A Message from Drs. Abbate and Salloum
Associate and Assistant Chairs for Research

Another year has passed, and so much has been achieved!!! Congratulations to all of our featured researchers. The number and breadth of publications by our faculty and staff continues to be outstanding. Many investigators have received new grants, while many others have renewed existing grants to continue their work. The department’s belief in the importance of research fosters the mentorship of students and junior faculty, and encourages those who have conducted research to continue to do so through expanding efforts, collaborating within and beyond the department and through new or advancing technologies.

We are truly excited about what we have achieved and where we are headed in 2019. We look forward to new discoveries and innovations.

Dr. Salloum’s Passion for Research

The Department of Internal Medicine would like to extend a warm welcome to Fadi N. Salloum, Ph.D., who was recently named as the department’s Assistant Chair for Research. Dr. Salloum is the Natalie N. and John R. Congdon Sr. Endowed Chair in the Pauley Heart Center and Associate Professor of Medicine (with Tenure) in the Division of Cardiology. He also holds an affiliate faculty appointment in the Department of Physiology and Biophysics. A native of Beirut, Lebanon, Dr. Salloum completed his Ph.D. in Physiology, with emphasis on molecular cardiology, at VCU. After completing his postdoctoral fellowship, he joined the cardiology faculty at VCU in 2009. Dr. Salloum is a Fellow of the American Heart Association (Council on Basic Cardiovascular Sciences), Fellow of the American Physiological Society (Cardiovascular Section), and a member of the International Society for Heart Research. He has authored or co-authored over 92 research articles, many of which are published in the leading cardiovascular journals, including Circulation, Circulation Research and Journal of the American College of Cardiology. Dr. Salloum’s research program has been supported by the American Heart Association and Novartis Pharmaceuticals and is currently funded by the National Institutes of Health (2 R01 grants from NHLBI and R21 from NIA).

Dr. Salloum is very excited to work with all research faculty in the DOIM and support their research endeavors and be a strong advocate and supporter of the research mission of the department.
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The answer to "what is the greatest question in science?" is -- "Where is the next grant coming from?"

“THE DELICATE BALANCE OF MENTORING SOMEONE IS NOT CREATING THEM IN YOUR OWN IMAGE, BUT GIVING THEM THE OPPORTUNITY TO CREATE THEMSELVES.”
- STEVEN SPIELBERG
Bradley Reuter, M.D. is in his third year as an internal medicine resident at VCU. Brad, originally from Fairfield, Connecticut, received his medical and undergraduate degrees from Wake Forest University in Winston-Salem, North Carolina. He also completed research fellowships at the National Cancer Institute and the NIH-sponsored Vanderbilt Summer Research Program. Under the leadership of Dr. Stephanie Call, internal medicine residency program director, Brad is able to work with a wide array of different divisions and attendings through the internal medicine residency program and has very much enjoyed his educational experience as a resident.

Brad chose to come to VCU to complete his residency because he valued the quality of the educators in the program and the strength of the Division of Gastroenterology, Hepatology and Nutrition. Specific attributes of the program such as the schedule, and the location in Richmond, Virginia, also contributed to Brad’s choice.

As a resident, Brad’s focus has been chronic liver disease — specifically decompensated cirrhosis. He hopes to improve the quality of care for this ever-growing patient population. Two years ago, Brad’s projects included a multi-center study using standardized patients to assess GI fellow and attendants’ abilities to diagnosis and manage hepatic encephalopathy patients and a health literacy project which evaluated cirrhotic patients’ health literacy and understanding of hepatocellular carcinoma. Last year, Brad began work on a cost-effective analysis of the use of FIT testing for screening patients less than 50 years old for colon cancer and on a study looking at how well VCU is managing nutrition in its inpatient cirrhotic patients. In general Brad likes to devote his time to patient-centered projects that can improve quality of care at both an individual and system-wide level.

Brad enjoys the complexity of this patient population and how much the liver intersects and works with all the other body systems. He became interested in quality improvement and patient care projects during medical school where he designed a special rotation that allowed him to receive training in this area. When Brad had his first opportunity to be involved in GI consultations during his third year of medical school, he felt he had truly found a field that aligned with his personality and interests.

Over the two and a half years, Brad’s patience, time management and ability to focus on issues from different perspectives have improved. He strives to become a well-rounded internal medicine resident and wants to solidify that foundation of his training and career before embarking on a future career in GI. During the rest of his residency, Brad hopes to have the opportunity to work with additional members of the Division of Gastroenterology, Hepatology and Nutrition and to work to collaborate between divisions, sub-specialties, departments and residency programs to generate interesting and more dynamic projects. Brad would like to see a more formal institutional research mentoring program to help direct younger residents in starting their research careers. Brad feels fortunate to have been able to work with Dr. Jasmohan Bajaj, his research mentor, because Dr. Bajaj is an excellent role model who has invested heavily in helping Brad become a better physician and researcher.

Brad relishes the experiences he has in residency program and cannot imagine a family we have become is special and residency experience.” After do a gastroenterology fellowship and gastroenterologist. He hopes to as an educator while continuing to During his free time, Brad volunteers at educational science program. Over the interested in photography. Brad also new restaurants, breweries and vineyards in

Brad likes to devote himself to patient-centered projects that can improve the quality of care at both an individual and system-wide level.

shared with his classmates in the better residency class. He said, “The has made all the difference in my completing his residency, Brad plans to then to pursue a career as an academic cultivate a career in which he can serve produce meaningful research. an animal shelter and with an past year, he has become very enjoys hiking, traveling and exploring and around Richmond.
Laura Cei, B.S., L.P.N., C.C.R.P., C.C.R.C., who is originally from Richmond is a Clinical Research Nurse Coordinator for the Department of Internal Medicine’s (DOIM) Division of Cardiology. As a research nurse, Laura works to coordinate multiple phase II, III and IV clinical trials as well as device studies. Specifically, she performs all aspects of recruitment and enrollment, which include educating and consenting patients who are eligible and interested in participating in research. Alongside the principal investigator, Laura follows patients’ progress, collects data and reports adverse events as patients advance through studies. Laura is also responsible for adhering to FDA regulations and GCP guidelines to ensure that human subjects are protected in an ethical and safe manner.

In 2002 Laura graduated from nursing school and joined VCU Health as a nurse on an acute medical-surgical floor. In 2010 she took a position as a research assistant with Emergency Medicine and fell in love with clinical research. She worked on many investigator-initiated studies and collaborated with the Department of Anesthesiology and the Surgical Trauma service as well. In 2012 Laura joined the Division of Cardiology as a clinical research nurse coordinator and has since enjoyed working that role. Over the past eight years, she also has had the opportunity to collaborate with Nephrology, Cardiothoracic Surgery, Electrophysiology, Pathology and Ophthalmology on a variety of studies in her role.

Laura reports to Dr. Antonio Abbate, vice-chair of Cardiology and medical director of the Clinical Research Services Unit; Clare Greene, division administrator; and Dr. Kenneth Ellenbogen, chair of Cardiology and director of the Electrophysiology Lab. As a research nurse, Laura is further responsible for communicating and reporting to the principal investigators who lead clinical trials.

