21 Shah S, Christianson A, Meganathan K, Leonard A, Schauer D, Thakar CV. Racial differences and factors associated with pregnancy in end-stage kidney disease patients on dialysis in the United States. J Am Soc Nephrol. 2019 Sept 25.
- 22 Shah S, Christianson A, Verma P, Meganathan K, Leonard A, Schauer D, Thakar CV. Racial differences and factors associated with pregnancy in kidney transplant recipients Plos One. 2019. Aug 9; 14(8).
- 23 Shah S, Gupta A. Hypertensive disorders of pregnancy. Cardiology Clinic. 2019 Aug; 37(3): 345-354.
- 24 Shah S. Thakar CV. Diabetes/Kidney/Heart Disease (Editorial). Cardiology Clinic. 2019 Aug; 37(3).

- 25 Agresta L., Lehn M., Lampe K., Cantrell R., Hennies C., Szabo S., Wise-Draper T.M., Conforti L., Hoebe K., Janssen E.M. CD244 Represents a New Therapeutic Target in Cancer. J Immunother Cancer. 2020 Mar;8(1). pii: e000245. doi: 10.1136/jitc-2019-000245
- 26 Chimote A. A., Gawali V. S., Newton H.S., Wise-Draper T.M., Conforti L., A compartmentalized reduction in membrane-proximal calmodulin reduces the immune surveillance capabilities of CD8+
- 27 Dirar Q., Russell T., Liu, L., Ahn, S., Dotti, G., Aravamudhan, S., Conforti, L., Yun YH. Activation and degranulation of CAR-T cells using engineered antigen-presenting cell surfaces. PLoS ONE 2020: 15(9): e0238819. https://doi.org/10.1371/journal.pone.0238819.
- 28 Khodoun M., Chimote A.A., Ilyas F. Z., Duncan H. J., Moncrieffe H., Kant S.K. and Conforti L., Targeted knock-down of Kv1.3 channels in T lymphocytes corrects the disease manifestations associated with Systemic Lupus Erythematosus (Science Advances, in press).
- 29 Newton H. S.\*, Gawali V.\*, Chimote A.A.\*, Lehn M., Palackdharry S., Jandarov R., Hildeman D., Janssen E.M, Wise-Draper T.M., and Conforti L. PD1 blockade enhances K+ channel activity, Ca2+ signaling, and migratory ability in cytotoxic T lymphocytes of head and neck cancer patients. J Immunother Cancer. 2020 Oct;8(2):e000844. doi: 10.1136/jitc-2020-000844. PMID: 33060146; PMCID: PMC7566435. \* first authors
- 30 Dao A, Cuffy M, Kaiser TE, Loethen A, Cafardi J, Luckett K, Rike AH, Cardi M, Alloway RR, Govil A, Diwan T, Sherman KE, Shah SA, Woodle ES. Use of HCV Ab+/ NAT- donors in HCV naïve renal transplant recipients to expand the kidney donor pool. Clin Transplant. 2019 Jul;33(7):e13598. doi: 10.1111/ctr.13598. Epub 2019 Jun 5. PMID: 31104346.
- 31 Kassam AF, Mirza A, Kim Y, Hanseman D, Woodle ES, Quillin RC 3rd, Johnson BL, Govil A, Cardi M, Schauer DP, Smith EP, Diwan TS. Long-term outcomes in patients with obesity and renal disease after sleeve gastrectomy. Am J Transplant. 2020 Feb;20(2):422-429. doi: 10.1111/ajt.15650. Epub 2019 Nov 16. PMID: 31605562.
- 32 Diwan TS, Cuffy MC, Linares-Cervantes I, Govil A. Impact of obesity on dialysis and transplant and its management. Semin Dial. 2020 May;33(3):279-285. doi: 10.1111/sdi.12876. Epub 2020 Apr 10. PMID: 32277512.
- 33 Cheung AY, Sarnicola E, Eslani M, Wright E, Goebel J, Hooper DK, Govil A, Kurji KH, Holland EJ. Clinical Outcomes of Allograft Ocular Surface Stem Cell Transplantation in Pediatric Patients. Cornea. 2020 Jun 4. doi: 10.1097/ICO.00000000002379. Epub ahead of print. PMID: 32501833.

- 34 Perwez Alam, Sihame Amlal, Charuhas V Thakar, Hassane Amlal. Acetazolamide causes renal HCO3- wasting but inhibits ammoniagenesis and prevents the correction of metabolic acidosis by the kidney. Am J Physiol Renal Physiol. 319(3):F366-F379, 2020
- **35 Gudsoorkar P, Anand M, Abu Jawdeh BG**. Apolipoprotein L1 Genotyping in African American Donors: Utility and Cost Effectiveness. Am J. Nephrol. 2020 Jan 15:1-3.
- **36 Abu Jawdeh BG**. COVID-19 in Kidney Transplantation: Outcomes, Immunosuppression Management, and Operational Challenges. Adv Chronic Kidney Dis. 2020 Jul 17.
- 37 Menon MC, Patel N, He JC. Novel protein synthesisbreakdown complexes: TASCCed with fibrosis after G2-M arrest. Kidney Int. 2019 Nov;96(5):1056-1058. doi: 10.1016/j.kint.2019.04.026. PMID: 31648692.
- 38 Patel N, Nadkarni GN. Apolipoprotein L1, Cardiovascular Disease and Hypertension: More Questions than Answers. Cardiol Clin. 2019 Aug;37(3):327-334. doi: 10.1016/j.ccl.2019.04.009. Epub 2019 May 14. PMID: 31279426.
- 39 Hilburg, Rachel, Patel N, et al. "Medical Education During the Coronavirus Disease-2019 Pandemic: Learning From a Distance." Advances in Chronic Kidney Disease, 23 Jun. 2020, doi:10.1053/j. ackd.2020.05.017
- 40 El Shamy O, Patel N, Abdelbaset MH, Chenet L, Tokita J, Lookstein R, Lee DS, Cohen NA, Sharma S, Uribarri J. Acute Start Peritoneal Dialysis during the CO-VID-19 Pandemic: Outcomes and Experiences. J Am Soc Nephrol. 2020 Aug;31(8):1680-1682. doi: 10.1681/ ASN.2020050599. Epub 2020 Jun 16. PMID: 32546597; PMCID: PMC7460897.



# Division of Pulmonary, Critical Care and Sleep Medicine

### ENDOWED CHAIR: Taylor Professor of Medicine

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.



Frank McCormack, MD DIVISION DIRECTOR

### **Research Focus Areas/Types:**

In our basic research, we focus on studies that have a human clinic trial on the horizon, at least conceptually. Current laboratory projects are focused on:

- Innate and adaptive
  - immunology of
    - Smoking
    - Trauma
- The role of collectins and lung epithelial cells in innate immune defense against inhaled bacteria, mycobacteria, fungi and viruses, especially influenza
- Preclinical studies in mouse models of:
  - Pulmonary Langerhans cell histiocytosis
  - Lymphangioleiomyomatosis
  - Pulmonary alveolar microlithiasis
  - Pulmonary alveolar proteinosis
  - Thermal trauma
  - Influenza
- Neutrophil NETs in cystic fibrosis
- Alveologenesis

Current clinical research focuses on:

- Investigator-initiated, multicenter, NIH supported, national and international randomized trials for lymphangioleiomyomatosis
- Investigator initiated phase II NIH combination therapy trial for lymphangioleiomyomatosis
- Pharmaceutical trials in pulmonary arterial hypertension, COPD, asthma, interstitial lung disease and critical care medicine
- Therapeutic Development Network and pharmaceutical trials in cystic fibrosis
- Phase 1 NIH trials of phosphate restriction and therapeutic EGTA lavage for pulmonary alveolar microlithiasis
- Safety and yield of cutting edge interventional and advanced diagnostic pulmonary procedures
- Investigator initiated study of the molecular pathogenesis of portopulmonary hypertension
- NIH funded federal network and pharmaceutical trials in Critical Care Medicine
- Investigator initiated home spirometry trials

### **Resources:**

Bronchoscopy Core, Translational Pulmonary Science Center Tissue Repository, four Pulmonary Function laboratories, three Sleep Laboratories.

### Investigators/Trainees:

We currently have 13 faculty investigators of about 30 total faculty members, 14 pulmonary fellows that conduct mentored research with faculty members, including one KO8 fellow, one IMStar fellow and one Rare Lung Disease Fellow.

### Funding Types for Investigator Initiated Research:

- National Institutes of Health and other federal agencies—VA, NCATS, FDA, DOD
- Heart and lung societies, ALA, AHA, ATS
- Patient Advocacy Foundations
- Pharmaceutical companies— Pfizer, United Therapeutics

# **Mentoring:**

We committed to the training of the next generation of basic scientists and clinicianinvestigators. We have a special interest in training physicianscientists who are comfortable both at the bench and in the clinic, and fully equipped with the skills, resources and personnel required to bring their research discoveries to trials.

### **Collaborations:**

We are part of the Translational Pulmonary Science Center, a collaborative project between pulmonary groups at UC and Cincinnati Children's Hospital Medical Center, and the Rare Lung Diseases Consortium.

# Kristin Hudock, MD

ASSISTANT PROFESSOR DIVISION OF PULMONARY, CRITICAL CARE AND SLEEP MEDICINE  or Kristin Hudock, University of Cincinnati assistant professor of medicine and pediatrics, the 'why' behind her research is quite simple.

"I love science and understanding why and how things happen," says Hudock, an ICU doctor with joint appointments in UC's Division of Pulmonary, Critical Care and Sleep Medicine as well as the Cincinnati Children's Hospital Medical Center (CCHMC) Division of Pulmonary Biology. "The potential to uncover mechanisms of disease that could be targeted to improve another human's health drives and fulfills me."

Hudock's current research focuses on understanding the balance between host defense and lung injury in Cystic Fibrosis.

"We have demonstrated that neutrophils expel neutrophil extracellular traps (NETs) that drive epithelial injury and inflammation via very specific pathways," Hudock explains. "We believe NETs are a therapeutic target to limit progression of lung disease in cystic fibrosis and prolong lives."

More immediately, Hudock's role in the ICU has also brought her in close contact with COVID-19 patients in the past year, and she has been part of the program that collects the blood from coronavirus patients for one of the first COVID-19 biorepository systems in the nation — being built by doctors and scientists in Cincinnati. The biorepository is basically a library of COVID-19 blood samples. UC researchers, along with the Cincinnati Veterans Administration Hospital and Children's Hospital, are working together to create the repository.

The goal of the blood library is to ultimately make research against the virus more efficient. Researchers hope to collect specimens from 500 patients in the end. The specimens will be used by Hudock and other researchers to learn more about COVID-19 and possible treatments and preventions for not only this disease but possibly diseases of the future.

"Really, the goal is to identify a biomarker, or something that's going to tell us if this person is likely to get sick and this person isn't," Hudock says. "I think the number of questions we can answer with this, and the number of people we can help, is phenomenal."

