RESEARCH *Matters*

Spring 2022

IN THIS ISSUE...

Association for the Accreditation of Human Research Protection Programs, Inc. — *Full* Accreditation

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RESEARCH AROUND McLAREN

MCRI SITE SPOTLIGHT:

McLAREN GREATER LANSING

Divyakant Gandhi, MD

McLaren Center for Research and Innovation is thrilled to announce the opening of its office at the new McLaren Greater Lansing Hospital. MCRI opened a clinical trials office at the Greenlawn campus approximately four years ago and has been conducting primarily cardiovascular and orthopedic research trials. With the completion of the new facility, research has caught the eye of four physicians who are new to MCRI and are now planning on opening trials at the new Greater Lansing location.

Dr. Divyakant Gandhi, Cardiothoracic Surgeon, and now Principal Investigator, has taken on an exciting Phase II drug trial called The START Study, that opened to enrollment in April of 2022. The START Study is evaluating an investigational drug and its effect on preconditioning response biomarkers in subjects undergoing CABG and / or cardiac valve surgery. "This is very exciting, to work with so many different departments of our beautiful new facility on such an exciting new trial," Dr. Gandhi said.

"The START Study is one of the first trials at McLaren Greater Lansing to involve multiple departments and really involve the whole hospital in the conduct of clinical research," says Pam Wills-Mertz, Corporate Research Director, "It's been a challenge to coordinate, particularly during the move, but this will lay the groundwork for many more trials to come."

Another new trial is opening at the new McLaren Greater Lansing facility under Dr. Khalil Kanjwal, Electrophysiologist and Principal Investigator. "The REAL-AF study is capturing a real-world experience of catheter ablation for treatment of atrial fibrillation," explains Dr. Kanjwal, "With this study, we will be able to see the long-term clinical outcomes of our current standard of care."

"Real-world studies like REAL-AF are a great compliment to Phase II or III drug studies like the START study. They each have their own utility for our patients and physicians," Pam Wills-Mertz expressed.

Managing all of MCRI's new and on-going studies at McLaren Greater Lansing is our research nurse coordinator, Katie Esckilsen, RN. Katie has five years of experience coordinating clinical trials at both McLaren and Michigan State University. Katie is based in the MCRI office located on the lower level of the Outpatient Care Center, in room LL-302A. "I'm looking forward to seeing how we can improve the flow of research here at our new hospital, being in

> "... THE ENERGY OF THE NEW HOSPITAL IS DRAWING MCRI TOWARDS EXCITING NEW GROWTH AND UNTAPPED POTENTIAL FOR RESEARCH OPPORTUNITIES AT McLAREN!"
>
> ***– Pam Wills-Mertz***

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MCRI SITE SPOTLIGHT: McLAREN GREATER LANSING

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close proximity to the cardiology clinic with Drs. Shah and Mughal, should really help enrollment efforts in their cardiology studies," Katie said.

McLaren Greater Lansing is developing a robust clinical trials portfolio and supports trials from orthopedic surgery registries with Dr. Mesko, cardiac stent and cardiology drug studies with Drs. Mughal and Shah, and our newest trials with Dr. Gandhi and Dr. Kanjwal. "We look forward to seeing what new therapeutic areas are drawn to clinical trials at this amazing new facility," says Pam Wills-Mertz, "The energy of the new hospital is drawing MCRI towards exciting new growth and untapped potential for research opportunities at McLaren!"

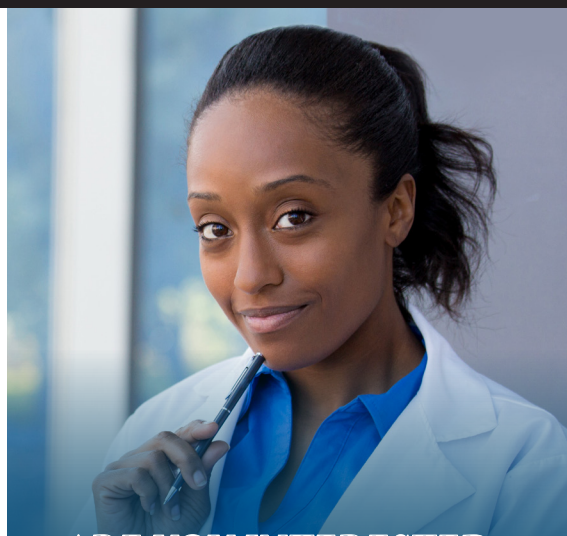
McLAREN NEUROSCIENCE RESEARCH EXPANDS TO McLAREN NORTHERN MICHIGAN

Neurologist Karl Meisel, MD, has recently opened McLaren Northern Michigan's first Neurology trial, ARCADIA. ARCADIA is a StrokeNet sponsored Phase III trial of apixaban versus aspirin in patients who have evidence of atrial cardiopathy and a recent stroke of unknown cause. At his previous institution, Dr. Meisel was the PI for ARCADIA and is excited to bring the trial to McLaren Northern Michigan. MCRI looks forward to working with Dr. Meisel to further develop the neuroscience research portfolio at this location. McLaren is pleased to be able to offer neuroscience clinical trial opportunities to our northernmost patients.