In the Division of Cardiology, Laura’s team consists of three research nurses besides herself: Melissa Sears, B.S.N., R.N., Laura Johnson, B.S.N., R.N. and Melissa Hockman, R.N. The team also includes one research assistant, Julia Collins, M.P.H., and a regulatory manager, Amy Ladd, Ph.D. In addition, Laura works closely with the division’s fiscal team, which consists of a fiscal administrator, Brenda Johnson, a fiscal assistant, Cheryl Rocha, and a grants specialist, Laniece Jones. Dr. Abbate leads a team of research coordinators as well, which includes two dieticians, Salvatore Carbone, Ph.D., and Hayley Billingsley, R.D., one research assistant, Brando Rotelli, and a Pharmacy Research Fellow, George Wohlford, Pharm.D. This dynamic group makes up the core of cardiology and electrophysiology research.

Laura is currently coordinating trials that primarily focus on heart failure, acute coronary syndromes or cardiac device implantation. These trials provide patients with access to novel therapies for their challenging conditions. Recently, Laura has been a part of studies wherein the FDA has approved medications to help reduce the risk of heart attacks, strokes and hospitalizations. It has been rewarding for Laura to witness these developments and know that her contributions have helped advance medicine. In the past, Laura has worked alongside Dr. Keyur Shah on rare disease trials for cardiac amyloidosis, which is a debilitating and burdensome genetic condition often leading to heart failure. Dr. Shah has worked tirelessly to educate the public and staff about this illness. Dr. Shah and Laura will continue working to increase visibility and to offer clinical trials as they become available. These trials often set VCU Health apart from other academic medical centers and Laura is proud to be part of a team that is able to provide patients with such exciting opportunities.
Research Administrator Profile:
Brian Washington, M.B.A.

Brian Washington, MBA, moved to Richmond and joined the Department of Internal Medicine (DOIM) as a grants and fiscal manager in June 2017. Brian is originally from Milwaukee, Wisconsin, and received a marketing degree from Concordia College and a master of business administration from Edgewood College in Madison, Wisconsin. Brian felt his prior experience as a financial officer at Kansas University’s Cancer Center would make him a good fit for his new position. Brian started his management career at AT&T and has always enjoyed the financial aspects of his roles. When he transitioned from telecommunications to healthcare finance, Brian felt like he had joined an industry that wasn’t just making widgets. At VCU he feels integral to organization that helps heal people, which is a wonderful team to be a part of.

In his role as a grants and fiscal manager, Brian provides financial management and oversight for all sponsored programs and clinical trials conducted in the divisions within the DOIM. He is also responsible for developing policies and guidelines pertaining to training and technical guidance for all of the Department’s divisions. Brian works closely with, and reports to Rashmi Pershad, the Department’s associate administrator for research. Brian also supports three grant specialists who manage the post-award activities for the DOIM. Brian says his work environment has the feel of a small startup company because it is composed of a team of relatively new members tackling a lot of work, developing processes and training others. Brian likes to use his knowledge and organizational skills to create tools for his colleagues, making their lives easier and more organized, and to provide solutions to challenges through the creation and implementation of policies and protocols.

In the two years that Brian has been in his position, he has worked to streamline post-award processes, has developed access databases and has developed financial reports. He has learned a lot about the systems and tools in place throughout the institution. There are some useful tools that Brian believes can help streamline work processes and is working to utilize and integrate them into his assignments. He hopes to develop Standard Operating Procedures (SOPs) for the department as well as to develop best practices that can be shared with all the divisions. Brian strives to help the DOIM become more efficient in its processes and workflows. He takes his cues from Rashmi Pershad, his supervisor and mentor, sharing that Rashmi has a lot of experience in research administration and is always willing to share that knowledge. Brian supports Rashmi’s vision for what the DOIM can be and is excited about moving that vision forward. He also hopes to facilitate the growth of the financial acumen of the DOIM’s staff and faculty, which in turn will increase the department’s overall financial performance.

First comes thought; then organization of that thought, into ideas and plans; then transformation of those plans into reality. The beginning, as you will observe, is in your imagination.

—Napoleon Hill (American Author of The Law of Success and other self-improvement books)

www.intmed.vcu.edu | Richmond, VA | VCU Department of Internal Medicine
The VCU DOIM has recently created a Rising Scholar Program under the direction of Antonio Abbate, M.D., Ph.D. and Rehan Qayyum, M.D., M.H.S. The Rising Scholar Program is a unique opportunity for clinicians to obtain dedicated training in Clinical and Translational Research, while progressing in their academic careers in Internal Medicine and Subspecialties and improving clinical skills.

The program is designed for individuals who are board certified or board eligible in Internal Medicine, and will last for 24 months with a start date of July first of the respective year. The program combines formal training within the VCU Master of Science Program in Clinical and Translational Research with hands-on research experience under the tutelage of a dedicated mentor. The Scholars are appointed as Clinical Instructors of Medicine within the DOIM, and work 14-16 hours per week (averaged over 4 weeks) within the Hospitalist Night Medicine Program. At the end of the program, trainees are expected to be competitive for appointment to an Assistant Professor faculty position and for a KL2 or K23 NIH training grant. There are currently three clinicians taking part in the program.

The current rising scholars are Graham Gipson, M.D., who joined the Division of Nephrology after completing a fellowship in Nephrology here at VCU, Georgia Thomas, M.D., Ph.D. who joined the Division of Hospital Medicine and Pauley Heart Center research efforts from the University of Maryland where she had been an assistant instructor in the Department of Medicine, and Eziafa Oduah, M.D., M.P.H., M.S., who joined the Division of Hospital Medicine and Massey Cancer Center’s research team from the Berkshire Medical Center, Department of Medicine, in Pittsfield, Massachusetts, where she was an Internal Medicine resident.

Dr. Oduah’s research interest lies in advancing our knowledge of cancer and translating these into developing new and better ways of treating the whole spectrum of the disease. Her inspiration comes from cancer patients for whom she has cared and has been forged by both clinical training and research experiences she has had in medical school and graduate studies. Her current research focus is in understanding the mechanisms regulating mutant P53 and how these can be used to develop new targets and treatment strategies.

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Dr. Thomas’s research focuses on the role cytokine IL-1 plays in changes to cardiac function following thoracic radiotherapy, with particular attention to the methods that best detect these changes. Dr. Thomas plans to enroll patients that have undergone thoracic radiotherapy and assess cardiac reserve through cardiopulmonary exercise testing and biomarker assessment. This project organically marries Dr. Thomas’ interest in cardiology with her background in cancer research.

Dr. Gipson’s research focuses on the exploration of human physiology and its direct application to the clinical evaluation and management of nephrologic problems. He is currently focusing his research efforts on (1) the investigation of the correlation between the degree of chronic kidney disease (CKD), reverse cholesterol transport dysfunction, and CKD-associated atherosclerotic cardiovascular disease (ASCVD); (2) the reappraisal of methods to rapidly monitor changes in urine electrochemistry in the management of hyponatremia (among other diseases); and (3) the exploration of the human lipidome with special attention to the association of certain lipidomes with hemodialysis vascular access thrombosis.

Though there are three participants currently, the table below shows the complete listing of mentors participating in the Rising Scholar Program as well as their areas of research and areas of interest in which rising scholars can partner through the program.

