HUNTINGTON Medical Research Institutes SCIENTIFIC DISCOVERY, MADE IN PASADENA Insights

Solving the Puzzle of Alzheimer's Disease

Solving the Puzzle of Alzheimer's Disease PAGE 4 HMRI Science Day Recap PAGE 6 Inaugural President's Event Series PAGE 8

A MESSAGE FROM OUR PRESIDENT & CEO



HMRI's culture of innovation continues to lead the way as we strive to improve human health and work towards a future free of heart and brain disorders. Our clinical neuroscientists presented their recent discoveries at the Alzheimer's Association International Conference in Amsterdam, featured on page 6, and continue to be on the frontier of detecting risk for Alzheimer's disease and other dementias.

After twenty-three years, our researchers remain committed to solving the complex puzzle of Alzheimer's disease, featured on page 4. Earlier this fall, we welcomed Dr. Astrid Suchy-Dicey to our distinguished neuroscience

research team as the Director of the Brain Aging Study. She is an accomplished epidemiologist renowned for her revolutionary research on Alzheimer's disease. Her extensive experience leading large government-funded studies and her expertise in neuroepidemiology will play a pivotal role in advancing HMRI's research initiatives, particularly in health equity and minority health in the Pasadena community.

It's been an exciting year as we've opened our doors again to the public for events after temporary closures due to the pandemic. We launched our quarterly President's Event Series on October 26, page 11, where Dr. Suchy-Dicey was a featured expert on Alzheimer's disease. Another highlight was HMRI's first Science Day, page 8, where scientists and students in the summer education programs presented their research to local supporters, community members, and industry professionals.

As we move forward on this journey of growth and positive change, I am grateful for all of our loyal supporters. You make impactful change possible, improving the trajectory for human health outcomes. We invite you to join us in advancing biomedical research by providing financial support and helping us build strategic partnerships to fulfill our mission.

With gratitude,

Julia E. Bradsher, PhD, MBA President and Chief Executive Officer

Organizational Officers

John Babcock, Board Chair Sonia K. Singla, Board Vice Chair Susan E. Kane, Immediate Past Board Chair Julia Bradsher, President Gabriel Rincon, Treasurer Wendy Welch-Keller, Secretary

Board of Directors

Cameron Boswell C. Joseph Chang Hilary J. Fausett James J. Femino Lawrence W. Jones Daniel R. Kimbell Ellen Lansden Alexandra Levine Edward A. Mena John L. Mothershead Terry Perucca Sandra B. Sharp Uma Shrivastava John C. Siciliano Rick Wentzel

Directors Emeritus

M. Helen Baatz John D. Baldeschwieler Michael C. Doyle Roger Engemann James D. Gamb Jerry M. Harrington Mitchell B. Howe Jr. R. William Johnston George D. Leal

HMRI Welcomes New Employees

Over the summer, HMRI welcomed four new employees to its diverse team of researchers and administrative professionals who are pictured below with HMRI President and CEO Julia E. Bradsher, PhD, MBA, center. To the left are Paul Roach, Senior Director of Development and Astrid M. Suchy-Dicey, PhD, Associate Professor, Director, Brain Aging Study, Scientific Director, Clinical Neurosciences. Sadaf Vakili, MPP, MNM, Director of Corporate and Foundation Relations; and Benjamin Russin, Data Entry Admin, Neuroscience Research, are pictured to the right.



HMRI Employees Receive Values in Action Award

HMRI employees vote for peers who exemplify the organization's values in their work. Recipients of this award innovate with creativity, collaborate for the greater good, operate with integrity and rigor, work with respect, and act with accountability. Congratulations to Jenny Park and Said El Bakri!



Jenny Park, HMRI's Payroll Manager and recipient of the HMRI Values in Action Award for the summer of 2023, works tirelessly behind the scenes, making others shine through her work. Jenny always has a smile on her face, a positive attitude, and is an excellent team player. She goes above and beyond to help others and portrays respect and integrity in her duties. Her friendly demeanor makes HMRI an inclusive work environment.