McLAREN TOP ENROLLER IN NEUROSCIENCE CLINICAL TRIAL

McLaren Center for Research and Innovation would like to congratulate Dr. Bharath Naravetla and his research teams at both McLaren Flint and McLaren Macomb for their amazing contribution to Stryker's ASSIST registry. ASSIST is a global post-market study designed to assess the procedural success and clinical outcomes with operator techniques utilizing Stryker Neurovascular Devices used in real-world situations. McLaren Health Care was the top enrolling site in North America, and the second highest enrolling site world-wide, contributing a total of 151 patients to the registry. Enrollment numbers of this caliber require a great deal of effort from the entire team. McLaren is proud to have participated at such a substantial rate.

Bharath Naravetla, MD



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

For information on enrolling in a clinical trial please visit our website at www.mclaren.org/main/clinical-research-trials. Here you will find a list of open enrolling studies at McLaren, including which hospital the research is being done at and contact information for each study.

We have enrolling studies for the following conditions (not a complete list):

- **Diabetes**
- **Orthopedic Surgery**
- **COVID-19**
- **High Blood Pressure (Hypertension)**
- **Stroke**
- **Heart Attacks / Heart Failure / Heart Disease**
- **Kidney Diseases**
- **Lung Diseases**
- **Peripheral Artery Disease**
- **Carotid Artery Disease**
- **Mastectomy**
- **Various Cancers**
  - **Breast**
  - **Lung**
  - **Prostate**
  - **Multiple Myeloma**
- **Patients who underwent intracranial aneurysm coiling**
- **Drug study for patients with recent acute coronary syndrome**

For a complete list of conditions, please visit our website listed above.

RESEARCH AROUND McLAREN

Clinical Trials at McLaren Health Care are conducted by the McLaren Center for Research & Innovation and the Karmanos Cancer Institute.

HAPPY CLINICAL TRIALS DAY

Clinical Trials Day is celebrated internationally on May 20 of each year to commemorate the date that English surgeon Dr. James Lind began the first randomized clinical trial to combat scurvy in 1747. Dr. Lind's research took place on a British naval ship where he divided ill soldiers into six groups, provided each group with various dietary supplements, and was able to determine a positive connection between Vitamin C and scurvy. This clinical trial laid the foundation for modern clinical research.

Clinical Trials Day is a celebration of clinical research professionals and participants, by recognizing their contributions to public health and medicine. It is a well-deserved time out to honor those who make clinical trials possible and raise awareness of clinical trials in the community. Clinical Trials are research studies with human volunteers that are intended to add to overall medical knowledge. Behind every medication and medical intervention are thousands of patients that volunteered to participate in Clinical Trials. Without Clinical Trials, devastating diseases like polio would not be all but eradicated in the United States. Nor would we have seen a 50 percent decline in coronary artery mortality rates between 1980 and 2000. Clinical Research Professionals and patients are the unsung heroes in the development of new drugs, devices, biologics and treatments to improve the care of all Americans.

McLaren Health Care would like to take this time to thank our clinical research professionals for their tireless efforts to advance medical science, as well as improving the health and well-being of our patients. McLaren patients involved in clinical trials are often provided choices for their care beyond the standard available treatment. This care is coordinated and provided by our highly skilled clinical research professionals. At McLaren, research matters for our patients, our organization, and our physicians. Growing our research program gives our patients access to the latest clinical trials and the confidence they are receiving the best treatments, proven by research conducted in our own hospitals, by physicians they know and trust.

DO YOU HAVE A RESEARCH PROJECT THAT NEEDS FUNDING?

McLaren Health Care has formed a corporate level Research Funding Committee. This committee has been created to establish a system-wide strategic plan and process for awarding research funding to investigators. One goal of this committee is to support and strengthen investigator-initiated research within the corporation. Awards of up to $5,000 will be awarded to individuals involved in Graduate Medical Education Research (GME - residents and fellows). Awards of up to $20,000 will be awarded to non-GME individuals interested in pursuing Investigator-Initiated research. Non-GME awards are open to all McLaren employees or affiliated providers. These funds are to be used for the conduct of the observational or interventional research study and will be awarded on a quarterly basis. Due dates for application submissions are January 1st, April 1st, July 1st, and October 1st of each year. The application process is now open for the July 1st deadline at **www.McLaren.org/FundingApplication**. Required information for the application includes a detailed description of the research project, as well as a proposed budget.

ATTENTION: McLAREN ST. LUKE'S PROVIDERS!

Do you have interest in conducting research at McLaren St. Luke's? We now have an active office of the McLaren Center for Research and Innovation located in the Heart Center and we are ready to support local investigators. Please email MCRI@mclaren.org to request information about the new site and to learn more about how we can support your research efforts.

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MICHIGAN CANCER PATIENTS CAN ENROLL IN CLINICAL TRIALS AT THE McLAREN PROTON THERAPY CENTER IN FLINT

The goal of eliminating cancer, while minimizing side effects, is ongoing as medical scientists continue research and development of new treatments. Some of that research is done through clinical trials. Clinical trials allow physicians to observe what new treatments work best and even help to improve current treatments for cancer patients.

“We can cure a lot of cancers today. This is a result of past research,” said Brian Yeh, MD, PhD.

The Karmanos Cancer Institute at McLaren Flint and the McLaren Proton Therapy Center want to offer patients the most advanced treatment options. They offer clinical trials through the Karmanos Cancer Network and the Proton Collaborative Group.