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<th>Area</th>
<th>Mentor</th>
<th>Area of Interest</th>
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<td>Addiction Medicine</td>
<td>F. Gerald Moeller, MD</td>
<td>Opioid and Cocaine Addiction</td>
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<td>Allergy/Immunology</td>
<td>Lawrence Schwartz, MD</td>
<td>Mast Cell Biology</td>
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<td>Cardiology</td>
<td>Antonio Abbate, MD</td>
<td>Inflammation and Heart Failure</td>
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<td>Endocrinology</td>
<td>Fancesco Celi, MD</td>
<td>Thyroid Function and Fat Metabolism</td>
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<td>Family Medicine</td>
<td>Alex, Krist, MD</td>
<td>Family Medicine and Population Health</td>
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<td>Hepatology</td>
<td>Jasmohan Bajaj, MD</td>
<td>Brain-Gut Axis, Microbiome, Liver Disease</td>
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<td>Arun Sanyal, MD</td>
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<td>Richard Sterling, MD</td>
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<td>Hospital Medicine</td>
<td>Rehan Qayyum, MD</td>
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<td>Gordon Ginder, MD</td>
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<td>Steven Grossman, MD</td>
<td>Lung Cancer</td>
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<td>Patrick Nana-Sinkam, MD</td>
<td>Lung Cancer/Exosomes</td>
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<td>Alpha (Berry) Fowler, MD</td>
<td>Acute Lung Injury/Sepsis</td>
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The DOIM has assembled a mentoring team for our junior faculty, which includes Drs. Abbate and Salloum, as associate and vice chairs for research, respectively, as well as Dr. Francesco Celi, chair of the Division of Endocrinology, Diabetes and Metabolism, Dr. Rehan Qayyum, chair of the Division of Hospital Medicine, and Dr. Patrick Nana-Sinkam, chair of the Division of Pulmonary Disease and Critical Care Medicine. The program officially began during the summer and fall of 2017, although mentoring is not new to any of the participants in the program and other senior faculty in the department. Currently, there are approximately 15 junior faculty members being mentored in the program. The members of the mentoring team periodically meet individually with junior faculty to promote their independent growth and provide guidance pertaining to study design and grant submission, while maintaining an efficient balance with clinical and/or teaching responsibilities.

Dr. Salloum explained why a formalized mentoring program was begun. He said:

Mentoring is so important in research, similar to any other field, and it can in fact greatly influence one’s future career. It is crucial for guiding junior faculty, teaching them how to ask the next ‘big’ question and also how to design a reasonable approach to address that question. The most common mistakes that junior scientists make include designing ‘overambitious’ research approaches. Having a good mentor is very helpful in encouraging junior faculty, while also reminding them of limitations and how to tactfully circumvent them. All these efforts should also be targeted at guiding junior faculty in balancing overall duties and setting a solid path towards scientific independence and growth.

Dr. Nana-Sinkam added:

The DOIM research mentoring program represents a unique opportunity to provide junior investigators with the guidance necessary to develop their own research programs. I have personally been very fortunate to have mentors throughout my career who were instrumental in my personal success. After joining VCU, I saw this program as a valuable way to give back and help train our next generation of scientists and physician scientists.

Dr. Qayyum shared why he was enthusiastic to take part in the mentoring program. He said:

Mentoring is a contact sport and I am thoroughly enjoying working with some of the brightest minds. When I was asked to join the research mentor group, I could only say yes; I have been blessed with excellent mentors and I thought it was about time to start returning the favor life has bestowed upon me.

Dr. Salloum’s aim for the future is to further develop the Mentor Program and grow it to encompass more of the department’s senior faculty with many more junior faculty mentees. He believes that having a culture that supports and fosters junior scientists may draw more faculty members into research and encourage them to make such an investment.
Principal Investigator Mario Acunzo, Ph.D.

Grant Project Entitled: “microRNA Editing in Lung Cancer Pathogenesis.”

Dr. Acunzo and his team hypothesized that the phenomenon of microRNA editing is involved in the regulation of the cancerous phenotype of Non-Small Cell Lung Cancer (NSCLC), which they are investigating through the analysis of NSCLC exosome samples.

RNA editing is a widespread post-transcriptional mechanism that modifies the sequence of primary RNA transcripts. The most common post-transcriptional modification in mammals has been found to be the deamination of Adenosine to Inosine (A-to-I). As a result of this modification, Inosine is then interpreted as Guanosine (G) by the cell’s splicing and translation machinery, effectively changing the sequence of the primary transcript, and directly influencing its function and/or regulation.

Recent reports indicate that RNA editing also occurs in microRNAs (miRNAs). It has been estimated that 10-20% of miRNAs undergo A-to-I editing at the pri-miRNA level. While A-to-I editing at the pri- or pre-miRNA editing sites (ESs) can change both the maturation and the expression of miRNAs, the edits occurring in the mature miRNA sequence can drastically alter its targetome and consequently modify its function, particularly in the seed regions (MSRs). Moreover, it has been suggested that RNA editing is aberrantly acting on human diseases, including lung cancer.

Cancer patients exhibit abnormally present, measurable miRNAs in their plasma, serum, and cellular vesicles. Circulating miRNAs present in the exosomal cargo play a crucial role in human cancers, including lung cancer. Using bioinformatic analysis coupled with Next Generation Sequencing (NGS), Dr. Acunzo’s team detected, for the first time, a deregulation in edited microRNAs in NSCLC patient exosomes. They intend to study the function of such edited microRNAs when delivered to lung cell lines.

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As with all research, the need for funding is paramount in order to sustain any academic inquiry, particularly when researching a lesser-known area such as RNA editing. The preliminary data Dr. Acunzo’s team has presented encouraged him to ask for funding, which allows his research to move forward and in turn produce more valuable data that will further elucidate the phenomenon of RNA editing in Non-Small Cell Lung Cancer.

In Dr. Acunzo’s research, receiving this grant has been crucial for the development of original preliminary data. One of the goals of the DOIM grant is the creation of preliminary data for the application of external funds. If selected, the continuation of this grant will allow Dr. Acunzo to better fund his research and further contribute to the DOIM goal of scientific development. Furthermore, Dr. Acunzo believes that more funding is necessary to support his research because it will help to understand NSCLC biology enough to contribute new therapies.

The grant money will be used partly to pay a technician and partly to buy regents needed for the research. In particular, the majority of the grant money will be used for designing and buying custom probes and regents needed for the research such as the edited microRNA-411-5p needed for the overexpression studies and the custom probe needed for the detection of such edited microRNA in vitro.

Dr. Acunzo and his team have already concluded the Specific Aim1 identifying NSCLC cell lines that express the edited miR-411-5p. They are in the process of ordering custom reagents for studying the effects of this edited microRNA in NSCLC cell lines (Specific Aim2). They will test the effect of the miR-411-5p overexpression in NSCLC recipient cell lines by measuring: a) Cell cycle and cell proliferation and b) migration and invasion. In the future they plan to globally profile the effect of the edited miRNA-411-5p on the transcriptome in NSCLC by Next Generation Sequencing.

