REMEMBERING OUR FOUNDER

James T. Willerson, MD
IMMPact Report is published by McGovern Medical School.
All correspondence should be addressed to:
Office of Communications
6431 Fannin, B.340
Houston, TX 77030
E-mail: m.darla.brown@uth.tmc.edu
Articles and photos may be reprinted with permission.

About the cover
The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases was the brainchild of founder James T. Willerson, MD, who died Sept. 16, 2020. This issue of the IMMPact Report is a tribute to him.

IMMPact Report is published by McGovern Medical School.
All correspondence should be addressed to:
Office of Communications
6431 Fannin, B.340
Houston, TX 77030
E-mail: m.darla.brown@uth.tmc.edu
Articles and photos may be reprinted with permission.

Editor
Darla Brown, Director, Office of Communications

Contributors:
Darla Brown
IMM Faculty

Design:
Roy Prichard

Photography:
Dwight Andrews
Archival Photography

The University of Texas Health Science Center at Houston (UTHealth) Leadership
Giuseppe N. Calasardo, MD
President
Kevin Dillon, MBA, CPA
Senior Executive Vice President, Chief Operating Officer
Michael Blackburn, PhD
Executive Vice President, Chief Academic Officer
LaTanya Love, MD
Executive Vice President, Student Affairs and Diversity
Richard Andrusy, MD
Executive Dean ad interim, McGovern Medical School

IMM Senior Administrator
John F. Hancock, MA, MB, BCHir, PhD, ScD, MRCP(UK), FRACP
Executive Director

IMM Advisory Council Members
Alan Baden
David Beck
John Beckworth
Louana Frois
Theodore Frois
Irma Gagli, MD
Steven Gordon
John F. Hancock, MA, MB, BCHir, PhD, ScD, MRCP(UK), FRACP
John Mackel
Rodney Margolis
John McDonald
Dudley Oldham
Charles Parker
Judith Perkins
Beth Robertson
Shavonnah Roberts Schreiber
Ralph Thomas
Damon McWilliams

The University of Texas System Board of Regents
Kevin P. Eltife, Chairman
Janiece Longoria, Vice Chairman
James C. “Rad” Weaver, Vice Chairman
David J. Beck
Christina Melton Crain
Patrick O. Ojuga, II
R. Steven Hicks
Jodie Lee Jiles
Nolan Perez, MD
Keley L. Warren

For information on supporting programs at the McGovern Medical School and the IMM, contact giving@uth.tmc.edu
713-500-3200

OOC-Marketing-4-300-3/21
## Contents

<table>
<thead>
<tr>
<th>Page</th>
<th>Section</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Director’s Message</td>
</tr>
<tr>
<td>3</td>
<td>Mission</td>
</tr>
<tr>
<td>8</td>
<td>Features</td>
</tr>
<tr>
<td>4</td>
<td>Dr. Willerson: A vision for excellence</td>
</tr>
<tr>
<td>8</td>
<td>Remembering Dr. Willerson</td>
</tr>
<tr>
<td>12</td>
<td>Constructing support for the IMM</td>
</tr>
<tr>
<td>18</td>
<td>Fayez S. Sarofim Research Building Timeline</td>
</tr>
<tr>
<td>20</td>
<td>Center for Cardiovascular Genetics</td>
</tr>
<tr>
<td>23</td>
<td>Center for Human Genetics</td>
</tr>
<tr>
<td>29</td>
<td>Center for Immunology and Autoimmune Diseases</td>
</tr>
<tr>
<td>33</td>
<td>Center for Metabolic and Degenerative Diseases</td>
</tr>
<tr>
<td>42</td>
<td>Center for Molecular Imaging</td>
</tr>
<tr>
<td>47</td>
<td>Center for Stem Cell and Regenerative Medicine</td>
</tr>
<tr>
<td>62</td>
<td>Center for Translational Cancer Research</td>
</tr>
<tr>
<td>70</td>
<td>Texas Therapeutics Institute</td>
</tr>
<tr>
<td>77</td>
<td>IMM Service Centers</td>
</tr>
<tr>
<td>79</td>
<td>By the Numbers</td>
</tr>
<tr>
<td>81</td>
<td>Gift Report</td>
</tr>
</tbody>
</table>
I am pleased to introduce the latest annual IMMpact report for The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM). The IMM is a stand-alone research institute that is embedded within McGovern Medical School. The IMM mission is to deliver translational outcomes from research in molecular medicine that benefit patients. This mission was proposed by Dr. James Willerson, whose passion for molecular medicine was the driving force for the founding of the IMM. It was his single mindedness coupled with phenomenal fundraising and philanthropy that saw phase one of the project completed in 2006 with the opening of the Fayez Sarofim Research Building that houses the IMM. I say phase one because the opening of this remarkable research building was just the beginning of the outstanding and innovative translational science that continues to define the IMM. Sadly, Dr. Willerson passed on the 16th of September this past year and so to honor him, we are dedicating this year’s report to him by going back to the symposium, which was scheduled in April because of COVID concerns. We have not yet decided on a new date, but if the COVID vaccination program, currently underway in Houston, continues to drive down new cases, then a fall symposium may be possible. In the interim we are in the process of developing an IMM Webinar series as an alternative to the symposium, which will showcase short research presentations from our faculty together with question-and-answer sessions and special video coverage of their respective laboratories. We hope to start releasing these webinars next month.

Despite these challenges I am pleased to report, that once again IMM faculty have nevertheless excelled in NIH, DOD, CPRIT and other extramural grant funding. Over the financial year just ended, our new grants and contracts matched last year, which has a best ever for new funding, capping increases in our extramural research programs pursued by each of our current IMM faculty. There are many metrics that can be used to define research and institutional success, including grant funding, scientific publications, spin our companies, and the capacity to recruit and retain stellar scientists from around the world. By all these metrics the IMM excels; an impressive and enduring legacy of our founder, Dr. Willerson. As with everywhere, COVID-19 impacted our operations this year although not as extensively as some of our sister institutions within the TMC. Research operations were scaled back in April whilst new operating procedures were put in place to ensure safe working in the laboratories and then ramped up again in May, such that by summer all labs were operating pretty much as normal, albeit with all workers masked and social distancing observed. Unfortunately, we had to cancel the IMMpact symposium, which was scheduled in April because of COVID concerns. We have not yet decided on a new date, but if the COVID vaccination program, currently underway in Houston, continues to drive down new cases, then a fall symposium may be possible. In the interim we are in the process of developing an IMM Webinar series as an alternative to the symposium, which will showcase short research presentations from our faculty together with question-and-answer sessions and special video coverage of their respective laboratories. We hope to start releasing these webinars next month.

Despite these challenges I am pleased to report, that once again IMM faculty have nevertheless excelled in NIH, DOD, CPRIT and other extramural grant funding. Over the financial year just ended, our new grants and contracts matched last year, which has a best ever for new funding, capping increases in our extramural research funding for each of the last seven years. It is a testament to the remarkable quality and creativity of our scientists that the IMM remains so successful in attracting research funds. That said, full implementation of our mission remains heavily dependent on attracting support from alternative sources, including research charities and foundations, industry collaborations, and, most importantly, the continuing generosity of our friends and donors. In this context, we are always deeply appreciative of the strong work and dedication of the IMM advisory council, which plays a key role in the continued growth and development of the IMM.

In conclusion I want to return to Dr. Willerson, his contributions to teaching, education, medical service and research at UTHealth and the broader TMC are too lengthy to list, but for all of us here paramount is his gift of the IMM, and the enduring legacy of scientific and medical discoveries that have only been possible because of it. In Dr. Willerson’s own words… “Our genes and proteins are the game official of our lives. They already know if you have a cancer in your future. Or dementia. Or some other devastating disease. We must identify these genes and proteins in our bodies and discover ways in which they might be altered to prevent these diseases from occurring in the first place . . . That research is the role of the IMM.”

We at the IMM are indeed privileged to be realizing Dr. Willerson’s vision for molecular medicine at UTHealth. If you would like to investigate how you also can help us further in this regard, I would be very pleased to talk with you personally.

John Hancock, MA, MB, BCHir, PhD, ScD
Executive Director, Institute of Molecular Medicine
John S. Dunn Distinguished Chair in Physiology and Medicine

The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM) is a research institute that seeks to investigate the causes of human diseases at the cellular and molecular levels, using DNA and protein technologies to elucidate disease mechanisms. This development and progress are of particular interest for future planning in the increasingly important area of clinical research. The institute endeavors to design methods of rational therapy and, wherever possible, strategies for the prevention of human diseases.

Advances in molecular and cell biology have enormous potential for innovative medical research and the future practice of medicine with more novel therapies. These approaches have been most successfully used to determine the causes of infectious disorders and genetic diseases.

However, it is clear that molecular and cell biology will play a major role in clarifying the causes of many unsolved problems of modern medicine, such as heart disease, hypertension, vascular disorders, major mental illnesses, and inflammatory and immunologic diseases. The research of the institute’s investigators is inspiring and promises to fulfill the mission of the IMM.

Because the applications of molecular and cell biology to medical practice are of major importance to product development in biotechnology and the pharmaceutical industry, the IMM has the potential and desire to form important links and collaborations between its own research activities and various industries to apply its discoveries and intellectual properties to pharmaceutical opportunities.

As an institute of McGovern Medical School, the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases strives to set the example for research excellence and collaboration locally, nationally, and internationally.
This was the vision of James T. Willerson, MD, which was realized as the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases rose from a plan to reality with the backing of UTHealth and UT System leadership, colleagues, community members, elected officials, and supporters who believed in the future of science.

Dr. Willerson was a pioneer who embraced a vision of excellence in a quest to create a scientific institute unlike any other. Today that institute is known as the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (IMM).

Born Nov. 16, 1939, Dr. Willerson grew up in San Antonio with both parents as doctors in private practice. Dr. Willerson had stated his firm intention to follow in their footsteps early in life. His introduction to Dr. Denton Cooley, founder of the Texas Heart Institute, as a teenager, had a profound impact on the direction of his career.

A proud graduate of The University of Texas at Austin, Dr. Willerson earned his medical degree from Baylor College of Medicine and completed postgraduate training at Harvard Medical School and Massachusetts General Hospital. Prior to his work in Houston, he was on the faculty of The University of Texas Southwestern Medical School in Dallas. As president of UTHealth, a position he held from 2001-2008, Dr. Willerson aimed to build a university foundation poised for greatness. The IMM was integral to that success.

“I am very proud of the fact that we were able, with Beth Robertson and Rodney Margolis and many friends in Houston, Legislature, UT Regents, to build the IMM and continue to recruit some of the world’s best scientists,” he said back in 2008. “As I’ve said about each of our schools, poised for greatness depends on our constant recruitment and retention of the best scientists with a commitment to basic medical science discovery to translate to patients for cure and prevention of their diseases so wonderfully placed in the world’s largest medical center with colleagues. I expect great discoveries that benefit mankind to come from our IMM to uplift scientific discovery and translate to our schools, to develop strong research efforts with collaborative grants and educational programs.”

Throughout his career, Dr. Willerson always stressed the importance of all three areas of the mission – education, patient care, and research, noting no one area was more important than the other. “We need to be outstanding in each area,” he said.

Dr. Willerson always led by example. Not only was he a mentor and teacher, a world-renowned expert pursuing gene therapy and stem cell research, he also was the caring physician for more than 2,000 patients.

The IMM was born in 1989. That was the year Dr. Willerson came to Houston – recruited as chair of the Department of Internal Medicine at The University of Texas Medical School at Houston (now known as McGovern Medical School).

Dr. Willerson imagined the institute as a collaborative environment of scientists not only elucidating the roles of genes in disease but also developing genomic-tailored therapies to combat the most challenging diseases. “Molecular medicine is a very exciting field, and we must be at the cutting-edge,” he once said. “Genes are the
Our success is dependent on scientific talent, and, most importantly, our will to discover and apply new knowledge in technology to better the human condition.

-James T. Willerson, MD

drugs of the future. Better yet, if you can predict disease or prevent it altogether, then we can reduce human suffering and the difficulties — including cost — that go with it.”

In 1993, Dr. David Low, then-president of the UT Health Science Center, formally announced the university’s support of the institute with the kick-off of a $40 million fundraising initiative headed up by Rodney Margolis.

