



Annual Research Report

ACADEMIC YEAR 2015-2016

DEPARTMENT OF
INTERNAL MEDICINE

University of

CINCINNATI

MISSION STATEMENT

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

Our mission is to improve health for all through:

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

DEPARTMENT OF **INTERNAL MEDICINE**

Annual Research Report

ACADEMIC YEAR 2015-2016



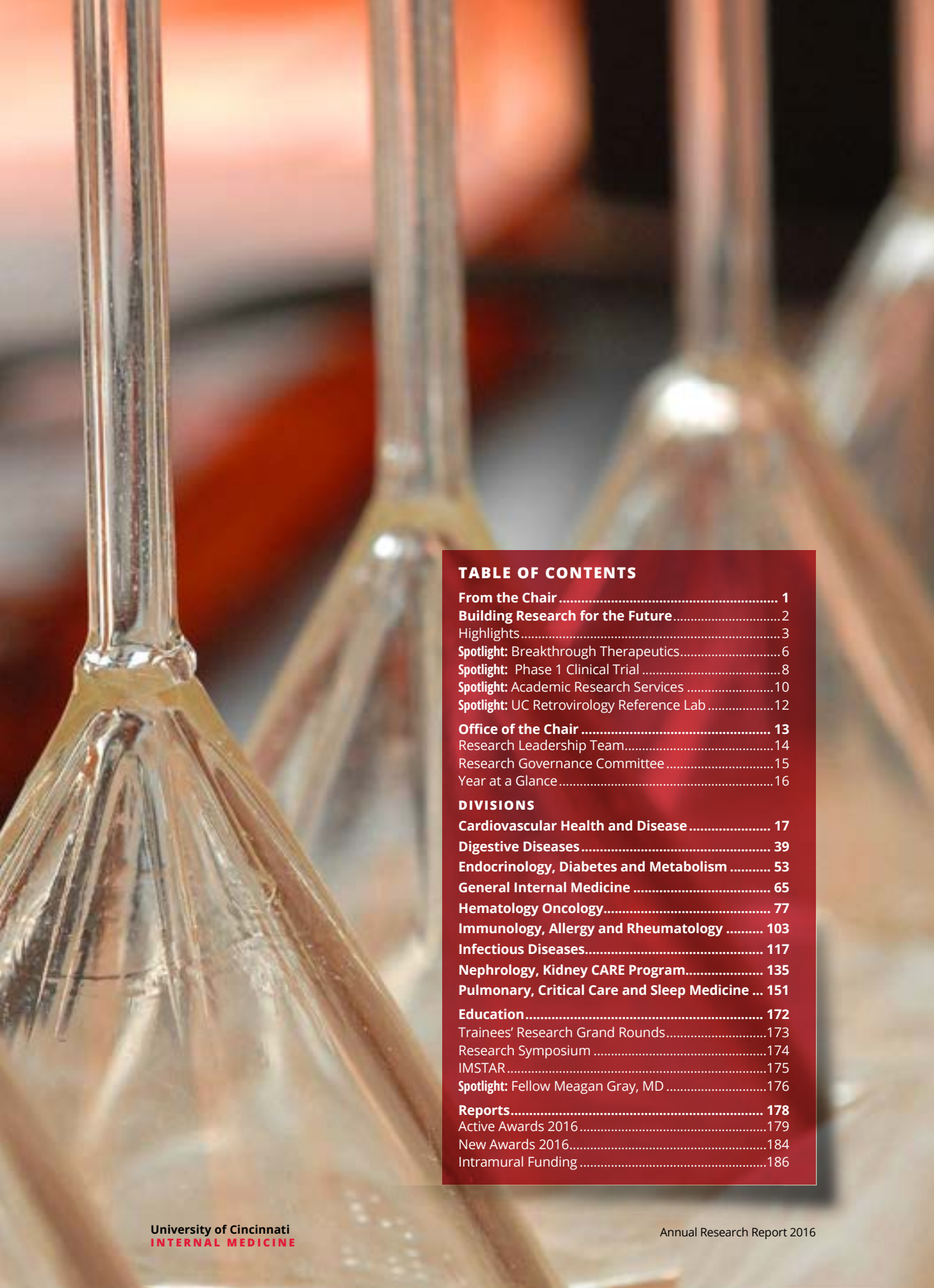


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Message from the Chair

WE APPRECIATE THE COMMITMENT, WORK AND SERVICE

of all the faculty, investigators, researchers, trainees and staff of the nine divisions of the Department of Internal Medicine. Manoocher Soleimani, MD, associate chair of research, and Carl Fichtenbaum, MD, associate chair of translational research, along with other faculty and staff on the research core governance committee deserve a great deal of credit for coordinating and preparing our annual research symposium, monthly research conferences, intramural research awards and annual research report.



A great deal has been accomplished in each of our tripartite missions over this past year and research is no exception. We currently hold 124 total grants in the department and 17 percent of these are held by primary investigators with R01 awards. The total award amount is \$64.9 million in direct costs, while more than \$9.2 million of this amount includes new grants awarded just since July 2015. Another \$5 million in additional direct awards comes from our research through Cincinnati VA Medical Center.

Most importantly, we continue to support our investigators with distinguished research achievement awards, junior and senior pilot awards, challenge awards, bridge funding and others. This investment of \$2.5 million in seed and interim funding over the past three academic years has resulted in a net of approximately \$8 million in new awards realized by these researchers. We plan to continue these very successful initiatives.

The UC and scientific community will be hearing impressive research news from many of these investigators in the months to come. Their work focuses on an array of topics, and their discoveries will be used to improve the health of our community on many levels.

Sincerely,

Gregory Rouan, MD

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

A great deal has been accomplished in each of our tripartite missions over this past year and research is no exception.

Building Research for the Future

The success of the Department of Internal Medicine hinges, in large part, on the new knowledge created by our research teams. Scientific discoveries lead by our basic, translational and clinical investigators are very important to the Cincinnati community and have enhanced our reputation both nationally and internationally. With a vision to create an environment that encourages, stimulates and promotes research, the leadership of this department will continue to provide the tools critical to support our mission.

In this annual report are success stories of translational research, interesting spotlights about our investigators along with summaries from researchers and staff in each division, and information about new administrative services developed to assist researchers and trainees with their research projects at the University of Cincinnati. We invite the public to learn about the department's research awards and awardees, and how we are cultivating a productive, innovative and growing research program to make a difference in the health of our community.

In addition to releasing this year's annual research report, we are happy to have hosted a successful research symposium and another round of intramural DOIM research awards to stimulate and support innovative investigator initiated ideas. Junior faculty and fellows presented pilot projects at the research symposium, which served as an excellent incubator for researcher collaboration and mentorship. These and other activities advance not only the research mission of our department but the entire UC Academic Health Center.

Spend time with our annual report, review our leading edge research and feel free to ask how you can support our initiatives if you value innovation and discovery.

Respectfully,

Carl Fichtenbaum, MD

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

Manoocher Soleimani, MD

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



Carl Fichtenbaum, MD



Manoocher Soleimani, MD

**Learn how we
are cultivating
a productive,
innovative and
growing research
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a difference in the
health of our
community.**

TOTAL GRANTS

124 17 percent are held by primary investigators with R01 awards

TOTAL FUNDING

\$64.9 million

OVER \$9.2 million
in NEW AWARDS IN FY2016

CLINICAL TRIAL REVENUE (FY2016)

\$4.7 million

INCREASE IN TOTAL FUNDING (FY2016)

> 17%

SUCCESS RECEIVING FUNDING

up from 18% to 25%

INTRAMURAL FUNDING (FY2016)

> \$240,000

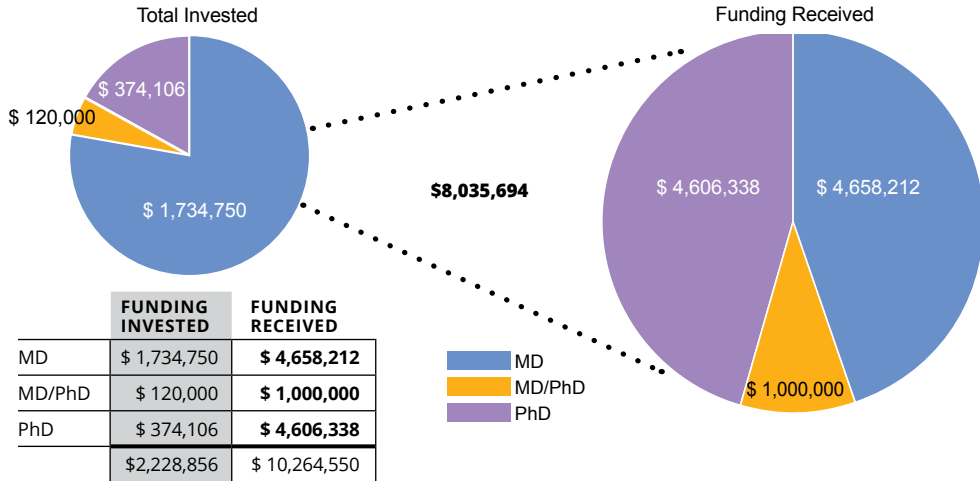
ROI ON INTRAMURAL FUNDING (3 YEAR):

\$2.2 million returned over \$8 million

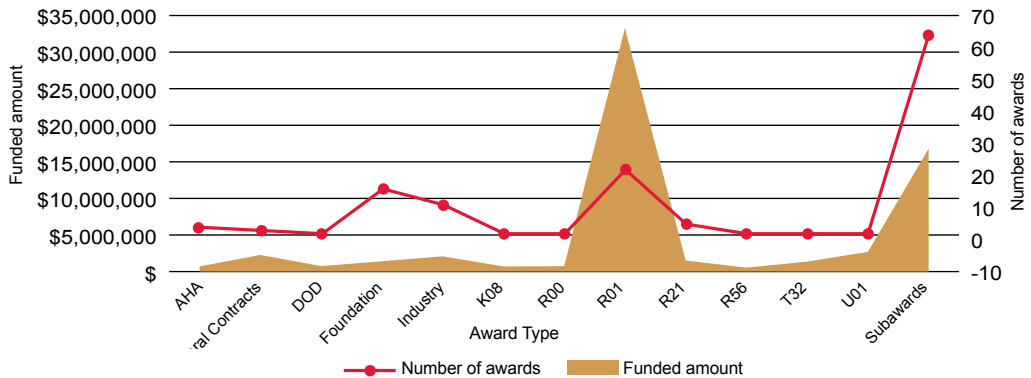
in direct and indirect funding; resulted in 34 original publications, 28 presentations

Return on Investment Intramural Funding

Over three years (FY2013-FY2015) the Department of Internal Medicine awarded more than \$2.2M in intramural research support to investigators to enhance research programs and stimulate new and innovative research ideas. The initial funds resulted in over \$10M in direct and indirect funding, 34 original publications and 28 presentations. The estimated return on the department's initial investment was approximately \$8 M.

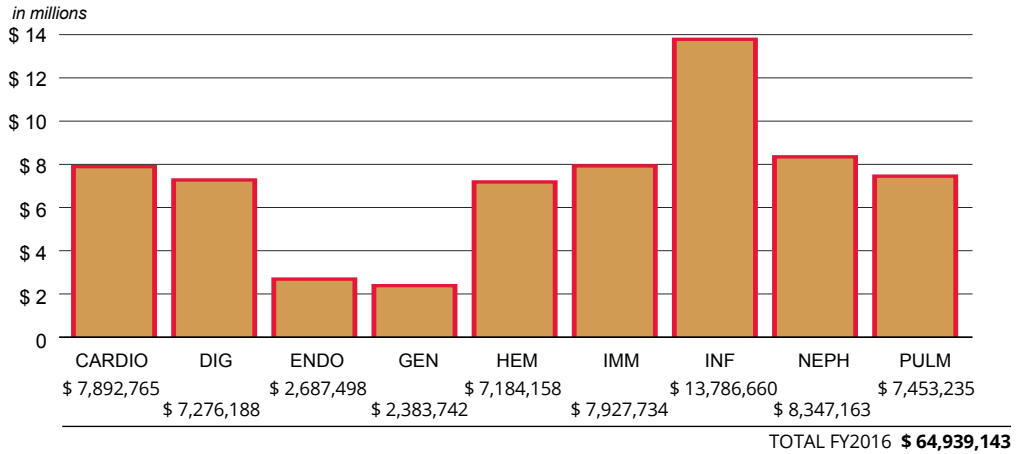


Funded Awards by Type

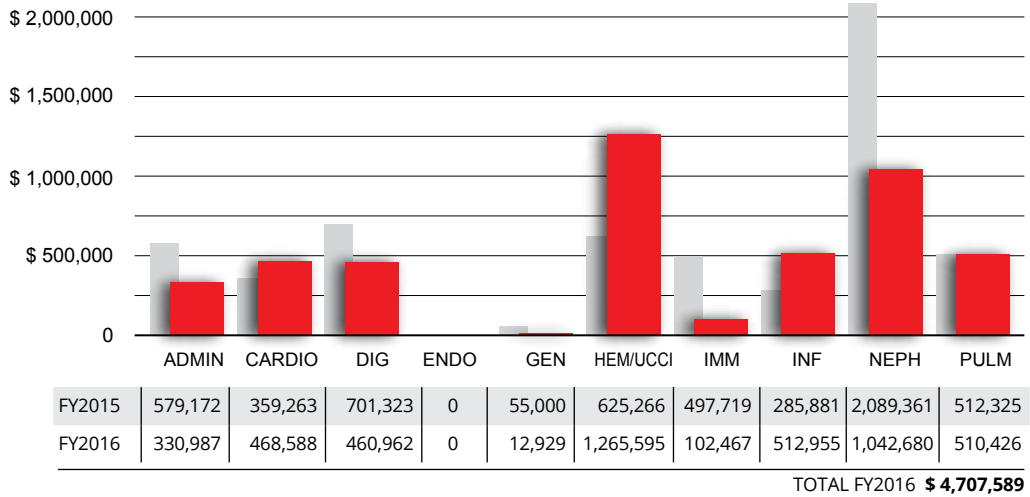


TYPE OF AWARD	# OF AWARDS	FUNDED AMOUNT
AHA	3	\$ 707,000
Federal Contracts	2	\$ 2,270,981
DOD	1	\$ 748,549
Foundation	15	\$ 1,406,057
Industry	10	\$ 2,084,141
K08	1	\$ 704,232
R00	1	\$ 735,572
R01	21	\$ 33,264,850
R21	4	\$ 1,517,121
R56	1	\$ 534,653
T32	1	\$ 1,361,995
U01	1	\$ 2,691,189
Subawards	63	\$ 16,802,471

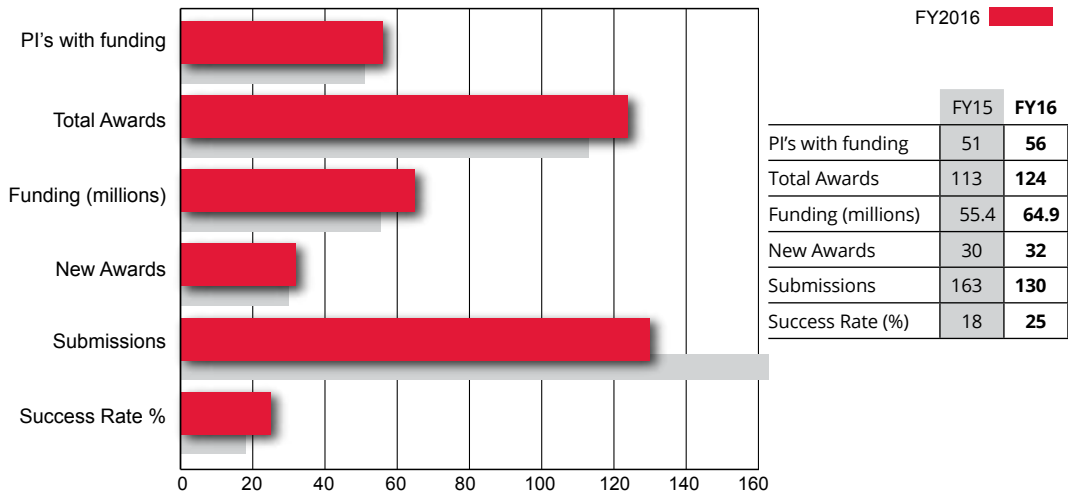
Funding by Division FY2016



Clinical Trial Revenue by Division FY2015 to FY2016



Research Funding Metrics FY2015 to FY2016



“Washing the lungs with an EDTA-containing solution reduced the burden of stones in airspaces. This finding could translate into a therapy for humans if toxicity studies demonstrate that the approach is safe.”

Frank McCormack, MD

Breakthrough Insights

Research revealing potential therapeutic approaches for rare lung disease

Frank McCormack, MD, Taylor Professor and Director of the Division of Pulmonary, Critical Care and Sleep Medicine, is an expert in the study of pulmonary alveolar microlithiasis (PAM), a rare lung disease that results in formation of crystals of calcium phosphate in the airspaces of the lung, chronic inflammation and scarring and respiratory failure in middle age or later in life.

McCormack and his investigative team identified biomarkers and developed an animal model to explore the disease. The team found that the animals with mutations in SLC34A2 developed abundant stone formation, followed by lung injury and inflammation, which were reflected by elevations in certain key serum markers.

The mouse studies have sparked ideas for potential therapeutic approaches that may hold the key to treating PAM. UC researchers learned that certain cytokines and surfactant proteins in serum tracked with the burden of stones in the lung, suggesting they may become useful tools for following disease progression and treatment response in patients. A surprising finding was that stones removed from the lung readily dissolved in EDTA, a calcium-binding molecule that is a component of many detergents, and is used as a treatment for heavy metal poisoning, explains McCormack.

“Washing the lungs with an EDTA-containing solution

reduced the burden of stones in airspaces,” says McCormack. “This finding could translate into a therapy for humans if toxicity studies demonstrate that the approach is safe.”

A low-phosphate diet was also found to prevent stone development in the lung and even to reverse lung calcification in the animals, says McCormack. However, phosphate-restricted diets must be tested in trials before they can be recommended because they can cause other medical problems such as osteoporosis if not properly administered. Other strategies for restoring normal phosphate balance in the lung include inserting a gene for a working phosphate pump back into the cells of the lung using viral vectors, explains McCormack.

Trials in humans are planned, but will be challenging for two reasons. First, PAM is exceedingly rare, with just over 1,000 documented cases worldwide since it was discovered in the 1960s. Second, cases are scattered around the globe. Forty cases of PAM have been identified worldwide in the network of pulmonary clinics within the Cincinnati-based NIH-grant-funded Rare Lung Disease

Consortium. Sixteen of those cases are in the United States.

McCormack says rare disease research can reveal surprising insights into the fundamental biology of the lung.

“Studies of the PAM mouse model have already revealed a potential role for phosphate in the regulation of surfactant balance in the lung and have attracted the interest of cystic fibrosis scientists interested in exploring the possible interaction between Npt2b and the defective chloride channel in that disease,” explains McCormack.

Other researchers assisting McCormack and associated with UC include: Nik Nikolaidis, PhD; Yasuaki Uehara, MD, PhD; Hassane Amlal, PhD; Jason Gardner, PhD; Kathleen LaSance; Lori Pitstick; James Bridges, PhD; Kathryn Wikenheiser-Brokamp, MD, PhD; Dennis McGraw, MD and Jason Woods, PhD.

The research has been funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health, the National Center for Advancing Translational Sciences through RDCRN and Carespring Health Care Management Research. •

UC researchers learned that certain cytokines and surfactant proteins tracked with the burden of stones in the lung, suggesting they may become useful tools for following disease progression and treatment response.

One Very Important Step

Basic laboratory research moves to Phase 1 clinical trial

After decades of laboratory research and promising findings, the discoveries of Xiaoyang Qi, PhD, professor in the Division of Hematology Oncology, researcher in the Cincinnati Cancer Center and Bexion's scientific co-founder, are being translated to clinical trials in humans, possibly helping thousands living with cancer.

On July 18, 2016, Bexion Pharmaceuticals LLC announced that the U.S. Food and Drug Administration cleared their application for a first-in-human Phase I clinical trial with the compound BXQ-350 for treatment of advanced solid tumors and glioblastoma

“This is an exciting announcement as this is the goal of every scientist—to actually make a difference in patient care.”

multiforme, the most common type of brain cancer.

“This is 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 that now, 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 co-principal 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.

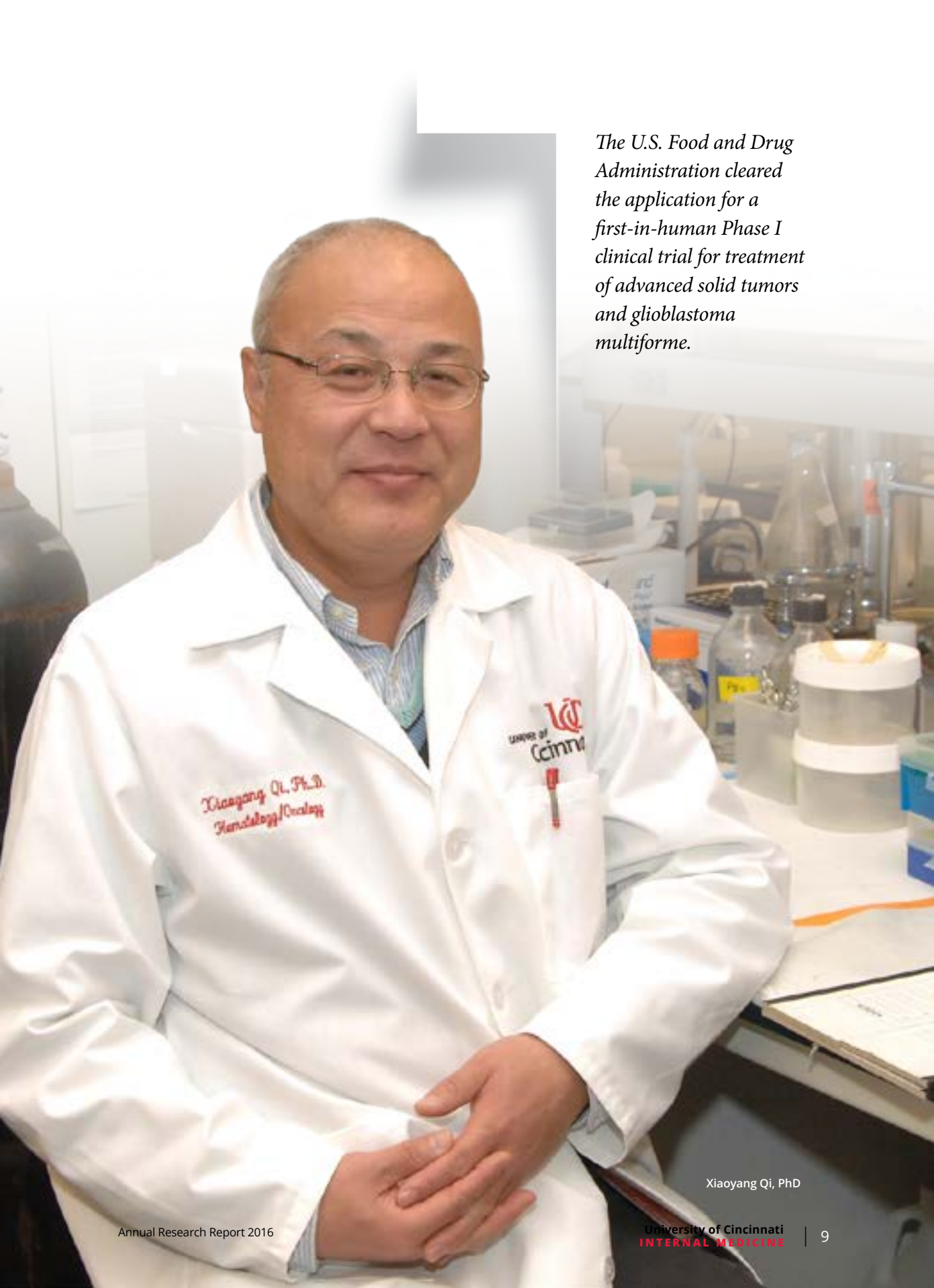
Qi says his lab found that the combination of these two natural cellular components, or SapC-

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 which will now be tested in a Phase I clinical trial.

“Phase 1 trials help us determine acceptable dosages and possible side-effects,” says John Morris, MD, director of the UC Cancer Institute’s Phase I Experimental Therapeutics Program where the trial will be housed. Morris, also a faculty member at the UC College of Medicine and a member of the Cincinnati Cancer Center, is principal investigator on the clinical trial at UC, which is one of several sites hosting the study.

“Phase 1 clinical research trials are the first step in moving tested scientific concepts from the laboratory bench to the patient; they typically include less than 50 people and are important for patients who may not have standard treatment options, as these therapies are novel and not widely available,” he says. “The UC Cancer Institute is the only facility in the Tristate area with a Phase I program.”

The trial is now being reviewed by the Institutional Review Board. •



The U.S. Food and Drug Administration cleared the application for a first-in-human Phase I clinical trial for treatment of advanced solid tumors and glioblastoma multiforme.

Xiaoyang Qi, PhD

Expanding the Research Culture

Launch of Academic Research Services increases resources for investigators

In June, researchers in the Department of Internal Medicine gained a new resource for making their cutting-edge research ideas a reality with the department's launch of Academic Research Services (ARS).

The goals of ARS are to minimize barriers to allow researchers to focus on scholarly activity; assist faculty, staff, and trainees with their research projects; and provide real-time support for researchers. ARS are provided by the department and include grant

writing, administrative tasks such as budgeting and progress reports, keeping track of regulatory protocols, funding searches, specimen processing, publishing and presentation assistance.

"We want to support researchers and trainees and enable them to focus on their science and not so much on the administrative work, such as finding grants," says Yolanda Wess, MEd, BSN, RN, research manager of ARS. Wess has spent more than 17 years at UC working in re-

search, clinical care and education with the Division of Infectious Diseases, including coordinating clinical trials and managing federally funded grants. "I'm excited about this unique opportunity to assist the Department of Internal Medicine in creating and expanding a research culture and improving upon some of our research systems and processes."

Joining Wess in leading ARS is research associate Eric Smith, MD, who also has more than 17 years of experience supervising

labs and supporting grant-writing efforts for the Division of Endocrinology, Diabetes and Metabolism. Smith says research funding is definitely the main challenge for young investigators. Smith and Wess have spent the first months in their new roles meeting with division directors and researchers throughout the department to determine how ARS can best meet the needs of current and new investigators. ARS also includes the UC Retrovirology Reference Lab (UCRRL), a specialty laboratory that offers tests concentrated in the areas of molecular biology, virology, immunology and pathology and is currently providing lab processing for more than six divisions.

“The funding is out there, and we can help them identify those sources,” Smith says. “But where we can particularly help is with the nuts and bolts of applying for

a grant. We can collaborate with their mentors and the department to help put young researchers in a position where they are competitive to receive these grants.”

For Wess, the chance to lead ARS was a natural progression in a career dedicated to medicine, discovery and helping others—and an intriguing opportunity to help researchers find answers that could improve real patients’ lives.

“I love science, and my nursing background has been very helpful in my new role,” Wess says. “There’s some magnificent work going on at UC, and we have these world-renowned researchers here who are devoting their lives to trying to cure diseases, to make a difference for humanity. I’m honored to support them and contribute to their efforts.” •

Academic Research Services

- grant writing
- budgeting
- generating progress reports
- tracking regulatory protocols
- funding searches
- publishing and presentation assistance
- specimen processing (see *UC Retrovirology Reference Lab* next page)

“We want to support researchers and trainees and enable them to focus on their science and not so much on the administrative work.”

Yolanda Wess, MEd, BSN, RN,
and Eric Smith, MD



UC Retrovirology Reference Lab

Specialty laboratory is part of Academic Research Services

The UC Retrovirology Reference Lab (UCRRL) is a specialty laboratory offering tests in, but not limited to, the areas of molecular biology, virology, immunology, and pathology. Josette Robinson-Eaton, research assistant and UCRRL laboratory manager, Chelsea Dietz, lab coordinator, and Molly Leibel, research

assistant, are the team going the extra mile to ensure that specimens are handled and processed to the highest quality standards.

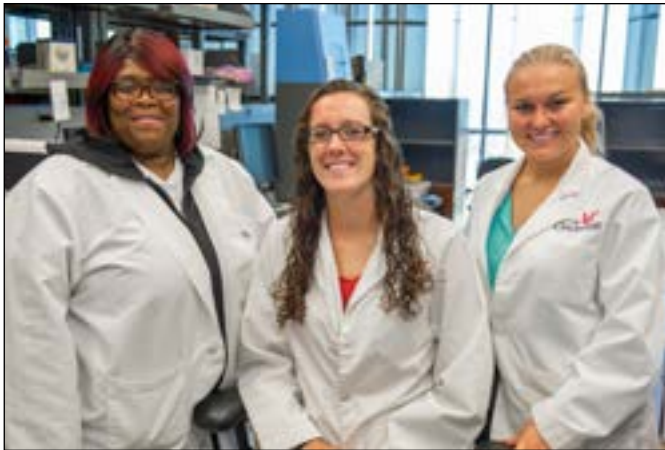
The UCRRL team currently provides lab processing for more than six divisions and 80 protocols for 15 principal investigators (PI). They work directly with the study coordinator, research nurse, lab

personnel or PI to ensure that specimens are picked up in a timely manner and processed per protocol specifications.

Client services are available to physicians, laboratories, pharmaceutical and clinical trial companies, test manufacturers, and others for the purposes of research, clinical diagnosis, and product/assay comparison/evaluation. As a reference laboratory, the tests performed for diagnostic purposes comply with ACTG, UC, ODH, CLIA, and CAP regulations.

Carl Fichtenbaum, MD, is the medical director and Yolanda Wess is the research manager.

To obtain a quote for services contact the lab manager, Josette Robinson-Eaton. •



“The UC Retrovirology Lab has played an essential role in our ability to complete our complicated clinical trials.

The staff is very efficient and easy to work with. There are several studies that require PK's and other research lab samples to be processed around the clock and the lab team has made that happen. Beyond the processing, their team ships all the specimens and maintains accurate records for our studies. This allows me as a coordinator the time needed to be with the patient and data collection.”

Patti Rose, BSN
Senior Research Nurse Coordinator
UC Cancer Institute





Office of the Chair



Research Leadership Team



Gregory Rouan, MD
*Gordon and Helen Taylor
Hughes Professor
and Chair*



Carl Fichtenbaum, MD
*Professor
Associate Chair
for Translational
Research*



Manoocher Soleimani, MD
*James Heady Professor
of Medicine
Associate Chair
for Research*



Peter Clayton, MPA
*Executive Director,
Business Affairs
Office of the Chair*



Kelly Niederhausen
*Asst. Director, Research
and Education
Sr. Business Administrator*



Angela Duke
*Associate To
Office of the Chair*



**Yolanda Wess, MEd,
BSN, RN**
*Research Manager
Office of the Chair*



Tina Sandfoss
*Program Director
Office of the Chair*



Eric Smith, MD
*Research Associate
Office of the Chair*



Leah Bischoff
*Administrative Assistant
Planning Committee*



Chandra DuBose
*Administrative Assistant
Planning Committee*

Research Governance Committee



Standing (left to right): Perez-Tilve, Niederhausen, Yacyshyn, Sadayappan, Steen, Eckman, Smith, Wise-Draper, Duke
 Seated (l to r): McGraw, Holland, Soleimani, Fichtenbaum, Rouan, Wess, Amlal
 Not pictured: Becker, Bernstein D., Bogdanov, Clayton, Falciglia, Kopras, McCormack, Rubinstein, Schauer, Smulian, Qi



Robert Baughman, MD

Professor
Office of the Chair

Robert Baughman, MD, along with longtime collaborator, Elyse Lower, MD, has a long standing interest in sarcoidosis and other interstitial lung diseases. Our group has established several novel agents for the treatment of sarcoidosis, including methotrexate, infliximab, aprelimast, mesenchymal stem cells, roflumilast, Acthar gel, and rituximab. Currently, we have National Heart, Lung, and Blood Institute funding to study a new combination of antibiotics for advanced sarcoidosis. We have also been developing other novel agents for pulmonary and extra-pulmonary disease.

During the past four years, we have headed a multi-nation registry of sarcoidosis associated pulmonary hypertension, which now includes

more than 200 patients—a quarter of whom are followed in Cincinnati. We have also led studies for treatment of sarcoidosis associated pulmonary hypertension and participate in the Foundation for Sarcoidosis Research Clinical Studies Network, a 10-center group looking at quality of life in sarcoidosis. We are planning to launch a new registry within this network to follow patients with advanced sarcoidosis. Our team continues collaborations with groups around the world and has hosted visiting scholars from the Netherlands, China, and Turkey during the past two years.

Funding support comes from the NHLBI, the Foundation for Sarcoidosis Research and several industrial partners.

