RESEARCH *Matters*

Winter 2022

IN THIS ISSUE...

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

McLaren | DOING WHAT'S BEST.®

RESEARCH AROUND McLAREN

Rachel Turek, Special Events Officer MGL Foundation and Lynn Griffor, VP MGL Foundation present a check to Pam Wills-Mertz, Director MCRI and Chandan Gupte, VP Clinical Excellence & Research.

FUNDRAISING FOR RESEARCH:

COCKTAILS FOR A CAUSE

The McLaren Corporate Research Funding Committee partnered with the McLaren Greater Lansing Foundation to strengthen McLaren's ability to fund internal research projects. This partnership allows potential donors to guide their charitable gifts to a specific therapeutic area of interest, such as cardiovascular research, or by providing funding to a specific community, if desired.

On October 14, 2021, the MGL foundation hosted a fund-raising event at the Country Club of Lansing. This "Cocktails for a Cause" event featured area restaurants competing for the most popular drink at the event. The drinks were served by celebrity bartenders, including McLaren's own Dr. Linda Peterson, CMO at MGL. In addition to cocktails and appetizers, information about McLaren's research program was provided.

According to Lynn Griffor, Foundation VP, "the MGL Foundation decided to dedicate proceeds from the inaugural Cocktails for a Cause event to research. We wanted to raise both money for, and awareness of, the innovative projects our physicians, residents and other clinicians are involved with. We think funding research projects both locally and throughout the McLaren system is a great way for our donors to make a huge impact on the health and wellness of our communities".

This successful event raised $19,000 to fund research programs at McLaren. It is the hope of the funding committee to partner with other subsidiary foundations to further elevate research funding opportunities within the corporation.

Celebrity Bartender, Dr. Linda Peterson.

FUNDS AWARDED FOR RESEARCH PROJECT

Daniel Dubay, MD

Dr. Daniel Dubay, Internal Medicine at McLaren Greater Lansing, has been awarded funds to conduct his research project titled Whole Food Plant-Based Diet Support Group Intervention. The purpose of the study is to determine if compliance with a whole food plant-based diet is better with nutrition support, as well as studying health outcome metrics compared to a standard medical care group of participants. The funds will be used for Dietician support and cooking demonstrations. Funding for this program was provided by the McLaren Corporate Research Funding Committee.

Congratulations, Dr. Dubay!

Do you need funding for your research project?

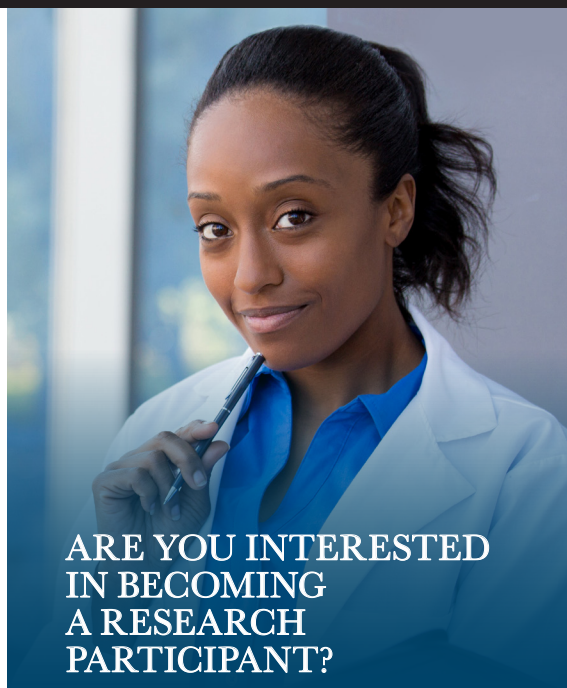
McLaren Health Care has formed a corporate level Research Funding Committee. This committee has been created to establish a system-wide strategic plan and process for awarding research funding to investigators. One goal of this committee is to support and strengthen investigator-initiated research within the corporation.

- Awards of up to $5,000 will be awarded to individuals involved in Graduate Medical Education Research (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. Please visit **mclaren.org/fundingapplication**.

MCRI OPENS NEW RESEARCH SITE

The McLaren Center for Research and Innovation is thrilled to announce that a research site has been established at McLaren St. Luke's in Maumee, Ohio. We have a part-time research coordinator, office space and a patient examination room in place. If you are a provider at McLaren St. Luke's with an interest in clinical trials, please email us at **MCRI@mclaren.org**. MCRI is excited to develop this site and we believe it will be very successful!



ARE YOU INTERESTED IN BECOMING A RESEARCH PARTICIPANT?

For information on enrolling in a clinical trial please visit our website at https://www.mclaren.org/main/research-trials1.aspx . 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

STUDY START-UP WITH MCRI

New study opportunities come to McLaren through a variety of avenues. Sometimes you as the investigator may be approached by a colleague at a conference, a representative in the cath lab, or receive an email directly from a drug or device manufacturer, asking if you would be interested in participating in a clinical trial. Other times, study opportunities get funneled in through the staff at the sites, the management staff in the Administration Office or even cold calls to our general research line. Whichever way a study gets to us, McLaren Center for Research and Innovation has a systematic study start up management plan.