In 1995, Dr. Willerson recruited the first scientific director of the IMM, Hans Muller-Eberhard, MD, PhD. His wife, Irma Gigli, MD, was recruited to lead the IMM’s Center for Immunology and Autoimmune Diseases. The next decade was spent growing and focusing the IMM as it moved into temporary space in the Texas A&M Institute of Biosciences and Technology, on the outskirts of the Texas Medical Center.

As the human genome sequencing race transfixed the world, Dr. Willerson capitalized on the scientific fervor, winning over the support of generous community members and elected officials with his vision of the IMM. A campaign was initiated — this one chaired by Beth Robertson and Ben Lowe, with a fund-raising goal of $200 million.

More than $236 million later, the seven-story Fayez S. Sarofim Research Building opened as the Institute’s home in 2006, ushering in a new era of research for UTHealth. With scientists in modern labs, pursuing the latest research in a modern environment created to further molecular medicine, the vision became reality.

By 2006, seven research centers had been established at the IMM — each staffed with outstanding faculty pursuing novel work: Cardiovascular Diseases, Cell Signaling, Human Genetics, Immunology and Autoimmune Diseases, Protein Chemistry, Stem Cell Studies, and Nanotechnology. Today’s eight centers are targeted to innovative areas to produce discoveries and translational outcomes.

Dr. Willerson never considered his job work. “It’s not work; it’s opportunity,” he once said. “My goal is to make The University of Texas Health Science Center at Houston what it is supposed to be — a health university with excellence at each of our schools.”

Following the 9/11 attacks on our nation, he sent a university-wide message, reminding “each one of us has an uncertain number of days on this earth in which to do meaningful things. Let us recommit ourselves to using them wisely and work together to create an environment here in which all of us have the opportunity to be the best we can be.”

Dr. Willerson died Sept. 16, 2020, leaving a legacy of excellence — the crown jewel of which was the IMM. At the time of his death, he was the president emeritus, director of cardiology research, and co-director of the Cullen Cardiovascular Research Laboratories at Texas Heart Institute at CHI St. Luke’s Health—Baylor St. Luke’s. On Nov. 19, 2020, the UT System Board of Regents unanimously named him president emeritus of UTHealth.
Remembering Dr. Willerson

Several of our current Institute of Molecular Medicine faculty were founding faculty members, on staff when Dr. James T. Willerson was leading the Institute. We asked them for their remembrances of our founder.

Ali J. Marian, MD
Professor and Director, Center for Cardiovascular Genetic Research, George and Mary Josephine Hamman Foundation Distinguished Professor in Cardiovascular Research

Dr. Marian published a full paper on the memory of Dr. Willerson in Circulation Research, which may be found at go.uth.edu/willerson. An excerpt is included below:

Leadership was natural to him. It was in his genes. It was coupled with his huge vision, the vision of unifying all forces against cardiovascular diseases. He led at The University of Texas at Southwestern and at The University of Texas Health Science Center at Houston. As the president of the university, he built institutions, established programs, and recruited world-class scientists. He was the founding father of the Institute of Molecular Medicine. He had the strong conviction that from the basic science discoveries will come the knowledge the predict, prevent, and cure cardiovascular diseases.

And he was truly a gracious man. When he was editor of Circulation, I was one of his associate editors, and we were at the annual meeting of the editorial board. He acknowledged several of the associate editors and forgot to mention my name and likely a few others. This is typically not a big deal as no one expects all of the editors to be acknowledged. A day later, he realized he had missed a few names. I received an apology in person, a personal handwritten note, and a beautiful bouquet of flowers. Of course, none of this was expected, and likely the others he forgot received the same treatment.

Ba-Bie Teng, PhD, FAHA
Professor of Molecular Medicine
The Jerry and Mauzy Rubinstein Distinguished Professorship in Heart Research Center for Human Genetics

I joined UTHouston, Institute of Molecular Medicine, in May of 1998 as a young faculty. I remember meeting Dr. Willerson to discuss a proposed collaborative research project. He greeted me and our other collaborators with his famous, fatherly, warm smile and gave us constructive criticism on how to proceed with our project. Dr. Willerson’s enthusiasm for science and medicine was infectious, and it was a motivating force in my career. It was his vision and perseverance that built the Institute of Molecular Medicine and helped it become an icon of research excellence in the Texas Medical Center. I am grateful to have known Dr. Willerson. He will be remembered.

Peter Doris, PhD
Professor and Director, Center for Human Genetics
Mary Elizabeth Holdsworth Distinguished University Chair in Metabolic and Inflammatory Disease Research

In 1979, I enrolled in the PhD program in physiology at the University of California, Riverside. One of the professors who served on my advisory and examination committees was recently arrived in California from her training at UT Southwestern. She was interested in cardiac glycoside drugs and heart function. As I spent time around her in the lab and in classes, I began to hear of a person who she viewed as a legend in cardiology … a person who bridged excellence in clinical medicine with outstanding innovation in heart research. That person was James T. Willerson, MD. I took note of her impressions and held on to them.

In 1997, I visited Houston in connection with a possible faculty opportunity in the newly created Institute of Molecular Medicine. As I learned about how this new institute had come into creation, I was told that, to attract the legendary James T. Willerson, MD from Dallas to Houston, he was offered the opportunity to bring to reality his vision that contemporary biomedical research needed to move into a new era wherein the tools of molecular biology were harmonized and integrated with the problems of clinical medicine.

As I understood whose vision this was, my past recollections about Dr. Willerson as a person committed to advocating for medical research that bridged bench and bedside, created a surge of excitement about the new opportunity I was exploring.

During that visit to Houston, I spent 30 minutes with the legend. Not all legends are larger than life. In my mind, such a person was supposed to be huge both in persona and in stature. But Jim Willerson was a compact person with a quiet, deliberate, and modest demeanor. I was impressed that he wasted no energy; his manner was concise and direct, and he was completely lacking in self-doubt. He knew what he believed, and he believed it because it was obvious to him from his own experience in medicine. This was no follower of the ideas of others. I was certain this was a leader who was completely harmonized with my own aspirations in medical science.

During the early years at IMM, Dr. Willerson was heavily engaged in advancing the nascent institute. He was patient, never hurried, but persevered. I saw his persuasiveness. It surprised me. I learned that leadership and innovation was not about loud or noisy claims regarding his own importance or that of his mission. He reached out to the audience of potential donors who might help build and support his vision in his typical earnest, but restrained manner. Quiet, calm, clear, moderate, and confident.

The combination was utterly persuasive. He generously moved the spotlight from his own aspirations to the actual investigators who were beginning to bring the vision of IMM to reality.

As we moved forward to actually raising and occupying the splendid building that is now our home and filling it with science, I was sometimes surprised to find that Jim Willerson had little interest in taking credit for the new institute that was forming. For him, I think, the accomplishment was not in being recognized for the achievement that was his vision, but in the knowledge that he had helped create something unique and good and valuable. His effort was genuinely for the benefit of the world he lived in and loved.
Dr. Willerson’s legacy in the IMM is a vision of how you can integrate human beings and different components. The IMM is his major contribution, and the opening of the new building of the institute was a very special day for both of us. I think Dr. Willerson loved the IMM, and his devotion to the institute cannot be denied.

I don’t think many people know of how the idea of the institute came about. I was chair of the Department of Dermatology at the University of California San Diego when I was asked to interview a candidate to be the head of cardiology. The candidate was Dr. Willerson. He walked into my office and saw a large poster of a lecture that my husband (Hans Eberhard) had given the year before for an important organization. He was sort of fixed looking at it, and said, “I have a great deal of admiration for that man.” And I burst out laughing and said perhaps it’s good to be interested in your own husband. We used different names and had our own careers. Dr. Willerson told me he was not interested in the job for which I was to interview him, but said he was looking for good faculty for when he took a position in Houston. He later met with my husband in Germany and said he had an idea of an institute that studied diseases from many different aspects. He continued to develop this in his mind with Hans as the director and me as the codirector. Finally, he got us to agree, and we then looked for architects and made all of the plans. Before the building was built, we had the top two floors of the A&M building on Holcombe and worked in the labs and recruited people. My husband developed advanced prostate cancer and died after a few years. I worked very hard with the architects to develop the concept that eventually became the building of the IMM. It’s a place that I love.
Constructing support for the IMM

Building and sustaining relationships with generous and supportive friends of the IMM has proven to be one of Dr. James Willerson’s most enduring legacies.

“I am very proud of the fact that we were able, with Beth Robertson and Rodney Margolis and many friends in Houston, the Legislature, the UT Regents, to build the IMM and continue to recruit some of the world’s best scientists,” Dr. Willerson once said.
Houston is a very generous city, and Dr. Willerson was an excellent and caring physician whose scientific knowledge and drive encouraged hundreds to understand, and finance, the power of molecular medicine. “He told me that when he arrived at UTHealth, nothing was singularly more important to him than accelerating and cementing the institution’s research capacity,” recalled Randa Safady, PhD, UT System vice chancellor for external relations, communications, and advancement services. “He knew it was the best way to recruit the best and brightest scientists to UTHealth and the TMC, to draw increased sponsored research support, and to be more competitive on a national and international level. He said he would always be ‘relentless and in a hurry’ with this pursuit. He successfully pushed for more research space to achieve those aspirations.”

Focused on growing research, Dr. Willerson recruited Hans J. Muller-Eberhard, MD, as director and his wife, Irma Gigli, MD, as chief director of the IMM. A team of scientists soon began working in two floors of the Texas Medical Center’s Texas A&M research building. Planning quickly started for an independent IMM building, on which Dr. Gigli worked hand-in-hand with the architects. “I put all of myself in what came to be, and the community was happy in seeing what the money could help to develop,” she said.

“I still remember vividly his vision for the IMM, which he told me about in 1990,” said Ralph Thomas, former chair of the UTHealth development board and senior vice president of Fayez Sarofim & Co. “He impressed me with his vision and dedication. It was inspiring.” In 1995, Dr. Willerson set his sights on realizing a new home for the IMM—a 223,000-square-foot state-of-the-art building, selecting Rodney H. Margolis, Houston community leader, philanthropist, and long-standing friend, to help lead a fundraising initiative to help construct it. “Jim asked me to head up the campaign and thought Dr. Eberhard was brilliant. We would solicit for philanthropy, and people were so receptive they would tell their story. “We would go to a couple of philanthropic groups who had never given money for molecular medicine, and after he spoke they would say, ‘how much money do you want?’” recalled Margolis, who had known Dr. Willerson since their student days at The University of Texas at Austin, where they both were members of the Texas Cowboys.

“A brilliant diagnostician and even better caregiver, Dr. Willerson was everybody’s doctor. He had a list of probably 2,500 or 3,000 patients. All ‘grateful patients’, but he knew all of them and found time for all of them,” said Beth Robertson, who in 2001 stepped up as co-chair, with the late Ben Love, of the New Frontiers Campaign, whose goal was to raise $200 million in support of the IMM. Dr. Safady recalled the New Frontiers Campaign’s early days. “Dr. Willerson was thrilled when Beth said she would lead the campaign. I remember she said she couldn’t head up another campaign, and Dr. Willerson said she was the only one he could go to, so she said yes. You can’t say no to Dr. Willerson, and she was so committed to him and the IMM, and the results showed,” Dr. Safady said. “We traveled around Houston and the state where he pitched the idea of the IMM—a world-class institute that would attract world-class researchers/MDs to UT and TMC to make big discoveries that would translate into curing human disease here,” Robertson recalled. “And we had amazing results from these grateful patients. They wanted to support Dr. Willerson and his crusade against human disease. We all believed in Dr. Willerson.”

“We were able to raise a great deal of money,” agreed Dr. Gigli, the Walter and Mary Muscher Distinguished Professor in Molecular Medicine and the Hans J. Muller-Eberhard Chair in Immunology director emeritus. “But the community won’t give money unless it is going to something worthwhile.” Dr. Gigli also remembered Robertson’s involvement. “Beth Robertson was unbelievable,” she recalled. “She was very involved and expanded our enthusiasm for the institute.” Throughout the life of both campaigns, more than $240 million was raised through 350 gifts. The largest gifts were $25 million from building namesake Fayez S. Sarofim, founder and owner of the investment firm Fayez Sarofim & Co., and $20 million from the Brown Foundation, Inc., for which the IMM is named.