For Hudock, both the cystic fibrosis and COVID work represent just the latest endeavors in a career spent striving to make lives better for patients through active research. Hudock attended the Georgetown University School of Medicine and completed her fellowship at the University of Pennsylvania in Philadelphia before moving to Cincinnati. At UC, she has collaborated with investigators in various disciplines, including: Bruce Trapnell, MD, MS; JP Clancy, MD; Frank McCormack, MD; Jeffrey Whitsett; MD and Scott Worthen, MD. Hudock also welcomes students in MD or PhD programs into her labs, passing on the support she has received from the department and mentors.

"The trial and error of research is tough, and there is a lot of failure, but that is why having an administration and department that invest in your potential is so crucial," Hudock says. "It is a bit like gambling, but with lots of preparation. I hope to see even more investment from the department and college in junior investigators like myself." • BOTH THE CYSTIC FIBROSIS AND COVID WORK REPRESENT JUST THE LATEST ENDEAVORS IN A CAREER SPENT STRIVING TO MAKE LIVES BETTER FOR PATIENTS THROUGH ACTIVE RESEARCH.

### **DISCOVER & INNOVATE**

#### Pulmonary, Critical Care & Sleep Medicine

#### PUBLICATIONS July 1, 2019 thru June 30, 2020

- Shaw BM, Shaw SD, McCormack FX. Pulmonary Alveolar Microlithiasis. Semin Respir Crit Care Med. 2020 Apr;41(2):280-287. doi: 10.1055/s-0040-1702211. Epub 2020 Apr 12. PMID: 32279298.
- 2 Walkup LL, Roach DJ, Hall CS, Gupta N, Thomen RP, Cleveland Zl, McCormack FX, Woods JC. Cyst Ventilation Heterogeneity and Alveolar Airspace Dilation as Early Disease Markers in Lymphangioleiomyomatosis. Ann Am Thorac Soc. 2019 Aug;16(8):1008-1016. doi: 10.1513/AnnalsATS.201812-880OC. PMID: 31038987.
- 3 Nalian A, Umstead TM, Yang CH, Silveyra P, Thomas NJ, Floros J, McCormack FX, Chroneos ZC. Structural and Functional Determinants of Rodent and Human Surfactant Protein A: A Synthesis of Binding and Computational Data. Front Immunol. 2019 Nov 7;10:2613. doi: 10.3389/fimmu.2019.02613. PMID: 31781112; PMCID: PMC6856657.
- Jönsson ÅLM, Bendstrup E, Mogensen S, Kopras EJ, McCormack FX, Campo I, Mariani F, Escribano-Montaner A, Holm AM, Martinez-Colls MDM, Pintos-Morell G, Taillé C, Crestani B, Hilberg O, Hvarregaard Christensen J, Simonsen U. Eight novel variants in the SL-C34A2 gene in pulmonary alveolar microlithiasis. Eur Respir J. 2020 Feb 27;55(2):1900806. doi: 10.1183/13993003.00806-2019. PMID: 31831582.
- 5 Liu H, Osterburg AR, Flury J, Swank Z, McGraw DW, Gupta N, Wikenheiser-Brokamp KA, Kumar A, Tazi A, Inoue Y, Hirose M, McCormack FX, Borchers MT. MAPK mutations and cigarette smoke promote the pathogenesis of pulmonary Langerhans cell histiocytosis. JCI Insight. 2020 Feb 27;5(4):e132048. doi: 10.1172/jci.nisight.132048. PMID: 31961828; PMCID: PMC7101136.
- 6 Krymskaya VP, Courtwright AM, Fleck V, Dorgan D, Kotloff R, McCormack FX, Kreider M. A phase II clinical trial of the Safety Of Simvastatin (SOS) in patients with pulmonary lymphangioleiomyomatosis and with tuberous sclerosis complex. Respir Med. 2020 Mar;163:105898. doi: 10.1016/j.rmed.2020.105898. Epub 2020 Feb 8. PMID: 32125970.
- 7 Shaw B, Borchers M, Zander D, Gupta N. Pulmonary Langerhans Cell Histiocytosis. Semin Respir Crit Care Med. 2020 Apr;41(2):269-279. doi: 10.1055/s-0039-1700996. Epub 2020 Apr 12. PMID: 32279297.
- 8 Wellmerling JH, Chang SW, Kim E, Osman WH, Boyaka PN, Borchers MT, Cormet-Boyaka E. Reduced expression of the lon channel CFTR contributes to airspace enlargement as a consequence of aging and in response to cigarette smoke in mice. Respir Res. 2019 Sep 2;20(1):200. doi: 10.1186/s12931-019-1170-3. PMID: 31477092; PMCID: PMC6720379.
- 9 Ochayon DE, Ali A, Alarcon PC, Krishnamurthy D, Kottyan LC, Borchers MT, Waggoner SN. IL-33 promotes type 1 cytokine expression via p38 MAPK in human NK cells. J Leukoc Biol. 2020 Apr;107(4):663-671. doi: 10.1002/JLB.3A0120-379RR. Epub 2020 Feb 4. PMID: 32017227; PMCID: PMC7229703.

- 10 Suzuki T, McCarthy C, Carey BC, Borchers M, Beck D, Wikenheiser-Brokamp KA, Black D, Chalk C, Trapnell BC. Increased Pulmonary GM-CSF Causes Alveolar Macrophage Accumulation. Mechanistic Implications for Desquamative Interstitial Pneumonitis. Am J Respir Cell Mol Biol. 2020 Jan;62(1):87-94. doi: 10.1165/rcmb.2018-0294OC. PMID: 31310562; PMCID: PMC6938130.
- 11 Knoell DL, Smith D, Bao S, Sapkota M, Wyatt TA, Zweier JL, Flury J, Borchers MT, Knutson M. Imbalance in zinc homeostasis enhances lung Tissue Loss following cigarette smoke exposure. J Trace Elem Med Biol. 2020 Jul;60:126483. doi: 10.1016/j.jtemb.2020.126483. Epub 2020 Feb 27. PMID: 32155573.
- 12 Liu H, Osterburg AR, Flury J, Swank Z, McGraw DW, Gupta N, Wikenheiser-Brokamp KA, Kumar A, Tazi A, Inoue Y, Hirose M, McCormack FX, Borchers MT. MAPK mutations and cigarette smoke promote the pathogenesis of pulmonary Langerhans cell histiocytosis. JCI Insight. 2020 Feb 27;5(4):e132048. doi: 10.1172/ jci.insight.132048. PMID: 31961828; PMCID: PMC7101136.
- 13 Osterburg AR, Lach L, Panos RJ, Borchers MT. Unique natural killer cell subpopulations are associated with exacerbation risk in chronic obstructive pulmonary disease. Sci Rep. 2020 Jan 27;10(1):1238. doi: 10.1038/ s41598-020-58326-7. PMID: 31988425; PMCID: PMC6985179.
- 14 Choi W, Choe S, Lin J, Borchers MT, Kosmider B, Vassallo R, Limper AH, Lau GW. Exendin-4 restores airway mucus homeostasis through the GLP1R-PKA-PPARy-FOXA2-phosphatase signaling. Mucosal Immunol. 2020 Jul;13(4):637-651. doi: 10.1038/s41385-020-0262-1. Epub 2020 Feb 7. PMID: 32034274; PMCID: PMC7664156.
- 15 Kai-Feng Xu, Wenshuai Xu, Song Liu, Jane J. Yu, Xinlun Tian, Yanli Yang, Shao-Ting Wang, Weihong Zhang, Ruie Feng, Tengyue Zhang. Lymphangioleiomyomatosis. Semin Respir Crit Care Med. 2020 Apr;41(2):256-268. doi: 10.1055/s-0040-1702195. Epub 2020 Apr 12. PubMed PMID: 32279296.
- 16 Yiyang Lu, Xiaolei Liu, Erik Zhang, Elizabeth J. Kopras, Eric P. Smith, Aristotelis Astrinidis, Chenggang Li, Yuet-Kin Leung, Shuk-Mei Ho and Jane J. Yu. Estrogen activates pyruvate kinase M2 and increases the growth of TSC2-deficient cells. PLoS One. 2020 Feb 20;15(2):e0228894. PMCID: PMC7032738.
- 17 Minzhe Guo, Jane J. Yu, Anne Karina Perl, Kathryn Wikenheiser-Brokam, Matt Riccetti, Erik Y. Zhang, Parvathi Sudha, Mike Adam, Andrew Potter, Elizabeth J Kopras, Krinio Giannikou, S Steven Potter, Sue Sherman, Stephen R. Hammes, David J. Kwiatkowski, Jeffrey A. Whitsett, Francis X. McCormack, Yan Xu. Single cell transcriptomic analysis identifies a unique pulmonary lymphangioleiomyomatosis cell. Am J Respir Crit Care Med. 2020 Jun 30. PMID: 32603599.

- 18 Liu H, Osterburg AR, Flury J, Swank Z, McGraw DW, Gupta N, Wikenheiser-Brokamp KA, Kumar A, Tazi A, Inoue Y, Hirose M, McCormack FX, Borchers MT. MAPK mutations and cigarette smoke promote the pathogenesis of pulmonary Langerhans cell histiocytosis. JCI Insight. 2020 Feb 27;5(4):e132048. doi: 10.1172/ jci.insight.132048. PMID: 31961828; PMCID: PMC7101136.
- 19 Polverino F, Hysinger EB, Gupta N, Willmering M, Olin T, Abman SH, Woods JC. Lung MRI as a Potential Complementary Diagnostic Tool for Early COPD. Am J Med. 2020 Jun;133(6):757-760. doi: 10.1016/j.amjmed.2019.12.009. Epub 2020 Jan 16. PMID: 31954683.
- 20 Shaw B, Borchers M, Zander D, Gupta N. Pulmonary Langerhans Cell Histiocytosis. Semin Respir Crit Care Med. 2020 Apr;41(2):269-279. doi: 10.1055/s-0039-1700996. Epub 2020 Apr 12. PMID: 32279297.
- 21 Singla A, Kopras EJ, Gupta N. Spontaneous pneumothorax and air travel in Pulmonary Langerhans cell histiocytosis: A patient survey. Respir Investig. 2019 Nov;57(6):582-589. doi: 10.1016/j.resinv.2019.07.004. Epub 2019 Sep 26. PMID: 31563637; PMCID: PMC6832853.
- Wajda N, Zhu Z, Jandarov R, Dilling DF, Gupta N. Clinical outcomes and survival following lung transplantation in patients with pulmonary Langerhans cell histiocytosis. Respirology. 2020 Jun;25(6):644-650. doi: 10.1111/resp.13671. Epub 2019 Aug 12. PMID: 31407478.
- 23 Cherian SV, Girvin F, Naidich DP, Machnicki S, Brown KK, Ryu JH, Gupta N, Mehta V, Estrada-Y-Martin RM, Narasimhan M, Oks M, Raoof S. Lung Hyperlucency: A Clinical-Radiologic Algorithmic Approach to Diagnosis. Chest. 2020 Jan;157(1):119-141. doi: 10.1016/j. chest.2019.06.037. Epub 2019 Jul 26. PMID: 31356811.
- 24 Khawar MU, Yazdani D, Zhu Z, Jandarov R, Dilling DF, Gupta N. Clinical outcomes and survival following lung transplantation in patients with lymphangioleiomyomatosis. J Heart Lung Transplant. 2019 Sep;38(9):949-955. doi: 10.1016/j.healun.2019.06.015. Epub 2019 Jun 21. PMID: 31303421.
- 25 Walkup LL, Roach DJ, Hall CS, Gupta N, Thomen RP, Cleveland ZI, McCormack FX, Woods JC. Cyst Ventilation Heterogeneity and Alveolar Airspace Dilation as Early Disease Markers in Lymphangioleiomyomatosis. Ann Am Thorac Soc. 2019 Aug;16(8):1008-1016. doi: 10.1513/AnnalsATS.201812-880OC. PMID: 31038987.
- 26 Obaidat B, Yazdani D, Wikenheiser-Brokamp KA, Gupta N. Diffuse Cystic Lung Diseases. Respir Care. 2020 Jan;65(1):111-126. doi: 10.4187/respcare.07117. Epub 2019 Oct 15. PMID: 31615921.
- 27 Smith BJ, Roy GS, Cleveland A, Mattson C, Okamura K, Charlebois CM, Hamlington KL, Novotny MV, Knudsen L, Ochs M, Hite RD, Bates JHT. Three Alveolar Phenotypes Govern Lung Function in Murine Ventilator-Induced Lung Injury. Front Physiol. 2020 Jun 30;11:660. doi: 10.3389/fphys.2020.00660. PMID: 32695013; PMCID: PMC7338482.