Dr. Acunzo and his team have already produced some interesting data about circulating edited microRNAs in lung cancer. Once they understand their function in NSCLC, they will be ready in the next 18 months to apply for external funds. In general, they believe that the data they will produce thanks to the DOIM grant will improve the knowledge of the NSCLC biology. The study of the edited microRNA functions will open a completely new frontier in the study of the relation between RNA editing and lung cancer. In the long run the team aims to profile the edited microRNA in the circulation and in tissues of a large number of human lung cancer samples trying to uncover their biomarker potential and real functions of the editing phenomenon in lung cancer.
2017-2018 DOIM Pilot Project Grant Recipients
Continued

Principal Investigator Jasmohan Bajaj, M.D.

Grant Project Entitled: “Application of Novel Neuroimaging Methods Based on Human Connectome Project in Hepatic Encephalopathy”

Dr. Bajaj and his team are investigating the neuro-anatomical and neuro-metabolic basis of brain dysfunction in cirrhosis (minimal and overt hepatic encephalopathy, MHE and OHE) using novel neuroimaging techniques via the human connectome project (HCP).

The current data regarding the neuro-anatomical and neuro-metabolic basis of MHE and OHE is inhomogeneous due to variation in techniques and processing. The human connectome project uses novel processing techniques providing more details. Details are also lacking on the effect of lactulose on the brain in MHE which Dr. Bajaj and his team aim to explore via HCP. Eventually they hope to translate their findings to clinical endpoints.

This is a novel study and as far as Dr. Bajaj and his team know has not been undertaken so far. Details regarding the neuro-pathophysiology of HE and the effect of lactulose on the brain, will help in developing new therapies for HE. In order to conduct a larger study Dr. Bajaj needs to provide a proof of concept pilot study. The generous grant from the DOIM has helped Dr. Bajaj and his team recruit subjects to gather preliminary data for this pilot study as well as pay for the MR scanning.

Currently, Dr. Bajaj and his team are actively recruiting subjects. They have six controls and 11 cirrhotic subjects. They plan to continue recruiting and hope to implement the next phase of lactulose prescription for the next patients. The next step will be to apply for a larger grant. The current grant funds payment to the subjects and pays the CARI center for their MRI facilities. It also helps pay for the lactulose Dr. Bajaj and his team will be prescribing.

Soon Dr. Bajaj and his preliminary data from spectroscopy and DTI in also have data in regard MHE patients before lactulose. This will be will be used to determine functional regions that condition and also set funding.

The team will have enough functional MRI, MR all groups. They will to brain changes in and after treatment with exciting new data that mine newer brain are associated with this the stage for future
Principal Investigator Salvatore Carbone, M.S., Ph.D.

Grant Project Entitled: “Unsaturated Fatty Acids Enriched-Diet to Improve Cardiorespiratory Fitness in Obese Patients: a Feasibility Study”

In this pilot clinical trial, Dr. Carbone and his team are assessing the feasibility of a dietary intervention aimed at increasing the consumption of unsaturated fatty acids (UFA), also known as ‘healthy fats’, for 12 weeks, to improve exercise capacity in patients with obesity and heart failure with preserved ejection fraction.

Dr. Carbone is a nutritionist by training, therefore understanding how diet affects the cardiovascular system has always been a central point of his research. Moreover, he and his team have recently published an original manuscript (Carbone S et al. J Am Coll Cardiol Basic Trans Science 2017;2(5):513-25) in which they have shown a correlation between the consumption of unsaturated fatty acids (UFA) and greater exercise capacity in obese patients with heart failure with preserved ejection fraction. They have also shown an improved cardiac function and reduced weight gain in mice fed with a diet rich in UFA, compared with mice fed with a diet with similar caloric intake, but with higher a amount of saturated fatty acids and a lower amount of UFA.

The associations found in the recently published manuscript, together with the interesting pre-clinical data obtained in the lab, clearly required an interventional clinical trial to support Dr. Carbone’s hypothesis. However, a pilot trial such as the one recently funded by the DOIM is needed to determine the feasibility of the intervention, and to obtain preliminary data to design an adequately powered randomized controlled trial in the future to measure the effects on clinical outcomes. This grant will allow Dr. Carbone and his team to obtain crucial preliminary data, which will be required for future submission for extramural funding from institutions such as the National Institutes of Health and the American Heart Association.

The project is going very well. So far, Dr. Carbone and his team have received IRB approval, and have enrolled about half of the participants they have planned to. The hope is that within a few months they will complete this pilot study and have enough preliminary data for extramural submissions.

The grant money is being used to pay for the use of the facilities, instruments (i.e., echocardiography, metabolic cart to perform cardiopulmonary test), to perform research labs and also to reimburse patients for their expenses related to the food Dr. Carbone and his team are recommending the patients eat on a daily basis (i.e., olive oil, canola oil, avocado, seeds, fatty fish...), and for their time and willingness to participate in this research study.

In addition to the DOIM grant, Dr. Carbone recently has been awarded with a VCU Pauley Heart Center Pilot Grant which will support a sub-study of the one proposed in the DOIM grant. In addition to measuring the effects of the dietary intervention on the cardiovascular system in the DOIM-funded grant, they will also measure the effect on metabolism using the new whole indirect calorimeter room located in the Clinical Research Unit, in a joint effort with the Division of Endocrinology, Diabetes and Metabolism. Additionally, they have ongoing clinical trials with glucose-lowering medications in patients with diabetes and heart failure, from which Dr. Carbone hopes to obtain important clinical data soon.
Grant Project Entitled: “The Timing and Predictors of Palliative Care Among Cancer Patients: A Population-Based Study”

This is a pilot study for population-based research in access to and use of specialist palliative care services. Palliative care inter-disciplinary teams provide an extra layer of support for patients with progressive, life-limiting diseases such as cancer and heart failure. They focus on prognostication, communication about goals of care, and expert symptom management. These services are in place at some but not all local hospitals.

Dr. Cassel has conducted a lot of research on the impact of palliative care, focusing on the impact on patients (such as improvement in symptom burden) and impact on hospitals and payers (such as a reduction in hospital admissions and costs of care). It is not clear from single-site studies, or even multi-site studies, who has access to palliative care and who is using it. This is especially important in the Richmond area where only some hospitals have palliative care services. Dr. Cassel and his team want to see if palliative care use is associated with cancer type and insurance type.

It is time in the evolution of the palliative care field to take a more public health approach to some outstanding questions: Are there inequities in access to palliative care in a given community? Is palliative care access and use related to the quality of end-of-life care, and its cost? How can the public health principles of health promotion, prevention and protection be applied to the lives of persons with advanced illnesses, and their families? For too long, research in palliative care has been stuck at the level of single sites or a small number of widely scattered in multi-site studies. Dr. Cassel believes there is much value in taking a community-level or population-level approach to questions about access, utilization, and impact.

With his colleagues Donna McClish PhD (Biostatistics), Egidio Del Fabbro MD (Dept of Internal Medicine), and Nevena Skoro (Massey Cancer Center), Dr. Cassel had submitted a proposal to the American Cancer Society for a 2-year pilot project in palliative care for a “Community-wide study of cancer care, palliative care, and hospice.” They received an “Outstanding” score (1.0-1.5) but they had insufficient funds to fund it, so they suggested that Dr. Cassel and his team get some of the preliminary data sharing steps completed before resubmitting. The DOIM funding will allow Dr. Cassel and his team to complete the initial phase of data acquisition steps so that they can re-submit the proposal to move directly on to acquiring additional data on hospitalizations and hospice use.

