May 2021

Ongoing news about MEHARRY RESEARCH

The Research Digest

ADVANCING RESEARCH AND INNOVATION · Writer/editor: Sheila T. Yong, Ph.D.

From the Meharry Medical College Office for Research and Innovation

ANNOUNCEMENTS

Upcoming/ongoing events:

- A special supplemental issue of *Journal of Health Care for the Poor and Underserved* is available on TechQuity. Click **here** to read.
- **Meharry School of Dentistry** established a partnership with **Eastman Institute of Oral Health (EIOH)** at University of Rochester. This partnership establishes research collaborations between the two institutes and will host lunch and learn meetings for residents, students, and faculty. Click **here** to read more.
- **Meharry Medical College/Vanderbilt-Ingram Cancer Center/Tennessee Statue University 20th Annual Symposium.**

  Date: May 22, 2021
  Time: 8:30 am—12:30 pm

  See **flyer** for details.
- **Meharry Medical College Center for Women's Health Research (CWHR)** seeks African-American women with a mother, daughter, or sister who have been diagnosed with breast cancer to participate in discussion groups.

  For more info or to sign up, call **615.327.6531** or email **CWHR**.

  Sign-up deadline: May 31, 2021
- **Johnson & Johnson (J&J) Innovation** seeks to increase diversity at HBCUs. The center is seeking proposals in the following areas:

  Novel approaches in defining the role of gut barrier dysfunction in driving

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THE VP'S CORNER

Dear Meharrians:

The extraordinary outpouring of support I have received following my campus-wide vision presentation last month underscores the significance of Meharry's research enterprise. Our collective commitment and enthusiasm are inspiring. Together, I am confident that we can achieve our transformational goal of establishing Meharry as an institution of excellence and eminence. I look forward to working with all of you as we advance Meharry intellectually, physically and financially. We will transform Meharry into a global academic health sciences center that is student-centered, research-focused, and service-oriented. More importantly, we will continue to impact the intellectual, social, cultural, and economic experiences of the underserved communities we care for.

As Meharry approaches its sesquicentennial anniversary in 2026, we are at a pivotal time of our journey. Fueled by the Meharrian spirit and legacy to succeed despite all odds, we will rise to the challenge and avail the opportunities presented to us to transform Meharry into one of the best institutions in the world—one that will revolutionize healthcare and eliminate health disparities in underserved populations. Thus far, our organizational complexity and perhaps complacency stifle our innovative spirit as well as poses an impediment to our academic excellence and research prowess. This is the main reason President Hildreth urged us to develop Meharry 2026 strategic plan. By establishing this strategic plan, we have arrived at a shared vision to find solutions to our major challenges, establish mechanisms for assessing success, and provide adequate resources to empower those who will realize this plan.

The three major areas we will focus on are:

- **Intellectual transformation:** We will devise a robust **faculty growth plan** that will nurture talent and expertise to shape new fields. Our aim is to provide our students with the knowledge and skills that can shape them into forward-looking next-generation leaders. It is vital that we promote transdisciplinary collaborations by uniting complementary minds across disciplines to create exceptional academic frameworks. This will tie in with our graduate student growth and excellence plan to expand our Ph.D. population, along with a pipeline of postdoctoral internships and exchange programs that will prepare our postdoctoral fellows for faculty positions. Thus far, we have developed such programs with the UNC Eshelman Institute of Innovation, University of Memphis, Florida A&M University, Icahn School of Medicine at Mount Sinai, and American Cancer Society, with several more currently under development. Faculty sabbaticals, research technology training programs, and collaborative research projects for junior faculty and postdoctoral fellows will bolster their path to independence. In addition to opportunities in basic and computational sciences, we will also create opportunities in clinical population sciences and translational research that will benefit our medical and dental students and residents. We will set up field-based research and educational hubs where campus and community members in marginalized neighborhoods can work together to address health concerns that impact the quality of life in marginalized communities as well as pertain to health disparities and social inequities. We will also expand our outreach efforts at local

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systemic inflammation and disease

New therapeutics strategies that promote resolution of inflammation

Improving the precision of immunotherapies through cell targeting

Submission Deadline: Jun 1, 2021

For details, click **here** to view flyers and announcement.