“The Brown Foundation is proud to join UTHealth in celebrating Dr. Willerson’s legacy of excellence and community impact. We are honored to have been an early supporter of his pioneering leadership,” said Will Mathis, on behalf of Foundation Trustees. The generous support from all donors resulted in the recruitment of world-renowned scientists—through the creation of 27 faculty endowments—and ultimately the 2006 grand opening of the Fayez S. Sarofim Research Building, home of the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases. IMM for short. “We recently had a good laugh about a meeting we had some 14 years earlier about the long name as it would appear in signage and on buildings. He initially insisted on signage in brightly illuminated orange— in fact, he wanted the whole UTHealth
Dr. Willerson created in the IMM what he envisioned as the standard for medical research. Robertson observed. “He came to UT because he loved the institution. He was a brilliant diagnostician, an incredible leader and had so much energy, doing everything at once.”

“He was prepared to demonstrate that this type of quality and world-class research was what he was thinking for the whole institution, that it would give us a vision of how we would take it from the lab to the bed,” she said.

His supporters and friends still marvel, remembering his unique abilities and talents.

“There won’t be another person like Jim Willerson to cross your path or my path again, for dedication or loyalty again – can’t find anyone stronger again,” Margolis added. “Jim was so dedicated to the concept of molecular medicine there are not words in the dictionary to celebrate his dedication to medicine.”

“How on earth does Jim do it?” Thomas wondered. “There are not that many hours in the day – he had at least three different roles going at the same time and not one was left beside by his emphasis on something else – he was dedicated and well-balanced.”

The IMM, most agree, is Dr. Willerson’s crowning achievement.

“The IMM has done what he hoped, I think,” Robertson said. “A high-quality pinnacle is what he wanted. Jim Willerson was the high-quality pinnacle person. There was never a dull moment raising money with him. He was not going to be denied. A big UT fan and former UT swimming star, he was very competitive. I admired him – not just for his energy/drive and his thoughtful and encyclopedic knowledge, but also but for his empathic kindness to others. I was blessed to have him as my doctor, but more blessed to have him for my friend.”

“Dr. Irma Gigli, a founding leader of the IMM.

“Community supporters included Mayor Bill White.

“The IMM and Sarofim building were gold-standard examples of how investments from the state, UT System, and philanthropy came together to advance discovery and health research and care for the people of Texas and beyond.”

- Dr. Randa Safady, UT System vice chancellor for external relations, communications and advancement services

Beth Robertson co-chaired the New Frontiers campaign.
<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1989</td>
<td>James T. Willerson, MD joins The University of Texas Health Science Center at Houston and announces his vision to develop an Institute of Molecular Medicine for the Prevention of Human Diseases (IMM) in Houston's Texas Medical Center. Fundraising begins.</td>
</tr>
<tr>
<td>1993</td>
<td>M. David Low, MD, PhD, president of the UT Health Science Center at Houston, formally announces a plan to establish an institute that specifically will target the prediction and prevention of human diseases – The Institute of Molecular Medicine for the Prevention of Human Diseases. He announces the first receipt of gifts totaling $7.2 million to enhance molecular research. A $40 million fundraising initiative is announced that will later be expanded to the $200 million New Frontiers Campaign to house and support the new institute.</td>
</tr>
<tr>
<td>1995</td>
<td>Dr. Gigli becomes the IMM’s first faculty member. Plans to house the IMM in the renovated UT Speeds and Herring Building are revised as space is leased and readied in the Albert Alkek Building of the Texas A&amp;M Institute of Biosciences and Technology.</td>
</tr>
<tr>
<td>1995</td>
<td>Müller-Eberhard, MD, PhD, arrives in Houston. Prior to his appointment he was director of the Berhard Hocht Institute for Tropical Medicine in Hamburg, Germany. He begins developing research programs in immunology, infectious diseases, cardiovascular diseases, neurobiology, and cancer research at the genetic level. Recruitment of scientists in these specialties begins.</td>
</tr>
<tr>
<td>1998</td>
<td>Dr. Müller-Eberhard dies at MD Anderson Cancer Center.</td>
</tr>
<tr>
<td>2003</td>
<td>The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases becomes the official name of the institute, in recognition of a $20 million gift by The Brown Foundation, Inc.</td>
</tr>
<tr>
<td>2006</td>
<td>UT System Regents approve naming the new building The Fayez S. Sarofim Research Building in recognition of the largest gift ever received by The University of Texas Health Science Center at Houston—$25 million to advance stem cell research.</td>
</tr>
<tr>
<td>2006</td>
<td>First faculty and staff occupy new Sarofim Research Building.</td>
</tr>
<tr>
<td>2006</td>
<td>John Hancock, MA, MB, BChir, PhD, ScD, is appointed executive director of the IMM.</td>
</tr>
</tbody>
</table>
T he IMM Center for Cardiovascular Genetics, established in 2006, focuses on elucidation of molecular genetics, genomics, and pathogenesis of cardiovascular diseases with the objective of utilizing the discoveries to prevent and treat cardiovascular diseases in humans. The Center provides specialized clinical services to patients with genetic cardiovascular disorders at the Cardiovascular Genetic Clinic. The Center also has a Research Clinic, which is utilized for clinical research activities, including NIH- and industry-sponsored clinical trials.

Mission: To prevent and treat cardiovascular diseases in humans through identification and targeting of the pathogenic genes and pathways. 

Faculty: Priyatansh Gurha, PhD, assistant professor; AJ Marian, MD, professor

General theme of the research programs: The research programs at the Center starts with human molecular genetic studies aimed at identifying the causal genes for human cardiovascular diseases. The focus is primarily on hereditary cardiomyopathies, which are important causes of sudden cardiac death and heart failure. Genetic analysis is performed by whole exome and genome sequencing. Genetic discoveries are then coupled with the genomic studies to identify differentially expressed coding and non-coding transcripts and dysregulated pathways, chromatin remodeling, and DNA methylation in cardiomyopathies. The integrated approach is used to identify the key pathogenic regulatory pathways for preventive and therapeutic genetic and pharmacological interventions. The findings in the model systems are extended to human patients through pilot randomized placebo-controlled double-blind clinical trials. The findings provide the platform for large-scale multi-center efficacy clinical trials.

Research Programs: The research programs are as follows:

I. Human molecular genetic studies of cardiomyopathies: We have a repository of several hundred cases and their family members with cardiomyopathies, including hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), and arrhythmogenic cardiomyopathy (ACM). Pathogenic and causal variants are identified by whole exome sequencing in the probands and family members. These studies have identification of new disease-causing genes and have advanced the genetic causes of heart failure.

II. Genomics and epigenetic studies of human heart failure and mouse models of cardiomyopathies: The studies predominantly relate to DCM and ACM and included whole transcriptome analysis by RNA-Seq, DNA methylation analysis, and analyzing chromatin remodeling by ChIP-sequencing. Specfific epigenetic regulators of gene expression are identified and targeted in order to delineate their functions in the heart.

III. DNA damage response in human hereditary cardiomyopathies: We have detected increased double stranded DNA breaks (DSBs) in human hearts from patients with hereditary cardiomyopathies and in mouse models. Studies are ongoing to define genomic characteristics of the DSBs and to define the pathogenic role of DNA damage response pathways in heart failure.

IV. Therapeutic targeting of dysregulated pathways in cardiomyopathies: Dysregulated pathways identified through integrated genomic studies are targeted through genetic and pharmacological interventions in model organisms and their effects on survival, cardiac function, and clinical outcomes are analyzed. A major focus currently is on the canonical WNT and the Hippo signaling pathways.

V. Clinical Studies: The Center participates in investigator-initiated single pilot clinical trials as well as industry-sponsored multi-center clinical trials in hereditary cardiomyopathy. An NIH-sponsored double-blind randomized pilot study (HALT-HCM) in patients with HCM was recently completed. The Center also participates in industry sponsored clinical trials in cardiomyopathies.

AJ Marian, M.D.
Center Director & Professor

Our long-standing research objectives have been to delineate the molecular genetics, genomics, and pathogenesis of hereditary cardiomyopathies in humans and apply the discoveries to prevent the evolving and reverse the established phenotypes of heart failure and sudden cardiac death. We have active research programs in three core themes of hereditary cardiomyopathies: Arrhythmogenic Cardiomyopathy (ACM): ACM is an enigmatic form of hereditary cardiomyopathies that clinically presents with cardiac arrhythmias, heart failure, and sudden cardiac death, particularly in the young. A unique feature of this disease is a gradual replacement of cardiac myocytes with fibro-adipocytes. There is no effective therapy for ACM. Hypertrophic Cardiomyopathy (HCM): HCM is the most common form of hereditary cardiomyopathies, affecting ~1 in every 500 individuals in the general population. The affected individuals are typically asymptomatic and sudden cardiac death is often the first manifestation of this disease. HCM is the most common cause of sudden cardiac death in the young. While there are effective therapeutics to alleviate patient’s symptoms, there is no effective therapy to prevent or reverse the disease process. Dilated Cardiomyopathy (DCM): DCM is genetically the most heterogeneous form of hereditary cardiomyopathies and a major cause of heart failure and heart transplantation in the young. The affected individuals often present with symptoms of heart failure, cardiac arrhythmias and sometimes, sudden cardiac death. There are a number of effective pharmacological and non-pharmacological therapies for DCM but currently there is no cure for DCM. The overall approach entails an integrated approach that includes human molecular genetic studies through high throughput whole exome and genome sequencing to identify the causal genes and mutations, followed by genomic studies including transcriptomics and epigenetics to define molecular remodeling of chromatin in the presence of causal mutations. The aim is to link the causal mutations to genomic remodeling and to the pathogenic pathways. The re- sponsible molecular mechanisms are identified through molecular mechanistic studies in genetically modified animal models and cultured cells. The molecular discoveries are then utilized to intervene in model organisms, utilizing genetic and pharmacological approaches that target the pathogenic pathways, in order to prevent the evolving phenotype and reverse or attenuate the established phenotype. These findings in the model organisms are extended to human studies through pilot randomized placebo-controlled double-blind clinical trials. The findings, if favorable, are pursued through collaborative large-scale clinical trials.

General theme of the research programs:

- Identification of causal genes for heart failure and sudden cardiac death
- Identification and characterization of epigenetic and transcriptomic changes in hereditary cardiomyopathies
- Identification and characterization of the pathogenic molecular pathways in patients with hereditary cardiomyopathies
- Delineation of the role of the mechanosensing signaling pathways in the phenotypic expression of hereditary cardiomyopathies
- Defining and characterizing the role of DNA damage in hereditary cardiomyopathies and the utilities of the DNA damage pathway in therapeutic targeting
- Vitamin A and Explore studies: Industry–sponsored clinical trials to test efficacy of an ATRA modulator on improving symptoms and exercise tolerance in patients with obstructive (Maverick) and non-obstructive (Explorer) hypertrophic cardiomyopathy.

**KEY PUBLICATIONS**


Exercise Restores Dysregulated Gene Expression in a Mouse Model of Hypertrophic Cardiomyopathy. Chen et al. JMC, 19, 1-10, e1360145-146. PMCID: 32484798

**LAB MEMBERS**

Post doctoral fellows: Shinha C Merchandy; Leila Roughanbould, PhD

Research assistant: Shang Tan

Research and clinical nurse: Tanvi Tal, RN
The main objective of my research is to understand the molecular mechanisms that coordinately regulate gene expression and contribute to the pathogenesis of heart failure. Within this theme, we are studying the function of epigenetics and non-coding RNAs in proliferation, differentiation, and maturation of myocytes and how alteration of these interlinked processes eventually leads to cardiac dysfunction and failure. My previous studies have identified epigenetic dysregulation of miRNA and its role in the pathogenesis of ACM. We have now begun to investigate how reprogramming of epigenetic code governsgene transcription and ensuing cardiac phenotype in human ACM heart failure (HF). Recently, we uncovered the role of DNA methylation and Lamin-Associated Domains in cardiac myocytes and heart failure.

**RESEARCH PROJECTS**
- Role of lncRNAs in the pathogenesis of cardiomyopathies and heart failure.
- Identification and characterization of molecular mechanisms and functions of lincRNA KDM5B in cardiomyopathies and heart failure.

**KEY PUBLICATIONS**


**LAB MEMBER**
Post-doctoral fellow: Manisha Deogharia

Heart plot of differentially expressed transcript and dysregulated upstream transcriptional regulators in human heart failure (HF).
High blood pressure is a frequent cause of renal injury, but the role of renal disease in patients with high blood pressure is best predicted by family history, indicating a genetic predisposition. At present we have almost no knowledge of why high blood pressure creates kidney disease in some people, but not others. To try to fill this knowledge gap, we study a genetic model comprising inbred laboratory rats that have high blood pressure. The divergence of hypertension in rats is known; is also present in these rats. Some lines get progressive renal injury, other lines don’t. Therefore, this model provides a means to investigate what genetic differences can influence kidney disease. We can take what we have learned and conceivably treat approaches to prevent and treat them in the model.