- 28 National Heart, Lung, and Blood Institute PETAL Clinical Trials Network, Ginde AA, Brower RG, Caterino JM, Finck L, Banner-Goodspeed VM, Grissom CK, Hayden D, Hough CL, Hyzy RC, Khan A, Levitt JE, Park PK, Ringwood N, Rivers EP, Self WH, Shapiro NI, Thompson BT, Yealy DM, Talmor D. Early High-Dose Vitamin D3 for Critically III, Vitamin D-Deficient Patients. N Engl J Med. 2019 Dec 26;381(26):2529-2540. doi: 10.1056/ NEJMoa1911124. Epub 2019 Dec 11. PMID: 31826336; PMCID: PMC7306117.
- 29 Fowler AA 3rd, Truwit JD, Hite RD, Morris PE, DeWilde C, Priday A, Fisher B, Thacker LR 2nd, Natarajan R, Brophy DF, Sculthorpe R, Nanchal R, Syed A, Sturgill J, Martin GS, Sevransky J, Kashiouris M, Hamman S, Egan KF, Hastings A, Spencer W, Tench S, Mehkri O, Bindas J, Duggal A, Graf J, Zellner S, Yanny L, McPolin C, Hollrith T, Kramer D, Ojielo C, Damm T, Cassity E, Wieliczko A, Halquist M. Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients With Sepsis and Severe Acute Respiratory Failure: The CITRIS-ALI Randomized Clinical Trial. JAMA. 2019 Oct 1;322(13):1261-1270. doi: 10.1001/jama.2019.11825. Erratum in: JAMA. 2020 Jan 28;323(4):379. PMID: 31573637; PMCID: PMC6777268.
- 30 Gollomp K, Sarkar A, Harikumar S, Seeholzer SH, Arepally GM, Hudock K, Rauova L, Kowalska MA, Poncz M. Fc-modified HIT-like monoclonal antibody as a novel treatment for sepsis. Blood. 2020 Mar 5;135(10):743-754. doi: 10.1182/blood.2019002329. PMID: 31722003; PMCID: PMC7059515.
- 31 Hudock KM, Collins MS, Imbrogno M, Snowball J, Kramer EL, Brewington JJ, Gollomp K, McCarthy C, Ostmann AJ, Kopras EJ, Davidson CR, Srdiharan A, Arumugam P, Sengupta S, Xu Y, Worthen GS, Trapnell BC, Clancy JP. Neutrophil extracellular traps activate IL-8 and IL-1 expression in human bronchial epithelia. Am J Physiol Lung Cell Mol Physiol. 2020 Jul 1;319(1):L137-L147. doi: 10.1152/ajplung.00144.2019. Epub 2020 Mar 11. PMID: 32159969; PMCID: PMC7468846.
- 32 Kramer EL, Madala SK, Hudock KM, Davidson C, Clancy JP. Subacute TGFβ Exposure Drives Airway Hyperresponsiveness in Cystic Fibrosis Mice through the PI3K Pathway. Am J Respir Cell Mol Biol. 2020 May;62(5):657-667. doi: 10.1165/rcmb.2019-0158OC. PMID: 31922900; PMCID: PMC7193791.
- 33 Gentene AJ, Guido MR, Woolf B, Dalhover A, Boesken TA, Mueller EW, Zafar MA. Multidisciplinary Team Utilizing Pharmacists in Multimodal, Bundled Care Reduce Chronic Obstructive Pulmonary Disease Hospital Readmission Rates. J Pharm Pract. 2019 Nov 26: 897190019889440. doi: 10.1177/0897190019889440. Epub ahead of print. PMID: 31769330.
- 34 Zafar MA, Loftus TM, Palmer JP, Phillips M, Ko J, Ward SR, Foertsch M, Dalhover A, Doers ME, Mueller EW, Alessandrini EA, Panos RJ. COPD Care Bundle in Emergency Department Observation Unit Reduces Emergency Department Revisits. Respir Care. 2020 Jan;65(1):1-10. doi: 10.4187/respcare.07088. PMID: 31882412.

### **DISCOVER & INNOVATE**

#### Pulmonary, Critical Care & Sleep Medicine

**PUBLICATIONS** CONTINUED

- 35 Jose A, Eckman MH, Elwing JM. Anticoagulation in pulmonary arterial hypertension: a decision analysis. Pulm Circ. 2019 Dec 23;9(4):2045894019895451. doi: 10.1177/2045894019895451. PMID: 31903185; PMCID: PMC6928543.
- 36 Jose A, Kher A, O'Donnell RE, Elwing JM. Cardiac magnetic resonance imaging as a prognostic biomarker in treatment-naïve pulmonary hypertension. Eur J Radiol. 2020 Feb;123:108784. doi: 10.1016/j. ejrad.2019.108784. Epub 2019 Dec 10. PMID: 31862635.
- 37 DesJardin JT, Kolaitis NA, Kime N, Kronmal RA, Benza RL, Elwing JM, Lammi MR, McConnell JW, Presberg KW, Sager JS, Shlobin OA, De Marco T; PHAR Investigators. Age-related differences in hemodynamics and functional status in pulmonary arterial hypertension: Baseline results from the Pulmonary Hypertension Association Registry. J Heart Lung Transplant. 2020 Sep;39(9):945-953. doi: 10.1016/j.healun.2020.05.005. Epub 2020 May 16. PMID: 32507341.
- 38 Jose A, Kher A, O'Donnell RE, Elwing JM. Cardiac magnetic resonance imaging as a prognostic biomarker in treatment-naïve pulmonary hypertension. Eur J Radiol. 2020 Feb;123:108784. doi: 10.1016/j. ejrad.2019.108784. Epub 2019 Dec 10. PMID: 31862635.
- 39 Jose A, Eckman MH, Elwing JM. Anticoagulation in pulmonary arterial hypertension: a decision analysis. Pulm Circ. 2019 Dec 23;9(4):2045894019895451. doi: 10.1177/2045894019895451. PMID: 31903185; PMCID: PMC6928543.
- 40 Grossoehme DH, Cole AG, Lewis K, Stamper SM, Teeters A, Joseph PM. Adults with cystic fibrosis: spiritual coping with lifelong disease. J Health Care Chaplain. 2020 Apr-Jun;26(2):45-57. doi: 10.1080/08854726.2020.1713647. Epub 2020 Mar 14. PMID: 32172686.
- 41 Shepherd RW, Radchenko C. Bronchoscopic ablation techniques in the management of lung cancer. Ann Transl Med. 2019 Aug;7(15):362. doi: 10.21037/ atm.2019.04.47. PMID: 31516908; PMCID: PMC6712260.
- 42 Radchenko CC, Cho PK, Kang L, Saettele TM. Performance of endobronchial-ultrasound guided miniforceps biopsy of targeted mediastinal and hilar lesions. Respir Med. 2019 Oct-Nov;158:92-96. doi: 10.1016/j.rmed.2019.10.001. Epub 2019 Oct 7. PMID: 31627081.
- 43 Radchenko C, Kang L. Response to respiratory medicine. Respir Med. 2020 Jun;167:105965. doi: 10.1016/j. rmed.2020.105965. Epub 2020 Apr 7. PMID: 32421547.
- 44 Smith MS, Bonomo J, Knight WA 4th, Prestigiacomo CJ, Richards CT, Ramser E, Adeoye O, Bertsch S, Shirani P, Vagal A, Fichtenbaum CJ, Housholder A, Khatri P, Kleindorfer DO, Broderick JP, Grossman AW. Endovascular Therapy for Patients With Acute Ischemic Stroke During the COVID-19 Pandemic: A Proposed Algorithm. Stroke. 2020 Jun;51(6):1902-1909. doi: 10.1161/STROKEAHA.120.029863. Epub 2020 Apr 30. PMID: 32352910; PMCID: PMC7199768.

- 45 Smith DF, Sarber KM, Spiceland CP, Ishman SL, Augelli DM, Romaker AM. Effects of Medical Therapy on Mild Obstructive Sleep Apnea in Adult Patients. J Clin Sleep Med. 2019 Jul 15;15(7):979-983. doi: 10.5664/ jcsm.7876. PMID: 31383235; PMCID: PMC6622504.
- 46 Singla A, Kopras EJ, Gupta N. Spontaneous pneumothorax and air travel in Pulmonary Langerhans cell histiocytosis: A patient survey. Respir Investig. 2019 Nov;57(6):582-589. doi: 10.1016/j.resinv.2019.07.004. Epub 2019 Sep 26. PMID: 31563637; PMCID: PMC6832853.

# Mentor and Support

# Caterina Bartolacci, PhD

POST-DOC FELLOW, DIVISION OF HEMATOLOGY ONCOLOGY

84

aterina Bartolacci didn't dream of becoming a researcher while growing up in Italy. Being fond of forensic television series where information from a DNA sample could solve any case, she wanted to become a forensic biologist, and earned a bachelor's degree in biology. Then her PhD work led her to the lab of Augusto Amici, PhD, and Cristina Marchini, PhD, at Italy's University of Camerino, where she focused on breast cancer biology and immunology.

"I realized I finally found what I really liked," Bartolacci says. "A lucky serendipity. Research found me."

Her love for research led Bartolacci to a life-changing decision: In 2016, she and her peer Cristina Andreani, PhD (they are still coworkers), left the tiny University of Camerino for the University of Texas Southwestern in Dallas.

There, in the lab of Pier Paolo Scaglioni, MD, Bartolacci started her postdoc fellowship. The University of Texas Southwestern gave Bartolacci the opportunity to collaborate with world-renowned scientists in lung cancer and lipidomics, the large-scale study of pathways and networks of cellular lipids in biological systems, a promising but still poorly understood area of cancer biology. The huge structural diversity of these molecules continues to pose a challenge for lipid analysis. Despite the obstacles, Bartolacci succeeded at establishing a novel high-performance lipidomics platform.