To learn more about J&J Innovation, click **here**.

- **Meharry - Florida A&M (FAMU) Research and Innovation Collaborative Award Opportunity.** This is a collaborative research award for Ph.D. students, postdocs, and faculty to accelerate the development of creative ideas that will lead to discoveries and transformative changes in research and health care. Available funds: Up to **$20,000** each for students or postdocs, and up to **$40,000** each for faculty.

  Submission deadline: **Jun 30, 2021**

  Virtual Pitch Day: **Jul 15, 2021.** Invitation only

  Funding start date: **Aug 1, 2021**

  Please visit the **Meharry research** and **FAMU** websites for institutional information. To discuss a potential project or the award process, please contact **Leola Hubert-Randolph** (FAMU) or **Jared Elzey** (Meharry)

- **Advanced Medical Technology Association** offers workshops on **diversity in clinical trials**.

  Apr 28, 2021: Ethics, trust, and engagement: Addressing the challenges of clinical trial diversity.

  May 19, 2021: Building trust by building networks:

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schools to inspire the next generation of STEM leaders, especially in underserved communities, by organizing learning activities through hands-on experience and mobile labs. These mechanisms will revitalize our workforce and identify impactful collaborative research areas that promote health equity.

- **An advanced physical, technological, and computational infrastructure:** Such infrastructure is necessary to enrich our scientific and intellectual activities, as well as to ensure the success of collaborative transdisciplinary research clusters. Thus far, we have acquired two additional state-of-the-art flow cytometers for our Consolidated Research instrumentation, Informatics, Statistics and Learning Integration Suite (CRISALIS) and purchased supercomputers for the newly established School of Applied Computational Sciences. The renovation of our BSL3 facilities and acquisition of an Exploris 120 mass spectrometer are underway. Our in-house GPU supercomputer cluster will provide a data ecosystem for our research enterprise and clinical operations in a secure and compliant manner. In addition, this computing infrastructure will provide the hardware and digital platforms necessary to advance Meharry's technology, research, and analytic capabilities. We also plan to build a genomics and biorepository facility. This facility, combined with our computing infrastructure and imaging core, will strengthen our capabilities to computationally map, analyze, and visualize cells and tissues across a broad range of spatial and temporal scales. Another ongoing effort is to establish a pipeline of CLIA-certified Molecular Diagnostics Lab, a GLP Clinical Pharmacology Lab, and the Clinical and Translational Research Center to enhance our bioanalytical and translational capabilities. This proposed pipeline of facilities will generate revenue through conducting bioequivalence studies for generic drug repurposing commissioned by our partners in the pharmaceutical industry. The plans for a new research building are also in the works.

  These new infrastructure efforts, coupled with new and improved research administration online systems (for example, e-Protocol, Kuali, and iLabs), will create a vibrant research environment. This will enhance student training as well as increase the impact of faculty teaching and engagement that are critical for our growth. The increasing importance of online education in the last year has also prompted us to retool our courses to help students learn remotely, as well as to provide information and education material in an accessible and affordable manner. Such improvements will be especially beneficial to our new data science courses.

- **The creation and strengthening of strategic alliances:** Local and global alliances are key to the advancement of our research goals. To achieve this, we will create an Innovation and Commercialization unit to facilitate technology transfer as well as the management of intellectual property, innovation design, and industry partnering. Such efforts will enable the sharing of resources, talent and ideas, as well as accelerate research and delivery to maximize our positive impact on society. One of several research partnerships we are developing is a comprehensive 10-year National Genomics and Equity Initiative for a multi-organizational consortium. This is a partnership between historically Black medical colleges (HBMCs), led by Meharry, and pharmaceutical partners, led by Regeneron. This initiative is designed to empower the African American community to pioneer the transformation in education, culture and science. This long-term, public-private partnership will provide support and expertise to researchers and faculty at HBMCs to fill a void in human genomics resulting from the absence of the African founder population genome. The creation of this genome database is an important step in addressing health disparities within the African American community. This initiative will also create financial sustainability at HBMCs as it will: (1) invest in research

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Engaging clinicians and researchers

Jun 9, 2021: Addressing diversity through patient-centered trials

For details and past recordings, click **here**.