Said El Bakri, Research Assistant for the Department of Neurosciences and recipient of the HMRI Values in Action Award for the fall of 2023, is caring and hard-working. He assists the postdoctoral fellows, students, and research faculty to see that the research goals of the neuroscience department are met. He has a strong work ethic, radiates positivity, and always has a smile. Said is kind to everyone, making HMRI a better place.



Dr. Alfred Fonteh pictured with HMRI's first mass spectrometer. It was installed on the first day he arrived at HMRI, October 1, 2001.



Dr. Xianghong Arakaki studies brain waves during an electroencephalogram (EEG) in the Cognition and Brain Integration Laboratory.

HMRI Researchers are Committed to Solving the Puzzle of Alzheimer's Disease

Alzheimer's disease is the leading cause of dementia, and currently, there is no cure. According to a recent report published by the Alzheimer's Association, an estimated 6.7 million US adults age 65 and older are living with Alzheimer's dementia, and this number could grow to 13.8 million by 2060. The massive impact of this pervasive disease is felt by families, caregivers, and society. From a cost standpoint alone, in 2022, unpaid dementia caregiving was valued at \$339.5 billion, and in 2023, payments for long-term care and hospice services for people aged 65 and older with dementia are estimated to be \$345 billion.

HMRI and its esteemed researchers understand this urgent healthcare need and have been committed to solving the complex puzzle of Alzheimer's disease for over two decades. The original Brain Aging Study at the Institute started in 2000 and was supported by funding from a few family foundations. The aim was to detect protein changes in Alzheimer's disease (AD) by analyzing 100 cerebrospinal fluid (CSF) samples in people with and without AD, using 2D-gel electrophoresis.

Findings showed inflammatory changes associated with lipids in CSF. This attracted the attention of Dr. Alfred Fonteh, who was using state-of-the-art technology to characterize lipids critical to human diseases at Wake Forest University School of Medicine, where he was a Research Associate and Professor of Internal Medicine. He contacted HMRI's researchers to request CSF samples so he could conduct advanced chemistry analysis using Gas Chromatography/Mass Spectrometry (GC/MS). Dr. Fonteh's results were promising – showing changes in lipids and enzyme activity in AD. His interest in the Institute's clinical studies grew, and in 2001, he joined the HMRI research team, where he continues to gain new insights into biomarkers and their role in aging and AD.

In 2011, the trajectory of the study changed when researchers at HMRI received a significant grant from a private foundation for neuroscience and imaging. This additional funding was transformative in the study's evolution. The study changed from cross-sectional to longitudinal, enabling scientists to follow the same people over time and observe changes in their brains related to aging; in fact, 227 of the original participants in the longitudinal study are still active participants today. New equipment was purchased for analysis, including a high-tech LC/MS in 2023 to include the measurement and role of omega 3/6 fatty acids. This also supported research for noninvasive biomarkers.

In 2015, electroencephalogram (EEG) analysis was added to the Brain Aging Study projects. Neuroscientist Dr. Xianghong Arakaki was studying migraine and traumatic brain injuries. She expanded her EEG studies to the aging cohort and found similar changes in brain wave measurements in cognitively healthy individuals with a high risk of cognitive decline compared to those with low risk. This led to Dr. Arakaki's studies on heart waves and heart rate variability to understand the vital connection between the heart and the brain. HMRI's multi-faceted Brain Aging Study has advanced because of its financial supporters, study participants, and the great team efforts of collaborators from leading institutions, including clinicians, neuropsychologists, radiologists, biochemists, neurophysiologists, and statisticians. Today, the study's goal is for HMRI to become a front-runner in the early detection of risk for cognitive decline and AD using non-invasive and minimally invasive biomarkers.