Year at a Glance

- DOIM introduces **Submission Incentive Program**
- Welcome **first trainees into IMSTAR**
- DOIM **Lab Services** opens to divisions
- \$1.86M **NIH award** (Marzieh Salehi, MD)
- \$1.27M **NCI award** (Laura Conforti, PhD)



2015

July



2015

August



2015

September



2015

November



2016

January



2016

February



2016

March



2016

April



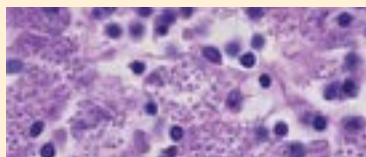
2016

May



2016

June

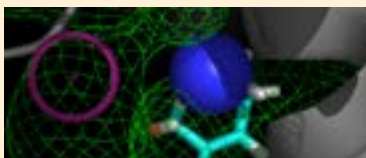


- RGC develops **initial plan** for Academic Research Services



- \$1.41M **NIH award** (Kenneth Sherman, MD, PhD)

- RGC begins to develop **faculty development plan** for research



- Two **Junior Pilot Awards** funded

- Call for **Senior Pilot and Rehn award** submissions
- \$1.49M **NIAID award** (Kenneth Sherman, MD, PhD)
- \$2M Joseph E. Palascak, MD **Endowed Chair in Bleeding Disorders and Clotting** established



- First **Collaborative Challenge Award** funded

- **Research Review Committee** formed
- \$2M Evelyn V. Hess, MD **Endowed Chair for Lupus Research** established
- \$5,000 **IMSTAR fund** established



- **Academic Research Services launched**
- 2nd Annual **Research Symposium**
- **Trainee Grand Rounds**

- **Clinical Scientist Training Program** graduates trainees Trisha Wise-Draper, MD, PhD, and Corey Clay, MD, PhD
- \$5,000 Pulmonary **Fellowship development fund** established



DIVISION OF
Cardiovascular Health and Disease





Cardiovascular Health and Disease

Richard C. Becker, MD
DIVISION DIRECTOR



Richard C. Becker, MD
DIVISION DIRECTOR

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

Our visibility on the local, regional, and national stage of academia is the end-result of collaboration among current faculty, support of early-stage faculty, retention of established investigators, and strategic recruitment of NIH-funded scientists and clinician-scientists.

The division employs a programmatic, theme-based approach to research that is aligned with strategic clinical services in advanced heart failure, heart transplantation, vascular medicine, thrombosis, arrhythmias, valve-related heart disease, cardiac imaging, recovery and rehabilitation science, and coronary artery disease. This approach was specifically chosen to engage all faculty, fellows, and clinical staff in one or more components of the division's research enterprise.

Our research includes the development of new drugs, devices, technologies, and cell-based therapies. Several new and exciting advances made within the past year by our faculty investigators include: ultrasonic sonochemistry for scavenging dissolved oxygen via acoustic droplet vaporization by Kevin Haworth, PhD; the role of HuR in pathological ventricular remodeling and cardiac fibrosis by Michael Tranter, PhD; the development of intravenous probenecid as a treatment for acute decompensated heart failure by Jack Rubinstein, MD; and new, app-based technology that provides a complete software solution to overcoming barriers to successful patient recruitment in clinical trials by Dylan Steen, MD. Each of these advances has been funded through the National Institutes of Health and intramural research grants offered through the University of Cincinnati, the College of Medicine, the UC Heart, Lung and Vascular Institute, and the Department of Internal Medicine.

In the coming year, new research initiatives will focus on cardiac myosin-binding protein C in myocardial ischemia and myocardial infarction, genome-phenome relationships in hypertrophic cardiomyopathy, and developing therapies for heart failure in patients with a preserved ejection fraction. The Division of Cardiovascular Health and Disease is fully committed to making major research contributions to the institution at large and its distinguishing academic signature.

The Fast Track

Assistant Professor Michael Tranter has found early-career research success at UC

In 2012, UC's Department of Internal Medicine invested in a young cardiovascular researcher named Michael Tranter—and won big. Tranter, who was just two years into his post-doctoral work at the time, stayed in Cincinnati for the chance to build a career as promising young scientist.

But by July 2016, Tranter, now an assistant professor in the UC College of Medicine's Division of Cardiovascular Health and Disease, had received two important grants. In January 2016, he received an American Heart Association Scientist Development Grant; and in July 2016 he received a five-year R01 grant of over \$1.7 million from the National Institutes of Health that will help his team of UC researchers continue their investigation of the protein human antigen R (HuR) and its role in cardiovascular disease, with the ultimate goal of translating this research to improve patient health.

Tranter, who is collaborating on the project with Jack Rubinstein, MD, associate professor in the UC College of Medicine and UC Health cardiologist, is just 35 years old—nearly a decade

younger than the average first-time NIH R01 grant recipient. The Division of Cardiovascular Health and Disease has made additional significant investments in new faculty under the leadership of Richard Becker, MD, and Tranter says there is definitely a youthful and optimistic buzz about the research outlook for the division.

But Tranter is not dwelling on his accomplishments—he is focused on the work, and is particularly excited about possible translation of the current NIH funded research to an impact on human health. Currently, Tranter is working with a cancer biologist at the University of Kansas who has developed an inhibitor for the HuR protein, which Tranter is applying to his cardiovascular models.

“We’re excited about pushing this small molecule inhibitor of HuR as a potential future therapy for heart patients in five to 10 years,” Tranter says. “Ultimately, you want to see how your research has changed human health in some way—our team wants to see the impact of our work help change the way people with cardiac hypertrophy and heart failure are managed clinically,

whether that’s just a change in how we handle current therapies or the advent of an entirely new therapy.”

Tranter also participated in the I-Corps@Ohio program this summer, which is modeled after a National Science Foundation program focusing on commercializing technology from research labs. Tranter collaborated with Laura Sagle, PhD, assistant professor of chemistry at UC, on a new type of drug screening technology that has also received a small pilot grant from UC for development. “The I-Corps program has taught us how to think about the commercialization value of what we’re doing in the lab, and we’re now starting our own business and looking for outside investments,” Tranter explains. “It would allow us to spin technology out of the lab every time something arises.” In the past year, Tranter has filed two separate provisional patents and is currently working with a team of engineering students to design a device for use in mouse models of cardiovascular disease that will likely yield a third patent application.

Tranter’s work hasn’t gone unnoticed by internal medicine’s leadership.

“Mike is exactly the kind of researcher that UC wants to attract and retain,” explains Carl Fichtenbaum, MD, associate chair for translational research. “He is a great example of the success of our junior investigators. We are all very proud of him and his accomplishments and look forward to a very bright future.” •

“...there is definitely a youthful and optimistic buzz about the research outlook...”

“Our team wants to see the impact of our work...whether that’s just a change in how we handle current therapies or the advent of an entirely new therapy.”





Richard C. Becker, MD

Fellow of the American Heart Association (FAHA)
 Stonehill Endowed Professor of Medicine
 Chief, Division of Cardiovascular Health and Disease

- coronary heart disease
- vascular biology
- thrombosis
- nucleic acid aptamers for thrombotic diseases and conditions
- nucleic acid scavengers for autoimmune and other inflammatory conditions
- molecular pathways in systemic hypertension and target organ injury
- role of intestinal microbiome in anticoagulant drug safety

I am currently the Stonehill Endowed Chair Professor of Medicine, chief of the Division of Cardiovascular Health and Disease, and director of the Heart, Lung and Vascular Institute in UC's College of Medicine. I'm also director of Cardiovascular Services for UC Health. My academic career has centered on coronary heart disease, vascular biology and thrombosis and is currently funded by a NHLBI R01, a Doris Duke Foundation Grant, an American Heart Association Collaborative Science Award and a NHLBI U54 grant from the Translational Centers for Thrombotic and Hemostatic Disorders. The U54 has supported doctoral candidates, post-doctoral fellows and early career investigators. I also have mentored fellows during their transition to faculty through American Heart Association Fellow-to-Faculty

awards, K12s, T32s and other career development pathways.

Our group is actively involved in the investigation of nucleic acid aptamers that are designed to target coagulation proteins and their complementary antidotes (drug-antidote pairs for the treatment of thrombotic diseases, disorders and conditions), nucleic acid scavengers for the treatment of autoimmune and other inflammatory conditions, molecular regulatory pathways in systemic hypertension and target organ injury, and the contributory role of the intestinal microbiome in anticoagulant drug safety.

My primary collaborators are at Duke University School of Medicine (Bruce Sullenger, PhD, Tom Povsic MD, PhD) and Cincinnati Children's Hospital Medical Center (Elaine Urbina, MD).



Stephanie H. Dunlap, DO

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

- clinical trials for cardiomyopathy and heart failure
- end-stage heart failure including assist devices and transplantation
- ultrafiltration machines
- implantable devices
- injected stem cells for heart failure

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

During the past year, we conducted a trial with biomarkers, and we are using these biomarker proteins found in the blood stream of patients with

heart failure to augment their medical therapy for heart failure. We are starting a very exciting new trial that will study the effects of injecting stem cells into the hearts of patients resistant to all other therapies for heart failure.

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

Mohamed A. Effat, MD

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



I am an active researcher in the Division of Cardiovascular Health and Disease. I have been involved in many investigator-initiated clinical and translational research studies, as well as national and international clinical trials. My research interests focus on exploring innovative concepts around incorporating fundamental fluid dynamics principles into the physiological evaluation of cardiovascular blood flow. My research also explores the application of new fluid dynamics-based measures for determining the severity of aortic valve stenosis, while linking these parameters to long-term survival status. We have recently concluded a large clinical outcome study (ClinicalTrials.gov identifier NCT01719016) funded by a VA Merit Review Grant.

I am currently seeking NIH multi-site clinical trial funding (PAR-12-128 Collaborative R01) for the next phase of our advanced research on the physiological assessment of coronary disease in the cardiac catheterization laboratory. I have been closely involved with the theory, design and conduct of the research studies that produced the proof of concept and provided the pilot data supporting the

feasibility of investigating our novel parameters in this planned clinical trial. This trial will determine the clinical applicability of our proposed indices for coronary and aortic valve disease evaluation. By providing evidence for improved clinical decision making on the basis of such novel endpoints, this body of work may help improve and refine the practice guidelines and open new horizons in relevant medical settings well into the future.

I have spearheaded a collaborative research effort between investigators from the Division of Cardiovascular Health and Disease and the College of Engineering and Applied Science. Our research team conducted numerous experiments in animal models and humans in order to illustrate and validate the functional role of novel parameters for improving the evaluation and diagnosis of coronary artery disease.

I have been living in the Cincinnati area for the past 11 years. My wife and I enjoy many outdoor activities, and I also enjoy watching and playing soccer with our children.

- innovative use of fluid dynamics in evaluating cardiovascular blood flow
- fluid dynamics-based measure of aortic valve stenosis
- indices proposed for coronary and aortic valve disease evaluation
- physiological assessment of coronary disease in the cardiac catheterization laboratory
- collaborations with College of Engineering and Applied Science

PERSONAL

- outdoor activities
- soccer with my children



David Feldman, MD, PhD

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

- improving heart failure management
- defining mechanisms of cardiac remodeling
- G protein-coupled receptor (GPCR) signaling
- mechanisms of immunity in heart failure

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

My long-term goal is to improve heart failure management and ultimately reveal novel opportunities for novel therapeutic options brought from the “bench” to the “bedside.” To accomplish these goals, I have developed a research environment that is highly organized and multi-disciplinary. I also have been fortunate to have long-term R01 funding in

mechanisms of reverse remodeling during CRT in heart failure, as well as several additional grants from other sources. I also study mechanisms of immunity in heart failure and mechanisms to improve heart transplant functions.

In addition, I remain active in clinical trials—I have been involved with more than 50 trials and have served as a national/international steering committee member on two of those trials. My accomplishments, recognized by my peers, have allowed me to serve on the guidelines and research committees for both the Heart Failure Society of America (HFSA) and the International Societies of Heart and Lung Transplant (ISHLT).

Myron C. Gerson, MD

Emeritus Professor of Medicine
 Director of Electrocardiography
 Director of the UC Medical Center Exercise Laboratory
 Division of Cardiovascular Health and Disease



My primary research program involves innovation related to the new generation of nuclear cameras for cardiac imaging involving cadmium-zinc-telluride (CZT) technology. This includes validation of diagnostic indices, new imaging protocols that improve clinical efficiency, and assessment of adjunctive findings that may improve diagnostic accuracy. The second major area of investigation involves application of a new stress-testing modality, the anti-gravity treadmill. Projects in this area include application of the anti-gravity treadmill for stress myocardial perfusion imaging for patients who are unable to exercise to target heart rate on a standard treadmill.

In our manuscript released electronically June 2016, validation and a cut-off value are provided for transient left ventricular cavity dilation (an indicator of extensive coronary artery disease) that is widely used with conventional nuclear cardiology cameras, but was not previously validated using an upright CZT camera. The exercise laboratories of UC Medical Center and West Chester Hospital use an upright CZT camera for research and clinical studies. Myocardial perfusion imaging is the most widely used method for diagnosis of coronary artery disease. The CZT camera is the most important hardware breakthrough for myocardial perfusion

imaging in decades. The UC Medical Center Exercise Laboratory is also using the AlterG anti-gravity treadmill, which is on loan for research only. It is likely to provide a major breakthrough in cardiac stress testing.

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

I am the faculty mentor for cardiology fellow Fahad Waqar, MD. As a first-year fellow, Waqar has already published a review article and an editorial in a major peer-reviewed journal and is a central figure in our CZT research program. I also have served as the principal investigator guiding Patrick Daly, MD, in his productive investigation of new applications of the anti-gravity treadmill. Additional supervision of research projects involves UC cardiology fellows Naseer Khan, MD; Steven Rudick, MD; and Mayhar Khaleghi, MD. I provide continued research mentoring for Zenith Jameria, MD, at the University of Illinois at Chicago on his investigations of the CZT camera. I also am mentoring UC medical student Nischelle Kalakota.

My hobbies include bicycling, travel and classical music.

- cardiac imaging involving cadmium-zinc-telluride (CZT) nuclear camera technology
- cardiac stress-testing using the anti-gravity treadmill
- collaboration with Department of Radiology, Nuclear Medicine division

PERSONAL

- bicycling
- travel
- classical music



David M. Harris, MD

Assistant Professor
 Medical Director, 6 South Cardiovascular Services
 Assistant Director, Cardiovascular Fellowship
 Division of Cardiovascular Health and Disease

- cardiac MRI
- echocardiography
- MRI evaluation and risk stratification of ischemic and non-ischemic cardiomyopathies, particularly stress-induced cardiomyopathy
- links between pericardial adipose and inflammation in HIV, coronary artery disease patients

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

I am interested in the MRI evaluation and risk stratification of

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

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



Kevin J. Haworth, PhD

Assistant Professor of Internal Medicine
 Division of Cardiovascular Health and Disease

- acoustic droplet vaporization for drug delivery, ablation, imaging
- signal processing for both ultrasound and other data sources
- oxygen scavenging to attenuate reperfusion injury

PERSONAL

- grilling
- pizza enthusiast

I am the principal investigator of the Biomedical Ultrasound and Cavitation Laboratory (BUCL) within the Image-guided Ultrasound Therapeutics Laboratories. The BUCL specializes in the application of acoustic droplet vaporization, signal processing and ultrasound imaging algorithms. Acoustic droplet vaporization is the phenomena of selectively creating microbubbles by phase-transitioning micron-sized liquid droplets using focused ultrasound. Acoustic droplet vaporization is being explored for drug delivery, thermal ablation, molecular imaging and gas scavenging. A main focus of our lab is oxygen scavenging to attenuate reperfusion injury, a project funded via an American Heart Association scientist development grant.

Our signal processing and imaging work is centered on processing ultrasound signals to increase the informa-

tion that can be garnered from them. We also have experience in applying our algorithms to non-ultrasound signals and images, such as optical microscopy. An example of a past collaboration was our analysis of video microscopy of fluorescently tagged zebrafish hearts to estimate heart rate and cardiac output. The laboratory includes one postdoctoral fellow, Karla Mercado, PhD, and several biomedical engineering undergraduate students.

We have active collaborations with Christy Holland, PhD, (internal medicine), Doug Mast, PhD, (biomedical engineering), James Lin, PhD, (biomedical engineering), Yoonjee Park, PhD, (chemical engineering) and Ian Papautsky, PhD, (electrical engineering).

Outside of work, I enjoy spending time with my wife and young daughters, as well as grilling and eating pizza.

Christy K. Holland, PhD

Professor of Internal Medicine
 Division of Cardiovascular Health and Disease and Biomedical Engineering Program
 Director of Research, UC Heart, Lung and Vascular Institute
 Editor-in-Chief, *Ultrasound in Medicine and Biology*



Having been trained as an applied physicist at Wellesley College and Yale University, but immersed in medical research and education for the last 27 years, I have come to value a multi- and interdisciplinary team approach to problem solving. My research program is housed in the Cardiovascular Center of Excellence.

I am the principal investigator of an NIH R01 grant entitled “Ultrasound-Assisted Thrombolysis for Stroke Therapy,” and an NIH Research Supplement to Promote Diversity. Collaborators on this project include David D. McPherson, MD, who is developing echogenic liposomes for the evaluation and treatment of atherosclerosis in coronary and peripheral vascular beds; and Todd Abruzzo, MD, who is using an interventional vascular porcine arterial thrombus model to test treatment efficacy. Successful completion of these studies will contribute significantly to our long-term goal to develop an ultrasound-assisted thrombolysis system that delivers and enhances thrombolytic therapy in the cerebral vasculature and rapidly restores perfusion after ischemic stroke.

Through NIH supplemental funds, Karla Mercado, PhD, Kevin Haworth, PhD, and I are developing an ultrasound elasticity imaging technique to predict the rt-PA lytic susceptibility in order to guide the choice of appropriate therapies for stroke patients.

Mentoring young scientists is one of the most enjoyable aspects of my job and one of the most important things that can be accomplished, as the impact will be long term. I direct the Image-Guided Ultrasound Therapeutics Laboratories in the UC Cardiovascular Center (IgUTL), which focuses on applications of biomedical ultrasound, including sonothrombolysis, ultrasound-mediated drug and bioactive gas delivery, development of echogenic liposomes, early detection of cardiovascular disease, and ultrasound-image guided tumor ablation.

Outside the lab, I have performed locally for the past 20 years with the Knox Presbyterian Church Choir under the direction of Earl Rivers. My husband Scott and I commission sacred music annually. When the sun shines, I enjoy gardening and beekeeping in my backyard, and when the snow falls, I enjoy skiing with my family in Bachelor Gulch, Colo.

- applications of biomedical ultrasound
- ultrasound-mediated drug and bioactive gas delivery
- ultrasound-assisted thrombolysis for stroke therapy
- development of echogenic liposomes
- ultrasound-image guided tumor ablation

PERSONAL

- choral performance
- gardening, beekeeping
- snow skiing



Robert O'Donnell Jr., MD

Associate Professor
Division of Cardiovascular Health and Disease

- advanced cardiac imaging modalities in prognosis and diagnosis
- cardiac involvement in amyloidosis using gadolinium-enhanced cardiac MRI
- imaging to predict obstructive multi-vessel coronary artery disease
- collaboration on chest pain protocol in ER
- statins for coronary atherosclerosis in patients with HIV
- validation of solid-state SPECT system and software
- collaborations on interdepartmental care coordination

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

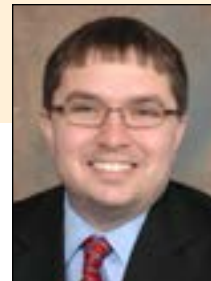
My ongoing collaborative studies focus on: the assessment of the emergency department chest pain protocol's ability to improve patient triage and outcomes; use of an antigravity treadmill to improve compliance with exercise myocardial perfusion testing; and assessment of the ability of statins to limit progression of coronary atherosclerosis (and prevent vascular events) in patients with HIV (a multi-institutional REPRIEVE cardiac CT substudy, in collaboration with the UC Division of

Infectious Diseases). Other areas of collaboration include a study on the retrospective assessment of CMR data for both research and quality control purposes, a study on the validation of solid-state SPECT system and software — including building normal files based on the Cincinnati patient population — and a study on the assessment of pericardial fat metabolism/inflammation by CMR in patients with HIV (I'm acting as mentor/co-investigator for the latter).

Evolving collaborative efforts include: work on the evaluation of prognosis and natural history of pulmonary hypertension in patients presenting to the emergency room with chest pain and found to have right ventricular abnormalities in the setting of normal myocardial perfusion imaging; reducing the impact of interdepartmental care coordination fall-out on patient outcomes in an urban population of chronically ill patients; and utilization of CMR to assess myocardial suitability for heart transplantation.

A. Phillip Owens III, PhD

Assistant Professor
Division of Cardiovascular Health and Disease



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

Our recent publication in the journal *Arteriosclerosis, Thrombosis and Vascular Biology* demonstrates that platelet accumulation and activation are detrimental in a mouse model of established AAAs. The results indicate that platelet inhibitors are beneficial in pre-existing aneurysms. Our future studies are examining the role of platelet signaling in AAAs.

My research is currently supported by an NIH R00 Pathway to Independence Grant to examine the role of

tissue factor and clot formation in AAAs, as well as two small university grants, and generous start-up funds from the College of Medicine.

I collaborate with several scientists at the University of Cincinnati including: Jack Rubinstein, MD (remote-ischemic preconditioning studies); Michael Tranter, PhD (obesity, remote-ischemic preconditioning studies and aneurysm); Sean Davidson, PhD (atherosclerosis and aneurysm studies); David Hui, PhD (atherosclerosis and aneurysm studies); and Vladimir Bogdanov, PhD (endotoxemia and coagulation). Outside of the university, I frequently collaborate with Matthew Flick, PhD (Cincinnati Children's Hospital Medical Center, obesity and fibrinogen studies); Alisa Wolberg, PhD (University of North Carolina at Chapel Hill, fibrinogen studies); Ryan Temel, PhD (University of Kentucky, hypercholesterolemia and coagulation studies); Wolfgang Bergmeier, PhD (University of North Carolina at Chapel Hill, platelet and aneurysm studies); and Scott Cameron, MD, PhD (University of Rochester, platelets) on several ongoing projects in my laboratory.

When I am not in the lab, I enjoy spending time with my wife and three young children. I am an avid movie watcher and a fierce fan of Cincinnati Bengals Football and Bearcats basketball.

- thrombosis in atherosclerotic and aneurysmal disease
- role of tissue factor and clot formation in AAAs
- platelet signaling in AAAs

PERSONAL

- movie enthusiast
- Cincinnati Bengals
- Bearcats basketball



Florence G. Rothenberg, MD

Associate Professor of Medicine
Division of Cardiovascular Disease and Health

- interventions for critically ill, non-acute coronary syndrome patients with troponin elevation
- PROMISE trial (role of CT angiography in detecting coronary artery disease)
- PRESERVE trial, on contrast-induced nephropathy in high-risk populations
- embryonic development of the heart and nervous systems
- serves on UC's "Women in Medicine and Science" to advance women in academic medicine

PERSONAL
• enjoy life

I am president-elect of the American Federation for Medical Research. Our group investigates interventions to reduce mortality in critically ill, non-acute coronary syndrome (ACS) patients with troponin elevation—a large high-risk population for whom we have little evidence-based research to guide management.

In a mixed population of nearly 20,000 medical and surgical ICU patients without ACS, we found that cTn was an independent predictor of 30-day mortality after adjusting for multiple variables, and that beta-blocker, aspirin and statin use was associated with 30-day mortality reductions in a cTn-dependent manner. This suggests that early cTn measurement may guide medical management of non-ACS critically ill patients. Ours is the first study to demonstrate mortality reduction with medical intervention in a cTn-dependent fashion. We are developing prospective investigations to test our findings.

I am a local-site investigator for the multicenter Veterans Administration Cooperative Study, the PRESERVE trial, designed to determine whether

N-acetylcysteine or sodium bicarbonate prevent contrast-induced nephropathy in high-risk populations. I served as the site principal investigator for the national PROMISE trial, which continues to yield insights into the role of CT angiography in detecting coronary artery disease. In the past I studied embryonic development of the heart and nervous systems, working with biomedical engineers to create high-resolution imaging technology to investigate embryonic physiology and hemodynamics.

I have served as a thesis committee member for five graduate students and have trained 11 post-graduate and eight medical students. I am the chair of the fundraising committee for Women in Medicine and Science, a new organization at UC whose goal is to advance “the full and successful participation and inclusion of women within academic medicine by addressing gender equity, recruitment and retention, awards and recognition, and career advancement,” according to the Association of American Medical Colleges.

In my free time I enjoy life.

Jack Rubinstein, MD

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



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

Our research has led us to investigate novel therapeutic options for the prevention and treatment of

heart failure, which are currently being developed for pre-clinical and early clinical trials. The research has been funded by multiple entities including the American Heart Association and the National Institutes of Health as well as various internal funding mechanisms.

I enjoy exercising, spending time with my family and drinking bourbon (usually not at the same time).

- therapeutics for heart failure
- role of transient receptor potential channels

PERSONAL

- exercising
- bourbon enthusiast

Sakthivel Sadayappan, PhD, MBA

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



I began my work at UC on August 15, 2016. My research is aimed at understanding the disease mechanisms underlying heart failure. Recent studies have found that the phosphorylation of cardiac myosin binding protein-C, a cardiac muscle myofilament protein, has a direct effect on the heart's contractile properties, sarcomere organization and cardioprotection in ischemia-reperfusion injury models. Current funding includes an ongoing AHA genome-phenome discovery grant and four NIH grants, including an NIH-NHLBI R01 grant, NIH-NHLBI R01 grant, NIH-NIAMS R01 grant and an NIH-NHLBI K02, as well as support from two industrial sources.

The long-term goals of the Sadayappan lab involve elucidating the causes of muscle-specific diseases at the molecular level and identifying therapeutic targets that will lead to the development of effective cures. Therefore, the short-term goals of current research studies involve identifying cardiac-specific early biomarkers of heart

failure; restoring sarcomere structure and function; and screening for compounds to improve sarcomere function during ischemia-reperfusion injury. In particular, hypertrophic cardiomyopathy (HCM) is a major genetic disorder among populations of South Asian descent, leading to contractile dysfunction, heart failure and sudden cardiac death. In an unrelated, but nonetheless pivotal, study, we are studying the differential roles of slow and fast myosin binding protein-C in skeletal muscles using both in vitro culture systems and animal models.

As part of our commitment to the development of young scientists, the Sadayappan lab provides expertise and training in cell biology, molecular biology, structural biology and physiology of the muscle and encourages collaborations in various areas of muscle biology.

I am a member of the Department of Internal Medicine Research Governance Committee and the UC Heart, Lung and Vascular Institute governance council in the UC College of Medicine.

- muscle biology
- disease mechanisms underlying heart failure
- cardiac-specific early biomarkers of heart failure
- restoring sarcomere structure and function
- hypertrophic cardiomyopathy among populations of South Asian descent
- differential roles of slow and fast myosin binding protein-C in skeletal muscles



Arnold Schwartz, PhD

Distinguished Professor of Internal Medicine
 Division of Cardiovascular Health and Disease
 Wendland Professor of Pharmacy

- first to clone human heart calcium channel
- sites for calcium channel blocking drugs
- mechanism of action of digitalis

Arnold Schwartz, PhD, is a 2016 Drake Medal recipient, awarded for his outstanding and unique contributions to medical education, scholarship and research. He was the first to clone and characterize a human heart calcium channel and identify the sites for the calcium channel blocking drugs diltiazem, verapamil and amlodipine, which are widely used to treat heart failure and hypertension. Prior to that, he established the mechanism of action of digitalis, the oldest known drug used to treat these heart conditions.

Schwartz earned his master's degree at Ohio State University and PhD at SUNY Downstate, Brooklyn.

Following postdoctoral fellowships in London and Aarhus, Denmark, he joined the faculty at Baylor College of Medicine.

Since 1977, Schwartz has nurtured hundreds of graduate and medical students and young faculty members at the UC College of Medicine as the principal investigator of a National Heart, Lung and Blood Institute training grant for 38 years, and a program project grant for 28 years.

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



Yukitaka Shizukuda, MD, PhD

Professor
 Division of Cardiovascular Health and Disease

- iron-overload cardiomyopathy
- echocardiography, cardiac MRI and coronary CT for clinical practice
- exercise physiology
- heart transplant

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

I also have assisted research projects with fellows and residents in our division and mentored numerous medical trainee-initiated research protocols for the Institutional Review Board for Protection of Human Subjects in the last 10 years. My research areas include iron-overload cardiomyopathy, utilization of echocardiography, cardiac MRI and

coronary CT for clinical practice, exercise physiology and heart transplant. My research is in part supported by intramural funds from the National Heart, Lung and Blood Institute.

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

Dylan L. Steen, MD, MS

Assistant Professor
 Division of Cardiovascular Health and Disease
 Director of Clinical Trials and Population Health Research
 for the UC Heart, Lung and Vascular Institute



My administrative role in the division and the UC Heart, Lung and Vascular Institute is to support the development of the clinical research infrastructure.

My personal research efforts are focused on two areas. The first is the control of modifiable, atherosclerotic risk factors including poor diet, sedentary lifestyles, tobacco use, obesity, hyperlipidemia, diabetes and hypertension. Current projects include a study of novel dietary interventions in partnership with the grocery industry to improve nutritional intake. Other current projects include the evaluation of lipid-lowering medication utiliza-

tion and cholesterol target achievement, and the determination of real-world cardiovascular event rates and risk model development in the United States, United Kingdom and France using large, generalizable, country-specific datasets.

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

- study of modifiable, atherosclerotic risk factors
- dietary interventions in partnership with the grocery industry
- medication utilization and cholesterol target achievement
- risk modeling using large, generalizable, datasets
- software development for clinical study patient recruitment

Michael Tranter, PhD

Assistant Professor
 Division of Cardiovascular Health and Disease



The long-term goals of my research are to increase understanding of the molecular mechanisms of cardiovascular disease. Within this realm, the ongoing work in the laboratory is broadly centered on post-transcriptional gene regulation in the setting of pathological left ventricular hypertrophy and fibrosis and the mechanisms of cardio-protection against ischemia/reperfusion injury.

My laboratory has identified human antigen R (HuR) as a new player in the development of pathological cardiac hypertrophy in response to pressure overload (e.g. chronic hypertension). A recent publication from the lab shows that HuR promotes cardiomyocyte hypertrophy downstream of p38 MAP kinase in an isolated neonatal cardiomyocyte model. Using a new inducible, cardiac-specific HuR knockout mouse created by our lab, we also show that deletion of HuR in the adult heart pre-

serves cardiac function while decreasing pathological ventricular remodeling following transverse aortic constriction (TAC), a model of hypertension-induced pathological cardiac hypertrophy. Ongoing projects are designed to identify the upstream signaling mediators of HuR in hypertrophic myocytes, the downstream target genes of HuR and the mechanisms by which regulation of these targets promotes pathology. This work is funded by an NIH R01 grant (HL132111).

Additional projects in the lab include the role of HuR in myocardial ischemia/reperfusion injury, ischemic preconditioning and diet-induced obesity. Finally, we are working to develop a novel drug-screening assay to allow for high-throughput screening and identification of unique small-molecule inhibitors of HuR for validation in our cell and animal models of HuR-mediated pathology.

- molecular mechanisms of cardiovascular disease
- identification of human antigen R (HuR) in cardiac pathologies
- HuR in hypertrophy, fibrosis, myocardial ischemia/reperfusion injury, ischemic preconditioning and diet-induced obesity

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Kenneth E. Sherman, MD, PhD
DIVISION DIRECTOR

The **Division of Digestive Diseases** has an active research agenda across the spectrum of gastrointestinal disorders. This includes basic, translational and research studies in esophageal disorders including: eosinophilic esophagitis and GERD; upper GI bleeding; pancreatobiliary disorders; inflammatory bowel disease; intestinal infections like C. difficile and liver disorders including viral hepatitis; NAFLD/NASH; PSC; PBC; and liver transplantation. Currently, the division has five active research laboratories. These laboratories are nationally recognized for their contributions to the understanding of new treatments of various areas of disease including: hepatitis C; the role of quasispecies in hepatitis C; interaction of HIV and hepatitis C viruses; viral host immunology; mechanisms of bilirubin transport and physiological roles of bilirubin; nutritional consequences of and treatment of liver diseases; inflammatory bowel diseases; and C. difficile infection.

These laboratories are available to medical residents interested in an elective experience in a basic research laboratory. A joint GI training grant with pediatric gastroenterology has recently been renewed and funded. This grant provides stipends for fellows interested in basic laboratory research. The division has an extensive and well-developed clinical research program. In addition to GI fellows, participation in the programs is also available to house staff. Some of these include treatment of chronic viral hepatitis, reflux esophagitis, upper GI bleeding, inflammatory bowel disease, irritable bowel syndrome and peptic ulcer disease. We anticipate even further expansion of our clinical trials program.

Real-World Impact

Professor Jason Blackard searches for answers to fight life-threatening viruses around the world



For Jason Blackard, an associate professor in the Division of Digestive Diseases, research isn't just about the excitement of discovery; it's also about making real societal impact. As a graduate student at Harvard University in 1995, Blackard found himself studying HIV—a virus that, although it had been discovered in 1981, still held numerous questions for researchers in the mid-90s.

“We knew that HIV existed but we didn't always know how it was killing people. We didn't have very good therapies,” Blackard says. “I was motivated by the fact that I was studying something

Research isn't just about the excitement of discovery; it's also about making real societal impact.

that had a lot of ethical questions and social considerations. I liked the complexity of it—not just the science behind it, the biology complexity—but what it meant at the societal level.”