As soon as a new opportunity comes to our attention, it gets sent directly to the Corporate Research Manager in charge of study start up. The study is entered into to a tracking system, then the work begins. The manager reaches out to the sponsor, telling them who we are, what we have to offer and why they should choose McLaren as a research site. From this, we often get a Confidentiality Disclosure Agreement (CDA) from the sponsor. The CDA is executed on behalf of McLaren Health Care so our whole team can receive confidential study information. Once we have a CDA, the sponsor will provide us with a study synopsis, or brief description of the trial opportunity.

The manager sends this information out to the research coordinators at all active McLaren research locations: Bay Region, Flint, Greater Lansing, Macomb, Northern Michigan, Oakland, and St. Luke's. The site staff review it and see if any of their local physicians would have a particular interest in conducting the trial. Once we identify interested investigators, the manager works with the sponsor and sites to get initial feasibility questionnaires completed. The sponsor often wants to do an on-site qualification visit to each site to complete their evaluation of our institution's capabilities. The sponsor will then use this information to determine if we are a suitable site for their study.

Once we are selected by the sponsor, we receive a contract and a budget and this starts the clock on our "study start up timeline". MCRI's goal is 90 days from contract receipt to IRB approval. Study sponsors expect a tight timeline to get studies enrolling as this process can be costly for them. The contract and budget specialist, in conjunction with McLaren's research legal

team, begins reviewing the contract and budget while regulatory specialists begin drafting consents and collecting regulatory documents for the sponsor. Meanwhile, the Feasibility Review Committee, chaired by Mark Zainea, MD, gets to work with the site staff to tease out the operational details of the protocol. FRC exists to ensure that each site has the manpower, equipment, space and local hospital resources to adequately conduct the study. The study is also evaluated for financial impact to the institution.

In the background, MCRI's contract and budget specialists and regulatory specialists are working to get study budgets, contracts, consents and other related material reviewed, prepared and ready for final execution and IRB submission. Our research informatics team and research finance teams are also on high alert during this time to prepare our Clinical Trials Management System and patient payment system for the new study.

The final step before IRB submission is Protocol Review Committee. PRC, as chaired by Hesham Gayar, MD, reviews research protocols for scientific merit. This committee is charged with ensuring McLaren embarks on research that has value to the scientific community and can be of potential value to our patients. The committee is made up of primarily McLaren physicians who conduct peer reviews of research protocols. This is a wonderful forum for scientific discussion and research related collaboration.

After PRC approval, the study can be released for IRB submission. Typically, once submitted, we can anticipate about 3 weeks to approval. Once the study is IRB approved, each participating site will have a Site Initiation Visit to ensure they are ready to begin enrollment. The SIV is conducted by the sponsor and includes detailed training on the study protocol, FDA regulations and responsibilities of the investigator and research team. This is also when study drug, devices or other study supplies will be shipped out to the study sites. Once the sponsor gives us the go ahead, we can begin the enrollment phase of the study.

The study start-up process is vital to the success of research at McLaren. Selecting studies that match our abilities and interests provides us a strong foundation to conduct valuable scientific inquiry and provide sponsors with high quality data. When we meet our contractual obligation with these high -profile industry leaders, they value McLaren as a partner in research and come back with future contracts. If MCRI continues to refine and improve our study start-up process, we can provide McLaren opportunity to grow research at our institution in ways we have yet to imagine.

ATTENTION NEW OR POTENTIAL MCRI INVESTIGATORS

In order to conduct research as an Investigator at McLaren, there are a few basic requirements you will need to complete to get started:

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

1. **Human Subject Protection Training www.CITIprogram.org Affiliate with McLaren Health Care and take the required Biomedical Research Human Subjects Protection Training Course, the required Conflict of Interest Course, and a Good Clinical Practice course. (*note, if you have completed CITI training under another institution, your completed modules may apply but additional modules may be required for completion of this institutional requirement.)**
2. **Have an updated CV with your McLaren affiliation listed and sign and date the first page.**
3. **Have a current medical or professional license**

Once you have met the three requirements above, please email the documents to MCRI@mclaren.org and indicate "New Investigator" in the subject line.

Please provide any available information about the study that you are interested in conducting and if industry sponsored, please provide a contact person from the sponsoring company. If you are interested in conducting your own study or simply interested in future projects, please explain what research opportunities you are looking for. Include your preferred method of contact and your best email address, so we will be able to reach you easily.

You will be contacted shortly after receipt of your email request to discuss how McLaren Center for Research and Innovation can best support your research interests.

RESEARCH AROUND McLAREN

Mahmoud Rayes, MD

MCRI SITE SPOTLIGHT:

McLAREN FLINT

McLaren Center for Research and Innovation at McLaren Flint has a long and robust history of conducting clinical trials. Originally established over 20 years ago with a focus on cardiology research, McLaren Flint experienced a recent shift to a focus on Neuroscience research. McLaren Flint was the first subsidiary to join StrokeNet, a National Institutes of Health research initiative involving approximately 500 hospitals in the U.S. designed to serve as the infrastructure as pipeline for potential treatments for patients with stroke and those at risk for stroke. "As the hub of the McLaren Stroke Network, McLaren Flint has the need for and capability to conduct acute stroke research trials like no other McLaren hospital can. We are uniquely positioned to succeed with very challenging trials because we have the population and a growing research department," explains Dr. Mahmoud Rayes, Neurointerventionalist and Principal Investigator. "If this is what we can accomplish in a few short years, I look forward to seeing what our future has in store."