- The **UNC-Duke collaborative clinical pharmacology T32 postdoctoral training program** offers training opportunities for promising under-represented MD and DDS scholars as well as PhD graduates with interests in clinical pharmacology and translational research. See **flyer** for details.
- The Department of Otolaryngology at Thomas Jefferson University offers **research fellowship opportunities. An additional scholarship to a underrepresented, minority student is also available.** Admission is rolling, so please apply ASAP. See their **website** and **this announcement** for details.
- Grant development "Chalk-talk" sessions available to junior investigators to help develop their specific aims. Request your session at VP-Research@mmc.edu

Past events:

- **May 15, 2021: Meharry's 146th Commencement.** For photos, click **here**. Recording of the hooding and conferral of diplomas is available on the **MeharryTube** channel. The virtual commencement is available **here**.
- **Apr 30, 2021: A vision for Meharry research & innovation.** Presentation by Dr. Anil Shanker, Interim VP for Research & Innovation. Click **here** to view the Zoom recording. Passcode: pD#tF11T
- **Apr 19, 2021: Meharry's sesquicentennial celebration.**

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enhancement and training at HBMCs; (2) develop a genetic counseling training program; (3) establish a Joint-HBMC Diaspora Human Genomics Institute; and (4) create a unique African ancestry genomics reference resource. These efforts will lead to unprecedented opportunities and partnerships that will contribute to Meharry's overall progress and advancement.

In time, our efforts will transform Meharry into a global hub of innovation that will act as a catalyst for social enrichment for underserved minorities and communities worldwide. Together, we will continue to shape and impact the world through addressing local, national, and global challenges that underserved populations encounter.

Kind regards,

Anil Shanker, M.S., Ph.D.
Interim Vice President for Research and Innovation
Professor of Biochemistry, Cancer Biology, Neuroscience and Pharmacology

SPOTLIGHT

Meharry graduate student wins the Ruth L. Kirschstein Predoctoral Individual National Research Service Award

Fifth-year graduate student Ky'Era Actkins (pictured) received the Ruth L. Kirschstein Predoctoral Individual National Research Service award (F31 predoctoral fellowship) from the National Institutes of Health. Funded through the Eunice Kennedy Shriver National Institute of Child Health and Human Development, this award will support her stipend, tuition and fees, and research expenses for one year.

"Receiving this fellowship is an honor and I am completely overjoyed," Actkins said. This funding will provide her with the tools and resources she needs to complete her dissertation project so that she can transition to the next step in her research career.

A Ph.D. candidate in the Department of Microbiology, Immunology, and Physiology at Meharry, Actkins studies the etiology of polycystic ovary syndrome (PCOS) in the laboratory of Dr. Lea Davis at Vanderbilt University Medical Center. "PCOS is a chronic endocrine disorder that affects up to 20% of reproductive-aged women and is one of the leading causes of infertility," she explained. Using electronic health records and genetic data, she aims to investigate the complex relationship between PCOS and its cardiometabolic comorbidities.

Such comorbidities disproportionately affect underrepresented females. While minority female patients experience higher incidence of type 2 diabetes, hypertension, and metabolic syndrome, PCOS remains understudied in these patients. It can take over two years to receive a diagnosis, and up to 75% of females with PCOS remain undiagnosed.

Actkins wants to bring more awareness to this disorder. "Electronic health records offer so many opportunities to understand PCOS risk and development," she explained. Therefore, she wants to capitalize on this resource to investigate why so many women with PCOS remain undiagnosed. Importantly, she wants to determine if this lapse in diagnosis contributes to health disparities among underserved women.