After two years in Dallas, Bartolacci moved to the University of Cincinnati's Division of Hematology Oncology. She is currently working with several external partners and the lab of Ken Greis, PhD, at UC, establishing the lipidomics platform at the university.

"I am fortunate to be able to count on the mentorship and expertise of Dr. Scaglioni, a world class expert in the field of lung cancer, and on the support of my coworkers," Bartolacci says. "Moreover, during my post-doc fellowship, I collaborated with John Minna, MD, and Jeff McDonald, PhD, experts in lung cancer and lipidomics, respectively. Their supervision helped me acquire a wide range of cancer biology, lung cancer and lipidomics knowledge while also gaining new skills in mouse lung cancer models and mass spectrometry technique. In this environment, I have undergone tremendous professional growth."

Bartolacci's current research objective is to significantly contribute to the understanding of the metabolic dependencies of mutant KRAS lung cancer, ultimately leading to innovative therapies. The KRAS gene belongs to a class of genes known as oncogenes. Mutated oncogenes can cause normal cells to become cancerous. The KRAS biomarker is mutated in approximately 30 percent of patients with non-small cell lung cancer. In particular, Bartolacci is focusing on how mutant KRAS regulates fatty acids metabolism.

"I intend to apply the skills and expertise I gained during my fellowship to test the hypothesis that the metabolism of fatty acids is indeed an 'Achilles' heel' of mutant KRAS lung cancer," says Bartolacci. "My long-term goal is to broaden the knowledge on lipid metabolism in lung cancer driven by oncogenes other than KRAS or harboring additional mutations on top of KRAS."

Outside of the lab, Bartolacci enjoys drawing, painting and dancing, mainly salsa and bachata. "I like the way dance brings such diverse people together," she says. "I always smile while dancing."

"I AM FORTUNATE TO BE ABLE TO COUNT ON THE MENTORSHIP AND EXPERTISE OF DR. SCAGLIONI, A WORLD CLASS EXPERT IN THE FIELD OF LUNG CANCER, AND ON THE SUPPORT OF MY COWORKERS.... IN THIS ENVIRONMENT, I HAVE UNDERGONE TREMENDOUS PROFESSIONAL GROWTH."

# Robert Burkes, MD, MSCR

IMSTAR FELLOW

linical Instructor Robert M. Burkes, MD, MSCR, is delighted to be able to continue his early career as a physician-scientist in the Division of Pulmonary, Critical Care and Sleep Medicine. He finds the division's long history of academic contributions, strong mentorship infrastructure, and emphasis on career development to be a great place for him to work towards his career goal of becoming an independently funded researcher.

Burkes' academic interests involve the clinical-translational study of the interface of measurable components of the immune system with clinicallyrelevant Chronic Obstructive Pulmonary Disease (COPD) outcomes. With COPD being the fourth leading cause of death in this country and worldwide, establishing markers which predict poor outcomes is an important and ongoing endeavor. Burkes studied the associations between levels of immune peptides and COPD outcomes prior to joining the faculty at the University of Cincinnati.

Currently, his focus is understanding the dynamic relationship between chronic cytomegalovirus infection, Natural Killer cell phenotypes, and loss of lung function and COPD exacerbations. Burkes works closely with his mentorship team of Frank McCormack, MD, Michael Borchers, PhD, and Ralph Panos, MD—world experts in their fields and distinctly suited to oversee the development of a young researcher like Burkes. While striving to become an independently funded researcher himself, Burkes is excited to have the opportunity to learn from his supportive team of mentors.

Prior to settling in Cincinnati with his wife, a community pediatrician, and his three daughters, Burkes was a medical student at The University of Toledo College of Medicine and Health Sciences where he studied mood disorders in cardiopulmonary rehabilitation participants with a highly regarded psycho-physiologist, Angele McGrady, PhD. He continued his medical training at the University of Louisville, where he solidified his interest in COPD and worked as a quality improvement leader mentored by Nancy Kubiak, MD, to perform a peer-to-peer quality improvement intervention in the care of COPD patients in his internal medicine residents' clinic. While at the University of Louisville, Burkes also worked on ICU outcomes studies with intensivist Rodrigo Cavallazzi, MD.

Immediately prior to coming to Cincinnati, Burkes was a fellow and then clinical instructor at the University of North Carolina-Chapel Hill, where he obtained a Master of Clinical Research and was awarded a NIH Ruth R. Kirschtein F32 award to study the innate immune peptide, cathelicidin, and COPD outcomes. During this time, he was mentored by thought experts in COPD, Brad Drummond, MD, MHS, and Jim Donohue, MD. The findings from this work were presented at international meetings and in manuscripts and is the basis for his continued work at the University of Cincinnati.

Burkes is enjoying working with his top-of-their-field mentors, supportive colleagues, and staff in the Department of Internal Medicine and feels supported in his quest to advance his career and achieve his career goals to better understand how mechanisms of COPD directly affect patient outcomes. •

# IMSTAR

**Internal Medicine Scholars Training for Academic** Research (IMSTAR) grew out of the department's desire to develop a highly competitive program that would train scholars in academic medicine. The program provides trainees opportunities for development of basic, translational, and clinical research programs. It also includes a focus on educational scholarship offering structured learning experiences in clinical teaching and leadership development. Burkes is a 2020 IMSTAR participant.

CURRENTLY, HIS FOCUS IS UNDERSTANDING THE DYNAMIC RELATIONSHIP BETWEEN CHRONIC CYTOMEGALOVIRUS INFECTION, NATURAL KILLER CELL PHENOTYPES, AND LOSS OF LUNG FUNCTION AND COPD EXACERBATIONS.

# Adeboye Adejare, PhD

GRADUATE ASSISTANT, BIOMEDICAL INFORMATICS PROGRAM GENERAL INTERNAL MEDICINE esearch graduate assistant Adeboye Adejare wants to create more equitable, better healthcare outcomes for everyone — all while empowering patients to make informed medical decisions. His lofty goals are becoming reality through his work at the University of Cincinnati with his mentor, Mark Eckman, MD, MS, and collaborating colleagues.

"There is no such thing as too much effort to combat disparities in healthcare, whether they are based on race, gender, sexual orientation or otherwise," Adejare says. "To reject that effort is to reject modern research."

Working with experts in UC's Department of Internal Medicine and the Center of Health Informatics, Adejare's team created a web based assessment tool, The Gambler, to help patients become more involved in making healthcare decisions. The Gambler acts as a shared decision-making tool for patients to express their ideas, preferences and values for different health conditions. During the process of expressing their values, patients can learn more about the different outcomes they might face from a disease by watching videos of people demographically matched to them. This method allows for patients to receive information about conditions from people like them, a method proven to make them more receptive to the information discussed.

"These expressions can allow for decision models to give researchers and patients guidance on how to approach the health care treatment," says Adejare. "Contributing software that gives patients more say in their healthcare truly means a lot since it may provide vulnerable patients more educated agency."

In clinical settings, Adejare's research can provide the mechanism for health equity. The Gambler demonstrates this purpose with their recent research with hemodialysis patients. The researchers acquired patients' preferences and values for different health states involved in End-Stage Kidney Disease (ESKD), including hemodialysis and kidney transplant. In particular, they wanted to know how patients, given appropriate information, would value a kidney successfully treated for a hepatitis C infection.

"African Americans wait longer for kidneys than other patients, and to remediate the issue, it requires more kidneys," Adejare explains. While a tragedy, deceased opioid users provide an option for kidney donation even with the kidneys infected with hepatis C. "Asking patients to consider a kidney transplant through shared decision making and The Gambler can alert clinicians to consider the option for patients, helping to ameliorate the kidney transplant disparities in African Americans."

Decreasing the disparity in kidney transplants is just one potential application of The Gambler; there are plans to use tool in multiple settings. For instance, Adejare's team is currently working to embed The Gambler in a shared decision-making pipeline to help prevent strokes in patients with atrial fibrillation (AF), providing doctors with treatment recommendations based on individual patient preferences. The researchers are also working with collaborators in Spain and Canada to implement The Gambler to improve outcomes in women who previously had venous thromboembolism and are either pregnant or want to become pregnant. For this work, the team created a mechanism to display The Gambler in multiple languages, opening even more potential applications for the tool.

"Developing innovations that can truly impact patients is what drove me to research," Adejare says. "Creating new techniques that can improve patients' health care experience, and overcome disparities, motivates my work every day." •

"THERE IS NO SUCH THING AS TOO MUCH EFFORT TO COMBAT DISPARITIES IN HEALTHCARE, WHETHER THEY ARE BASED ON RACE, GENDER, SEXUAL ORIENTATION OR OTHERWISE."

# **Office of the Chair**



# Robert Baughman, MD

Professor

Our group has a registry to follow patients with advanced sarcoidosis. We are part of the Foundation for Sarcoidosis Research Clinical Studies Network, an eight-center group focused on sarcoidosis. We have also initiated and contributed in clinical trials of diagnosis and treatment of sarcoidosis, including sarcoidosis associated pulmonary hypertension.

Collaborators: Elyse Lower, MD

Keywords: Sarcoidosis; Pulmonary hypertension; Pulmonary fibrosis

# PUBLICATIONS July 1, 2019 thru June 30, 2020

- Shlobin OA, Kouranos V, Barnett SD et al. Survival of patients with sarcoidosis associated pulmonary hypertension: the impact of baseline hemodynamics, pulmonary function, and six minute walk test in a multi-national registry cohort. Eur Respir J 2020;in press.
- 2 Rahaghi FF, **Baughman RP**, Saketkoo LA et al. Delphi consensus recommendations for a treatment algorithm in pulmonary sarcoidosis. Eur Resp Rev 2020;in press.
- 3 Rahaghi FF, Sweiss NJ, Saketkoo LA et al. Management of repository corticotrophin injection therapy for pulmonary sarcoidosis: a Delphi study. Eur Respir Rev 2020; 29(155):29-155-292019.
- 4 Rahaghi FF, **Baughman RP**, Saketkoo LA et al. Delphi consensus recommendations for a treatment algorithm in pulmonary sarcoidosis. Eur Respir Rev 2020; 29(155):29-155-292019.
- 5 **Baughman RP**, Scholand MB, Rahaghi FF. Clinical phenotyping: role in treatment decisions in sarcoidosis. Eur Respir Rev 2020; 29(155):29-155-292019.
- 6 Crouser ED, Maier LA, Wilson KC et al. Diagnosis and Detection of Sarcoidosis. An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med 2020; 201(8):e26-e51.
- 7 Harper LJ, Gerke AK, Wang XF et al. Income and Other Contributors to Poor Outcomes in U.S. Patients with Sarcoidosis. Am J Respir Crit Care Med 2020; 201(8):955-964.
- 8 Sellares J, Francesqui J, Llabres M et al. Current treatment of sarcoidosis. Curr Opin Pulm Med 2020; 26(5):591-597.
- 9 Syed H, Ascoli C, Linssen CFM et al. Infection prevention in sarcoidosis: proposal for vaccination and prophylactic therapy. Sarcoidosis Vasc Diffuse Lung Dis 2020; 37(2):87-98.
- 10 Lo KH, Donohue J, Judson MA et al. The St. George's Respiratory Questionnaire in Pulmonary Sarcoidosis. Lung 2020;10-00394.