The Brain Aging Study will continue to grow, positively impacting society and aging populations, under the leadership of its new Director, Dr. Astrid Suchy-Dicey, who was welcomed to HMRI in October. She is an accomplished epidemiologist renowned for her revolutionary research on AD and dedication to unraveling health disparities in neurodegenerative diseases. Her research focuses on enhancing methodology for analyzing and interpreting data related to imaging, biomarkers, cognitive testing, and social determinants pertaining to Alzheimer's and vascular diseases, especially in American Indians, Alaska Natives, and other marginalized populations. She is committed to risk and resilience factors as she leads multiple large, landmark population-based studies on Alzheimer's disease and related dementias. "I'm eager to lead HMRI's passionate team of scientists on the Brain Aging Study," says Dr. Suchy-Dicey, "I look forward to advancing research on Alzheimer's disease, especially insofar as it differentially affects underserved minorities." Dr. Suchy-Dicey's vision for the future of the Brain Aging Study includes expansion of recruitment to reflect the population of Pasadena and surrounding communities, including more representation of Hispanic-Latino, African-American, Asian, and other racial/ethnic groups. She also envisions more focus on biomarkers for early detection and prevention of Alzheimer's disease, especially non-invasive biomarkers. "New studies are emerging with novel biomarkers such as changes in language patterns, changes in walking gait, changes in retinal biology, and others, which are not only detectable in early disease but do not require invasive lumbar puncture for cerebrospinal fluid collection or expensive imaging, which can be barriers to healthcare access for many people." Dr. Suchy-Dicey hopes that the Brain Aging Study programs at Huntington Medical Research Institutes can be a leader in these innovative research programs: "HMRI is dedicated to creating a future world without heart and brain disorders, and I'm grateful and honored to be part of that."



Drs. Astrid Suchy-Dicey, Alfred Fonteh, and Xianghong Arakaki at the 2023 Alzheimer's International Conference (AAIC) in Amsterdam.

HMRI Neuroscientists Highlight Research on Early Detection at Alzheimer's Association International Conference in Amsterdam



Alfred Fonteh, PhD (center) and Xianghong Arakaki, MD, PhD (right) attended AAIC in Amsterdam over the summer to present HMRI research focused on early detection of Alzheimer's disease, pictured with postdoctoral fellow and co-author Abdulhakim AI-Ezzi, PhD (left).

Alzheimer's Association International Conference (AAIC), held in Amsterdam earlier this year, brought together 10,000 dedicated scientists and other professionals from around the world to advance research for dementia. HMRI was represented by Drs. Alfred Fonteh and Xianghong Arakaki who presented research abstracts with significant updates and focused on the early detection of risk for cognitive decline.

Dr. Fonteh, who leads the Biomarker Neuro-disease Mechanism Lab (BNML) at HMRI, reported on biomarkers in plasma and urine dicarboxylic acid levels. He predicts that they will soon lead the way in early detection diagnostics because of their minimally invasive or non-invasive nature, compared to analyzing cerebrospinal fluid (CSF) – one of the current methods used to diagnose Alzheimer's disease (AD) via lumbar puncture. "Alzheimer's disease remains a challenge because there is no viable cure, and a long incubation phase before cognitive decline makes it difficult for early diagnosis or to predict populations at risk. HMRI is on the forefront of researching biomarkers to test for AD before symptoms appear," Dr. Fonteh pointed out. "By 2029, we hope to offer a five-part biomarker test, which could help stop or slow the onset of this devastating disease for millions."

Dr. Xianghong Arakaki, head of HMRI's Cognition and Brain Integration Laboratory, presented two posters on neural biomarkers for the early detection of Alzheimer's disease. The first abstract examined the correlation between resting heart rate variability and cognitive function, while the second, co-authored with Dr. Abdulhakim Al-Ezzi, a postdoctoral fellow on her research team, outlined the methods and results of quantitative electrography (qEEG), which measures electrical activity in the form of brain wave patterns. Dr. Al-Ezzi examined specific brain regions and their connections and determined that it has the potential to detect the risk of cognitive decline years before symptoms appear.

Dr. Arakaki is enthusiastic about their findings, "If people have a way to know and understand their risk factors, then it is possible to intervene and slow the progression."



Dr. Astrid Suchy-Dicey at AAIC 2023 presenting her research prior to joining HMRI, "Plasma AT(N) biomarkers, cognitive impairment, and MRI measures of Alzheimer's disease in American Indians: the Strong Heart Study."