What we have learned so far: 
**Genes influencing antibody formation affect the emergence of hypertensive renal disease.** We have identified important genetic variation in the immunoglobulin heavy chain gene, which encodes antibodies. We also have identified genetic deletions in the gene, Stim1. This is a key gene in immune function and B lymphocytes comprise the adaptive immune system.

**Gene variants that control modifiable risk factors.** We have studied the role of genetic factors in the development of hypertensive renal disease in rats. We have identified genetic variants that influence risk for renal injury and hypertension in humans, and we have tested them in the model.

**Genes influencing antibody formation affect the emergence of hypertensive renal disease.** To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury.

We have identified important genetic variation in the immunoglobulin heavy chain gene, which encodes antibodies. We also have identified genetic deletions in the gene, Stim1. This is a key gene in immune function and B lymphocytes comprise the adaptive immune system.

**Gene variants that control modifiable risk factors.** We have studied the role of genetic factors in the development of hypertensive renal disease in rats. We have identified genetic variants that influence risk for renal injury and hypertension in humans, and we have tested them in the model.

**Genes influencing antibody formation affect the emergence of hypertensive renal disease.** We have identified important genetic variation in the immunoglobulin heavy chain gene, which encodes antibodies. We also have identified genetic deletions in the gene, Stim1. This is a key gene in immune function and B lymphocytes comprise the adaptive immune system.

**Gene variants that control modifiable risk factors.** We have studied the role of genetic factors in the development of hypertensive renal disease in rats. We have identified genetic variants that influence risk for renal injury and hypertension in humans, and we have tested them in the model.

**Genes influencing antibody formation affect the emergence of hypertensive renal disease.** To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.

Genes influencing antibody formation affect the emergence of hypertensive renal disease. To prove that antibodies cause hypertensive renal injury in our model species, we deleted the immunoglobulin gene. These animals cannot generate antibodies. They have high levels of blood pressure but have no renal injury. An immunosuppression drug that inhibits B cell function has a similar effect.
Role of non-coding cis-regulatory sequence variation in cardiac arrhythmias and sudden death risk

Ashish Kapoor, PhD
Assistant Professor

Overview of cardiac arrhythmias and sudden cardiac death (SCD)

SCD, defined as a cardiac arrest leading to death within one hour of onset, is a major cause of death in the United States and worldwide. A variety of underlying conditions can lead to SCD, including coronary artery disease, cardiac arrhythmias, and congenital heart defects. Understanding the genetic basis of SCD is crucial for developing personalized prevention strategies.

Role of non-coding cis-regulatory sequence variation

Recent advances in genome-wide association studies (GWAS) have identified numerous genetic variants associated with the QT interval, a measure of cardiac electrophysiology. However, the majority of these variants are non-coding, suggesting a role in regulatory mechanisms.

Molecular characterization of QT interval genetic factors

By integrating computational and experimental approaches, our lab has identified a role for non-coding cis-regulatory sequence variation in cardiac arrhythmia risk.

Enrichment analyses (reporter expression) for QT interval-associated variants

We performed reporter assays in mouse embryonic heart cells and human embryonic kidney (HEK) cells to assess the transcriptional activity of non-coding variants.

Correlation with functional effects

Key findings include the identification of variants that alter the expression of key cardiac genes, such as the sodium channel Nav1.5, which plays a critical role in cardiac repolarization.

Future directions

Further studies are needed to validate these findings in human populations and to understand the functional implications of non-coding variants in cardiac arrhythmia risk.

KEY PUBLICATIONS

Lab Members

Assistant Professor: Ashish Kapoor
Post-doctoral fellow: Parul Singh
Research Assistant: Ankita Smith
PhD student: Varun Singh

Supported by the National Heart, Lung, and Blood Institute and the American Heart Association.
Regulation of gene expression is fundamental to a wide range of biological processes. From cell fate determination during development to malignant transformation during tumor genesis, precise control of gene expression forms the basis of these processes. Our current understanding of gene regulation is, however, far from complete. Most published studies that profile gene expression are transcript-centric (i.e., they focus on measuring mRNA levels and levels of transcription factor binding). While these efforts revealed intricate networks of cooperation amongst transcription factors in shaping complex biological processes, much of the post-transcriptional regulation are left unexplored. It remains unclear whether the process of protein translation is regulated by a network of factors in an extent of complexity similar to transcription regulation. We ask questions such as “Do sequence specific RNA binding proteins (RBP) cooperate in controlling translation?” and “Are there translational regulatory networks that orchestrate critical biological processes?”

We have reported a systemic survey of uORF regulation of protein translation at HMSD locus. Using RNA binding protein footprint sequencing to investigate translational regulation of protein synthesis, RNA binding proteins are known to regulate protein translation. We aim to develop a general and effective tool to facilitate research in this area.

• Identification of functional novel coding regions across multiple tissues. We have previously identified 2,733 novel coding regions from a single cell type using ribosome profiling data. While we provided evidence of active translation at these loci, the biological function and importance of these loci remains unknown. We are following up on this line of research by designing knockout and knockdown screens to identify loci that are essential for cell survival. We are also expanding our efforts in identifying novel coding regions through performing ribosomal profiling experiments in additional cell types and tissues.

• Gene expression buffering at the post-transcriptional level. Gene expression at the transcript level are often assumed to propagate to the protein level. In a series of studies, we have demonstrated that, in our cell line model system, the variations observed at the transcript level is often buffered at the protein level through post-translational processes. In order to evaluate how general this phenomenon is, we are now expanding our analysis to other tissue types and species.

KEY PUBLICATIONS


LAB MEMBERS

Post-doctoral fellow: Sandeep Bansal

Sidney Wang, PhD
Assistant Professor

Deciphering the regulatory code: A functional genomics approach to protein translation

The investigators of the Hans J. Müller-Eberhard and Irma Gigli Center for Immunology and Autoimmune Diseases are examining the molecular, cellular, and genetic bases of several different allergic, autoimmune, and infectious diseases. These studies explore the nature, structure, and function of specific cell membrane receptors and their ligands in modulating immune and inflammatory responses.

In concert with the molecular studies, the Center’s scientists have engineered mice with specific targeted gene mutations or deletions that are used as models for human disease. These animal studies have facilitated the identification of key gene products that play significant roles in regulating the immune system, as well as contributing to the pathogenesis of human disease.

Results from these research efforts have identified several therapeutic targets for the treatment of asthma, septic shock, and lupus erythematosus.

The Center recently established a robust research program focused on the development of stem cell therapeutics for the treatment of acute and chronic lung diseases and for genetic deficiencies that affect normal lung function as well as for major eye diseases, including macular degeneration and diabetic retinopathy.

Research interests include:

• Asthma and Sinusitis
• Diabetic Retinopathy
• Mucosal Immunology & Autoimmunity
• Microbial Infectious Disease
• Acute Lung Injury and COPD
• Lung Surfactant Deficiencies
• Macular Degeneration
• Pulmonary Regenerative Medicine

Rick Wettel, PhD
Center Director & Professor
Hans J. Müller-Eberhard, MD, PhD and Irma Gigli, MD Distinguished Chair in Immunology

Genotype of a genetic variant is associated with a URF regulation of protein translation at HMSD locus in HepG2 cells. Negative correlation in the levels of protein translation between the two Open Reading Frames at HMSD locus is clearly shown through strand-specific ribosome profiling data by genotype.
Chronic diseases of the lung and eye are often the result of dysregulation of the immune and inflammatory response to pathogenic or toxic substances, resulting in the destruction of healthy tissue, establishment of debilitating pathologies due to tissue loss, and impairment of normal tissue repair mechanisms. However, the beauty of cellular and molecular knowledge regarding lung and eye immunity, inflammation, and repair mechanisms has slowed the development of novel therapeutics that could be used for the effective treatment of chronic diseases of the lung and eye. Accordingly, our laboratory has for the past several years focused on delineating the key molecules that mediate the inflammatory and immune responses in the lung and eye during both normal and pathological conditions. Much of this research has involved studies of the complement system, the complement system is a major arm of the innate immune system and is well known for being the first line of defense against bacterial and viral pathogens. It is comprised of over 30 plasma proteins and cell surface receptors. It has become evident that the complement system is required to sustain inflammation and to orchestrate the recruitment and activation of innate immune cells. This is exemplified by the fact that complement system deficiencies are associated with the susceptibility to a variety of diseases, including AIDS, hepatitis B, and multiple sclerosis.

**RESEARCH PROJECTS**

- Determine the role of vascular and inflammatory responses in the development and progression of chronic lung disease.
- Determine how the function of vascular and immune cells is regulated during chronic lung disease.
- Evaluate the therapeutic potential of gene therapy for the treatment of chronic lung disease.
- Develop novel strategies for the treatment of chronic lung disease.

**KEY PUBLICATIONS**


**LAB MEMBERS**

Senior research scientist: Alexey F. Domoshnik, MD

Senior research scientist: Stacey Mueller-Ortiz, PhD

Assistant professor: Tingting Weng, PhD

Senior research scientist: Kelly Volcik, PhD

Research associate: Ning Yue Chen

Research scientist: Jose Mohola, Sr.

Graduate student: Josh Ko, PhD

**Model illustrating how the vascular endothelium on stimulation by the complement anaphylatoxin C3a activates B cells and polarizes T cells in the absence of complement.** Vascular lumen

Intestinal tissue

Model illustrating how the vascular endothelium on stimulation by the complement anaphylatoxin C3a activates B cells and polarizes T cells in the absence of complement. Endothelial cells shown in brown with letter T. B cells and T cells in brown and green, respectively. The elongated cells depict activated B cells and polarized T cells as they transmigrate through the endothelium.

**Adenose signaling and the regulation of chronic lung disease**

- Novel regulation of nNOS phosphorylation in the regulation of pulmonary fibrosis. The role of Adenosine signaling in the regulation of chronic lung disease.
- Understanding novel mechanistic roles for A2B receptor in the regulation of chronic lung disease.
- Investigation of adenosine transport in acute lung injury.
- Understanding novel mechanistic roles for A2B receptor in the regulation of chronic lung disease.

**KEY PUBLICATIONS**


**Increased expression of proteinase 3 in pulmonary macrophages in mice with pulmonary fibrosis (BOLD).**
Environmental triggers regulating innate immune responses in chronic airway inflammation

Over 40 million Americans suffer from chronic rhinosinusitis (CRS), which causes facial pain and pressure, nasal congestion, and obstruction. These symptoms ultimately drive, consecu-
tively, 18.2 million visits per year with an annual direct healthcare treatment cost of over 3 billion dollars. In addition, patients suffering from CRS often are diagnosed with asthma. Together, CRS and asthma as chronic respiratory diseases represent some of the most prevalent chronic illnesses in the United States. Despite this healthcare burden, much remains unknown about its pathophysiology, and current treatment options, which typically involve recurr-
rent surgeries and anti-inflammatory agents, are not curative. CRS represents an ideal human research model for studies in chronic inflammatory respiratory diseases. CRS patients often undergo surgery providing an opportunity to harvest critical diseased tissue and are seen regularly in clinic, which allows periodic evalua-
tion of the patient and diseased mucosa. CRS is clinically classified into 2 groups, defined by the absence or presence of nasal polyps (see image 1). This classification has been supported generally by immuno-
logic profiles of the inflamed sinonasal tissue. CRS without nasal polyps is characterized by predominance of neutrophils and elevated T helper cell type 1 (Th1), Th2, and Th17, while CRS with nasal polyps (CRSwithP) has high presence of eosinophils, mast cells, and basophils and expression of type 2 cytokines such as IL-4, IL-
5, and IL-13. However, recent study by our labs using cluster analysis of genetic information has identified endotypes within these clinical phenotypes, allowing for possible personalized treatment.