A fifth-year graduate student, Actkins is no stranger to the challenges in research. "I learned very quickly that science does not always work out the way we want it to, and it requires a lot of patience and hard work," she said. She is fortunate to have a great mentor in Dr. Davis and a support system, both professionally and personally, to help her navigate the challenges she faces in graduate school.

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- **Apr 14-16, 2021: Graduate Student Appreciation Week** celebrated Meharry graduate students to highlight their contribution to science, public health, and service to Meharry. For list of awards, click **here**.
- **Mar 16, 2021:** President's Town Hall. President Hildreth announced the creation of the **School of Applied Computational Sciences (SACS)**. Lead by **Dr. Fortune Mhlanga**, SACS will begin offering courses for Masters of Science degrees and Biomedical Data Science in Aug 2021. Courses towards a doctoral degree in Biomedical Data Science will be available in Fall 2022. For details, click **here**.

MORE INFORMATION?

Meharry Research

OfRI Services and Support Unit

Meharry Community Engagement Core

Meharry's research history

COVID-19 lab safety guidelines

ResearchPoint

Yammer

Autumn Acklin (*top*) and Dr. Richard Martin (*bottom)*

She also acknowledges the difficulties she faced while preparing her application for the F31 fellowship. There were many requirements to meet and the documents took a long time to prepare. She is grateful for the help she received from her mentor, her committee members, the graduate school, the grants management office at Meharry, and several of her fellow graduate students while preparing her application. Therefore, she advises those interested in applying for the fellowship to start early so that they can seek feedback from their mentors and peers on ways to improve their application.

In the future, Actkins hopes to continue her research in women's health. In particular, she wants to use her training in genomic and clinical analysis to investigate other disorders that are understudied in women. "I want to make sure that women get the proper treatment and care they need to improve their quality of life."

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The MVTCP Program – Meharry medical student assesses the impact of hospital policies on oncology clinical trial enrollment

Medical student Autumn Acklin is passionate about community-based research and health equity. As a participant in the 2020 Meharry-Vanderbilt-Tennessee State University Cancer Partnership (MVTCP) summer research program, she studied the impact of hospital policies on oncology clinical trial enrollment.

Currently in its 20th year, the MVTCP is the longest consecutively funded Comprehensive Partnership to Advance Cancer Health Equity (CPACHE) program (principal investigator: Dr. Samuel Adunyah). The CPACHE Program develops and maintains comprehensive, long-term, and mutually beneficial partnerships between institutions serving underserved populations and underrepresented students and NCI-designated cancer centers. The program aims to achieve a stronger national cancer program and address challenges in cancer and cancer disparity research, education, and outreach, as well as their impact on underserved populations. In its newest iteration, the MVTCP seeks to broaden its scope to include more comprehensive population and community engagement aspects through its Population Research and Clinical Trials in Cancer Equity (PRACTICE) core. Within this core, Dr. Maureen Sanderson, Professor of Cancer Epidemiology, and Dr. Richard Martin, Assistant Professor of Hematology/Oncology, supervised Acklin's research.

Dr. Martin also serves as a medical oncologist at Nashville General Hospital (NGH) and co-director of theClinical Oncology Trials Network. As an MCTVP co-investigator, he aims to expand the clinical trial portfolio at NGH as well as develop a cancer cohort at NGH and Meharry as a resource for future studies. "Meharry has a strong track record of providing access to cancer trials," he said. "With so many new and experimental treatments leading to improved survival, access to cancer trials is more important than ever in ensuring health equity."

In the US, cancer disproportionately affects minority populations. Yet, participation of minority patients in oncology clinical trials trends well below cancer prevalence in these communities. Meharry, a trusted healthcare resource among underserved and minority communities, provides medical care through a partnership with NGH. Using NGH as her target site, Acklin investigated how hospital policies may influence enrollment of minority patients in oncology clinical trials.

Specifically, Acklin focused on a 2017 proposal to close NGH and its hospital-based clinics and to replace them with an outpatient facility. Such a proposal would hugely impact NGH patients, who are predominantly from black and minority communities. In fact, between 2008 and 2017, roughly half the patients at NGH/Meharry oncology were Black. As the only state-funded hospital within a 50 -mile radius of Davidson county, TN, NGH also provides a healthcare safety net to uninsured individuals in the area. Understandably, the announcement of this proposal triggered a multitude of concerns among not only community members, but also NGH employees and researchers.