Dr. Cassel and his team are working through the data acquisition steps with the palliative care practices at CJW and Bon Secours hospitals, as well as the Virginia Cancer Registry (VCR). The hospitals are providing data on who used palliative care services in the past 6 years (including when and what form – for example inpatient versus outpatient), and Dr. Cassel’s team will link those to data on cancer decedents from the VCR (including cancer diagnosis date, cancer type, cancer stage, demographics, census track, and date of death). They will then add VCUHS data and link census track to socio-economic characteristics such as neighborhood poverty level, educational attainment, and employment. With those data in hand, they can answer their pilot questions which are focused on the characteristics of cancer patients associated with using palliative care services.

Dr. Cassel hopes to publish the pilot data in a cancer, public health, or palliative care journal, and then receive funding from the ACS to incorporate outcomes data regarding hospitalizations and hospice enrollment. In fact, we were recently notified that Dr. Cassel received funding notice from the ACS based on the data generated with the support of his DOIM pilot grant. We are very pleased with this outcome and the excellent return on investment in our talented faculty members.
2017-2018 DOIM Pilot Project Grant Recipients
Continued

Principal Investigator Zachary Gertz, M.D.

Grant Project Entitled: “Remote Ischemic Preconditioning to Prevent Doxorubicin-Induced Cardiotoxicity”

Anthracyclines are a group of chemotherapy drugs that can cause heart failure. Remote ischemic preconditioning is a process of causing brief, controlled episodes of ischemia (occluding a blood vessel), that has been shown to make the heart better able to tolerate certain insults. The purpose of this study is to see whether remote ischemic preconditioning can prevent or reduce heart failure from doxorubicin, an anthracycline chemotherapy agent. Dr. Gertz and his team are working with mice in this study.

Doing this kind of in depth research is expensive. Because of this reality, Dr. Gertz knew he needed to find funding to support his research. The pilot grant will enable Dr. Gertz and his team to study over 100 mice. All of the mice will receive doxorubicin, but only half will get remote ischemic preconditioning. So far Dr. Gertz and his team have studied over half of the mice, and the mice with preconditioning appear to be living longer. This suggests the treatment has worked. Now they will use the rest of the mice to confirm this finding and to try to understand the mechanism of how preconditioning works. The team will explore things like fibrosis of the heart, free radical formation, and mitochondrial function. Dr. Gertz believes his team should be finished collecting data by the spring 2018. They hope to have a manuscript prepared for publication by fall 2018, and will also be applying for external funding during that time.

Principal Investigator Genta Kakiyama, Ph.D.

Grant Project Entitled: “Biomarker Development for Assessing Severity of Non-alcoholic Fatty Liver Disease (NAFLD)”

This proposal aims to demonstrate that serum oxysterol levels and markers of the activated inflammasome correlate with steatohepatitis and its severity; establishing a liver specific approach for those in early stage progression from steatosis to steatohepatitis (NASH). Upon completion of this study, Dr. Kakiyama is expecting to identify noninvasive biomarkers for assessing severity of Non-alcoholic fatty liver disease (NAFLD).

It is believed that NASH, the progressive form of NAFLD, represents an inflammatory response to the accumulation of toxic lipids within hepatocytes triggering development and progression of fibrosis. However, it remains unclear why lipid accumulation does not always result in progression to NASH. This inconsistency in disease progression may be attributed to different cytotoxic potentials of lipids that accumulate in the liver and the ability of the liver to reduce exposure to these toxic molecules. Potential toxic/injurious lipids include free fatty acids, phospholipids, cholesterol, and oxysterols, but in vivo there is no clear evidence of a direct ‘cause and effect’ to these potential injurious agents, therefore, Dr. Kakiyama and his team have been studying (Continued on page 15)
2017-2018 DOIM Pilot Project Grant Recipients

Continued

the role of the ‘acidic pathway of bile acid synthesis,’ on lipid metabolism and cholesterol homeostasis. This is a hepatic pathway of metabolism of cholesterol in which hepatocyte mitochondria generates two potentially injurious key intracellular regulators of lipid homeostasis, 25-hydroxycholesterol (25HC) and 27-hydroxycholesterol (27HC). Preliminary data suggested that the liver of western diet-induced NAFLD mice accumulated high levels of these oxysterols due to significant suppression of Oxysterol 7α-hydroxylase (Cyp7b1).

Of note, our investigations have shown Cyp7b1 controls intercellular oxysterol levels. Since it is known that genetic absence of CYP7B1 in the first year of life leads to accumulation of oxysterols (and their unusual metabolites) along with rapid progression to inflammation and liver fibrosis, they hypothesized that in NAFLD there is chronic suppression of CYP7B1; and, the subsequent chronic increase in oxysterols/oxysterol metabolites becomes the major driving force for transition from NAFLD to NASH (Figure 1). Dr. Kakiyama and his team think serum oxysterol/metabolites levels as well as inflammasome activation could be utilized as new noninvasive biomarkers to establish the disease activity and progression.

Recently the presence and progression of liver fibrosis has become increasingly recognized as the most reliable predictive marker of NAFLD outcomes. At present, diagnosis of NASH and definitive fibrosis staging is achieved only by liver biopsy; this “imperfect gold standard” carries high costs, a non-negligible risk of complications, and is associated with some degree of sampling biases. Current non-invasive blood tests for the assessment of fibrosis largely focus only on detection of advanced stage fibrosis, and are yet unable to monitor modest changes in fibrosis progression. Therefore, there is a critical need for development of new, non-invasive diagnostic tests that can effectively detect steatohepatitis as well as discriminate between minimal fibrosis (F0-1) and significant fibrosis (F2-4).

It has been more than five years since Dr. Kakiyama began working on the research regarding regulation of cholesterol metabolism and lipid homeostasis in Dr. William Pandak’s laboratory. Much of the preliminary data

![Figure 1: Summary of the central hypothesis: CYP7B1 mediated progression from steatosis to steatohepatitis. Chronic excess of lipids causes suppression of hepatic CYP7B1, and generates accumulation of lipotoxic oxysterols and their unusual metabolites, which initiates/incites liver inflammation. Present study showed that the hepatocyte mitochondria generated not only common 25HC and 27HC but also 24HC. Under suppression of Cyp7b1, the metabolisms of these oxysterols were routed to hydrophobic 3β-hydroxy-5-cholestenolic acid (3βOH-Δ5-ChA) and lithocholic acid (LCA), creating hepatotoxic pathway. This mechanism shows oxysterols and their unusual metabolites, as well as inflammasome markers (Caspase-1, 1L-1β) may serve as biomarkers for risk evaluation of disease progression from steatosis to steatohepatitis.](image-url)

(Continued on page 16)
presented in this proposal were accumulated under his supervision. Last year, Dr. Kakiyama received an award for young investigator in liver research from Gilead Sciences Inc, and was promoted to an Assistant Professor with university support. He feels it is now time to take the next steps, which is to be independent. This pilot grant will give Dr. Kakiyama an opportunity to collect sufficient data to justify his central hypothesis and apply for federal funding independently.

