SCIENCE IN A CHANGING WORLD

HMRI | Huntington Medical Research Institutes

2024 ANNUAL REPORT

HMRI's Impact on Science and Education

IMPROVING HUMAN HEALTH

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SOURCES OF FUNDING

Contributions, grants, and bequests	$2.7M
Government grants and contracts	$2.4M
Legacy Gift Income	$5.6M
Other	$1.3M
Total	**$12M**

Julia E. Bradsher and John C. Babcock

Advancing Biomedical Research in a Changing World

More than seventy years ago, two Pasadenans founded the institutes that would one day join forces to become the Huntington Medical Research Institutes. They held a simple conviction: **science driven by curiosity, courage and compassion can transform human health**. Today, in a world marked by social, political and environmental change, our researchers embrace complexity and press on when others hesitate. Every advance depends on a community of individuals who trust discovery's power to shape a better future.

The same perseverance that once drove HMRI scientists to confront smog and shape national automobile safety standards now propels our mission into a new era. We see this spirit in researchers like Dr. Lawrence Jones, whose work revolutionized prostate cancer care. We see it in the enduring support of community leaders like the women of the Altadena Guild, who have championed biomedical research in Pasadena for more than seven decades. We see it in the pioneering efforts of today's scientists: exploring stem cell treatments for mental illness, leveraging AI to accelerate heart attack diagnosis, and leading studies on neurodegeneration and aging, especially in veterans. These efforts reflect our conviction that **science must adapt: it is rigorous yet resilient in a world that won't wait**.

At HMRI, **our scientists refuse to pause for perfect conditions**. Global health threats, rapid technological shifts and evolving priorities make biomedical research both urgent and vulnerable. History shows us that when we invest in science during moments of uncertainty, **we do more than respond to a changing world — we help shape its future**. We move forward because delay costs lives and discovery demands boldness.

As you explore HMRI's 2024 milestones in the pages ahead, consider what it means to have a thriving research community at Pasadena's heart. Together, we have a generational opportunity: to reaffirm our shared commitment to discovery, health, and hope — and to keep Pasadena a beacon of scientific progress and human flourishing.

In a changing world, science endures. With your partnership, it advances — and so does human progress.

Julia E. Bradsher, PhD, MBA
President and CEO

John C. Babcock,
Chair, HMRI Board of Directors

CARDIOVASCULAR

Instantaneous detection of acute myocardial infarction and ischaemia from a single carotid pressure waveform in rats
Alavi R, Dai W, Matthews RV, Kloner RA, Pahlevan NM
European Heart Journal Open, October 2023

Impact of symptom-to-reperfusion-time on transmural infarct extent and left ventricular strain in patients with ST-segment elevation myocardial infarction: a 3-dimensional view on the wavefront phenomenon
Demirkiran A, Beijnink C, Kloner RA, Hopman LHGA, van der Hoeven NW, van Pouderoijen N, Janssens GN, Everaars H, van Leeuwen MAH, van Rossum AC, van Royen N, Robbers LFHJ, Nijveldt R
European Heart Journal of Cardiovascular Imaging, October 2023

Flavoring agents in e-cigarette liquids: A comprehensive analysis of multiple health risks
Sachdeva J, Karunananthan A, Shi S, Dai W, Kleinman MT, Herman D, Kloner RA
Cureus, November 2023

Association of the COVID-19 pandemic on treatment times for ST-elevation myocardial infarction: observations from the Los Angeles County Regional System
Shavelle DM, Bosson N, French WJ, Thomas JL, Niemann JT, Gausche-Hill M, Rollman JE, Rafique AM, Klomhaus AM, Kloner RA
American Journal of Cardiology, November 2023

Princeton IV consensus guidelines: PDE5 inhibitors and cardiac health
Kloner RA, Burnett AL, Miner M, Blaha MJ, Ganz P, Goldstein I, Kim NN, Kohler T, Lue T, McVary KT, Mulhall JP, Parish SJ, Sadeghi-Nejad H, Sadovsky R, Sharlip ID, Rosen RC
Journal of Sexual Medicine, December 2023

Effects of electronic cigarette vaping on cardiac and vascular function, and post-myocardial infarction remodeling in rats
Dai W, Shi J, Siddarth P, Carreno J, Kleinman MT, Herman DA, Arechavala RJ, Renusch S, Hasen I, Ting A, Kloner RA
Cardiovascular Toxicology, February 2024

The association of tadalafil exposure with lower rates of major adverse cardiovascular events and mortality in a general population of men with erectile dysfunction
Kloner RA, Stanek E, Desai K, Crowe CL, Paige Ball K, Haynes A, Rosen RC
Clinical Cardiology, February 2024

An urgent call for studies that address the cardiovascular consequences of legalization of marijuana
Rezkalla SH, Kloner RA
Cardiovascular Research, April 2024

Proceedings of Princeton IV: PDE5 inhibitors and cardiac health symposium
Rosen RC, Miner M, Burnett AL, Blaha MJ, Ganz P, Goldstein I, Kim N, Kohler T, Lue T, McVary K, Mulhall J, Parish SJ, Sadeghi-Nejad H, Sadovsky R, Sharlip I, Kloner RA
Sexual Medicine Reviews, June 2024

Increased PHLPP1 expression through ERK-4E-BP1 signaling axis drives nicotine induced oxidative stress related damage of cardiomyocytes
Mohammed Abdul KS, Han K, Guerrero AB, Wilson CN, Kulkarni A, Purcell NH
Journal of Molecular and Cellular Cardiology, June 2024

The Princeton IV consensus recommendations for the management of erectile dysfunction and cardiovascular disease
Köhler TS, Kloner RA, Rosen RC, Burnett AL, Blaha MJ, Ganz P, Goldstein I, Kim NN, Lue T, McVary KT, Mulhall JP, Parish SJ, Sadeghi-Nejad H, Sadovsky R, Sharlip ID, Miner M
Mayo Clinic Proceedings, August 2024

Adverse cardiovascular effects of nicotine delivered by chronic electronic cigarettes or standard cigarettes captured by cardiovascular intrinsic frequencies
Alavi R, Dai W, Mazandarani SP, Arechavala RJ, Herman DA, Kleinman MT, Kloner RA, Pahlevan NM
Journal of the American Heart Association, September 2024

IMMUNOLOGY

NAD+ prevents septic shock-induced death by non-canonical inflammasome blockade and IL-10 cytokine production in macrophages
Iske J, El Fatimy R, Nian Y, Ghouzlani A, Eskandari SK, Cetina Biefer HR, Vasudevan A, Elkhal A
eLife, February 2024