To examine these concerns and the potential impact of this policy on clinical trial enrollment, Acklin first

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analyzed publicly available reporting on the policy. From these reports, she identified the correlation between the policy announcement, along with subsequent major events, and changes in clinical trial enrollment. She found that while clinical trial enrollment at NGH had been declining gradually, its decline became more apparent beginning in 2018, shortly after the policy announcement in November 2017. In fact, enrollment continued to decline in 2019 to a level below the accreditation threshold.

Next, she interviewed NGH staff and researchers as well as community members and policy makers to explore the relationship between policy implementation or changes and clinical trial support. To ensure an objective interview process, the team avoided language that would place blame on any of the involved parties. Rather, the interview questions focused on gathering information that would help strategize subsequent actions. All interviewees answered the same questions. To avoid interview bias, the team only reviewed the responses after completing the entire interview process.

Responses from the interviews indicate job security, awareness of the patient population served, and the impact of the relationship between NGH and MMC to be the major concerns regarding the proposal to close NGH. Such concerns appear to have ultimately affected the patient population and clinical trial enrollment at NGH.

Acklin's research highlights the importance of understanding how policy changes can affect patient care and clinical trial participation. It also indicates that perspectives from all parties—policy makers, medical professionals, staff, and community members—are crucial to crafting policies that are most likely to benefit everyone involved. In the future, the team hopes to improve public access to clinical trial information, to disseminate such information to black and minority communities, and ultimately, to increase patient participation.

Acklin will present her findings at the upcoming MVTCP Cancer Outreach Community Advisory Board quarterly meeting. The team is also currently preparing a manuscript for submission. Acklin hopes that her research will garner the interest of not only the scientific community, but also policy makers whose decisions may impact access to clinical trials.

Acklin, who is Black American, takes healthcare access very seriously. "As a future physician, I want to make it my duty to explore avenues in which those who look like me can benefit from clinical trials," she said. She acknowledges that past and present experiences with the healthcare system have created hesitancy within communities of color. Therefore, it is important to engage these communities and educate them on how the medical community is working to address these grievances. "Clinical trials offer a unique way for patients to get care while allowing scientists to learn more about how potential treatments can affect Black and other minority populations," she explained. "If we can educate these communities on the benefits of clinical trials while addressing and acknowledging their concerns, we can ultimately increase participation and regain our patients' trust."

Dr. Martin concurs. "Ms. Acklin's efforts demonstrate that with continued commitment from our academic and community partners, the future of clinical cancer research at Meharry is bright."

PUBLICATION HIGHLIGHTS

Want your publications featured in the Publication Highlights? Please complete this ***REDCap survey*** *to share the information with us!*

From the groups of Drs. Jui Pandhare and Chandravanu Dash:

Activation of proline biosynthesis is critical to maintain glutamate homeostasis during acute methamphetamine exposure. Bobby Jones, Muthukumar Balasubramaniam, Joseph J. Lebowitz, Anne Taylor, Fernando Villalta, Habibeh Khoshbouei, Carrie Grueter, Brad Grueter, Chandravanu Dash, Jui Pandhare. *Scientific Reports.* 2021 Jan 14. DOI: 10.1038/s41598-020-80917-7

Glutamate homeostasis is essential to many aspects of normal brain functioning, including learning, memory, and cognition. In this study, the authors examined how methamphetamine (METH), a highly addictive psychostimulant, perturbs glutamate balance and alters brain chemistry. Using cultured cells, the authors showed that METH exposure increased the levels of enzymes that catalyze the synthesis of proline from glutamate. However, when they knocked out the expression of pyrroline-5-carboxylate synthase (P5CS), a key proline biosynthesis enzyme, they observed an increase in glutamate levels in cells exposed to METH. These findings indicate that 1) METH exposure increases glutamate levels; and 2) proline biosynthesis increases upon METH exposure to use up the excess glutamate as a strategy to restore glutamate homeostasis.

