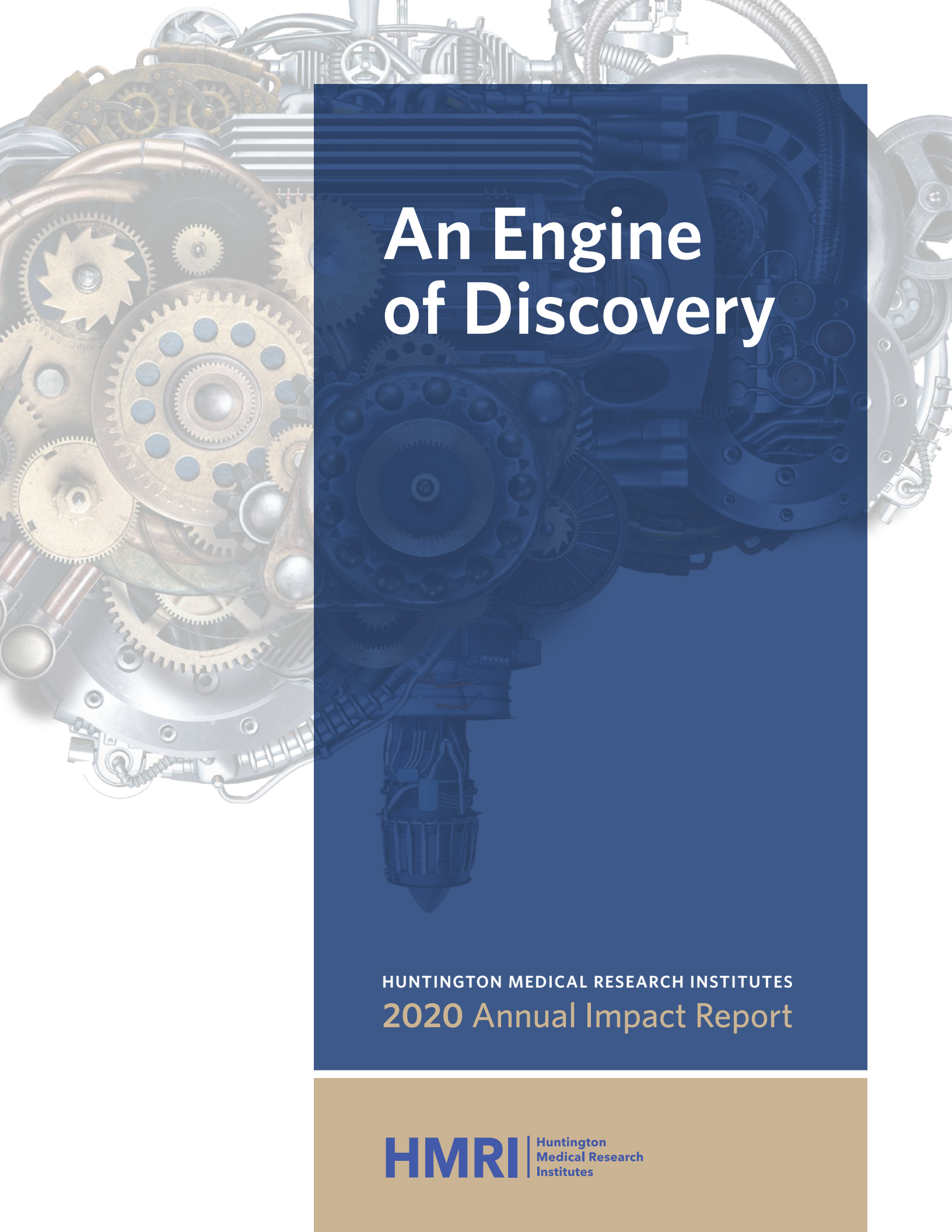




An Engine of Discovery

HUNTINGTON MEDICAL RESEARCH INSTITUTES
2020 Annual Impact Report

Letter from Our Leadership

"It was the best of times, it was the worst of times." This line opens Charles Dickens' classic novel *A Tale of Two Cities*, but his words find new relevance more than 160 years later and ring especially true for HMRI in 2020. The worst of times was, of course, the COVID-19 pandemic.

When we committed in 2019 to a strategic plan that sharpened our research focus on heart and brain diseases affecting millions of people each year, we had no idea about the grave challenge for humanity that would emerge just a few months later. But we also found the best of times as we devised new ways to interact with colleagues and the public, new ways to conduct our operations safely and effectively, and new ways to deliver on our mission to improve lives through biomedical research.