McLaren Flint is currently enrolling in 8 Neuroscience trials, many of which are for acute stroke patients. MCRI is working to open 3 additional neuroscience trials to add to that portfolio. "We recognize that McLaren Flint is primarily a neuroscience research site, but we were very excited to expand to infectious disease during the COVID-19 pandemic and provide our physicians and patients with clinical trial options for COVID treatment," said Pamela Wills-Mertz, MCRI Director, "We hope to continue working with our infectious disease physicians and bring more COVID research to McLaren Flint."

The Flint MCRI office on 3 North is supported by two full-time Research Coordinators and a part-time Research Assistant. Marci Roberts has been working in clinical trials for close to 20 years and is one of MCRI's most experienced coordinators. Marci's strong coordination skills have been invaluable not only supporting the complex acute stroke trials, but training and on-boarding new coordinators across the system. Stephanie Bruma, RN has recently transitioned from a floor nursing position to a research nurse position and is quickly learning the industry. Jonathon Stern is a new addition in 2021 and has taken on a part-time research assistant position while preparing to go to medical school. "With Marci's experience and Stephanie's clinical expertise supported by Jonathon this team is a force to be reckoned with!" says Dr. Rayes.

Rounding out the MCRI team, the Neuroscience Advanced Practice Providers and Stroke Coordinator assist on many trials. "Participating in clinical trials expands the knowledge base of our providers and gives them the opportunity to connect with patients on a different level," says Julie Snyder, Corporate Neuroscience Director, "As an accredited Comprehensive Stroke Center with the Joint Commission we are always looking for ways to explore novel treatment options and participate in trials that could change the standard of care for our patients."

McLaren Flint is a bustling hub for clinical trials activity and is proud to offer unique and ground-breaking treatment options for our patients, while contributing to scientific advancement of numerous therapeutic areas.

THE AMERICAN SOCIETY OF HEMATOLOGY (ASH)

RECOGNIZES KCI/WSU RESEARCHER'S WORK WITH AN ORAL PRESENTATION AT ITS UPCOMING ANNUAL MEETING

Suresh Balasubramanian MD, hematologist oncologist at the Barbara Ann Karmanos Cancer Institute and assistant professor at the Wayne State University (WSU) School of Medicine's Department of Oncology, has identified a novel approach to treat aggressive non-Hodgkin's lymphoma. This work has been selected for oral presentation at the prestigious ASH Annual Meeting.Dr. Balasubramanian considers his selection to be an honor because of the society's rigorous review process.

Suresh Balasubramanian, MD

Dr. Balasubramanian is exploring novel therapeutics preclinically in the field of malignant hematology. His team has shown that targeting p21 activated kinase 4 (PAK4) and nicotinamide phosphoribosyl transferase (NAMPT) could be a synthetic lethal strategy for aggressive lymphomas. Dual targeting PAK4/NAMPT in preclinical models by small molecules inhibitors in vitro and in mice showed excellent efficacy with barely noticeable toxicity in animals.

THESE FINDINGS ARE INDEED PROMISING AND IF PROVEN TO BE EFFECTIVE IN CLINICAL TRIALS, COULD SERVE AS A VIABLE OPTION IN THE EXPANDING ARMAMENTARIUM OF CANCER THERAPEUTICS FOR PATIENTS.

These findings are indeed promising and if proven to be effective in clinical trials, could serve as a viable option in the expanding armamentarium of cancer therapeutics for patients. This work is a result of a joint effort between Dr. Balasubramanian and Asfar Azmi, PhD, associate professor at WSU.

RESEARCH AROUND McLAREN

Asfar Azmi, PhD

ASFAR AZMI, PhD RECEIVES 2021 KALES AWARD FOR BREAKTHROUGH IN PANCREATIC DUCTAL ADENOCARCINOMA TREATMENT

Asfar Azmi, PhD, associate professor, Department of Oncology at the Barbara Ann Karmanos Cancer Institute and Wayne State University School of Medicine, has been selected as the winner of the 2021 Anthony and Joyce Danielski Kales Endowed Faculty Award for Innovative Cancer Researcher for his research on Selinexor with Gemcitabine and Nab-Paclitaxel for the treatment of pancreatic ductal adenocarcinoma.

Dr. Azmi's research, "Preclinical Assessment with Clinical Validation of Selinexor with Gemcitabine and Nab-Paclitaxel for the Treatment of Pancreatic Ductal Adenocarcinoma," was published in Clinical Cancer Research.

Co-authors on this research include Husain Yar Khan, Irfana Muqbil, Amro Boukameel, Jasper E. Neggers, Dirk Daelemans, Amit Mahipal, Gregory Dyson, Mandana Kamgar, Mohammad Najeeb Al-Hallak, Anteneh Tesfaye, Steve Kim, Vinod Shidham, Ramzi M. Mohammad and Philip A. Philip.

"I am really humbled to be honored with this wonderful award," said Dr. Azmi. "Pancreatic ductal adenocarcinoma (PDAC) is a deadly disease in urgent need of newer treatments, and I am proud to contribute research to this field."

Dr. Azmi's research demonstrates that the nuclear exporter protein exportin 1 (XPO1) is critical in enabling PDAC tumors to grow and persist. Targeting XPO1 using drugs such as selinexor has shown antitumor activity in stem cell-derived models, and multiple patient-derived models when combined with standard-of-care treatment or used alone. In a phase I clinical study, Dr. Azmi and his team observed remarkable response in a patient with metastatic PDAC tripling the survival on a regimen of selinexor–gemcitabine–nab-paclitaxel. His team's studies bring forward a new and clinically effective therapy for PDAC.