From the group of Dr. Amosy E. M'Koma:

Linking bacterial enterotoxins and alpha defensin 5 expansion in the Crohn's colitis: A new insight into the etiopathogenetic and differentiation triggers driving colonic inflammatory bowel disease. Tanu Rana, Olga Y. Korolkova, Girish Rachakonda, Amanda D. Williams, Alexander T. Hawkins, Samuel D. James, Amos M. Sakwe, Nian Hui, Li Wang, Chang Yu, Jeffrey S. Goodwin, Michael G. Izban, Regina S. Offodile, Mary K. Washington, Billy R. Ballard, Duane T. Smoot, Xuan-Zheng Shi, Digna S. Forbes, Anil Shanker, Amosy E. M'Koma. *PLoS ONE*. 2021 Mar 9. DOI: 10.1371/journal.pone.0246393

Crohn's colitis (CC) and ulcerative colitis (UC) are two subtypes of chronic colonic inflammation. However, they are difficult to distinguish using currently available diagnostic methods. Inability to distinguish between UC and CC often leads to a diagnosis of indeterminate colitis and subsequent mismanagement of the disease.

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In this study, the authors demonstrated their ability to accurately categorize these disease subtypes. Using immortalized colon cells and colonoids, they revealed alpha defensin 5 (DEFA5) to be the key factor for distinguishing between CC and UC. DEFA5 is a peptide involved in host defense that normally exists in the Paneth cells of the ileum, the final section of the small intestine that precedes the large intestine. The authors uncovered the presence of DEFA5 in CC samples. This is because these samples contained crypt-cell like cells (CCLCs) that express Paneth cell markers. The extent of CCLC expansion correlated directly with the severity of the disease. The presence of DEFA5 in the CC samples also triggered distinct expression and secretion signatures. While the significance of DEFA and its accompanying signatures in CC remains to be determined, this study uncovered DEFA5 as a potential therapeutic target for CC.

From the group of Dr. Pius N. Nde:

piRNAs as modulators of disease pathogenesis. Kayla J. Rayford, Ayorinde Cooley, Jelonia T. Rumph, Ashutosh Arun, Girish Rachakonda, Fernando Villalta, Maria F. Lima, Siddharth Pratap, Smita Misra, Pius N. Nde. *International Journal of Molecular Sciences*. 2021 Mar 22. DOI: 10.3390/ijms22052373

Small non-coding RNAs (sncRNAs) encompass small interfering RNAs (siRNAs), microRNAs (miRNAs), and PIWI-interacting RNAs (piRNAs). This review focuses on piRNAs, the least studied among the three. piRNAs interact with PIWI proteins, which are highly conserved RNA-binding proteins previously thought to exist only in germline cells and adult stem cells. However, more recent research has shown PIWI proteins to also exist in somatic cells, indicating a broad function of piRNAs. piRNAs guide PIWI proteins to their target destinations where they can cleave specific RNAs, promote heterochromatin formation, and methylate target DNA sequences. Consequently, piRNAs play a role in epigenetic regulation. Emerging research have also uncovered other novel functions of piRNAs, including its role in cardiomyopathy and cancer pathogenesis. These discoveries highlight the potential of piRNAs as disease biomarkers and therapeutic targets.

From the group of Dr. Jennifer Cunningham-Erves:

Training researchers in dissemination of study results to research participants and communities. Jennifer Cunningham-Erves, Elizabeth Stewart, Jillian Duke, Sylvie A Akohoue, Nicole Rowen, Omaran Lee, Stephania T Miller. *Translational Behavioral Medicine*. 2021 Apr 5. DOI: 10.1093/tbm/ibab023

This article describes the process of developing a training module to teach researchers and academicians how to disseminate research findings beyond academic publications. The authors then conducted a training session with 25 research professionals. At the end of the session, more than half the participants strongly agreed that they now have a better understanding of research dissemination, the dissemination process, and how to identify stakeholders and develop a dissemination plan. This knowledge is important in translational research so that a greater audience can access research findings that may help improve health outcomes.