Dr. Yeh is the medical director of network research for the Karmanos Cancer Network. In this role, he works with the network sites at each McLaren hospital to implement research and clinical trials for cancer treatments. The clinical trials that the network offers are multi-institutional, nationwide trials, which also include clinical trials that begin at the Karmanos Cancer Institute in Detroit.

According to Dr. Yeh, there are many reasons why it is important to offer clinical trials to cancer patients in Michigan. One reason is to make sure that Michigan’s patients are represented in the nationwide results.

“We want to be able to use the results of these trials confidently when we make decisions to treat our patients. Every state and every city’s population are unique and made up differently. This means we need to enroll patients from our population into these important studies,” Dr. Yeh explained.

Available Clinical Trials in Flint

Karmanos Cancer Institute at McLaren Flint offers clinical trials for patients

going through medical oncology treatments, receiving surgery to remove their cancer, or having radiation therapy. With the McLaren Proton Therapy Center in the same building, patients also have access to clinical trials that involve proton therapy.

"Right now, we are one of the most active centers in the country," said Christian Hyde, MD, DABR, radiation oncologist and proton therapy specialist at the McLaren Proton Therapy Center. "It's because of our network [the Karmanos Cancer Network] that we have a lot of patients throughout Michigan being cared for through clinical trials, from Petoskey down to the Detroit area and the larger cities in between."

One study offered to eligible patients directly compares two therapies, photon and proton radiation, to determine which one has better disease control for prostate cancer patients and fewer patient-reported and physician-reported side effects.

"The patient must be willing to fill out annual surveys related to side effects, including bowel, bladder, and sexual function. We follow-up with the participating patients for ten years. They also need regular PSA check-ups over the course of those ten years," Dr. Hyde said.

Another study available in Flint looks at the side effects of using proton radiation therapy for women with breast cancer. Investigators are looking to learn more about how effective and safe this treatment is in comparison to other kinds of radiation treatment.

The Karmanos Cancer Institute at McLaren Flint and the McLaren Proton Therapy Center offer many more clinical trials.

"If a patient is interested, during their consultation we can explain to them and show them which clinical trials they are eligible for," said Dr. Yeh. "We want to offer the best care for our patients. Being involved with clinical trials puts us on the edge of cancer research and cancer knowledge, and that allows us to give the best care for our patients, whether they are involved in a clinical trial, or not."

For more information on the clinical trials through Karmanos, visit karmanos.org/clinicaltrials.

DRS. FARES ALSAWAH AND DIPESH UPRETY PUBLISHED IN *INTERNATIONAL JOURNAL OF CANCER CARE AND DELIVERY*

Congratulations to Fares Alsawah, M.D., Hematology/Oncology Fellow, and Dipesh Uprety, M.D., member of the Thoracic Oncology and Phase I Clinical-Pharmacology Multidisciplinary Teams, who were recently published in the *International Journal of Cancer Care and Delivery*. The paper titled, "Advances in Neoadjuvant and Adjuvant Immunotherapy and Targeted Therapy for Resectable NSCLC," reviews important studies utilizing immunotherapy (IO) in both the neoadjuvant and adjuvant settings for resectable NSCLC. Great job, Dr. Alsawah and Dr. Uprety!

Dipesh Uprety, MD

Fares Alsawah, MD

RESEARCH AROUND McLAREN

THE NEW McLAREN GREATER LANSING, KARMANOS CANCER INSTITUTE, OUTPATIENT CARE CENTER NOW OPEN

Clinicians at McLaren Greater Lansing's new $600 million health care campus began treating its first patients on February 28 at the new outpatient care center and Karmanos Cancer Institute. The historic event was marked by a ceremonial ribbon cutting attended by leaders from McLaren, Michigan State University (MSU), Karmanos Cancer Institute, MSU Health Care, clinicians, support staff, construction workers, and elected officials.

"Today marks the beginning of a new chapter in McLaren and Michigan State University's history of collaborating on caring for the communities we serve, advancing medical research, and training the next generation of caregivers to serve our patients in mid-Michigan and beyond," said Phil Incarnati, President and CEO of the McLaren Health Care system. "The possibilities of a greater partnership between McLaren and MSU combined with a common vision for healthy communities led to the creation of this new, next-generation health care campus. With nearly 900,000 square feet of new inpatient and ambulatory care space, this project is the largest capital project in our system's history and one of the largest single investments in the health of the greater Lansing community ever."

Incarnati noted the legacy of McLaren's hospitals in Lansing date back more than a century. Now McLaren, MSU, and the area's independent physician partners are looking forward to what can be accomplished together over the next 100 years.

"Community partnerships are the basis of MSU's medical education and outreach across the state of Michigan, and it is wonderful to have these new facilities and our partners at McLaren Health Care in such close proximity to MSU," MSU President Samuel L. Stanley Jr., MD said. "The new McLaren campus will expand services and help improve health care outcomes for residents across our entire region."

The new health care campus, including the seven-story, 240-bed hospital and Level 3 trauma center with certified primary stroke center designation is located at 2900 Collins Road in Lansing.

"We would not be here today without the dedication of our team members, physician partners, and community as a whole, who all offered invaluable input on the design and operations of our new health care campus," said Kirk Ray, president and CEO, McLaren Greater Lansing. "We must also thank and recognize our entire design build team and the thousands of trades people who dedicated their time to this project. It is a testament to their knowledge and skill to be opening our campus right on schedule, having weathered a global pandemic and unheard-of supply chain challenges throughout design and construction of the facilities."