Transplanting old organs promotes senescence in young recipients
Iske J, Roesel MJ, Martin F, Schroeter A, Matsunaga T, Maenosono R, Tripathi U, Xiao Y, Nian Y, Caldarone BJ, Vondran FWR, Sage PT, Azuma H, Abdi R, Elkhal A, Pirtskhalava T, Tchkonia T, Kirkland JL, Zhou H, Tullius SG
American Journal of Transplantation, February 2024

NEUROSCIENCES

Practice makes imperfect: stronger implicit interference with practice in individuals at high risk of developing Alzheimer's disease
Hung SM, Adams SW, Molloy C, Wu DA, Shimojo S, Arakaki X
GeroScience, October 2023

Choriocapillaris and retinal vascular alterations in presymptomatic Alzheimer's disease
Corradetti G, Oncel D, Kadomoto S, Arakaki X, Kloner RA, Sadun AA, Sadda SR, Chan JW
Investigative Ophthalmology and Visual Science, January 2024

Plasma biomarkers of Alzheimer's disease and related dementias in American Indians: The Strong Heart Study
Suchy-Dicey AM, Longstreth WT Jr, Rhoads K, Umans J, Buchwald D, Grabowski T, Blennow K, Reiman E, Zetterberg H
Alzheimer's & Dementia, January 2024

HMRI's scientists lead the way, thinking creatively about complex diseases in new ways, exploring therapies that have the power to disrupt science, push the boundaries of what's possible and transform lives.

Psychometric reliability, validity, and generalizability of 3MSE scores among American Indian adults: The Strong Heart Study
Suchy-Dicey AM, Vo TT, Oziel K, Buchwald DS, Nelson LA, Verney SP, French BF
Journal of the International Neuropsychological Society, January 2024

Incidence of stroke in indigenous populations of countries with a very high Human Development Index: A systematic review
Balabanski AH, Dos Santos A, Woods JA, Mutimer CA, Thrift AG, Kleinig TJ, Suchy-Dicey AM, Siri SRA, Boden-Albala B, Krishnamurthi RV, Feigin VL, Buchwald D, Ranta A, Mienna CS, Zavaleta-Cortijo C, Churilov L, Burchill L, Zion D, Longstreth WT Jr, Tirschwell DL, Anand SS, Parsons MW, Brown A, Warne DK, Harwood M, Barber PA, Katzenellenbogen JM
Neurology, March 2024

Psychometric properties of Controlled Oral Word Association (COWA) test and associations with education and bilingualism in American Indian adults: The Strong Heart Study
Suchy-Dicey AM, Vo TT, Oziel K, King R, Barbosa-Leiker C, Rhoads K, Verney S, Buchwald DS, French BF
Assessment, April 2024

Epidemiology and prevalence of dementia and Alzheimer's disease in American Indians: Data from the Strong Heart Study
Suchy-Dicey AM, Domoto-Reilly K, Nelson L, Jayadev S, Buchwald DS, Grabowski TJ, Rhoads K
Alzheimer's & Dementia, May 2024

Parallel electrophysiological abnormalities due to COVID-19 infection and to Alzheimer's disease and related dementia
Jiang Y, Neal J, Sompol P, Yener G, Arakaki X, Norris CM, Farina FR, Ibanez A, Lopez S, Al-Ezzi A, Kavcic V, Güntekin B, Babiloni C, Hajós M
Alzheimer's & Dementia, May 2024

Mid-life sleep is associated with cognitive performance later in life in aging American Indians: Data from the Strong Heart Study
Fonseca LM, Finlay MG, Chaytor NS, Morimoto NG, Buchwald D, Van Dongen HPA, Quan SF, Suchy-Dicey A.
Frontiers in Aging Neuroscience, June 2024

Associations of plasma glutamatergic metabolites with alpha desynchronization during cognitive interference and working memory tasks in asymptomatic Alzheimer's disease
Leong VS, Yu J, Castor K, Al-Ezzi A, Arakaki X, Fonteh AN
Cells, June 2024

Algorithm-defined memory impairment in older American Indians: The Strong Heart Study
Suchy-Dicey AM, Grabowski T, Buchwald D, Longstreth WT, Rhoads K
Neuropsychology, July 2024

Differential patterns of gut and oral microbiomes in Hispanic individuals with cognitive impairment
Wadop YN, Vasquez EL, Mathews JJ, Muhammad JAS, Mavarez RP, Satizabal C, Gonzales MM, Tanner J, Maestre G, Fonteh AN, Seshadri S, Kautz TF, Fongang B
bioRxiv, July 2024

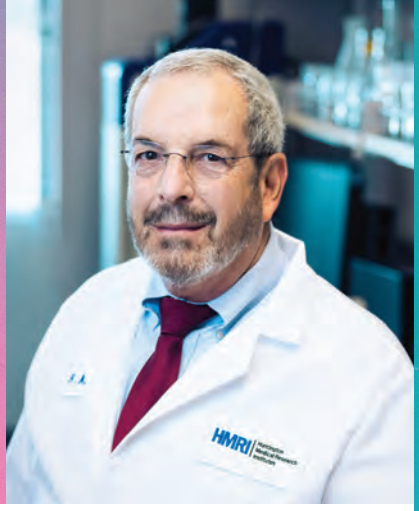
Psychometric reliability, validity, and generalizability of MoCA in American Indian adults: The Strong Heart Study
Suchy-Dicey AM, Vo TT, Oziel K, Buchwald DS, Rhoads K, French BF
Assessment, July 2024

Disrupted brain functional connectivity as early signature in cognitively healthy individuals with pathological CSF amyloid/tau
Al-Ezzi A, Arechavala RJ, Butler R, Nolty A, Kang JJ, Shimojo S, Wu DA, Fonteh AN, Kleinman MT, Kloner RA, Arakaki X
Communications Biology, August 2024

Higher sodium in older individuals or after stroke/reperfusion, but not in migraine or Alzheimer's disease - a study in different preclinical models
Xia C, Dai W, Carreno J, Rogando A, Wu X, Simmons D, Astraea N, Dalleska NF, Fonteh AN, Vasudevan A, Arakaki X, Kloner RA
Scientific Reports, September 2024

Science in a Changing World

A Letter from the Chief Science Officer



In a world that's changing faster than ever — where public health threats, chronic disease, and health disparities are growing more complex — the need for forward-thinking, life-changing research has never been greater. At Huntington Medical Research Institutes (HMRI), we're committed to leading with science, translating discoveries into real solutions that improve lives. Thanks to your support, our scientists are meeting the challenges of today — and preparing for those of tomorrow — with bold ideas, innovative tools, and compassionate purpose.