Postdoctoral Fellows Work to Understand the Mechanisms of Brain Aging

Abdulhakim Al-Ezzi, PhD joined HMRI's Cognition and Brain Integration Laboratory as a postdoctoral fellow in 2022. He received his PhD from the Universiti Teknologi Petrona in Perak, Malaysia, where he studied Biomedical engineering. Prior to joining HMRI, he researched mental health conditions such as anxiety and depression, mild exercise on attention performance, cognitive function, and artificial intelligence. His research interests are the neural basis of cognition, memory, and emotion in humans. Dr. Al-Ezzi was awarded two scholarships during his university studies, and his research has been published in high-impact journals.



Abdulhakim Al-Ezzi, PhD, Postdoctoral Fellow, in the Cognition and Brain Integration Laboratory, reviewing brain waves from an EEG analysis.

At HMRI, Dr. Al-Ezzi focuses on cognitive processing in the clinical Brain Aging Study through EEG data collection and correlation analysis with other aging-related datasets to understand the subtle cognitive dysfunctions in cognitively healthy participants who may be at risk for developing Alzheimer's disease. His research aims to find noninvasive methods to detect risk factors before symptoms appear. Earlier this year, Dr. Al-Ezzi's research was presented at the Alzheimer's Association International Conference in Amsterdam and Society for Neuroscience in Washington DC by his mentor and collaborator, Xianghong Arakaki. Dr. Al-Ezzi explains, "I have a desire to make a positive impact and a deep curiosity about the complex mechanisms of mental health conditions, driven by the potential for breakthroughs that can improve the quality of life for those affected and address a growing global health challenge."



Joby Jose, PhD, Postdoctoral Fellow, in the Biomarker and Neuro-disease Mechanism Laboratory with the new mass spectrometer.

Joby Jose, PhD joined HMRI earlier this year as a postdoctoral fellow in the Biomarker and Neuro-disease Mechanism Lab (BNML) under the mentorship of Dr. Alfred Fonteh. Dr. Jose received his PhD in Biochemistry from Kannur University in India, where he investigated the potential anti-carcinogenic effects of selected flavonoids and their derivatives. He conducted bioavailability studies and assessed the biodegradation of these compounds in the intestines utilizing *in vivo* techniques. In the BNML lab, his research aims to identify novel biomarkers for Alzheimer's disease in early disease conditions in cognitively healthy patients.

Dr. Jose discusses the pressing need to advance research for early detection. "Alzheimer's disease is the most common form of dementia and the sixth leading cause of death in the US. Currently, there is no cure, methods of detection are limited to select patients, and they lack potential biomarkers to predict the onset of the disease. Current diagnostic techniques are only widely available or applicable to some patients due to the high invasiveness of CSF collection and PET imaging and the high expense of these procedures. So, there is an urgent requirement for a cheaper, non-invasive biomarker." Jose continued, "As a researcher in the early stage of my career, I envision a future where simple, commercially available tests will be available as part of routine clinical screenings. This will empower people to manage their aging process, modify their lifestyles to improve their health, predict the eventual development of Alzheimer's disease in cognitively healthy conditions, and thereby delay the onset of the disease."

INSPIRING THE NEXT GENERATION

HMRI'S First Science Day Showcases Biomedical Research



Postdoctoral fellows, students, interns, and research technicians prepare to present their research at HMRI's first Science Day.

HMRI's biomedical researchers gathered on July 26 to host its first Science Day, a new addition to the education program, to celebrate the scientific discoveries of its early career scientists, including postdoctoral fellows, SURF students, interns, and research technicians. Some of their research projects included topics related to the early detection of Alzheimer's disease and how vaping impacts the cardiovascular system.

Representatives from the biotech industry attended, along with members of the local Pasadena area communities and the High School STEM Students.



"Science Day challenged researchers to disseminate their science to the general public and younger students in lay terms, allowing them to work on their communication and presentation skills," said Dr. Nicole Purcell, Scientific Director of Education Programs and Associate Professor of Cardiovascular Research.

Postdocs and student researchers excelled at presenting their research and enjoyed networking with industry professionals. Emily Abad, a SURF student in the Neurosciences laboratory, was proud of the data she produced in the program and the opportunity to present her findings. "Science Day was one of the SURF program highlights for me. I've always had an interest in teaching. Science Day was fun because I had the opportunity to explain difficult scientific concepts to people in ways that were easy to understand."