The multi-specialty outpatient care center includes endoscopy services, a comprehensive heart and vascular institute with direct cath lab access, and a training center to support graduate medical education featuring expanded classroom spaces and advanced simulation labs, along with an expanded lounge and sleep rooms for resident physicians.

The 46,000-square-foot cancer center is a collaboration between McLaren Greater Lansing and the Karmanos Cancer Institute, in partnership with MSU Health Care. The partnership will recruit top clinicians to the region, provide outstanding patient care, and "bench-to-bedside" access to new life-changing therapies and treatments. The comprehensive cancer center is home to the latest radiation oncology technology, medical and surgical oncology clinicians, and chemotherapy and infusion services. Another hallmark of the cancer center is its patient-centric design that includes larger exam rooms to support a multidisciplinary approach to care, and flexible infusion areas to offer patients options for the setting where they will receive their treatments. The cancer center also houses a state-of-the-art breast imaging center offering 3D mammography, biopsies, and surgical and reconstructive services.

"The partnership between McLaren Greater Lansing, Karmanos Cancer Institute, and MSU will bring comprehensive cancer services conveniently accessible under one roof to ensure an excellent patient experience," said Justin Klamerus, M.D., MMM, president of Karmanos Cancer Hospital and Network. "By offering a seamless continuum of care, patients experience less disruption in care, and the burden of treatment is reduced. We are committed to staying at the forefront of cancer treatment and offering patients tomorrow's standard of care today – giving them their best chance to beat the disease. This investment enables our teams to keep moving forward in the fight against cancer."

Michigan State University Cancer is a founding member of the Big Ten Cancer Research Consortium. The Big Ten cancer centers work together and conduct innovative clinical trials using the expertise of Big Ten universities.

"One of the greatest challenges in health care is being able to bring accessible, affordable care to all," said Norman J. Beauchamp, Jr., M.D., MHS, executive vice president for health sciences at Michigan State University. "No single organization can transform health and health care delivery, alone. With this collaboration, we are bringing together the strengths of MSU radiology and McLaren to bring better diagnosis and treatment for cancer in our community."

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Left to right: U CAN-CER VIVE Foundation members, Liz Schumacher, Events Committee: Carol Peters, Events Committee; Kelley LaFontaine, Co-Founder; and Todd McKay, Grants Committee.

Gerold Bepler, MD, PhD; Asfar Azmi, PhD; M. Najeeb Al Hallak, MD; and Linda Filipczak, RN, BSN, MBA.

KARMANOS CANCER INSTITUTE AWARDED $352,000 GRANT FROM U CAN-CER VIVE FOUNDATION

THE DONATION WILL FUND PANCREATIC CANCER RESEARCH

The Barbara Ann Karmanos Cancer Institute recently received a $352,437 grant from the U CAN-CER VIVE Foundation to help fund a pancreatic cancer research study. The outcomes of this study will help define new standards of care for patients undergoing chemotherapy for this disease.

Asfar Azmi, Ph.D., associate professor, Department of Oncology, leader, Molecular Therapeutics Research Program and director, Pancreatic Cancer Research Initiative at Karmanos Cancer Institute and Wayne State University School of Medicine (WSU SOM), and M. Najeeb Al Hallak, M.D., MS, member of the Gastrointestinal and Neuroendocrine Multidisciplinary Team at Karmanos and assistant professor in the Department of Oncology at WSU SOM, are leading a pilot study titled, “A pilot study of serial blood profiling for micro-RNA expression signature to Gemcitabine/Nab-Paclitaxel in pancreatic ductal adenocarcinoma patients.”

“There are limited, effective therapies for this disease, and more importantly, there are no strategies to date to tell us early on if a treatment is working or not,” Dr. Azmi said. “In our study, we collect blood from the patient during the course of chemotherapy treatment and analyze the blood for certain markers. If those markers predict response or resistance to chemotherapy, we will then have new knowledge to help produce scientific advances for the best treatment option for those faced with this disease.”

Pancreatic cancer is the third leading cause of cancer death in the United States, and the state of Michigan is among the states with higher rates of pancreatic cancer diagnoses. Pancreatic cancer is considered incurable in the majority of patients due to advanced stage at diagnosis, and often once diagnosed, the only treatment option is chemotherapy.

“It will be a groundbreaking research finding if we are able to identify that microRNA signature in the blood that tells us ‘this chemotherapy is the best treatment option for the patient,’ and avoid ineffective treatments that allow a

RESEARCH AROUND McLAREN

patient's symptoms to worsen and the cancer to spread," said Dr. Al Hallak. "This grant will significantly help improve testing quality and even expand the testing beyond just the microRNA to find other signatures for those patients, which can even influence future research into new drug therapies for pancreatic cancer treatment."

"At U CAN-CER VIVE, we have focused a great deal of our cancer grant funding towards research tackling pediatric cancers, as well as those with a very low survival rate. This research specifically looks at pancreatic cancer, which in addition to having a low survival rate, is also underfunded," said Kelley LaFontaine, co-founder of the U CAN-CER VIVE Foundation. "Our hope at U CAN-CER VIVE is that this grant funding will provide the doctors and researchers with the necessary support to fulfill their mission and hopefully discover findings that raise the quality of life and outlook for those afflicted with this disease."