This past year, **epidemiologist Astrid M. Suchy-Dicey, PhD, joined HMRI to lead our long-standing Brain Aging Study (the BAS)**, which was first launched more than two decades ago with support from visionary local donors. Under her leadership, the study has expanded its focus on the **early detection and prevention of Alzheimer's disease**, utilizing promising new biomarker technologies that are both non-invasive and accessible. Supported by a generous $8 million grant from a private foundation, the BAS is now poised to help us recognize Alzheimer's-related changes in the brain years before symptoms begin — opening the door to earlier intervention and care.

In addition to directing the BAS, Suchy-Dicey leads several large, NIH-funded studies examining brain aging in American Indian and Alaska Native populations, who have been historically overlooked in dementia research. In a landmark finding published in "Alzheimer's & Dementia: The Journal of the Alzheimer's Association," her team found that nearly half of American Indians over age 65 show signs of cognitive impairment, with about 10% experiencing dementia — rates that are significantly higher than previously thought. These discoveries help to ensure that the **future of Alzheimer's research is more inclusive, equitable, and accurate.**

To support this critical work, we reorganized HMRI's Department of Neurosciences into two complementary divisions: Clinical and Translational Neurosciences, led by Suchy-Dicey, and Basic and Translational Neurosciences, headed by **Anju Vasudevan, PhD**. This structure enhances collaboration and accelerates the transfer of discoveries from the bench to the bedside — an essential part of our strategy.

Vasudevan and her team have made breakthrough discoveries around a new type of GABA signaling in the brain's vascular system, which operates differently from traditional neuronal pathways. These findings are helping explain the **developmental origin of psychiatric disorders like schizophrenia, autism, and depression**, and how brain blood flow may play a critical role. This foundational research is crucial for developing more effective and personalized treatments.

Fueled by the generosity of a local donor, Vasudevan launched the Pluripotent Stem Cell Program and recruited the talented Dr. John M. Boyle to HMRI. Using induced pluripotent stem cells, scientists can model brain-like cells in the laboratory — enabling scientists to examine how psychiatric illnesses develop at the cellular level and to develop new methods for diagnosis. Dr. Boyle, who passed unexpectedly in August, was a wry and enthusiastic scientific partner, and we are grateful for the brief time we shared together.

In another vital area of research, **Abdala Elkhal, PhD**, is tackling one of the deadliest critical care emergencies: septic shock. Each year, millions die from sepsis, yet there are no approved therapies to prevent or reverse it. Elkhal discovered that **NAD+**, a molecule found in all living cells**, can block the body's dangerous overreaction to sepsis and improve survival by up to 80%** in preclinical models. With further development, this could be **a revolutionary treatment for sepsis, saving countless lives**.

Another exciting area of progress is the integration of **AI and wearable technology** to monitor heart health. **James G. Boswell Postdoctoral Fellow, Rashid Alavi, PhD,** along with me and collaborators **Niema Pahlevan, PhD,** a visiting scientist to HMRI from USC, and **Wangde Dai, MD,** an associate professor at HMRI and USC, have developed a noninvasive method — utilizing AI to analyze waveforms from the carotid artery — that can **detect "silent" heart attacks with 90% accuracy.** These events often go unnoticed and untreated, especially in women and people with diabetes. **With further support, this technology could be made available through smartphones or wearable devices, offering a powerful new tool for early detection and prevention.**

Alavi and his collaborators also applied a novel technique to **predict the long-term risk of cardiovascular damage from e-cigarettes**, particularly those with nicotine. Using cardiovascular intrinsic frequency and a smartphone app, he detected subtle signs of damage in the cardiovascular system that might otherwise go undetected by routine medical exams. This type of early warning system could help reduce future heart disease, especially in young users of nicotine products.

Meanwhile, **Nicole Purcell, PhD**, and her team in the Cardiovascular Signaling Laboratory have made important strides in understanding **how nicotine damages heart cells**. Her research uncovered a specific molecular pathway — involving a protein called PHLPP1 — that is triggered by nicotine exposure and increases vulnerability to cardiac injury. By identifying how this process works, Purcell's lab is **paving the way for new therapies that could protect the heart from nicotine-related harm**, whether from traditional cigarettes or vaping products.

This year, the scientists and physicians who convened at HMRI for the national 2023 Princeton IV Symposium concluded that **PDE-5 inhibitors remain safe for the cardiovascular system**. They published expanded clinical recommendations for men who present with erectile dysfunction (ED). I was honored to be the principal investigator of Princeton IV, co-chaired by Raymond Rosen, PhD, of UC San Francisco.

Recent studies from our lab have shown that men taking tadalafil (trade name Cialis), originally developed for ED, experience **lower rates of Major Adverse Cardiac Events — heart attacks, hospitalizations, and cardiovascular death, — with a reduction of 55% in cardiovascular mortality**. The research, published in the Journal of Clinical Cardiology and Journal of Sexual Medicine, emphasizes how **ED can serve as an early warning sign for heart disease —** and how these **medications may offer a double benefit by improving both sexual and heart health.**

These accomplishments, spanning neuroscience, cardiovascular science, mental health, immunology, and digital innovation, are a direct result of your belief in our mission. Every discovery, every breakthrough, every life improved begins with support from individuals like you.

Your generosity enables our investigators to take calculated risks, pursue innovative ideas, and address urgent health needs. Whether it's launching a new program, funding a clinical trial, or equipping a lab with the tools it needs, **your impact is woven into every step we take**.

As we look ahead, we are filled with hope and determination. **Science alone cannot solve all of the world's challenges — but science powered by people who care deeply can**. Thank you for being our partners in this work. Together, we are building a future where health innovation is more inclusive, more proactive, and more impactful than ever before. ❖

With deepest gratitude,

Robert A. Kloner

Robert A. Kloner, MD, PhD
Chief Science Officer, HMRI
Professor of Medicine (Clinical Scholar)
Keck School of Medicine, USC

Advancing Science Through Shared Resources — Powered by Donors

HMRI's **Core Resource Program (CRP)** was established to provide researchers at HMRI and its affiliated institutions with access to specialized services, equipment, and technical expertise that extend beyond the capabilities of individual laboratories. Made possible through the generous support of our donors, the CRP delivers vital infrastructure that enables HMRI scientists and external collaborators to access standardized laboratory services and state-of-the-art biomedical technologies.

Led by **Natalie Astraea**, the CRP team provides technical consultation, equipment training, and technician-supported laboratory testing. From project inception to completion, the program prioritizes safety, quality, and efficiency — allowing researchers to focus on groundbreaking scientific discovery.