Allergic fungal sinusitis (AFS) is a clinical subtype of CRSwithP that is associated with an accumulation of thick entrapped mucous laden with fungal hyphae and eosinophils between the nasal polyps and within sinus cavities. This trapped mucous can cause expansion of sinus cavities and ultimately erosion of bone separating the sinuses from the intranasal and orbital cavities, which can result in intracranial complications and blindness, respectively. Epithelial cells

Respiratory epithelial cells represent the first line of defense against the environment for sinonasal mucosa. Recent studies have shown that epithelial cells serve an active role through regulation of cytokines and release of anti-microbials. Three identified epithelial cell--derived cytokines, thymus stromal lymphopoi-

ete, interleukin (IL)-25 and IL-33, have been linked to the type 2 immune response. Our lab has focused on the role of IL-33 in orchestrating the type 2 immune response characteristic of CRS with nasal polyps. We con-

firmed that the receptor of IL-33 is upregulated in the diseased sinonasal mucosa of CRSwithP. We demonstrated an increased presence of in-

tracytoplasmic type 2 cells (ICL2) preferentially in CRSwithP patients relative to health controls. These ICL2 express ST2, the receptor for IL-33, and represent the major cell type producing IL-

13 in response to IL-33. Interestingly, we found that fungal antigens, specifically Aspergillus, can stimulate respiratory epithelial cells to release IL-33. Given the appreciation of the innate immunity and known data of the role of the adaptive immune response in CRS, we are currently interested in the distribution and ultimately in the function of innate (epithelial cells and ILC2) helper cells in various CRS subtypes. In addition, our lab is interested in the molecular characterization of fungi-mediated signaling pathway(s) and the fungal component responsible for signaling in the inflammatory response in some CRS subtypes. We currently believe allergic fungal sinusitis may result from a defect in local anti-fungal immune response. This has led us to our recent interest in establishing a mouse model of eosinophilic upper and lower airway inflammation and the protocols to evaluate the sinus inflammation. Current studies are focused on the pathways that regulate antimicrobial peptides with antifungal activity as it relates to CRS.

ENVIRONMENTAL TRIGGER PROJECTS

- Characterization of immunologic and molecu-

lar defects contributing to pathophysiology of allergic fungal rhinosinusitis.

- Molecular signaling through respiratory epithelial cells of fungal alone and with other environmental triggers responsible for initiat-

ing and/or maintaining the characteristic Th2 response.

- Clinical characterization and identification of biomarkers for CRS subtypes.

KEY PUBLICATIONS


Shaw, J.L.; Fakhri, S.; Ostrander, M.L.; Porter, P.C.; Corry, D.B.; Khawand, F.; Lu, L.Y.; Luang, A. IL-33-responsive innate lymphoid cells are an important source of IL-13 in chronic rhinosi-


Tyler, M.A.; Russell, C.B.; Smith, D.E.; Rothman, J.K.; Deo, C.J.; Hu, R.; Parast, M.L.; Fakhri, S.; Assassi, S.; and Luong, A. Large scale gene expression profiling reveals distinct type 2 inflammatory patterns in chronic rhinosi-


LAB MEMBERS

Hua Sun, MD, PhD

Amber Luong, MD, PhD

Associate Professor, Center for Immunology and Autoimmune Diseases and Department of Otolaryngology – Head and Neck Surgery

T he eight laboratories of the Center for Metabolic and Degenerative Diseases investigate aging-associated diseases, including type-2 diabetes, muscle wasting, vascular insufficiencies, neurodegeneration, and cancer. Mechanisms of aging, stress, and obesity-associated changes in brain activity, energy metabolism, vascular function, cell signaling, protein homeostasis, and cell fate determination that lead to physiological abnormalities are being interrogated in animal models and through studies on clinical specimens. The specific questions being addressed by the center’s faculty include the following:

- How does replicative senescence of adipocyte progenitors underlie diabetes-development?

- How do adipocyte-derived fatty acids contribute to diabetes and cancer progression?

- Can cells of adipose tissue be targeted for therapeutic purposes?

- How is angiogenesis, fibrosis, and inflammation implicated in metabolic dysfunction?

- How do stress hormones regulate energy utilization in diabetes?

- What vascular genes can be targeted to treat muscle disease and diabetes?
Adipocyte progenitor cells: Dysfunction in disease and aging

Our group is interested in the mechanisms underlying aging-related diseases and developing new approaches to target them. Specifically, we focus on the role of fat (adipose) tissue in the context of obesity, type 2 diabetes, muscle degeneration, and cancer. While white adipocytes store lipids to insulate them in times of energy scarcity, brown adipocytes burn lipids off to keep the body warm. In obesity, overgrown white fat becomes inefficient in holding fats, hence causing diabetes, cardiovascular disease, and cancer. In contrast, active brown fat can prevent the onset of metabolic disease. Both white and brown adipocytes are continuously replaced as they undergo senescence, and these pools in fat tissue are maintained by adipose stem cells (ASCs). In obesity, increased numbers of white fat ASCs are generated. We have discovered that tumors recruit these ASCs that fuel cancer progression. Taking advantage of our report in targeted therapies, we have developed the first experimental drug (D-CAN) targeting ASCs. Our publications demonstrate that D-CAN prevents obesity and suppresses tumor growth in mice. In more recent work, we used this experimental drug to investigate the mechanism through which ASC promote cancer progression to chemotherapy resistance and metastasis and validated them as a drug target. We are also applying ablation of ASC as a new therapeutic approach to Duchenne muscular dystrophy treatment. In collaboration with plastic surgeons, we recently showed that D-CAN targets human ASCs. Our reports indicate that D-CAN treatment spares brown fat ASCs, leads to generation of brown adipocytes, and enables a short-term metabolic benefit. However, our recent data indicate the importance of maintaining functional ASCs and preventing their replicative senescence in healthy aging. As we age, fat cell numbers decrease and the deficient fat tissue fails to effectively deplete lipids, which start spilling into other organs. This can cause inflammation and metabolic disorders accounting for cancer and organ failure in the elderly. Our experiments in mice lacking telomerase (TERT) in adipose stroma. PLN1: adipocyte senescence marker p16 in PDGFRa-positive stromal cells accumulating Immunofluorescence on sections of adipose tissue showing expression of senescence marker p16 in PDGFRα-positive stromal cells accumulating in mice lacking telomerase (TERT) in adipose stroma. PhLM: adipocyte marker yellow. Nuclei (DNA) are blue.

**RESEARCH PROJECTS**

- **Ablate senescent adipocytes in PDGFRα-positive stromal cells**
- **Identify gene networks that drive muscle stem cell replication after injury**
- **Novel pathways regulating type 2 diabetes and muscle regeneration**

**KEY PUBLICATIONS**

Age-associated telomere attrition in adipocyte progenitors predisposes to metabolic disease.

**RESEARCH PROJECTS**

- **Proapoptotic Peptide Suppresses Cancer and metastasis and treated with chemotherapy (cisplatin) alone (Left) or a combination of chemotherapy and a peptide D-CAN targeting adipose stromal cells. Note the suppression of metastases (M) by D-CAN.**

**KEY PUBLICATIONS**

- **Comprehensively define muscle stem cells and inflammatory cells in human muscle during recovery from traumatic muscle and bone injury**

**LAB MEMBERS**

Post-doctoral fellows: Maria Estrella, Crystal Wilkerson

Graduate assistant: Krista Wolf

Undergraduate student: Alexandria Aragon

Research assistant: Michael C. Moreland, PhD

Medical student: Victor Gonzalez

Graduate tutorial student: Didier van der Wall

Research assistants: Elena Dyukova, Chase Fussell, Rebecca Berdeaux, PhD

**CENTER FOR METABOLIC AND DEGENERATIVE DISEASES**

**Novel pathways regulating type 2 diabetes and muscle regeneration**

**RESEARCH PROJECTS**

- **Determine how a stress activated kinase tunes sugar and fat utilization in skeletal muscle in obesity**
- **Identify gene networks that drive muscle stem cell replication after injury**
- **Comprehensively define muscle stem cells and inflammatory cells in human muscle during recovery from traumatic muscle and bone injury**

**KEY PUBLICATIONS**

- **Comprehensively define muscle stem cells and inflammatory cells in human muscle during recovery from traumatic muscle and bone injury**

**LAB MEMBERS**

Post-doctoral fellows: Laura Bahm, Mariane Martinez

Research assistant: Elena Dyukova, Chase Fussell, Rebecca Berdeaux, PhD

Graduate student: Daniel Hancock

Undergraduate student: Daisy Díaz-Rehena

Research assistant: Rebecca Berdeaux, PhD

**LAB MEMBERS**

Post-doctoral fellows: Maria Estrella, Crystal Wilkerson

Graduate assistant: Krista Wolf

Undergraduate student: Alexandria Aragon

Research assistant: Michael C. Moreland, PhD

Medical student: Victor Gonzalez

Graduate tutorial student: Didier van der Wall

Research assistants: Elena Dyukova, Chase Fussell, Rebecca Berdeaux, PhD

**CENTER FOR METABOLIC AND DEGENERATIVE DISEASES**
with its clock. In normal circadian conditions, the brain's central clock, known as the suprachiasmatic nucleus (SCN), synchronizes the body's rhythms with the 24-hour day-night cycle. This synchronization is critical for maintaining a healthy balance of sleep and wake, metabolic processes, and hormone release. However, when the body's internal clock (circadian clock) is disrupted, it can lead to various health issues, including diabetes and obesity, as well as mental health conditions such as depression.

Our research aims to understand the mechanisms that control the circadian clock and its impact on health. We are particularly interested in how disruptions to the circadian clock can lead to metabolic disease and how these disruptions might be mitigated.

The goals of my lab center on the role of our internal clock in physiology and tissue-specific function. Experiments in peripheral organs are heavily influenced by other zeitgebers, or "time-givers," such as light and food. Poor quality nutrients as well as food rhythms can lead to metabolic disease. We are trying to understand why circadian disruption produces these effects.

Mechanisms linking circadian disruption to metabolic disease.

Mechanisms by which circadian disruption...

In these cells causes tumor cell death and impairs metabolic disease in these cells.

Rhythmic, daily proliferation of adipocyte progenitor cells.

Understanding the role of the circadian clock in human adipose tissue.

High levels of stress cause anxiety that if continuously present leads to devastating mental illness, most commonly depression, generalized anxiety disorder and PTSD. Stress impacts the progression of other diseases, in part due to elevated levels of the stress hormone, cortisol, which is released in response to stress.

Key publications:


Labor members:

Instructors: Baharan Feikey, PhD
Post-doctoral fellows: Ralat Indy Santos, PhD
Graduate student: Rachel Van Duren, Janine Tran

Labor projects:

Local signaling that controls endocrine, autonomic, and behavioral stress responses via direct signaling with stress-activated CRF neurons.

At the VMH, we have developed new genetic tools, allowing the discovery and functional interrogation of specific stress-responsive circuits in the brain. Our first discovery was a new type of neuron in the hypothalamus that controls release of stress hormone, by stress. We have now discovered in published experiments a new mechanism that functions to control hormone release in response to stress and limit our own production of cortisol. Our continued study of this circuit has revealed additional roles for this new type of neuron that is responsive to Corticotropin Releasing Factor (CRF) and thereby can coordinate hormone release with autonomic, endocrine, and behavioral changes made in response to stress exposure. This new class of neurons can be selectively manipulated allowing interrogation of the function to an unprecedented degree. We are determined to find the mechanisms used by these neurons to control the stress response to help us avoid diseases that are caused or negatively impacted by stress.

- CRF and other neuropeptide neurons in the VMH project to key cortical circuits to influence movement choice.

We identified another unprecedented neuronal circuit that connects stress hormone release with the central circuits responsible for coordinating movement. This movement circuit, termed "the basal ganglia" is the system that malfunctions in Parkinson’s Disease as well - in other neurodegenerative disorders and is associated with loss in the ability to move and control movement. We hypothesize that this newly found circuit communicates stress-relevant information to the basal ganglia to influence which movements are made in response to threats in our environment. In this way, stress circuits shape our reaction to a stressful threat, perhaps causing escape behavior and running away from a threat in certain contexts, and hiding from the threat in other contexts. Given our identification of this new circuit connecting stress hormone release and core neural circuits that guide movement, endless possibilities for future discovery lay ahead for which we pursue with passion.

- Oxytocin neurons become responsive to CRF only in mothers who have had offspring: an array of transgenic animals designed to visualize and manipulate CRF receptor neurons, we found that Oxytocin neurons, which are involved in parturition and lactation, but only see CRFR1 positive Oxytocin neurons in mothers; both virgin females and male animals lack CRFR1 expression in Oxytocin neurons. Moreover, CRFR1 is expressed by Oxytocin neurons for the rest of the mother’s life. We are just beginning to understand how CRF responsiveness alters Oxytocin neurons, some their known functions in pup-mothering behavior. However, this molecular change that occurs only in mothers has the potential to alter how mothers respond to stress long after they have finished raising children. This project has introduced a new field in our study of stress biology: how stress influences maternal behaviors. We are determined to uncover how, and perhaps, why oxytocin neurons receive information about the stress status of an animal surrounding the time of parturition, and whether it is beneficial or detrimental to successful reproduction.