Currently, there are 10 patients enrolled in the pilot study. The U CAN-CER VIVE grant makes it possible to double the number of participants to 20. Karmanos Cancer Institute is a national leader in clinical trials and at the forefront of offering treatments that define the new standards of care. In fact, Karmanos offers more cancer treatments and clinical trials not found elsewhere in Michigan.

"There is so much more to learn and understand about cancer and cancer treatments, and at Karmanos, it's a team effort," said Gerald Bepler, M.D., Ph.D., president and CEO of Karmanos Cancer Institute. "The collaborative relationship between researchers and physicians in this study, and funding like the U CAN-CER VIVE grant help to advance our ability to give patients their best advantages in surviving a cancer diagnosis and living longer."

THE NEW McLAREN GREATER LANSING, KARMANOS CANCER INSTITUTE, OUTPATIENT CARE CENTER NOW OPEN

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The McLaren Health & Wellness pavilion is now open. Designed to meet the physical and emotional needs of our patients in today's high-paced society, this elegant facility provides a variety of ambulatory patient care services in a convenient, comfortable, and restorative environment. Some of these clinical care services include a hyperbaric wound care center, sleep medicine, and physical rehabilitation, with more services to be added in the future.

The $600 million health care campus has already spurred additional economic development in the area, including an additional medical services building set to open in 2023 on the new campus, and will attract even more investment in the region in the future.

"This investment in Lansing and the development it will spur is truly transformational for our city, especially south Lansing, and the entire region," said Andy Schor, Mayor of Lansing. "I am excited that our residents will continue to have access to world-class health care in this incredible new facility and look forward to the future growth of the campus here."

RESEARCH AROUND McLAREN

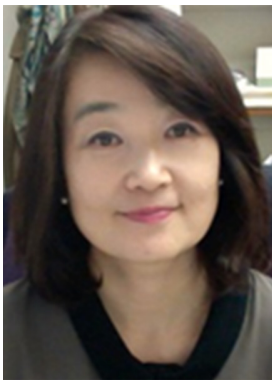
KARMANOS RESEARCHERS NAMED RECIPIENTS OF DMC FOUNDATION GRANTS

Three Karmanos Cancer Institute scientific members recently received grants from the DMC Foundation to support their research.

The DMC Foundation is dedicated to promoting the well-being of people in the metropolitan Detroit area through the support of health-related research, education and community benefit activities. DMC Foundation grants enhance and supplement current peer-reviewed funding.

Hyeong-Reh Kim, PhD

Project Title: "Targeting the lipid signaling network in prostate cancer bone metastasis" – Total budget: $77,144



Hyeong-Reh Kim, PhD

More than 90 percent of patients with castrate-resistant prostate cancer eventually develop bone metastasis, an incurable disease. Studies indicate that disseminated tumor cells (DTCs) arrive in the bone marrow at a relatively early stage of PCa and often survive as dormant cells in the marrow for long periods of time before they can be activated to form metastases. Based on our novel findings, we hypothesize that the disturbance of lipid profiling in the bone microenvironment serves as a trigger for dormant bone-resident prostate cancer cells to enter a highly proliferative phase. The goals of this study are to identify therapeutic targets in lipid signaling networks and test their therapeutic values.

Our research indicates that disturbance of lipid profiling in the bone microenvironment serves as a trigger for the intraosseous growth of prostate carcinoma. Although the current study focuses on prostate cancer, this may apply to intraosseous growth of tumors of other origins such as breast, lung, and kidney. Thus, patients battling other forms of cancer in the metropolitan Detroit area may eventually benefit from our research.

Kristen Purrington, PhD

Project Title: "Racial disparities, epigenetics, and environmental stressors in colorectal cancer in metropolitan Detroit" – Total budget: $73,085

Kristen Purrington, PhD

African Americans (AAs) are 20 percent more likely to both develop and die from colorectal cancer (CRC), yet AAs remain drastically underrepresented in existing molecular resources for cancer research. The social and economic disadvantage that is experienced by many AAs in metropolitan Detroit can increase inflammation through chronic stress, which directly impacts the gastrointestinal tract and can initiate CRC through DNA damage and other mechanisms. Tumor methylation profiling

is a powerful tool that can reveal prognosis-related subtypes; signatures of chronic inflammation and immune response; and exposure to chemical and environmental agents.

Existing resources for studying molecular characteristics of CRC vastly underrepresent racial minorities, including AAs. Recent reports, including our preliminary data, suggest that CRC tumors in AAs are more likely than those of Non-Hispanic Whites (NHWs) to harbor specific molecular features associated with aggressive disease. While there is strong evidence for racial differences in tumor molecular phenotypes in CRC, existing studies of molecular differences in CRC tumors by race are consistently limited by highly selected (i.e. not population-based) small sample sizes, and lack of attention to social disadvantage as a biologic factor in aggressive disease. This research will address social disadvantage and CRC in a biologically relevant way. A better understanding of the high burden of aggressive CRC subtypes among AAs in metropolitan Detroit and the role of potentially modifiable environmental factors is critical to ensure equitable approaches to targeted cancer prevention and treatment in this racially and economically diverse population.

