March 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:

- The **Meharry-Vanderbilt-TSU Cancer Partnership** turns 20 this year! Click **here** to learn about its impact on cancer health equity.
- A group of 20 Meharrians from the School of Medicine, the School of Dentistry, the School of Graduate Studies and Research, and the administrative branch have been selected to join the **Advancing Women in Nashville (AWIN) Leadership Development Cohort.** The year-long program began on Mar 8, 2021. Click **here** to learn more about AWIN.
- Drug development grant opportunities:

  i) Harrington scholar-innovator award

  Open to physician-scientists. M.D. required.

  Deadline: Apr 16, 2021

  ii) ADDF-Harrington scholar award

  Open to researchers. Ph.D. or M.D. or equivalent required.

  Deadline: Apr 23, 2021

  Click **here** for award details.
- 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.

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THE VP'S CORNER

Dear Meharrians:

In 2015, President Obama declared precision medicine a national priority. Thanks to scientific advances and the advent of high-throughput technologies, precision medicine is now possible. Researchers cracked the genetic code of SARS-CoV-2 virus in record speed, thus allowing Pfizer-BioNTech to deliver a safe and efficacious COVID-19 vaccine in 11 months. Advances in genetics research and tools enabled them to shorten the vaccine development process, which would normally take years, to mere months. Cancer immunologists and BioNTech founders Uğur Şahin and Özlem Türeci played a major role in developing the Pfizer-BioNTech vaccine, vetting the promise of transdisciplinary research as a path forward. Rightly so, the Meharry 2026 vision compels us to dive into transdisciplinary research and innovation.

The study of genetics at the individual and population level offers the potential to address health disparities and inequity, which is central to Meharry's mission. In the early 1970s, Meharry established the Division of Genetics and Molecular Medicine. During this time of Meharry's **"Renaissance Period"**, the College also launched the Meharry Sickle Cell Center, an initiative ahead of most medical schools at the time. These establishments have allowed Meharry to educate and train medical doctors and researchers in genetics research, many of whom come from racial minorities or represent underserved communities.

One pertinent issue that Meharry aims to address is the underrepresentation of minority populations in clinical trials and health professions. For instance, representation of African, Hispanic, or indigenous participants is less than 5% in the majority of clinical trials in the US. Moreover, African Americans make up less than 1% of genetic counselors in the US. Such disparities hinder our ability to design healthcare and treatment strategies that cater to these communities.

Lately, extensive studies that traced conserved maternal genes through mitochondrial genetics showed that *Homo sapiens* began migrating from Africa to other parts of the world about 170,000 years ago. Their first stop was in South Asia about 70,000 years ago. By about 15,000 to 20,000 years ago, they reached the Americas. A proportion of the genetic differences between any two people (about 15%) reflects divergence between groups defined according to the continents of their ancestral origin. This genetic variation links to disease susceptibility and response to pharmacologic agents. Knowledge regarding pathogenic variants for people of African ancestry is lacking due to insufficient information. Clinical research findings generated in populations of European descent and extrapolated to the treatment of non-European populations are neither equitable nor proven safe for the latter. This has led to, for example, inaccurate predictions of kidney function in African American patients and inappropriate dosing for drugs.

To address these issues, a deliberate engagement of communities under the safeguard of ethical rigor is needed. This will encourage the participation of African Americans and other underrepresented communities in clinical trials and research. Their participation will allow us to build reliable databases that will help us better understand and address genetic and phenotypic variations that exist among these populations. Therefore, an African ancestry reference genome is urgently needed to fill the knowledge gap in diaspora genetics and provide new insights into human biology.