Based on the central hypothesis, Dr. Kakiyama proposed two specific aims: 1) To study, in a mouse NAFLD model, the effect of down-regulation of Cyp7b1 on liver/serum oxysterol and its metabolites levels, and the ability of those metabolites to activate the inflammasome; and 2) To demonstrate, in humans, that serum oxysterol levels and markers of the activated inflammasome correlate with steatohepatitis and its severity. Currently, Dr. Kakiyama and his team are working on aim 1. Following is the summary of results they have obtained so far. First, they have confirmed 2 weeks Western Diet (WD) feeding on the NAFLD mice (B6/129) suppressed Cyp7b1 mRNA expression to 80±10% (n=5) as compared to chow diet fed controls. This suppression was well-correlated to increases in their 25HC and 27HC levels as well as inflammasome activity levels as determined by IL-1β (Table 1).

<table>
<thead>
<tr>
<th>Table 1: Hepatic Oxysterol, Cyp7b1 mRNA expression, ALT and IL-1β levels in the NAFLD model mice (B6/129).</th>
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<tr>
<td></td>
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<tr>
<td>RC</td>
</tr>
<tr>
<td>WD</td>
</tr>
<tr>
<td>WD (STARD1 overexpression)</td>
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<td>*n=3-5 each group</td>
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</table>

Since ‘histologic’ inflammation was not yet evident in these steatosis mice, Dr. Kakiyama and his team believe this inflammasome activation represents an initial step of inflammation. In addition to the mice model, Dr. Kakiyama and his team have analyzed human steatosis livers which were obtained from the NIH Liver Tissue Cell Distribution System. What they found was a comparable 62±13% (n=3) CYP7B1 mRNA suppression and well-correlated 27HC levels (Figure 2).
In these NAFLD mice of Cyp7b1 suppression, they have found that the hepatic mitochondria generate not only common 25HC and 27HC but also 24(S)-hydroxycholesterol (24HC). This 24HC can be metabolized to lipotoxic 3β-hydroxy-5-cholestenoic acid and lithocholic acid (LCA), creating a potential hepatotoxic pathway. These unusual metabolites can also be candidates for specific NAFLD markers (See Figure 1).

In the next step, they will work on aim 2. After obtaining the IRB approval, Dr. Kakiyama and his team will recruit patients who are seen in the Hepatology clinic with imaging-confirmed diagnosis of NAFLD and receiving standard of care work-up for NASH including a liver biopsy. They will determine whether serum oxysterol/oxysterol metabolites levels and markers of the activated inflammasome (i.e. IL-1β) correlate with steatohepatitis and its severity.

The mice used in the present study, such as B6/129 (NAFLD model), and Cyp7b1−/−, have been bred in Dr. Kakiyama’s lab for several years, and are necessary for keeping these colonies going for these studies. Therefore, most of the budget is directed towards animal purchase and maintenance fees, and personnel for the animal handling technicians. The rest of the funding is used to purchase lab supplies such as reagents, solvents, and enzymes for the bioanalytical assays.

Given the known interacting homeostatic regulation found amongst cholesterol, lipid, and glucose metabolism, it is reasonable to consider the insulin signaling pathway is involved in the regulation of CYP7B1. The hyperglucagonemia associated with the insulin resistance found with type 2 diabetes is now well appreciated; and its potentiating hyperglycemic effects to insulin resistance have led to treatment goals to approach it. In fact, Dr. Kakiyama and his team have initial evidence in the direct effects of glucagon on the regulation of CYP7B1 in primary murine hepatocytes. The direct coupling of glucagon and CYP7B1 would give immediate relevance as to why NAFLD appears to progress more rapidly in the setting of insulin resistance. Within the next 1-2 years, they will collect more data regarding evidence of CYP7B1 ties to insulin resistance. If Dr. Kakiyama and his team successfully collect data, they will apply for an external grant in this regard.
2017-2018 DOIM Pilot Project Grant Recipients

Continued

Principal Investigator Mohammad Siddiqui, M.D.

Grant Project Entitled: “The Relationship Between Metabolic Flexibility and Obesity in Liver Transplant Recipients with Non-alcoholic Fatty Liver Disease”

Obesity is a complicated chronic medical disease that has rapidly grown to epidemic proportions over the past 30 years. Although often stigmatized, obesity results from complex interplay between genetics, environment, and behavior. Similar to the general population, obesity is a major healthcare challenge in the field of solid organ transplantation, particularly in liver transplant recipients (LTR). Although the survival rates in liver transplant recipients are at an all-time high, it remains considerably lower when compared to age- and gender matched cohorts from the general population. A key driver of the reduced mortality in liver transplant recipients is obesity, which can occur in up to 80% of LTR depending on the etiology of chronic liver disease. Post-transplant increase in BMI has also been associated with an increased risk of de novo nonalcoholic fatty liver disease, increased graft failure, and development of cardiometabolic risk factors. Interestingly, weight gain after liver transplantation appears to be universal and even patients who are underweight or optimal weight tend to gain weight after liver transplantation. The exact mechanism underlying the pathophysiology is complex and not well understood and appears to be further compounded in LTR due to chronic exposure to immunosuppression.

There is data that the inability to utilize non-carbohydrates as food sources can lead to weight gain and obesity. This is linked to several factors including chronic inflammation, insulin resistance, gut hormones to name a few. All of these factors are common in LTR and may explain weight gain and particularly the severity of weight gain. Thus, in his project Dr. Siddiqui and his team will take LTR and analyze their ability to utilize various biofuels for energy sources linking them to weight, distribution of weight and severity of liver disease.

Dr. Siddiqui became interested in this topic as he has a keen interest in the overlap between liver, heart and insulin resistance. This hypothesis leverages the strength at VCU to generate preliminary data for hopefully a competitive R-type grant application. The current DOIM grant provides Dr. Siddiqui with the resources necessary to generate data to not only write a competitive grant but also improve the quality and quantity of care of liver transplant recipients. He is currently in the process of enrolling patients, as well as working on the R21 application. The money from the grant is being used to pay for the metabolic chamber (to measure metabolic flexibility) and serum blood tests.
Sarcoidosis is an inflammatory disease with an unpredictable clinical course that can affect many different organs (especially the lungs and heart), and while we can recognize features of the disease, we do not yet understand the underlying cause. Dr. Iden, Dr. Syed, and Dr. Ward’s research hopes to elucidate the antigens that initiate the immune system’s response in sarcoidosis.

Drs. Iden and Syed, both pulmonologists who treat sarcoidosis, realized that they could not tell their patients what caused their disease or what the optimal treatment should be. Because of Dr. Ward’s basic science immunology background, Drs. Iden and Syed approached him to help elucidate the immunology of sarcoidosis. Together, the three then came up with the idea for a bottom-up approach to identifying the causative antigens in this disease.

The estimated prevalence of sarcoidosis in the US is about 60 cases per 100,000 persons, but within certain areas, the prevalence can be much higher. One such area is the southeast US, which includes the patient population here at VCU. There are large numbers of patients coming through the VCU clinics, but currently we cannot be sure the treatments will be successful, nor can physicians be sure which patients will go into remission and which will progress. Drs. Iden, Syed and Ward felt that they could do more for these patients, and the first step was to understand more about the disease.