"Our research team has shown that overexpression of XPO1 contributes to therapy resistance and poor survival in solid tumors. Therefore, XPO1 inhibition and subsequent realignment of TSPs to the nucleus is an attractive anticancer strategy," Dr. Azmi explained.

Dr. Azmi will be honored for his research at a virtual Grand Rounds ceremony on November 18. He will speak about his research, specifically on nuclear protein transport biology and the publication for which he is being recognized.

The Kales Award was created in 2012 at the WSU School of Medicine to recognize exemplary and innovative cancer research. It is supported by the Drs. Anthony and Joyce Danielski Kales Endowed Faculty Award for Innovative Cancer Research Endowment. Selection is based on a comprehensive review of published articles within the previous year.

RADHIKA GOGOI, MD, RECEIVES GERI FOURNIER OVARIAN CANCER RESEARCH GRANT

Karmanos is pleased to congratulate Radhika Gogoi, MD, PhD, member of the Gynecologic Oncology Multidisciplinary Team at Karmanos for securing a Geri Fournier Ovarian Cancer Research Grant in the amount of $50,000. The annual award is given by The Michigan Ovarian Cancer Alliance to recognize and provide funding for the critical research happening in the state.

Dr. Gogoi received the grant award for a research project that aims to identify differences between BRCA1 and BRCA2 proteins that may lead to more effective targeted treatments. Currently, treatment with PARP inhibitors does not differentiate between BRCA1 and BRCA2 mutated tumors. (PARP inhibitors are cancer drugs that help repair DNA when it becomes damaged. In cancer treatment, blocking PARP may help keep cancer cells from repairing their damaged DNA, causing them to die.) However, preliminary data suggests that there are molecular differences that contribute to varied treatment responses. Dr. Gogoi's research aims to identify unique gene targets, biomarkers, and potential new therapeutic combinatorial approaches to provide better treatment options for patients with BRCA 1 and 2, the most common cause of hereditary breast and ovarian cancer.

Radhika Gogoi, MD, PhD

FDA APPROVAL GRANTED FOR NEW BREAST IMAGING TOOL DEVELOPED IN DETROIT

SoftVue™ 3D Whole Breast Ultrasound Tomography System developed by Karmanos Cancer Institute spinoff Delphinus Medical Technologies, LLC

Karmanos Cancer Institute is pleased to celebrate the FDA approval of SoftVue™ 3D Whole Breast Ultrasound Tomography System (SoftVue™) for use as an adjunct to digital mammography in screening asymptomatic women with dense breast tissue. This technology was developed by Delphinus Medical Technologies, LLC, which originated as part of Karmanos Cancer Institute.

This unique technology helps to accurately detect many early stages of breast cancer, even in women with dense breast tissue. Mammography alone misses about half the cancers in women with dense breasts. Forty percent of women in the U.S. have dense breast tissue, so that increased risk, combined with decreased sensitivity, creates a significant challenge for this population.

How it works: During the exam, the patient relaxes on her stomach with her breast submerged in a warm water bath. The breast is comfortably stabilized and centered with a disposable Sequr™ Breast Interface gel pad. Imaging is performed with a proprietary 360-degree ring transducer, scanning each breast from chest wall to nipple in an average of three minutes, capturing new images every two millimeters. The captured signals are then analyzed using sophisticated algorithms that provide cross-sectional slices of the entire volume of breast tissue.

Clinical evidence has demonstrated that SoftVue identifies up to 20 percent more cancers with greater accuracy than full-field digital mammography (FFDM) alone. Additionally, the SoftVue exam is completed with no compression or radiation, and exams can be performed at the same appointment as screening mammograms without the need for an extra appointment.

RESEARCH AROUND McLAREN

Ann Schwartz, PhD, MPH

Gerold Bepler, MD, PhD

KARMANOS CANCER INSTITUTE RECEIVES MULTI-MILLION DOLLAR GRANT TO DETERMINE WHY ADVANCED CANCER TREATMENT FAILS AFRICAN AMERICANS

The Barbara Ann Karmanos Cancer Institute and Wayne State University recently received a $2,997,215 federal grant to help determine why African Americans show poorer responses than whites when treated with one of the most advanced immunotherapies for lung cancer. The specific focus of the grant is to study immune checkpoint inhibitor (ICI) treatment for metastatic non-small cell lung cancer.

The grant is through the NCI's SPORE, or Specialized Program of Research Excellence, which funds collaborative, interdisciplinary translational cancer research. It will fund two projects under the title Reducing Cancer Health Disparities in Detroit.

Project 1:
Characterizing race-specific immune profiles with respect to the tumor environment and host genetic background to determine their contribution to response to ICIs

Project 2:
Understanding racial differences in patients' responses to ICI treatment

The projects will be led by principal investigators Ann Schwartz, PhD, MPH, Deputy Center Director, Karmanos Cancer Institute and Professor and Associate Chair of Oncology, Wayne State University School of Medicine and Gerold Bepler, MD, PhD, Thoracic Oncologist, President and CEO of Karmanos Cancer Institute.

Recent breakthroughs in immunotherapy, particularly ICIs with Food and Drug Administration approval, have offered significant advancements for lung cancer treatment. Unfortunately, African American patients have accounted for less than four percent of ICI clinical trial representation. In the limited data available, African Americans show poorer responses to ICIs than whites,

contributing to racial disparities in cancer treatment.