Throughout the year, our teams continued to achieve remarkable results and growth. We hired a new mid-career scientist to help advance HMRI's expertise and reach: Anju Vasudevan, PhD, who joined us as an associate professor and scientific director of neurovascular research (read more on page 4). We secured 36 new grants to fund our research and continued to engage with donors to raise unrestricted support. We prepared for the launch of our formal postdoctoral and STEM education programs in 2021. Our scientists produced 30 peer-reviewed publications and five peer-reviewed presentations at scientific meetings.

Our research teams achieved unparalleled insights, including groundbreaking discoveries about abnormal brain cell development leading to mental illness, irregular brainwaves surrounding Alzheimer's disease, the risk of immediate damage brought on by vaping, several intersections of COVID-19 and cardiovascular disease, as well as advances in the treatment of pelvic floor disorders, post-surgical pain management and more.

This 2020 Annual Impact Report highlights the great strides we made to improve the lives of millions through biomedical research. We invite you to learn more about our work and to share our passion for helping others. Our continued efforts and success rely on the generosity of supporters like you.

With much gratitude,



Julia E. Bradsher, PhD, MBA
President and CEO



James D. Gamb
HMRI Board Chair,
January 2019 to January 2022



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Fueling the Engine of Discovery

HMRI's expert researchers pursue revolutionary discoveries about the nature of Alzheimer's disease, cardiovascular disease, mental illness, and other serious health conditions. Their work is made possible by the unflagging contributions and service of a long list of supporters. We are grateful for the steadfast guidance of our Board of Directors—particularly in a year of unprecedented challenges—and to all those who support our continued success with generous gifts of time, talents and finances. The donors who fuel our progress are vital members of the HMRI family. Thank you!

SUPPORTER SPOTLIGHT: ROGER ENGEMANN

Pasadena resident Roger Engemann is known as a successful businessman and generous philanthropist. He was the founder, principal and president of Roger Engemann & Associates from 1969 until his retirement in 2008. He has held a number of volunteer leadership roles, including serving on the Board of Directors of HMRI for more than thirty years, on the Boards of Trustees of the University of Oregon and Scripps College, and on the Board of Governors of The Huntington Library, Art Museum, and Botanical Gardens.

Mr. Engemann accepted an invitation to join the HMRI Board of Directors in 1990. "It seemed both worthwhile and exciting to support a local organization," he says. "At the time, HMRI was the only biomedical research laboratory in Pasadena."

In the 32 years since then, Mr. Engemann has been a true champion of HMRI. His thoughtful guidance and hands-on leadership have helped shaped HMRI into the organization it is today. He has been an integral member of the executive committee, serving as board chair for six years, as investment committee chair for 20 years and as chair of the capital campaign to fund HMRI's new building.

"Roger and Michele have played key roles in HMRI's continued growth," says Julia Bradsher, president and CEO. "I am truly grateful for their passion, vision, and dedication to the work we are doing here at HMRI.

Supporters like Roger—and so many others—are crucial to our research towards life-changing cures."

"Where we're going—it's exciting," says Mr. Engemann. "In the last ten years we've recruited some very high quality scientists who can move us up to the next level. We have a beautiful building, they have freedom to work and they've got a leader who understands their needs. We're set to go places."



Board member Roger Engemann and his wife, Michele, have provided invaluable leadership and support to HMRI for more than 30 years.