The grant Drs. Iden, Syed and Ward received is critical in that it allows them to validate their long-term research plan. Advances in research technologies have made it possible to sequence the genes of individual T cells and to reconstruct likely antigens from T cells. But as far as they can tell, no one has combined these techniques and directly applied them to a human disease. Drs. Iden, Syed and Ward want to know that they can obtain all the data they need from real patients with sarcoidosis.
Drs. Iden, Syed and Ward are currently optimizing their techniques for obtaining DNA from tissue and blood samples from subjects with sarcoidosis, and shortly they will begin sequencing the DNA of T cells found in the blood and lung tissue of persons with sarcoidosis. They will use this information to help identify the T cell clones most likely responsible for directing the formation of granulomas, the type of immune response characteristic of sarcoidosis.

The funds from the grant allow Drs. Ideny, Syed and Ward to pay for the sequencing of the subjects’ T cells and to discern the subjects’ HLA haplotypes. In the next 18 months, they hope to have identified subgroups of T cells associated with the develop of granulomas in their first group of subjects. Additionally, Drs. Iden, Syed and Ward aim to have identified themes within the HLA proteins expressed by persons with sarcoidosis. They plan to use this data to secure funding to identify both T cell clones and bacterial signatures from individual subjects with sarcoidosis. Combining these data should let them discover which bacterial antigens are associated with the formation of sarcoidosis granulomas by T cells.

Please see the accompanying schematic of the long-term “bottom-up” approach to the project.
Principal Investigator Stefano Toldo, Ph.D.

Grant Project Entitled: “Differential Signaling of the Interleukin-18 Receptors in Obesity and Heart Failure”

The goal of the research project is to understand the role of a pro-inflammatory cytokine, Interleukin-18 (IL-18), and the two receptors it activates, named IL-18R and NCC, in the development of obesity and heart failure. IL-18 has opposite effects in the setting of diet induced obesity. On one hand it seems to suppress the appetite and the gain of weight, but on the other hand it induces heart dysfunction. Dr. Toldo and his team believe that by understanding how IL-18 promotes this dual effect they may be able to develop targeted therapies to block the detrimental effects associated with obesity.

Cytokines are proteins that are produced during an inflammatory process with a function to change the function of target cells. Most of the times, the effects of these cytokines are good, because they help to fight infections. However, when these proteins are activated in response to chronic diseases, they may cause more harm than benefits. These proteins are elevated during heart or metabolic diseases and Dr. Toldo and his team believe that they have a role in negatively affecting organ function. Over the past years Dr. Toldo’s group and others have recognized that blocking IL-18 with drugs prevents the development of heart diseases. However, before testing it in patients Dr. Toldo and his team need to understand as much as possible about the biological effects of this protein.

There are millions of people affected by heart failure, and still physicians do not have a complete understanding of why many patients do not respond to the current therapies. The association of obesity and unhealthy diet with the development of cardiovascular diseases and heart failure is very strong. Dr. Toldo believes that by understanding the biology of IL-18 it will be possible to better understand obesity and find a treatment for heart failure patients.

This award has an enormous importance. Many times, for junior faculty like Dr. Toldo it is difficult to find resources to cultivate their ideas. To apply for external funding, they need good ideas but also supporting evidences. This type of grant makes it possible to retrieve those supporting evidences necessary to apply for external funding in a competitive manner.

Dr. Toldo has characterized the metabolic and cardiac phenotype of mice with genetic mutations of the IL-18 receptors. After 6 months, he and his team have learned more about the physiological role of one of the protein.

(Continued on page 22)
involved in the IL-18 signaling, the NCC receptor. They are currently developing a mouse that lacks the IL-18R and NCC. This mouse will be a key piece to understand the biology of IL-18 and its receptors. The grant is supporting the purchase of materials, the expenses associated with developing and maintaining the mice and the support for the stipend of a laboratory assistant.

After the completion of this project and the development of the all the mouse lines proposed, Dr. Toldo will be able to support a project to present for funding to the federal government and to foundations such as the American Heart Association or the American Diabetes association. The acquisition of new data is also sparking new ideas and Dr. Toldo and his team believe that they can identify some key function of the NCC protein that may be important to understanding the effects of mutations of the NCC gene that cause genetic diseases in humans. 

Principal Investigator Victor Yazbeck, M.D., M.S.
Grant Project Entitled: “Developing Animal Models for Indolent Lymphomas”

Dr. Yazbeck’s research project involves developing genetically engineered mouse models (GEMM) of human indolent non-hodgkin's lymphomas (NHL). In general, Dr. Yazbeck’s clinical and translational research efforts are focused on developing novel treatment strategies for lymphoid malignancies, in particular indolent NHL. Unlike aggressive lymphomas, indolent NHL lack reliable preclinical models including cell lines, which have hampered the rationale drug development for these common lymphoid malignancies. Given the underlying indolent nature and slow progression of iNHL, it has been extremely hard to generate human cell lines and/or patient-derived xenograft (PDX) mouse models for these tumors. Hence, the need to generate these GEMMs for iNHL, that might provide insights of the underlying tumor biology, understand the mechanism of resistance to current and novel therapies, inform the development of biomarkers for patient selection, and the design of future clinical trials.

(Continued on page 23)
In a disease where the immune system and tumor micro-environment play a crucial role in the underlying lymphomagenesis, the widely used xenograft models from established tumor cell lines and/or PDX-models that use immunodeficient mice, will fail to recapitulate many critical features of the underlying human tumor, especially for iNHL. Therefore, Dr. Yazbeck felt the need to develop these clinically relevant novel GEMMs for indolent NHL, as they not only provide proof of concept, but more importantly can inform the clinical process.

Given the indolent nature of the underlying human disease, developing these GEMMs is challenging as it requires both money and time. Therefore, the DOIM pilot grant was crucial in securing funding for this pilot project, and allowed Dr. Yazbeck to generate preliminary data that will support future grant submissions. The current grant is supporting the mouse project in full: including mice breeding, genotyping, colony management, generating slides, H&E and immuno-histochemistry staining, western blot, and more.

Dr. Yazbeck and his team have generated these novel GEMMs and are currently in the phase of monitoring for tumor formation, and characterizing these tumors upon collection. Preliminary results are promising. The next step will be to understand the mechanisms of resistance to novel therapies.

The most exciting part of the project is the establishment of a clinically relevant GEMM for one of the most common subtype of lymphomas: a similar model to the widely used Eμ-TCL1 transgenic mice that develop chronic lymphocytic leukemia at 8-12 months of age.
Rashmi Pershad, M.Phil., C.R.A., C.C.R.P. joined the Department of Internal Medicine (DOIM) in June of 2015 as its associate administrator for research. Since then she has helped the research team grow from one member to seven members, through centralizing some of the divisions, which better serves the research needs of the department’s faculty.

Plans are also in place to hire a few research coordinators centrally to provide much needed support for clinical trials. The current research administration team includes Rashmi Pershad, the research administrator; Meagan Sok, the grant and fiscal manager, Elizabeth Demro, a pre-award grant specialist; Aston Charlton, Chanin Consoer and Sabris Harris, post-award grant specialists, and David Lett, a fiscal technician. The team is looking to hire an additional grant and fiscal manager, as well as a project manager.