Overall, African Americans continue to have worse outcomes after a lung cancer diagnosis than whites, and there are known differences between African Americans and whites in many aspects of cancer treatment, including time to initiation and dose of chemotherapy, symptom burden and treatment of side effects.

Poorer response to treatment and worse outcomes are compounded because lung and bronchus cancers were leading sites of cancer diagnosis among African American men and women from 2019 to 2021, according to the American Cancer Society. Lung and bronchus cancers were the number two cause of cancer death in African American people, following prostate cancer in men and breast cancer in women.

Work funded by the grant will provide the basis to move toward a more race-inclusive, equity-focused, precision medicine approach to the use of ICIs and serve as a model for future research on other cancer sites and new agents.

“With this grant, we will work to address racial disparities in Metropolitan Detroit, a uniquely important underserved population where great cancer disparities exist,” said Ann Schwartz, PhD, MPH, Deputy Center Director, Karmanos Cancer Institute and Professor and Associate Chair of Oncology, Wayne State University School of Medicine, one of two principal investigators for the study. “Racial disparities in cancer outcomes will likely widen without a comprehensive understanding of the biologic mechanisms driving treatment response in diverse populations and the applicability of clinical guidelines to all populations.”

In their efforts to understand racial treatment-response differences, researchers will directly evaluate sociodemographic, individual and disease-specific predictors of response to ICI treatment in African American and white patients. While ICIs hold promise for improved outcomes, little is known about whether potential predictors of patient-reported side effects and quality of life and immune-related adverse events vary by race.

By identifying drivers of potential disparities, health care professionals can better identify patients at high risk for side effects and immune-related adverse events, which are a significant concern. Health care providers can also develop interventions to reduce risk factors, thereby improving patients’ quality of life and reducing racial disparities in outcomes.

Unfortunately, little is known about potential racial differences in response to ICI treatment. This is largely due to a lack of inclusion of African American patients in the clinical trials leading to FDA approvals. Thus, there is a critical need to explore whether African American and white patients are affected differently by side effects related to ICI treatment.

RESEARCH AROUND McLAREN

THE NATIONAL CANCER ACT

The Barbara Ann Karmanos Cancer Institute, along with hospitals, researchers, advocates and policymakers across the country, recognizes the 50th Anniversary of the National Cancer Act (NCA).

In 1971, President Richard Nixon amended the Public Health Service Act of 1944 to create legislation that would wage a "war on cancer." The National Cancer Act established the current iteration of the National Cancer Institute (NCI) and enabled the development of a national cancer program. It also empowered researchers by creating a clinical trial network, provided additional funding for cancer control programs and established an international cancer research data bank. Additionally, the National Cancer Act created a presidentially-appointed committee known as the National Cancer Advisory Board (NCAB) to guide the development of NCI programs and the President's Cancer Panel (PCP), which holds public hearings on cancer topics and submits a yearly report to the president.

"The National Cancer Act was a game-changer for cancer treatment and research," said Gerold Bepler, MD, PhD, president and CEO of Karmanos Cancer Institute. "This legislation laid the groundwork for enhanced communication and elevated the nation's commitment to curing cancer."

Dr. Bepler recently spoke about the 50th anniversary of the NCA and what it means to be an NCI cancer center with Kevin Stevenson on the I Don't Care podcast, which highlights health care executives and administrators who are solving unique issues in their industries. Hear his interview at **https://marketscale.com/industries/healthcare/the-inspirational-quest-to-eradicate-cancer/**.

The NCI Cancer Centers Program, a critical part of the 1971 act, recognizes centers around the country that meet rigorous standards for transdisciplinary, state-of-the-art research focused on developing new and better approaches to preventing, diagnosing and treating cancer.

In 1978, just seven years after its inception, the National Cancer Institute (NCI) designated Karmanos Cancer Institute as a comprehensive cancer center. At this time, Karmanos was known as the Cancer Center of Metropolitan Detroit. This designation is awarded to only 51 cancer centers throughout the country, and Karmanos is only one of two cancer centers with this designation in Michigan. To receive this designation, a hospital must

demonstrate expertise in laboratory, clinical and population-based research. Hospitals must also provide early-phase clinical trials and conduct community outreach and educational activities. This means patients can access treatments exclusive to Karmanos, as well as cancer prevention programs and multidisciplinary teams of cancer specialists.

NCI-designated cancer centers play a vital role in advancing our goal of reducing morbidity and mortality from cancer. During our 43 years as an NCI-designated cancer center, Karmanos has contributed to many meaningful advancements in cancer treatment. Highlights include:

- **1989** - Dr. Soule developed MCF-10, an immortal line of normal human breast cells. The cell line was the first of its kind to be cultured without the use of transforming agents and was used to study the earliest changes a normal cell undergoes in becoming cancerous.
- **1998** - The National Breast Cancer Prevention Trial released news that the drug Tamoxifen, can reduce the incidence of breast cancer in healthy women at high risk for the disease by 50 percent. The drug was created with the MCF-7 breast cancer cell line established by the Institute in 1973.
- **1999** - Dr. Wei-Zen Wei developed the HER-2 DNA breast cancer vaccine in 1999, which has been shown to be effective on drug-resistant tumors in mice.
- **2017** - CAR T-cell therapy received FDA approval; Karmanos is one of 18 sites in the world that participated in its development.
- **2021** - SoftVue™ 3D Whole Breast Ultrasound Tomography System receives FDA approval for use as an adjunct to digital mammography in screening asymptomatic women with dense breast tissue. This technology was developed by Delphinus Medical Technologies, LLC, which originated as part of Karmanos Cancer Institute.