The CRP is composed of five core facilities:

- **Analytical Biochemistry Core (ABC)**
- **Research Services Core**
- **Imaging Core**
- **Central Biorepository**
- **Vivarium**

These core labs utilize advanced methodologies and detection systems to identify, characterize, and quantify cells, compounds, and their interactions across various biological and synthetic matrices. HMRI has also leveraged CRP capabilities to secure and fulfill external contract research projects, making meaningful contributions to t he global scientific community.

HMRI's **Institutional Biosafety Committee (IBC)**, approved by the **National Institutes of Health (NIH)**, reviews research involving recombinant DNA and other non-recombinant materials. The IBC ensures compliance with NIH guidelines by evaluating containment protocols, laboratory procedures, personnel training, and facility standards. Complementing these efforts, HMRI launched a comprehensive **Cal/OSHA safety training program** and introduced a streamlined **2023–2024 Compliance Calendar** to align with all relevant regulatory requirements.

The **Analytical Biochemistry Core (ABC)** plays a central role in accelerating scientific progress. In the past year alone, the lab processed and analyzed more than 3,000 clinical and preclinical samples. One key advancement was the **adaptation of the Brain Aging Study (the BAS) biomarker methods from cerebrospinal fluid (CSF) to plasma**, a less invasive approach that expands testing capabilities. The ABC now supports both HMRI's BAS and external collaborators with a comprehensive panel of neurodegeneration biomarkers, including:

- Beta-amyloid 42/40
- Tau, ptau217, ptau231, and ptau181
- Neurofilament light (NfL)
- Glial fibrillary acidic protein (GFAP)

Further expanding its services, the ABC began offering a broader range of scientific domains by implementing new methods to quantify **alpha-synuclein** in human plasma and CSF, as well as a panel of **inflammatory cytokines** (TNFα, IFNγ, IL-5, IL-10, IL-13, IL-23), widening its utility across a range of scientific fields.

Significant infrastructure improvements — partially funded by donor contributions — include the implementation of a centralized inventory management system, an upgraded chemical management program, and a custom **Laboratory Information Management System (LIMS)**. Serving as an essential tool for standardized test results, the LIMS tracks and barcodes biobank specimens, enhancing data accuracy and reporting. The Core team has cataloged thousands of clinical and preclinical samples in the Biobank and Brainbank, unifying legacy data with current testing resources.

Facility and operational enhancements continued this year with the consolidation of general and specialized lab equipment, a multi-phase building evaluation and structural reinforcement project, and targeted resource optimization efforts. As part of HMRI's commitment to responsible financial stewardship, the MRI facility was decommissioned, and the BAS scans are now outsourced — allowing donor funds to be more effectively allocated toward active research initiatives.

HMRI welcomed **GrittGene Therapeutics** into the biomedical research community as a new tenant. Using a disease-centric approach, GrittGene is a start-up driven by its mission to cure patients with **myotonic dystrophy type 2**. ❖

Driving Early Detection in a Changing World: The Brain Aging Study

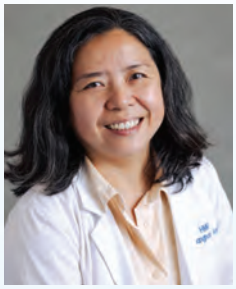
In today's fast-paced scientific landscape, the search for solutions to complex diseases, such as Alzheimer's, requires collaboration and data-driven innovation, with a focus on the future. As Alzheimer's disease reaches epidemic proportions — affecting over 47 million people worldwide — **scientists are urgently working to shift the paradigm from late-stage diagnosis to early detection and prevention.**

A Collaborative Approach to Biomarker Discovery

Twenty-five years after HMRI researchers first investigated protein changes in patients with Alzheimer's disease, the Brain Aging Study team, directed by Astrid Suchy-Dicey, PhD, has narrowed its focus to identify indicators of Alzheimer's disease before symptoms arise. This ambitious, multidisciplinary effort harnesses expertise in neuroscience, data science, and clinical practice, positioning HMRI scientists at the forefront of early detection. These subtle early signs could transform how — and when — we intervene, offering hope for delaying or even preventing disease onset.

The **Biomarker and Neuro-disease Mechanism Laboratory (BNML)** led by Alfred Fonteh, PhD, has developed highly sensitive assays that measure fatty acids in urine — potential early markers of neurodegenerative injury. Utilizing ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-LC/MS), this advanced method is over 1,000 times more sensitive than previous techniques, enabling the detection of a broader and more nuanced range of biomarkers.

Simultaneously, the BNML has examined cerebrospinal fluid samples from cognitively healthy individuals who later experienced cognitive decline. Their findings reveal changes in extracellular matrix (ECM) proteins and metabolites related to sleep regulation and neuronal health. This suggests that intervention strategies to support ECM integrity or sleep hormone levels could help preserve cognitive function.



Meanwhile, the **Cognition and Brain Integration Laboratory (CBIL)**, led by Xianghong Arakaki, MD, PhD, is integrating neurophysiology and technology to enhance biomarker discovery. By analyzing brainwave (EEG) and heartwave (ECG) data during cognitive testing, researchers are identifying distinct neurophysiological patterns associated with preclinical Alzheimer's pathology. Even in participants who appear cognitively healthy, subtle signs of autonomic dysfunction and changes in brain connectivity may indicate the earliest stages of Alzheimer's-related processes.

These signatures, which differ by cognitive task and brain region, present exciting potential as low-cost, noninvasive tools for early detection.

Data Science as a Unifying Force

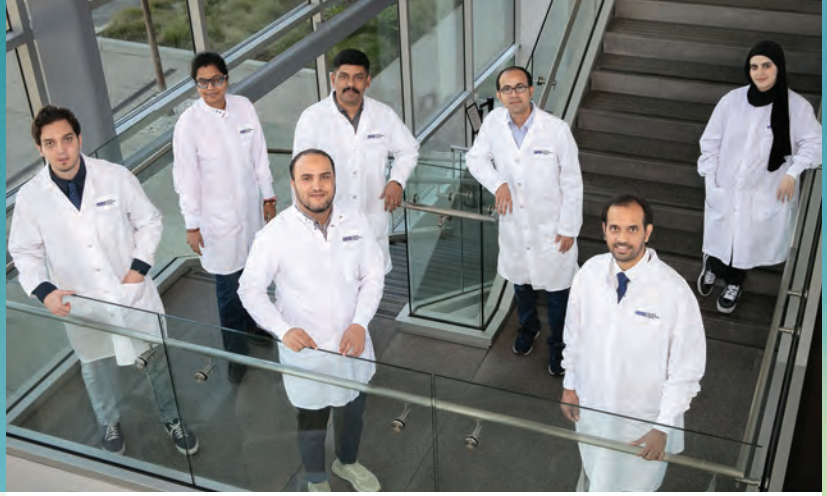
Central to the success of the Brain Aging Study is the integration of extensive, multimodal data. Study teams are collecting and curating high-quality data from imaging (MRI, OCT), electrophysiology (EEG, ECG), biofluid biomarkers, and neuropsychological assessments. This initiative offers a comprehensive snapshot of each participant's cognitive and biological status over time.