Cardiovascular Research

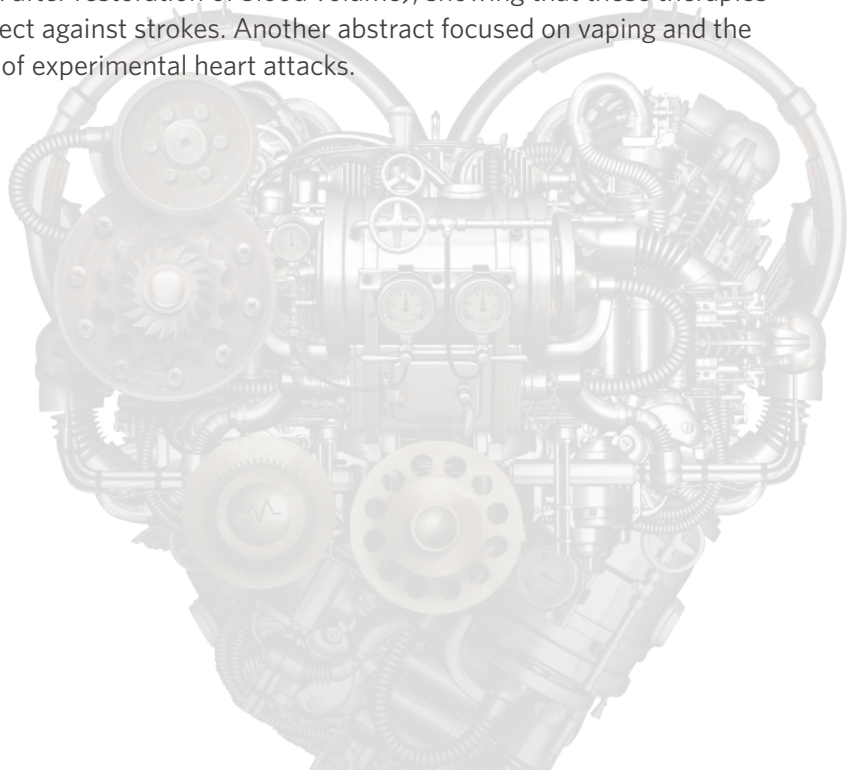
"We continue to study novel ways to reduce heart damage during heart attack and extend that work into vascular insufficiency and stroke to the brain. Over the years, we've studied a number of ways of reducing cell death during heart attack and have now applied that knowledge to other disease models, including hemorrhagic shock. With HMRI's collective interest in the heart-brain connection, the goal is to extend that work to see how the concepts could apply to brain diseases such as stroke and dementia. Applying what we've learned in the heart to the brain and the blood vessels in the brain is very exciting."

— Robert A. Kloner, MD, PhD
Chief Science Officer
Professor and Scientific
Director, Cardiovascular
Research

Our cardiovascular scientists were deep into a complex vaping study when COVID-19 restrictions were implemented in spring 2020. These restrictions slowed down our research, but we kept our laboratories open and continued our experimental work—including our investigation of the effect of smoking, nicotine and electronic cigarettes on the heart and lungs. We found that e-cigarettes increased lung inflammation and caused abnormalities in heart function. Additional studies indicated that the heating element in vaping devices can cause lung injury, and that nicotine use near or at the time of a heart attack can increase the size of the heart attack—which could have a significant impact on recovery. These results contribute to a greater understanding of heart health and the potential adverse effects of smoking, nicotine and e-cigarette vapors.

We had many other bright spots in what could have been a year overshadowed by COVID-19. The cardiovascular research team won supplemental grant funding to carry out additional research on e-cigarettes and published 10 full-length papers. Chief Science Officer Robert Kloner co-authored a scientific statement from the American Heart Association about the cardiovascular effects of marijuana.

At the national American Heart Association Scientific Sessions, we presented six abstracts and delivered a lecture on the adverse effects on the heart of marijuana use—all virtually, as necessitated by pandemic protocols. One of these abstracts examined therapies for hemorrhagic shock (the condition in which severe blood loss leads to inadequate oxygen delivery and blood pressure does not recover even after restoration of blood volume), showing that these therapies protect against strokes. Another abstract focused on vaping and the size of experimental heart attacks.



Neurosciences Research

Our neurosciences research team also made forward progress in the face of the pandemic, even though many of our studies relied heavily on study participants who were no longer allowed onsite at HMRI. Nevertheless, we forged ahead with our investigations of Alzheimer's disease, traumatic brain injury, migraine and more. We tested new theories and made game-changing discoveries that brought us closer every day to our dream of developing screenings and finding cures for a range of brain diseases.

We secured key funding for our brain aging study from local foundations as well as from the National Institutes of Health and National Institute of Aging. Our researchers published 12 peer-reviewed papers and 15 conference abstracts in the course of the year, representing significant contributions in the field.

Key work in 2020 included examining two groups of biomarkers, including several metabolic changes in body fluids (urine and cerebrospinal fluid), as well as systemic brain and heart wave changes in study participants that occur before development of Alzheimer's disease. These discoveries could lead to simpler, noninvasive tests to help predict risk for the disease. We also found that plasma metabolism is related to chronic migraine and influenced by non-steroidal anti-inflammatory drugs—exciting advances in understanding these chronic illnesses.



"Science is not a one-person project. Success depends on an entire team working together. Every tiny detail requires the efforts of an entire team of people – and every detail is important. The key is understanding each other, and being grateful for the different ideas and insights each person brings."