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- 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:

- **Feb 24 & 25, 2021:** Penn Center of Global Genomics & Health Equity organized a symposium entitled **"Importance and challenges of increasing ethnic diversity in human genomics research"**. Click **here** to learn more about the Center.
- **Feb 17, 2021:** Fireside chat entitled "**Health integration, innovation and racial justice: A call to action**" featuring Dr. Anthony Fauci and Dr. James Hildreth. Dr. Fauci is the director of NIAID and chief medical advisor to President Biden. Meharry President Dr. Hildreth is a non-federal member of the Biden-Harris COVID-19 Health Equity Task Force. Watch the program **here**.
- **Feb 1, 2021:** In conjunction with **Black History Month**, the American Lung Association (ALA) featured **Dr. Donald Alcendor** on LungCast™, the ALA podcast. He discussed how health disparities among Black, Brown, and other communities of color impact the COVID-19 pandemic. Dr. Alcendor is the first Meharrian to serve on the ALA expert advisory panel for COVID-19 and the prestigious ALA Scientific Advisory Board. Listen to Episode 7 **here**.

Such information is crucial for improving strategies for genetic prediction, precision medicine, and genetic counseling that target these populations.

In this regard, Meharry's recent success in clinical trials has allowed the College to elevate its status as a trusted healthcare resource among racial minority and underserved communities. Thus, the College is able to recruit clinical trial participants from these communities, including for cancer trials where the enrollment of African American patients continues to trend far below the true cancer prevalence in the community. As such, Meharry has been and will always be at the forefront of achieving health equity.

The diversity of Meharry's campus also sets the College apart from other schools. The College is home to a diverse body of students, faculty, and staff with respect to gender, race, and geographical origin. In time, Meharry will revolutionize healthcare and succeed in its mission to eliminate health disparities in underserved communities.

I thank all Meharrians for your commitment to Meharry's mission. Let's continue to strive for a safe, constructive, and engaging environment for greater success!

With gratitude and hope,

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

SPOTLIGHT

Meharry lands funding to study the impact of social determinants of health on COVID-19 health disparities and to develop novel approaches to optimize health equity

The week of Christmas 2020 bore good news for Dr. Bryan Heckman (pictured), an associate professor in Psychiatry and Behavioral Sciences at Meharry Medical College and Director of Meharry's Center for the Study of Social Determinants of Health (CSSDOH).

The Truist Foundation and Blue Cross Blue Shield Tennessee (BCBS-TN) announced their grant awards to Dr. Heckman and colleagues to study and address the public health and social consequences of COVID-19. Totaling over $1.4 million, these grants will fund research to develop tools to address health disparities and vaccine hesitancy among underserved communities.

Central to these projects are the role of social determinants of health (SDOH). SDOH reflect the contexts in which people are born, grow, live, work, worship, and age. They are shaped largely by resource or power (mis)distribution and account for up to 80% of health outcomes. Examples include economic stability, access to quality education and healthcare services, neighborhood, and social or community context. Dr. Heckman believes that in order to adequately address issues pertaining to health equity, it is necessary to account for these upstream environmental factors. "Data on SDOH are essential for identifying what factors drive disparities," he said. "Then, we can create more precise programs to meet the needs and positively impact our communities."

The $1.1 million Truist Foundation grant will fund the development of a multi-faceted mHealth platform that will benefit the community and researchers alike. One component of this platform is a contact-tracing app for COVID-19. "Meharry has a unique status of a trusted community resource that is already reaching individuals through testing sites and its general patient network," Dr. Heckman explained. Many of these individuals are underserved, older adults, residents of rural areas, or

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MORE INFORMATION?

You can find them here:

Meharry Research Website

OfRI Services and Support Unit

Meharry Community Engagement Core

Meharry's research history

COVID-19 lab safety guidelines

ResearchPoint

Yammer

represent communities of color who have limited access to broadband services. Therefore, they are more likely to rely on smartphones, rendering them the ideal target population for this app. Those without access may also be afforded devices to enhance connectivity to much needed resources. The app will also help identify COVID -19 hotspots and gather data that will inform resource allocation efforts in underserved areas. Importantly, it will also serve as a trusted source of accurate information and provide access to useful resources to overcome SDOH.