The data and administrative teams are working closely with partners from UCLA, Caltech, Fuller Theological Seminary, and others to ensure the dataset is clean, organized, and ready to support novel insights and future publications. These collaborations underscore HMRI's commitment to open scientific exchange and the collective advancement of knowledge.

A Vision for the Future

As the study progresses, so does the potential to shape the future of Alzheimer's research — bringing together collaborators, community members, and donors in a shared mission to improve health outcomes with compassion and precision for those at risk of Alzheimer's disease. ❖

Educating Future Scientists for a Changing World



2024 POSTDOCTORAL FELLOWS

Abdulhakim Al-Ezzi, PhD
Faculty mentor: Xianghong Arakaki, MD, PhD
Cognition and Brain Integration Laboratory

Tanimul Alam, PhD
Faculty mentor: Nicole Purcell, PhD
Cardiovascular Signaling Laboratory

Amina Ghouzlani, PhD
Faculty mentor: Abdala Elkhal, PhD
Neuro- Cardio- Immunology Laboratory

Kazi Helal Hossain, PhD
Faculty mentor: Anju Vasudevan, PhD
Angiogenesis and Brain Development Laboratory

Joby Jose, PhD
Faculty mentor: Alfred Fonteh, PhD
Biomarker and Neuro-disease Mechanism Laboratory

Divya Mishra, PhD
Faculty mentor: Anju Vasudevan, PhD
Angiogenesis and Brain Development Laboratory

Khaja Shameem Mohammed Abdul, PhD
Faculty mentor: Nicole Purcell, PhD
Cardiovascular Signaling Laboratory

Chenchen Xai, PhD
Faculty mentor: Xianghong Arakaki, MD, PhD
Cognition and Brain Integration Laboratory (Migraine)

JAMES G. BOSWELL POSTDOCTORAL FELLOW

Rashid Alavi, PhD
Faculty Mentors:
Robert A. Kloner, MD, PhD, HMRI
Morteza Gharib, PhD, Caltech
Niema Pahlevan, PhD, USC-HMRI
Cardiovascular Research Laboratory (HMRI)
Department of Medical Engineering (Caltech)

In a world where science is rapidly evolving — shaped by technological innovation, shifting global health challenges, and new frontiers in discovery — the need to prepare the next generation of scientists and physicians has never been more vital. At HMRI, we acknowledge that the future of biomedical research relies on empowering young minds to adapt, lead, and innovate in this dynamic landscape.

As part of our commitment to advancing science in a changing world, HMRI continues to invest in immersive STEM education programs that equip students with the skills and perspectives needed to thrive in an unpredictable future. In 2024, we expanded these initiatives to reach even more aspiring researchers.

Thanks to a new partnership, medical students studying at the Western University of Health Sciences participated in biomedical research projects at HMRI for the first time, gaining firsthand experience in tackling today's most pressing health issues. Furthermore, the American Heart Association (AHA) chose HMRI as a partner in its prestigious Supporting Undergraduate Research Experiences (SURE) scholars program. HMRI is proud to be the only independent research institute invited to take part in a program historically reserved for elite universities.

Over the next three years, HMRI will receive $117,000 through the AHA SURE program to support nine undergraduate students in cardiovascular research. The 2024 summer session marked the launch of our first AHA SURE cohort, welcoming scholars Christopher Munoz, Lorraine Tam, and Sona Ayvazyan.

At HMRI, students work side by side with leading researchers on scientific questions that impact millions — heart failure, stroke, Alzheimer's disease, and neuropsychiatric conditions. Within our nonprofit, hands-on research environment, students develop independent projects, use cutting-edge tools and technologies, and learn to navigate the complexity of biomedical science with critical thinking and curiosity.

This personalized mentorship experience doesn't just teach students how to do science — it prepares them to do science differently. In a field where the only constant is change, HMRI's education programs help young scholars become adaptable, innovative, and resilient leaders ready to tackle the challenges of tomorrow. ❖

Summer Undergraduate Research Fellows (SURF)

Cardiovascular Research Laboratory
Jason Lin, Mt. San Antonio College

Cardiovascular Signaling Laboratory
Angel Calles, California State Dominguez Hills
Xiaoxue Jiang, Mt. San Antonio College
Marco Renteria, Mt. San Antonio College
Alexa Sen, Pasadena City College

Angiogenesis and Brain Development Laboratory
Karina Kachler-Glynne, Occidental College

Biomarker and Neuro-disease Mechanism Laboratory
Andrea Barrera Cruz, Pasadena City College
Cindy Martinez, California State Dominguez Hills

Cognition and Brain Integration Laboratory
Isabella Man, Pasadena City College

Isabella Man receives certificate of completion at the conclusion of the 2024 SURF program, pictured with her HMRI postdoctoral mentor, Dr. Abdulhakim Al-Ezzi (R) and her father, Dr. David Man (L), infectious disease specialist in Pasadena, CA.

American Heart Association Supporting Undergraduate Research Experiences (AHA SURE)

Cardiovascular Signaling Laboratory
Christopher Munoz, Pasadena City College
Sona Ayvazyn, Glendale Community College

Angiogenesis and Brain Development Laboratory
Lorraine Tam, University of California Berkeley

Biomedical Research Internships

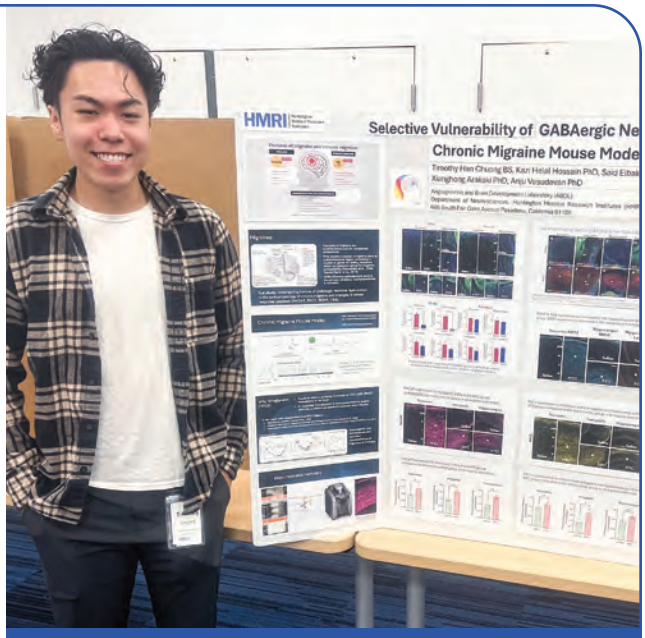
Cardiovascular Research Laboratory
Jianjun Lin, University of Southern California