From the group of Dr. Smita Misra:

SUMO-Modification of human Nrf2 at K^{110} and K^{533} regulates its nucleocytoplasmic localization, stability and transcriptional activity. Treniqka S Walters, Deneshia J McIntosh, Shalonda M Ingram, Lakeisha Tillery, Evangeline D Motley, Ifeanyi J Arinze, Smita Misra. *Cellular Physiology and Biochemistry*. 2021 Mar 27. DOI: 10.33594/000000351

Nuclear factor (erythroid-derived 2)-like 2 (Nrf2) is a transcription factor that activates genes that respond to oxidative stress. It does so by binding to the antioxidant response elements (AREs) in their target gene promoters. This study examined the post-translational modification (PTM) on the Nrf2 protein that may affect its subcellular and function. Specifically, the authors focused on SUMOylation, a PTM that attaches small ubiquitin-like modifier (SUMO) proteins onto other proteins. Using in silico, molecular biology, and tissue culture methods, the authors identified two lysine (K) residues (K^{110} and K^{533}) in human Nrf2 that undergo SUMOylation to influence nuclear localization and stability of Nrf2 as well as the transcription of Nrf2 target genes. These K residues are also conserved in mouse Nrf2.

From the group of Dr. Consuelo H. Wilkins:

The astounding breadth of health disparity: phenome-wide effects of race on disease risk. Jill M. Pulley, Rebecca N. Jerome, Gordon R. Bernard, Jana K. Shirey-Rice, Yaomin Xu, and Consuelo H. Wilkins. *Journal of the National Medical Association*. 2021 Apr. DOI: 10.1016/j.jnma.2020.08.009

Using data from almost two million patients at a medical center in Tennessee, the authors conducted a phenome-wide association study (PheWAS) to compare diagnoses among black patients to those among white patients. A PheWAS is an approach for investigating the association between different types of DNA variants across many different phenotypes. In this study, the authors wanted to compare the risks of diagnoses associated with Black patients to those associated with White patients. This approach allowed them to predict the extent of health disparities among these patients. This study is important for the understanding of risk factors that contribute to poorer health in the Black population.

From the group of Dr. Christine Lovly:

Beyond PD-L1: B7-H6 emerges as a potential immunotherapy target in small cell lung cancer. Portia L. Thomas, Sarah M. Groves, Yun-Kai Zhang, Jia Li, Paula Gonzalez-Ericsson, Shamilene Sivagnanam, Courtney B. Betts, Hua-Chang Chen, Qi Liu, Cindy Lowe, Heidi Chen, Kelli L. Boyd, Prasad R. Kopparapu, Yingjun Yan,

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Lisa M. Coussens, Vito Quaranta, Darren R. Tyson, Wade Iams, and Christine M. Lovly. *Journal of Thoracic Oncology*. 2021 Apr 8. DOI: 10.1016/j.jtho.2021.03.011

Programmed death ligand-1 (PD-L1) is a transmembrane immune regulatory protein that binds to PD-1, an inhibitory checkpoint molecule. This interaction allows cells that express PD-L1 to escape immune surveillance. Many types of cancer cells use this mechanism to bypass the host's immune system. Immune checkpoint inhibitors atezolizumab and durvalumab are FDA-approved first-line treatments for small cell lung cancer (SCLC). However, these treatments are only moderately effective because they increase overall survival by only two to three months. Here, the authors used RNA sequencing and tissue microarrays to investigate possible reasons for this moderate effect. By analyzing almost 200 samples of SCLC cell lines and primary tissues, they found 26 other inhibitory checkpoint molecules with higher expression levels than that of PD-L1. Particularly, high expression of B7-H6 correlated with longer progression-free survival and higher infiltration of immune cells that target tumor cells. Therefore, they proposed future studies to investigate other immune checkpoint molecules besides PD-L1, particularly B7-H6, as targets in treatments for SCLC.