— Xianghong Arakaki, MD, PhD
Assistant Professor,
Neurosciences and
Electrophysiology



"For me, the innovative research environment we are building is setting us up to be a well-known, well-respected lab. It will enhance translational research at HMRI and increase collaboration, such that we will make better use of the fantastic resources that are available to us. And someday, that will provide the forward momentum we need to get to the major breakthroughs of brain disease—breakthroughs that will allow for cost-effective screenings for Alzheimer's disease and new means of preventing chronic migraine."

— Alfred Fonteh, PhD
Research Associate Professor,
Neurosciences and Lipidomics/
Proteomics

Neurovascular Research

"Tough times reveal true colors and character. What I experienced at HMRI during the lab move and the pandemic was an incredible team spirit that overcame all sorts of difficulties. It created a bond of trust with everyone here, which builds a strong foundation to pursue our studies with confidence and freedom.... There is a vibrancy here that is perfect for bold new scientific pursuits. Good science takes patience and resilience. The research that we are doing is filled with energy and positivity and promise."

— Anju Vasudevan, PhD
Associate Professor
and Scientific Director,
Neurovascular Research

2020 marked the birth of our Neurovascular Research Department, with the recruitment of accomplished neurovascular scientist Anju Vasudevan. Dr. Vasudevan relocated her lab from Harvard Medical School to HMRI, where she is continuing her studies of angiogenesis and brain development. This work sits at the intersection of our other



The Neurovascular Research Team successfully relocated their laboratory from Boston to Pasadena in 2020.

research pillars—the heart and the brain—and could someday improve the lives of millions who suffer from mental illness.

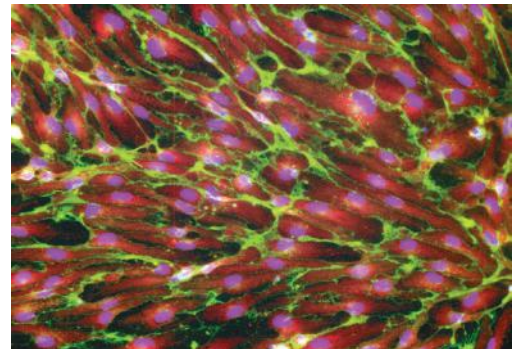
Her team published four peer-reviewed articles that shared new insights on the role of angiogenesis and the origins of mental illness.

These findings mark an exciting transition from

basic to translational research—a decade of work that has blossomed into new fundamental concepts in developmental neuroscience and psychiatry that may lay the foundation for treatments.

The neurovascular research team showed how prenatal NAD+ treatment can repair defects in blood vessel formation, normalize brain development and prevent mental illness. They also developed a stem cell-based vascular therapy for repair and regeneration in the adult brain that improves behavioral outcomes in a pre-clinical model of psychiatric disorder, within just one month of transplantation.

The formation of the neurovascular research team positions HMRI to continue its growth as a world-renowned biomedical research institution, pushing the boundaries of medical discovery.



Dr. Vasudevan and her team have successfully generated human embryonic forebrain endothelial cells (above) in the neurovascular laboratory—an important technique in studying the role blood vessels play in brain development and the potential onset of mental illness.

Colorectal Research

Our colorectal research team relocated in 2020 to the HMRI building, where it enjoys upgraded laboratory facilities and equipment and more opportunities to collaborate with other scientists. As we continue the quest to improve lives, we work towards opioid-free clinical pathways and enhanced recovery programs with the dual goals of keeping patients safer and improving the overall patient experience.

Clinical Director Howard Kaufman recruited two surgeons to the colorectal research team: Gabriel Akopian, MD, as a visiting scientist and Juliane Golan, MD, as a clinical instructor. These three doctors are also engaged in a private surgical practice that allows us to involve more patients in our research program. We added two residents to the research program (now totaling four), doubled our support staff from three to six, and acquired 3D ultrasound equipment.

Although much of our colorectal and pain management research was slowed because elective surgeries—even those for cancers—were canceled in 2020, we still produced solid evidence showing that robotic elective colorectal surgery allows for more complex operations and also can result in decreased hospital stays compared to laparoscopic surgery. We also determined that higher body mass index (BMI) is associated with increased opioid use following minimally invasive colon and rectal surgery—knowledge that can help lead to improved patient outcomes.

Liver Research

The liver research team continued investigations in the areas of hepatitis B, hepatitis C and hepatocellular cancer. We collaborated with expert peers to find innovative methods to detect liver cancer and bring about novel clinical treatments.