Key publications:


Labor members:

Post-doctoral fellow: Shewkar Rahmanians, PhD
Research assistant: Jonathan Tao

Tracing connections between CRF receptor positive Serotonin neurons (red) and the neurons that make direct synapses onto these neurons to control their activity.
Our laboratory broadly studies transcriptional regulations of metabolic and vascular homestasis using nuclear receptors as model signaling molecules. Currently, we are investigating the cellular and physiological functions of orphan nuclear receptors (e.g. estrogen related receptors) and their co-regulators (e.g. PGC1’s). We use a wide ranging approach, including genetically engineered mice, murine disease models, high throughput gene expression analysis (e.g. RNA sequencing, ERP sequencing), pharmacology, cell signal and in vitro systems in our studies. These tools are being used to investigate the role of ERRs and PGC1’s in (1) cellular processes such as genome-wide gene expression, histotrophic biogenesis, and angiogenesis; (2) physiological phenomena, such as exercise adaptation and whole-body metabolism; as well as (3) diseases such as obesity/diabetes, peripheral arterial disease and muscular dystrophy. Our ongoing work has uncovered the therapeutic role of estrogen-related receptors (ERRs) via metabolic and angiogenic regulation in peripheral arterial disease (PAD), and in Duchenne muscular dystrophy (DMD). Similarly, our studies on estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functions of orphan nuclear receptors (e.g. PPAR alpha and beta, estrogen-related receptors) and their co-functional regulation of metabolic and vascular diseases.
**Brain control of feeding, body weight, and glucose metabolism**

**RESEARCH PROJECTS**

- Mice neurons and neural pathways for feeding regulation and its relation with emotional states.
- Brain different pathways controlling peripheral metabolism.
- Brain mechanisms mediating blood hormone action on energy and glucose, and their involvement in obesity and diabetes pathogenesis.
- Chronic stress and obesity development.

**KEY PUBLICATIONS**


**LAB MEMBERS**

- Instructor: Yuanzhong Xu, MD, PhD
- Research assistants: Xin Ye, PhD; Mrs. Lili Ye
- Research assistants: Qingchun Tong, PhD; Hongli Li (visiting)
- Instructor: Shiyu Xu, PhD
- Research assistants: Xin Ye, PhD; Mrs. Lili Ye
- Research assistants: Yuzhi Li, PhD; Xi Xue

**LAB MEMBERS**

- Instructor: Yuzhi Li, PhD
- Research assistants: Xin Ye, PhD; Mrs. Lili Ye
- Research assistants: Hongli Li (visiting)

**CENTER FOR METABOLIC AND DEGENERATIVE DISEASES**

**Research projects**

- Mechanisms of protein folding and cellular clearance pathways in brain invertebrates, including human and species.
- Novel functions of Huntington’s disease and its perturbation in Huntington’s disease.
- Biogenesis of autophagosomes and lysosome-related organelles.

**KEY PUBLICATIONS**


**LAB MEMBERS**

- Instructor: Shiyu Xu, PhD
- Graduate Students: Yuzhi Li, Mrs. Lili Ye

**Molecular mechanisms of neurodegenerative diseases**

As we live longer and enjoy unprecedented longer life expectancy, we are also becoming increasingly vulnerable to aging-related neuronal degenerative disorders, including Alzheimer’s disease (AD), Parkinson’s disease (PD) and Huntington’s disease (HD). As these incapacitating brain diseases are relentless unalterable emotional and financial tolls to patients and their families, they are becoming a pressing threat to our society. However, now there is little effective prevention and treatments against these maladies.

**Research projects**

- Mechanisms of protein folding and cellular clearance pathways in brain invertebrates, including human and species.
- Novel functions of Huntington’s disease and its perturbation in Huntington’s disease.
- Biogenesis of autophagosomes and lysosome-related organelles.

**Key publications**

Sheng Zhang, PhD

**Assocate Professor**

Becky Family Foundation Professor in Diabetes Research

**Research projects**

- Mechanisms of protein folding and cellular clearance pathways in brain invertebrates, including human and species.
- Novel functions of Huntington’s disease and its perturbation in Huntington’s disease.
- Biogenesis of autophagosomes and lysosome-related organelles.
The Mission of the Center for Molecular Imaging (CMI) is to develop and translate new medical imaging technologies, molecular imaging agents, and companion diagnostics to accelerate discoveries. The CMI houses a diverse, interdisciplinary team of scientists and engineers who develop and use multi-modality molecular diagnostics and imaging techniques, including nuclear imaging, X-ray computed tomography, bioluminescence, fluorescence, and near-infrared fluorescence (NIRF) to enable new understandings of disease and chronic conditions. Sponsored industry, philanthropic, and federal research funding focuses upon autoimmune disorders, neuroinflammation, cancer metastases, hemo- and lymph-vascular diseases, and lymphedema. The team has expertise in instrumentation, imaging agent development, antibody engineering, animal models of human disease, and translational science that effectively moves inventions and discoveries, “bench to bedside,” and when discoveries are made in the clinic, “from bedside back to bench.”

A highlight of the CMI is the development of the Center Director & Professor
Eva Marie Sevick-Muraca, PhD
Nancy and Rich Kinder Distinguished Chair in Cardiovascular Disease Research

LAB MEMBERS
Post-doctoral fellows: Carolina Manilla-Bejar, PhD
Research assistants/associates: Janelle Morton, BS, Fred Christian “CJ” Velasquez, BA

RESEARCH PROJECTS
• Evaluating the role of CSF outflow in brain health and Alzheimer’s.
• Assessing the role of lymphatics in metabolic disorders.
• Refining measurements of lymphatic anatomy and function.

CENTERS FOR MOLECULAR IMAGING
IMMPACT REPORT
IMMPACT REPORT
Imaging in immunology

I have participated as a team member imaging treatment responses to head and neck LE, which affects ~90% of head and neck cancer patients. The treatment used, protonic compression therapy, removes stagnant lymph in LE patients, but needs NIR-LI to visualize the source of regional and remote disease activity. Green fluorescent dye is visualized through the skin, pumping through lymphatics, revealing delayed cranial drainage when the head is tilted. The use of NIR-LI allowed us to better understand the cranial lymphatic system, which now enables patients to locate health care professionals and clinicians direct optimal care.

The lymphatic system is a vital, yet poorly understood, component of the circulatory system. It has been known for many years that gravity aids lymphatic drainage, laying on their back and sitting up. The images were imaged in a head down tilt position to mimic microgravity conditions as well as while laying on their back and sitting up. The images revealed delayed cranial drainage when the subject was in the head down position, indicating that under normal conditions gravity aids cranial lymphatic drainage. We continue the development of this imaging technology, including assessing novel imaging and drug delivery technologies, improving device sensitivity, automating different aspects of the hardware, and developing analytical tools to facilitate lymphatic image processing and analysis, with the ultimate goal of answering new biological and clinical questions not addressed by other technologies.

One of our primary focuses is the relationship between the lymphatics and the circulatory system. It has been known for many years that regional tissue changes and poor immune response. We recently imaged a group of patients with early cancer and showed that under normal conditions gravity aids cranial lymphatic drainage. We continue the development of this imaging technology, including assessing novel imaging and drug delivery technologies, improving device sensitivity, automating different aspects of the hardware, and developing analytical tools to facilitate lymphatic image processing and analysis, with the ultimate goal of answering new biological and clinical questions not addressed by other technologies.

Research projects

- Longitudinal study of breast cancer-related LE
- Longitudinal study of reparative microsurgeries for LE
- Imaging of lymphatics in lymphedema
- Imaging of neonatal chylous and pediatric lymphovenous anomalies

Key publications

- Lab members: Medical student: Kay Pham
- Assistant Professor: Melissa B. Aldrich, MBA, PhD
- Assistant Professor: John Rasmussen, PhD
- Assistant Professor: Carolyn F. Keen

The lymphatic system is a vital, yet poorly understood, component of the circulatory system. As blood flows through the arteries and veins, water leaks from the vessels entering the small gaps between the tissue cells. As the water moves through the tissues it pools into cell wells, foreign contaminants, proteins, etc., and the resulting solution is taken up by the lymphatics, processed for immune response, and is already returned to the veins. In addition, the lymphatics provide a pathway for the absorption of patients from the gut. However, because the lymphatics are typically small and primarily transport clear fluids, they are difficult to distinguish from the surrounding tissue. With our new near-infrared clinical imaging modalities such as spectroscopy, X-ray, MRI, and ultrasound, over the past five years, my research has focused upon the development and translation of near-infrared fluorescence imaging (NIRF) optical imaging as a way to noninvasively image lymphatic and characterize human lymphatics and quantify their contractile function in health and disease using microfluidic amounts of a fluorescent contrast agent.

One of our primary focuses is the relationship between the lymphatics and the circulatory system. It has been known for many years that gravity aids lymphatic drainage, laying on their back and sitting up. The images were imaged in a head down tilt position to mimic microgravity conditions as well as while laying on their back and sitting up. The images revealed delayed cranial drainage when the subject was in the head down position, indicating that under normal conditions gravity aids cranial lymphatic drainage.

In addition, the lymphatic pumping rate initially increases when the head is tilted, reaching a peak when the head is tilted. The use of NIR-LI allowed us to better understand the cranial lymphatic system, which now enables patients to locate health care professionals and clinicians direct optimal care.

One of our primary focuses is the relationship between the lymphatics and the circulatory system. It has been known for many years that gravity aids lymphatic drainage, laying on their back and sitting up. The images were imaged in a head down tilt position to mimic microgravity conditions as well as while laying on their back and sitting up. The images revealed delayed cranial drainage when the subject was in the head down position, indicating that under normal conditions gravity aids cranial lymphatic drainage. We continue the development of this imaging technology, including assessing novel imaging and drug delivery technologies, improving device sensitivity, automating different aspects of the hardware, and developing analytical tools to facilitate lymphatic image processing and analysis, with the ultimate goal of answering new biological and clinical questions not addressed by other technologies.

Research projects

- Assessing the role of lymphatics in the development of peripheral venous disease
- Assessing the development of cancer related lymphedema and its response to intervention
- Understanding the role of lymphatics in the development of neurological conditions.

Key publications

Brain network dysfunction from cerebral palsy, a birth-related stroke, or epilepsy contributes to developmental delays in children. Although MRI can diagnose brain network dysfunc-
tion, the complexities and general anesthesia needed to obtain motion-free BOLD fMRI data limit their practical use in young children. Recently, we report a transcranial near infrared (NIR) optical imaging system, called Cap-based Transcranial Optical Tomography (CTOT), able to image whole brain hemodynamic activity in an awake child. With recent advances to couple fast read-out scientific CMOS (sCMOS) devices and with optical switching of detector fiber optics, rapid dynamic CTOT mapping should be possible, which would then enable evaluation of functional connectivity in awake infants.

The lymphatic vasculature is an essential highway for the immune system, enabling local resolution of innate and mounting of adaptive immune responses in regional draining lymph nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs. In addition more meningeal and cribriform lymphatics that drain subarachnoid space into the newly rediscovered nodes (LNs). In the brain, CSF drains from the subarachnoid space into the newly rediscovered meningeal and cribriform lymphatics that drain via gravity to cervical LNs.

In the pages following you will find examples of Center faculty exploring the potential therapeutic value of stem cells for repairing tissues such as spinal cord, brain, muscle, lung, and blood, as well as elucidating the role of stem cells in cancer. If I may provide any additional information, please do not hesitate to contact me.

For patients presenting with genetically inherited diseases, Center faculty are utilizing recently developed gene editing technologies to correct the disease-causing mutations in either tissue-resident stem cells or iPSCs. The goal of these studies is development of therapies that include correcting the mutations in a patient’s own stem cells, then delivering either the corrected stem cells or cells/tissues derived from them back into the same patient.

The faculty, research staff, and trainees of the Center for Stem Cell and Regenerative Medicine (CSCRM) are focused on experimental studies of the biological properties of stem cells in both health and disease. The interest in healthy stem cells is motivated by their essential role in both normal development as well as in maintenance of tissues and organs throughout life. One of the hopes of regenerative medicine is that this fundamental understanding of stem cells may be effectively translated into therapies in which healthy stem cells, or their derivatives, can be employed to replace cells and tissues lost as a consequence of normal aging, injury, or disease.