Cardiovascular Signaling Laboratory
Gregory Ayzenberg, Western University of Health Sciences (medical school)
Inca Stienhans, California State Los Angeles
Shaira Santos, Western University of Health Sciences (medical school)
Henry Lyu, San Marino High School
Hollis Rausch, High School (homeschool)

Angiogenesis and Brain Development Laboratory
Emily Abad, Pasadena City College
Timothy Choung, Western University of Health Sciences (medical school)

Brain Aging Study
Sofia Stellar, University of Southern California (post-bac)

Cognition and Brain Integration Laboratory
Isabella Man, Pasadena City College
Mengxiang (Daniel) Gao, Pasadena City College



Biomedical research intern in the Angiogenesis and Brain Development Laboratory, Timothy Choung, presents his independent research project, Selective Vulnerability of GABAergic Neurons in a Chronic Migraine Model at Science Day.

Students accepted into the afternoon session on the first day of the 2024 High School STEM program.

PUSD High School STEM Program

John Muir High School
Suri Almasi
Esmeralda Gonzalez Salcedo

Marshall Fundamental School
Giovanni Benitez
Saray Bolanos
Michael Gerst
Sophia Hammer
Carlanne La Compte
Leo Lou
Garabet Marmarian
Fernanda Morales
Dylan Obsenares
William Peddie
Cynthia Rocha
Jonathan Sercel
Makena Sweet

Pasadena High School
Adia Estebane
Willow Johnson
Giselle Leya
Annika Tamppari

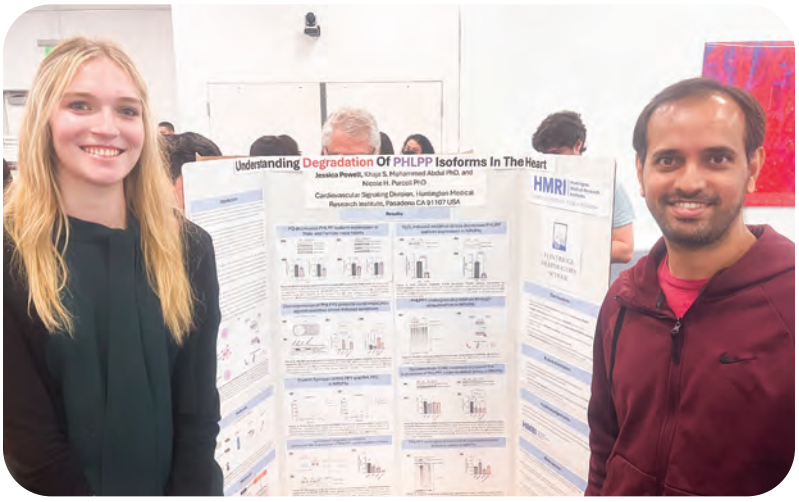
Blair High School
Jordan Fleischman
Augustus Kemp
Elias Torres
Layah Winn

CIS Academy
Kelly Ortiz Torres

Students receive certificates after their individual research presentations on the closing day of the 2024 High School STEM program.

Connecting Scientific Discovery in a Changing World

In a world where the pace of scientific advancement continues to accelerate, connecting groundbreaking research with the broader community is more important than ever. On July 24, 2024, HMRI welcomed 150 guests from across the Pasadena area to its second annual Science Day — a vibrant showcase of discovery, collaboration, and education in action.



This year's event featured 24 research exhibits spanning neuroscience, cardiovascular health, and translational research, highlighting the work of undergraduate students, postdoctoral fellows, and HMRI scientists. The program also included a dynamic panel discussion, focused on creating equitable opportunities in STEM education, moderated by HMRI President and CEO Julia E. Bradsher, PhD, MBA. The discussion examined how science education and workforce development must evolve to remain inclusive and responsive in today's shifting global landscape.

Science Day is one of many efforts by HMRI to make **research more accessible and meaningful to the public**, which is part of a broader **mission to foster deeper community engagement as science adapts to new challenges**. Following the end of the COVID-19 pandemic in May 2023, the need to reestablish in-person connections became evident. In response, HMRI launched the **President's Event Series** in the fall of 2023. These quarterly events bring together **leading voices** from both inside and outside the institute — researchers, clinicians, educators, and caregivers — **to discuss critical issues** such as Alzheimer's disease, cardiovascular health, and youth mental health.

As scientific discovery becomes increasingly interdisciplinary and global, **HMRI remains committed to transparency, public engagement, and community partnership**. Events like Science Day and the President's Event Series allow us to celebrate the progress being made in our laboratories while also demonstrating the real-world impact of that work, made possible through the ongoing support of donors, partners, and community members.

In a changing world, **science must not only advance — it must connect, include, and inspire**. At HMRI, we believe that sharing our discoveries with the community is essential to building a healthier future for all. ❖

A Legacy of Generosity:
Honoring the Altadena Guild's 70 Year Commitment

For more than 70 years, the Altadena Guild has been a steadfast partner of Huntington Medical Research Institutes, providing strength and support during periods of growth, challenge, and change. In a world where science must constantly adapt to address new health threats and emerging technologies, the Guild's unwavering commitment has ensured that HMRI remains at the forefront of biomedical discovery.

In this year's annual report, we reflect with deep gratitude on the Altadena Guild's role in helping us navigate decades of change. **Their efforts have fueled progress in neuroscience, cardiovascular health, imaging research, and beyond — contributing to better health outcomes for our community and the world**. It is with heartfelt appreciation that we dedicate this report to the incredible women of the Altadena Guild.


Society
WOMAN'S WORLD
Huntington Auxiliary's Expansion Initiated as Altadena Guild Born

The Guild's journey began in February 1952 with a visionary idea: a home tour to raise funds for medical research. Admission was $1.50 — or $2.00 with dessert — and the event raised $428 for the small research facility that would become HMRI. That inaugural effort sparked a 70-year tradition of service and generosity, resulting in over $2.5 million raised for HMRI and a legacy that continues to shape the future of science.