From the group of Dr. Dorin-Bogdan Borza:

Laminin-521 is a novel target of autoantibodies associated with lung hemorrhage in anti-GBM disease. Cong-Rong Shen, Xiao-Yu Jia, Wentian Luo, Florina Olaru, Zhao Cui, Ming-Hui Zhao, Dorin-Bogdan Borza. *Journal of the American Society of Nephrology*. 2021 Apr 23. DOI: 10.1681/ASN.2020101431

Antiglomerular basement membrane (anti-GBM) disease is an autoimmune disease where the patient produces antibodies that attack α345(IV) collagen, which is present in the glomerular and alveolar basement membranes. Consequently, anti-GBM disease often causes damages in the kidney and lungs. In this study, the authors revealed laminin-521 (LM521) as a novel autoimmune target in anti-GBM disease. LM521 is a type of αβγ heterotrimeric glycoprotein. The laminin family of proteins is common in all basement membranes. Here, the authors examined the circulating antibodies in 101 patients with anti-GBM disease and 85 controls. They found about 30% of the patients to present with anti-LM521 IgG in their circulation. Conversely, the antibody was absent among controls who were healthy or had other types of glomerular diseases. Autoreactivity against LM521 was also more prevalent among anti-GBM disease patients also suffering from lung hemorrhage.

From the group of Dr. Pandu Gangula:

Mechanistic role of antioxidants in rescuing delayed gastric emptying in high fat diet induced diabetic female mice. Chethan Sampath, Mohammad Tabatabai, Michael L. Freeman, Pandu R. Gangula. *Biomedicine & Pharmacotherapy*. 2021 May. DOI: 10.1016/j.biopha.2021.111370

Diabetic gastroparesis, often manifesting as delayed gastric emptying (GE), is common among people who are obese and diabetic, especially females. The leading cause is the reduction or loss of nuclear factor (erythroid-derived 2)-like 2 (Nrf2), atranscription factor that promotes the expression of neuronal nitric oxide synthase alpha (nNOSα). nNOSα is an enzyme that catalyzes the production of nitric oxide, a signaling molecule that regulates smooth muscles such as those in the digestive tract. Using female mouse models of obesity-induced diabetes, the authors found Nrf2 activators cinnamaldehyde (CIN) and curcumin (CUR) to restore gastric motility and GE in obese and diabetic mice. CIN and CUR are the active compounds in cinnamon and tumeric, respectively. These compounds also altered the expression patterns of genes associated with oxidative stress. However, they had no effect in *Nrf2*-knockout mice. Additionally, the author also reported a physical interaction between nNOSα and Nrf2.

RESEARCH GRANT HIGHLIGHTS

Dr. Xinhong Dong received an R01 award for the following proposal:

HIV interactions with host cell proteins in particle release

This project aims to examine the role of host proteins and pathways in the tetherin-Vpu interaction involved in HIV-1 release and cell-to-cell transmission.

Dr. Waldemar Popik received an R21 award for the following proposal:

Mitochondrial DNA content in blood extracellular vesicles as a biomarker of neuronal mitochondrial DNA damage induced by cigarette smoking in virally suppressed, HIV-positive African Americans

This proposal aims to determine the relationship between mitochondrial DNA damage and cigarette smoking in HIV positive African Americans.

Congratulations!

Want to share your research news, highlights, and announcements with us? Want your stories featured in The Research Digest? Please submit this ***REDCap survey*** *to share your updates with us. We look forward to celebrating your achievements!*

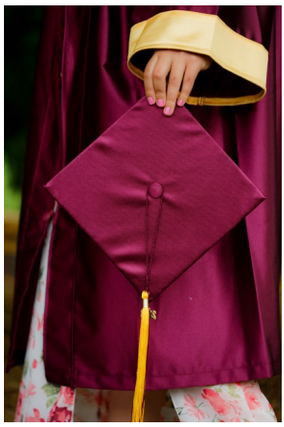

Photo by Tai's Captures on Unsplash

Congratulations, Class of 2021!

Best wishes from the Office for Research and Innovation to all 2021 Meharry graduates and their families.

Your future awaits!