There are at least two distinct classes of stem cells under active investigation within the Center for such therapeutic applications. The first of these are tissue-resident stem cells: such cells present throughout life in various organs such as bone marrow, intestine, and lung are involved in active regeneration of cells and tissues lost due to normal cell turnover, aging, injury, or disease. A second class of stem cells of significant therapeutic interest to Center investigators is induced pluripotent stem cells (iPSCs). iPSCs are patient-specific stem cells that can be generated from easily obtained cells from any individual and, in principle, may be specifically guided into the various cell types and tissues present within the human body. Faculty within the Center are seeking to develop efficient and robust methodologies to convert iPSCs into various cells/tissues of therapeutic interest, including neural, blood, lung, and muscle – as well as how to best deliver and maintain such cells/tissues for therapeutic benefit.

The C. Harold and Lorine G. Wallace Distinguished University Chair

For patients presenting with genetically inherited disease, Center faculty are utilizing recently developed gene editing technologies to correct the disease-causing mutations in either tissue-resident stem cells or iPSCs. The goal of these studies is development of therapies that include correcting the mutations in a patient’s own stem cells, then delivering either the corrected stem cells or cells/tissues derived from them back into the same patient.

Finally, there is increasing evidence for the presence within cancers of cells having specific properties typically associated with stem cells. Center faculty are investigating the role of such cells in the initiation and maintenance of cancers of the blood such as mantle cell lymphoma and multiple myeloma.

In the pages following you will find examples of Center faculty exploring the potential therapeutic value of stem cells for repairing tissues such as spinal cord, brain, muscle, lung, and blood, as well as elucidating the role of stem cells in cancer. If I may provide any additional information, please do not hesitate to contact me.

For patients presenting with genetically inherited disease, Center faculty are utilizing recently developed gene editing technologies to correct the disease-causing mutations in either tissue-resident stem cells or iPSCs. The goal of these studies is development of therapies that include correcting the mutations in a patient’s own stem cells, then delivering either the corrected stem cells or cells/tissues derived from them back into the same patient.

Finally, there is increasing evidence for the presence within cancers of cells having specific properties typically associated with stem cells. Center faculty are investigating the role of such cells in the initiation and maintenance of cancers of the blood such as mantle cell lymphoma and multiple myeloma.

In the pages following you will find examples of Center faculty exploring the potential therapeutic value of stem cells for repairing tissues such as spinal cord, brain, muscle, lung, and blood, as well as elucidating the role of stem cells in cancer. If I may provide any additional information, please do not hesitate to contact me.
Our laboratory has as its primary objective the sequence-specific genetic correction of mutations in the chromosomal DNA of induced pluripotent stem (iPS) cells and/or tissue-specific stem cells derived from patients with inherited disorders affecting the lung or blood system. This is being pursued with the ultimate goal of developing stem cell-based therapeutic approaches.

We have utilized DNA sequence-specific nuclease-mediated homology-directed repair to correct the most common genetic mutations in iPS cells derived from patients with cystic fibrosis - and have demonstrated genetic and functional correction in lung epithelial cells derived from these corrected iPS cells. We have introduced lung-specific fluorescent reporters into iPS cells and utilized it specifically to isolate early lung progenitors and then airway basal stem cells for purposes of molecular and functional characterization. Specifically, we have now demonstrated that our iPS-derived airway basal cells (iBCs) correspond closely to airway basal cells of patients with cystic fibrosis - and have now demonstrated genetic and functional correction in lung epithelial cells derived from these corrected iPS cells. We have introduced lung-specific fluorescent reporters into iPS cells and utilized it specifically to isolate early lung progenitors and then airway basal stem cells for purposes of molecular and functional characterization.

Key Publications


Lab Members

Post-doctoral Fellow: Dr. John M. Avila, Dr. Cristiana Barilla, Dr. Shin悟 Suzuki
Research staff: Dr. Balliang Wang, Huiqeng Xue

Derivation of airway basal stem cells from induced pluripotent stem cells (iPSCs). (A) Summary of protocol with critical steps highlighted. (B) iPS-derived airway basal cells are able to generate airway epithelium. (C) Detection of NKX2.1, TII and TP63 in iPS-derived airway epithelium.

The research in my laboratory focuses on developing biomaterials to be used in clinical treatments for spinal cord injury, traumatic brain injury, and stroke. The laboratory was an interdiscipliary approach involving techniques from cell, molecular, and stem cell biology, chemistry, and material science. Utilizing engineering approaches, the laboratory seeks to optimize scaffold design for the expansion of clinically relevant cell sources for use in stroke cell therapy and to support the cells after implantation into patients.

By examining cell-material interactions, we seek to understand which aspects of the native extracellular matrix facilitate tissue repair and regeneration with the surrounding host tissue. Once optimal composition, architecture (porosity, feature size, fiber alignment, etc.), mechanical properties, and bioactive signaling peptide concentrations have been identified using combinatorial methods, they are integrated into advanced hybrid matrices. These matrices can then be evaluated in in vivo models.

Tissue engineering approaches for the treatment of CNS injuries

The number of viable cells for transplant produced from current differentiation protocols is extremely low. Both biochemical and mechanical properties of the cell culture surface have shown to significantly affect cellular differentiation but have not been studied significantly in respect to iPSC differentiation. The laboratory seeks to extend our knowledge of three dimensional culture systems to optimize two dimensional cell culture surfaces for differentiation of neural stem cells and oligodendrocyte progenitor cells from iPSC. Preliminary studies have focused on the coating of proteins to the surface of hydrogels with containing a TGF-β/Modulating gradient to study the effect of mechanical properties on iPSC lineage choice.

Key Publications


Laura A. Smith Callahan, PhD

Assistant Professor

Tissue engineering approaches for the treatment of CNS injuries

KEY PUBLICATIONS


Stem cells for neurological diseases

Recent advances in the field of stem cell biology have shown promise in the treatment of neurological disorders. One approach involves the reprogramming of reactive astrocytes into neuronal precursor cells, which can then be transplanted to replace lost neurons after SCI or stroke.

**RESEARCH PROJECTS**

- In vivo reprogramming of reactive astrocytes and chemotactic approach for SCI repair.
- Treating neurotoxic path by in vivo reprogramming of astrocytes after SCI.
- Combinatorial approaches to promote axonal regeneration and functional recovery after SCI.
- Human iPSC-derived neural stem or precursor cells for spinal cord injury and stroke.

**KEY PUBLICATIONS**


**LAB MEMBERS**

- Undergraduate student: Matthew Carey
- Graduate student: Chrystine Gallegos
- Post-doctoral fellow: Yuan Zhang

**Professor Qi Lin Cao, MD**

**Professor George and Cynthia Mitchell Distinguished University Chair**

**Cellular therapies for neurological injury**

Our current research program focuses on the use of cellular therapies for neurological disorders. We have been interested in the modulation of the innate immune response to TBI and how cellular therapies have been successful without significant engraftment in the brain-long term. Cell-cell interactions in the peripheral microenvironment have resulted in Th2 polarization and modulation of the microglia/macrophage phenotypes in the brain. We use these types of data to help us determine dosing regimens (number of cells, type, and route of delivery, as well as timing), which may be very specific to the pathophysiology in question. We use in vivo models of injury and in vitro cell culture models to help us determine dosing regimens (number of cells, type, and route of delivery, as well as timing), which may be very specific to the pathophysiology in question.

**RESEARCH PROJECTS**

- Development of Phase 1 and 2 Clinical Trials using non-ESC stem/progenitor cells for traumatic brain injury.
- MD enabling studies using aPFC for traumatic brain injury.
- Intranasal fluid derived MOG-MS for the treatment of neurological injury associated with congenital heart disease and cardiomyopathy.
- Hydrocortisone delivery, as well as timing, which may be very specific to the pathophysiology in question.
- Novel delivery systems for stem cells in neurological injury.
- Imaging of microglial activation in vivo.

**Professor Charles Cox, Jr., MD**

**Professor and George and Cynthia Mitchell Distinguished University Chair**

**Development of a novel biocarrier for stem cell production.**
Human induced pluripotent stem cells (iPSCs) to treat skeletal muscle disorders

RADROB DARIABI, MD, PhD
Associate Professor

**Human induced pluripotent stem cells (iPSCs) to design strategies for correction of (POGLUT1) and use them to study disease from novel types of muscular dystrophy patients**

Our lab uses cutting edge technologies to therapy in degenerative disorders.

**Skeletal muscle disorders consist of a diverse and heterogeneous group of disorders affecting patient’s function and mobility. Common disorders include muscular dystrophies and muscle injuries.**

Skeletal muscle injuries are hypertrophic and genetic disorders of the skeletal muscle. In this group of disorders due to a mutated gene, a structural protein of the skeletal muscle becomes defective, which leads to progressive muscle inflammation and degeneration.

Depending on the affected gene, patients may show different degrees of progressive muscle weakness with early or late onset. Another major group of muscle disorders are muscular skeletal mass (VML) injuries and defects, which are very common in traumatic patients, such as car accidents or combat injuries or after tumor resection in cancer patients. These also often lead to a coagulopathy and different levels of disabilities. Skeletal muscle disorders are often incurable and are a major cause of disabilities and create a big burden on the health system.

Here at the IMM and stem cell center, we are interested in using induced pluripotent stem cells (iPSCs) for skeletal muscle repair. iPSCs can be easily reprogrammed from adult skin or blood cell and can generate a source of stem cells capable of unlimited differentiation to all cell types in the human body. In addition, since iPSCs are derived from patients, they are fully compatible with the patient with minimal immune rejection risk. Therefore, iPSCs are considered as the top candidate for stem cell therapy in degenerative disorders.

Our lab uses cutting edge technologies to create iPSCs from muscle disorder patients and use them for generation of large quantities of muscle cells useful for for drug development applications. So far, we have generated patient iPSC's from novel types of muscular dystrophy patients (GORD1) due to a defect in a novel gene (POGLUT1) and used them to study disease mechanisms and pathophysiology. We also use advanced genome correction methods, such as CRISPR, to design strategies for correction of defective genes in these disorders. In addition, we use different rice models for muscular dystrophy (Sarm1) and muscle loss injury mouse models (to model muscle injuries after trauma or combat injury) to validate regeneration and reparative potential of human iPSCs.

So far our lab has pioneered new methods for derivation of engraftable muscle cells from human iPSCs and demonstrated their application for skeletal muscle repair in these models. The long-term goal of our lab is to pave the way toward clinical application of human iPSCs to treat skeletal muscle disorders. Our research program is currently funded by two NHLBI grant awards from National Institute of Arthritis and Musculoskeletal and Skin Diseases (NAMS) to support these exciting and novel projects.

**Research Projects**

- **Evaluation of the engraftment and functional recovery potential of human iPSCs in the mouse models for Duchenne muscular dystrophy (DMD).**
- **Therapeutic application of human iPSCs for muscular volume loss injuries (VML) and evaluation of their innovation and functional recovery**
- **Gene correction of muscular dystrophies using CRISPR/Cas9 system**

**Key Publications**


**Lab Members**

- Investigator: Juwuo Wu Research assistant: Nasa Bu

---

**Engraftment of human iPSC in a mouse model for volumetric muscle loss (VML) injury.** Red and green colors mark human iPSCs expressing specific markers of dystrophin and lamin A/C.

---

**Simplified pathway for NAD metabolism.** NAD+ is synthesized from two metabolic pathways: a de novo synthesis pathway from (fam and amino acids) or a recycling pathway. Sarm1 is a NAD+ consuming enzyme. Its activity is thought to play a key role in axonal degeneration. One of the enzymes that metabolizes NAD+ in axons is Sarm1 (Sarm1 Alpha and TIR Motif Containing 1), and its activity is thought to play a key role in axonal degeneration. We have been examining the role of Sarm1 in axonal injury and cognitive outcome after repeated mild closed head injury (rmCHI). Our results indicate that degradation of NAD+ contributes to axonal damage after repetitive closed head injury.

**Simplified pathway for NAD metabolism.** NAD+ is synthesized from two metabolic pathways: a de novo synthesis pathway from (fam and amino acids) or a recycling pathway. Sarm1 is a NAD+ consuming enzyme. Its activity is thought to play a key role in axonal degeneration. One of the enzymes that metabolizes NAD+ in axons is Sarm1 (Sarm1 Alpha and TIR Motif Containing 1), and its activity is thought to play a key role in axonal degeneration. We have been examining the role of Sarm1 in axonal injury and cognitive outcome after repeated mild closed head injury (rmCHI). Our results indicate that degradation of NAD+ contributes to axonal damage after repetitive closed head injury.