Some highlights of our work in 2020 included reviewing clinical guidelines related to the reactivation of hepatitis B and collaborating with Jihane N. Benhammou, MD, of Los Angeles Westwood Veterans Hospital to investigate the incidence of gastrointestinal cancers, especially liver cancer, in veterans exposed to Agent Orange while serving in the Vietnam War.



"My goal is to build more bridges between clinicians and scientists. There are huge cross-disciplinary opportunities to further the studies at HMRI, and it's very exciting."

— Howard S. Kaufman, MD
Clinical Professor and Clinical Director, HMRI Colorectal Research



"HMRI's innovative research keeps our scientific discovery accelerating, even during the COVID-19 pandemic. The year 2020 was a tremendous challenge to continue our work, establish new projects and secure needed funding. HMRI is very supportive of our staff and research and very adept at keeping the forward momentum, no matter what."

— Myron J. Tong, MD, PhD
Clinical Professor and Clinical Director, HMRI Liver Center



Inspiring the Next Generation

We find joy in the curiosity of young students, the commitment of rising fellows, and the tenacity of budding scientists. 2020 was a banner year for educational opportunities at HMRI, as we prepared for the launch of our formal Postdoctoral Fellowship Program and inaugural High School STEM Program.

POSTDOCTORAL FELLOWSHIP PROGRAM

Though HMRI has long hosted postdoctoral fellows, we began planning our first formal program in 2020, thanks to a transformational grant we received from a generous supporter. Our Postdoctoral Fellowship Program provides one-on-one time with a supervisor, guaranteed salary support, research funds, personalized laboratory training and a friendly environment that supports interaction with supervisors, peers and senior scientists. Through innovative projects, new technologies and multidisciplinary collaborations, fellows enjoy the opportunity to demonstrate originality, creativity and productivity, all of which contribute to a successful career in research. We received applications from more than 70 potential fellows and dove into planning under the direction of Dr. Anju Vasudevan.

SUMMER UNDERGRADUATE RESEARCH FELLOWSHIP

For more than 50 years, HMRI has hosted a Summer Undergraduate Research Fellowship, providing students with hands-on experience in biomedical research. The eight- to ten-week program offers participants the opportunity to experience the day-to-day workings of a research laboratory and develop a better understanding of the scientific process. At the end of the program, students give a presentation outlining their experience and research findings. This year, three fellows assisted our neurosciences team in chronic migraine research, studying the cortical cortex

area of the brain and using RNA sequencing to identify proteins specific to migraines. They also worked with Dr. Kloner and the cardiovascular team in a study detailing the effects of the novel coronavirus on the cardiovascular system.

STUDENT VOLUNTEER PROGRAM

In addition to our educational programs, HMRI offers volunteer opportunities for current undergraduate students who are interested in experiencing biomedical research. These aspiring scientists commit at least a quarter (and up to a year) of volunteer time working alongside our researchers, studying a variety of topics. They receive hands-on laboratory experience and develop essential technical skills. Though 2020 necessitated a virtual format for much of our work, we still were able to involve undergraduate volunteers in several projects.

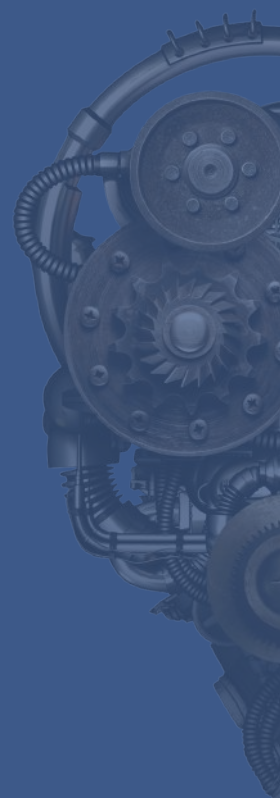
HIGH SCHOOL STEM PROGRAM

A bright spot in 2020 was announcing our High School STEM Program, Pasadena's first in the biomedical research field. Such learning opportunities can be an important tool for increasing students' exposure to the disciplines of science, technology, engineering and mathematics—especially for girls and students of color, who are underrepresented in these fields. We received applications and teacher recommendations from several rising juniors and seniors in the Pasadena Unified School District and prepared for the 2021 inaugural program.