Rashmi and her team help faculty with everything from identifying funding opportunities and administrators of the www.intmed.vcu.edu | Richmond, VA | VCU Department of Internal Medicine

Congratulations to our Colleagues on New Extramural Grant Funding

The table below depicts the Federal, State and Foundation Funding received by researchers in the VCU Department of Internal Medicine for the period from January 2018—September 2018

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<tr>
<td>Ellenbogen, Kenneth</td>
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<td>Huizar, Jose</td>
<td>Mechanistic Insights of Premature Ventricular Contractions-induced Cardiomyopathy</td>
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<td>Kukreja, Rakesh</td>
<td>Amelioration of Doxorubicin-Induced Muscle Dysfunction with Embryonic Stem Cells-Derived Exosomes</td>
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<td>PDE5 inhibitor (Sildenafil) for ameliorating androgen deprivation therapy (ADT)-induced cardiotoxicity</td>
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<td>Ghosh, Shobha/ Hu Yang</td>
<td>Modulating macrophage function in atherosclerosis by functionalized nanoparticles</td>
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<td>Ginder, Gordon</td>
<td>VCU Massey Cancer Center Minority NCI Community Oncology Research Program</td>
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<td>Structural and functional diversity of the methyl-binding domain protein family</td>
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<td>Achieving a Cancer-Free and Productive Workforce in Virginia</td>
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<td>Wee1 and HDAC inhibition in relapsed/refractory AML</td>
<td>$1,554,073</td>
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(Continued on page 25)
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<table>
<thead>
<tr>
<th>PI Name</th>
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<td>Matin, Khalid</td>
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<td>and Antonio Abbate</td>
<td>Versus Weekly Gemcitabine Alone in the Treatment of Patients with Persistent or</td>
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<td>Relapsed Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma.</td>
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Always plan ahead - Ideally, if the idea for which you are seeking grant funding is entirely new, then plan to spend **three months** preparing prior to submitting your grant proposal.

The first month focus on planning out your idea. Conduct a literature search to develop your concept and see what others are doing in the field. By conducting a thorough review of existing literature, you will be able to fine tune your idea and see what others have already done. The information you gather in this step can be used in your research plan to provide background and context for your research idea. Also check the NIH website and others relevant to your field to determine what similar projects have already been funded in order to further refine your idea.

If you are planning to submit your application for a standard R01 submission then planning early allows you to take advantage of speaking with the project officers at the agency to see if your idea is a good fit for the agency or if they recommend you talk with someone else or apply to a different institute. **Remember there are 27 institutes within the NIH and for standard R01 applications you can submit an assignment form to request that your application be reviewed by a specific agency, setting yourself up for the best chance of success.**

In order to communicate with a project officer at the NIH, you will need to first contact the project officer and ask for a phone meeting to discuss your idea. Then prepare a few slides that present your idea and share your specific aims. Send the slides to the project officer prior to the review. Utilize the feedback you receive from the project officer to further develop your idea. Make sure you thoroughly read the program announcement so you can tailor your application to appropriately meet the program announcement’s requirements.

Remember to look at the budget early on so the scope of the project you propose is within budget. Frequently, ideas for projects are more ambitious than the budget will allow and reviewers can gauge that when they are reviewing proposals. Great ideas beyond the scope of budget will not be funded.

Allow sufficient time for colleagues and mentors to review your submission. Ideally you will want to distribute your proposal to internal reviewers two weeks before your submission is due so you have time to modify your proposal and include their feedback. And make sure you’ve conferred with colleagues about your timing needs so that they can realistically plan to help you.

Allow the last week to check your application to make sure everything requested in the program announcement has been included and there are no errors, typos, or ambiguous language in your application.

**The Most Common Errors that Reviewers See:**

1. **Number of Contributions** – In the biosketch the maximum number of contributions should not exceed **five** and the number of publications per contribution should not exceed **four**. However, on reviews we frequently see more publications listed.

2. **Completed Support** – only research grants that were completed in the last three years should be included. We frequently see older grants included here and they should not be included. The NIH may disqualify a submission if this is not corrected.

3. **Discrepancies in personnel** – Personnel effort must be consistent from budget to budget justification.
Rashmi Pershad, M.Phil., C.R.A., C.C.R.P. joined the Department of Internal Medicine (DOIM) in June of 2015 as its associate administrator for research. Since then she has helped the research team grow from one member to seven members, through centralizing some of the divisions, which better serves the research needs of the department's faculty.

Plans are also in place to hire a few research coordinators centrally to provide much needed support for clinical trials. The current research administration team includes Rashmi Pershad, the research administrator; Meagan Sok, the grant and fiscal manager, Elizabeth Demro, a pre-award grant specialist; Aston Charlton, Chanin Consoer and Sabris Harris, post-award grant specialists, and David Lett, a fiscal technician. The team is looking to hire an additional grant and fiscal manager, as well as a project manager.

Rashmi and her team help faculty with everything from identifying funding opportunities and administrators of the NIH Grants — Tips for a Successful Submission Continued

Advantages of Submitting Before 5pm on the Due Date
Did you know if you submit 48 hours prior to the due date you have time to fix errors identified by Grant.gov and Commons Validation? This means if errors are found you have time to fix them and you don’t need to wait to submit until the next funding cycle. For more information on preparing a successful grant application go to: https://grants.nih.gov/grants/how-to-apply-application-guide/write-application.htm

VCU Internal Routing Timelines
The DOIM central administration team reviews all proposals for the department prior to submission to ensure all administrative requirements are met. This may take 24-48 hours depending how many proposals are waiting to be reviewed. The School of Medicine and Office of Sponsored Programs request that all proposals are submitted 5-7 days prior to the deadline.

NIH Changes Effective January 25, 2018
As of January 25th of this year changes were made mainly pertaining to the submission of grants that include human subjects, research and clinical trials. Program announcements now clearly specify whether or not a grant proposal may contain a clinical trial component. The three options are: Clinical Trial Not Allowed, Clinical Trial Required or Clinical Trial Optional.

Clinical Trial Proposal Submissions
If you plan to submit a grant that includes a clinical trial it must be submitted to a specific program announcement that references clinical trials. The NIH will no longer accept clinical trial proposals submitted as part of the standard RO1 applications, unless Clinical Trial Required or Clinical Trial Optional are listed in the RFA.

The application requirements for submitting information on the human subject section and requirements for what information needs to be provided regarding clinical trials has changed. The annotated document called “Preview of Form E Grant Application Form Changes” highlights the changes to the forms and changes regarding clinical trials. It can be found at: https://grants.nih.gov/grants/how-to-apply-application-guide/resources/annotated-form-sets.htm

The NIH has made the form changes to consolidate the human subject information in one location and to gather more information on clinical trial data collection in order to assist in proposal review and to prepare the NIH for future data exchanges with Clinical Trials.gov.

DOIM Application Review Deadline
For DOIM review, it is requested that all documents be in final format except the research plan and publications which may be submitted as drafts. Final research plans and publications should be submitted 2 days prior to the grant due date to avoid missing the deadline.

Questions
Please reach out to Rashmi Pershad at Rashmi_Pershad@vcuhealth.org if you are in the Department of Internal Medicine and you have any questions regarding your grant application. Thank you for your cooperation.
If you have questions or would like to share information to be included in future issues of the VCU Department of Internal Medicine’s Research Newsletter please contact someone from the DOIM Research Team:

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Thank you for reading.

For more information about the Department of Internal Medicine, please visit us online at:

www.intmed.vcu.edu