In addition to these accomplishments, Karmanos has served thousands of individual patients and saved lives with outstanding care, research and clinical trials. The past 50 years have seen remarkable progress in eradicating cancer, the second leading cause of death in the United States, but there is more work ahead of us. Karmanos looks forward to leading the way, along with other NCI-designated centers and the backing of the National Cancer Institute. Nothing will stop us.

EQuIP CORNER

Andrea Klaver, MBA, CHRC

2022 AAHRPP REACCREDITATION SITE VISIT PREPARATION:

WHAT SHOULD I KNOW?

By Andrea Klaver, MBA, CHRC

In the Spring 2021 edition of Research Matters, I wrote about AAHRPP (pronounced "ay-harp"), the Association for the Accreditation of Human Research Protections Programs, the accreditation process, and why we do what we do throughout our research programs to retain the AAHRPP "golden seal."

McLaren first earned initial AAHRPP accreditation in 2013 and was awarded full reaccreditation in 2016. We are tentatively scheduled for AAHRPP to conduct our next reaccreditation site visit this summer. We have already submitted our Step 1 Application Materials to AAHRPP and are awaiting a response from them reviewing our Application, which should occur by mid-February. These materials included an overview of our Human Research Protections Program (HRPP), our policies, IRB information, Education and Quality Improvement Program (EQuIP) documents, and much more.

During the site visit, representatives from AAHRPP will conduct confidential interviews and review records to ensure that these policies and procedures have been implemented effectively and are being adhered to throughout McLaren. As an investigator or research team member, you are an integral part of the McLaren HRPP.

As the site visit draws nearer, the AAHRPP site visit committee members will select individuals to be interviewed during their visit. Anyone who has a role in human research at McLaren has a chance of being selected, and several researchers and their team members will be interviewed. Questions are generally focused on regulatory and ethical issues related to research with human participants.

The following is a high-level overview. Additional information and training will be provided in the coming months.

Preparing for the Site Visit: General Tips

First, it is central to know and understand the McLaren HRPP 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. 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. More information on the McLaren HRPP may be found at https://www.mclaren.org/main/research-integrity.

McLaren's reaccreditation depends largely on the interviews. If interviewed, we recommend that you respond directly to the question asked. If a question seems unrelated to the type of work you do, please let the interviewer(s) know. For example, if a question regarding Food and Drug Administration (FDA) regulations is asked, a behavioral health researcher should let the interviewer(s) know that drugs or medical devices are not part of their research.

Some topics you will be expected to be familiar with include:

- Clearly describing your role in supporting the protection of research participants
- Be familiar with McLaren Research Integrity Policies and Procedures (and where to access them) and the McLaren HRPP's general structure
- Know how to report non-compliance and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)
- Understand and describe the ethical aspects, the purpose, and the value of your work
- Know the regulatory standards that apply to your research
- Know IRB application (iRIS) submission terminology, and describe your IRB submissions
- Describe the human subject training that you've had (e.g., CITI Training, EQuIP sessions)
- Know how to recruit participants ethically and in an equitable manner while adhering to inclusion/exclusion criteria

Roles and Responsibilities of Investigators and Research Staff

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. The principal investigator (PI), co-investigator (Co-I), and other members of the study team are expected to be knowledgeable about and adhere to:

- **The Belmont Report**, created as a result of the National Research Act of 1974:
- **Respect for Persons.** Study subjects are treated as autonomous agents, and should that autonomy be diminished, they are entitled to protection. We give weight to each patient's choices and opinions, while ensuring they are participating in the study voluntarily after being supplied

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EQuIP CORNER

UPCOMING RESEARCH EDUCATION

SOCRA
31st Annual SOCRA Conference
September 16 - 18, 2022
Orlando, Florida
Disney's Coronado Springs Resort

MAGI
MAGI's Clinical Research Hybrid Conference – East
May 1 - 4, 2022
Boston, Maine
Sheraton Boston Hotel
Physical or Virtual Event

ACRP 2022
Annual Conference
April 22 – 25, 2022
Orlando, Florida
Hyatt Regency Orlando

BROWN BAG SERIES

Our next Brown Bag Session is tentatively scheduled for Tuesday, March 8, 2022. Please watch your email and the EQuIP Education webpage at https://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.

2022 AAHRPP REACCREDITATION SITE VISIT PREPARATION: WHAT SHOULD I KNOW?

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adequate information (e.g., **Informed Consent**).

- A note on **Informed Consent:** Informed Consent 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 involving the investigator (or designees) and the research participant.
- To review, please see policies MHC_RP0115, "Obtaining Informed Consent from Research Subjects" and MHC_RP0116, "Vulnerable Subjects in Research" on the McLaren Research Policies & Procedures page at **https://www.mclaren.org/main/research-policies-procedures**.
- **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. You may review The Common Rule requirements at https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html.
- **21 CFR 50 and 21 CFR 56**, which serve as the regulatory framework for research regulated by the FDA (i.e., research involving drugs, devices, biologics), and any other federal or state laws and regulations that apply to research (e.g., HIPAA).

It is critical to remember that minimizing risks to participants and ensuring participants' rights and welfare are key components of human subjects protections. Be prepared to discuss some strategies through which this is accomplished at McLaren (e.g., the design and implementation of protocols, equitable recruitment procedures, adequate participant monitoring, etc.).