Originally formed to extend the work of the Women's Auxiliary of Huntington Memorial Hospital, **the Guild has carried forward a mission rooted in healthcare, innovation, and community**. Their signature fundraising event, the Altadena Home and Garden Tour, has showcased more than 270 homes and gardens, celebrating the rich architectural and cultural history of the region.

The most recent tour, "Poppies on Meadowbrook," took place on May 5, 2024. Guests enjoyed live music, artisan vendors, a pop-up café, and stunning homes and gardens — all set against the backdrop of a vibrant and welcoming Altadena neighborhood. It was a delightful celebration of tradition and purpose. Unfortunately, it was also the last Home Tour for the foreseeable future.

In the wake of the devastating Eaton Canyon Fires, the 2025 tour was canceled. Many Guild members and community supporters have suffered the loss of their homes and businesses. As the world changes in unpredictable ways, HMRI stands in solidarity with our Altadena partners. **Their resilience in the face of**

hardship exemplifies the spirit that drives innovation in times of uncertainty.

The Guild's commitment extends beyond events. Through personal philanthropy and volunteerism, members champion research to detect, prevent, and ultimately eradicate diseases such as Alzheimer's disease, heart disease, and mental illness. **"HMRI is a critical cause,"** one Guild member shared, **"and we are proud to support science that improves lives**."

In 1992, the Guild also hosted the first annual Lynn Smith Memorial Golf Tournament at Annandale Golf Club, which continued for more than two decades. The tournament, benefiting HMRI, honored Lynn A. Smith, a Pasadena businessman, longtime HMRI Board member, and passionate supporter of medical research. His legacy of service lived on through this cherished fall event, which united donors, local businesses, and community leaders in support of scientific excellence.

As we look to the future of medicine, the Altadena Guild partners with HMRI in their dedication to educate and inspire the next generation of scientists. Their generosity supports the Summer Undergraduate Research Fellowship (SURF), a 10-week immersive program that offers students hands-on experience in cutting-edge biomedical research. Many SURF alumni have become leaders in medicine, biotech, and academia — demonstrating that science in a changing world starts with mentorship and opportunity.

Through shifting landscapes, both in science and society, the Altadena Guild has remained a constant force for good. Their generosity, vision, and resilience have helped HMRI adapt and thrive in a rapidly evolving world.

To the Altadena Guild: thank you. In this changing world, **your commitment is the steady foundation upon which innovation is built**. Together, we move science forward — and lives are better for it. ❖

Honoring a Legacy:

Dr. Lawrence W. Jones' Lifelong Influence: Shaping the Field of Urology and Changing Countless Lives

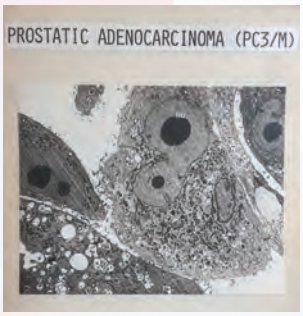
In the ever-evolving world of medicine, few individuals leave a legacy as far-reaching and deeply felt as that of Dr. Lawrence W. Jones. **A pioneering urologist, dedicated educator, and transformative leader in cancer research,** Dr. Jones spent a lifetime bridging the gap between science and humanity, advancing how prostate cancer is diagnosed and treated, while mentoring generations of physicians to lead with both knowledge and compassion.

Dr. Jones' journey toward a career in medicine did not begin in the classroom or a hospital, but in the backyard of his childhood home. Encouraged by his grandmother — a high school teacher who defied his mother's protests — he began dissecting squirrels to explore anatomy and to discover how the body worked. His early experiments ignited a passion for science and surgery, marking the beginning of a remarkable journey that would ultimately shape the field of urology and change countless lives.

Dr. Jones' academic path was as rigorous as it was distinguished. He attended Yale University and the University of California, Berkeley, before earning his medical degree from the University of California, San Francisco (UCSF). He completed residency programs at LA County-USC Medical Center and returned to UCSF for a research fellowship, specializing in both pediatric and adult urologic surgery. Following his advanced training and military service, he joined the Pasadena Urological Medical Group, where his expertise as a clinician and researcher became the foundation for a career that would blend innovation, leadership, and care.

His passions — patient care, research, and teaching — guided every step of his professional journey. At a time when prostate cancer diagnosis was limited to invasive biopsies following abnormal rectal exams, Dr. Jones was on the front lines of a transformative era. He was an early adopter of blood screening, utilizing Prostate-Specific Antigen (PSA), which revolutionized the early detection of prostate cancer. **But beyond embracing change, Dr. Jones created it.**

At Huntington Medical Research Institutes, he became a key collaborator in the institutes' cell culture and prostate cancer research programs. It was there, alongside his colleagues, that he co-developed the now-famous **PC-3 cell line — a tool that continues to serve researchers worldwide in the study of prostate cancer growth and response to treatment.** His research laid the groundwork for pre-clinical trials that tested cancer-controlling agents and even explored the role of lifestyle and nutrition in disease progression.



Prostatic Adenocarcinoma (PC-3) electron micrograph in monolayer culture, second passage.

Dr. Jones' involvement in the use of cultured human prostate cells stemmed from the successful recruitment and support of Dr. M. Edward Kaighn at the W. Alton Jones Cell Science Center in Lake Placid, NY. Together with Drs. Shankar Narayan and Yasushi Ohnuki, the team was the first to develop an immortal line of cells bearing markers of human prostate cancer origin. The live cell line, PC-3, remains in use today as a model for prostate cancer research.

Dr. Shankar Narayan examines PC-3 cells in the laboratory.

Equally significant was Dr. Jones' work with Magnetic Resonance (MR) during the 1980s when HMRI installed the first magnetic imaging unit on the West Coast. Working alongside innovators such as Drs. C. Hunter Shelden, Robert H. Pudenz, and William G. Bradley, Dr. Jones addressed a major limitation in prostate imaging: poor-quality imaging due to the prostate's anatomical location and signal noise. He engineered an inflatable balloon-based carrier for a newly designed surface coil and partnered with radiologist

Dr. William Bradley

Dr. William G. Bradley Jr. to optimize the electronics. The resulting device — the MR Endorectal Coil — transformed prostate imaging and is still used today, improving early detection and treatment planning for patients around the world.