- 11 Baughman RP, Judson MA, Beaumont JL et al. Evaluating the Minimal Clinically Important Difference of the King's Sarcoidosis Questionnaire (KSQ) in a Multi-center, Prospective Study. Ann Am Thorac Soc 2020;10-607OC.
- 12 Gupta R, **Baughman RP**. Advanced Pulmonary Sarcoidosis. Semin Respir Crit Care Med 2020; 41(5):700-715.
- 13 Baughman RP, Cremers JP, Harmon M et al. Methotrexate in sarcoidosis: hematologic and hepatic toxicity encountered in a large cohort over a six year period. Sarcoidosis Vasc Diffuse Lung Dis 2020; 37(3):c2020001.
- 14 Drake WP, Culver DA, **Baughman RP** et al. Phase II investigation of the efficacy of antimycobacterial therapy in chronic pulmonary sarcoidosis. Chest 2020; in press.
- 15 Baughman RP, Tillinger M, Qin Y et al. A composite score to assess treatment response in pulmonary sarcoidosis: the Sarcoidosis Treatment Score (STS). Sarcoidosis Vasc Diffuse Lung Dis 2019; 36:86-88.
- 16 Ramos-Casals M, Kostov B, Brito-Zeron P et al. How the Frequency and Phenotype of Sarcoidosis is Driven by Environmental Determinants. Lung 2019;10-00243.
- 17 Kampstra NA, Grutters JC, van Beek FT et al. First patient-centred set of outcomes for pulmonary sarcoidosis: a multicentre initiative. BMJ Open Respir Res 2019; 6(1):e000394.
- 18 Brito-Zeron P, Bari K, Baughman RP et al. Sarcoidosis Involving the Gastrointestinal Tract: Diagnostic and Therapeutic Management. Am J Gastroenterol 2019;10.
- 19 Voortman M, Drent M, Baughman RP. Management of neurosarcoidosis: a clinical challenge. Curr Opin Neurol 2019; 32(3):475-483.
- 20 **Baughman RP**, Wells AU. Advanced sarcoidosis. Curr Opin Pulm Med 2019; 25:497-504.

- 21 Lower EE, Sturdivant M, **Baughman RP**. Presence of onconeural antibodies in sarcoidosis patients with parasarcoidosis syndrome. Sarcoidosis Vasc Diffuse Lung Dis 2019; 36(4):254-260.
- 22 Singha A, Liao SY, Herman DD et al. Summary for Clinicians: Clinical Practice Guideline for the Diagnosis and Detection of Sarcoidosis. Ann Am Thorac Soc 2020; 17(12):1510-1515.
- 23 Obi ON, **Baughman RP**. Mixed Obstructive and Restrictive Ventilatory Defect in Sarcoidosis: A New Phenotype? Chest 2020; 158(5):1816-1817.
- 24 Kirkil G, Lower EE, **Baughman RP**. Chest CT scan: The best predictor of mortality in advanced pulmonary sarcoidosis? Respir Med 2020; 170:106059. doi: 10.1016/j.rmed.2020.106059. Epub@2020 Jun 10.:106059.
- 25 **Baughman RP**, Judson M. Sarcoidosis: Advances in Therapy. Semin Respir Crit Care Med 2020; 41(5): 605-606.

### **MENTOR & SUPPORT**

Research Governance Committee (RGC) Academic Research Services (ARS); Regulatory Staff Retrovirology Reference Laboratory (RRL)

# **Research Governance Committee**

- Senu Apewokin, PhD Khurram Bari, PhD Rebecca Cason, BA Laura Conforti, PhD Alexandru Costea, MD Angela Duke, BS Heather Duncan, PhD Carl Fichtenbaum, MD
- Jason Gardner, PhD Robert Hite, MD Marat Khodoun, PhD Suzanne Morris, PhD, Kelly Niederhausen, BA Helen Regina Shelton Sakthivel Sadayappan, PhD, MBA Silvi Shah, MD
- Eric Smith, MD Davendra Sohal, MD Kavitha Subramanian, PhD Yolanda Wess, MEd, RN, BSN Jason Winnick, PhD Jane Yu, PhD



# **Academic Research Services Staff**

Yolanda Wess, MEd, RN, BSN Eric Smith, MD Angela Duke, BS

# **Regulatory Staff**

Helen Gina Shelton Liz Arustamyan, BS Amber Crowther, MPH Romana Saeed, MS Jessica Truong, BS



# IM Division Lab Service-Retrovirology Reference Laboratory

Sierra Bennett Angelique Collins Gabrielle Cook Anissa Moussa Marlena Petrie

# Reports

# Active Awards June 30, 2020 Department of Internal Medicine

DIVISION	PI	AWARD	PROJECT PERIOD	А	AWARD	C	URRENT ERIOD †
ADMIN	Baughman	1015264 / 2019 Foundation for Sarcoidosis Research	06/01/19 - 05/31/21	\$	20,000	\$	10,000
ADMIN	Baughman	1013987 / Validation of a Sarcoidosis Diagnostic Score (SDS)	07/01/18 - 06/30/20	\$	80,000	\$	40,000
CARDIO	Ahmad	1014896 / SPIRRIT study	08/27/18 - 07/31/22	\$	17,908	\$	4,480
CARDIO	Costea	1014008 / Sub DECAAF II Efficacy of DE-MRI guided abla- tion	01/15/18 - 12/31/20	\$	1,999	\$	1,999
CARDIO	Crocker	1015928 / Autonomic remodeling and optogenetic targeted modulation therapy for arrhythmic sudden cardiac death	02/01/20 - 01/31/23	\$	111,023	\$	38,201
CARDIO	DeMazumder	1013213 / Autonomic Remodeling and Modulation Therapy in Heart Failure and Sudden Death	02/01/18 - 01/31/21	\$	747,000	\$	248,997
CARDIO	DeMazumder	1015296 / CHAOS-sleep: a novel strategy for developing the personalized polysomnog- raphy-based mortality risk scoring system	07/01/19 - 06/30/21	\$	200,000	\$	100,000
CARDIO	DeMazumder	1015915 / Transforming sympathetic nerves to parasympathetic in vivo prevents sudden death in males and females with heart failure	07/01/19 - 06/30/22	\$	175,458	\$	58,255
CARDIO	DeMazumder	1015733 / Genetic Autonomic Modulation In Vivo to Protect Against Oxidative Stress and Sudden Cardiac Death (SCD)	09/01/19 - 08/31/20	\$	91,152	\$	91,152
CARDIO	Desai	1015776 / Human cardiac organoids for hypertrophic cardiomyopathy .	01/01/20 - 12/31/21	\$	62,032	\$	31,016
CARDIO	Green	1015777 / The role of Human Antigen R (HuR) in pathological cardiac remodeling	01/01/20 - 12/31/21	\$	62,032	\$	31,016
CARDIO	Green	1015707 / 1014461 / Lisa Green T32	07/02/18 - 07/01/20	\$	33,700	\$	33,700
CARDIO	Haworth	1015155 / Ultrasound-mediat- ed Controlled Hypoxemic Reperfusion for Inhibition of Reperfusion Injury	07/01/19 - 04/30/24	\$	3,651,316	\$	739,145
CARDIO	Haworth	1012816 / Ultrasound-mediat- ed oxygen scavenging for inhibition of reperfusion injury	08/01/16 - 06/30/21	\$	630,964	\$	156,874

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD	C P	URRENT ERIOD †
CARDIO	Holland	1015996 / 1014971/1014086/ Echogenic Targeted Lipo- somes: Transfectin/Drug Delivery	04/15/17 - 03/31/21	\$	1,045,413	\$	249,416
CARDIO	Holland	1011436/2R01NS047603-9- Ul- trasound Assisted Thromboly- sis	08/15/14 - 07/31/20	\$	2,764,157	\$	545,685
CARDIO	Holland	1013888 / Chronic Thrombus ablation with histotripsy and thrombolytics	12/15/17 - 11/30/22	\$	1,057,183	\$	194,459
CARDIO	Lynch	1015810 / Inflammation driven platelet loss following transcatheter aortic valve replacement	11/15/19 - 11/14/20	\$	20,000	\$	20,000
CARDIO	Owens	1015248 / Determine the Mechanism by which Rivaroxaban Reduces	01/28/19 - 07/31/20	\$	64,000	\$	64,000
CARDIO	Owens	1014105 / R01 The role of prostease activated receptor 2 in atherosclerosis	05/01/18 - 03/31/23	\$	2,004,383	\$	401,250
CARDIO	Owens	1016115 / Role of the Gut Microbiota in Abdominal Aortic Aneurysm	06/01/20 - 05/30/24	\$	2,556,707	\$	658,280
CARDIO	Owens	1015332 / The Role of Pulmonary Alveolar Microli- thiasis in Cardiovascular Disease	07/01/19 - 06/30/21	\$	200,000	\$	100,000
CARDIO	Owens	1015427 / The role of protease-activated receptor 2 (PAR2) in the pathogenesis of Alzheimer?s Disease (AD)	09/01/19 - 03/31/20	\$	396,631	\$	396,631
CARDIO	Rubinstein	1013966 / Endocrine Distruptors and Heart Heath (Wang)	02/01/18 - 01/31/23	\$	148,906	\$	32,444
CARDIO	Sadayappan	1013068 / Molecular mechanism of hypertrophic cardiomyopathy in popula- tions of South Asians descendants	08/15/16 - 12/31/20	\$	1,326,009	\$	-
CARDIO	Sadayappan	1014763 /American Heart Association - Summer Undergraduate Research Fellowship (AHA-SURF)	01/01/19 - 12/31/21	\$	60,000	\$	20,000
CARDIO	Sadayappan	1013101 / Cardiac Mosin Binding Protein-C: Structure and Function (NCE)	12/01/16 - 03/31/21	\$	1,555,018	\$	-
CARDIO	Sadayappan	1015065 / Hypertrophic cardiomyopathy in popula- tions of South Asian descendents	04/19/19 - 01/31/21	\$	250,000	\$	250,000
CARDIO	Sadayappan	1015162 / Master Cisitin Post Doc Amgen	06/10/19 - 06/09/22	\$	120,000	\$	40,000