Blackard began focusing particularly on HIV in the developing world, with his thesis on mother to infant transmission in Tanzania. After earning his doctorate in biological sciences in public health from Harvard and completing a postdoctoral fellowship at Massachusetts General Hospital, Blackard joined the College of Medicine faculty in 2005. Since then, spurred in part by a personal passion for traveling to remote areas, he has developed study abroad programs in Ghana, South Africa, China, and Botswana for UC students interested in public health and international research, and conducts federally funded research in South Africa. Blackard is also currently director of the UC College of Medicine Office of Global Health.

In 2007, Blackard received an American Society for Microbiology Young Investigator Award for research excellence in microbiology and infectious disease. More recently, his work has focused on new treatments for hepatitis C, the cases of which have risen in Cincinnati in recent years due to

“It's difficult to challenge the norm; but I take pride in the fact that I can do so.”

the heroin epidemic that's taken hold in many Midwestern areas. “Similar to studying HIV, focusing on hepatitis C has important consequences for people—in this case, intravenous drug users—who may not have a lot of advocates in the community,” Blackard says.

But no matter the research topic, he considers his most significant accomplishment to be collaborating with colleagues to challenge conventional thinking on issues that affect lives every day. “Just because we don't have data on something doesn't mean that it's not important,” Blackard says. “I like studying viruses in a geographic setting or context where there's not a lot of information. We're asking, in a petri dish, does it do something that nobody has ever characterized? It's difficult to challenge the norm; but I take pride in the fact that I can do so.” •



Khurram Bari, MD

Assistant Professor
Division of Digestive Diseases

- clinical research focus on viral hepatitis and non-alcoholic steatohepatitis
- efficacy of synthetic corticosteroid Budesonide for liver transplant recipients
- non-invasive tests for diagnosis and monitoring of hepatic sarcoidosis

PERSONAL

- coach youth soccer
- home improvement projects
- movie enthusiast

I am an assistant professor in the Division of Digestive Diseases and actively involved in clinical research. I am a co-investigator in 16 industry-sponsored clinical trials focusing on prevention and treatment of viral hepatitis and non-alcoholic steatohepatitis. The trials are conducted at the liver research center at the University of Cincinnati. I am principal investigator for a pilot clinical trial aimed at evaluating the efficacy and safety of Budesonide as an immune suppressing agent in place of prednisone for liver transplant recipients. Prednisone is an essential component of liver transplant immune suppression, but is also associated with many well-known adverse effects including hyperglycemia, new onset diabetes after transplant, increased rates of infections and metabolic bone disease. Budesonide, on the other hand, is a synthetic

corticosteroid with extensive first pass hepatic metabolism and only 10% systemic bioavailability and thus has the potential to provide liver specific immune suppression with minimal systemic toxicity. The goal is to improve long term outcomes of liver transplant recipients.

I am collaborating with investigators focused on transplant surgery and transplant pharmacy and have received a clinical research grant from the American College of Gastroenterology (ACG) to conduct a pilot study. I am also designing a study to evaluate non-invasive tests for diagnosis and monitoring of hepatic sarcoidosis in collaboration with Robert Baughman, MD, at Cincinnati Sarcoidosis Center.

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

Jason T. Blackard, PhD

Director, UC College of Medicine Office of Global Health
Associate Professor
Division of Digestive Diseases



I direct a basic and translational research laboratory that focuses on human and mechanistic studies to understand the interactions between various viral pathogens.

Hepatitis C virus (HCV) is a positive-strand RNA virus that infects over 170 million people worldwide. Multiple studies have demonstrated the adverse effects of human immunodeficiency virus (HIV) co-infection on liver fibrosis, HCV RNA levels, HCV disease progression, and response rates to HCV treatment. The mechanisms by which these two viruses interact remain unclear, as no direct virus-virus interactions have been demonstrated to date. Using a variety of cell culture, immunologic, and molecular virology techniques, as well as patient-derived samples, we are investigating the pathogenic and evolutionary mechanisms by which viruses interact with the host and cause disease. Current work in the laboratory involves studies of several hepatitis viruses, including hepatitis B (HBV), hepatitis E (HEV), and GB virus C (GBV-C), as well as HIV.

Funded Research Projects

- Characterizing genotypic and phenotypic diversity of the HCV RNA-dependent RNA polymerase (NIH R01)
- Investigating HBV infection and drug resistance in the context of HIV co-infection
- Evaluating extrahepatic replication of HCV

Collaborations

Current collaborators within the Department of Internal Medicine include:

- Kenneth Sherman, MD, PhD
- M. Tarek Shata, MD, PhD; and
- Carl Fichtenbaum, MD.

Collaborators outside of UC include:

- Department of Virology at the University of Limpopo (Pretoria, South Africa)
- Department of Clinical Virology at the University of Pretoria (Pretoria, South Africa)
- Department of Medicine at Bonn University Hospital (Bonn, Germany)
- Botswana-Harvard AIDS Partnership (Gaborone, Botswana)
- HIV Epidemiologic Research Study (HERS)
- Centers for Disease Control and Prevention; and
- University of Ghana Medical School (Accra, Ghana).

- virus-host mechanisms
- viral co-infections
- pathogens including hepatitis B, hepatitis E, GB virus C, HIV
- basic and translational studies



Mohamed Tarek M. Shata, MD, MSc, PhD

Adjunct Associate Professor
Division of Digestive Diseases

- cellular immune responses to HEV
- use of cART on the development of hepatic fibrosis
- characterization of gut-associated lymphocytes (GALT) in HIV, HCV and coinfecting patients
- role of immune responses in the emergence of drug mutants during therapy

PERSONAL

- soccer
- international travels

My research activities have been continuously supported by extramural funding, with funds from federal, international and industry sources. I have generated interesting data on the cellular immune responses to hepatitis E (HEV), using experimentally HEV-infected chimpanzees (from NIH), sera from chronic liver disease patients, and samples from an endemic area (Egypt). These data allowed us to be awarded an R21 grant (R21 A1067868), and an R01 (1R01 DK108362-01) from the NIH to evaluate the role of HEV in the United States. I was also a co-investigator in the R01 (2R01AI065256-06A1) grant titled "Antiretroviral Therapy and Hepatic Injury." The major goals of this project were to understand the relationship between initiation and use of cART, which includes the use of CCR5 blocking and its effect on the development of hepatic fibrosis. I was also awarded two grants from the Merck Investigator-initiated studies program. The major goals of those

grants were to characterize the gut-associated lymphocytes (GALT) in HIV, HCV and coinfecting patients and to identify the role of the immune responses in the emergence of drug mutants during therapy.

Internationally, I was awarded a grant from the USAID-Egypt Science and Technology. The primary goal of this project is to investigate the role of Th17 lymphocytes in the pathogenesis of Schistosoma infection in humans, in Egypt.

I served as a reviewer to international funding agencies such as Wellcome Trust and in the study sections of the NIH as a member the NIH International and Cooperative Projects-1 (ICP1) study section (2013-2016) and as ad hoc member of the NIH ACE study section and NIH Special Emphasis Panel. My teaching activities involve medical and graduate students, as well as, residents and fellows.

My hobbies include soccer and international travels.

Kenneth E. Sherman, MD, PhD

Gould Professor of Medicine
 Division Director
 Division of Digestive Diseases



I serve as director of the Division of Digestive Diseases, and have a research agenda focused on viral hepatitis with a secondary interest in autoimmune hepatitis and drug-associated hepatotoxicity. My research group has several NIH-funded studies designed to examine the relationship of viral evolution and host response to natural history and treatment response. We also devoted some effort to development and validation of new diagnostic tools. Current research projects are focused on hepatitis B, C, D and E.

Our group is closely associated with the AIDS Clinical Trials Group (ACTG), with an emphasis on laboratory and translational studies of viral hepatitis in those with HIV infection. We have approximately 25 active clinical trials, primarily in the area of hepatitis C treatment.

Collaborations**UC:**

- Jason Blackard, PhD
- Tarek Shata, MD, PhD, and
- Mario Medvedovic, PhD

Cincinnati Children's:

- Bruce Aronow, PhD

Outside Institutions:

- Adeel Butt, MD
(University of Pittsburgh)
- Lynn Taylor, MD
(Brown University)
- Valerie Lin, MD
(Harvard-Massachusetts General Hospital)
- Zachery Goodman, MD, PhD
(Innova Medical Center, VCU); and
- multiple national/international investigators in the ACTG.

- primary focus on viral hepatitis (B, C, D and E)
- associated with AIDS Clinical Trials Group, emphasis on viral hepatitis in those with HIV infection
- autoimmune hepatitis
- drug-associated hepatotoxicity



Bruce R. Yacyshyn, MD

Professor
Division of Digestive Diseases

- adhesion molecule (integrin) research in inflammatory bowel disease (IBD)
- biomarker and personalization of IBD therapy
- large data sets to study unmet GI needs
- clinical therapeutics and treatment of Clostridium difficile
- first non-Asian recipient of Thousand Talent award of the government of China
- academic appointment at Xiangya University, Changsa, China

PERSONAL

- outdoor enthusiast
- muscle car hobbyist
- sports geek of all types

Translational research in gastroenterology (GI) is the theme of my work in this area. I have been the lead investigator and principal investigator for a range of work. Notably, work in antisense DNA as a human therapy was the first in human for systemic applications of this technology. Adhesion molecule (Integrin) research in inflammatory bowel disease (IBD) led to several new drugs being developed including the first human description of Vedolizumab (ACT-1).

Our work now focuses on biomarker and personalization of IBD therapy, use of large data to study unmet GI needs, and clinical therapeutics and treatment of Clostridium difficile. I share research interests with my wife, Mary Beth Yacyshyn, MD, an immunologist.

I am a mentor to faculty, trainees and students. I represent the medicine faculty at the Faculty Forum, and serve on the University Honors Council. I am a member of the university’s advisory committee on China. I am the

first non-Asian recipient of the Thousand Talent award of the government of China, (8th cycle, Biotechnology). Together with this award, I have an academic appointment at the Xiangya University in Changsa, China, as a professor of translational medicine.

I have new drug approval letters from my short period mid-career working in industry at Procter & Gamble. There I developed opportunities to learn and collaborate at multiple levels in the drug development area. These are areas that we still focus on in our current research. With the sale of this company almost a decade ago, I have been at UC since. I have lived in Cincinnati for 12 years and worked at UC for almost 9 of them.

I have three grown daughters—two in medical school and one in veterinary medical school. During my spare time, I am an outdoor enthusiast, muscle car hobbyist, and sports geek of all types.

Mary Beth Yacyshyn, PhD

Adjunct Associate Professor Division
of Digestive Diseases



I have been involved in translational academic research for the past 20 years and my lab projects have focused on various aspects of human mucosal immunology. At present, I am concentrating on two projects. My lab is studying human-host innate immune differences in recurrent *C. difficile* infection (CDI). Using flow cytometry, cell culture, qPCR, immunohistochemistry, metabolomics and lipidomics, we are determining how cellular inflammatory differences effect recurrence or clearance. With our industry-sponsored funding, we are developing methods for early detection of recurrent CDI with the hope of preventing recurrence and changing initial therapeutic algorithms. To this end, we are collaborating with the lab medicine and surgical pathology groups at the UC Medical Center to set up clinical lab tests using our research. Secondly, we are developing a project in the area of obscure gastrointestinal bleeding and angioectasia. In the past five years there has been a dramatic increase in the detection of these intestinal bleeding

sites. Currently, there are no drugs available to treat this condition. We hypothesize that the development of aberrant capillaries and formation of these bleeding sites may be due to microbiome dysbiosis and host inflammatory process. We have just begun to study this underdeveloped area and through novel targeted bioinformatics, immunochemistry and qPCR, we hope to develop new guided therapeutics.

In the past seven years at UC, I have developed broad collaborations with basic scientists, clinical physicians and clinical scientists at UC Medical Center and Cincinnati Children's Hospital Medical Center. I have enjoyed mentoring and setting up lab projects for over 30 students in my 25 years of work in Canada and the United States.

My family and I have lived in Cincinnati for the past 10 years. My husband and I now enjoy spending time with our three grown daughters and two dogs. I love to cook, garden, travel, and spend time outdoors in the mountains or by the sea.

- human mucosal immunology
- human-host innate immune differences in recurrent *C. difficile* infection
- microbiome dysbiosis and host inflammatory process in obscure GI bleeding

PERSONAL

- cook
- garden
- travel
- time outdoors, in the mountains or seaside

DIGESTIVE DISEASES

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DIVISION OF
Endocrinology, Diabetes and Metabolism





Endocrinology, Diabetes and Metabolism

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



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

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

Current research activities in the Division of Endocrinology, Diabetes and Metabolism are focused on diabetes, integrated mechanisms causing obesity, metabolic signaling, lung and brain development and rare genetic lipid disorders. Clinical trials in the division focus on new treatments for diabetes and provide opportunities for physicians and patients to have access to the latest medications and treatments. For example, Robert Cohen, MD, is a co-investigator in a National Institutes of Diabetes and Digestive and Kidney Disease sponsored multi-center trial called GRADE (Glycemia Reduction Approaches in Diabetes).

Our faculty have many collaborative research efforts with other disciplines including adult and pediatric hematology, pediatric gastroenterology, hepatology and nutrition, pediatric human genetics and the Department of Pathology and Laboratory Medicine. Our overall goal is to build a robust, multi-disciplinary program that supports both laboratory-based and patient-based research in our clinical care, research and education programs for endocrinology disorders.

Inspired Investigation

Researcher challenges traditional thinking on what causes obesity



“Science and research are more important than ever. And with the technical advances and tools now available, this is the most exciting time in history to become a researcher.”

Assistant Professor Diego Perez-Tilve’s decision to pursue research was influenced by Santiago Ramón y Cajal, a Spanish neuroscientist who discovered the cellular organization of the central nervous system. “I always felt interested in science so becoming a researcher was a pretty straightforward choice,” Perez-Tilve says. “It gripped me because of the reward associated with unveiling a fragment of reality, of how things work, and the possibility of using that new knowledge to treat a disease.”

Perez-Tilve, who earned his PhD at the University of Vigo in Spain before joining UC’s Obesity Research Center and Genome Research Institute as a post-doctoral fellow in 2004, is now a researcher in the Department of Internal Medicine’s Division of Endocrinology, Diabetes and Metabolism. His most prominent research has focused on the hormone leptin, which has been of interest to researchers since 1994, when scientists discovered that a particular strain of obese mouse couldn’t produce leptin at all—which made them hungry, all the time.

But in 2015, a research team headed by Perez-Tilve conducted a study funded by the National Institutes of Health in which they blocked leptin action in both lean and obese mice. Both sets of mice ate more and gained weight to the same extent, debunking the theory that leptin action is

impaired in obese individuals—and proving the need for scientists to look for other potential therapy agents besides the hormone to treat obesity.

“Our research focuses on unveiling physiological mechanisms involved in controlling metabolism that, when disrupted, result in the development of obesity, diabetes and other associated comorbidities,” says Perez-Tilve. The researcher is currently working on the implementation of new techniques that allow temporal control of neuronal activity, allowing researchers to assess the contribution of a specific subset of cells in maintaining energy homeostasis within the human body. “Understanding how those mechanisms are regulated may provide novel drug targets or lifestyle interventions to improve patients’ health,” says Perez-Tilve.

Describing himself as a “fearless cook,” Perez-Tilve spends much of his free time with his two young toddlers and believes that the next generation of researchers should be inspired by the fact that their work is crucial to improving human health.

“Science and research are more important than ever,” Perez-Tilve says. “And with the technical advances and tools now available, this is the most exciting time in history to become a researcher.” •



Robert M. Cohen, MD

Professor of Medicine
Division of Endocrinology, Diabetes and Metabolism

- clinical and basic physiology research expertise in diabetes mellitus and metabolic disease
- HbA1c and blood glucose relationship
- red blood cell age/survival data and disease implications

My primary areas of research interest have focused on diabetes mellitus and its complications and the challenges to assessment of blood glucose control resulting from physiologic variation in the relationship between hemoglobin A1C (HbA1c) and blood glucose. This interest in HbA1c has led to an additional area of focus—the measurement of variation in red blood cell (RBC) survival and mean RBC age with implications for both diabetes and for hematologic diseases. As a result, I have extensive collaborations in hematology.

I have participated as a site principal investigator for NIH multi-center studies. The GRADE Trial is currently in progress for which we have recruited over 100 subjects in Cincinnati. The GRADE Trial is an NIH-funded multi-center comparative effectiveness study of the durability of second drugs for Type 2 diabetes in maintaining glycemic control. There are opportunities for ancillary studies, several of which the Cincinnati site is already participating in.

The ACCORD Trial and its ACCORDION extension have been completed, as have a number of industry-initiated clinical trials. I also provide expertise on clinical and basic

physiology research in diabetes mellitus and metabolic disease to a variety of collaborators across UC, Cincinnati Children’s Hospital Medical Center and the Cincinnati VA Medical Center.

Current funding includes a NIDDK GRADE Trial Department of Internal Medicine faculty pilot research award with pending grants for HbA1c and red blood cell lifespan studies.

Collaborations

UC collaborators:

- Robert Franco, PhD
- Christopher Lindsell, PhD
- Eric P. Smith, MD
- Shahriar Arbabi, MD
- Anastasios Angelopoulos, PhD
- Jonathan Bernstein, MD
- Khurram Bari, MD
- Jason Blackard, PhD
- Trudy Gaillard, PhD
- Hyon Kim, MD, PhD
- Matthew Tubbs, MD, PhD
- Ann Vuong, PhD.

External collaborators:

- Cincinnati Children’s Charles Quinn, MD.
- Emory University Clinton Joiner, MD, PhD.

Mercedes Falciglia, MD

Associate Professor
Division of Endocrinology, Diabetes and Metabolism



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

Through my participation in national and local efforts, focused on systems-based diabetes management, including roles as medical director of trans-disciplinary diabetes programs at UC Medical Center and Cincinnati VA Medical Center, I have gained experience in facilitating collaborative and interdisciplinary groups towards

performance improvement practices throughout our academic health center. Among the opportunities arising from these efforts is my role as the lead endocrinologist nationally for the NIH-sponsored SHINE Trial, a multicenter RCT to determine the efficacy and safety of glycemic control in patients admitted with ischemic stroke. In recent years, I have expanded the breadth of my focus to examine the implementation and processes of diabetes care during and surrounding the time of hospitalization.

Together with collaborators from the Division of General Internal Medicine, College of Nursing and College of Arts and Sciences, I have recently submitted a proposal for a pragmatic trial, "Sweet Transitions: The Coordination of Diabetes Care Between Hospital and Primary Care Settings."

- hyperglycemia and diabetes during acute illness
- causes of inpatient hyperglycemia
- glycemic control in patients admitted with ischemic stroke
- diabetes care during and surrounding hospitalization
- performance improvement practices

Shailendra B. Patel, BM, ChB, DPhil

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



My research interests include genetic disorders affecting cholesterol metabolism, genetic disorders of bile acid metabolism such as cerebrotendinous xanthomatosis, genetic disorders of cholesterol synthesis such as Smith-Lemli-Opitz-Syndrome and desmosterolosis. My interests also focus on genetic disorders of cholesterol, such as low cholesterol or high cholesterol and genetic disorders of cholesterol trafficking, such as sitosterolemia.

Clinical Phase II and Phase III trials

- Endocrine disorders
- Diabetes
- Lipid disorders

Pre-clinical models for obesity

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

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

- genetic disorders of cholesterol
- cholesterol synthesis, metabolism, trafficking
- bile acid metabolism
- cerebrotendinous xanthomatosis
- Smith-Lemli-Opitz-Syndrome
- desmosterolosis
- sitosterolemia



Diego Perez-Tilve, PhD

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

- neuroendocrine control of metabolism
- afferent endocrine signaling (GLP-1, ghrelin and leptin) in metabolism
- efferent mechanisms of metabolism control
- nutrient and environmental impacts on metabolic regulatory interactions

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

We have ongoing collaborations with the pharmaceutical industry to develop new therapies to treat obesity and diabetes.

Funding and Collaborations

UC collaborators:

- James Herman, PhD
- David Hui, PhD
- Yve Ulrich-Lai, PhD; and
- Charles Caldwell, PhD.

External collaborators:

- Richard Dimarchi, PhD, Indiana University at Bloomington;
- David D'Alessio, MD, Duke University;
- Kirk Habegger, PhD, University of Alabama at Birmingham;
- Matthias Tschöp, MD, Helmholtz Zentrum, Munich, Germany.

I am a member of the Digestive Health Center at Cincinnati Children's Hospital Medical Center. Our research group includes five staff members and has been supported by UC start-up funds, NIH and industry partners.

Jason J. Winnick, PhD

Assistant Professor
Division of Endocrinology, Diabetes and Metabolism



In humans, the liver plays a central role in the regulation of blood glucose homeostasis—consuming the sugar and storing it as glycogen during the fed state, then releasing it back into the blood on a need-basis when fasting. Unfortunately, these processes become dysfunctional in some people, thereby leading to diabetes which, if left uncontrolled, can hasten the development of micro- and macro-vascular disease.

The research that my colleagues and I perform revolves around the study of how hepatic glucose metabolism is regulated in both the healthy and diseased states. As such, one area of focus is hypoglycemic counter regulation. In preliminary animal studies, we showed that an acute increase in liver glycogen content can augment hepatic glucose production (HGP) in response to insulin-induced hypoglycemia. As a result, current NIH-funded studies are underway to investigate the translational potential of this finding to healthy humans and to people with Type 1 diabetes whose counter regulatory responses to hypoglycemia are diminished.

Chronic exercise training, with and without weight loss, can lower fasting HGP and improve blood glucose homeostasis in people with Type 2 diabetes. Accordingly, a second arm of the research that we perform relates to the whole body mechanisms responsible for these improvements and the study of how the intrahepatic pathways that contribute to HGP respond to lifestyle modification.

Finally, there is now overwhelming evidence demonstrating that Roux-en-Y gastric bypass (RYGB) surgery not only leads to significant weight loss in people who are obese, but it also markedly improves blood glucose homeostasis in people with Type 2 diabetes. The two primary metabolic improvements, as a result of RYGB, include increased insulin responsiveness to a mixed meal and lowered fasting HGP. Hence, we are interested in better understanding the mechanisms leading to reduced HGP after RYGB in people with Type 2 diabetes as well as the effect that the increased insulin responsiveness has on the liver.

- hepatic glucose production (HGP) in both healthy and diseased states
- hypoglycemic counter regulation and HGP
- how HGP pathways respond to lifestyle modification
- impact on HGP resulting from Roux-en-Y gastric bypass (RYGB) surgery



Matthew Wortman, PhD

Research Scientist
Division of Endocrinology, Diabetes and Metabolism

- integration of circulating and cellular metabolic signals in maintaining energy balance
- mitochondrial mediation of energy sensing pathways
- identified drug-like small molecules that modulate mitochondria function
- computational screening for drug targets
- allosteric activators of enzyme activity

PERSONAL

- gearhead activities
- nature photography

My work is focused upon understanding how organisms integrate circulating and cellular metabolic signals in order to maintain energy balance. Of particular interest is that both severely obese and lean animals maintain precise control of their body weight. This suggests that obesity is a shift in energy homeostasis rather than a failure to match energy intake to expenditure. Thus, a control system much like a thermostat enables all animals to defend their body weight and considerable effort is being spent to identify the factors that cause the ‘thermostat’ to move from lean to obese. Because the ‘thermostat’ is intact in obese animals, I believe it represents a viable drug target thus we are searching for small molecule ‘thermostat’ modulators that would enable obese and diabetic animals to defend a healthier body weight. Recently we identified the mitochondria as a key mediator of energy sensing pathways and identified drug-like small molecules that modulate mitochondria function and influence body weight.

My lab uses a combination of computational and molecular biology to identify and test drug targets.

Biological evidence is used to select drug targets then *in silico* techniques are used to screen for chemicals with binding potential from either our in-house library of ~250,000 drug-like compounds or public screening libraries. Hits from computational screening are tested in the lab for activity and the top modulators are reprocessed by computers to refine/improve activity. We have used this workflow to identify many first-in-class modulators of receptors and enzymes and we are particularly interested in identifying modulators of non-traditional targets like allosteric binding sites and protein and protein interactions. Example projects include allosteric activators of enzyme activity, inhibitors of protein and protein interactions and stabilizers of protein.

Current and past collaborators include researchers from UC and other universities around the United States and Canada, as well as a few industry partners. My lab has received funding/support from the NIH, NSF, U.S. Department of Defense, and U.S. Department of Energy.

In my spare time I enjoy gearhead activities and nature photography.

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DIVISION OF
General Internal Medicine





Mark H. Eckman, MD
DIVISION DIRECTOR

Research and clinical practice activities in the **Division of General Internal Medicine** bring together staff and faculty as well as investigators from a broad range of disciplines and departments. Primary focus research areas include: decision sciences, patient-centered outcomes research, health services research, clinical informatics, performance improvement and implementation research.

The focal point for research within the division is our Center for Clinical Effectiveness. The center provides a meeting place where investigators from multiple divisions, departments and professions gather to share their ideas and research expertise. Many projects, including funded research, have arisen through these interprofessional collaborations. A major strategic goal of the center is the development of a suite of analytically driven decision support tools. These tools take a variety of forms, including interactive web pages, and ultimately integration into the electronic health record and computerized physician order entry. They are designed to help clinicians, as well as patients, and their families grapple with complicated therapeutic and diagnostic decisions.

Decision analytic models can synthesize comparative effectiveness data from multiple clinical studies, as clinical trials seldom perform head-to-head comparisons of all of the treatment alternatives clinicians have for any particular disorder. In addition, these tools can incorporate patient preferences and values for health outcomes, which are of particular importance for preference sensitive decisions in which patients are trading off significant treatment side effects and adverse outcomes in the hopes of preventing further disease progression. Examples of current projects in this area include the development and research evaluating the impact of implementing an Atrial Fibrillation Decision Support Tool, which is now available to clinicians throughout UC Health as a tool embedded with our Epic electronic health record. This project has involved collaborations across a diverse group including cardiology, neurology, the Center for Health Informatics, the Center for Continuing Professional Development, the Department of English, the College of Design, Architecture, Art, and Planning, UC Health Information Technology, and the UC Health Primary Care Network. Another project in collaboration with the Division of Pulmonary, Critical Care and Sleep

Medicine involves the development of shared decision-making tools to assist patients with cystic fibrosis in prioritizing the slew of home therapies they must use on a daily basis. Yet another project in collaboration with an international group of investigators is studying the benefit of tools to support shared decision-making about antepartum thromboprophylaxis for pregnant women with a history of prior venous thromboembolism.

At a policy level, the center conducts cost-effectiveness analyses of diagnostic, treatment and screening strategies for both adults and children. Areas of particular interest include management of anticoagulation therapy in atrial fibrillation and venous thromboembolic disease, public health screening strategies for hepatitis B and C infections, neonatal infections and HIV/AIDS. In addition, through collaboration with the James L. Winkle College of Pharmacy, center staff and fellows investigate pharmaco-economic issues such as the impact of obesity on costs and outcomes of kidney transplantation. Members of the division are involved in NIH-funded research examining bariatric surgery for patients with morbid obesity. Projects include epidemiologic studies of the impact of bariatric surgery on the incidence of a variety of cancers, issues surrounding bariatric surgery in obese patients being considered for solid organ transplantation, such as kidney transplants, and shared decision-making approaches to the consideration of bariatric surgery. Other significant foci of research in the division include migraine headache, the impact of innovations in medical education, and implementation of performance improvement and system redesign. Faculty in our division have

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

Faculty in the division have conducted a number of studies examining the impact of various educational and operational innovations in the residency program, particularly related to the EIP (Educational Innovations Program) award granted by the ACGME. Other research foci have included predicting performance of house-staff on standardized certifying examinations, and medical student self-assessment using matrix evaluation, and the effect of changes in duty hours on resident education and patient care.

Medicine-pediatrics faculty in the division have received HRSA funding to establish a medical home for patients with sickle cell disease who are transitioning from pediatric to adult care. Infrastructure has been developed and studied to coordinate care between the medical home, pediatric and adult sickle cell centers at Cincinnati Children's Hospital Medical Center and UC Medical Center, and between community primary care sites. Faculty also address patients' educational needs about sickle cell disease and its complications. A variety of other implementation studies have included the development and evaluation of clinical pathways for chronic pain management, and performance improvement focused on optimizing pneumococcal vaccination.

Designing Discoveries

Research coordinator combines healthcare and graphic design skills

After 25 years in the nursing field, Ruth Wise, a senior research assistant in UC's College of Medicine's Department of Internal Medicine, knew she needed to expand her skill set to stay competitive in a changing healthcare landscape. The direction she chose, though, differed from—and surprised—many of her peers.

"I realized that changes in healthcare delivery required me to return to school to obtain either a PhD or DNS in nursing or become a nurse practitioner. Instead, I decided to switch careers to something that fit better with my later-in-life interests," says Wise, who started her career at UC in 1988 as a psychiatric liaison/substance abuse clinical nurse specialist (CNS) at UC Medical Center. In 2000, she enrolled at UC's College of Design, Architecture, Art, and Planning, earning her master's degree in graphic/digital design and later, a specialty in medical information design. She now combines her passions and abilities in her role as the research coordinator for two UC physician researchers: Mark Eckman, MD, the Posey Professor of Clinical Medicine, and Daniel Schauer, MD, assistant professor. Schauer's research focuses on decision-making related to bariatric surgery—currently, he is conducting a multi-center study

using data to examine the association between weight reduction through bariatric surgery and cancer risk.

Eckman, an expert in decision modeling, focuses most of his research on developing clinical strategies and informatics to prevent strokes in patients with atrial fibrillation including the development, refinement and testing of a computerized decision support tool to assist physicians and patients in deciding whether or not to use anticoagulants. "We have assembled a well-functioning, multi-disciplinary team of experts, called the Cincinnati Atrial Fibrillation Initiative (CAFI)," Wise says. "This team is composed of cardiologists, neurologists, internists, pharmacists, informaticists, nurses and patients. The AF decision-support tool is innovative and different from others like it; it incorporates both stroke and bleeding risks and patient preferences."

Besides coordinating the AF decision-support tool studies, Wise has designed the navigation and screens of CAFI's web-based applications, along with the CAFI newsletter. She also led and produced the re-design of the Center for Clinical and Translational Science and Training website. Though she regularly receives comments on the difference in her skillsets, Wise says the chasm is not as wide as it seems. "There is a connection

between both fields—as a psych CNS, I became an expert in human behavior and communication," she explains. "Graphic design involves solving visual communication problems. Same knowledge, different media."

Most of all, Wise says she loves the detail-oriented, goal-driven atmosphere of research coordination. "I love working with colleagues and patients, working through all the logistics of doing a study, operationalizing it and being curious about the outcome," explains Wise. "I love seeing the results of clinical research translated into reality." •

"I love working through all the logistics of doing a study, operationalizing it and being curious about the outcome. I love seeing the results of clinical research translated into reality."

Besides coordinating decision-support tool studies, Wise has designed the navigation and screens of web-based applications.





Tiffany Diers, MD

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

- interprofessional collaborative care models in primary care and underserved community settings
- quality improvement and implementation research
- Treatment Demonstration Project (sickle cell)
- group care programs (chronic pain; prenatal/infant care)

PERSONAL

- integrative health practices
- yoga
- relaxation coaching
- hiking

Coming from a background in improvement science, I became interested in studying the implementation of interprofessional collaborative care models to improve the health of vulnerable populations in primary care and underserved community settings. In my first research experience, I led a HRSA-funded Sickle Cell Disease Treatment Demonstration Project (SCD-TDP) from 2009-2015 in which we worked with people living with sickle cell and community-based organizations to develop primary care capacity, an adult patient advocacy group, a self-management program and an expanded interprofessional team including a pharmacist and a community health worker at the UC Medical Center Adult Sickle Cell Center. I was fortunate in the middle of that experience to become connected with interprofessional colleagues through the Cincinnati Interprofessional Care Collaborative, led by Jack Kues, PhD, and with Amy Short, MHSA, who became the project director of the SCD-TDP. Our work in sickle cell and later in chronic pain walked the interface between quality improvement and implementation research.

With Jill Boone, PharmD, James L. Winkle College of Pharmacy, and partners in the UC Center for Integrative Health and Wellness and in the Department of Family and Community

Medicine, I led the development of an integrative group visit program in Hoxworth Center for people living with chronic pain. This program showed benefit to patients in terms of pain, mood and function and has now been adopted by the practices as an ongoing clinical program. This project and several others in chronic pain were funded through Pfizer Independent Grants for Learning and Change.

Currently, Debora Dole, PhD, CNM, APRN, in the Center for Women's Health and I are seeking funding to study the impact of another group care program based on the Centering® model for women and infants.

Lastly, I work with interprofessional colleagues through the Health Professions Education Collaborative and we have collaborated on several funded projects with the St. Vincent de Paul agency in the West End as part of our Institute for Healthcare Improvement Open School chapter with students from the UC Academic Health Center.

On the personal front, I am a Cincinnati native, married to Fernando Martinez, who works as an orthodontist in private practice, and we have two teenage daughters, Nina and Maya. I have an interest in integrative health and enjoy yoga, hiking and learning to coach others in relaxation practices by practicing on my two teens.

Mark H. Eckman, MD

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



For the past 31 years, I have followed my passion as a general internist and a decision scientist, first as an active member of the Division of Clinical Decision Making at the New England Medical Center (1984-1999) and more recently as director of the Center for Clinical Effectiveness at the University of Cincinnati Medical Center (1999 – present). As both a researcher and a clinician, this environment has supported my interests in combining both clinical and theoretic applications of decision analysis to the care of individual patients and to broader issues of health policy. In particular my methodological interests have included the development of patient-specific decision support tools, cost-effectiveness analysis, and the continued study and development of new decision analytic methods.