"The day was a huge success," said Dr. Purcell, "It was rewarding to see the students gain confidence in their ability to hone their public speaking skills and communicate their research to peers and the community, which will be beneficial for their future careers."



"I've always had an interest in teaching. Science Day was fun because I had the opportunity to explain difficult scientific concepts in ways that were easy to understand"

Emily Abad, 2023 HMRI SURF Student

Alzheimer's Researchers Inspire the Next Generation of Scientists

Drs. Xianghong Arakaki and Alfred Fonteh are dedicated mentors who inspire the next generation of scientists every summer when students join their labs for the Summer Undergraduate Research Fellowship.

Melanie Ly, a student at UC Irvine, majoring in Biochemistry and Molecular Biology, worked under the mentorship of Dr. Arakaki and postdoctoral fellow, Chenchen Xia, PhD. Ly worked on behavioral testing in a migraine model to study quality of life and anxiety. She also worked with Dr. Xia to test the expression of neurotransmitters in the brain in preclinical migraine models.



Researchers in the Cognition and Brain Integration Laboratory (CBIL), pictured left to right, with 2023 SURF student Melanie Ly; Dr. Chenchen Xia, Postdoctoral Fellow; Dr. Xianghong Arakaki, Assistant Professor and Head of CBIL; and Dr. Abdulhakim AI-Ezzi, Postdoctoral Fellow.

For Dr. Arakaki, the most rewarding part of the program is the student's enthusiasm for the research, including reviewing the literature, summarizing methods, data collection and analysis, and presenting their work. "It is a pleasure to see them take an active part in the research topic and present their work."

Ly shared highlights from her experience. "Practicing presentation skills taught me how to explain findings, to correlate them to existing research, and ask questions to guide future research." She continued, "This program is a valuable learning experience for those interested in STEM careers. It offers hands-on lab experiences and helps guide career development; for me, it solidified my career decision to go into laboratory research."

Yzabella Ragaza, a student at Cal State LA and aspiring dentist, joined Dr. Fonteh and postdoctoral fellow Joby Jose, PhD, in the

Biomarker Neuro-disease Mechanism Lab (BNML), where she investigated the measurement of tricarboxylic acid cycle components. She was joined by a fellow SURF student, Ashanti Miller, a Chemistry major at Howard University in Washington DC, who researched the quantification of neurotransmitters in migraines.



Researchers with 2023 SURF students in the Biomarker Neuro-disease Mechanism Lab (BNML), pictured from left to right, Dr. Alfred Fonteh, Associate Research Professor, Head of BNML; Dr. Joby Jose, Postdoctoral Fellow; and their mentees, Ashanti Miller and Ysabella Ragaza.

"I want the students to develop a passion for the fundamental principles of research and to think creatively."

Dr. Alfred Fonteh, Associate Research Professor and Head of Biomarker and Neuro-disease Mechanism Lab

Dr. Fonteh said, "I want the students to develop a passion for the fundamental principles of research and to think creatively about the molecular basis of Alzheimer's disease or migraine. I challenged them to identify a problem and think about solutions; to understand that the jigsaw puzzle of research is always fun." Both students had positive experiences in the program under Dr. Fonteh's mentorship. Ysabella said, "I learned that I do fit in, I can persevere to overcome challenges, work with tight time constraints, and collaborate with my team to find solutions to complicated problems." Ashanti, expressed her gratitude, "I am a nerd for science and grateful that this nonprofit was willing to invest in me."

The most rewarding part of the program for Dr. Fonteh is seeing the students grow. "My joy of being a mentor comes from the students developing confidence in themselves and their ability to succeed in life, knowing the sky is the limit to what they can achieve."

Altadena Guild Presents Check to HMRI to Support Student Education Programs



Altadena Guild of HMH check presentation of \$35,000 to support HMRI's SURF program on October 16, 2023. Pictured left to right: Susan Kane, PhD, Chair, Board of Directors, HMRI; Karen Skinner-Twomey, Past President, Altadena Guild of HMH; Elizabeth Polenzani, Co-Chair, Altadena Guild Home & Garden Tour 2023; Julia Bradsher, PhD, MBA, HMRI President and CEO; Paula Orlandini, President, Altadena Guild of HMH.