Statement of Financial Position

September 30, 2020 (with comparative totals for September 30, 2019)

	2020	2019
ASSETS		
Cash and cash equivalents	\$ 4,366,776	\$ 4,322,171
Government and contract receivables	577,584	514,064
Other receivables	124,251	91,723
Promises to give, net	1,773,586	3,631,878
Prepaid expenses	59,540	12,771
Investments	34,396,538	29,803,299
Property and equipment, net	33,600,928	34,947,756
Beneficial interest in a charitable remainder unitrust	104,630	105,862
Patents, net	66,595	72,615
Patent deposits	318,051	303,334
Total assets	\$ 75,388,479	\$ 73,805,473
LIABILITIES AND NET ASSETS		
Liabilities		
Accounts payable	\$ 279,926	\$ 339,988
Accrued expenses and deposits	858,527	547,310
Refundable advance	438,898	822,468
Refundable advance - Paycheck Protection Program	1,039,287	-
Accrued pension cost	4,581,528	4,224,918
Total liabilities	7,198,166	5,934,684
Net Assets		
Net assets without donor restrictions		
Undesignated	30,941,507	33,791,407
Designated by the Board	20,764,177	17,701,733
Total net assets without donor restrictions	51,705,684	51,493,140
Net assets with donor restrictions	16,484,629	16,377,649
Total net assets	68,190,313	67,870,789
Total liabilities and net assets	\$ 75,388,479	\$ 73,805,473



Statement of Activities

Year Ended September 30, 2020 (with comparative totals for September 30, 2019)

	2020			2019
	Without Donor Restrictions	With Donor Restrictions	Total	
REVENUE, SUPPORT, AND GAINS				
Gain on sale of property and equipment	\$ 5,088,130	\$ -	\$ 5,088,130	\$ -
Government grants and contracts	2,685,370	-	2,685,370	2,206,191
Contributions, grants and bequests	1,092,523	1,378,557	2,471,080	5,009,406
Investment return utilized for operations	1,442,522	84,518	1,527,040	3,058,912
Clinical and royalty income	478,467	-	478,467	786,525
Rental income	113,873	-	113,873	345,302
Gain on charitable remainder unitrust	-	2,538	2,538	1,297
Net assets released from restrictions	2,391,168	(2,391,168)	-	-
Total revenue, support and gains	13,292,053	(925,555)	12,366,498	11,407,633
EXPENSES AND LOSSES				
Program services	8,188,475	-	8,188,475	6,978,613
Supporting services				
Management and general	3,382,261	-	3,382,261	2,927,725
Fundraising	476,953	-	476,953	458,060
Total supporting services	3,859,214	-	3,859,214	3,385,785
Loss on uncollectable promises to give	365,000	-	365,000	-
Total expenses and losses	12,412,689	-	12,412,689	10,364,398
CHANGE IN NET ASSETS FROM OPERATIONS	879,364	(925,555)	(46,191)	1,043,235

Statement of Activities

Year Ended September 30, 2020 (with comparative totals for September 30, 2019)

			2020	2019
	Without Donor Restrictions	With Donor Restrictions	Total	
NET INVESTMENT RETURN				
Interest and dividends	\$ 609,042	\$ 431,546	\$ 1,040,588	\$ 1,006,993
Realized gains on investments	388,933	232,275	621,208	319,023
Unrealized gains (losses) on investments	166,881	453,232	620,113	(12,423)
Investment fees	(32,544)	-	(32,544)	(45,934)
Total net investment return	1,132,312	1,117,053	2,249,365	1,267,659
LESS INVESTMENT RETURN DESIGNATED FOR CURRENT OPERATIONS	(1,442,522)	(84,518)	(1,527,040)	(3,058,912)
Investment return reduced by the portion of net investment return designated for current operations	(310,210)	1,032,535	722,325	(1,791,253)
Change in net assets before change in accrued pension cost	569,154	106,980	676,134	(748,018)
Change in Accrued Pension Cost	(356,610)	-	(356,610)	(1,045,021)
Change in Net Assets	212,544	106,980	319,524	(1,793,039)
Net Assets, Beginning of Year	51,493,140	16,377,649	67,870,789	69,663,828
NET ASSETS, END OF YEAR	\$ 51,705,684	\$ 16,484,629	\$ 68,190,313	\$ 67,870,789

2020 Achievements at a Glance

Despite community shutdowns and stay-at-home orders, HMRI achieved notable success in 2020. Our Bob Mackin Memorial Scientific Lectures, convened via Zoom, drew a higher attendance than ever before. We secured critical grant funding for our groundbreaking research. And our scientists contributed to the growth and sharing of medical knowledge not only through research, but also through articles, abstracts and online presentations.