Methodologically, my interests also extend to more generic issues of health policy planning and cost-effectiveness analyses, attempting to use quantitative methods to help make decisions about the allocation of increasingly scarce health care resources. I also have a long-standing interest in decision analytic issues surrounding anticoagulation therapy

within a variety of clinical situations, including atrial fibrillation, venous thromboembolism, and thrombophilic states.

Within our institution in particular and the profession in general, I am also deeply committed to pursuing the continued development and application of computational and information technologies to the practice of medicine and medical education. I believe that the challenges we encounter as both clinicians treating individual patients and as administrators managing and leading systems of care, provide the most fertile soil for interesting research and innovative problem solving. The model we are striving to create in our Center for Clinical Effectiveness is one that balances a portfolio of research projects that on the one hand address the operational and strategic needs of our own institution, but also utilize these real world challenges and investigations as the nidus for more scholarly work.

We have lived in Cincinnati for 16 years now and have two grown children. To unwind from work, I am the lead guitarist for a folk-rock band—The Creeky Knees.

- application of decision sciences to both individual patient care and to broader health policies
- development of patient-specific decision support tools
- decision analytics impacting anticoagulation therapy in various clinical conditions
- developing new methods of decision analysis
- pursuing computational and information technologies to medical practice and education

PERSONAL

- folk-rock guitarist



Vincent T. Martin, MD

Professor of Medicine
Division of General Internal Medicine
Co-director, Headache and Facial Pain Center, UC Gardner Neuroscience Institute

- risk factors for migraine headache attacks
- ovarian hormones as migraine trigger
- weather as migraine trigger
- role of comorbid medical disorders on migraine frequency

PERSONAL

- travel
- Italian culture and language enthusiast

Our research group has primarily focused on the identification of risk factors responsible for the triggering of attacks of migraine headache. We are best known for our studies defining the role of female ovarian hormones in the precipitation of migraine headache. We first conducted an interventional study regarding the effect of medical oophorectomy on the course of migraine headache in premenopausal women.

More recently we have performed an epidemiological study to determine if headache attacks are more common in perimenopausal women with migraine as compared to premenopausal women. We just completed an observational cohort study to determine whether ovarian hormones trigger attacks of migraine headache in pre-pubertal and pubertal girls with migraine headache.

Another primary area of research involves the role of weather as a trigger factor for migraine. We have recently completed a study in which mathemat-

ical models of surface weather variables were developed to predict attacks of migraine headache. We were also later able to link these models to the specific types of low and high pressure symptoms seen on surface weather maps. Other research areas have included how comorbid medical disorders (e.g. chronic rhinitis, asthma and Ehlers Danlos syndrome) influence the frequency of migraine headache.

We have a team of researchers that includes physician scientists, psychologists, meteorologists and biostatisticians. The epidemiological studies have been funded by the National Headache Foundation, pharmaceutical companies, and private donations.

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

Daniel P. Schauer, MD, MSc

Associate Professor
Division of General Internal Medicine



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

I am the principal investigator on an R01 that was funded by the NCI that will examine the relationship between obesity, cancer and intentional weight loss. I have experience using

many of the large publicly available datasets including the National Health Interview Survey that is linked to the National Death Index and the Nationwide Inpatient Sample in my research.

I have also collaborated with the HMO Research Network using their data sources. Additionally, as associate program director for resident research, I oversee all of the resident research in the Department of Internal Medicine.

- decision sciences
- patient-centered outcomes research
- comparative effectiveness research
- skills with large public datasets
- focus on obesity and bariatric surgery outcomes

Joel Tsevat, MD, MPH

Professor of Medicine
Associate Dean for Clinical and Translational Research
Co-Director of the Center for Clinical and Translational Science and Training
Research Director in the Center for Clinical Effectiveness, College of Medicine
Director of the R&D Committee at the Cincinnati VA Medical Center
Director of the Research Sub-Council for the Veterans Healthcare System of Ohio (Veterans Integrated Service Network [VISN] 10).



I am a past-president of the Society for Medical Decision Making. My primary expertise is in health-related quality of life, in particular, health status vs. utility assessment, along with HIV/AIDS outcomes research, spirituality/religion, cost-effectiveness analysis and decision analysis.

I have served as principal investigator on multiple federally-funded grants from NIH, VA, and AHRQ and I am one of the two principal investigators (with James Heubi, MD) on the University of Cincinnati's Institutional Clinical and

Translational Science Award (CTSA) grant.

I have published over 160 peer-reviewed papers, reviews, book chapters, and editorials.

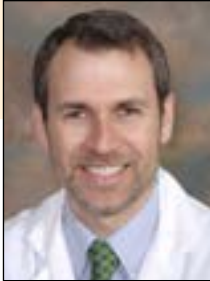
I mentor junior faculty, fellows, and residents doing clinical and translational research.

I am married and have two daughters in medical school. My hobbies include golf, running, and visiting major league baseball stadiums. I have watched a game in all 30 current stadiums and 24 that are now defunct.

- health-related quality of life assessment
- HIV/AIDS outcomes research
- spirituality/religion impacts
- cost-effectiveness analysis
- decision analysis
- CTSA co-PI

PERSONAL

- golf
- running
- MLB stadium lifelist



Eric Warm, MD

Richard W. and Sue P. Vilter Professor of Medicine
Division of General Internal Medicine
Program Director, Residency Program

- medical education research
- validation of observable activities for assessing resident practice competence
- assessment of procedural competence
- improving wellness and resilience among trainees
- improving clinical handoffs
- created educational dashboard for faculty and programmatic performance

I am involved in medical education research. Our team has a number of ongoing projects divided into several themes. Our assessment team is studying a new system we developed based on entrustment of observable practice activities mapped to milestones and entrustable professional activities. To date we have collected nearly 500,000 discrete data points. Our current work centers on validity interpretation of this data. Can a system such as ours determine when a resident is ready for unsupervised practice based on competence and not simply time-based metrics (e.g. after 3 years of training)? We have also created an educational dashboard for faculty and programmatic performance, and are studying ways to measure and

improve individual, rotation level, division, and departmental performance. Our team is also working on assessment of procedural competence, attempting to determine how we know a resident is competent for a given procedure, and at what rate competence declines over time.

Other members of our team are working on improving wellness and resilience among trainees and improving clinical handoffs. Team members have also collaborated with educators within our medical center, and in many other medical centers across the country. We are participating in and leading multiple national learning and teaching collaborative initiatives.

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GENERAL INTERNAL MEDICINE

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DIVISION OF
Hematology Oncology





Hematology Oncology

Tahir Latif, MBBS, MBA, FACP
INTERIM DIVISION DIRECTOR



**Tahir Latif, MBBS,
MBA, FACP**
INTERIM DIVISION
DIRECTOR

The **Division of Hematology Oncology** has seen tremendous growth over the last few years and currently has more than 30 faculty members. Many of them were recruited primarily to focus on providing state-of-the-art clinical care to patients, but they are increasingly becoming involved in clinical, translational, and basic science research pursuits. All faculty members contribute to advancing the field in different ways, either through leading clinical trials, enrolling patients in clinical trials, conducting fundamental laboratory research, or educating the next generation of leaders in the field. Our division faculty work closely and collaboratively with other faculty in our UC Academic Health Center in multidisciplinary clinics, tumor boards, and academically focused, disease-based groups, as well as through outside institutions.

CLINICAL RESEARCH: The division currently has 75 open clinical trials that are actively enrolling patients and these trials include pharmaceutical, cooperative group, and investigator-initiated trials. Over the past year, 121 patients were enrolled in these trials, which is the highest enrollment of any division in the University of Cincinnati Cancer Institute. The studies involve all types of cancer and therapies at different phases of their development. Our phase 1 studies program is one of a kind in the region providing patients, who generally had exhausted all standard treatment options, access to emerging promising therapies. Several of our faculty have developed investigator-initiated concepts and been awarded millions of dollars from industry sponsors to conduct these trials.

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

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

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

Going with the Flow

For one UC researcher, a passion to improve treatment outcomes runs in his veins



Associate Professor Vladimir Bogdanov, director of the Hemostasis Research Program in the Division of Hematology Oncology, chose his specialty based on an answer to a simple question—what research could help save the most lives?

While studying cardiology as a medical student, Bogdanov realized that it's the blood or vessel issues associated with many cardiovascular conditions that most affect outcomes for patients with cardiovascular disease. "It seemed to me that patients with these diseases very often die not because they have a faulty heart tissue, but because of issues that arise when blood fails to 'feed'

Bogdanov discovered a molecule called alternatively spliced Tissue Factor (asTF), which is part of the blood coagulation protein set and activates a number of intracellular pathways that promote cancer progression.

heart tissue adequately, and so I got more and more interested in blood and blood vessels," Bogdanov says.

He carried that interest through graduate school at Mount Sinai School of Medicine in New York, where Bogdanov worked in a vascular biology lab. Soon, he found himself immersed in blood coagulation and other hematological topics. "The more I studied, the more I realized that blood coagulation has quite a bit to do with malignancies as well—dozens of labs have found the hemostatic system to be disturbed by cancer," Bogdanov says. "That was the final turn that put me on the avenue that I'm on now."

And where Bogdanov finds himself currently is at the center of potentially groundbreaking research on pancreatic cancer, which has the highest mortality rate of all cancers—only about 8 percent of patients survive more than five years after diagnosis. During his post-doctoral work, Bogdanov discovered a molecule called alternatively spliced Tissue Factor (asTF), which is a part of the blood coagulation protein set that spurs the spread and progression of pancreatic cancer. "asTF activates a number of intracellular pathways that promote cancer progression," says Bogdanov, who is working with his colleagues to create a new therapeutic approach to slow down the progression of pancreatic cancer by targeting this molecule.

They are also studying whether asTF can serve as a circulating biomarker in devising personalized therapy approaches

that could enhance the chances of no-relapse post-surgery. "We're very, very hopeful that this will change, at least to some meaningful extent, the outlook on pancreatic cancer," says Bogdanov, adding that their findings could also lead to new treatment options in other cancers as well, most significantly breast cancer.

"We're very, very hopeful that this will change, at least to some meaningful extent, the outlook on pancreatic cancer."

In addition to his research on asTF, Bogdanov is studying the contribution of red blood cells (RBC) to obesity-related vascular pathologies, specifically chronic inflammation. He hopes that better understanding RBC biology could lead to new diagnostic or therapeutic strategies in obese patients suffering from vascular diseases as well as cancer. "Most of the research on RBC so far has been about their role in diseases such as sickle cell anemia, but not so much in cardiovascular disease or cancer," Bogdanov says. "We are thrilled because this research opens up an area that's not well studied yet potentially important, which is always good when we try to achieve significant progress." •



El Mustapha Bahassi, PhD

Research Assistant Professor
Division of Hematology Oncology

- brain tumor etiology, treatment strategies, biomarkers
- role of IDH1 mutation in gliomas
- using high throughput genomics (HTG) to study chromothripsis as possible factor in cancer initiation and progression
- developing non-invasive biomarkers to enhance tumor monitoring

PERSONAL

- hiking
- painting
- gardening
- carpentry

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

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

We have also been using high throughput genomics (HTG) to develop new hypotheses on brain tumors initiation and progression. We are investigating the initiating factors

of chromothripsis, a single catastrophic event that leads to massive chromosomal rearrangements that may not only contribute to cancer initiation but also possibly drive tumor progression. This new finding challenges the notion that all cancers progress as a result of the gradual acquisition of mutations over an extended period of time.

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

Our research is funded through the Neuroscience Foundation/Mayfield Clinic, the National Center for Advancing Translational Sciences of the National Institutes of Health, the Gromada Foundation and the UC Brain Tumor Center.

Outside of work, I like to hike with my wife or play soccer with my kids. I also enjoy painting, gardening and carpentry.

Vladimir Bogdanov, PhD

Associate Professor of Medicine
Division of Hematology Oncology



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

Our newly developed inhibitory antibody against asTF is currently being tested in animal models. The second is red blood cells (RBC) as novel contributors to vascular dysfunction in acute and chronic inflammatory states. We recently discovered that RBC can contribute to heightened clotting and obesity-related atherosclerosis, in large part because the levels of pro-inflammatory chemokines bound to RBC become

high on a high-fat diet. We hope that these observations will improve our understanding of RBC biology, and help develop new diagnostic and/or therapeutic strategies aimed at ameliorating obesity-related vascular disease.

Funding and Collaborations

My key collaborators are

- Nigel Mackman, PhD, University of North Carolina at Chapel Hill
- Henri Versteeg, PhD, Leiden University, The Netherlands
- Xiaoyang Qi, PhD, University of Cincinnati
- Neal Weintraub, MD, Georgia Regents University
- Theodosia Kalfa, MD, PhD, Cincinnati Children’s Hospital Medical Center.

My current trainees are Dusten Unruh, PhD, Albert J. Ryan, Fellow, 2014-15; Richard Godby, MS4, and 2016 HONORS Award from the American Society of Hematology; and Clayton S. Lewis, PhD, who began his postdoctoral fellowship in the fall of 2015.

My funding sources are as follows: R01CA190717; 2015 Rehn Award (UC College of Medicine).

- Hemostasis Research Program
- blood coagulation system in health and disease
- alternatively spliced tissue factor (asTF) as a therapeutic target in pancreatic cancer
- red blood cells as novel contributors to vascular dysfunction in acute and chronic inflammatory states
- role of RBC in obesity-related vascular disease



Mahmoud Charif, MD

Associate Professor of Medicine
Director, Mid-Level Providers
Program Director, Hematology Oncology Fellowship
Division of Hematology Oncology

- focus on clinical questions related to breast cancer
- breast cancer resistance to endocrine therapy
- interaction between HER-2 overexpression and endocrine resistance
- developed standardized scoring method for expression of estrogen receptor regulator MED-1
- the relationship between MED-1 expression and response to anti HER-2 therapy

As a member of the breast cancer team, I collaborate with researchers in my division as well as clinical researchers in other specialties including pathology and surgical oncology, and basic scientists to investigate clinical questions related to breast cancer.

I am particularly interested in breast cancer resistance to endocrine therapy and the interaction between HER-2 overexpression and endocrine resistance as well as the effect of HER-2 targeting on tumor response to endocrine therapy and possible mediators of that response. In a preliminary result of our investigation, we have shown improved response to the estrogen receptor antagonist fulvestrant with targeting of HER-2 overexpression with trastuzumab.

In collaboration with other clinical researchers and basic scientists, we have developed a standardized scoring method for the expression of the estrogen receptor regulator MED-1; and, we are investigating the relationship between MED-1 expression and response to anti HER-2 therapy.

I am the director of the Hematology Oncology Fellowship Program and I am currently mentoring some of our fellows and residents with projects related to breast cancer including patterns of utilization of dual anti-HER-2 therapy and cases of prolonged survival with metastatic triple negative breast cancer.

Rekha Chaudhary, MD

Adjunct Associate Professor of Medicine
Division of Hematology Oncology



I have been practicing neuro-oncology since 2010 and, therefore, most of my research centers on this topic. I am a primary investigator on multiple industry and cooperative group sponsored clinical trials. I am also chairperson of the UC Brain Tumor Center’s marketing committee and the co-chairperson of its clinical trials committee. Since I also have an interest in integrative oncology, I am writing and have received funding for a prospective trial looking at the feasibility of ketogenic diet in glioblastoma multiforme. Ketogenic diet in conjunction with radiation therapy in mice has been shown to significantly prolong survival and decrease tumor size. This trial is in conjunction with Robert Krikorian, PhD, and Amanda Stein, PhD, both from the Department of Psychiatry and Behavioral Neuroscience. They will be looking at neurocognitive outcomes with the ketogenic diet and the correlation with mitochondrial respiration in platelets. Tammy Ward,

registered dietitian from the UC Cancer Institute, has been trained in prescribing this diet and will be training trial patients. This trial has been funded by the UC Brain Tumor Center John C. Tew Endowed Chair Fund. We are also applying for funding to look at the effects of the ketogenic diet with MRIs performed with spectroscopy.

In my personal life, I enjoy trying to apply integrative medicine techniques to my own life including reading, practicing meditation and yoga and cooking a whole-food plant-based diet. I am currently writing a cookbook with Megan Tysoe, chef and owner of the Cincinnati restaurant, Rooted. I was featured in a small role in the documentary, “Plant Pure Nation,” and I present annually at a wellness conference called, “Sempre Sano,” in Tuscany, Italy. I have three children ages 12, 10 and eight, and my husband, Haleem Chaudhary, MD, is a total joint surgeon with Beacon Orthopedics.

- neurooncology research
- integrative oncology
- trial of ketogenic diet in glioblastoma multiforme

PERSONAL

- integrative medicine approach to lifestyle
- meditation and yoga practice
- cooking a whole-food plant-based diet
- present annually at a wellness conference called, “Sempre Sano,” in Tuscany, Italy



Zhongyun Dong, MD, PhD

Professor of Medicine
Division of Hematology Oncology

- prostate and lung cancer focus
- novel anti-cancer small molecules
- elucidate new class of proliferating cell nuclear antigen (PCNA) inhibitors
- studies on secretory phospholipase A2-IIa (sPLA2-IIa) as significant biomarker
- developing magnesium alloy-based drug delivery devices for cancer therapy

PERSONAL

- backyard fruit and vegetable garden

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

PCNA is essential for DNA replication and repair, cell growth, and survival. PCNA inhibitors bind to the interfaces of two monomers in the PCNA homotrimers, induce DNA damage and apoptosis, attenuate glycolysis, selectively inhibit tumor cell growth in culture, and retard tumor growth in animals without significant toxic effects on the host. We are currently conducting studies to further elucidate the molecular mechanisms underlying the differential effects of these compounds on tumor and normal cells and evaluate the therapeutic potentials of the compounds, alone or in combination with other DNA

damage drugs in several mouse models of human prostate cancer and lung cancer.

With respect to biomarkers, we have found that the secretory phospholipase A2-IIa (sPLA2-IIa) is significantly elevated in the plasma of patients with advanced lung and prostate cancer and is associated with poor prognosis. Moreover, sPLA2-IIa stimulates tumor cell growth and is a potential target for cancer therapy.

Another ongoing project is to develop magnesium alloy-based drug delivery devices for cancer therapy.

Our research, completed and ongoing, was supported by grants from NIH-NCI, DOD-PCRP, American Cancer Society, Natural Science Foundation, several pharmaceutical companies, and our institution.

I moved to Cincinnati in 2004 and have enjoyed living here ever since. My son is now a medical school student and my daughter is the first violinist in her high school. I enjoy having parties with friends and working in the small vegetable and fruit garden in our backyard.

James J. Driscoll, MD, PhD

Assistant Professor of Medicine
Division of Hematology Oncology



Our recent advances in genomics and proteomics in multiple myeloma (MM) have increased our understanding of disease pathogenesis, helped to identify novel therapeutic targets, and provided the scientific rationale for combining targeted therapies to increase tumor-cell cytotoxicity which abrogates drug resistance. Specifically, gene microarray profiling has shown major differences between normal plasma cells and cells from monoclonal gammopathy of unclear significance (MGUS) and MM cells, with further modulations within MM cells and in cells progressing to plasma cell leukemia. Therefore, we have profiled individual patients newly diagnosed with MM in order to tailor targeted therapy for them; it is likely that cocktails of therapeutics will be needed to overcome resistance.

My laboratory is also interested in understanding the role of the highly conserved ubiquitin+proteasome system (UPS) that plays a pivotal role in protein homeostasis and is critical in regulating normal and cancer-related cellular processes. The hierarchical nature of the UPS provides a rich source of molecular targets for specific intervention and has therefore arisen as a promising approach to innovative anti-cancer therapies. Pharmacologics

that inhibit the UPS have yielded unprecedented results which have doubled the survival of certain patients diagnosed with MM. However, many MM patients do not respond to proteasome inhibitors and those that do respond inevitably develop drug resistance.

In recent studies, many from our laboratory, we have demonstrated that the genetic heterogeneity strongly regulates the response of myeloma cells to proteasome inhibition. We have employed a multi-pronged approach using molecular and cellular biology tools, novel 3-D and murine models with MM cell lines, and patient tumor cells to validate the role of novel small molecules and immunotherapy as a clinically-relevant therapeutic strategy for MM. The long-term objective of this research project is to develop an integrated understanding of plasma cell signaling and to develop novel, investigator-initiated inhibitors of this pathway. Our work has laid a foundation for the new field of targeting the UPS and will eventually guide the design of current clinical trials for MM patients. These studies will advance our laboratory's long-term goal of developing novel therapies to treat MM patients.

- multiple myeloma (MM) focus
- plasma cell profiling for therapeutics
- targeting the ubiquitin+proteasome system (UPS)
- MM immunotherapy



Hala Elnakat Thomas, PhD

Research Assistant Professor
Division of Hematology Oncology

- pancreatic neuroendocrine tumors (pNETs)
- targeted therapies that inhibit mTOR signaling
- tumor-associated pathological manifestations such as carcinoid syndrome
- role of mTOR inhibitors in delay of cardiac carcinoid disease
- patient-derived tumor xenografts and cell lines from pNETs

My research is primarily focused on identifying novel treatments for pancreatic neuroendocrine tumors (pNETs) with special emphasis on targeted therapies that inhibit mTOR signaling. Our laboratory relies on biochemical, genetic and in vivo mouse preclinical studies to determine the mechanisms of response and acquired resistance to these treatments. Our studies extend to scoring these therapeutics not only at the level of tolerability and anti-tumor efficacy but also at the level of tumor-associated pathological manifestations such as carcinoid syndrome. In collaboration with Jack Rubinstein, MD, we have particularly focused on understanding the mechanism by which mTOR inhibitors delay onset of cardiac carcinoid disease and protect heart valves from fibrosis.

We collaborate with a number of oncologists both internally and nationally to establish feasibility of developing patient-derived tumor xenografts and cell lines from pNETs (obtained from the UCCI tumor bank). Our vision is to eventually contribute significantly to the development of a personalized medicine program for pNET patients in our institution and to expand into additional NETs.

Funding sources include Division of Hematology Oncology support (JIT and HOTSAs/HOPGA awards), departmental support (Faculty Pilot Project grant award), CCC JIT award and R21 funding through NCI as a co-investigator.

Robert S. Franco, PhD

Professor Emeritus
Division of Hematology Oncology



As an emeritus, I no longer have my own laboratory, but I continue to work with several principal investigators in areas that allow me to apply the expertise and techniques that we developed over many years. These projects are in the areas of cancer, diabetes, and sickle cell disease.

For cancer projects, Xiaoyang Qi, PhD, and I have examined the mechanism of phosphatidylserine externalization in cancer cells and the role it plays in the targeting of SapC-DOPS microvesicles for both imaging and therapeutic purposes.

For diabetes projects, Robert Cohen, MD, and I have applied novel red cell labeling techniques to determine the importance of red cell

lifespan in the interpretation of HbA1c and the importance of its variation in the mismatches that occur between HbA1c and blood glucose.

For projects related to sickle cell disease, Charles Quinn, MD, Cincinnati Children’s Hospital Medical Center and our UC red cell lifespan group have introduced an easy to use stable isotope technique for measuring red cell turnover and have compared this direct measurement to the surrogate markers that have been used in the past.

These collaborations have made this part of my career very enjoyable while also having the flexibility to travel and enjoy my semi-retirement.

- collaborations as emeritus
- mechanism of phosphatidylserine externalization in cancer cells (with Qi)
- red cell lifespan variability in HbA1c (with Cohen)
- red cell turnover measurement (with Quinn)

Saulius Girnius, MD

Assistant Professor of Medicine
Division of Hematology Oncology

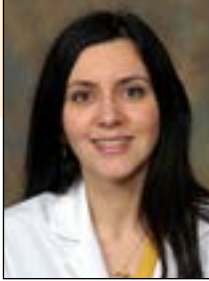


I am involved primarily in clinical research in hematology, both benign and malignant. My primary interest in hematologic malignancies is multiple myeloma (MM), for which I am the institutional principal investigator for a prospective, Phase 2 industry-sponsored trial. Likewise, I am a steering committee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

observational INSIGHT-MM trial, which is an industry-sponsored, international registry with planned accrual of >5,000 patients with MM.

I have active clinical and research collaboration with the hematologists at Cincinnati Children’s Hospital Medical Center, focusing on hemophilia, platelet disorders, and coagulopathy of vascular malformations.

- clinical hematology
- multiple myeloma (MM) focus
- INSIGHT-MM trial
- hemophilia
- platelet disorders
- coagulopathy of vascular malformations



Nooshin Hashemi Sadraei, MD

Assistant Professor of Medicine
Division of Hematology Oncology

- head and neck cancer clinical trials
- biomarkers that predict efficacy or toxicity
- DNA repair inhibition
- EGFR inhibition in combination with immune therapy

PERSONAL

- family hiking, traveling
- World Cup Soccer

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

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

therapy and DNA repair inhibition.

Conducting and designing these studies has allowed me to interact closely with my friends and colleagues at UC as well as leaders in the field nationally, and to collaborate with outside academic institutions, industry, and NCI cooperative groups. I have been working as medical chair on a concept to address the roles of immune therapy and stereotactic radiation. I am also working on a sub-study of an intergroup trial as a co-primary investigator to address the role of EGFR inhibition in combination with immune therapy. These studies, once open to accrual, will be available to all member sites in the United States and Canada. Finally, I am a member of NCI Head and Neck Task Force under the Head and Neck Cancer Steering Committee (HNSC).

In my free time, together with my husband and two young daughters, we enjoy hiking and traveling. I watch a lot of Soccer World Cup and Olympic Games on television, and hope to attend in person someday.

Nagla Karim, MD, PhD

Associate Professor of Medicine
Division of Hematology Oncology



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

inhibitor might improve the response to pemetrexed (Ceppi et al 2012). Moreover, there is an association between the K-ras wild type and SRC overexpression (Abel Karim, et al IASLC-AACR 2014).

I currently collaborate with Jiang Wang, MD, PhD, Department of Pathology and Laboratory Medicine; El Mustapha Bahassi, PhD, Division of Hematology Oncology; and John Morris, MD, Division of Hematology Oncology.

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

- lung cancer
- therapeutic/early phase clinical trials
- role of SRC overexpression

Tahir Latif, MBBS, MBA, FACP

Associate Professor of Clinical Medicine
Interim Division Director
Division of Hematology Oncology



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

intrathecal prophylaxis of high risk patients.

I am currently collaborating with Imran Arif, MD, Division of Cardiovascular Health and Disease; Mohammad Azam, PhD, Cincinnati Children's Hospital Medical Center; E. Steve Woodle, MD, Department of Surgery; and James Driscoll, MD, PhD, Division of Hematology Oncology. I will collaborate with researchers in the Division of Cardiovascular Health and Disease to define best treatment approaches of malignant pericardial effusions.

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

- clinical trial focus
- fostering patient enrollment in lung, head and neck, GI cancers
- treatment of CNS involvement by diffuse large B cell lymphoma



Carol Mercer, PhD

Research Assistant Professor
Division of Hematology Oncology

- mTOR pathway and autophagy regulation
- biological implications of therapeutic targeting of autophagy
- impact of mTOR inhibitors on different tumor subtypes
- metabolic impact of mTOR inhibition
- hepatocellular carcinoma (HCC)

My research interests are centered on the mammalian target of rapamycin (mTOR) pathway and the regulation of autophagy. My long-term goal is to understand the mechanisms that positively and negatively regulate autophagy and the biological implications of therapeutically targeting autophagy in tumor growth. An understanding of the role of autophagy in cancer is important because autophagy has been argued to either inhibit or promote tumor survival, depending on tumor type and tumor context. Allosteric mTOR inhibitors known as rapalogs are FDA approved for some cancers, and next generation ATP-site competitive inhibitors are currently in clinical trials. Importantly, these inhibitors also induce autophagy, making it critical to understand autophagy's role in the tumor setting. Using both cargo-based autophagy

assays and traditional LC3-II flux assays, we have demonstrated that a combination of two mTOR inhibitors potently induces autophagy and mitophagy in cultured cells and inhibits tumor growth in a mouse model of hepatocellular carcinoma (HCC). We suspect that autophagy may contribute to the growth inhibition of the bulk of the tumor, while promoting the survival of a small population of tumor initiating cells. We are currently investigating the mechanistic role of autophagy and mitophagy in the response of tumors to mTOR inhibitors; determining the impact of mTOR inhibitors on different tumor population subtypes; examining the metabolic impact of mTOR inhibition; and looking for drug combinations that will improve the tumor response in patients with HCC.

John C. Morris, MD

Professor of Medicine
Division of Hematology Oncology



My research focuses on immunotherapy of lung cancer. Lung cancer is the leading cause of cancer death with more people succumbing to it than the next four most common cancers combined. Despite recent advances in diagnosis and treatment, the mortality for lung cancer remains unacceptably high. We are studying the application of the immunostimulatory cytokine interleukin-15 (IL-15) for the treatment of lung cancer. Our laboratory has focused on using IL-15 in a vaccine strategy by expressing IL-15 and its receptor (IL-15Ra) in lung cancer stem cells (CSCs) as an antitumor vaccine. We have generated a series of lentiviral vectors expressing IL-15 and/or IL-15Ra under the control of a promoter that expresses in stem cells that were used to transduce a series of mouse lung cancer cell lines. Cancer cells transduced with these vectors demonstrated the ability to stimulate the proliferation of a T cell line in a bioassay. These cells were cultured under conditions that increase the number of CSCs that will then be used to vaccinate tumor-bearing mice in hopes of generating an effective

vaccine. Experiments in mouse lung cancer models are underway.

Currently, I have two postdoctoral fellows working with me, Donatien (Kamden) Toukam, PhD, and Ihab Eldoussouki, MD, PhD, and I collaborate with Jason C. Steel, PhD, Queensland University, Australia. We are funded through a generous grant from the Lcs Foundation.

I am the director of the Thoracic Oncology, Head and Neck Cancer, and Experimental Therapeutics/Phase I Programs. I am a full member of the Cincinnati Cancer Center, and co-director of the Lung Cancer Center of the University of Cincinnati Cancer Institute. I'm also a member of the Cancer Gene Therapy committee of the American Society of Gene and Cell Therapy (ASGCT) and sit on the Experimental Therapeutics Subcommittee of the American Society of Clinical Oncology (ASCO) Education Committee. I have clinical interests in lung and head and neck cancer and have an extensive background in early phase and first-in-human clinical trials, and drug development.

- lung cancer immunotherapy
- expressing interleukin-15 (IL-15) and its receptor in lung cancer stem cells as a vaccine strategy
- testing underway in mouse models
- early phase, first-in-human clinical trials, drug development



Olugbenga O. Olowokure, MD

Associate Professor of Clinical Medicine
Division of Hematology Oncology

- clinical research focus
- GI cancers
- gemcitabine plus cisplatin in advanced biliary cancers
- Sorafenib in hepatocellular carcinoma
- gemcitabine plus Nab-paclitaxel in pancreatic cancer
- pancreatic cancer epidemiology
- novel agents in colorectal cancer management

PERSONAL

- travel
- watch, play soccer
- running
- racquet sports

I specialize in gastrointestinal cancers such as malignancies of the pancreas, colon, rectum, anus, esophagus, stomach, small intestine, GIST tumors, carcinoid tumors, liver, gallbladder, and bile ducts/cholangiocarcinomas. My clinical research efforts focus on novel treatment approaches for gastrointestinal cancers and on improving current existing standards of care with an aim to preserve the patient's ability to function as normally as possible while on chemotherapy.

As our most senior GI oncologist, I am the principal investigator or sub PI on all GI related malignancy protocols at the University of Cincinnati Cancer Center. Enrolling patients, when possible, on clinical trials remains one of my top priorities.

I work with a multidisciplinary team that includes surgeons, radiation oncologists, pathologists, interventional radiologists, the liver transplant team, and basic scientists. Through these collaborations, we have opened up two investigator-initiated clinical trials at UC, UCC-GI 001 and UCC-GI 002 clinical protocols. In addition, a cholangiocarcinoma transplant protocol through collaboration with the liver transplant team was initiated.

I am collaborating with Xiaoyang

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

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

I have lived in Cincinnati for seven years. My wife also works at UC, and we have three children. My hobbies include playing with our kids, travelling, watching and playing soccer, running, tennis and racquetball.

Xiaoyang Qi, PhD

Professor
Division of Hematology Oncology



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

A variety of animal tumor models, including neuroblastoma, pancreas, brain, lung, skin, breast, prostate, and

leukemia, have been used for efficacy and toxicity studies of this new anti-cancer agent. I am the exclusive inventor for nine issued U.S. and foreign patents of SapC-DOPS technology. Based on intellectual property developed in my laboratory, over 30 patents have been filed worldwide at Cincinnati Children's Hospital Medical Center and the University of Cincinnati. SapC-DOPS patents have been licensed to USA-based Bexion Pharmaceuticals. Our translational research with Bexion has led to the development of a first-in-human (Phase I) clinical trial approved in 2016. We are confident that SapC-DOPS has the potential to be a targeted, potent, broad, and safe therapeutic agent for cancer patients. Other applications might include the development of novel diagnostic and imaging strategies.

My research projects are currently supported by multiple NIH grants (R01s, R21, R44Ib). My collaborators include Vladimir Bogdanov, PhD; T. Cripe (Nationwide Children's Hospital, Columbus); Ying Sun, PhD, Cincinnati Children's Hospital Medical Center; and R. Takigiku (Bexion Pharmaceuticals, Covington, KY).