Part of HMRI's vital mission is its commitment to inspire and educate the next generation of scientists, a tradition that began in 1955. The education programs are sustained through donations from devoted supporters.

The Altadena Guild of Huntington Memorial Hospital has supported HMRI since 1952 with funds traditionally raised through its annual Home and Garden Tour, held each spring. This year, they raised a record number of funds and presented HMRI with a generous check for \$35,000 on October 16, 2023. "Our unwavering support to HMRI continues uninterrupted. Altadena Guild of HMH is very proud to donate to HMRI's Summer Undergraduate Research Fellowship (SURF)," said Paula Orlandini, President of Altadena Guild of HMH, at the check presentation. HMRI's SURF program provides 10 weeks of hands-on biomedical research and mentorship to bright, talented undergraduate students. In 2023, the program attracted over 700 students from across the United States to fill 16 coveted spaces. Historically, students from HMRI have gone on to successfully join the medical community, advance scientific discovery, and lead biotech companies.

Dr. Julia Bradsher, President and CEO of HMRI, expressed, "We're grateful to the Altadena Guild for their support over the years and shared dedication to making a direct impact on the students."



Panelists with Moderator Julia Bradsher, HMRI President and CEO (center); Dr. Yafa Minazad and Jamie Jackson, pictured to the left; Dr. Tabia Richardson and Dr. Astrid Suchy-Dicey, pictured to the right.

HMRI kicked off its President's Event Series on October 26. The series will be held quarterly and will feature topics on diseases of the heart and brain, moderated by President and CEO, Julia Bradsher, PhD, MBA. This inaugural event featured distinguished expert panelists on Alzheimer's disease.

"As leaders in early detection, we are committed to bringing new knowledge about Alzheimer's disease to our community."

Julia Bradsher, PhD, MBA, HMRI President and CEO



Panelists discuss Alzheimer's disease, health equity, and minority health at the inaugural President's Event Series.

Spotlight on Alzheimer's Disease at HMRI's Inaugural President's Event Series

Major donors supporting HMRI's Clinical Brain Aging Study enjoyed a private cocktail reception where they engaged with distinguished panelists. John Siciliano, HMRI donor and board member, said, "This is an important event for the people in Pasadena. We're aging; the risk of Alzheimer's disease is a growing concern for our community. The event helped us better understand this scary condition that many of us have witnessed in loved ones."



Donors enjoy time with the panelists at a private reception before the event.

Panelists included Jamie Jackson, former coach and college athletics administrator, now a full-time Alzheimer's caregiver to her father; Yafa Minazad, DO, MMM, Board Certified Neurologist and Neurophysiologist, HMRI Visiting Scientist; Tabia Richardson, PhD, MPH, Associate Vice President, Community Education and Health Equity, Alzheimer's LA; and Astrid Suchy-Dicey, PhD, HMRI Associate Professor, Clinical Neurosciences, Director of the Brain Aging Study.

They discussed important topics from their diverse perspectives – risk factors and prevention for Alzheimer's disease, research, health equity and minority health, the caregiver journey, and resources for support. Bradsher commented on the event, "A key part of our mission at HMRI is to improve human health through scientific discovery. Alzheimer's disease and other dementias impact every single one of us – our families and loved ones. As leaders in early detection, we are committed to bringing new knowledge about this disease to our community."



GIVING TO HMRI IS **YOUR** CHANCE TO **IMPROVE HUMAN HEALTH AND INSPIRE THE NEXT GENERATION OF SCIENTISTS Thank you for supporting our vital research!**

hmri.org/donate | Development@hmri.org | 626-389-3408

GIVE TO HMRI TODAY!



HMRI Muntingion Matters Insights FALL/WINTER 2023 DIRECTOR OF MARKETING AND COMMUNICATIONS Jessica West DESIGN AND ART DIRECTION Russo Design PHOTOGRAPHY HMRI Contributors

HMRI

686 South Fair Oaks Avenue Pasadena, California 91105 Web: hmri.org | Email: info@hmri.org | Phone: 626.795.4343

Copyright © 2023 by HMRI. All rights reserved.