Nerissa Viola, PhD

Project Title: "Molecular Imaging of Immune Cell Activity" – Total budget: $75,000

Nerissa Viola, PhD

Because of the disadvantages in biopsy sampling due to tumor heterogeneity, limitations on sampling frequency, reader bias and depth of location of the lesion, there is a need to develop tools to detect changes within the tumor microenvironment before and after immunotherapy in a non-invasive and quantitative manner to lower patient burden. This proposal aims to evaluate a positron emission tomography (PET) agent specific for interferon (IFN), a cytokine released by an activated immune system to facilitate tumor clearance. This new imaging agent will be tested for its potential monitor tumor response to radiotherapy, which has been associated to incur anti-tumor response. If proven successful, clinical translation of the PET agent will potentially benefit cancer patients by identifying responders versus non-responders to both radiotherapy and immunotherapy.

The development of this imaging agent has major implications particularly for cancer patients receiving immunotherapy. If successful, the imaging probe can be used as a tool to identify patients who are responders versus those who are non-responders to treatment in a timely manner, without waiting for the tumors to regress in size, which usually takes many months. Consequently, this guides clinicians to either keep the patient on the treatment regimen or identify new ones within the early stages of treatment.

EQuIP CORNER

Andrea Klaver, MBA, CHRC

WHAT INVESTIGATORS NEED TO KNOW ABOUT IRB REVIEW:

A REVIEW OF THE COMMON RULE AND ITS APPLICATION

By Andrea Klaver, MBA, CHRC

To kick off this month's EQuIP Corner, I want to emphasize how essential it is to know and understand the McLaren HRPP (Human Research Protection Program) mission, which is:

- To safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety, and well-being are protected; and
- To facilitate excellence in human subjects research.

To carry out this mission, the McLaren IRB must follow all federal regulations guiding human subjects research as prescribed by the appropriate federal institutions, including the Common Rule. Through their reviews, the IRB is committed to developing and implementing policies, procedures, and guidelines to ensure continued compliance and maintain the highest ethical standards, while pledging to minimize the administrative burden on researchers and administrators and expedite and facilitate research activity.

To that end, in this article we will (1) discuss how the Federal regulations for human subjects research came about, (2) clarify the role of OHRP (Office for Human Research Protections), and (3) review how the Common Rule works, including what human subjects research and exemption means.

Human Research: An Inherent Ethical Tension

Federal regulations define research as "a systematic investigation, including development, testing, and evaluation, designed to develop or contribute to generalizable knowledge" (45 CFR 46.102(l)). Research, at its heart, is about promoting the common good.

However, in the pursuit of the common good, it is not always easy to manage competing interests and the rights and welfare of individual research subjects could be easily overlooked.

Where Did the Regulations Come From?

Investigators have primary responsibility for protecting the rights and welfare

of humans participating in research. Safeguarding research subjects takes precedence over the goals and requirements of any research endeavor. McLaren IRB staff and members are knowledgeable about and adhere to:

- The Belmont Report, and its three basic principles:
  - Respect for Persons. Subjects are treated as autonomous, and should that autonomy be diminished, they are entitled to protection. We ensure they are participating in the study voluntarily after being supplied adequate information (e.g., Informed Consent).
- A note on Informed Consent: This is the voluntary choice of an individual to participate in research based on a complete and accurate understanding of the study. Informed Consent is not a single event or document, but rather an ongoing process.
  - Beneficence. Beneficence is understood to mean "do no harm," while at the same time maximizing potential benefits and minimizing potential risks.
  - Justice. Who receives the benefits of research and who will bear its burdens? This principle stresses the fair selection of subjects and sharing the risks and benefits of the study considered in the beneficence discussion equitably.
- The Common Rule (45 CFR 46), which is the federal regulatory framework that governs federally funded research with human subjects and codifies the ethical principles of The Belmont Report. Interestingly, the "Common Rule" is named such because so many Federal government agencies have adopted it.

Remember that *minimizing risks to participants and ensuring participants' rights and welfare are key components of human subjects protections*. Regulations are not there to trip researchers up; they are there to protect subjects.

The Federal Regulatory Framework for Human Research Protections

OHRP holds the regulatory authority for 45 CFR 46 and provides leadership in protecting human subjects in research conducted or supported by the Department of Health and Human Services (HHS). Regulatory requirements for protections apply to non-exempt human subjects research that is conducted or supported by HHS.

- NIH sponsors research
- FDA regulates research (involving drugs, devices, and biologics)
- OHRP regulates HHS-conducted research or supported human research

The Federal regulations represent the bare minimum ("the floor") and institutional IRBs may set more stringent criteria to befit their locale. The expectation of the IRB is that the researchers will do more than simply adhere.

When Do Regulations Apply and What Does That Mean?