In 1994, Dr. Jones partnered with Dr. John Arcadi to study **Rhodamine 123 (R-123)**, a fluorescent dye originally developed by Eastman Kodak. Dr. Arcadi discovered that R-123 had a unique affinity for cancerous mitochondria. It selectively entered cancer cells, starving them of oxygen and energy, while leaving healthy cells largely unaffected. Preclinical studies showed remarkable success, and by 1999, with a **$500,000 grant from the California Cancer Research Center, the FDA approved the first-ever Phase I clinical trial of R-123 in humans.** Although later results were insufficient to proceed to a Phase II trial, this work was an unprecedented exploration into **mitochondrial-targeted cancer therapy**.

Drs. Jones and Arcadi conducting Phase I clinical trials of Rhodamine-123 for use against hormone-resistant metastatic prostate cancer.

Beyond his groundbreaking research, **Dr. Jones was a revered educator.** Appointed a full clinical professor of urology at the University of Southern California in 1974 by Dr. Allen Mathies, Jr., Dr. Jones regularly participated in clinical rounds at Huntington Hospital and delivered lectures that blended medical rigor with moral clarity. One lesson he repeated to every student was simple yet profound: **"Always put yourself in the position of the patient." For Dr. Jones, empathy was not optional — it was essential.**

His leadership extended well beyond the exam room, the laboratory, and the classroom. In 1994, **Dr. Jones joined the Board of Directors at HMRI, where he contributed his extensive medical knowledge to inform the research strategy and enhance its clinical relevance.** He played a crucial role in helping the board achieve one of its most ambitious goals: the completion of HMRI's state-of-the-art research facility in 2018. He regarded this milestone as one of his proudest accomplishments as a Board member, as it expanded the institute's capacity for scientific innovation. He continued to serve with distinction until the end of 2024, when he was named Director Emeritus in recognition of his lifetime of service.

Dr. Jones was named Director Emeritus in 2024. He is pictured here with John Babcock and Dr. Julia Bradsher

Throughout his career, Dr. Jones held numerous prestigious leadership positions. He served as president of the California Urological Association, the Western Section of the American Urological Association (AUA), and the American Association of Clinical Urologists (AACU). Additionally, he was a board member of the AUA, AACU, the American Foundation of Urologic Disease. For 17 years, he represented the AUA in the American Medical Association's House of Delegates, advocating for policies that supported both patients and physicians.

A scholar of medicine's past as well as its future, Dr. Jones served as editor-in-chief of the *AUA Centennial History: 1902–2002*, earning the William P. Didusch Art and History Award for his lifelong commitment to urologic history. He was also the first recipient of the Western Section's Miley B. Wesson Resident's Essay Award and received the AUA President's Citation Award for his outstanding advocacy.

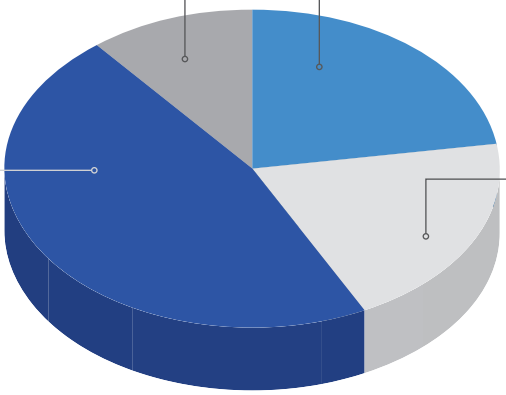
A prolific researcher and writer, **Dr. Jones authored 46 peer-reviewed scientific articles and received numerous awards for laboratory investigations**. He was also a member of the American Association for Cancer Research, which further extended his influence within the scientific community.

Dr. Jones' impact serves as a powerful reminder of what can be achieved when curiosity meets commitment, supported by the generosity of donors like you who continue to believe in our mission.

Thank you for being part of this enduring legacy. Together we honor the past, celebrate the present, and invest in a healthier future — just as Dr. Lawrence W. Jones envisioned. ❖

Revenue & Support

2024 TOTAL **$12M**



2023

Revenue and Support

2023 Total: **$11.5M**

Contributions, grants, and bequests
$3.3M (28.7%)

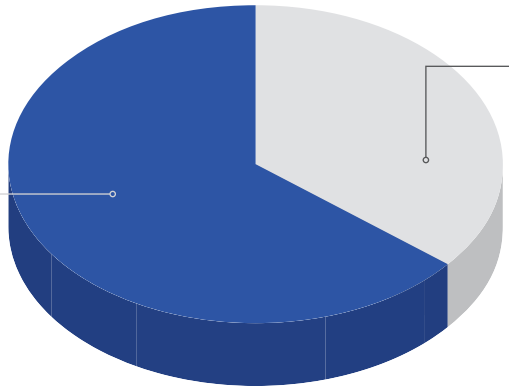
Government grants and contracts
$2.6M (22.6%)

Legacy Gift Income
$3.2M (27.8%)

Other
$2.4M (20.9%)

Operating Expenses

2024 TOTAL **$14.2 M**



2023

Operating Expenses

2023 Total: **$14.6M**

Supporting Services
$4.9M (33.6%)

Program Services
$9.7M (66.4%)

	Sept 30, 2024	Sept 30, 2023
ASSETS		
Cash	10,608,445	3,738,954
Government and contract receivables	138,931	194,225
Other receivables, net	296,132	703,299
Promises to give, net	1,398,039	2,148,099
Prepaid expenses	126,498	130,384
Investments	21,911,049	28,414,993
Property and equipment, net	29,645,236	30,810,177
Patents, net	199,862	208,991
Total Assets	**64,324,192**	**66,349,122**
LIABILITIES AND NET ASSETS		
Liabilities		
Accounts payable	436,652	340,624
Accrued expenses	535,326	462,251
Deferred revenue	17,300	
Accrued pension cost	1,085,716	1,317,307
Total Liabilities	**2,074,994**	**2,120,182**
Net Assets		
Net assets without donor restrictions		
Undesignated	34,759,437	25,519,950
Board designated endowment	10,095,702	17,180,184
Total net assets without donor restrictions	44,855,139	42,700,134
Net assets with donor restrictions	17,394,060	21,528,806
Total Net Assets	**62,249,199**	**64,228,940**
Total Liabilities and Net Assets	**64,324,193**	**66,349,122**

AT HMRI, WE'RE ON A MISSION

TO IMPROVE THE LIVES OF PEOPLE WORLDWIDE.

THROUGH INNOVATIVE BIOMEDICAL RESEARCH,

OUR SCIENTISTS COMBINE THEIR EXCEPTIONAL TALENTS

AND UNWAVERING PASSIONS TO FEARLESSLY PURSUE SCIENCE AND

CONTRIBUTE TO A WORLD FREE FROM

HEART AND BRAIN DISORDERS.

HMRI | Huntington Medical Research Institutes

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