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD MOUNT *	C P	URRENT ERIOD †
CARDIO	Sadayappan	1012990 / Umass Sub R01 AR067279- Sketal myosin- binding protein C	08/15/16 - 06/30/20	\$	65,925	\$	16,557
CARDIO	Sadayappan	1015125 / Molecular Mechanisms of Cardiac Arrhythmias in Patients with Compound Mutations	07/01/19 - 06/30/22	\$	162,471	\$	54,157
CARDIO	Sadayappan	1015830 / Preclinical studies to improve contractile function in Humanized mouse model expressing R14del-phosphol- amban with heart failure.	09/01/19 - 08/31/20	\$	60,000	\$	60,000
CARDIO	Sanagala	1015253 / 1014321/ CHAOUS- ICU	07/01/18 - 06/30/20	\$	100,000	\$	50,000
CARDIO	Slone	1015775 / HuR-dependent regulation of inflammatory remodeling following myocardial ischemia/ reperfusion injury	01/01/20 - 12/31/21	\$	62,032	\$	31,016
CARDIO	Song	1014768 / AHA 19 Postdoc fellowship	07/01/19 - 06/30/21	\$	106,532	\$	52,216
CARDIO	Tranter	1012547 / Investigation of Human Antigen R (HuR) as a Novel Mediator of Cardiac Hypertrophy	07/01/16 - 03/31/21	\$	1,777,500	\$	355,500
CARDIO	Tranter	1015133 / A novel role for HuR in UCP1-independent thermogenesis and energy expenditure	07/01/19 - 06/30/21	\$	300,000	\$	100,000
CARDIO	Tranter	1015141 / RNA aptamer homing beacons to reduce obesity	07/01/19 - 06/30/21	\$	200,000	\$	100,000
DIG	Blackard	1014863 /Omics analysis of HIV during synthetic opioid exposure	03/01/19 - 12/31/23	\$	1,181,407	\$	608,272
DIG	Blackard	1016344 / The COVID-19 / Opioid / HIV Syndemic R61 Supplement	03/01/19 - 12/31/21	\$	279,889	\$	150,215
DIG	Blackard	1014625 / Memorandum of Understanding-Instituto Nacio- nal de Saude of Mozambique	08/01/18 - 07/31/20	\$	4,000	\$	2,000
DIG	Blackard	1015780 / An evaluation of vertical transmission of hepatitis C virus and natural history of chronic HCV in pregnant women with subsequent treatment	08/01/19 - 09/30/20	\$	106,536	\$	106,536
DIG	Reynolds	1013317 / Comparative effectiveness of specific carbohydrate and mediterra- nean diets to induce remission in patients with crohns disease	03/20/17 - 07/31/20	\$	25,800	\$	8,600

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD MOUNT *	C P	URRENT ERIOD †
DIG	Reynolds	1014353 /Study of a Prospective Adult Research Cohort with Inflammatory Bowel Disease (SPARC IBD)	07/13/18 - 08/31/21	\$	256,060	\$	126,755
DIG	Sherman	1014780 / A randomized, placebo-controlled pilot study of sulfasalazine for the treatment of Primary Sclerosing Cholangitis (SHIP)	01/01/18 - 12/31/20	\$	10,500	\$	10,500
DIG	Sherman	1012450 / HIV Antiretroviral Therapy and Hepatic Injury	02/15/16 - 01/31/21	\$	1,849,870	\$	500,045
DIG	Sherman	1016281 / 1015170 / 1014224 / 1012602 / 1012513-FIU U01-DA040381	08/01/15 - 05/31/21	\$	1,226,275	\$	161,007
DIG	Sherman	1016316 / 1015291/1014330/ Subaward-R01 Maryland	02/01/18 - 05/31/22	\$	101,987	\$	11,749
DIG	Sherman	1012724/ The Prioritize study: PCORI	03/01/16 - 08/31/21	\$	258,209	\$	57,402
DIG	Sherman	1012223 / Hepatitis E in HIV-Infected Patients	09/23/15 - 08/31/20	\$	1,374,995	\$	274,999
DIG	Sherman	1015763 / 1014941/(LOC), AIDS Clinical Trials Group (ACTG)	12/01/18 - 11/30/20	\$	40,044	\$	20,045
DIG	Yeboah-Ko- rang	1015477 / AASLD Foundation Advanced/ Transplant Hepatology Award	07/01/19 - 06/30/20	\$	26,000	\$	26,000
ENDO	Cohen	1012554 / GRADE EDS	09/01/15 - 03/31/21	\$	56,423	\$	12,126
ENDO	Cohen	1015313 / 1014391 /1013659 (Yr 6) /1012844 (Yr 5) /1012028 (Yr 4) /1011388 (Yr 3) /1010749 (Yr 2) /1010368 (Yr 1) - GRADE	01/01/12 - 07/31/20	\$	2,054,669	\$	431,453
ENDO	Patel	1014913 / The Role of Abcg4 in Alzheimer's Disease	04/01/19 - 01/31/21	\$	320,875	\$	160,377
ENDO	Patel	1015403 / 1014536/Role of Cholesterol Biosynthesis in Development	09/01/18 - 08/31/20	\$	127,626	\$	59,903
ENDO	Winnick	1013196 / Effect of liver glycogen content on hypoglyce- mic counterregulation	09/01/16 - 05/31/21	\$	1,653,483	\$	338,817
GEN MED	Eckman	1015561 / Children's Research Institute	08/01/19 - 07/31/23	\$	200,867	\$	25,600
GEN MED	Martin	1013209 / Determining the optimal treatment strategy for patients who have chronic migraine with medication overuse	05/01/16 - 04/30/21	\$	212,364	\$	41,721
GEN MED	Martin	1014451 / 1R03 HD094236- 01-A1	08/07/18 - 07/31/20	\$	22,954	\$	11,477

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	ļ	AWARD	C	URRENT ERIOD †
HEMONC	Bogdanov	1012102 /1011805/1 R01 CA190717-01Alternatively Spliced Tissue Factor and Pathobiology of Pancreatic Cancer	04/09/15 - 03/31/21	\$	1,396,170	\$	268,008
HEMONC	Bogdanov	1015348 / Post-Graduate Cancer Research Translational (PG-CART) Training Program	07/05/19 - 06/30/24	\$	2,083,649	\$	296,167
HEMONC	Charif	1015387 / Back to Bedside Initiative	07/01/19 - 12/31/20	\$	5,000	\$	5,000
HEMONC	Chaudhary	1011153 / SWOG Purchase Service Agreement	06/09/14 - 06/30/20	\$	415,654	\$	122,821
HEMONC	Dong	1014339 / R21 Preclinical safety and efficacy assessment of a novel PCNA inhibitor for prostate cancer therapy	08/01/18 - 07/31/20	\$	364,010	\$	162,232
HEMONC	Dong	1006682 / NSF sub	09/01/08 - 07/31/20	\$	1,200,000	\$	61,767
HEMONC	Palascak	1016170 / 1015060/1014197 /1013325 /1012909 /1012312 /1011659 /1010330 /1011222 /1011659 - HFM MCHB	06/01/20 - 05/31/21	\$	15,000	\$	15,000
HEMONC	Palascak	1016172 / 1015026/1014171/1 012610/1011826/1009394/101 1157/1010442 - HFM Cascade	06/01/20 - 05/31/21	\$	175,620	\$	175,620
HEMONC	Qi	1015024 / Preclinical studies of BXQ-350 therapy for DIPG	03/01/19 - 12/31/20	\$	99,877	\$	28,580
HEMONC	Sasaki	1015376 / 1014351/Targeting the metabolic vulnerability of GTP-metabolism in IDH mutated glioma	07/01/18 - 06/30/20	\$	30,000	\$	30,000
HEMONC	Sasaki	1011482 /1 R01NS089815-01	09/30/14 - 08/31/20	\$	1,670,215	\$	337,450
HEMONC	Wise-Draper	1014740 / RSG-18-148-01 CCC-Oral Rinse Methylation for follw-up	01/01/19 - 12/31/22	\$	134,787	\$	44,929
HEMONC	Wise-Draper	1015666 / Harnessing the Natural Killer Cytotoxic Response in Head and Neck Cancer	01/01/20 - 12/31/23	\$	792,000	\$	198,000
HEMONC	Wise-Draper	1013562 / CA160714P1: lonic Mechanisms of Resistance to Immunotherapy in Head and Neck Cancer	07/01/17 - 06/30/20	\$	533,631	\$	173,922
IMM	Bernstein, J	1014733 / Investigation of	01/02/19 - 01/01/21	\$	135,200	\$	45,067
		Pathomechanisms of Chroic Cough using in Vitro Approach					
IMM	Finkelman	1013239 / Wimpy antibody isotypes protect against antibody-mediated disease	01/25/17 - 12/31/21	\$	1,833,210	\$	365,342
IMM	Finkelman	1014203 / suB r01 Regulation of gene expression in the anaphylactic pathway	05/15/18 - 04/30/23	\$	254,905	\$	59,466

\* NOA Project Period Award Amount † NOA Current Budget Period

#### CURRENT PERIOD † AWARD AMOUNT \* IMM Finkelman 1011228 / 1 R01 AI113162-01 07/15/14 - 06/30/20 \$ 1,334,589 \$ 332,784 IMM Finkelman 1012921 / Administrative 08/22/16 - 06/30/20 \$ 100,000 \$ 100,000 Supplement to 5R01Al113162 IMM Finkelman 1015242 / Rapid, safe 07/05/19 - 06/30/24 \$ 2.643.173 \$ 585.704 suppression of IgE-mediated disease with monovalent anti-FceRla mAb 1015630 / Genome Research IMM Khanna 09/12/19 - 09/11/24 \$ 21,660 \$ 4,458 in African American Scleroderma Patients (GRASP) IMM Shao 1014923 / Axl receptor 709,889 235,640 04/01/19 - 03/31/22 \$ \$ tyrosine kinase, a potential therapeutic target in glomerulonephritis IMM Shao 1015429 / AAI Travel grant 07/01/19 - 06/30/20 \$ 2,500 \$ 2,500 INF Apewokin 1015459 / John Hopkins 01/01/19 - 07/31/20 \$ 3,541 \$ 5,081 clinical trial INF Apewokin 1016128 / Harnessing iHIOs 06/01/20 - 05/31/25 \$ 1,160,380 \$ 233,957 and Metagenomics to Unravel Host Immune-microbiota Interactions During Cancer Chemotherapy-associated Clostridium difficile Infections INF 1014862 / HOPE in Action: A \$ \$ 3,539 Apewokin 08/01/18 - 07/31/23 39.158 Clinical Trial of HIV-to-HIV Liver Transplantation INF 1014781 / 1 R01 HL146266-01 Cushion 02/01/19 - 01/31/23 \$ 1,932,006 \$ 477,062 the role of sex in the life cycle and transmission of pneumocystis INF Cushion 1015527 / 1015522/Copper 07/01/19 - 06/30/21 \$ 249.225 \$ 124.909 tolerance and homeostasis in Pneumocystis species INF Cushion 1013660/ 07/14/17 - 07/13/24 \$ 3.500 \$ 3.500 HHSN272201700034 / T1 INF Cushion 1012927 / SUNY 73370 Sub 12/01/15 - 11/30/20 \$ 211,430 \$ 42,616 R01 Pharmacy Sec INF Cushion 1012928 / SUNY 73370 Sub 08/01/16 - 11/30/20 \$ 274,285 \$ 51,878 R01 1013979 / HIF Regulation of INF 02/15/18 - 01/31/23 Deepe \$ 2,002,500 \$ 401,250 Histoplasma Pathogenesis INF Deepe 1012686 / Dendritic cell KLF2/ 06/10/16 - 05/31/21 \$ 2,292,933 \$ 394,129 Notch Axis and Th2 Responses to Eukaryotic Pathogens INF 1014290 / 1014322/ 531,019 Deepe 07/01/18 - 06/30/23 \$ 2,668,531 \$ AI106269-06 GM-CSF-Induced Metal Sequestration and Histoplasma INF 1015624 / Identification of 09/30/19 - 09/29/24 \$ 549,239 \$ 124,436 Deepe