Regulatory requirements apply when a project is non-exempt human subjects research. What does that mean? This generally means that: (1) the IRB review is performed according to regulatory requirements and criteria; (2) the informed consent form is created and reviewed according to regulatory requirements (unless waived); and (3) the Institution has a Federal Wide Assurance (FWA) which assures the government that the Institution is carrying out ethical research and provides certification of all IRB approvals.
Requirements typically do not apply when: (1) the project is not research; (2)

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EQuIP CORNER

UPCOMING RESEARCH EDUCATION

SOCRA
31st Annual SOCRA Conference
September 14 - 17, 2022
Virtual Event Only
Early bird registration ends August 22, 2022
For upcoming educational opportunities, please visit www.socra.org/conferences-and-education

MAGI
MAGI's Clinical Research Hybrid Conference – East
May 1 - 4, 2022
Boston, Maine
Sheraton Boston Hotel
Physical or Virtual Event
For upcoming educational opportunities, please visit www.magiworld.org

ACRP 2022
For upcoming educational opportunities, please visit www.acrpnet.org/events

BROWN BAG SERIES

Our next Brown Bag Session is tentatively scheduled for Tuesday, June 7, 2022. Please watch your email and the EQuIP Education webpage at www.mclaren.org/main/research-education for more details as the time approaches.

For more information, contact Andrea Klaver at (248) 484-4987 or andrea.klaver@mclaren.org.

WHAT INVESTIGATORS NEED TO KNOW ABOUT IRB REVIEW

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the project is not human subjects research; or (3) the project is Exempt human subjects research. So, while Investigators and Institutions do have some flexibility outside of the regulations, ethical responsibilities for participants' rights and welfare remain.

Determining If a Study Is Human Subjects Research

A good place to start is with the regulatory definition for human subject: a living individual about whom an investigator conducting research:

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. (45 CFR 46.102(e)(1)(i)(ii))

If (i) is true, it is primary human subjects research. This research may qualify for an exemption, but if not, the McLaren IRB will follow all regulatory requirements for review and informed consent.

If (ii) is true, it is secondary human subjects research. Materials are identifiable at the time of access, and again, this research may qualify for an exemption, but if not, the McLaren IRB will follow all regulatory requirements for review and informed consent.

What does identifiable mean under the Common Rule? Identifiable private information or biospecimens refers to private information or biospecimens for which the identity of the subject is or may be readily ascertained by the investigator or associated with the information or biospecimens. (45 CFR 46.102(e)(5)(6))

If neither (i) or (ii) are true, it is secondary research with non-identifiable data or specimens. Only non-identifiable materials will be used, and this is not human subjects research. In this case, there are no Common Rule requirements. This research involves human specimens and/or data, but no human subjects are involved.

What Does It Mean That Research Is Exempt?

If researchers indicate that their research is Exempt, they must be prepared to justify why. So, what constitutes Exempt research?

- The study is human subjects research.
- The entire study meets the conditions for one or more Exempt categories described in the Common Rule.

Exempt studies are exempt from the requirements of the Common Rule (i.e., IRB review according to the criteria at §46.111 and the informed consent requirements at §46.116). Institutions generally rely on experienced individuals, including the IRB staff and members, to make exemption determinations instead of leaving this to investigators. Further, making an Exempt determination does not equal an IRB review or approval.

What Does the McLaren IRB Look for When Reviewing Submissions?

The criteria for IRB review and approval of research are outlined in §46.111. These criteria are rigorously examined by McLaren IRB staff and members during each submission review as the level of risk is determined.

- Risks to subjects are minimized.
- Risks to subjects are reasonable in relation to anticipated benefits, if any.
- Selection of subjects is equitable.
- Informed consent will be obtained and documented accordingly (if applicable).
- Adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data are in place.
- Safeguards for vulnerable subjects are in place (if applicable).

These are, in essence, the Belmont Report put into practice. If for any reason the IRB cannot make these determinations, the submission cannot be approved. In this case, the IRB could return to research team for more information, bring in a consultant, etc. to work with the IRB to make changes and successfully move the submission through the IRB approval process.

Protecting study subjects is a shared responsibility, including staff, researchers, the McLaren IRB and other external IRB's, our Institution, our funding organizations, all the way up to the Office for Research Protections (OHRP). The McLaren IRB follows all federal regulations guiding human subjects research as set by federal institutions, including the Common Rule. The McLaren IRB is committed to ensuring continued compliance and maintaining the highest ethical standards, while minimizing the administrative burden on researchers and administrators to expedite and facilitate research activity.

LAUREN HAMEL, PhD, NAMED CO-PROGRAM LEADER OF THE POPULATION STUDIES AND DISPARITIES RESEARCH PROGRAM

Congratulations to Lauren M. Hamel, PhD, who was recently named co-program leader of the Population Studies and Disparities Research (PSDR) Program at the Karmanos Cancer Institute and Wayne State University School of Medicine. Dr. Hamel is an Associate Professor in the Department of Oncology with research expertise in health care disparities, health equity, patient-provider communication and the building and testing of interventions to improve clinical communication and organizational processes.

Lauren M. Hamel, PhD

Dr. Hamel is currently the principal investigator of a five-year Research Scholar Health Equity Grant from the American Cancer Society to test the effectiveness of a patient-focused intervention she and her team designed to improve patient-provider treatment cost discussions, and other patient outcomes related to the financial consequences of cancer treatment. Dr. Hamel is also working to enhance the methodological sophistication of how investigators examine the dynamics of human communication, and how race-based attitudes influence that communication. Dr. Hamel was awarded grants from the National Cancer Institute and the National Institute of Minority Health and Health Disparities to support this work. Dr. Hamel is also leading the design and implementation of an evidence-based, longitudinal implicit bias training curriculum designed for healthcare providers, students, and staff members. Dr. Hamel's scholarship and leadership have been recently recognized with awards from the Wayne State University School of Medicine, the Academy of Communication in Healthcare, the Association for Community Cancer Centers and Crain's Detroit Business.