- discovery of saposin C coupled dioleoylphosphatidylserine (SapC-DOPS) anticancer nanovesicles
- identified phosphatidylserine (PS) as the unique receptor for SapC-DOPS
- translation to preclinical research
- exclusive inventor on 9 issued U.S. and foreign patents
- phase 1 clinical trial approved in 2016



Neetu Radhakrishnan, MD

Adjunct Associate Professor of Clinical Medicine
Division of Hematology Oncology

- breast cancer
- lymphomas
- myeloproliferative disorders
- MS patients on taxane/platinum chemotherapy
- ethnic Asian, Southeast Asian, Middle Eastern cancer epidemiology

PERSONAL

- badminton
- dancing
- fine-tuning EPIC

My main areas of interest are breast cancer, lymphomas, myeloproliferative disorders, aHUS, and TTP. I am also interested in assessing the response of multiple sclerosis patients to taxane and platinum containing chemotherapy and includes assessing tolerability and outcomes at preliminary stages.

I am also interested in identifying, quantifying and characterizing the prevalence of breast cancer and prostate cancer in the Asian, Southeast Asian and Middle Eastern populations as data on these ethnicities are scarce in the United States.

I am the principal investigator for an open trial: tBRE 12-158: A Phase II Randomized Controlled Trial of Genomically Directed Therapy After Preoperative Chemotherapy in Patients with Triple Negative Breast Cancer. Also, I participate in cooperative group trials and facilitate tissue collection for various cancer biology programs through the University of Cincinnati Cancer Institute.

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



Atsuo T. Sasaki, PhD

Associate Professor
Division of Hematology Oncology

- pioneering focus on GTP and roles in primary/metastatic brain tumors
- discovered the missing GTP sensor
- collaborative, multidisciplinary research

We are pioneering a new field by focusing on an energy molecule, GTP (guanine triphosphate) and its roles in primary/metastatic brain tumors. With R01 funding, we have discovered the missing GTP sensor and published the finding in *Molecular Cell* and featured in *F1000Prime*, *Cancer Discovery*, and *Science Signaling*. I have published 47 research papers with more than 6,500 total citations (Hirsch citation H-index of 32). Since joining UC in 2012, I have received nine external sources of funding totaling over \$2.2 million.

Among factors for successful research, my lab most appreciates our many collaborators. We have active collaborations with two local, four national and six international research groups. The multidisciplinary research approach has resulted in multiple funding awards including an R01 grant, manuscripts including *Molecular Cell*, and the application of cutting-edge

research technologies, such as stable-isotope labeled metabolomics, NMR and X-ray structural analyses, and chemical library screening to identify new inhibitor/activator for the target enzyme.

As a mentor, I have assisted in the development of students, resident and post-doctoral fellows. All of my three previous post-doctoral fellows have received fellowship grants under my mentorship and have now become faculty members either in Japan or at UC. I have provided guidance to young researchers by lecturing to students and post-doctoral fellows locally, nationally and internationally. (I have delivered 37 invited lectures since joining the UC faculty in 2012).

My activities besides grant/manuscript writing are to discuss science, walk our dog, and spend quality time with my wife.

Trisha Wise-Draper, MD, PhD

Assistant Professor of Medicine
Division of Hematology Oncology



I am the principal or sub-investigator on several pharmaceutical and investigator initiated clinical trials. I am the lead investigator of a phase I study in head and neck cancer (HNC) patients studying the addition of metformin to cisplatin and a multicenter phase II trial studying the addition of pembrolizumab to standard of care treatment. Many samples obtained from these studies are analyzed in our own and collaborator laboratories of Pankaj Desai, PhD, Laura Conforti, PhD and Edith Janssen, PhD.

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

Specifically, we are interested in identifying mechanisms important for immunotherapy (anti-PD-1) resistance. We have identified a couple of potential mediators that we plan to target in tissues from patients resistant to immunotherapy. We have also identified the DEK oncogene as a possible blood biomarker and immune cell stimulator in HNC patients. We are now studying its role in cancer immune surveillance and outcomes. These studies are fundamental to identify patients likely to respond to particular treatment modalities and to develop new therapies that can easily be translated into phase I clinical trials.

I am the associate director of the Hematology Oncology Fellowship Program and assist trainees in their research pursuits. I am also integral in the execution and monitoring of phase I trials in our experimental therapeutics clinic. Funding includes institution pilot grants as well as a KL2 mentored award through the Center for Clinical & Translational Science & Training.

My hobbies include running, soccer and most recently Krav Maga.

- therapeutic resistance and biomarkers in cancer
- head and neck cancer (HNC) focus
- identifying key mechanisms for anti-PD-1 resistance
- addition of metformin to cisplatin for HNC in phase 1 trial
- addition of pembrolizumab in multicenter phase 2 trial
- DEK oncogene as biomarker

PERSONAL

- running
- soccer
- Krav Maga

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HEMATOLOGY ONCOLOGY

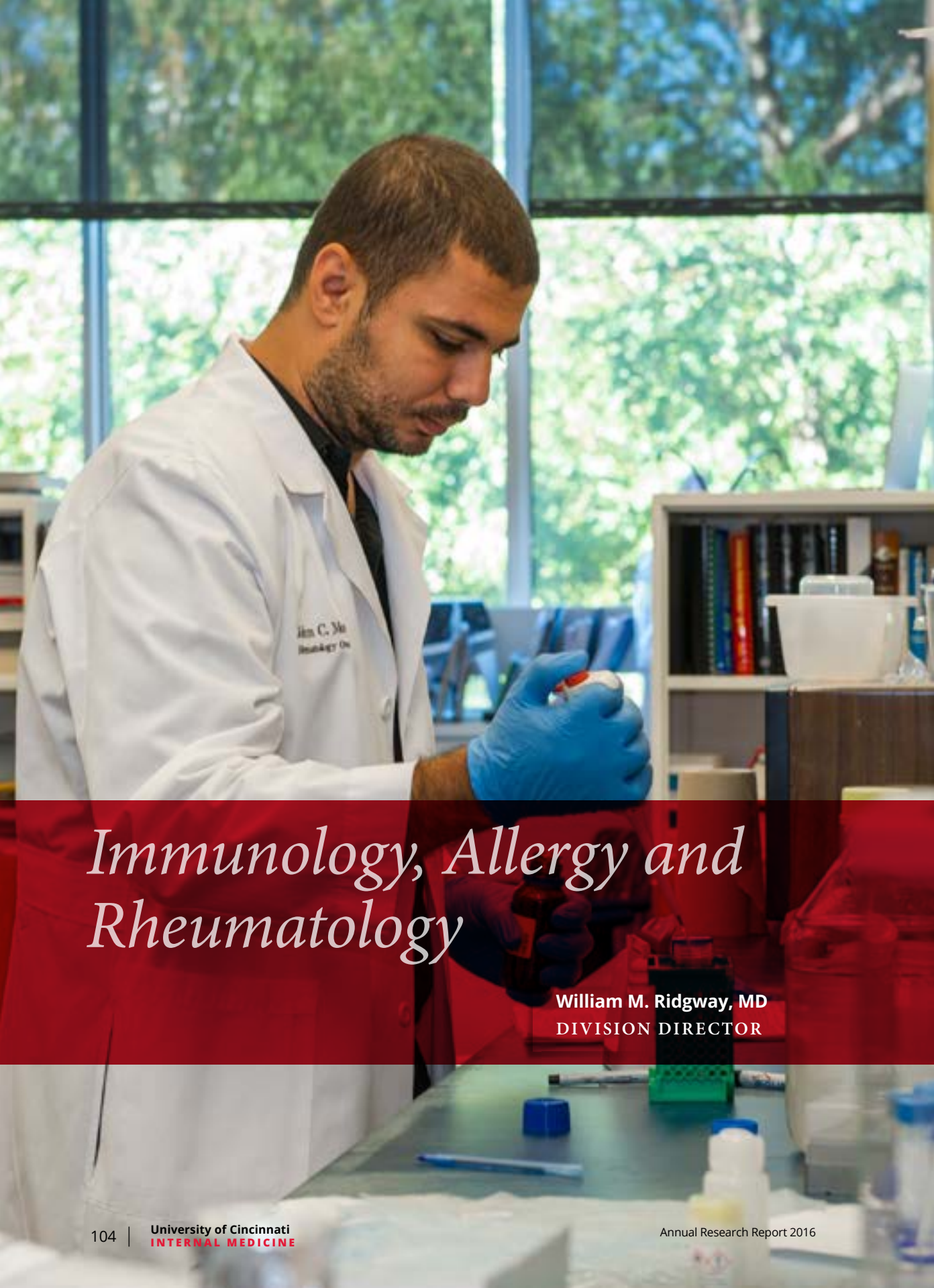
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DIVISION OF
Immunology, Allergy and Rheumatology





John C. Ma
Immunology Division

Immunology, Allergy and Rheumatology

William M. Ridgway, MD
DIVISION DIRECTOR



William M. Ridgway, MD
DIVISION DIRECTOR

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

Research in the division spans the spectrum of basic immunological research. Research projects include the following efforts: investigations to the pathogenesis of food allergy/hypersensitivity; anaphylaxis; new therapies for asthma and allergic diseases; mechanisms of occupational lung disease; pathogenesis of primary biliary cirrhosis and type 1 diabetes (organ specific autoimmunity); pathogenesis of cutaneous systemic lupus erythematosus (SLE); and novel therapies for autoimmune disease. The division has a T32 in allergy/immunology and has been an active participant in the CSTP program. Two separate ACGME accredited fellowship programs in the division produce academic allergists and rheumatologists. A recently hired investigator in immunology, Wenhai Shao, PhD, specializes in SLE mouse models and immune cell signaling.

Highlights of this year's research include the following achievements: publication of a novel approach to reverse acute type 1 diabetes by targeting innate immunity in the journal *Diabetes* by the Ridgway laboratory; a review highlighting work in Human IgE-independent systemic anaphylaxis was published in the *Journal of Allergy and Clinical Immunology* by the Finkelman lab; a collaborative study between the division and Cincinnati Children's Hospital Medical Center on defects of B-cell terminal differentiation in patients with type-1 kabuki syndrome was published in the *Journal of Allergy and Clinical Immunology* by the Jonathan Bernstein lab in collaboration with Andrew Lindsley, MD, PhD; and a study on genetic variants in TNF α , TGF β 1, PTGS1 and PTGS2 genes are associated with diisocyanate-induced asthma, published in the *Journal of Immunotoxicology* by the David Bernstein laboratory. Overall, researchers in the division published more than 50 articles this year.

A major effort during the next year 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. The Evelyn V. Hess, MD, Endowed Chair of Lupus Research is now officially established and the search for its first occupant will begin. The division will organize seminars to encourage cross disciplinary research in SLE that involves both basic investigators and clinicians.

Science as Art

One senior research assistant and artist finds beauty in the pursuit of new ideas



For Banurekha Kesavalu, pursuing a career in research was an easy choice—she has had a passion for biology since childhood. “Exploring new possibilities, trying out new hypotheses—these are the most interesting aspects of research to me,” says Kesavalu, now a senior research assistant at UC’s College of Medicine for Professor David Bernstein in the Department of Internal Medicine’s Division of Immunology, Allergy and Rheumatology.

Working with Bernstein, Kesavalu focuses on occupational (workplace) asthma—airway hyperresponsiveness caused by exposure to a specific agent or chemical present in a work environment. Specifically, the lab is studying the genes that have been found to be associated with occupational asthma and the underlying mechanisms related to their susceptibility. “It’s a wonderful feeling when hard work pays off, when you come up with results that help answer questions related to a project, and when peer-reviewed publications support your work.”

Kesavalu’s current position is the latest in a lifetime dedicated to science. After acquiring a master’s degree in life sciences in her native India, she worked on a mycobacterium tuberculosis genome project there, learning molecular and immunology techniques. Kesavalu came to Cincinnati when her husband was offered a position at UC. She joined the Department of Internal Medicine in 2006.

When she’s not in the lab, Kesavalu spends much of her free time creating award-winning polymer clay art and jewelry, and teaching jewelry and handicrafts courses for UC’s Communiversity on the weekends. She also enjoys reading, running, cooking and spending time with her two daughters.

Her advice for those just starting research careers is simple: tap into the thirst for discovery, every day. “Be curious, collect lots of background information before working on a project, and treat each experiment as a work of art,” Kesavalu says. “Above all, set a goal and stay motivated.” •

“Be curious, collect lots of background information before working on a project, and treat each experiment as a work of art.”

“Exploring new possibilities, trying out new hypotheses—these are the most interesting aspects of research to me.”



David I. Bernstein, MD

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

- focus on isocyanate induced occupational asthma
- lead a multicenter international cooperative genotyping project
- sequencing for genetic markers and mechanisms of action
- co-investigator on study of the respiratory microbiome

PERSONAL

- ballroom dance
- sports cars
- golf
- family vacationing

I lead a multicenter international cooperative genotyping project conducted in collaboration with investigators from Canada and Spain. The laboratory is focused on identification of genetic markers and mechanisms of occupational asthma caused by diisocyanates. DNA samples have been collected from workers recruited in these countries who have a confirmed diagnosis of isocyanate induced occupational asthma. The work involves analyzing results of genome-wide association studies conducted in this cohort. Next generation sequencing has been performed on informative loci to identify functional variants associated with disease and interactions with transcription factors in human cells are currently being studied. This work is funded through an R01 renewal of a grant from NIOSH-CDC. I am also collaborating as coinvestigator in a study of the respiratory microbiome with Tiina Reponen, PhD, professor of environmental health at UC.

Currently, I am director and principal investigator of the allergy-immunology T32 training grant sponsored by the National Institute of Allergy and Infectious Diseases. The mission of this training program, now in its 12th year, is to prepare physicians for successful careers in academic research. Currently there are four trainees enrolled in this research training program. I have served as mentor and co-mentor for many of these trainees. I also served as co-director of the Allergy Immunology Fellowship Training Program.

Current professional activities include membership in the Joint Task Force for Practice Parameters, a committee that designs national guidelines for allergy practice, as well as serving as vice chair and incoming chair of the American Board of Allergy and Immunology.

During my spare time, I enjoy learning ballroom dancing, sports cars, golf and vacationing with my family.

Jonathan A. Bernstein, MD

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



Current research in my laboratory is focused on the effect of environmental determinants on asthma. I am the protocol chair and co-principal investigator of a NIAID U44 funded multicenter trial investigating the health effects of UV irradiation units installed as an environmental in the furnace ducts of asthmatic children's homes. An exploratory objective is to assess the effect of UV irradiation on denaturing allergens. We are also investigating potential peripheral blood biomarkers for diagnosis and management of hereditary angioedema attacks as part of an IIS funded by Shire. Our current study involves identification of expression profiles of endothelial cell surface receptors (g-C1qR-, cytokeratin-k and uPAR) from skin biopsies of HAE patients between and during swelling attacks and determination of serum kallikrein and serum albumin levels, as markers of Kallikrein Kinin System (KKS) activation and of endothelial permeability.

Other ongoing projects include investigation of biomarkers for Trimellitic anhydride sensitization in the workplace, allergenicity of cyanobacteria, phenotyping and mechanistic evaluation of non-allergic rhinitis, seminal plasma hypersensitivity and progesterone induced autoimmune dermatitis.

I have several collaborations on main campus, Cincinnati Children's Hospital Medical Center, and at UC Medical Center on a number of projects. I am also a DIA certified investigator involved as a principal investigator or sub-principal investigator in over 30 clinical trials. I have provided mentorship to numerous allergy fellows, medical residents and medical students over the past 26 years.

I am actively involved in non-profit organizational work related to allergy and immunology. I am married with four grown children and one grandchild on the way. My hobbies are travel related to work, road biking and golf.

- environmental determinants of asthma
- UV irradiation for allergens
- biomarkers for hereditary angioedema
- trimellitic anhydride sensitization biomarkers
- allergenicity of cyanobacteria
- non-allergic rhinitis
- seminal plasma hypersensitivity
- progesterone-induced autoimmune dermatitis

PERSONAL

- non-profits related to allergy
- road biking
- golf



Fred Finkelman, MD

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

- anaphylaxis and food allergy
- allergenicity
- antibody-mediated immunopathology
- allergens and epithelial cell unfolded protein response stimulate IL-25, IL-33, and TSLP production
- evaluating IgG antibody isotypes in strength of effector response

PERSONAL

- classical music
- non-fiction reading
- walking

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

Using live mouse models disease modes we note key findings:

- Treatment of mice with small doses of anti-FcεRI monoclonal antibodies induces mast cell anergy, then removes nearly all IgE from these cells.

- Several allergens promote the development of an epithelial cell unfolded protein response and stimulate IL-25, IL-33, and TSLP production by these cells. Agents that inhibit an unfolded protein response block expression of these cytokines. Treatment of mice that have food allergy with a combination of monoclonal antibodies to IL-25, IL-33 and TSLP abolishes this disorder.
- Mouse IgG1, which is relatively poor at activating complement and IgGFc receptors and at crosslinking antigens, suppresses disease models that are induced by mouse IgG2a and IgG3, which better induce these effector mechanisms.

Collaborators:

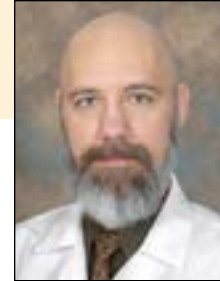
- E. Steve Woodle, MD, Department of Surgery
- Jonathan Katz, PhD, Department of Pediatrics and Cincinnati Children’s
- Harinder Singh, PhD, Department of Pediatrics and Cincinnati Children’s
- David Hildeman, PhD, Department of Pediatrics and Cincinnati Children’s.

I mentor Christopher McKnight, MD, and Corey Clay, MD, PhD, in the Division of Allergy, Immunology and Rheumatology.

My hobbies and personal interests include classical music, non-fiction reading and walking.

Christopher McKnight, MD

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



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

My second pathway of investigation studies how airway epithelial cells and smooth muscle cells independently and cooperatively produce airway hyperresponsiveness after the allergic response has been established. I show

that airway hyperresponsiveness is extinguished when both epithelial and smooth muscle cells cannot bind interleukin-13 or interleukin-4 when potent allergen or cytokine is administered at generous doses. Importantly, this work also shows that smooth muscle cell binding of IL-13 and IL-4 is superfluous in generating airway hyperresponsiveness when administering potent allergen but not when administering cytokine alone. Both findings have implications for treatment of human disease and future funding.

I collaborated with Atin Adhikari, PhD, Department of Environmental Health, on a model of non-allergic airway disease and currently collaborate with Ian Lewkowich, PhD, Department of Pediatrics and Cincinnati Children’s Hospital Medical Center, to categorize asthmatic patients by disease severity.

My research has been funded by the Department of Internal Medicine’s Fellow to Faculty Award.

When not in the office, you can find me tending a perennial garden or hiking in the woods.

- human allergic asthma
- effectors of humoral immunity (IgE and its high affinity receptor) and effectors of cellular immunity (CD4+ T cells, CD8+ T cells, invariant NKT cells and innate lymphoid cells)
- airway hyperresponsiveness after allergic response (role of interleukin-13 and interleukin-4)

PERSONAL

- perennial gardening
- outdoors hiking



William M. Ridgway, MD

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

- molecular pathogenesis of autoimmunity
- immunogenetic mechanisms of autoimmune disease
- focus on primary biliary cirrhosis (PBC) and type 1 diabetes (T1D)
- developing novel immunotherapies for autoimmunity

I hold the Alice W. and Mark A. Brown Chair of Internal Medicine and I am director of the Division of Immunology, Allergy and Rheumatology. I am a tenured professor of medicine at the University of Cincinnati College of Medicine, board-certified in Internal Medicine and Rheumatology by the American Board of Internal Medicine and a fellow of the American College of Physicians and the American College of Rheumatology. I was a tenured faculty member at University of Pittsburgh School of Medicine in the Division of Rheumatology, with a secondary appointment in the Department of Immunology, before moving to Cincinnati in 2008.

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

Collaboration

I have collaborated here in Cincinnati with:

- Jonathan Katz, PhD
- Fred Finkelman, MD
- Claire Chougnet, PhD
- Larry Dolan, MD
- Andy Herr, PhD
- Jorge Bezzera, MD
- Michael Jordan, MD
- Bruce Aronow, PhD.

Funding

Current funding includes: two R01 grants (“dnTGF Beta RII Mice and PBC”, 2010-2018; and “Mechanistic and therapeutic role of the CD137-CD137L axis in Type 1 Diabetes,” 2016-2021), an R21 (“Mechanism of restored immune tolerance in anti-TLR4 antibody reversal of NOD T1D,” 2015-2017), an R56 (“Molecular Vaccines for Type 1 Diabetes” (Liu, P.I., 2014-2016), a VA merit grant (BX000827-01A1, “Immunogenetic control of autoimmune biliary disease,” in no-cost extension), and an ADA Foundation grant (“Mechanistic role and therapeutic potential of CD137 in T1D,” 2016-2019).

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George Smulian, MD
DIVISION DIRECTOR

The **Division of Infectious Diseases** has a long-standing reputation as a research focused division where the vast majority of faculty members have active roles in clinical, translational, and basic science research. In addition to the seasoned senior investigators in the division who have spearheaded the traditional research focus in basic fungal-host pathogen interaction research and HIV clinical research, recent junior faculty recruits have expanded the clinical, translational and basic research areas in host cellular immunity and diarrheal and respiratory pathogens.

The program has an international reputation as a mycology powerhouse based on the research programs of George Deepe, MD, in *Histoplasma capsulatum* and Melanie Cushion, PhD, in *Pneumocystis* species. Close collaborations allow access to UC-based fungal research on aspergillus and candida and international programs in *Paracoccidioides* and *Cryptococcus*. Recent recruits have expanded the basic and translational focus examining the pivotal interface between host cellular, metabolism and *Clostridium difficile* in mouse models and in immunocompromised humans. The role of the host inflammatory response elicited by microbes in the pathogenesis of cardiovascular disease is a new area of exploration. The clinical research program under Carl Fichtenbaum, MD, continues to conduct studies on persons with HIV infection; prevention of HIV infection; hepatitis C; influenza and appropriate antibiotic usage.

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

The Long View

Infectious disease expert Rajat Madan links obesity, inflammation in latest research

While earning his PhD at the University of Cincinnati, Rajat Madan, assistant professor of clinical medicine, knew he wanted to choose a research specialty where he could potentially touch many lives—and make a tangible difference.

The India native, who originally came to Cincinnati as part of a developmental biology program at Cincinnati Children's Hospital Medical Center, found the perfect fit in infectious disease research. "I wanted to do research that crossed borders—that didn't just focus on a single organ, but on issues that affected all parts of the human body," Madan says.

Earning his medical degree at Jawaharlal Nehru Medical College in Ajmer, Rajasthan, India, Madan is well-versed in the clinical side of disease as well as the basic science research. After finishing his PhD at the University of Cincinnati, he completed his residency at Cincinnati's Christ Hospital and his fellowship at the University of Virginia. "I wanted to be sure to understand the real-world, actual problems faced in the field of medicine so that I could direct my research energy toward solving them," Madan says. "I chose infectious disease because it's a branch of medicine which is very global in its reach and impact."

Today, Madan's research is focused on understanding how infectious diseases manifest in patients who are obese—in particular, how overweight

"I chose infectious disease because it's a branch of medicine which is very global in its reach and impact."

patients respond to an infection caused by *Clostridium difficile*, the number one cause of healthcare-associated diarrhea in the United States. It's long been thought that obesity is linked to reduced sensitivity to the hormone leptin, which helps regulate appetite and body weight. Madan believes that leptin is also likely to play an important role in directing inflammation to infections in obese patients, who represent a rapidly expanding population demographic worldwide. In the lab, Madan is currently looking at disease susceptibility, severity and outcomes in patients with *C. difficile* infection; at the same time, he is working with investiga-

tors at Cincinnati Children's to study how leptin signaling impacts immune response during *C. difficile* infections in diet-induced obese mice.

Madan believes the studies have the potential to replace the current treatments for *C. difficile* with more effective therapies directed at the host immune response. "Basically, we are studying the response to infection—inflammation," Madan says. "So even in cases of non-infectious inflammatory diseases, I think our studies will provide new insights into how nutrition and metabolism impact the outcomes for both infectious and non-infectious diseases. The applicability is going to be very broad."

The potential to positively affect the lives of so many patients—and the excitement of discovery—is what keeps Madan looking forward, even when the rewards of research lie far ahead. "Practicing medicine provides you with more instantaneous results—you go to the hospital, give patients medicine, they feel better," Madan says. "But think about how much effort went into creating that medicine. That solution exists because of research. There's always something new coming out that you don't know about yet. Research is a life-long learning process." •

**“Practicing medicine you go to the hospital,
give patients medicine, they feel better.
That solution exists because of research.”**

Rajat Madan, MD, PhD
Infectious Diseases

UCC Health



Senu Apewokin, MD

Assistant Professor of Medicine
Division of Infectious Diseases

- infectious complications associated with immunosuppression
- genetic tools to guide risk stratification
- humoral and microbial correlates of protection
- biomarkers such as procalcitonin for infectious processes in immunocompromised host

I am the director of the Transplant Infectious Disease Program. I have been involved in investigator-initiated and industry-sponsored studies with a focus on improving outcomes of infectious complications associated with immunosuppressive events. My recent efforts employ genetic tools such as GWAS to guide risk stratification and predict these complications. This approach has been applied to pathogens such as *Clostridium difficile*, *Candida* sp and respiratory viruses. Additionally, I am examining humoral and microbial correlates of protection. Other interests include the utility of biomarkers such as procalcitonin for surveillance and early detection on infectious processes in immunocompromised hosts. I plan to apply for K23 funding in the winter of 2017.

Collaborations

Collaborators at UC include:

- Allison Weiss, PhD
- Rajat Madan, MD, PhD
- Madison Cuffy, MD
- Shimul Shah, MD
- Steve Medlin, MD.

At Cincinnati Children's Hospital Medical Center collaborators are:

- Tesfaye Mersha, PhD
- David Haslam, MD.

Other collaborators include:

- Ciaran Kelly, MD, Harvard Medical School.

Melanie T. Cushion, PhD

Senior Associate Dean for Research, UC College of Medicine
 Research Career Scientist, Cincinnati VA Medical Center
 Professor, Division of Infectious Diseases



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

My colleagues, Alexey Porollo, PhD, and Mike Linke, PhD, and my lab, discovered that *Pneumocystis* were myo-inositol auxotrophs, meaning that these fungi cannot synthesize myo-inositol, an essential nutrient necessary for viability. We then identified the inositol transporters that

were capable of sequestering myo-inositol from the mammalian host. Since myo-inositol is essential for life and the only means these fungi are able to obtain it is through transport, inhibiting these transporters would result in death of these fungi and cure of the pneumonia. Thus, we now have a new drug target which we are developing for treatment of PCP.

We are working with Eddie Merino, PhD, in the Department of Chemistry to synthesize a dye-tagged myo-inositol reporter as a critical component of a high throughput screening system (HTS) to identify candidate drugs/inhibitors. Once identified, the selected candidates will be analyzed for pharmacodynamics/ pharmacokinetics in collaboration with Pankaj Desai, PhD, James L. Winkle College of Pharmacy, and tested in an animal model of PCP. We are able to measure ATP content of cells using a bioluminescent assay based on the evolution of light driven by ATP in a luciferin: luciferase system. My lab uses the ATP assay to identify potential anti-PCP drug candidates. We complement yeast mutants with *Pneumocystis* genes to assess function, as there is no sustainable long term in vitro cultivation system for these fungi.

I enjoy running as a form of exercise and meditation. It is also a great time to design experiments.

- focus on *Pneumocystis* fungi, fungal pneumonia
- pre-clinical drug development
- discovered that *Pneumocystis* cannot synthesize myo-inositol
- identified transporters that sequestered myo-inositol as a new drug target
- bioluminescent assay to identify potential anti-PCP drug candidates

PERSONAL

- running as exercise and meditation



George Deepe, MD

Professor of Medicine
Division of Infectious Diseases

- *Histoplasma capsulatum* infection/immunity
- role of regulatory T cells in impairing immunity
- *Histoplasma* antigens as vaccine candidates
- role of zinc in macrophage and dendritic cell function

PERSONAL

- running
- reading

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

Specific projects that are underway include:

- analysis of transcription factors in macrophages and dendritic cells that regulate immunity to the fungus;
- analysis of the role of regulatory T cells in impairing immunity;
- utility of *Histoplasma* antigens as vaccine candidates; and
- the role of zinc as a regulator of macrophage and dendritic cell function.

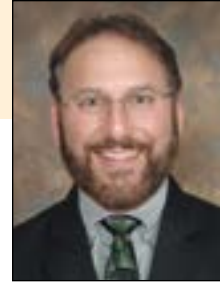
We are funded by a VA Merit Review, 2 NIH R01s and a subcontract on an NIH R01, and a grant from the CCTST.

I am one of the associate directors of the Medical Scientist Training Program at the College of Medicine and co-direct the multi-systems course for second year medical students.

My hobbies include running and reading.

Carl J. Fichtenbaum, MD

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



I am the principal investigator of the clinical trials unit in the Division of Infectious Diseases. I conduct studies on persons with HIV infection; prevention of HIV infection; hepatitis C; and influenza. We currently have 43 ongoing open clinical trials. My research focus has been on the end-organ diseases in HIV infection like cardiovascular disease and dyslipidemia. HIV infection elevates the risk of cardiovascular disease about two-fold and events occur at an early age. Bone disease, liver disease, kidney disease, diabetes, cancer and bacterial infections all occur at higher rates in persons with HIV infection. The link appears to be chronic inflammation.

I am vice-chair of the REPRIEVE study, a 6,500-person trial of pitavastatin versus placebo for prevention of cardiovascular disease and inflamma-

tory conditions in persons with HIV infection. I provide assistance to students, residents, fellows, faculty and staff in the Department of Internal Medicine to assist them in conducting research. I have provided mentorship to five junior faculty, 12 fellows, 10 residents and 15 medical students during the past two decades.

We have a population of 2,200 persons with HIV infection at UC Medical Center that facilitates our research program. Our research unit consists of 14 staff members and six research clinical investigators.

Funding sources include NIH and industry contracts.

I have lived in Cincinnati for 16 years and have two grown children. My hobbies include coaching soccer, singing and songwriting and playing golf.

- clinical trials on HIV infection; prevention of HIV infection; hepatitis C; and influenza
- end-organ diseases in HIV infection like cardiovascular disease and dyslipidemia

PERSONAL

- coaching soccer
- singing
- songwriting
- golf



Lisa Haglund, MD

Associate Professor of Clinical Medicine
Division of Infectious Diseases

I am the Medical Director of the Hamilton County Tuberculosis Control Clinic and with special interest in the areas of treatment of HIV and of M. tuberculosis, non-tuberulous mycobacteria, and Nocardia.

- HIV and M. tuberculosis
- non-tuberulous mycobacteria
- Nocardia

PERSONAL

- outdoor trail enthusiast

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



Pamposh Darbari Kaul, MD

Professor of Clinical Medicine
Division of Infectious Diseases

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

- focus on HIV clinical services
- Clinician Scholars Program
- HIV Practice Transformation Project
- HIV Interprofessional Education Project

PERSONAL

- cooking
- traveling
- reading
- movie enthusiast

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

becoming a patient-centered medical home.

The HIV Interprofessional Education Project improves outcomes along the HIV care continuum by providing hands-on learning in HIV care and treatment for UC students in medicine, nursing and pharmacy. The goal is to expand and strengthen the HIV clinical workforce. Activities in clinical consultation and technical assistance have primarily focused on prevention of mother to child transmission of HIV. This is accomplished through a multi-disciplinary team with both academic and community members that meet on a monthly basis to review cases, collaborate on care and promote patients' adherence to anti-retroviral medications. In addition to special programs, more than 50 educational presentations have been given around the state to physicians, nurse practitioners, social workers and counselors on a wide range of HIV related topics.

Outside of work, I enjoy cooking, traveling, reading, watching movies and spending time with my twin daughters and family.

Stephen Kralovic, MD

Professor of Medicine
Division of Infectious Diseases



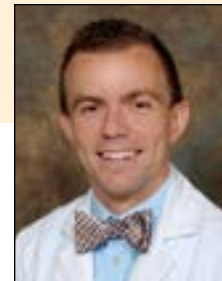
My interest in infectious diseases epidemiology and quality in medical care has helped me to develop a broad interest in healthcare epidemiology in large populations, with a focus on infection prevention and control. While not “classical” research in the sense of NIH-funded or industry-sponsored research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

I have applied this interest to evaluating and analyzing infection prevention and control programs both locally and nationally within the Veterans Health Administration healthcare system with respect to healthcare-associated infections. The national sustained reduction in healthcare-associated methicillin-resistant Staphylococcus aureus (MRSA) infections 8+ years into the Prevention Initiative is one such area of focus, as well as expansion into a Clostridium difficile (C diff) Prevention Initiative, and implementation of a healthcare-associated Legionella Prevention Initiative.