**ACTIVE AWARDS JUNE 2020 CONTINUED** 

ΡI

AWARD

PROJECT PERIOD

DIVISION

\* NOA Project Period Award Amount

human T cell epitopes of pathogenic fungi

† NOA Current Budget Period

Annual Research Report 2020

DIVISION	PI	AWARD	PROJECT PERIOD	ŀ	AWARD	C P	URRENT ERIOD †
INF	Fichtenbaum	1011786 /MGH 225707 1U01HL023336-02 REPRIEVE A5332 and A5333	08/08/14 - 04/30/21	\$	628,213	\$	150,000
INF	Fichtenbaum	1016088/ 1015197 /1014152 /1012586/Randomized trial to prevent vascular events in HIV (REPRIEVE)	05/01/16 - 04/30/21	\$	77,565	\$	13,710
INF	Fichtenbaum	1016185 / CWRU Viiv/FHI360 - HPTN Personal Protective Equipment	05/01/20 - 08/31/20	\$	10,080	\$	10,080
INF	Fichtenbaum	1015027 /Pitavastatin to REduce Physical Function Impairment and Frailty in HIV (PREPARE)	06/15/19 - 05/31/21	\$	36,482	\$	18,034
INF	Fichtenbaum	1016164 / ADMIN SUPPLE- MENT for ACTG - CWRU Core & PF	06/01/20 - 11/30/20	\$	296,270	\$	296,270
INF	Fichtenbaum	1016329 / UCLA ACTIV/ACTG A5401 - start-up funds	06/01/20 - 11/30/20	\$	176,287	\$	176,287
INF	Fichtenbaum	1015200 / 1013130 / Effect of pitavastatin on kidney function in HIV-infected person REPRIEVE kidney study	07/01/16 - 06/30/20	\$	42,775	\$	42,775
INF	Fichtenbaum	1015314 / 1014414/1013895/ HIV Cure Trailblazer	08/05/17 - 07/31/20	\$	248,191	\$	91,917
INF	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	01/01/17 - 11/30/22	\$	3,599,441	\$	587,796
INF	Fichtenbaum	1014653 ACTG Protocol Funds for all "A" protocols	01/01/14 - 11/30/20	\$	2,085,104	\$	363,133
INF	Fichtenbaum	1014835 / ViiV HPTN	01/01/17 - 11/30/20	\$	735,241	\$	44,146
INF	Fichtenbaum	1015728 / 1014680- BWH sub Al68636 Protocol and Core Funds ACTG	12/01/14 - 11/30/20	\$	3,086,841	\$	737,193
INF	Fichtenbaum	1015729 / Case Western Sub HPTN PF	12/01/19 - 11/30/20	\$	373,014	\$	373,014
INF	Fichtenbaum	1015779/ Exec committee_ UM1Al068636- ACTG Executive committee	12/01/19 - 11/30/20	\$	4,920	\$	4,920
INF	Fichtenbaum	1015806 /1014652-REPRIEVE Co-Chair	12/01/18 - 11/30/20	\$	20,534	\$	4,494
INF	Kaul	1016002 / 1015512/ Washington sub CDC	04/01/19 - 03/31/21	\$	60,019	\$	15,000
INF	Kaul	1015195 / 1014292 /1013632 /1012677 /1012148-MAETC 2019-2020	07/01/19 - 06/30/20	\$	230,216	\$	230,216

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD	C P	URRENT ERIOD †
INF	Kaul	1015302 / 1014479/HIV Training for Professionals and Consumers-UC	07/01/18 - 06/30/20	\$	553,153	\$	187,500
INF	Kaul	1015480 / 1014929/HRSA U01 MINHC	09/01/18 - 08/31/20	\$	123,396	\$	67,313
INF	Robertson	1015960 / 1014871 /1014030 /1013322 /1012460 /1011782 /1011016-CHN Ryan White 5H76HA0011-20-00	04/01/14 - 03/31/21	\$	3,143,935	\$	607,835
INF	Subramanian	1015882 /1014965/Metallo- thionein 3 shapes the polarization and metabolism of M2 macrophages	04/01/19 - 03/31/22	\$	231,000	\$	77,000
NEPH	Abu Jawdeh	1013450 / Investigating Comoliment-Split Products as Potential Biomarkers for Antibody-Medicated Rejection in Renal Allografts	04/01/17 - 03/31/21	\$	25,000	\$	25,000
NEPH	Abu Jawdeh	1016270 / 1015622/1014890/5 U01 DK116067 ASK-CCC	06/01/18 - 05/31/21	\$	19,824	\$	6,608
NEPH	Alloway	1015778 / BEST Study - Evalua- tion of serum belatacept concentrations in renal transplant recipients	12/01/19 - 11/30/20	\$	48,317	\$	48,317
NEPH	Amlal	1014632 / Mechanism(s) of adenine-induced fluid loss in the kidney	10/01/18 - 09/30/20	\$	238,764	\$	131,534
NEPH	Conforti	1011985 / 2 R01CA095286-10	07/01/15 - 06/30/20	\$	1,489,455	\$	280,276
NEPH	Conforti	1013561 / CA160714P1: lonic Mechanisms of Resistance to Immunotherapy in Head and Neck Cancer	07/01/17 - 06/30/20	\$	533,619	\$	176,172
NEPH	Shah	1014674 / DCI Reserve funds- Pregnancy outcomes in women with kidney treatment	11/01/18 - 10/31/20	\$	25,000	\$	25,000
NEPH	Thakar	1015347 / 1014366/Grand Rounds	07/02/18 - 07/31/20	\$	60,000	\$	30,000
PULM	Borchers	1014743 / Natural Killer Cell Functions in Lymphangioleio- myomatosis	01/01/19 - 12/31/22	\$	1,588,190	\$	379,952
PULM	Gardner	1015773 / 1014774/1013898/ Erythropoietin resistant anemia induced by thermal injury	01/01/18 - 12/31/21	\$	958,000	\$	239,500
PULM	Gupta	1015774 / 1014930/CCHMC R01 Cleveland	01/01/19 - 12/31/23	\$	44,774	\$	8,510
PULM	Gupta	1016072 / Sirolimus treatment in hopitalized patients with COVID-19 pneumonia	04/20/20 - 04/19/21	\$	30,000	\$	30,000

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD MOUNT *	C P	URRENT ERIOD †
PULM	Gupta	1013553 / Resveratrol and sirolimus in LAM Trial (RESULT)	07/01/17 - 06/30/20	\$	712,443	\$	228,918
PULM	Gupta	1014752 / Impact of Menstraul Cycle Related Variation in Lung Function on Disease Progression in LAM	09/01/18 - 08/31/21	\$	10,000	\$	3,333
PULM	Hite	1016047 / ORCHID	04/20/20 - 04/19/21	\$	74,925	\$	74,925
PULM	Hite	1016089 / 1015006/1014142/1 012550/1011868/1011505/ CCLCM-CWRU/ U54HL123023-01 PETAL	06/17/14 - 04/30/21	\$	215,368	\$	61,327
PULM	Hite	1015744 / Dissecting the molecular mechanisms of lung injury during mechanical ventilation	09/01/19 - 08/31/20	\$	30,287	\$	30,287
PULM	Hudock	1014270 / CLOVERS: Crystalloid Liberal or Vasopressors Early Resuscita- tion in Sepsis	11/01/17 - 04/30/21	\$	179,708	\$	37,833
PULM	Hudock	1013705 / The NET effect: Human CF epithelial responses to NETosis	09/01/17 - 08/31/22	\$	846,560	\$	169,312
PULM	Hudock	1015998 / K-boost The NET effect: Human CF epithelial responses to NETosis	09/01/19 - 08/31/22	\$	150,000	\$	50,000
PULM	Indihar	1015971 / 1014900/1013873/1 013361/1012969/A CF C3N Care Model of the Future: Proposal for Piloting a Learning Health System	07/01/16 - 12/31/20	\$	92,494	\$	30,464
PULM	Indihar	1016048 / TDN - Cystic Fibrosis Foundatipn Therapeutics Development Center	04/01/20 - 03/31/21	\$	45,770	\$	45,770
PULM	Indihar	1016117 / 1015743/ Implementation of Outpatient Clinical Pharmacy Services: Award for a Pharmacist abd or/Pharmacy Technician	04/01/19 - 03/31/22	\$	168,480	\$	54,160
PULM	Indihar	1016124 / 1014762/Improving research participation at UC Adult center	01/01/19 - 03/31/21	\$	59,025	\$	26,260
PULM	Indihar	1015807 / Personalizing Cystic Fibrosis Research Translation, CCHMC RDP - Translational Studies Core	07/01/19 - 06/30/23	\$	21,783	\$	5,417
PULM	Indihar	1016365 / 1015259/CFF Center Grant	07/01/19 - 06/30/20	\$	112,020	\$	112,000
PULM	McCormack	1015929 / U01 Sub harvard- The molecular and Genetic Pathogenesis of LAM	03/01/20 - 02/28/24	\$	561,750	\$	112,350

\* NOA Project Period Award Amount † NOA Current Budget Period

DIVISION	PI	AWARD	PROJECT PERIOD	A	AWARD MOUNT *	C P	URRENT ERIOD †
PULM	McCormack	1015989 / 1015017/Prevention of Preterm Birth Using the Collectin Surfactant Protein A (SP-A) Northshore	04/01/19 - 03/31/23	\$	170,421	\$	45,438
PULM	McCormack	1015297 / 1015298/A population-based chort study to monitor safety and effectiveness of sirolimus in patients with sporadic lymphangioleimyomatosis	05/01/19 - 04/30/21	\$	250,000	\$ 158	,443
PULM	McCormack	1016134 / 1015033 /1014131 /1013505 /CCHMC-WT1 regulation of pulmonary fibrosis	05/22/17 - 04/30/22	\$	48,340	\$	10,210
PULM	McCormack	1014180 / Single Cell RNA Sequencing in LAM	06/01/18 - 05/31/21	\$	80,000	\$	40,000
PULM	McCormack	1014329 / 1013475/1013010/ Multicenter Interventional Lymphangioleiomyomatosis Early Disease Trial (MILED)- CCC	09/20/16 - 08/31/21	\$	3,606,817	\$	649,490
PULM	McCormack	1015705 / 1014886/1013850/ Therapeutic benefit of HSP90 inhibition in pulmonary fibrosis	09/30/17 - 09/30/20	\$	132,715	\$	19,939
PULM	McCormack	1013865 / Pulmonary Epithelial Dynamics and Innate Host Defense	12/07/17 - 11/30/21	\$	2,026,868	\$	480,973
PULM	Romaker	1015927 / Impact of Low Flow Nocturnal Oxygen Therapy On Hospital Readmission/ Mortality in Patients with Heart Failure and Central Sleep Apneal (LOFT-HF)	09/01/19 - 08/31/24	\$	206,395	\$	36,125
PULM	Yu	1015407 / Dysregulation of sphingolipid metabolism and actions in tuberous sclerosis complex	01/13/20 - 01/14/23	\$	157,500	\$	37,500
PULM	Yu	1015757 / Role of homeobox genes in hormonal regulation of transcriptional activation in LAM progression	01/15/20 - 01/14/22	\$	150,000	\$	75,000
PULM	Yu	1013642 / Targeting prostaglandin biosynthesis and action in lymphangioleio- myomatosis	08/01/17 - 06/30/20	\$	1,843,109	\$	590,928
PULM	Yu	1015544 / TS180051 Development of remission- inducing therapy for TSC tumors	07/15/19 - 07/14/21	\$	119,914	\$	59,957