Congratulations, Dr. Hamel!

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

Carlos F. Rios-Bedoya, ScD

NEW HUMAN SUBJECTS RESEARCH PRE-DETERMINATION PROCESS

FOR GRADUATE MEDICAL EDUCATION SCHOLARLY ACTIVITY PROJECTS

By Carlos F. Rios-Bedoya, ScD

The Division of Scholarly Activity has decided to establish a separate process for the Human Subjects Research Pre-Determination (HSRPD) process for scholarly activity projects. This new HSRPD process has been implemented by McLaren Graduate Medical Education effective on February 1, 2022. All scholarly activity projects, except case reports, case series and systematic literature reviews without meta-analysis, must follow this new process. The new HSRPD does NOT require using the IRB iRIS submission system. However, if the scholarly project is determined to be human subjects research by the new process, an IRB application will be required to be completed and submitted using the electronic submission system. The new process uses two new PDF fillable forms (HSRPD form and checklist) and a supporting template. These forms and supporting template are available through New Innovation, the scholarly activity website, as well as through the PhDs.

> "... IF THE SCHOLARLY PROJECT IS DETERMINED TO BE HUMAN SUBJECTS RESEARCH BY THE NEW PROCESS, AN IRB APPLICATION WILL BE REQUIRED TO BE COMPLETED AND SUBMITTED USING THE ELECTRONIC SUBMISSION SYSTEM."
>
> *– Carlos F. Rios-Bedoya, ScD*

The forms have instructions on completion and signature requirements. It is recommended that you read and follow them carefully. In addition, the PhDs are available for questions and to provide guidance. In beginning this process, as with ALL scholarly activity procedures, PhDs should be contacted first for any needed advice or clarification.

Briefly, the process is as follows:

- Answer ALL the questions to the best of your knowledge.
- Consult a PhD if you are not sure on how to answer specific questions.
- Provide as much detail as possible when answering open-ended questions to assist reviewers in making a valid and accurate pre-determination.
- Make sure you gather the required signatures.
- Initialize the appendix

Note: An incomplete form will delay the review and the pre-determination decision. To assist in making sure the HSRPD form has been completed, a checklist must be completed, initialized, and submitted together with the HSRPD form to the email presented in the instructions (mhc.sarc@mclarenmeded.org).

"THE NEW PROCESS USES TWO NEW PDF FILLABLE FORMS (HSRPD FORM AND CHECKLIST) AND A SUPPORTING TEMPLATE."

– Carlos F. Rios-Bedoya, ScD

In addition to the HSRPD form and checklist, a supporting work template must be completed and included in the submission email. Please provide as much detail as possible when completing the template to expedite the process. Specific supporting templates for secondary data analysis and meta-analysis projects are also available. Consult with your PhD before using any of these project-specific templates. Selecting the wrong supporting template could cause delays in the review process. The estimated turnaround time for a properly completed and submitted application is five business days.

After receiving the pre-determination outcome letter, you still CANNOT start your scholarly activity project. The next step is to either submit a SARC application if your project was determined as non-human subjects research OR submit an IRB application if your project was determined as human subjects' research. Your scholarly activity project cannot start until after receiving either a SARC or IRB letter of approval. Please consult with your PhD if you have process questions.

The Division of Scholarly Inquiry is committed to support and facilitate scholarly activity for McLaren residents, fellows, and faculty. For additional information contact Dr. Carlos F. Ríos-Bedoya at **carlos.rios@mclaren.org**.

ANNOUNCEMENTS AND WHAT'S NEW

Alek Tasich

Research Integrity is pleased to welcome **Alek Tasich**, our newest IRB Analyst at the Auburn Hills corporate office! Alek brings a Bachelor of Arts degree in developmental psychology from the University of Detroit Mercy, in addition to five years of psychological and neurological research experience from his time as a National Institutes of Health BUILD scholar and as a Clinical Research Coordinator at the Wayne State University School of Medicine. We are glad to have him join our team.

CONGRATULATIONS!

McLaren Health Care would like to congratulate the ENT Residency program for their publication efforts. This team has had a combined total of 43 articles published from 2020 to present! This is an extraordinary accomplishment by this residency program and their attending physicians.

NEW GUIDANCE ON INFORMED CONSENT POSTING

The Revised Common Rule requires all clinical trials to post an unsigned informed consent form on a publicly available website. The Revised Common Rule is in effect for studies approved on or after January 21, 2019. This is a requirement for studies meeting the definition of a clinical trial and funded or supported by a **Common Rule department or agency**, which includes NIH. The goal of this requirement is to increase transparency for federally funded clinical trials and simultaneously create a repository of sample consent forms that may be used as a reference for future research. Recently the federal Office of Human Research Protections (OHRP) announced a new guidance document, ***General Instructions on the Informed Consent Posting Requirement***, now posted on the OHRP website at **https://www.hhs.gov/ohrp/regulations-and-policy/informed-consent-posting/informed-consent-posting-guidance/index.html**. This guidance addresses the basic scope of the posting requirement, and responds to questions regarding how to comply with the requirement at 45 CFR 46.116(h) including which consent form to post, considerations for cooperative research, and special circumstances.

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