- analyzing infection prevention and control programs
- large population epidemiology
- MRSA Prevention Initiative
- Clostridium difficile Prevention Initiative
- Legionella Prevention Initiative

Keith Luckett, MD

Assistant Professor of Medicine
Division of Infectious Diseases



My research focuses on infections in solid organ transplant recipients, specifically cytomegalovirus. Currently, we are enrolling high (D+/R-) and intermediate (R+) risk kidney transplant patients to assess the ability of a T-SPOT assay to diagnose and monitor CMV activity post-transplant. In addition, a separate T-SPOT assay is also being evaluated to detect allograft rejection. This is an industry-sponsored trial, guided by Oxford Immunotec. Previously, I was involved in pharmaceutical studies with a novel CMV drug, but this trial has since closed.

My research is a collaboration with the Department of Nephrology, Kidney CARE Program, and the Department of Surgery’s Division of Transplant Surgery, aided by Charuhas Thakar, MD, and E. Steve Woodle, MD, Department of Surgery.

I currently also serve as the associate program director for the Internal Medicine Residency Program as well as the medical director of Infectious Diseases in Solid Organ Transplant.

- infections in solid organ transplant recipients
- cytomegalovirus



Rajat Madan, MD, PhD

Assistant Professor of Medicine
Division of Infectious Diseases

- cellular and molecular mechanisms linking nutrition, metabolism, and immune responses
- leptin-directed gut mucosal immunity after *C. difficile* challenge
- human clinical studies and mouse models

PERSONAL

- travel
- gardening
- golf
- interest in physics, evolutionary biology

The overall research goal of my laboratory is to understand the cellular and molecular mechanisms by which nutrition, metabolism, and immune responses to infections are fundamentally linked. The current projects are focused on studying the role of obesity-associated cytokine, leptin, in directing mucosal immune responses during *Clostridium difficile* infection.

Clostridium difficile is the number one cause of healthcare-associated infections and leptin is an adipose tissue-secreted cytokine that affects multiple physiological processes. Interestingly obesity is a state of high serum leptin levels, thus leptin by virtue of its multiple physiologic effects is likely to play an important role in directing inflammation. Host inflammatory response is believed to be a key determinant of clinical disease.

We are using multiple different strains of leptin receptor transgenic mice to interrogate the mechanism(s) of leptin-directed gut mucosal

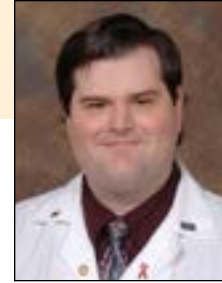
immunity after *C. difficile* challenge. In parallel, we are investigating the role of BMI (as a marker of obesity) in affecting disease susceptibility, severity and outcomes in a cohort of patients with *C. difficile* infection. In our lab, we use core molecular biology, tissue culture and immunology techniques including qRT-PCR, transfection assays, flow cytometry, ELISAs, and luminex assays to address these questions.

Our studies (using both human clinical samples and mouse models) are aimed at defining the role of leptin in mucosal defense of *C. difficile* colitis and thus bridge metabolism with infection and inflammation. This research is funded by an NIH K08 and the Department of Internal Medicine.

Outside of work, I like to travel and hike with my wife and 8-year old son. In my free time, I enjoy gardening, playing golf, watching football and reading books on evolutionary biology and physics.

Jaime Robertson, MD

Assistant Professor of Clinical Medicine
Division of Infectious Diseases



I am an assistant professor in the Division of Infectious Diseases. As a post-doctoral fellow, I conducted HIV clinical research examining immune reconstitution as a determinant of the adverse effects of antiretroviral therapy. Since completing my fellowship, I have been an HIV care provider and an investigator with the Clinical Trials Unit in the Division of Infectious Diseases. We have a population of ~1800 persons with HIV infection at UC Medical Center that facilitates our research. I have been the site principal investigator for two AIDS Clinical Trials Group studies and I am currently on the protocol development team for A5298, a randomized, double-blinded, placebo-controlled, phase III trial of the Quadrivalent Human Papillomavirus (HPV) Vaccine to Prevent Anal HPV in HIV-Infected Men. I have conducted two investigator-initiated HIV clinical research studies and I am currently conducting a third K-23 funded study to determine the association between epidemiological, HPV virological, and host cellular markers and the progression of anal dysplasia in HIV.

I have expertise in performing

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

I am currently collaborating with a network of providers to conduct STI research in collaboration with the Department of Emergency Medicine, Cincinnati Health Department and Cincinnati Children’s Hospital Medical Center Adolescent Clinic. I am currently providing research guidance for a fellow who is interested in HPV and viral-associated malignancies in transplant patients.

My research interests to date have primarily included studies in persons with HIV infection, HPV infection, and sexually transmitted diseases. As a member of the antimicrobial stewardship committee, however, I also have an interest in studies relating to appropriate antibiotic use. I have completed EPIC physician builder basic training and I am proficient in the design of EPIC reports for clinical and research applications.

- HIV clinical research studies
- HPV infection
- appropriate antibiotic use
- high resolution anoscopy and infrared coagulation expertise
- EPIC design for clinical and research use



George Smulian, MD

Ward E. Bullock Professor of Medicine
Division Director
Division of Infectious Diseases
Chief, Infectious Diseases Section, Cincinnati VA Medical Center

- *Pneumocystis carinii* and *Histoplasma capsulatum*
- clinical antibiotics, particularly Staphylococcal infections
- antibiotic needs in individuals with opioid use disorder

PERSONAL

- woodworking
- home renovation
- maintaining 1974 MG

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

My clinical research program focuses on appropriate and novel antibiotic use particularly with respect to prevention and management of Staphylococcal infections. We currently have two investigator-initiated clinical trials: one examining a novel agent for perioperative surgical prophylaxis for high risk surgical procedures such as joint replacement and cardiac surgery

with sternotomy and a second addressing antibiotic needs in individuals with opioid use disorder. Research funding over the years has included NIH and VA Merit Review funding, in addition to foundational, departmental and industry support.

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

Outside of work, I enjoy woodworking, home renovation and construction and car repair (maintaining my 1974 MG in running order).

Madhuri Sopirala, MD

Associate Professor of Medicine
Division of Infectious Diseases



My research interests are in clinical epidemiology, more specifically in the prevention of healthcare-acquired infections. I am the medical director of infection control and antimicrobial stewardship for UC Health. I have used my clinical research to enhance the quality improvement efforts of the hospital. Multidrug resistant organisms have emerged to be a healthcare burden in many ways. Hospital acquired infections cause major morbidity and mortality and significantly add to healthcare burden in the forms of treatment and extended lengths of hospital stay. A key strategy to tackling these infections is prevention.

Some of my previous work was related to epidemiology of multidrug resistant organisms such as Acinetobacter and carbapenem resistant Enterobacteriaceae infections in

immunocompromised patients and their treatment strategies in the setting of having no effective antibiotics for treatment of these organisms. A bulk of my research has been related to quality improvement strategies in prevention of hospital-acquired infections such as central line associated blood stream infections and methicillin resistant Staphylococcus aureus infections, as well as antimicrobial use. I routinely use clinical and molecular epidemiological techniques in my research.

I have mentored several ID fellows, some residents and many medical students in research projects since I joined UC in June 2012.

I love to spend time with my kids, mostly chaperoning them either to the zoo, Newport Aquarium or Kings Island. I love to cook with new recipes, paint and travel to new places.

- multidrug resistance in immunocompromised patients
- quality improvement strategies in hospital acquired infections
- molecular epidemiological techniques

PERSONAL

- time with my children
- cooking
- painting
- travel



Kavitha Subramanian Vignesh, PhD

Post-Doctoral Fellow
Division of Infectious Diseases

- zinc modulation strategies in immune response
- phagocyte metabolism
- tolerogenicity
- inflammasome activation
- T cell lineage differentiation

PERSONAL

- connect with inner consciousness
- meditation

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

We use diverse in vitro and in vivo techniques combining molecular, metabolic, cytometry, NMR and mass-spectrometry approaches. Our research has shed light on intricacies of zinc regulation in frontline defenders, macrophages and dendritic cells. Inflammatory macrophages sequester “free” zinc, rendering it unavailable to microbes. This strategy gives the host a dual-advantage in killing the pathogen—microbial access to zinc is curtailed, and the hosts’ oxidative defenses are bolstered.

Another flavor of macrophages, however, regulates zinc very differently. They “harbor” a zinc-rich pool that is exploited by microbes. Molecular cues involving metallothioneins, zinc transport proteins, proteolysis and superoxide generation all converge to yield a highly organized immune response centered on zinc regulation. These findings have seeded several exciting ideas that we currently pursue—phagocyte metabolism, tolerogenicity, inflammasome activation and T cell lineage differentiation.

I deeply value the excellence of George Deepe, MD. I enjoy collaborating with investigators from various disciplines including: Julio A. Landero Figueroa, PhD, Department of Chemistry; Bruce Klein, MD, University of Wisconsin; Senad Divanovic, MD, Cincinnati Children’s Hospital Medical Center; and others, training MS and undergraduate students in the lab.

My work is funded by grants from the Center for Environmental Genetics and American Heart Association.

When not thinking about research, I connect with nature, invest in raising the inner consciousness and promote meditation at a meditation center and through social media.

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DIVISION OF
Nephrology, Kidney CARE Program





*Nephrology,
Kidney CARE Program*

Charuhas Thakar, MD
DIVISION DIRECTOR



Charuhas Thakar, MD
DIVISION DIRECTOR

The **Division of Nephrology, Kidney CARE (Clinical Advancement, Research and Education) Program** is dedicated to the advancement of basic and applied translational research, clinical outcomes and implementation research, clinical trials and quality improvement and patient safety research. Currently, basic and translational research projects have a primary focus on ion-channels and immune regulation, epithelial transport, vascular biology, phosphate metabolism, acid-base physiology, and acute and chronic kidney injury. Our expanding clinical outcomes research program includes the disease areas of acute kidney injury, chronic kidney disease, dialysis, and transplantation.

The division has enhanced its capabilities through collaborations with pharmacy and nursing services to conduct implementation research in the areas of medication adherence and patient compliance. The focus on quality improvement and patient safety spans across all of our practice locations. Realizing the importance of quality improvement research in the future of clinical medicine, the division co-directs a program at the Cincinnati VA to develop and train a fellow in quality and safety. This is a year-long training which focuses on developing QI projects, and teaches residents and students about systematic methods of incorporating quality improvement methodology within the fabric of clinical practice.

Our program is at the forefront of planning or participating in national and international clinical trials of new drug development, devices, and other technology. There are more than 15 active clinical trials in a variety of disease areas including: polycystic kidney disease, diabetic kidney disease, anemia in kidney disease, and kidney transplantation.

The National Institutes of Health, U.S. Department of Veterans Affairs, Department of Defense, FDA, and industry, in part, support the research conducted within the division. Research publications by investigators in the Division of Nephrology, Kidney CARE Program have appeared in the most prestigious medical journals over the last decade, including the *Journal of Clinical Investigation*, *PNAS*, *Science*, *Translational Medicine*, *Journal of American Society of Nephrology*, *Kidney International*, *Critical Care Medicine and Stroke*, among others.

Moving forward, the division will continue to grow its outcomes research program, basic science program, and clinical translational research through strategic recruitment to develop research programs in the areas of AKI, CKD, and ESRD/Transplantation.

A Lifelong Pursuit

UC's Begoña Campos-Naciff's childhood experiences launched a desire to fight disease

"I was a dreamer; I wanted to find the magic, the solutions, that would help everybody. I still think that's possible."



Begoña Campos-Naciff's interest in research started as a child in Mexico. "I grew up with sick parents," says Campos-Naciff, whose father suffered from Crohn's Disease and heart issues and her mother developed Alzheimer's disease when Campos-Naciff was in postgraduate studies. "You think that nothing is happening, that they are OK. Then you see it. So you start looking for the magic that will make them better. I was a dreamer; I wanted to find the magic, the solutions, that would help everybody. I still think that's possible."

That ambition drove Campos-Naciff to first study chemistry, pharmacy and biology as an undergraduate at Mexico's University Autónoma of San Luis Potosí, then earn her PhD in biochemistry. She came to the University of Cincinnati in 1991 to work with John Dedman, PhD, professor emeritus in the department of cancer biology, after previously working as a postdoctoral student under Dedman at the University of Texas in Houston.

At UC, Campos-Naciff has been a visiting scientist and research assistant professor. Her research focused on endothelial

dysfunction and oxidative stress and she was a pioneer on the role of micro-particles in diseases. Campos-Naciff is currently a senior research associate and laboratory manager in the Division of Nephrology, Kidney CARE Program's kidney injury translational research unit, a program that explores the pathobiology of kidney injury using state-of-the-art technology. She works with the Vascular Access Research Group which develops and evaluates, through clinical trials, novel therapies that target the problem of hemodialysis vascular access dysfunction.

Campos-Naciff's most recent task is to identify early biomarkers among dialysis patients that may make them more susceptible to acute kidney injury. "People come to dialysis because they have a problem with their kidneys—sometimes this started because they had a stroke or heart attack,

cancer, or an infection. Some of them need to have a CT scan, an antibiotic, or another procedure, all of which can damage the kidneys," Campos-Naciff explains. "There are some patients who come to the clinic without an underlying issue and are borderline for acute kidney damage, but they develop it because of the procedures that they undergo at the clinic, as a side effect of the treatment."

The lab has collected and is already analyzing the new biomarker data, which could help improve outcomes for dialysis patients and, potentially, patients with other conditions as well. "My goal is to try to help every day," Campos-Naciff says. "When I have a difficult day here at the lab, I always think about how someone is having a worse day than I am. I want to help those who have harder lives. If you have passion for what you do, it makes a big difference. Whatever you decide to do, you need to do it with all your heart." •

Campos-Naciff's most recent task is to identify early biomarkers among dialysis patients that may make them more susceptible to acute kidney injury.



Rita R. Alloway, PharmD

Research Professor of Medicine
Division of Nephrology, Kidney CARE Program
Director, Transplant Clinical Research

- pharmacokinetic and pharmacogenetic aspects of immunosuppressants to create an individualized regimen and improve post-transplant outcomes
- tacrolimus generic products in kidney and liver transplant recipients
- novel immunosuppression in kidney transplant recipients to minimize toxicity
- use of cancer chemotherapeutic agents for desensitization in patients awaiting kidney transplant
- impact of laparoscopic gastric sleeve procedure on immunosuppressant pharmacokinetic profiles

I am director of the Transplant Clinical Research Program which spans the clinical research efforts between the Department of Internal Medicine and the Department of Surgery conducting studies at UC Medical Center and The Christ Hospital. We have a research unit consisting of six research coordinators, two fellows, and 12 faculty members. Our program has approximately 20 ongoing studies of which two are federally funded, five investigator initiated, and 13 industry sponsored. For the five investigator initiated studies, we serve as the sponsor and hold FDA approved INDs. These studies focus on novel immunosuppression in kidney transplant recipients to minimize toxicity and the use of cancer chemotherapeutic agents for desensitization in patients awaiting kidney transplant. One of these studies, Belatacept Early Steroid Withdrawal Trial (BEST), is a 315-patient, eight-center study where we serve as sponsor and coordinating center. The BEST study explores concomitant calcineurin inhibitor and steroid withdrawal with a new immunosuppressant, first-in-class belatacept (NCT01729494). Enrollment is over 95% completed with two-year follow-up, and has passed all DSMB reviews.

We maintain significant collaborations for complementary basic science studies with James Driscoll, MD, PhD, Division of Hematology Oncology, and Dave Hildeman, PhD, Cincinnati

Children's Hospital Medical Center, as well as with Minnie Sarwal, MD, PhD, University of California San Francisco, for biomarkers for rejection and post-transplant diabetes.

My overall research goal is to better understand the pharmacokinetic and pharmacogenetic aspects of immunosuppressants to create an individualized regimen, and subsequently improve post-transplant outcomes. I currently hold a U01 grant and FDA contract to explore the impact of tacrolimus generic products in kidney and liver transplant recipients. As part of these awards, I collaborate with Uwe Christians, MD, PhD, at University of Colorado, Denver, to develop tacrolimus assays from dry blood spot sample collections and Alexander Vinks, PharmD, PhD, Cincinnati Children's Hospital Medical Center, to incorporate pharmacogenetic results into research and clinical activities. I have conducted several pharmacokinetic studies with once daily tacrolimus dosage forms to facilitate dose conversion between formulations.

In addition, we collaborate with Tayyab Diwan, MD, Department of Surgery, to study the impact of laparoscopic gastric sleeve procedure on immunosuppressant pharmacokinetic profiles.

I am also director of the Transplant Pharmacy Specialty Residency and Fellowship Program, of which I have trained over 30 candidates in my career.

Hassane Amlal, PhD

Research Associate Professor
Division of Nephrology, Kidney CARE Program



My research interest is to study the role of renal transport physiology and understand the cellular and molecular mechanisms responsible for abnormal changes in various homeostatic functions of the kidney, including electrolytes and minerals balances, acid-base homeostasis and water metabolism. My current research program covers three specific areas of active research.

Regulation of inorganic phosphorus (Pi) metabolism by estrogen. The objective of these studies is to determine the phosphate transport pathways targeted by estrogen in the kidney, and dissect the molecular mechanisms and signaling pathways mediating the effects of this hormone on its targets. Our current working hypothesis is to test the effects of specific estrogen receptor modulators (SERMs) on renal and intestinal handling of Pi, and determine whether these SERMs can be used as therapeutic agents to correct and/or prevent hyperphosphatemia in patients with abnormal production of phosphaturic hormones. These studies have been supported by NIH/NIDDK RO1 since August 2010.

Role of glutamine transport and metabolism in the development of diabetic nephropathy. We have generated extensive preliminary data demonstrating that the onset of hyperglycemia in animal models of both type I and type II DM is associated with the stimulation of ammoniogenesis in the kidney. These studies will allow us to discover new therapeutic targets (transporters and/or enzymes) and identify new risk factors that could exacerbate CKD in diabetic patients. Both of these outcomes will open novel avenues for better management of DM, and prevention of kidney disease and/or its progression to ESRD in diabetic patients.

Adenine as a new water balance regulating factor. The molecular mechanisms and subsequent physiologic events

responsible for adenine-induced kidney disease remain elusive. Our studies will dissect the molecular and cellular mechanisms by which adenine regulates water transport in the kidney, and test whether low doses of adenine can be used as a new therapeutic agent to treat hyponatremia and polycystic kidney disease.

Methodologies and techniques: We use whole animal physiologic balance studies in metabolic cages using rats and mice (wild-type and mutated mice), as well as in vitro experiments using both renal cell lines for cloning/expression studies, as well as freshly isolated renal tubular suspensions. We study gene and protein expression using standard molecular and biochemical methods. We measure the activity of transporters using radio-isotopes or fluorimetry and perform assays to measure hormones, renal function, electrolytes, minerals and acid base components in both urine and blood samples.

Directorship: I direct the qualifying exam course for the second-year graduate students of the Pathobiology and Molecular Medicine Program. I teach students how to develop and structure their proposals, organize a mock NIH study section for the review of the proposals, and provide guidance on how to address the critics and flaws discovered by the reviewers.

Collaborators:

- Sulaiman Sheriff, PhD, Department of Surgery
- Rafeeq Ahmed P. Habebahmed, PhD, Department of Pathology and Laboratory Medicine
- Gary Shull, PhD, Department of Molecular Genetics
- Frank McCormack, MD, Division of Pulmonary, Critical Care and Sleep Medicine
- Robert Cohen, MD, Division of Endocrinology, Diabetes and Metabolism

- renal transport physiology
- phosphate transport pathways targeted by estrogen in the kidney
- Role of glutamine transport and metabolism in diabetic nephropathy
- Adenine as a new water balance regulating factor
- molecular and cellular mechanisms of adenine-induced kidney disease



Laura Conforti, PhD

Professor
Division of Nephrology, Kidney CARE Program

- cancer and autoimmunity
- role of microenvironments in tumor progression
- nanotechnology delivery of gene therapy to ion channels
- systemic lupus erythematosus

My laboratory studies cancer and autoimmunity. The main focus areas of my laboratory include:

- Understanding the role that ion channels and the tumor microenvironment play in the failure of the immune system to fight cancer and the limited response of patients to immunotherapies
- Studying how ion channels contribute to the development and persistence of the autoimmune disease systemic lupus erythematosus
- Developing nanoparticles that can be used as new targeted therapies in autoimmune diseases and cancer

My research in the cancer field has been supported since 2003 by a National Institute of Health R01 grant. This grant has been renewed to 2020 to continue studying how the tumor microenvironment can lead to cancer progression. In this study, we are trying to discover by which mechanisms hypoxia and adenosine inhibit ion channels and ultimately T cell function to find out how we can manipulate

them to improve T cell infiltration and functionality in the tumor, and stop tumor growth. I also have funding from the DCI Paul Teschan Foundation to explore how nanotechnology could be used to deliver gene therapies targeting ion channels in selective T cell subsets in individuals with autoimmune diseases, particularly systemic lupus erythematosus.

Collaborators:

- Trisha Wise-Draper, MD, PhD
Division of Hematology Oncology
- Edith Janseen, PhD
Division of Immunobiology,
Cincinnati Children's Hospital
Medical Center.
- Marat V. Khodoun, PhD, DVM
Division of Allergy, Immunology and
Rheumatology.
- Shashi Kant, MD
Division of Nephrology, Kidney
CARE Program.
- Heather Duncan, PhD
Division of Nephrology, Kidney
CARE Program.

Heather J. Duncan, PhD

Field Service Professor
 Division of Nephrology, Kidney CARE Program
 Director, Clinical Trials, Nephrology



Beginning as a post-doc in a UC College of Medicine lab in 1987, I have published research in neuroanatomy, neurophysiology, behavior and psychophysics of the olfactory and gustatory systems in both animal models and human subjects. From my work with patients at the University of Cincinnati Taste and Smell Center (Department of Otolaryngology–Head and Neck Surgery), I learned to apply my scientific expertise to the clinical problems of patients with chronic kidney disease (CKD). From there, I began management of the clinical trials program in nephrology.

Since 1996, we have expanded this program to many indications in CKD, including anemia of CKD, iron deficient anemia, secondary hyperparathyroidism, lupus nephritis, uremic pruritus, infections, nutrition, hyperphosphatemia, hemodialysis vascular access, and various other indications. We have conducted over 90 clinical trials, contributing data that has resulted in FDA approval of several medications now in use for CKD. Our

program trains physicians and other clinical research professionals to become principal investigators in sponsored clinical trials.

Our program also provides an environment and the expertise to support the research of nephrology fellows and other graduate students from within the College of Medicine and main campus, thus expanding our interdisciplinary interests and facilitating collaborations with basic science faculty from both campuses. In addition, with the extensive patient database maintained by our partner, Dialysis Clinic, Inc., our team of physicians can evaluate unique problems in chronic kidney disease, and develop new therapeutic approaches for these conditions.

I have served on multiple College of Medicine committees, primarily related to the quality of research and the protection of human subjects.

When not working, I like to travel to any ocean, listen to Scottish music, and sew.

- published in neuroanatomy, neurophysiology of olfactory and gustatory systems
- applied expertise to clinical problems of CKD
- currently clinical trials management in nephrology
- expanded program to many CKD indications

PERSONAL

- seashore visits
- Scottish music
- sewing



Karthik Ramani, MD

Assistant Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program

- dialysis vascular access
- vascular access database
- device innovation in dialysis/extracorporeal therapies
- fistula maturation study
- collaboration with Biomedical Engineering department

PERSONAL

- travel
- try other cuisines
- movie enthusiast

I am an interventional nephrologist with an interest in clinical and translational research on dialysis vascular access, device innovation and development of innovative teaching tools.

I am the principal investigator in the creation of a vascular access database. The vascular access database will hope to create both a clinical and biological database on access. I have collaborated on a R21 grant in the past which involved reducing tunneled dialysis catheter dysfunction through nitric oxide release and have been a sub investigator in numerous clinical trials (Medtronic, Shire, and Novel Biolog-

ics) and HFM or fistula maturation study.

Currently, I have collaborations with the Department of Biomedical Engineering on device innovation in vascular access and dialysis/extracorporeal therapies for which two patents are currently pending; future projects include development of innovative teaching tools for renal physiology for medical students using virtual reality technology. Prior funding sources include NIH and industry contracts.

In my free time, I like to travel, try different cuisines and watch movies.

Manoocher Soleimani, MD

James Heady Professor of Medicine
 Division of Nephrology, Kidney CARE Program
 Associate Chair for Research



My research over the last 30 years has focused on the identification and characterization of transporters and molecules responsible for electrolyte and acid-base transport in the kidney and gastrointestinal tract, with the ultimate goal of ascertaining their role in health and disease states. We have cloned several relevant genes and characterized their role and regulation in the kidney and/or GI tract in pathophysiologic states. Further, we have generated over 12 genetically-engineered mouse models lacking one or more transporters in order to examine their role in vascular volume homeostasis, blood pressure regulation and acid base balance. We were the pioneer group to clone and identify several electrolyte or acid base transporters in the kidney and gastrointestinal tract. The results have been published in very prestigious journals such as the *Journal of Clinical Investigation* and *Proceedings of the National Academy of Sciences*.

In addition to generating mice lacking a single gene we have started to

generate mice deficient in two or more genes. We were able to show that the double knockout of pendrin and NCC causes severe salt wasting and volume depletion. Our recent studies have identified Slc26a11 (KBAT) as a chloride transporter with a unique localization in the kidney and neurons in cerebellum and hippocampus. Our recent work focuses on the identification of roles of Slc2611 (KBAT), Slc4a8 (NDCBE) and Slc26a4 (Pendrin) in the kidney and brain.

We have also identified four injury-activated genes that play important roles in mediating tissue damage in kidney, liver and heart. We are currently examining the effect of blocking these genes on the kidney injury caused by the anti-cancer medication cis-platinum. My research over the last three decades has been funded by Merit Review from the U.S. Department of Veterans Affairs, NIH and Cystic Fibrosis Foundation.

Outside of work, I like to read on the history of evolution and revolutions and attempt not to play golf.

- electrolyte and acid-base transport molecules in kidney and gastrointestinal tract
- roles of Slc2611 (KBAT), Slc4a8 (NDCBE) and Slc26a4 (Pendrin) in kidney and brain
- injury-activated genes and impact of cis-platinum in kidney injury

PERSONAL

- history of evolution, revolutions
- golf



Ajay Srivastava, MD, FASN

Associate Professor of Medicine
Associate Program Director, Nephrology Fellowship
Division of Nephrology, Kidney CARE Program

I have research interests in interventional nephrology, cardio-renal interactions, and quality improvement and education.

- *Interventional Nephrology*
Clinical outcomes and clinical trials regarding vascular access for patients with end-stage renal disease
Topics include:
 - long-term outcomes
 - process of care guidelines
 - AV fistula maturation
 - PTFE graft stenosis
 - surgical vs endovascular intervention
 - tunneled hemodialysis catheter coatings
 - vascular and access cannulation techniques

- vascular access in end-stage renal disease
- process of care guidelines
- AV fistula maturation
- PTFE graft stenosis
- surgical vs endovascular intervention
- tunneled hemodialysis catheter coatings
- cannulation techniques
- CKD-induced cardiac impairments

PERSONAL

- astronomy
- cosmology
- tennis
- outdoor activities

- *Kidney and Cardiovascular Disease:*
All-cause cardiovascular risk increases with decreasing renal function. The cardio-renal interaction involves numerous risk factors that significantly contribute to the CKD-induced development of pathogenetic disease states including accelerated atherosclerosis and impairment in cardiac function which in turn also negatively impacts kidney function.
- *Quality improvement and education research*

My hobbies include astronomy, cosmology, watching and playing tennis, travelling and outdoor activities.

Charuhas Thakar, MD

Arthur Russell Morgan Professor in Internal Medicine
 Division Director
 Division of Nephrology, Kidney CARE Program



I have led several interdisciplinary investigations related to the clinical epidemiology, and translational research in acute kidney injury (AKI) and progression of chronic kidney disease (CKD). My thematic interests include clinical and health outcomes research, quality improvement and patient safety research, and clinical trials. I have developed and validated local and regional patient databases, and led investigations on national registries to assess risk factors and outcomes of kidney disease in both acute care and chronic care settings. An example of active funded studies include clinical outcomes in patients with kidney disease/end stage renal disease and cardiovascular complications (data sources include United States Renal Data System, Cerner Health, industry contracts and the U.S. Department of Veterans Affairs).

My other research interest revolves around biomarkers of acute kidney injury and chronic kidney disease. Some examples of active funded projects include: phenotyping drug related versus biological causes of acute kidney injury; identifying markers/

mediators of dual organ ischemic injury (kidney – brain and kidney – heart connections); biomarkers of kidney injury in kidney cancer.

Lastly, I also lead several clinical trials at University of Cincinnati and the Cincinnati VA Medical Center. The disease areas currently under investigation include diabetic nephropathy (SONAR trial); chronic kidney disease and ischemic heart disease (Ischemia CKD Study); anemia management in chronic kidney disease (OLYMPUS and ASCEND trials); glomerular disease (FSGS trial); and acute kidney injury (PRESERVE trial – Co-operative Study Program; Sepsis associated AKI trial).

My research accomplishments have been recognized through the receipt of extramural funding. Current active funding includes U.S. Department of Veterans Affairs, U.S. Department of Defense, NIH (NHLBI) and other research foundations. I have also been recognized for my research expertise, by national and international institutions, and organizations such as the American Society of Nephrology.

- clinical and health outcomes research, quality improvement and patient safety research, and clinical trials
- clinical epidemiology and translational research in acute kidney injury and chronic kidney disease
- risk factors and outcomes of kidney disease in both acute care and chronic care settings
- cardiovascular complications in kidney disease/end stage renal disease
- biomarkers of acute kidney injury and chronic kidney disease
- phenotyping drug related versus biological causes of AKI
- identifying markers/ mediators of dual organ ischemic injury (kidney–brain and kidney–heart connections)
- biomarkers of kidney injury in kidney cancer



Ganesh Yadlapalli, MD

Professor of Clinical Medicine
Division of Nephrology, Kidney CARE Program

Ganesh Yadlapalli, MD, is a clinician-teacher interested in medical education with a special focus on global health. His approach to improve global health is by providing educational material to health care providers in places with limited resources. He is involved in

developing practical, simple, and relevant information on common medical problems, incorporating the information developed by the World Health Organization and various other global organizations relevant to countries with limited resources.

- focus on global health
- education materials for providers in situations of limited resources

PUBLICATIONS July 1, 2015 thru June 30, 2016

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DIVISION OF
Pulmonary, Critical Care and Sleep Medicine





Pulmonary, Critical Care and Sleep Medicine

Frank McCormack, MD
DIVISION DIRECTOR



Frank McCormack, MD
DIVISION DIRECTOR

The **Division of Pulmonary, Critical Care and Sleep Medicine** conducts both basic and clinical research programs focused primarily on the development of pathogenesis-driven molecular diagnostics and therapeutics for rare lung diseases. The division is an integral part of the Translational Pulmonary Science Center, which is a collaborative project between pulmonary groups at UC and CCHMC, the Rare Lung Diseases Consortium (principal investigators Bruce Trapnell, MD, and Frank McCormack, MD), an NIH and NCATS supported platform for conducting studies in rare lung disease.

In our basic research, all projects have a human clinical trial on the horizon, at least conceptually. The laboratory has used mouse models of pulmonary Langerhans cell histiocytosis, Hermansky Pudlak syndrome, lymphangioleiomyomatosis, and pulmonary alveolar microlithiasis in preclinical studies to determine mechanisms of alveolar homeostasis in health and disease. Researchers in the division are also interested in the role of pulmonary airway cells, collectins and lung epithelial cells in innate immune defense against inhaled bacteria, mycobacteria, fungi and viruses, especially (and most recently) influenza.

Clinical research is focused on investigator-initiated, multicenter, international randomized trials for lymphangioleiomyomatosis, one of which recently led to discovery of an effective treatment and to FDA approval. There is optimism that our laboratory findings will support the design and execution of trials of phosphate restriction for pulmonary alveolar microlithiasis, BRAF inhibitors for pulmonary Langerhans cell histiocytosis, KGF treatment for pulmonary non tuberculous mycobacterial disease, and mTOR inhibitor prophylaxis and therapy for influenza.

Helping Patients Breathe Easier

Researcher Michael Borchers has a hypothesis that could change the lives of patients with COPD

For Cincinnati native and UC College of Medicine associate professor Michael Borchers, following an interest in environmental health research led him to an unlikely place—back home. Although Borchers had finished his PhD at the University of Cincinnati, he had completed his post-doctoral fellowship at Scottsdale’s Mayo Clinic and was looking at research positions in biotech, big pharma, and academia when UC offered him the opportunity to focus on studying immune function in chronic pulmonary diseases such as COPD.

For Borchers, it was the perfect next step in a career that has evolved organically—and started on a hunch. After earning his undergraduate degree in biology, Borchers became interested in air pollution and the effects of toxicants, such as ozone and aldehydes, on the airways, which eventually led him to pursue post-doctoral work in molecular biology and immunology. From there, he found his true research calling.

“There was hardly any literature on the effects of toxicants on immune function,” Borchers says. “Unlike your lung cells, your immune system doesn’t typically come into direct contact with environmental toxicants.”

Borchers found that under many conditions, certain compartments of the immune system actually become hyperactive when exposed to toxicants, instead of being killed off or functionally inhibited. “I was operating on the theory that the chronic damage created by toxicant exposure over time has as much effect as the toxicant itself. The damage activates the immune system and leads to disease.”