Investigator Compliance with the IRB and Other Requirements

Investigators and research staff have a responsibility for ensuring research is conducted in compliance with McLaren IRB policies and procedures, as well as other institutional and applicable regulatory requirements. These are outlined in McLaren policy MHC_RP0125, "Investigator Responsibility." Below are some requirements that investigators and research staff should be aware of related to this responsibility:

- Ensure that all research involving human subjects receives IRB review and approval in writing before commencement of the research
- Comply with all IRB decisions, conditions, and requirements
- Ensure that protocols receive timely continuing IRB review and approval
- Obtain IRB review and approval in writing before changes are made to approved protocols or consent forms

- Report unanticipated problems involving risk to subjects or others (UPIRSO) and any other reportable events to the IRB according to McLaren policy [MHC_RP0121, "Reporting Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)" and MHC_RP0122, "Protocol Deviations, Violations, and Exceptions"]

For additional details, please visit **https://www.mclaren.org/main/research-policies-procedures** to view all the McLaren Research Policies & Procedures.

Regarding IRB compliance, AAHRPP may ask you questions like:

- How do you notify the IRB about proposed changes to your research?
- What would you do if you lost your research data and who would you tell?
- Do you know how to report a participant complaint or a problem with your study?
- What is an Unanticipated Problem? Have you ever had one on a study? How would you report it to the IRB?

In Summary

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). While it is important that we know where to find the information discussed in this article and familiarize ourselves with it, we do not need to memorize everything! AAHRPP interviews are not meant to be interrogations. However, adequate preparation can put your mind at ease.

The McLaren Research Integrity staff are available to answer your questions and to help you have a successful interview, should you be selected to participate in our AAHRPP reaccreditation process. If you have any questions, don't hesitate to contact us at: **hrpp@mclaren.org**.

WHAT'S NEW WITH THE FDA: DIETARY SUPPLEMENTS

Recently, there has been an uptick in FDA enforcement activity related to studies involving dietary supplements. Specifically, when such studies are evaluating the effectiveness of supplements for a therapeutic purpose, or "diagnosis, cure, mitigation, treatment, or prevention" of disease, the FDA is classifying the supplements as drugs and requiring an IND unless the study qualifies for an IND exemption or the FDA itself issues a letter waiving the IND requirement for a study. For more information, please visit https://www.fda.gov/food/dietary-supplements.

FACULTY, FELLOWS & RESIDENTS

SCHOLARLY ACTIVITY NEWS

Carlos F. Rios-Bedoya, ScD

DIVISION OF SCHOLARLY INQUIRY – A YEAR IN REVIEW

By Carlos F. Rios-Bedoya, ScD

During the past year the Division of Scholarly Inquiry was involved in the design, development, modification, and implementation of several procedures aiming at standardizing, encouraging, and facilitating scholarly activity from residents and teaching physicians. In addition, findings from a resident research gap analysis were used to identify and measure the skill level of first year residents to conduct a review of literature. It has been a busy and challenging year, but also a very rewarding one.

Scholarly activity projects must comply with all federal regulations for safeguarding safety and privacy of participants. The Scholarly Activity Review Committee is working to implement these regulations as they apply to resident research. Case reports and case series are not considered research and hence are not reviewed by these committees The Division of Scholarly Inquiry together with the Office for Corporate Compliance developed a process to review all case reports and case series to ensure compliance with privacy and HIPAA regulations. Since the implementation of the process in January 2021, all case reports and case series audited have been in compliance with the privacy and HIPAA regulations.

In early 2019, a resident research gap analysis was conducted as part of an internal GME self-evaluation and quality improvement process to identify areas

> "IN EARLY 2019, A RESIDENT RESEARCH GAP ANALYSIS WAS CONDUCTED AS PART OF AN INTERNAL GME SELF-EVALUATION AND QUALITY IMPROVEMENT PROCESS TO IDENTIFY AREAS OF POTENTIAL VARIABILITY IN THE SCHOLARLY ACTIVITY PROCESS."
>
> *– Carlos F. Rios-Bedoya, ScD*

of potential variability in the scholarly activity process. One area identified was lack of appropriate literature review skills. It was unclear about the skill set of residents in completing an online literature review, which is one of the first steps in the scholarly activity process. A standardized assessment tool was developed in collaboration with subsidiary librarians to assess first year residents. Data analysis is in progress at this time.

Division of Scholarly Inquiry also conducted quarterly didactics for first year residents, USMLE Step 3 training, journal clubs, developed new templates for scholarly activity projects, and many other activities that cannot be included given space limitations. A lack of statistical support for residents was identified as another area of concern. To address this, we have coordinated with the Statewide Campus Office of Michigan State University to provide statistical analysis support for our scholarly activity projects.

"DIVISION OF SCHOLARLY INQUIRY ALSO CONDUCTED QUARTERLY DIDACTICS FOR FIRST YEAR RESIDENTS, USMLE STEP 3 TRAINING, JOURNAL CLUBS, DEVELOPED NEW TEMPLATES FOR SCHOLARLY ACTIVITY PROJECTS, AND MANY OTHER ACTIVITIES THAT CANNOT BE INCLUDED GIVEN SPACE LIMITATIONS."

– Carlos F. Rios-Bedoya, ScD

The Division of Scholarly Inquiry is establishing a pre-determination process prior to IRB submission which is expected to expedite scholarly activity projects' approval. Further details will be forthcoming.