While the pressing goal is to tackle immediate and secondary COVID-19 consequences in Tennessee, the team envisions the platform to serve other purposes well beyond the COVID-19 pandemic. Several promising avenues such as remote symptom monitoring, real-time risk assessment, and telehealth portals for medical and mental health appointments are in the works. Dr. Heckman believes that such measures are also applicable to the management of other chronic health conditions that plague underserved populations, such as cardiovascular diseases, diabetes, and the social and justice-involved consequences of substance use. Particularly, these measures will facilitate efforts that predict and assess risk and risk prevention behaviors, engagement with healthcare resources, and comorbidity. Ultimately, the platform aims to use artificial intelligence (AI) to learn how to best serve our communities and enhance treatment engagement through automation and evidence-based behavioral psychology approaches.

Another critical public health challenge that the CSSDOH aims to address is vaccine hesitancy among the underserved communities. The BCBS-TN award will allow the transdisciplinary Meharry team to understand how SDOH impact COVID-19 outcomes and disparities, and then use this information to tailor strategies to address vaccine hesitancy and healthcare disparities. "We are excited to blend precision medicine with population health approaches to meet the needs of our communities and optimize health equity," said Dr. Heckman.

This project focuses on black Americans, who are disproportionately impacted by COVID-19. They are nearly three times more likely to contract the virus and experience a death rate that is over two times higher than that for white Americans. Yet, among the black Americans surveyed, fewer than half are willing to take the COVID-19 vaccine due to concerns regarding safety and effectiveness.

To address these issues, the team plans to develop empirical methods to systematically identify communities that are most vulnerable to COVID-19 and those that may benefit most from vaccination. These methods involve the use of vulnerability indices, which measure the likelihood of an individual or a community experiencing harm in certain aspects of daily life. Examples include safety concerns, food insecurity, financial strain, discrimination, language barrier, and access to transportation. In other words, the level of comfort and security in one's daily life can influence one's decisions and beliefs regarding healthcare. Using AI tools, the team aims to develop and refine models that predict and assess these vulnerabilities. Such assessments will inform decisions on policy, resource distribution, and intervention strategies.

Dr. Heckman is collaborating with several Meharry experts and organizational partners to ensure the success of these projects. Among his Meharry collaborators are Executive Director of Meharry's Center for Health Policy Dr. A. Dexter Samuels, Director of the National Community Mapping Institute Dr. Wansoo Im, Dr. Ashutosh Singhal of Meharry's Data Science Institute, and Meharry faculty Dr. Donald Alcendor and Dr. Lauren Brown. These individuals are experts in the fields of infectious diseases, geographic information system, big data analysis, behavioral sciences, digital healthcare, and social justice.

Organizational partners include software company Emmito World, clinical study platform Ambitna, Microsoft, BCBS-TN, NashvilleHealth, Nashville Health Care Council, and Nashville Area Chamber of Commerce. These partners will provide support in app development, AI usage, health data sharing, and strategic planning for improving public health outcomes.

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Dr. Heckman emphasizes the relevance of these projects beyond the COVID-19 pandemic. Ultimately, he aims to build a solid infrastructure foundation and establish relationships with community partners to enhance community engagement approaches that address disparities at the individual and population levels. He believes that the outcomes of these projects will not only benefit Tennesseans, but also represent a model that can help underserved communities nationwide. Therefore, he looks forward to sharing his work with community leaders and cultural influencers across the country.

Interested in collaborating with Dr. Heckman? Contact him directly at bheckman@mmc.edu.

Visit the following websites to learn more about SDOH:
Social Determinants of Health - Healthy People 2030 | health.gov
WHO | Social determinants of health

PUBLICATION HIGHLIGHTS

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

From the group of Dr. Lea Davis:

Characterizing the clinical and genetic spectrum of polycystic ovary syndrome in electronic health records. Ky'Era V Actkins, Kritika Singh, Donald Hucks, Digna R Velez Edwards, Melinda Aldrich, Jeeyeon Cha, Melissa Wellons, Lea K Davis. *The Journal of Clinical Endocrinology & Metabolism*. 2021 Jan 1. DOI: 10.1210/clinem/dgaa675

The authors developed three algorithms and evaluated their performance in identifying patients with polycystic ovary syndrome (PCOS). Their aim was to improve currently available diagnostic criteria that often miss patients with symptoms that lie outside these strict criteria. They also wanted to characterize the clinical features of PCOS within and across different racial and ethnic groups. To do this, they tested their algorithms using information from electronic health records. They found their best-performing algorithm to have a positive predictive value of 98%. They were also able to characterize a spectrum of PCOS symptoms and detect their differences across different racial and ethnic groups.