After testing his theory, Borchers found he was right—and 10 years ago, began applying his findings to studying cigarette smoke exposure and immune function in diseases like COPD and in two rare chronic lung diseases, Lymphangioleiomyomatosis (LAM), and pulmonary Langerhan’s cell histiocytosis (PLCH). Borchers also studies the exacerbation of COPD symptoms caused by pathogens such as viruses, bacteria and fungi that affect the airway and can actually cause the disease to progress, he says.

In fact, Borchers considers his 2009 research on COPD patients—the first study to show that natural killer cells, one type of immune system component, were not inhibited but hyperresponsive and contributed to damage of lung tissue—his most significant accomplishment to date. He is hopeful that such studies will pave the way for therapeutic, customized medicine for patients with COPD in the

“You have to have a passion for exploration.”

future. “If we can identify patients with specific immune defects, then we might treat them differently,” Borchers says. “I’m working on ways to define those patients. That would have a huge impact.”

For Borchers, the promise of potentially improving real patients’ lives drives his passion to pursue answers—and he says students interested in research need to find their own motivation to see them through the long-term rollercoaster of lab life. “The fear of failure is crippling. You need to be patient because there is a lot of failure. Solutions may be years down the road,” Borchers says. “You can’t go looking at research as a 9-to-5 job. You have to have a passion for exploration.” •



Borchers found that certain compartments of the immune system actually become hyperactive when exposed to toxicants, instead of being killed off. The damage activates the immune system and leads to disease.



Sadia Benzaquen, MD, FACP, FACC

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Director of Interventional Pulmonology
Director of the Interventional Pulmonology Fellowship Program

- interventional pulmonology
- advanced diagnostic procedures (endobronchial ultrasound, navigation bronchoscopy, transthoracic needle biopsy)
- therapeutic procedures (rigid bronchoscopy, endoluminal therapies)
- multicenter trials
 - endobronchial valves
 - epithelial markers for lung cancer
 - idiopathic pulmonary fibrosis

- PERSONAL**
- soccer
 - basketball

I specialize in advanced diagnostic procedures such as endobronchial ultrasound (EBUS), navigation bronchoscopy and transthoracic needle biopsy as well as advanced therapeutic procedures such as rigid bronchoscopy and endoluminal therapy (laser, Argon plasma coagulation and cryotherapy). Additional procedures that are part of my practice include endobronchial valve placement, thermoplasty, percutaneous tracheostomy, medical thoracoscopy, chest tube insertion and Pleur x catheter insertion.

I am the principal investigator at UC on the following multi-center trials: the Emprove trial is a randomized controlled trial to evaluate the use of endobronchial valves for endoscopic volume reduction in emphysema; the Navigate study is a prospective investigation of the complication rates

associated with the Super Dimension Navigation system; the Precepta registry is looking for specific epithelial markers for lung cancer in patients undergoing bronchoscopy for lung cancer; the Brave study is looking for specific markers for Idiopathic Pulmonary Fibrosis using cryo-transbronchial biopsies; and the VAST study is a randomized controlled trial that compares endobronchial valves and conventional treatment in patients with alveolopleural fistula.

I have trained three dedicated Interventional Pulmonology fellows at UC. The first one is now the current director of the IP program at the University of Bangkok in Thailand.

My hobbies include playing soccer and basketball.

Michael Borchers, PhD

Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine



I am the principal investigator of multiple research grants from the NIH, the VA and private organizations. The primary focus of my laboratory is to understand alterations in the immune system (natural killer cells, T cells, dendritic cells and macrophage) of smokers and COPD patients and how these alterations in immunity affect susceptibility to exacerbations. We utilize a mouse model of long-term cigarette smoke exposure, and we have an ongoing study using low-dose secondhand smoke exposure. We routinely perform immune-cell isolations, flow cytometry, cell cytotoxicity assays and adoptive transfer studies in immunodeficient mice. We have developed unique transgenic mouse models, reporter-cell

lines and antibodies as part of our research. I provide training to graduate and undergraduate students, Internal Medicine residents and Pulmonary/ Critical Care fellows.

I am currently collaborating with Ralph Panos, MD, in the study of immune function in COPD patients at the VA. I am collaborating with Frank McCormack, MD, and Nishant Gupta, MD, on clinical projects focusing on lymphangiomyomatosis (LAM) and basic science projects on pulmonary Langerhan's cell Histiocytosis (PLCH).

I am the associate chair of the University Institutional Animal Care and Use Committee (IACUC) and serve as a member of the department's Reappointment, Promotion and Tenure Committee.

- immune system alterations in smokers and COPD patients
- clinical collaborations on LAM
- research collaborations on PLCH

Jean Elwing, MD

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine



I am the principal investigator for several clinical trials in the Division of Pulmonary, Critical Care and Sleep Medicine, evaluating existing and novel therapies for pulmonary arterial hypertension (PAH). Currently, there are 10-12 ongoing phase II and III clinical trials or registries available to PAH patients, with the main focus of examining therapeutics and treatment regimens in hopes to determine the optimal strategies.

The UC PH program follows a large cohort of patients affected by PAH. All patients seen in clinic are evaluated for possible participation in clinical trials or registries; the goal is to offer every patient an opportunity to

participate in clinical research. At least 25 percent of patients actively participate in clinical trials at some point in their care. The UC PH Program actively collaborates with Cincinnati Children's Hospital Medical Center and several other divisions at the University of Cincinnati on various research projects. The pulmonary research unit consists of five staff members and three clinical investigators who are focused on pulmonary hypertension. Funding sources include NIH and industry contracts. The program also participates in investigator-initiated projects and often collaborates with trainees who are interested in clinical research.

- pulmonary hypertension focus
- clinical trials and registries for PAH patients
- promoting clinical research to patients



Jason Gardner, PhD

Research Instructor
Division of Pulmonary, Critical Care and Sleep Medicine

- hematopoietic response to injury
- determinants of post-injury susceptibility to pneumonia, lung injury and anemia
- KGF post-burn
- erythropoietin-resistant anemia following injury

The primary research focus of my laboratory is related to the hematopoietic response to injury. My laboratory utilizes a mouse model of injury to define the axis of cytokines, signaling pathways and cellular responses that determine post-injury susceptibility to pneumonia, lung injury and anemia.

I am currently collaborating with Frank McCormack, MD, to determine the role of keratinocyte growth factor (KGF) in the development of post-

burn pneumonia and lung injury. We are also investigating the utility of recombinant human KGF as a novel therapeutic for the treatment of *Mycobacterium avium* infections. I am collaborating with McCormack and Jose Cancelas, MD, PhD, to determine the mechanisms responsible for the development of erythropoietin-resistant anemia following injury.



Nishant Gupta, MD

Adjunct Assistant Professor
Division of Pulmonary, Critical Care and Sleep Medicine

- cystic lung diseases, clinical and basic research collaborations
- LAM, BHD, PLCH
- management of spontaneous pneumothoraces in these patients

My clinical research program focuses on rare, diffuse cystic lung diseases such as lymphangioleiomyomatosis (LAM), Birt-Hogg-Dube syndrome (BHD) and pulmonary Langerhans cell histiocytosis (PLCH). We have recently completed analysis examining the cost effectiveness of using high-resolution computed tomography (HRCT) to screen patients who present with an apparent primary spontaneous pneumothorax. I am currently working on better defining the natural history of some of these cystic lung diseases, especially pertaining to the clinical manifestations and management of spontaneous pneumothoraces in these patients.

I work very closely with Francis McCormack, MD, on various research projects. In addition, I frequently collaborate with other investigators from the Rare Lung Diseases Consortium on these projects. Among basic science collaborators, I work with Michael Borchers, PhD, in our division on two separate projects aimed at developing mouse models of BRAF-mutated PLCH and on investigating the role of natural killer cells in the pathogenesis of LAM.

Outside of the work, I enjoy spending time with my two-year old son, Nathan.

Kristin Hudock, MD, MSTR

Assistant Professor of Medicine and Pediatrics
 Division of Pulmonary, Critical Care and Sleep Medicine
 Division of Pulmonary Biology, Cincinnati Children's Hospital Medical Center



The primary focus of my lab is to determine what regulates the balance between host defense and injury in diseases characterized by pulmonary infections including cystic fibrosis, acute respiratory distress syndrome (ARDS) and rare neutropenias. We use human-induced pluripotent stem (iPS) —and soon, CRISPR/Cas—to elucidate crucial genes-to-function relationships that modify neutrophil behaviors. With the help of the Cystic Fibrosis Center at Cincinnati Children's Hospital Medical Center, we are also defining the impact of human airway epithelia and

neutrophil interactions in models of inflammation in vitro.

My mentors are Bruce Trapnell, MD; Frank McCormack, MD; and JP Clancy, MD (at Cincinnati Children's). Our work is funded by the UC CCTST CT2 Scholar program, Parker B. Francis Foundation, Cystic Fibrosis Foundation, UC College of Medicine and Cincinnati Children's.

I recently moved to Cincinnati from Philadelphia and enjoy regular hikes in Eden Park with my dogs.

- regulatory relationships in pulmonary infections (CF, ARDS, neutropenias)
- airway epithelia, neutrophil interactions in inflammation

PERSONAL

- hiking with canine companions

M. Veronica Indihar, MD

Assistant Professor of Clinical Medicine
 Division of Pulmonary, Critical Care and Sleep Medicine



My clinical research program focuses on cystic fibrosis, with an emphasis on clinical trials and patient-centered outcomes. I am also interested in building a non-CF bronchiectasis, with the goal of joining a national network. Clinicians with an interest in this should contact me. Our trials are generally funded by the Cystic Fibrosis Therapeutics Development Network, with some industry support. We also have Cystic Fibrosis Foundation

funding for a quality improvement program. I collaborate with the other CF clinicians including: Patricia Joseph, MD; Bruce Trapnell, MD; Lisa Burns, MD; Cheryl McCullumsmith, MD, PhD; and Mark Eckman, MD.

In my free time, I enjoy life with my two children and husband. Since we are from Argentina, we are looking forward to attending FC Cincinnati games.

- clinical research focus on cystic fibrosis
- building a non-CF bronchiectasis

PERSONAL

- enjoying FC Cincinnati games



Patricia Joseph, MD

Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Director, Adult Cystic Fibrosis Program

- cystic fibrosis care
- CF clinical trials
- CF quality improvement/patient-centered outcomes research

I dedicate most of my clinical and research time to cystic fibrosis care, CF clinical trials and quality improvement. I am currently the principal investigator on multiple CF-related clinical trials with more planned for the near future. Our team is involved with several new investigational drugs designed to correct the defect in CF. Other studies include trials designed to improve lung function in CF patients, to evaluate patient methods of coping with chronic illness or to review aminoglycoside dosing and complications in CF. Our Adult CF program has a long history of involvement in quality improvement, and we have recently received a grant from the Cystic

Fibrosis Foundation to identify components of our CF care delivery that can be altered to increase patient engagement and improve health outcomes.

I collaborate with John P. Clancy, MD; Lisa Burns, MD; Veronica Indihar, MD; Bruce Trapnell, MD; Christopher Droege, PharmD, on CF clinical trials; Daniel Grossoehme, UC associate professor and chaplain in the Division of Pulmonary Medicine at Cincinnati Children's Hospital Medical Center, on coping with chronic disease; and with Mark Eckman, MD, on patient-centered outcomes research.

Peter H. Lenz, MD, MEd

Associate Professor
 Program Director, Pulmonary and Critical Care Fellowship
 Division of Pulmonary, Critical Care and Sleep Medicine



My academic investigations are focused around teaching physicians-in-training and creating appropriate programs and curricula to support aspiring clinician educators. The core components of my medical education mission are focused on audience engagement and promoting active teaching modalities. We recently surveyed program directors to assess existing teaching content and structure in U.S. pulmonary and critical care medicine (PCCM) fellowships. We found that only one-third of respondents had a formal curriculum for teaching medical education skills. This appears to be discordant with a recent fellows survey that reports that over 70 percent of fellows in training want formal instruction on teaching.

To meet this need, we have created a teaching curriculum for all of our fellows and have created a specific clinician educator track for fellows wishing to get more in depth training and experience in curriculum

development, delivering effective learner feedback and creating evaluative assessment tools. In our publication, qualitative analyses identified several barriers to implementing formal teaching skills curricula, and I am interested in developing the effective strategies that are needed to design, implement, sustain and assess teaching skills curricula for PCCM fellowships.

I mentor our fellows in the clinician educator track and our track's first graduate, Adam G. Cole, MD, won the Internal Medicine Residency Fellow Teaching Award this year. Cole also developed an assessment tool to evaluate our fellows' active teaching capacity and presented this at the American Thoracic Society annual conference in May. Cole will join our faculty as our associate program director.

My hobbies include coaching youth football, playing baseball and biking.

- medical education focus
- design, implement teaching skills curricula for fellows
- created a specific clinician educator track for fellows
- effective learner feedback and creating assessment tools

PERSONAL

- coaching youth football
- playing baseball
- biking



Frank McCormack, MD

Gordon and Helen Hughes Taylor Professor of Internal Medicine
 Division Director
 Division of Pulmonary, Critical Care and Sleep Medicine

- genetic interstitial lung diseases and pulmonary innate immunity
- translational research of rare lung disease
- inspired by patients we have met
- develop strategies for experimental plans that have a human trial on the horizon
- LAM, PAM and the role of the alveolar epithelium in influenza, mycobacterial and bacterial infection

Our group is broadly interested in translational research of rare lung diseases, which allows us to approach disease pathogenesis from the vantage point of a known molecular defect. Our goal is to develop new biomarkers and therapies with the potential to favorably impact human health in a short time frame. Many of our laboratory directions have been inspired by patients we have met, which gives our work purpose and meaning, and motivates us to ask questions that matter.

The McCormack laboratory is interested in genetic interstitial lung diseases and pulmonary innate immunity. Current projects are focused on lymphangioleiomyomatosis (LAM), pulmonary alveolar microlithiasis (PAM) and the role of the alveolar epithelium in influenza, mycobacterial and bacterial infection. We use animal models to develop biomarkers and strategies for trials, and try to focus on experimental plans that have a human trial on the horizon. As an example, we developed the PAM mouse model by deleting the phosphate transporter, Npt2b, from the alveolar epithelium, as mutations in that protein are known to cause the disease in humans. The animals develop diffuse pulmonary alveolar microliths, which produce hyperdense infiltrates on radiographs and C/T scans that are easily measured and quantified. The cytokine MCP-1 is elevated in the lungs of the PAM animals, and also appears in their serum. We also found that the very large alveolar space protein, surfactant protein D (SP-D), was elevated in PAM mouse serum, suggestive of lung injury and barrier dysfunction. We contacted

a dozen PAM patients around the world to obtain blood, and found that MCP-1 and SP-D are also elevated in the serum of patients, and are now developing promising biomarkers for disease progression and response to therapy. We found that stones isolated from the lungs of the PAM mice readily dissolve in calcium chelators such as EGTA and EDTA, suggesting therapeutic chelation lavage as a treatment approach; an idea we intend to test in monkeys and bring to the bedside if proven safe. We have also found that a low phosphate diet reduces the stone burden in the lung, suggesting that a simple dietary intervention (perhaps together with a phosphate binder) could be developed as a treatment. Our lab is actively trying to understand the mechanism of stone clearance due to phosphate restriction, focusing on the effect of phosphate hormone mediators such as VitD3 and FGF-23 on expression of alternative phosphate transporters in the alveolar epithelium.

We intend to conduct a trial in PAM patients through the NIH Rare Lung Disease Consortium, a network of 55 rare lung disease clinics located around the world, with Cincinnati as the hub, with co-investigators Bruce Trapnell, MD, and Frank McCormack, MD. The RLDC conducted the MILES trial for LAM, which demonstrated that sirolimus is an effective treatment. On the basis of the MILES result, the FDA approved sirolimus for LAM in 2015, and over 40 percent of LAM patients in North America are now taking the drug. Other past and present Cincinnati-based RLDC projects have included developing a pathologic classification system for the pediatric

interstitial lung diseases, developing diagnostic tests for pulmonary alveolar proteinosis, developing CT scanning as a biomarker of progression for alpha-1 antitrypsin deficiency, developing a longitudinal registry for LAM (MIDAS), and conducting a MILES-like trial of sirolimus in asymptomatic patients with LAM who have normal lung function (the MILED trial).

McCormack and Trapnell have also developed a collaborative UC/CCHMC program called the Translational Pulmonary Science Center, which organizes the resources necessary for translational research in pulmonary disease and operates a CCTST-funded bronchoscopy core for the collection of lung samples.

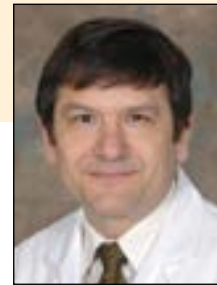
Dennis McGraw, MD

Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine

The primary focus of my laboratory is to understand how G-protein-coupled receptors (GPCR) regulate airway smooth muscle tone, with particular emphasis on the role of b2-adrenergic receptor regulation/dysregulation in asthma. We utilize cell models (including primary cultures of airway smooth muscle from genetically modified mice) to investigate multiple aspects of GPCR regulation including agonist/antagonist binding, receptor trafficking, membrane microdomain localization, dimer/oligomer formation and second messenger signaling. We also have developed transgenic models to target GPCR signal alterations specifically to smooth muscle in order to assess the consequences of receptor and/or signal transduction alterations on physiologic responses of intact tissues and animals.

Current collaborations with Frank McCormack, MD, include an investigation of pulmonary mechanics (airway hyperreactivity and compliance) in different murine models of rare human lung diseases such as pulmonary microlithiasis. I also serve as the director of a newly created Research Bronchoscopy Core that acquires lung samples (bronchoalveolar lavage, epithelial cell brushings and endobronchial biopsies) from human subjects.

Clinically, I serve as the section chief for the Division of Pulmonary, Critical Care and Sleep Medicine at the Cincinnati VAMC. I also serve as a principal investigator and co-principal investigator for pharmaceutical studies that primarily focus on agents for treating asthma and COPD.



- GPCR regulation of airway smooth muscle
- b2-adrenergic receptor regulation/dysregulation in asthma
- asthma, COPD pharmaceuticals
- Research Bronchoscopy Core



David Norton, MD

Associate Professor of Clinical Medicine
Division of Pulmonary, Critical Care and Sleep Medicine
Director, UC Medical Center Medical Intensive Care Unit

- severe acute respiratory distress syndrome (ARDS)
- Prevention and Early Treatment of Acute Lung Injury Trials (PETAL) Network

PERSONAL

- U.S. Air Force service
- running
- NFL and SEC football
- modern presidential politics, foreign policy reading

I am a principal investigator at the College of Medicine for the NIH/ National Heart, Lung, and Blood Institute (NHLBI)-sponsored Prevention and Early Treatment of Acute Lung Injury Trials (PETAL) Network. The grant was awarded in 2014 and will produce four to six prospective, randomized, controlled studies designed to prevent or treat severe acute respiratory distress syndrome (ARDS). The first trial — Reevaluation of Systemic Early Neuromuscular Blockade (ROSE) — began in the winter of 2016, and UC has enrolled several patients. The goal of the study is to help understand whether early chemical paralysis is beneficial in the care of patients with severe acute hypoxemic respiratory failure secondary to ARDS. The second trial (LOTUS-FRUIT) is a prospective cohort study looking at mechanical ventilation practices in the hospitals that are part of the PETAL Network. This work will help shape a low tidal volume for acute respiratory failure protocol for patients with risk factors for subsequent ARDS development

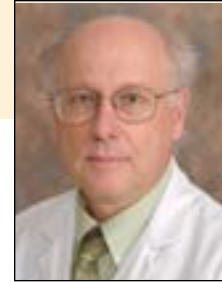
that will be tested later this year in the LOTUS trial. Finally, the VIOLET study will evaluate the benefit of vitamin D supplementation as a strategy for prevention of ARDS in patients with acute respiratory failure who are at risk for this complication. Several other future prospective studies are being evaluated for the remainder of the PETAL Network grant.

This research is supported in the MICU by the Division of Pulmonary, Critical Care and Sleep Medicine, the Division of Trauma and Critical Care, the Department of Neurology and the Department of Emergency Medicine.

I am originally from the Washington, D.C. area and was fortunate to live in many places during my time in the U.S. Air Force before arriving in Cincinnati in 2009. I am married to a Cincinnati family practitioner named Lisa, who also served in the Air Force, and have two boys ages 8 and 4 who keep me young. I love running, football (NFL and SEC), anything 80s and reading about modern presidential politics and foreign policy.

Ralph Panos, MD

Professor
Division of Pulmonary, Critical Care and Sleep Medicine



Cincinnati is the epicenter of the chronic obstructive pulmonary disease (COPD) epidemic that has made COPD the third leading cause of death in the United States. The high prevalence of COPD is due in large part to the high smoking rate as well as significant industrial exposures to various chemicals, dusts and fumes. Our epidemiologic studies have estimated the prevalence of COPD among veterans at the Cincinnati VA Medical Center to be 33-44 percent and two of every three veterans with COPD are not yet diagnosed. COPD health care expenditures account for nearly 10 percent of the entire Cincinnati VAMC budget, and 20 percent of patients with COPD incurred over 90 percent of the expenditures and 70 percent of the encounters for which COPD was the primary diagnosis. Thus, COPD is a common disorder of veterans that causes significant morbidity and mortality, and its treatment is a major expense within the Veterans Health Administration.

Over the past five to six years, we have developed a multidisciplinary and multifaceted clinical research effort into many different aspects of COPD that spans the spectrum of clinical research from local investigator-initiated projects and pharmaceutical trials to multicenter NIH- and VHA-sponsored trials. We obtained nearly \$1 million in funding from the VHA office of specialty care to develop a patient centered approach to the management of COPD. That program developed a VHA-specific screening instrument for the detection of airflow limitation that performed as well as previously validated COPD screening tools, initiated telespirometry, which has now spread throughout the VHA, and led to the publication of The COPD Primer, a comprehensive book for the management of COPD.

Our research team includes students, residents and fellows, and we collaborate with several basic science researchers including Michael Borchers, PhD, and Daniel Hassett, PhD.

- multidisciplinary and multifaceted clinical research into many aspects of COPD
- patient centered approach to COPD management
- COPD screening tool



Bruce Trapnell, MD

Professor, Departments of Pediatrics and Internal Medicine
 Director, Translational Pulmonary Science Center,
 Cincinnati Children's Hospital Medical Center
 Co-Director, NIH Rare Lung Diseases Clinical Research Consortium, RDCRN-3
 Co-Director, Pilot Clinical and Translational Collaborative Studies Core, CTSA, UC

- pathogenesis, diagnosis and therapy of rare lung diseases
- role of GM-CSF in lung homeostasis and defense
- human gene therapy
- pathway-based diagnostic and therapeutic development
- CF, PAP, LAM, indium lung disease
- pulmonary macrophage transplantation therapy for children with hereditary PAP

The Trapnell laboratory has had a long-standing focus on the pathogenesis, diagnosis and therapy of rare lung diseases, the role of GM-CSF in lung homeostasis and defense, human gene therapy, and translational, pathway-based diagnostic and therapeutic development. Approaches involve mouse and non-human primate disease models, molecular and cell biology methodologies, natural history trials, and human-treatment trials. We have contributed to the development of new diagnostics and therapeutics for multiple rare lung diseases including cystic fibrosis (CF), pulmonary alveolar proteinosis (PAP), lymphangioleiomyomatosis (LAM), indium lung disease and others.

Recent key findings include: development of a novel gene correction and cell transplantation therapy approach (pulmonary macrophage transplantation therapy) with extraordinary efficacy and potential to be the first specific therapy for children with hereditary PAP; identification of a reciprocal feedback loop by which pulmonary GM-CSF regulates the size of the AM population; and discovery and characterization of hereditary PAP. Our group has been continuously funded by the NIH in lung disease research since Trapnell came to Cincinnati and has provided training in basic, clinical and translational research at multiple levels. As director of the Cincinnati Cystic Fibrosis Therapeutics Development Network Center for more than a decade, Trapnell served as principal investigator on multiple clinical trials, including studies leading to FDA approval of Creon® and Pancreaze®. He has worked

with patient foundations for CF, alpha-1-antitrypsin deficiency, LAM, and childhood interstitial lung diseases. Trapnell is co-founder and current scientific director of the PAP Foundation. The current research portfolio includes human, non-human primate and mouse studies to determine the pathogenesis of several autoimmune PAP and hereditary PAP. We are preparing to initiate several clinical trials of therapies for PAP including oral pioglitazone and inhaled GM-CSF and a trial of gene correction and pulmonary macrophage transplantation therapy of hereditary PAP.

Current trainees in the Trapnell laboratory include Anthony Saltese, a graduate student in pathobiology and molecular medicine studying cholesterol homeostasis in pulmonary diseases, and Research Instructor Paritha Arumugam, who is focused on stem cell gene therapy for inherited diseases. Recently, the lab received the CCTST Mentored T1 award while Cormac McCarthy, a research fellow in clinical research in rare lung diseases, received the Rare Lung Diseases Scholar award. Assistant Professor Kristin Hudock, who studies the role of neutrophils in rare diseases, also received the following awards: Parker B. Francis Fellowship Grant for 'Uncovering Mechanisms of Lung Injury in CF using iPSC-derived Neutrophils'; the Cystic Fibrosis Foundation Pilot & Feasibility Award, 'CF iPSC-derived Neutrophil Responses in Lung Injury'; and the CCTST CT2 Scholar Award for 'SEQing Mechanisms for Rare Neutropenias: Deciphering the Neutrophil Transcriptome.'

Jane Yu, PhD

Associate Professor
Division of Pulmonary, Critical Care and Sleep Medicine



I lead a research laboratory focusing on investigation of the role of tumor suppressor proteins tuberin (TSC2) and hamartin (TSC1) in steroid action, cell survival, cellular metabolism, tumorigenesis and metastasis, and signaling transduction pathways. My laboratory also develops animal models to test the efficacy of FDA-approved drugs on the progression and metastasis of mTORC1 hyperactive cells, lung inflammation and injury. Current studies include determining the role of estrogen in the progression of lymphangioleiomyomatosis (LAM), a female predominant rare lung disease, from the alteration of signaling pathways, to the integrity of alveolar epithelium and microenvironment in the lung, and to the pulmonary functions. We are also investigating the potential application of using blood-based biomarkers in LAM. Our research has been funded by NIH/the National Heart, Lung and Blood Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, the Department of Defense and the LAM Foundation.

My laboratory developed the first LAM-associated, patient-derived primary cell line and the first metastatic model of LAM. We also have identified mTORC1-independent but mTORC2-mediated activation of prostaglandin biosynthesis in TSC and LAM, and used metabolomics profiling to identify dysregulation of glucose metabolism and pentose phosphate pathway addiction in TSC2-deficient cells.

Specialized equipment available for collaborative research includes the IVIS Spectrum pre-clinical in vivo imaging system.

I'm currently collaborating with Frank McCormack, MD, who provides access to human samples from patients with rare lung diseases; Darcy Krueger, MD, PhD, and David Neal Franz, MD, on studying tuberous sclerosis complex (TSC) neurologic manifestation; Brian Siroky, PhD, on investigating TSC renal abnormalities; and Jiang Wang, MD, PhD, El Mustapha Bahassi, PhD, and Nagla Abdel Karim, MD, PhD, on dissecting the interplay of steroid hormone receptors, autophagy and lung cancer.

- tumor suppressor proteins tuberin (TSC2) and hamartin (TSC1) in cell survival, cellular metabolism, tumorigenesis and metastasis
- animal models to test impact of FDA-approved drugs on mTORC1 hyperactive cells, lung inflammation and injury
- role of estrogen in the progression of LAM



Muhammad Ahsan Zafar, MD

Clinical Instructor
Medical Director of Pulmonary Rehabilitation
Division of Pulmonary, Critical Care and Sleep Medicine

- outcomes research
- quality improvement initiative for COPD exacerbation patients

My focus includes improving outcomes of patients with COPD exacerbations through system redesign and improvement science methodologies. COPD exacerbations are a major health expense in the United States. They also lead to poor quality of life, rapid decline in functional status due to disease progression and higher mortality. This quality improvement initiative aims to improve patient-level outcomes through creating a reliable care delivery system that provides evidence-based best practices consistently to all COPD exacerbation patients in the UC Health network.

I am the team leader of this multi-disciplinary team project that includes physicians, respiratory therapists, pharmacists, care coordinators, nurses and patients. Improvement science methodologies—including system appreciation, understanding

variations, change psychology and learning from rapid tests of change—are utilized. We use model-for-improvement systems for learning, testing and measurements. Successful interventions are continually modified for best results before moving to implementation. In the first phase of the project, we have successfully mitigated 75 percent of system-level failures that were prevalent at time of discharge transition from inpatient to outpatient care. This has led to a 35 percent reduction in 30-day, all-cause readmissions of patients with COPD exacerbation. In the next phase, we will redesign care delivery in the emergency-room setting to reduce 30-day health care utilization and return visits, reduce admission rates from the ER, days spent in the hospital (leading to better quality of life) and reduce the cost of care by minimizing wastes.

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Education

Trainees' Research Grand Rounds

The 2016 Trainees' Research Grand Rounds was held on Friday, June 10, 2016. There were 43 posters presented and 39 mentors. Gregory Rouan, MD, chair, Department of Internal Medicine, Manoocher Soleimani, MD, associate chair for research, and Carl Fichtenbaum, MD, associate chair for translational research, would like to recognize the efforts of the trainees and their mentors in putting together the excellent research presentations for this year's event. They also would like to thank the 49 faculty who served as judges. Their time, support, and efforts are integral to the success of this event.

Basic Science Awards:

1st place

Jamie Tweedle, MS

"TNF α Antagonism Promotes Gut to Lung Migration of CD11b+CD103+ Dendritic Cells that Amplify Regulatory T Cells in Lung Infection"

Mentor: George Deepe, MD, Infectious Diseases

2nd place

Megan Vogel, BS

"Bilirubin Prevents Atherosclerotic Lesion Formation in LDL Receptor-deficient Mice by Inhibiting Endothelial VCAM-1 and ICAM-1 Signaling"

Mentor: Stephen D. Zucker, MD, Digestive Diseases

Honorable Mention

Cindy Hochstetler, BS

"Impact of an Abnormal Bone Marrow Endothelial Niche on Hematopoiesis"

Mentor: Yi Zheng, PhD, Experimental Biology and Cancer Biology

Clinical Research Awards:

1st place (tie)

Mariam Anis, MD

"Successful Treatment of Idiopathic Pulmonary Vasculopathy with Targeted Pulmonary Vasodilator Therapy"

Mentor: Jean Elwing, MD, Pulmonary, Critical Care and Sleep Medicine

1st place (tie)

Su Ah Bae, MD

"Autosomal Dominant Hypophosphatemic Rickets (ADHR) Presenting in an Adult Patient Without Growth Restriction or Skeletal Deformities"

Mentor: Abid Yaqub, MD, Endocrinology, Diabetes and Metabolism

Honorable Mention

Adam Rose, MD / Muhammad Zafar, MD

"Impact of Lung Volume Reduction Surgery (LVRS) versus Endobronchial Valves (EBV) in Patients with Heterogeneous Emphysema: A Decision Analysis"

Mentor: Mark H. Eckman, MD, General Internal Medicine

Judges

Amlal Hassane, PhD

Arun Sendilnathan, MD

Bassam Abu Jawdeh, MD

Begoña Campos-Naciff, PhD

Chris Lindsell, PhD

Daniel Schauer, MD

David Bernstein, MD

Dennis McGraw, MD

Dylan Steen, MD, MS

El Mustapha Bahassi, PhD

Elizabeth Kopras, BA

Elsayed Abo Salem, MD

Enass Abdel-Hameed, MD, PhD

Florence Rothenberg, MD, MS

Fred Finkelman, MD

George Deepe, MD

Gregory Rouan, MD

Hala Elnakat Thomas, PhD

Heather Duncan, PhD

Houman Varghai, MD

Jack Rubinstein, MD

Jaime Robertson, MD

Jane Yu, PhD

Jean Elwing, MD

Jennifer Forrester, MD

Kenneth Bader, PhD

Kevin Haworth, PhD

Laura Conforti, PhD

Mark Eckman, MD

Mary Beth Yacyshyn, PhD

Matthew Wortman, PhD

Melanie Cushion, PhD

Mohammed Inayat, MD

Phillip Owens, PhD

Rajamouli Pasula, PhD

Rajat Madan, MD, PhD

Robert Cohen, MD

Robert Luke, MD

Ruchi Bhabhra, MD, PhD

Shailendra Patel MD, PhD

Stephanie Dunlap, DO

Trisha Wise-Draper, MD, PhD

Vinita Takair, MD, PhD

Vladimir Bogdanov, PhD

William Ridgway, MD

Xiaoyang Qi, PhD

Yukitaka Shizukuda, MD, PhD

Zhongyun Dong, MD, PhD

Research Symposium

2016

The research symposium—occurring simultaneous to Trainee’s Grand Rounds—furthers our efforts at innovation and collaboration by facilitating dialogue within and across our divisions, faculty, and trainees.

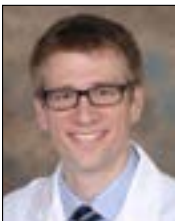


Internal Medicine Scholarly Training in Academic Research (IMSTAR)

The IMSTAR program grew out of the Department of Internal Medicine's desire to promote excellence in research among residents and fellows and 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 by pairing them with mentors within the department. It also includes a focus on educational scholarship offering structured learning experiences in clinical teaching and leadership development. The 2015-2016 academic year marked the program's first year in operation.