\* NOA Project Period Award Amount † NOA Current Budget Period

# New Grants FY 2020 Department of Internal Medicine

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIR	ECT COSTS
CARDIO	DeMazumder, D	CHAOS-ICU	AHA - 19AIML34930039	7/1/19 - 6/30/21	\$	181,818
CARDIO	DeMazumder, D	Transforming sympathetic nerves to parasympathetic in vivo prevents sudden death in males and females with heart failure	AHA Subaward (Sawti Dey - VUMC)	7/1/19 - 6/30/22	\$	159,077
CARDIO	DeMazumder, D	Genetic Autonomic Modulation in Vivo to Protect Against Oxidative Stress and Sudden Cardiac Death	DOD subaward (Sawti Dey - VUMC)	9/1/19 - 8/31/20	\$	56,793
CARDIO	DeMazumder, D	Autonomic remodeling and modulation as mechanism and therapy for sudden cardiac death in heart failure	Jeff Crocker F32	2/1/20 - 1/31/23	\$	111,023
CARDIO	Desai (Sadayappan)	Human cardiac organoids for hypertrophic cardiomyopathy	AHA 20PRE35120272	1/1/20 - 12/31/21	\$	62,032
CARDIO	Green (Tranter)	Bill Agreement for T32	CCHMC 134161/ 5 T32 HL125204	7/2/19 - 11/30/19	\$	13,835
CARDIO	Green (Tranter)	The Role of Human Antigen R in Pathological Cardiac Remodel- ing	AHA 20PRE34210795)	1/1/20/12/31/21	\$	62,032
CARDIO	Haworth, K	Ultrasound-mediated Controlled Hypoxemic Reperfusion for Inhibition of Reperfusion Injury	R01 HL148451	7/1/19 - 4/30/24	\$	2,693,676
CARDIO	Lynch, D	Inflammation driven platelet loss following transcatheter aortic valve replacement	NHLBI SRP-2019- 01 (Pride Award)	11/15/19 - 11/14/20	\$	20,000
CARDIO	Owens, P	The Role of Pulmonary Alveolar Microlithiasis in Cardiovascular Disease	AHA - 19IPLO134760319	7/1/19 - 6/30-21	\$	181,818
CARDIO	Owens, P	The role of protease-activated receptor 2 (PAR2) in the pathogenesis of Alzheimer's Disease	R01 HL141404- 02S1	9/1/19 - 3/31/20	\$	250,000
CARDIO	Owens, P	Role of Gut Microbiota in Abdominal Aortic Aneurysm	R01 HL147171	6/1/20 - 5/30/24	\$	1,739,142
CARDIO	Sadayappan	Molecular Mechanisms of Cardiac Arrhythmias in Patients with Compound Mutations	AHA- 19TPA34830084	7/1/19 - 6/30/22	\$	272,727
CARDIO	Sadayappan	Master Visiting Post Doc Yr 1 Funding -	Amgen - visiting postdoc -	1/1/19 - 12/31/20	\$	40,000
CARDIO	Sadayappan	Preclinical studies to improve contractile function in Humanized mouse model expressing R14del-phosphol- amban with heart failure	Netherlands Heart Institute PLN Award	9/1/19 - 8/31/20	\$	60,000
CARDIO	Tranter	A novel role for Human Antigen R (HuR) in uncoupling protein 1 (UCP1)- independent thermogenesis and energy expenditure	AHA- 19TPA34910086	7/1/19 - 6/30/22	\$	272,727
CARDIO	Tranter	RNA aptamer homing beacons to reduce obesity	AHA- 19iPL0134770131	7/1/19 - 6/30/21	\$	181,818

### **NEW GRANTS FY 2020** CONTINUED

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIF	RECT COSTS
CARDIO	Slone (Tranter)	HuR dependent regulation of inflammatory remodeling following myocardial ischemia / reperfusion injury	AHA - 20PRE34230020	1/1/20 - 12/31/21	\$	62,032
CARDIO	Song (Sadayappan)	Molecular mechanisms	AHA - POST34380448	7/1/19 - 6/30/21	\$	106,532
DIG	Blackard, J	An evaluation of vertical transmission of hepatitis C virus and natural history of chronic HCV in pregnant women	Christ Hospital	10/22/19 - 10/31/20	\$	106,536
DIG	Blackard, J	Omics analysis of HIV during synthetic opioid exposure	R61DA048439- 02S1	1/1/20 - 12/31/21	\$	180,794
DIG	Yeboah-Korang, A	AASLD Foundation Advanced/ Transplant Hepatology Award	Research SEED-AASLD Foundation	7/1/19 - 6/30/20	\$	26,000
GEN MED	Eckman, M	Improving the detection of STIs in the Pediatric Emergency Department: A Pragmatic Trial	Children's Research Institute - sub	8/1/19 - 7/31/23	\$	125,150
HEMONC	Bogdanov, V	Post-Graduate Hematology/ Oncology Translational (PG-HOT) Training Program	1T32CA236764-01	6/7/19 - 6/30/24	\$	1,943,354
HEMONC	Charif, M	Back to Bedside Initiative	ACGME	7/1/19 - 6/30/21	\$	5,000
HEMONC	Wise-Draper, T	ACS Harnessing the Natural Killer Cytotoxic Response	ACS RCG-19-111- 01-CCE	1/1/20 - 12/31/23	\$	792,000
IMM	Finkelman, F	Rapid, safe suppression of IgE-mediated disease with monovalent anti-ceRla mAb	R01 Al145991	7/5/19 - 6/30/24	\$	2,375,293
IMM	Khanna, S	Genome Research in African American Scleroderma Patients (GRASP)	GRASP	6/1/19 - 5/31/24	\$	21,659
IMM	Shao, W	AAI Travel Grant	AAI	7/1/19 - 6/30/20	\$	2,500
INF	Apewokin, S	Harnessing Induced Human Intestinal Organoids (iHIOs) Meta	K08 CA237735	6/1/20 - 5/31/25	\$	1,026,769
INF	Cushion, M	Copper tolerance and homeostasis in Pneumocystis species	R21 Al143467	7/1/19 - 6/30/21	\$	155,280
INF	Deepe, G	Identification of human T cell epitopes of pathogenic fungi	University of Massachusetts Worcester	9/30/19 - 9/29/20	\$	124,436
INF	Kaul, P	Midwest Capacity Building Assistance Network (MCBAN)	Wash U WU-20-13 Sub 1 NU65PS923676	4/1/19 - 3/31/20	\$	15,000
NEPH	Alloway, R	BEST Study - Evaluation of serum belatacept concentra- tions in renal	DCl Paul Teschan award	12/1/19 - 11/30/20	\$	48,317
PULM	Gupta, N	Sirolimus treatment in hospitalized patients with COVID-19 pneumonia	Pfizer, Inc	4/20/20 - 4/19/21	\$	30,000

### **NEW GRANTS FY 2020** CONTINUED

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIR	ECT COSTS
PULM	Hite, D	Dissecting the molecular mechanisms of lung injury during mechanical ventilation	OU Sub- R56HL142767	9/1/19 - 8/31/20	\$	18,870
PULM	Hite, D	ORCHID	Cleveland Clinic sub	4/20/20 - 4/19/21	\$	59,661
PULM	Hudock, K	K-Boost Award	CFF	9/1/19 - 8/31/22	\$	150,000
PULM	Hudock, K	CLOVERS-STEM	Cleveland Clinic sub	6/10/19-5/31/20	\$	27,205
PULM	Jose, A	Biomarker Discovery in Portopulmonary Hypertension	Entelligence	4/1/20 - 3/31/21	\$	90,909
PULM	Joseph, P	R1226 Dartmouth CF Lung Transplant Transition - Regional Dissemination Network	Cystic Fibrosis Foundation - Dartmouth sub	1/1/19 - 12/31/19	\$	9,000
PULM	McCormack, F	The Molecular and Genetic Pathogenesis of LAM	Brigham and Women's	3/1/20 - 2/28/25	\$	350,000
PULM	Romaker, A	Impact of Low Flow Nocturnal Oxygen Therapy on Hospital Readmission	OSU Sub	9/1/19 - 8/31/20	\$	41,201
PULM	Yu, J	DOD TS180051	DOD	10/1/19 - 9/30/21	\$	37,356
PULM	Yu, J	Role of Homeobox Genes in Hormonal Regulation of Transcriptional Activation in LAM Progression	LAM Foundation LAM0141E01-20	1/15/20 - 1/14/22	\$	150,000
PULM	Indihar, V	CFF Center grant	Cystic Fibrosis Foundation	7/1/19 - 6/30/20	\$	112,020
TOT					¢	14 551 202

### IMAGE, FACING PAGE:

#### "No Filters; Back to RENALity"

Mice Renal Tubular Epithelial Cells after ischemia-reperfusion injury. The four different colours represent proteins affected by oxidative stress. Live Microscopy Core was used on March 4, 2019, with a Leica DMi8 wide-field fluorescent microscope, 20x objective.

2020 limage Gallery, Basic Research Images

CREDIT: Sabrina Bernardo, Undergraduate student worker, Nephrology: Begona Campos, PhD; Charuhas Thakar, MD

#### MAIN IMAGE, BACK COVER:

### "B cell infiltration in head and neck cancer patients on anti-PD-1 therapy"

Using NanoString's Molecularly Guided Highly Multiplexed Spatial Profiling, we investigated B cell infiltration in head and neck cancer tissue from patients on PD-1 inhibitors. The image shows CD20+ B cells (yellow) and CD138+ plasma cells (pink), and tumor characterized by pan-cytokeratin (green). Patient tissue was obtained from Dr. Trisha Wise-Draper's Phase II clinical trial, "Investigation of Adjuvant Combined Cisplatin and Radiation with Pembrolizumab in Resected Head and Neck Squamous Cell Carcinoma"

2020 Image Gallery, Clinical Research Images

CREDIT: Sarah Palackdharry, MS, College of Medicine UC Cancer Program

# 106 University of Cincinnati
## **Annual Research Report 2019-20 Committee**

Yolanda Wess, MEd, RN, BSN *(lead)* Angela Duke, BS *(co-lead)* Kelly Niederhausen, BA Eric Smith, MD Amanda Chalifoux

## Annual Research Report 2019-20 Admin Team

Connie Adkins Melissa Baker Sheryl Carns Beverly Cunningham Justina Dunigan Jastina Dunigan Jamie Morgan Lauren Phipps Lynn Richmond Christina Salyers Priscilla Schmidt



## Department of INTERNAL MEDICINE

University of Cincinnati College of Medicine

Academic Office 6065 Medical Sciences Building 231 Albert Sabin Way PO Box 670557 Cincinnati, OH 45267-0557 513-558-4231

imoffice@uc.edu

med.uc.edu/intmed

## **Gregory Rouan, MD**

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