From the group of Dr. Aramandla Ramesh:

Benzo(a)pyrene-induced cytotoxicity, cell proliferation, DNA damage, and altered gene expression profiles in HT-29 human colon cancer cells. Jeremy N Myers, Kelly L Harris, Perumalla V Rekhadevi, Siddharth Pratap, Aramandla Ramesh. *Cell Biology and Toxicology*. 2021 Jan 7. DOI: 10.1007/s10565-020-09579-5

Benzo(a)pyrene is a toxicant that exists in exhaust fumes, cigarette smoke, and grilled foods. In this study, the authors examined the effects of benzo(a)pyrene on HT-29 human colon cancer cells. These cultured cells simulate real colon tissues and thus can provide insights into how human colon tissues may behave when exposed to benzo(a)pyrene. The authors showed that benzo(a)pyrene exposure led to DNA damage, cytotoxicity, and gene expression changes that affected various cellular processes, all of which were detrimental to the cells.

From the group of Dr. Mekeila Cook:

A longitudinal study of justice characteristics among girls participating in a sex trafficking court program. Mekeila C. Cook, Ryan D. Talbert, Breanna Thomas. *Health & Justice.* 2021 Jan 6. DOI: 10.1186/s40352-020-00127-1

The authors examined the justice-related outcomes among girls who participated in a sex trafficking court program. They defined justice-related outcomes as number of bench warrants, citations, placements, and times the girls ran away. These outcomes would generally involve the justice system or law enforcement authorities. Their findings revealed that younger girls are more vulnerable to worse outcomes, rendering them more vulnerable to continued exploitation. The authors also recommended interventions that do not involve the justice system, such as the involvement of dependency or family courts, decriminalization of prostitution among juveniles, and organization of community-based programs.

From the group of Dr. Robert L. Cooper:

The effects of perceived stress and cortisol concentration on antiretroviral adherence when mediated by psychological flexibility among southern Black men living with HIV. Robert L Cooper, Lauren L Brown, Mohammad Tabatabai, David W Haas, Bryan E Shepherd, Hector F Myers, Ryan D Edgerton, Castro Bonny, Julia A Watson, Vladimir Berthaud. *AIDS and Behavior*. 2021 Feb. DOI: 10.1007/s10461-020-03016-8

The correlation between stress and adherence to antiretroviral therapy among Black males living with HIV is well-established. In this study, the authors examined whether psychological flexibility affects this correlation among southern Black men living with HIV. Psychological flexibility refers to an individual's ability to stay connected to the present moment without succumbing to the control of or changing one's thoughts andemotions. It also refers to one's ability to adjust one's actions and behaviors to achieve specific goals or adhere to specific values. The authors are the first to use hair cortisol levels in samples from Black HIV-positive males from the South as a stress indicator and determine its correlation to ART adherence. Cortisol is a hormone that mediates our fight-or-flight response and helps control our mood, fear, and motivation. While this study did not uncover a statistically significant relationship

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between cortisol levels and ART adherence, it highlights the limitations and research directions that future studies may address.

From the groups of Dr. Donald J. Alcendor and Dr. James E. K. Hildreth:

JC polyomavirus and transplantation: Implications for virus reactivation after immunosuppression in transplant patients and the occurrence of PML disease. James E. K. Hildreth, Donald J. Alcendor. *Transplantology*. 2021 Feb 2. DOI: 10.3390/transplantology2010004

JC polyomavirus (JCV), which exists ubiquitously among the global population, usually causes asymptomatic infection and subsequent latency in the renal urinary tract. Unfortunately, immunocompromised individuals may suffer dire consequences due to the reactivation of latent JCV. Examples include transplant patients on immunosuppressive therapy, patients with immune diseases, and HIV patients. In these patients, reactivated JCV may cause a rare and likely fatal disease called progressive multifocal leukoencephalopathy (PML), that affects the white matter of the brain. Currently, there is no cure for PML. This review describes current approaches for managing PML and new studies on potentially promising treatment strategies.