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**.

McLAREN MACOMB CARDIOLOGY PUBLICATION

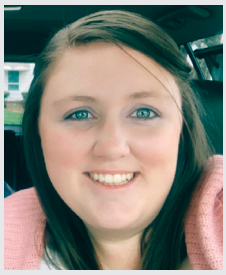
Parekh A, **Sengupta V**, **Hunyadi V**, **Ianitelli M**, **Zainea M.** – *Aortic Valve Leaflet Rupture Causing Delayed Left Main Coronary Ostial Obstruction During Valvuloplasty Preceding* TAVR. JACC: Case Reports. 2021;3(17):1822-1827. doi:10.1016/j.jaccas.2021.09.022

We sincerely regret if we left out any fellow or resident, due to our publication deadline. Nevertheless, our congratulations to all of you that received any recognition for your scholarly activity work. We also would like to recognize faculty, program directors, and all medical education staff for their support and assistance. Without you, none of this would have been possible.

ANNOUNCEMENTS AND WHAT'S NEW

Drita Nuculovic

Karmanos Cancer Network is pleased to welcome **Drita Nuculovic** as our Proton Research Nurse Navigator. She brings with her over 15 years' experience related to patient care. She has worked extensively on patient quality metrics with Patient-Centered Medical Home through BCBS. She, along with former colleagues, created a patient registry based on the most common chronic conditions in the practice. We believe Drita's experience will be an asset to the McLaren Proton Therapy Center. She will be assisting with activation of several clinical trials and a registry trial at the proton center this year. Drita is excited to join a great team and apply skills needed through our program in Flint.



Katlyn Greenawalt

MCRI is pleased to welcome **Katlyn Greenawalt** as a Clinical Research Coordinator at McLaren St. Luke's. She brings a Bachelor of Science degree in physics from Adrian College, as well as and two years of oncology research experience to her role. Katlynn is excited to return to the world of research after spending nearly three-years as a stay-at-home mom. She enjoys the fast-paced work of research and the ability to get to know her patients more in depth. Katlynn loves working within the clinical aspects of the research coordinator position, such as lab processing. She is very excited to open clinical trials at the newest MCRI site!

Katie Wray Esckilsen

MCRI is pleased to welcome **Katie Wray Esckilsen** back to her Clinical Research Nurse position at McLaren Greater Lansing. She graduated from the University of Saint Francis in Ft. Wayne, Indiana in 2012 with her nursing degree. Katie started her nursing career working on a Telemetry Unit and Critical Care Unit for several years until she moved to Michigan and began working in the MCTVS office. This is where she was originally introduced to Clinical Research. Since that time, Katie has coordinated several clinical trials including but not limited to Cardiovascular and Neurological trials over the past 5 years. She started her research career at McLaren and is happy to be back!

Mary Catton

MCRI would like to congratulate **Mary Catton**, Clinical Research Nurse at McLaren Northern Michigan, on receiving her Certification as a Clinical Research Coordinator (CCRC) through the Association of Clinical Research Professionals in October of 2021. Congratulations, Mary!

Office of Clinical Excellence
VICE PRESIDENT
Chandan Gupte
chandan.gupte@mclaren.org

ADMINISTRATIVE ASSISTANT
Tamara Leo
tamara.leo@mclaren.org

McLaren Corporate Research
2701 Cambridge Court, Ste. 110
Auburn Hills, MI 48326

McLaren Center for Research and Innovation
mclaren.org/Main/Research.aspx
(248) 484-4960

CORPORATE DIRECTOR. MCLAREN CENTER FOR RESEARCH AND INNOVATION
Pam Wills-Mertz
pamela.wills-mertz@mclaren.org

CORPORATE RESEARCH MANAGERS
Jill George
jill.george@mclaren.org

Melissa Szemites
melissa.szemites@mclaren.org

REGULATORY SPECIALISTS
Tanya Gardner-Mosley
tanya.gardner-mosley@mclaren.org

Vidya Yarlagadda
srividya.yarlagadda@mclaren.org

FINANCIAL ANALYST
Quinn Warwick
quinn.warwick@mclaren.org

CONTRACT AND BUDGET SPECIALIST
Lakeeshi Williams
lakeeshi.williams@mclaren.org

DIRECTOR OF RESEARCH FUNDING
Barb Rauschendorfer
barb.rauschendorfer@mclaren.org

CLINICAL RESEARCH INFORMATICS MANAGER
Donna Mott
donna.mott@mclaren.org

Research Integrity
hrpp@mclaren.org
(248) 484-4950

CORPORATE RESEARCH INTEGRITY MANAGER
Patricia Ivery
patricia.ivery@mclaren.org

IRB ANALYSTS
Markeda Richards
markeda.richards@mclaren.org

Mahjabeen Waris
mahjabeen.waris@mclaren.org

QI & EDUCATION SPECIALIST
Andrea Klaver
andrea.klaver@mclaren.org

Karmanos Cancer Institute Clinical Trials Office
VICE PRESIDENT
Lisa Lange
langel@karmanos.org

MANAGERS
Elizabeth Bowie
bowiee@karmanos.org

Sarah Bigelow
bigelows@karmanos.org

Jaclyn Ventimiglia
ventimij@karmanos.org

Kasha Donahue
krulk@karmanos.org

Elizabeth Cunningham
cunninge@karmanos.org