2015-2016 IMSTAR Fellows Matt Kelleher, MD, and Dana Sall, MD, are Education Pathway Scholars while Muhammad Ahsan Zafar, MD, FCCP, is a Clinical/Translational Outcomes Research Pathway Scholar. Our scholars have had a very successful first year with two first-author publications, multiple national and regional presentations, manuscripts reviewed and accepted; and IRB protocols approved.

Matt Kelleher, MD, is presently collaborating with Osmosis to develop a testing platform for our residents. The concept of exposure to regular board-style



questions promotes the theories of testing, spacing and interleaving to allow for improved knowledge acquisition and retention. Kelle-

her is in the process of studying the impact of this new program on multiple measures of resident performance. This scholarly work dovetails with the current movement towards lifelong learning for maintenance of certification and embraces the concepts of "testing for learning and not of learning."

Dana Sall, MD, is currently developing and studying a rigorous



procedural simulation program for internal medicine residents. In the current healthcare

environment internal medicine physicians are doing fewer and fewer procedures, while at the same time the patient safety movement is demanding that we have better systems in place to demonstrate physician competency in procedures. To address this, Sall has developed a state-of-the-art simulation program for internal medicine residents to learn the correct techniques of paracentesis in the simulation lab, and then return on a regular basis for "booster training" to maintain these skills. These periodic refreshers in the simulation lab allow one to receive some just in time training and for the residency program directors to document continued competency in this skills. Sall will be critically evaluating how this training improves resident procedural performance and attempting to identify the interval length that is best to bring residents back for these "booster sessions." While starting with only one procedure, there are

plans for this training to spread to all procedures that Internists are commonly asked to perform in the hospital. This work has the potential to have major implications on the future of procedural training for internal medicine residents as well as patient safety outcomes at an institutional level.

Muhammad Ahsan Zafar, MD, is a Quality Scholar at the James Anderson Center for Health Care



Excellence at Cincinnati Children's Hospital Medical Center. His work involves health deliv-

ery system improvement through redesign and innovation to improve patient outcomes and value of care. He worked with a multidisciplinary team that includes hospitalists, nurses, respiratory therapists, pharmacists and care co-coordinators to tackle the high hospital readmission rates after COPD exacerbation. System-level failures and unmet patient needs were identified and a COPD care bundle was designed to mitigate these failures. Using improvement science, the care delivery process was redesigned and 90 percent compliance to the bundle was achieved. This has led to a 35 percent relative reduction in COPD 30-day all-cause readmissions, from 22.7 percent to 14.7 percent. Zafar will next extend the bundle to the Emergency Department (ED) to reduce ED revisits and will also explore ways to reduce the cost of COPD care. •

Bedside Study

Fellow Meagan Gray's passion for patients drives her to discover better ways to help those living with liver disease

For Meagan Gray, a fellow in the College of Medicine's Division of Digestive Diseases, medicine is personal. "I really love getting to know patients and their families," Gray says. In fact, the gastroenterologist was drawn to study liver disease specifically because she liked the idea of working closely with patients from pre- to post-transplant, helping them through a difficult transition process in their health and lives. "You follow patients for a long period of time and develop a relationship with them."

Gray, who went to medical school at the University of Louisville and completed her residency at the Medical University of South Carolina, has plenty of opportunity to work directly with patients during her busy fellowship at UC. A typical day starts with performing procedures, including upper endoscopies and colonoscopies, at University of Cincinnati Medical Center; in the afternoons, she consults on hospitalized patients with complex gastrointestinal and liver problems. Somehow, she also finds time to focus on research that could improve patients' lives—the promise of which particularly excites her.

Her latest project collected hemoglobin A1C—a marker for diabetes—from patients prior to liver transplant to see if higher levels correlated with worse outcomes following transplant, something that previous research has found to be true in vascular and heart surgeries. To her surprise, though, Gray found that for the most part, higher levels of hemoglobin A1C did not correlate with worse outcomes post-transplant, and is now hoping to find out whether that's because liver disease patients have lower levels of hemoglobin A1C in general—and whether there is a better test for glucose control in these patients—a potentially important finding for physicians treating the disease.

"We're seeing more patients with fatty liver disease because our population is becoming more obese, with more diabetes, high-blood pressure and high cholesterol," Gray says. "We want our patients to do well, and understanding the role of hemoglobin A1C is just one thing that's going to help us care for our patients better and help them have better long-term outcomes after their transplant."

Throughout her fellowship research, Gray says she has relied on faculty members in her division—particularly gastroenterologist Stephen Zucker, MD—for guidance and support. "I think that for research, finding a good

mentor—someone who is doing something you're interested in and is willing to teach and show you the ropes—is so important because research isn't something that you can learn from a book," Gray says. "You have to do it to understand it."

Throughout her fellowship research, Gray says she has relied on faculty members in her division for guidance and support.

But Gray, who ultimately hopes to become a transplant hepatologist, says her research interests will always be led by her passion for helping patients in person. "Being sick is a very vulnerable time in someone's life," Gray says. "They're just looking for someone not only to give them medical advice, but to listen to them and give them real hope that things are going to get better." •



Gray found that higher levels of hemoglobin A1C did not correlate with worse outcomes post-transplant, and is now hoping to find out whether there is a better test for glucose control in these patients—a potentially important finding for physicians treating the disease.



Reports



Active Awards June 2016 Department of Internal Medicine

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
CARDIO	Attari	1012669 / Recurrence of atrial fibrillation following non-cardio-thoracic surgery or acute medical illness	5/14/16 - 5/13/19	\$ 20,000	\$ 20,000
CARDIO	Becker	1012566 / 1011829 / CCHMC xxxxxx Sub AHA 155FRN241100000 SHIP AHOY Project	4/1/15 - 3/31/19	\$ 339,658	\$ 68,772
CARDIO	Becker	1012561 / 1011861-DUKE sub 5U54HL112307 ACC DTMI-Center for Thrombotic and Hemostatic Disord	5/1/16 - 4/30/17	\$ 8,787	\$ 8,787
CARDIO	Becker	1012562 / 1011862-DUKE sub 5U54HL112307 Project 2	5/1/16 - 4/30/17	\$ 33,948	\$ 33,948
CARDIO	Becker	1012488 / 1012247 - Duke sub 2R01 HL065222-14A1-Anti-thrombotic Aptamers and Antidotes	9/1/15 - 8/31/16	\$ 8,473	\$ 8,473
CARDIO	Costea	1009540/Duke University Subaward U01HL089709	2/16/14-2/16/17	\$ 39,327	\$ 39,327
CARDIO	Dunlap	1011478/UNC Chapel Hill sub Roche Guide-it POC Substudy	8/1/14 - 7/31/17	\$ 23,999	\$ 23,999
CARDIO	Dunlap	1010824/Roche GuideIT Substudy-Echo	9/1/13 - 4/30/17	\$ 48,000	\$ 48,000
CARDIO	Dunlap	1010828/Duke Subaward GuideIT	4/30/13 - 4/30/17	\$ 172,997	\$ 172,997
CARDIO	Dunlap	1009098/Brigham & Women's Subaward 5R01HL091069	7/1/11 - 2/29/17	\$ 26,450	\$ 26,450
CARDIO	Dunlap	1010832/Roch GuideIT Substudy-Biomarkers	9/1/13 - 4/30/17	\$ 16,800	\$ 16,800
CARDIO	Feldman	1012457 / Grant Integrity in Heart Transplant Mediated by MicroRNAs	2/15/16 - 9/30/16	\$ 242,810	\$ 242,810
CARDIO	Haworth	1012341-Ultrasound-mediated Oxygen Scavenging for Inhibition of Reperfusion Injury	1/1/16 - 12/31/19	\$ 308,000	\$ 77,000
CARDIO	Holland	1011436/2R01NS047603-9- Ultrasound Assisted Thrombolysis	8/15/14 - 7/31/19	\$ 2,764,157	\$ 545,685
CARDIO	Knochelmann	1012335-CHMC 134433 / 5HL121230-02-Nurse Adjudicator for Childhood CV Risk and Adult CVD	12/1/15 - 11/30/16	\$ 36,852	\$ 36,852
CARDIO	Owens	1011730/4R00HL116786-03	3/15/13 - 2/28/18	\$ 735,572	\$ 248,937
CARDIO	Rubinstein	1011578/R01ES024744 Puga	10/11/14 - 10/31/19	\$ 2,417,354	\$ 132,099
CARDIO	Rubinstein	1010831/DHHS-R21 ES023319-02	8/29/13-7/31/16	\$ 110,992	\$ 38,485
CARDIO	Rubinstein	1012408/ Development of IV Probenocid	2/1/16 - 1/31/17	\$ 117,301	\$ 117,301
CARDIO	Tranter	1012321-Investigation of Human antigen R (HuR) as a novel mediator of cardiac hypertrophy	1/1/16 - 12/31/19	\$ 308,000	\$ 77,000
CARDIO	Tranter	1012674 /Development of a HuR inhibitor for the treatment of cardiac hypertrophy	6/1/16 - 7/31/16	\$ 23,700	\$ 23,700

* NOA Project Period Award Amount
 † NOA Current Budget Period

CONTINUED

REPORTS

ACTIVE AWARDS JUNE 2016 CONTINUED

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
DIG	Abdel-Hameed	1012373 / Evaluating Changes in Host-Immune Response during HCV Therapy in Cirrhotic Patients	12/1/15 - 11/30/16	\$ 25,000	\$ 25,000
DIG	Blackard	1010277/1008288 - Bronx VA	10/1/13 - 2/29/16	\$ 152,500	\$ 50,000
DIG	Blackard	1011103 / 1010456 - R01 GM105414	5/2/13 - 4/30/18	\$ 1,496,850	\$ 295,229
DIG	Sherman	1011584- Med Immune Way	12/10/14 - 6/9/16	\$ 151,594	\$ 151,594
DIG	Sherman	1011233 - R56 AI065256 HIV Antiretroviral	7/15/14 - 6/30/16	\$ 534,653	\$ 534,653
DIG	Sherman	1012142-Ultra-deep Sequencing of NS5A Resistance Variants in HCV/HIV Coinfected Patients	9/1/15 - 8/31/16	\$ 78,073	\$ 78,073
DIG	Sherman	1012223-Hepatitis E in HIV-Infected Patients	9/23/15 - 8/31/20	\$ 1,374,995	\$ 274,999
DIG	Sherman	1012602 / 1012513-FIU 800005519-01UG/DA040381	8/1/15 - 7/31/20	\$ 1,065,268	\$ 161,007
DIG	Sherman	1012450-HIV Antiretroviral Therapy and Hepatic Injury	2/15/16 - 1/31/21	\$ 1,815,419	\$ 562,690
DIG	Sherman	1012724/ The Prioritize study: PCORI	3/1/16 - 2/28/21	\$ 258,209	\$ 57,402
DIG	Sherman	1012673/Prevalence of Significance of PNPLA3 Gene Polymorphisms in HCV/HIV infected Persons	6/1/16 - 11/30/16	\$ 70,546	\$ 70,546
DIG	Yacyshyn	1011708 - Emory T317401 sub R01DK087694	12/1/14 - 2/28/17	\$ 60,000	\$ 60,000
DIG	Yacyshyn	1012080 - Cubist	8/4/15 - 2/28/17	\$ 193,081	\$ 193,081
ENDO	Cohen	1012028/1011388 (Yr 3) /1010749 (Yr 2) / 1010368 (Yr 1) - GRADE	1/1/12 - 7/31/20	\$ 2,054,669	\$ 207,271
ENDO	Cohen	1012554 / GWU GRADE sub R01DK104845	9/1/15 - 3/31/20	\$ 221,585	\$ 44,297
ENDO	Falciglia	1012315/1011348 - Falciglia Sub University of Virginia SHINE	8/1/14 - 7/31/18	\$ 8,000	\$ 2,000
ENDO	Patel	1012792 / GCF UN16-00269	6/1/16 - 5/31/17	\$ 55,000	\$ 55,000
ENDO	Perez-Tilve	1012381-Novo Nordisk	1/1/16 - 6/30/16	\$ 348,244	\$ 348,244
GEN	Diers	1010868-Pfizer- Interprofessional Pain Group Visits thru Gen Med 1010868	1/1/14 - 6/30/16	\$ 385,024	\$ 385,024
GEN	Schauer	1010970-Impact of Bariatric Surgery on Cancer Incidence Patients	3/1/14 - 2/28/17	\$ 1,998,718	\$ 629,199
HEM	Bogdanov	1012102-1011805 - 1 R01 CA190717-01 Alternatively Spliced Tissue Factor and Pathobiology of Pancreatic Cancer	4/9/15 - 3/31/20	\$ 1,396,170	\$ 276,298
HEM	Dong	1006682 - NSF sub	9/01/08 - 8/31/18	\$ 1,200,000	\$ 150,000
HEM	Hashemi	1011944-HNCF-Pharmacogenomic Profiling of Circulating Tumor Cells to Guide Head and Neck	7/1/15 - 6/30/16	\$ 20,000	\$ 20,000
HEM	Mercer	1011874-R21CA191814-01A1	6/1/15 - 5/31/17	\$ 406,316	\$ 184,663

* NOA Project Period Award Amount
 † NOA Current Budget Period

CONTINUED

ACTIVE AWARDS JUNE 2016 CONTINUED

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
HEM	Palascak	1011826 / HFM CASCADE	6/1/15 - 8/31/16	\$ 69,161	\$ 69,161
HEM	Palascak	1012312/ 1011659 / 1010330/ 1011222/ 1011659-HFM/CDC	9/30/14 - 9/29/16	\$ 14,000	\$ 14,000
HEM	Palascak	1012610 / 1011826/ 1009394/ 1011157/ 1010442-HFM	6/1/16 - 5/31/17	\$ 69,161	\$ 69,161
HEM	Palascak	1012611 / 1011915 / 1011317-Cascade Home Svc	6/1/16 - 5/31/17	\$ 10,000	\$ 10,000
HEM	Palascak	1012612 / 1011917 / HFM Cascade Pilot Prog	6/1/16 - 5/31/17	\$ 20,000	\$ 20,000
HEM	Qi	1009291 - R01 CA158372-03	9/27/11 - 7/31/16	\$ 1,640,857	\$ 325,282
HEM	Qi	1011394-Bexion U44	9/1/14 - 8/31/16	\$ 103,028	\$ 103,028
HEM	Qi	1012136- Intravenous Enzyme Replacement Therapy for CNS Disorders	8/31/15 - 8/30/17	\$ 565,250	\$ 250,450
HEM	Sasaki	1011482-1 R01NS089815-01	9/30/14 - 8/31/19	\$ 1,670,215	\$ 329,809
IMM	Bernstein, D	1012019/1005596/ 1010751/ 1011196-R01 OH 008795-04-06	9/1/06 - 8/31/17	\$ 1,642,007	\$ 443,832
IMM	Bernstein, D	1011860 / 1009656/ 1010499/ 1011351-T32 AI060515-09-11	9/1/04 -8/31/19	\$ 1,361,995	\$ 276,909
IMM	Bernstein, D	1012564 / 1011794/ 1012564/1010316 - CCHMC/ ES019890	7/1/12 - 3/31/17	\$ 18,026	\$ 3,054
IMM	Bernstein, J	1012158/ 1011380-sub 2U44AI074918-02	7/10/14 - 7/31/17	\$ 487,231	\$ 167,478
IMM	Finkelman	1010808-CFBRE sub ARMY	9/30/13 - 9/29/16	\$ 748,549	\$ 255,749
IMM	Finkelman	1011267 - FARE	7/22/14 - 9/30/17	\$ 734,986	\$ 246,426
IMM	Finkelman	1011228 - 1 R01 AI113162-01	7/15/14 - 6/30/18	\$ 1,334,589	\$ 331,764
IMM	Mina	1012120/1011631-CCHMC sub AR067166	9/15/14 - 7/31/16	\$ 44,600	\$ 14,852
IMM	Ridgway	1011901 - 1 R21AI120084-01A1	6/15/15 - 5/31/17	\$ 434,563	\$ 197,500
IMM	Ridgway	1011903/1011320-UC Davis/ dnTGF Beta RII Mice and PBC-COMPETITIVE RENEWAL	8/11/14 - 6/30/18	\$ 916,511	\$ 213,975
IMM	Ridgway	1012008-Wayne State U-Design Molecular Vaccines for Type 1 Diabetes	9/1/15 - 8/31/16	\$ 49,577	\$ 49,577
IMM	Ridgway	1012461-MCW/ADA-Mechanistic role and therapeutic potential of CD137 in T1D	1/1/16 - 12/31/17	\$ 155,100	\$ 51,700
INF	Cushion	1010974/1010504 Metatranscrip- tomimics HL119190	5/22/13-2/28/18	\$ 1,156,482	\$ 371,529
INF	Cushion	1011916-St. Jude sub AI070271	7/1/12 - 6/30/17	\$ 141,310	\$ 51,966
INF	Cushion	1009523- Duquesne sub R01	2/1/12-1/31/17	\$ 194,484	\$ 194,484
INF	Cushion	1012453 / 1011904-3R01 HL119190 -03S1-Directed Culturing of Pneumocystis Using Metatranscriptomi.	7/1/15 - 6/30/16	\$ 99,894	\$ 99,894
INF	Deepe	1010447 5R01AI106269-02	5/15/13-4/30/18	\$ 2,334,463	\$ 462,463
INF	Deepe	1010697 UMASS SUB	8/6/13-7/31/17	\$ 364,179	\$ 364,179
INF	Deepe	1012686-Dendritic cell KLF2/ Notch Axis and Th2 Responses to Eukaryotic Pathogens	6/10/16 - 5/31/21	\$ 2,292,933	\$ 512,675

* NOA Project Period Award Amount

† NOA Current Budget Period

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REPORTS

ACTIVE AWARDS JUNE 2016 CONTINUED

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
INF	Fichtenbaum	1011864/1011413 Reprieve Site Selection Committee	8/8/14-4/30/20	\$ 111,045	\$ 12,221
INF	Fichtenbaum	1011409 - BWH sub 5R01HL117713-02 ACTG Protocol Funds A5314	12/1/13 - 1/31/16	\$ 62,177	\$ 62,177
INF	Fichtenbaum	1011401 ACTG Protocol Funds for all "A" protocols	1/1/14-11/30/20	\$ 1,721,971	\$ 267,649
INF	Fichtenbaum	1011726- BWH sub AI68636 Protocol Funds ACTG	12/1/14 - 11/30/20	\$ 2,349,648	\$ 391,608
INF	Fichtenbaum	1012428-REPRIEVE Co-Chair	3/23/15 - 11/30/16	\$ 26,621	\$ 26,621
INF	Fichtenbaum	1011786-MGH 225707 1U01HL023336-02 REPRIEVE A5332 and A5333	8/8/14 - 4/30/2021	\$ 627,150	\$ 125,400
INF	Fichtenbaum	1012290-CWRU RES510456 SUB AI69501 Yr 3-	12/1/15 - 11/30/16	\$ 374,060	\$ 374,060
INF	Fichtenbaum	1012333-ACTG Scientific Agenda Steering Committee (SASC) Support	12/1/15 - 11/30/16	\$ 12,000	\$ 12,000
INF	Fichtenbaum	1012651 / HPTN 083: A phase 2b/3 double blind safety and efficacy study of injectable cabotegravir compared to daily oral tenofovir	5/1/16 - 11/30/16	\$ 178,000	\$ 178,000
INF	Fichtenbaum	1012586 / Randomized trial to prevent vascular events in HIV (REPRIEVE)	5/1/16 - 4/30/20	\$ 50,444	\$ 12,221
INF	Fichtenbaum	ACTG Protocol Funds A531412	2/1/16 - 1/31/17	\$ 92,157	\$ 92,157
INF	Fichtenbaum	1012711 / CRB-SSS-S-16-004872	11/1/15 - 6/30/16	\$ 3,401	\$ 3,401
INF	Kaul	1012148-MAETC 2015-2016	9/1/15 - 6/30/16	\$ 216,256	\$ 216,256
INF	Madan	1011574-7 K08 AI108801	8/1/14 - 7/31/19	\$ 704,232	\$ 176,058
INF	Robertson	1012460/1011782/1011016-CHN Ryan White 5H76HA0011-20-00	4/1/14 - 3/31/17	\$ 582,753	\$ 582,753
INF	Subramanian	1011877-AHA 15POST25700182	7/1/15 - 6/30/17	\$ 91,000	\$ 91,000
NEP	Alloway	1010884/FDA HHSF223201310224	9/26/13 - 9/25/16	\$ 2,250,981	\$ 2,250,981
NEP	Alloway	1010125/1U01FD004573/FDA Pharm. Studies of Tacrolimus in Transp.Pts.	9/15/12 - 9/30/16	\$ 2,691,189	\$ 2,691,189
NEP	Amlal	1008340/1R01DK083582	8/26/10 - 7/31/16	\$ 1,504,155	\$ 290,266
NEP	Conforti	1011985-2 R01CA095286-10	7/1/15 - 6/30/20	\$ 1,498,123	\$ 314,805
NEP	Conforti	1012300-Targeted Nanoparticle-based therapy in SLE	12/1/15 - 11/30/16	\$ 60,000	\$ 60,000
NEP	Soleimani	1012274- Dialysis Clinic, Inc. (DCI) Reserve Funds Project #C-3559 / Cincinnati (011)	7/1/15 - 10/31/16	\$ 139,738	\$ 139,738
NEP	Thakar	1012339-Kidney CARE Grand Rounds/Acute Care Nephrology Symposium	1/5/16 - 6/30/16	\$ 25,000	\$ 25,000
NEP	Thakar	1012657 / Hemodynamics and vascular wall biology determine arteriovenous fistula maturation	7/1/15 - 6/30/16	\$ 11,057	\$ 11,057
NEP	Thakar	1012777 / ISCHEMIA clinical trial- CKD study	3/1/16 - 2/28/18	\$ 75,630	\$ 75,630

* NOA Project Period Award Amount

† NOA Current Budget Period

CONTINUED

ACTIVE AWARDS JUNE 2016 CONTINUED

DIVISION	PI	AWARD	PROJECT PERIOD	AWARD AMOUNT *	CURRENT PERIOD †
NEP	Thakar	1012776/ ISCHEMIA clinical trial- Main study	3/1/16 - 2/28/18	\$ 91,290	\$ 91,290
PULM	Baughman	1011957-VUMC 42525 1R01HL117074-03	7/1/15 - 6/30/16	\$ 111,840	\$ 111,840
PULM	Baughman	1011898- fdn for Sarcoidosis Res/FSR-CSN	4/1/15 - 3/31/17	\$ 60,000	\$ 30,000
PULM	Borchers	1011007/R01 HL119538-01A1	4/1/14 - 3/31/18	\$ 1,581,563	\$ 395,000
PULM	Borchers	1011615/Ohio State University Sub R01HL118268-02	1/1/15 - 12/31/16	\$ 120,532	\$ 38,162
PULM	Borchers	1012316-NKG2D Receptor-Ligand Interactions in LAM Pathogenesis	1/15/16 - 1/14/17	\$ 25,000	\$ 25,000
PULM	Elwing	1012454 / CCHMC 137829 R21HL 105333-05	3/3/12 - 2/28/17	\$ 95,000	\$ 15,060
PULM	Gardner	1011988/1011324/CHMC sub T32HLHL007752-21	7/1/14 - 6/30/16	\$ 55,594	\$ 55,594
PULM	Gupta	1012472-Improving Intensive Care Patient Safety Through EHR-based Algorithms	9/1/15 - 8/31/19	\$ 110,332	\$ 20,093
PULM	Hudock	1012324-PBF Fellowship Hudock Uncovering Mechanisms of Lung Injury in CF	10/5/15 - 12/31/17	\$ 131,000	\$ 48,038
PULM	Hudock	1012443 / CFF Hudock15IO	10/1/15 - 9/30/17	\$ 108,000	\$ 54,000
PULM	Joseph	1012329/1011765 / CFF Transforming CF Care Through Shared Decision Making (QI)	1/1/15 - 12/31/16	\$ 92,161	\$ 92,161
PULM	Joseph	1011113/EmoryT164877	7/1/13-6/30/16	\$ 54,494	\$ 27,247
PULM	Li	1012060 - Estradiol and mTORC2 orchestrate to enhance prostaglandin biosynthesis and tumorigenesis in LAM	7/1/15 - 1/14/17	\$ 82,573	\$ 32,573
PULM	McCormack	1011731/1R01HL127455-01	4/1/15 - 3/31/19	\$ 2,593,162	\$ 409,364
PULM	McCormack	1011990 / 1011548/HL127672 RLDC Admin Unit	9/18/14 - 7/31/19	\$ 216,656	\$ 40,605
PULM	McCormack	1011989/1011549/HL12762 RLDC Project 1	9/18/14 - 7/31/19	\$ 476,052	\$ 88,339
PULM	McCormack	1012055/1010758/Baylor Subaward UH2TR00961	9/1/15 - 8/31/16	\$ 167,210	\$ 167,210
PULM	McCormack	1012358 / 1011608 Shriners	1/1/13 - 12/31/17	\$ 439,352	\$ 93,407
PULM	Norton	1012550 / 1011868/ 1011505/ CCLCM-CWRU/U54HL123023-01 PETAL	6/17/14 - 4/30/21	\$ 181,231	\$ 29,299
PULM	Norton	1012421-Reevaluation of Systemic Early neuromuscular blockade (ROSE)	11/17/15 - 4/30/17	\$ 66,526	\$ 66,526
PULM	Yu	1012306-Cornell 16050776 / R01 HL121266-03-	1/1/16- 12/31/16	\$ 32,213	\$ 32,214
PULM	Yu	1012220-7 R01 HL098216-06 Targeting the Estrogen Pathway Prevention & Treat of LAM-NCE	7/1/15- 3/31/17	\$ 178,744	\$ 178,744
PULM	Yu	1012103-7R01DK098331-02	7/1/15 - 6/30/17	\$ 474,000	\$ 237,000

* NOA Project Period Award Amount

† NOA Current Budget Period

REPORTS

New Awards FY 2016 Department of Internal Medicine

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIRECT AWARD AMOUNT *
CARDIO	Becker	Antithrombotic Aptamers and Antidotes	Duke - subaward	09/01/15 - 03/31/19	\$17,668
CARDIO	Feldman	Graft Integrity in Heart Transplant Mediated by MicroRNAs	Roche Organ Transplant Research Foundation	02/15/16 - 09/30/16	\$220,736
CARDIO	Haworth	Ultrasound-mediated Oxygen Scavenging for Inhibition of Reperfusion Injury	AHA	01/01/16 - 12/31/19	\$280,000
CARDIO	Rubinstein	Development of IV Probenicid for ADHF	NCAI	02/01/16 - 01/31/17	\$74,007
CARDIO	Tranter	Human antigen R (HuR) as a novel mediator of cardiac hypertrophy	AHA	01/01/16 - 12/31/19	\$280,000
DIG	Abdel-Hameed	Evaluating Changes in Host-Immune Response During HCV Therapy in Cirrhotic Patients	Bristol Myers-Squibb	01/01/16 - 12/31/16	\$15,385
DIG	Sherman	Hepatitis E in HIV infected patients	NIH	09/23/15 - 08/31/20	\$1,416,937
DIG	Sherman	Ultra-deep sequencing of NS5A Resistance Variants in HCV/HIV Coinfected patients	Merck	09/01/15 - 08/31/16	\$60,053
DIG	Sherman	HIV Antiretroviral Therapy and Hepatic Injury	NIH	02/15/16 - 01/31/20	\$1,232,354
DIG	Sherman	The Prioritize Study/PCORI subaward	University of Florida/ NIH	03/01/16 - 02/28/17	\$101,903
DIG	Yacyshyn, B	Phenotypic stratification of recurrent Clostridium difficile infected patients using circulating P BMC at point of initial infection	Cubist Pharmaceuticals, Inc.	08/04/15 - 02/28/17	\$154,965
ENDO	Perez-Tilve	Novel peptide-based therapies for the treatment of diabetes	Novo Nordisk	01/01/16 - 06/30/16	\$240,168
HEM	Hashemi / Bahassi	Pharmacogenomic Profiling of Circulating Tumor Cells to Guide Head and Neck Cancer Therapy	Brandon C. Gromada Head and Neck Cancer Foundation	07/01/15 - 06/30/16	\$20,000
HEM	Qi	Intravenous Enzyme Replacement Therapy for CNS Disorders	NIH	08/31/15 - 08/30/17	\$328,900
IMM	Bernstein, D	sub 5R01 ES019890	CCHMC	04/01/16 - 03/31/17	\$1,933
IMM	Ridgway	Design Molecular Vaccines for Type 1 Diabetes	Wayne State University	09/01/15 - 08/03/16	\$31,378
IMM	Ridgway	Mechanistic Role and Therapeutic Potential of CD137 in T1D	Medical College of Wisconsin/ADA	01/01/16 - 12/31/21	\$47,000

* NOA Project Period Direct Award Amount

CONTINUED

NEW AWARDS FY 2016 CONTINUED

DIVISION	PI	TITLE	AGENCY	PROJECT PERIOD	DIRECT AWARD AMOUNT *
INF	Kaul	MAETC 2015-2016	University of Illinois-sub NIH	09/01/15 - 08/03/16	\$200,237
INF	Subramanian	Interleukin-4 regulates zinc homeostasis to weaken acrophage antifungal defense	American Heart Association-Great Rivers Affiliate	07/01/15 - 06/30/17	\$91,000
INF	Fichtenbaum	Brigham & Women's ACTG Scientific Agenda Steering Committee	Brigham & Women's	12/01/15 - 11/30/16	\$12,000
INF	Deepe	Dendritic cell KLF2/Notch Axis and Th2 Responses to Eukaryotic Pathogens	NIH	06/10/16-05/31/21	\$2,292,885
PULM	Li	Estradiol and mTORC2 orchestrate to enhance prostaglandin biosynthesis and tumorigenesis in LAM	LAM Foundation	07/01/15 - 06/30/16	\$32,573
PULM	Borcher	NKG2D Receptor-Ligand Interactions in LAM Pathogenesis	LAM Foundation	01/15/16 - 01/14/17	\$25,000
PULM	Gupta	Improving Intensive Care Medication Safety through HER-bas	CCHMC	09/01/15 - 08/31/19	\$76,646
PULM	Hudock	Fellowship Hudock Uncovering Mechanisms of Lung Injury in CF	Parker B Francis	10/05/15 - 12/31/17	\$131,000
PULM	Hudock	iPSC-derived neutrophil responses in lung injury	CF	10/01/15 - 09/30/17	\$100,000
PULM	Yu	Prostaglandin biosynthesis: anovel therapeutic target in TSC disorders	NIDDK	07/01/15 - 06/30/17	\$237,000
PULM	Yu	Molecular and biochemical basis of Lymphangioliomatosis	Cornell sub NIH	07/01/15 - 12/31/15	\$32,704
PULM	Yu	Targeting the Estrogen Pathway for the Prevention and Treatment of LAM	NIH	07/01/15 - 03/31/16	\$113,128
TOTAL					\$9,232,199

* NOA Project Period Direct Award Amount

REPORTS

Intramural Funding Opportunities

The DOIM's commitment to growing research interests and supporting established research programs at all levels continued in FY2016 as the department funded awards for nine investigators totaling over \$240k.

For FY 2016

INVESTIGATOR	DIVISION	AMOUNT	TITLE	PROJECT PERIOD
Rehn Award				
Vladimir Bogdanov, PhD	HEM	\$16,000	Red blood cells and pathobiology of obesity-related cardiovascular disease	9/1/15 – 8/31/16
Megan Vogel, BS	PhD Student	\$16,000	Unconjugated bilirubin inhibits atherogenesis by preventing plaque formation through the inhibition of VCAM-1-mediated monocyte migration	9/1/15 – 8/31/16
		\$32,000		
Junior Pilot Awards				
Hyon Kim, MD, PhD	HEM	\$30,000	Role of atorvastatin to reduce inflammation and acute sickle cell related complications in adult sickle cell patients	1/1/16 – 12/31/16
Radat Madan, MD, PhD	INF	\$30,000	Regulation of neutrophil recruitment during Clostridium difficile infection by a single nucleotide polymorphism in leptin receptor	1/1/16 – 12/31/16
		\$60,000		
Challenge Award				
Fred Finkelman, MD	IMM	\$30,000	Murine models for development of targeted therapies for antibody-mediated disease	3/1/16 – 2/28/17
		\$30,000		
Senior Pilot Awards				
Jason Blackard, PhD	DIG	\$30,000	Treatment and virologic evaluation of hepatitis C virus infection in persons with injection drug use in Ohio	10/1/15 – 9/30/16
Robert Cohen, MD	ENDO	\$30,000	Expanding availability of mean red blood cell age determination to improve HbA1c interpretation	4/1/15 – 5/31/16
Xiaoyang Qi, PhD	HEM	\$30,000	Phosphatidylserine-targeted therapy for pancreatic cancer by SapC-DOPS nanovesicles	4/1/15 – 5/31/16
William Ridgway, MD	IMM	\$30,000	Mechanism of reversal of Type 1 diabetes by soluble CD137	4/1/15 – 5/31/16
		\$120,000		



**UNIVERSITY OF CINCINNATI
COLLEGE OF MEDICINE**

William S. Ball, MD

*Senior Vice President for Health Affairs
Christian R. Holmes Professor and Dean,
College of Medicine*

**College of Medicine
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University of Cincinnati
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