From the group of Dr. Anil Shanker:

Bortezomib sustains T Cell function by inducing miR-155-mediated downregulation of SOCS1 and SHIP1. Ariana N. Renrick, Menaka C. Thounaojam, Maria Teresa P. de Aquino, Evan Chaudhuri, Jui Pandhare, Chandravanu Dash, Anil Shanker. *Frontiers in Immunology*. 2021 February 25. DOI: 10.3389/fimmu.2021.607044

Bortezomib is a compound that inhibits protein degradation *via* the ubiquitin-proteasome pathway. It is used to treat multiple myeloma and mantle cell lymphoma because proteasomal function has been shown to support the resistance of these cancers to cell death. In this study, the authors found bortezomib to induce the expression of microRNA (miRNA) miR-155. miRNAs are short non-coding RNAs that influence various cellular processes by regulating gene expression. To do this, they bind to complementary messenger RNAs (mRNAs) and repress their translation, subsequently reducing the levels of proteins these mRNAs encode. Here, miR-155 targets SOCS1 and SHIP1 in T cells. SOCS1 inhibits cytokine signaling whereas SHIP1 inhibits PI3K/AKT signaling. These two signaling pathways are crucial to T cell function because they prevent T cell exhaustion, a state in which T cells die after performing their antigen-specific effector function. By repressing SOCS1 and SHIP1 protein levels *via* miR-155 induction, bortezomib can prolong the effector function of cytotoxic T cells that play a key role in tumor surveillance. Consequently, these T cells can survive longer and are more effective in attacking their target tumor cells. The findings provide a strong rationale for combining bortezomib with T cell immunotherapy, particularly in the immunosuppressive microenvironment of solid tumors.

From the Meharry Sickle Cell Center:

Newborn screening practices and alpha-thalassemia detection — United States, 2016. M.A. Bender, Careema Yusuf, Tim Davis, M. Christine Dorley, Maria del Pilar Aguinaga, Amanda Ingram, Ming S. Chan, Joseph C. Ubaike, Kathryn Hassell, Jelili Ojodu, Mary Hulihan. *Morbidity and Mortality Weekly Report*. 2020 September 11. DOI: 10.15585/mmwr.mm6936a7

Alpha-thalassemia is an inherited and a potentially life-threatening condition. Affected individuals have red blood cells that are smaller in size and lower in number. Although methodologies in state newborn screening (NBS) programs that detect sickle cell disease also detect alpha-thalassemia, the latter is not a core condition on the United States Recommended Uniform Screening Panel. This report highlights the importance of standardizing the testing and reporting procedures for alpha-thalassemia in NBS programs. This measure will ensure accurate data reporting as well as improve the public health impact and clinical outcomes of babies with this condition.

RESEARCH GRANT HIGHLIGHTS

Dr. Dorin Bogdan Borza received funding from the Department of Defense for the following proposal:

PLA2R1 gene as a novel SLE susceptibility locus: Mechanistic insights from African-specific, common loss-of-function variant

Congratulations!

CLINICAL & SERVICE GRANT HIGHLIGHTS

Under principal investigator **Dr. Maria del Pilar Aguinaga**, the **Meharry Sickle Cell Center (MSCC)** received two grants totaling **over $1.4 million** for its work in sickle cell surveillance.

First, the $1.44 million grant from the Tennessee Department of Health funds the sickle cell confirmatory laboratory, newborn follow-up, and patient care for three years.

Next, the $50,000 grant from the CDC, received through a partnership with the UT Memphis TN Sickle Cell Surveillance Program, funds a statewide surveillance initiative of newborn and adult cases of sickle cell disease as well as their healthcare utilization.

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!*

Happy Spring!

Photo by Kouji Tsuru on Unsplash