---

**Concussion and stress-related disorders**

**Simplified pathway for NAD metabolism.** NAD+ is synthesized from two metabolic pathways: a de novo synthesis pathway from (fam and amino acids) or a recycling pathway. Sarm1 is a NAD+ consuming enzyme. Its activity is thought to play a key role in axonal degeneration. One of the enzymes that metabolizes NAD+ in axons is Sarm1 (Sarm1 Alpha and TIR Motif Containing 1), and its activity is thought to play a key role in axonal degeneration. We have been examining the role of Sarm1 in axonal injury and cognitive outcome after repeated mild closed head injury (rmCHI). Our results indicate that degradation of NAD+ contributes to axonal damage after repetitive closed head injury.

**Simplified pathway for NAD metabolism.** NAD+ is synthesized from two metabolic pathways: a de novo synthesis pathway from (fam and amino acids) or a recycling pathway. Sarm1 is a NAD+ consuming enzyme. Its activity is thought to play a key role in axonal degeneration. One of the enzymes that metabolizes NAD+ in axons is Sarm1 (Sarm1 Alpha and TIR Motif Containing 1), and its activity is thought to play a key role in axonal degeneration. We have been examining the role of Sarm1 in axonal injury and cognitive outcome after repeated mild closed head injury (rmCHI). Our results indicate that degradation of NAD+ contributes to axonal damage after repetitive closed head injury.

**Simplified pathway for NAD metabolism.** NAD+ is synthesized from two metabolic pathways: a de novo synthesis pathway from (fam and amino acids) or a recycling pathway. Sarm1 is a NAD+ consuming enzyme. Its activity is thought to play a key role in axonal degeneration. One of the enzymes that metabolizes NAD+ in axons is Sarm1 (Sarm1 Alpha and TIR Motif Containing 1), and its activity is thought to play a key role in axonal degeneration. We have been examining the role of Sarm1 in axonal injury and cognitive outcome after repeated mild closed head injury (rmCHI). Our results indicate that degradation of NAD+ contributes to axonal damage after repetitive closed head injury.
Human pluripotent stem cells for lung regeneration and disease modeling

My laboratory is interested in applying human pluripotent stem cell (hPSC) models to the study of lung diseases. We have developed a step-wise differentiation strategy of clinically applicable cell types. As a first, we realized stem cell therapy in lung development and pathogen infection. We also develop new experimental models to study lung diseases.

Human pluripotent stem cells (hPSCs) are derived from human embryos and have the potential to differentiate into all three germ layers. They can be used to model human diseases at the cellular and molecular levels. In my lab, we focus on applying hPSCs to study lung diseases, including airway development and diseases.

We have developed a step-wise differentiation strategy of clinically applicable cell types. As a first, we realized stem cell therapy in lung development and pathogen infection. We also develop new experimental models to study lung diseases.

Our research efforts are directed towards understanding the basic mechanisms of lung development and disease pathogenesis. We use these models to address important clinical questions, such as the role of genetic and environmental factors in the development of lung diseases. We are also interested in using these models to develop novel therapeutic strategies for lung diseases.

In summary, my laboratory is dedicated to advancing the field of neuroscience by developing novel models and approaches to study lung diseases and develop new treatments. We are committed to translating our research findings into clinical applications to improve patient outcomes.

Sarah Xuellian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuellian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xuelian Huang, MBBS, PhD
Assistant Professor

Sarah Xue...
Development of hematopoietic stem cells and innate-like B cells in the mouse embryo

Momoko Yoshimoto, MD, PhD
Associate Professor

Center for Stem Cell and Regenerative Medicine

The hematopoietic stem cells (HSCs) that produce all types of blood cells in the body are first generated in the aortic region of the mouse embryo at embryonic day (E) 10.5. Interestingly, though, there are multiple waves of blood cell production prior to the emergence of the first HSC from hemogenic endothelial cells (referred to as hemogenic endothelial cells, HECs), and these blood cells include erythro-myeloid, T-lymphocytes, and B-lymphocytes. We have recently found that innate-like B-1 lymphocytes and the first HSCs are produced simultaneously from HECs. We are elucidating 1) what molecular signals determine the divergent point between innate-like B-1 lymphocytes and first HSCs, 2) how embryonic-derived B-1 progenitors contribute to postnatal B-1 cell pool, and 3) how HSC precursors mature into adult-constituting HSCs in a limited window of embryonic development.

B-1 cells are unique murine innate immune cells that are differentiated from conventional B-1 cells (B-2 cells). B-1 cells localize in the peritoneal and pleural cavities and secrete IgM and IgA antibodies. We have identified important molecules for HSC maturation in the mouse embryo utilizing single-cell RNA-sequencing. Examining the contribution of fetal-derived B cells to IgM secreting cells in the lamina propria of intestine. Producing human B-1 cells from human iPSCs.

Our research is dedicated to understanding cancer pathological mechanisms by applying patient-specific iPSCs and/or engineered ESCs. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma. We have developed patient-specific and/or engineered ESCs. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma.

After leukemia, osteosarcoma is the second leading cause of cancer mortality among children. Genetic alterations (e.g., p53 mutation and RB1 deletion) are strongly associated with osteosarcoma development. Patients with Li-Fraumeni syndrome (LFS), a genetically inherited autosomal dominant cancer disorder caused by germline mutations in the TP53 tumor suppressor gene, have increased incidence of osteosarcoma development, which provides a perfect model system to study osteosarcoma. Modeling human genetic disease has recently become feasible with induced pluripotent stem cell (iPSC) methodologies developed by Dr. Shinya Yamanaka in 2006. Characterized by their ability to self-renew indefinitely and differentiate into all cell lineages of an organism like embryonic stem (ES) cells, iPSCs provide a powerful and unlimited source of cells to generate differentiated cells that can be used to elucidate disease pathogenesis, for drug discovery and development, and personalized healthcare and eventually cell transplantation based therapies.

Our research is dedicated to understanding cancer pathological mechanisms by applying patient-specific iPSCs and/or engineered ESCs. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma. We have established the first human Li-Fraumeni syndrome (LFS) disease model by using LFS patient specific iPSCs to delineate the pathological mechanisms caused by mutant p53 in osteosarcoma.
Our research focuses on dissecting the neural developmental pathways and the corresponding pathogenesis in CNS injury and neurodegenerative diseases. Our long-term goal is to identify therapeutic targets for the treatment of CNS diseases.

Human induced pluripotent stem cells (iPSCs) provide autologous materials for patients, which theoretically could meet the need for immune-suppressed. We have optimized the more clinically relevant, integration-free CRISPR generation protocol and performed directed differentiation of patient-specific iPSCs into neural stem cells, neuronal and glial progenitors, as well as mature cell types for disease modeling, transplantation studies, neural regeneration and repair, and drug screening and testing. The highly efficient CRISPR gene editing tool adapted in the lab allows for quick creation of neural lineage reporters and malignance activation for lineage induction. These neural lineage-specific cells are applied to in-depth study of signal transduction in disease and development.

RESEARCH PROJECTS

- Generation of patient-specific, integration-free iPSCs
- Identification of optimal neural lineage progenitors for cell-based therapy in spinal cord injury
- Down syndrome disease modeling using patient derived iPSCs and neural populations
- Molecular changes in gene expression regulatory networks is glioblastoma.

KEY PUBLICATIONS


RFID (C, G). (D) and (H) are overlapped images. A Neurogenin 2 knockin human iPSC reporter cell line made using the CRISPR/Cas9 system. NEUROG2-mCherry human iPSC clones are induced as embryoid bodies (EBs) which glow red under the fluorescence microscope (A). NEUROG2 antibody staining (green) confirms that mCherry (red, native signal) expression faithfully reflects the endogenous NEUROG2 expression along the differentiation pathway (B, C).

Rapid generation of astrocytes from human-iPSCs by endogenous activation of astrocyte lineage specific transcription factors with the piggyBac CRISPR activation system. Human-iPSC cell line was transplanted with all-in-one vectors expressing guinea RNAs that activate SDRF NRIR-NIRF transcription factors. Fourteen days post transplantation, nearly all cells expressed astrocyte markers SOX9 (A), GFAP (B) and CSV (C). While it did not express glial progenitor marker ASB25 (D). Nuclei are revealed by DAPI (C, G) and (D) and (H) are overlapped images.

Human induced pluripotent stem cells (iPSCs) provide autologous materials for patients, which theoretically could meet the need for immune-suppressed. We have optimized the more clinically relevant, integration-free CRISPR generation protocol and performed directed differentiation of patient-specific iPSCs into neural stem cells, neuronal and glial progenitors, as well as mature cell types for disease modeling, transplantation studies, neural regeneration and repair, and drug screening and testing. The highly efficient CRISPR gene editing tool adapted in the lab allows for quick creation of neural lineage reporters and malignance activation for lineage induction. These neural lineage-specific cells are applied to in-depth study of signal transduction in disease and development.

RESEARCH PROJECTS

- Generation of patient-specific, integration-free iPSCs
- Identification of optimal neural lineage progenitors for cell-based therapy in spinal cord injury
- Down syndrome disease modeling using patient derived iPSCs and neural populations
- Molecular changes in gene expression regulatory networks is glioblastoma.

KEY PUBLICATIONS


RFID (C, G). (D) and (H) are overlapped images. A Neurogenin 2 knockin human iPSC reporter cell line made using the CRISPR/Cas9 system. NEUROG2-mCherry human iPSC clones are induced as embryoid bodies (EBs) which glow red under the fluorescence microscope (A). NEUROG2 antibody staining (green) confirms that mCherry (red, native signal) expression faithfully reflects the endogenous NEUROG2 expression along the differentiation pathway (B, C).

Rapid generation of astrocytes from human-iPSCs by endogenous activation of astrocyte lineage specific transcription factors with the piggyBac CRISPR activation system. Human-iPSC cell line was transplanted with all-in-one vectors expressing guinea RNAs that activate SDRF NRIR-NIRF transcription factors. Fourteen days post transplantation, nearly all cells expressed astrocyte markers SOX9 (A), GFAP (B) and CSV (C). While it did not express glial progenitor marker ASB25 (D). Nuclei are revealed by DAPI (C, G) and (D) and (H) are overlapped images.

The behavior of cancer cells is not only dependent on their genetic abnormalities but also requires complex relationships between malignant cells and their local bone marrow niche, which provides an environment for multiple myeloma cell growth as well as protection from chemotherapy-induced apoptosis. The bone marrow niches provide a “hiding place” for dormant clones, which are often resistant to chemotherapeutic agents. The major goals of my research program are to decipher molecular pathways that confer selection, growth and survival advantages to malignant B cells and delineating their interaction with the bone marrow microenvironment. One of these factors is paired box 5 (PAX5), a determinant of normal B cell lineage development. We discovered that PAX5 silencing in mantle cell lymphoma leads to increased tumor formation in xenograft model, indicating that PAX5 is a potential tumor suppressor. Moreover, PAX5 silencing led to increased cancer cell survival in the bone marrow. We have conducted high throughput drug screening using libraries comprised of 2391 compounds of NCI oncology, custom clinical, and prestwick libraries. We discovered that select compounds target the survival pathways of PAX5 silenced cells. Greater that PAX5 silenced cells are highly drug-resistant, discovery of compounds that target drug resistance populations in cancer cells will have direct translational applications. We are also conducting research delineating roles of the quiescent multiple myeloma and their interaction with the bone marrow microenvironment. MM is a plasma cell malignancy that proliferates primarily in bone marrow and causes osteolytic lesions. Since quiescent cells can escape the chemotherapeutic treatment and potentially led to drug resistance and increased tumor formation, it is important to understand the molecular mechanisms of their survival in bone marrows. Characterization of quiescent cells and their interaction with microenvironment is underway.

RESEARCH PROJECTS

- Survival mechanisms of dormant multiple myeloma cells and their microenvironment in the bone marrow
- Development of small molecule inhibitors to target drug-resistant lymphomas
- Conducting protein synthesis, folding, transport, and degradation
- Inappropriate protein assembly or modification promotes protein misfolding, which can lead to not only disruptions to protein homostasis but also to normal cellular functions. We focuses on delineating functions of protein homostasis control in cancer progression.
Our lab studies how biomechanical force generated by the flow of blood in the circulatory system impacts cell fate and behavior. One of our primary research projects addresses how frictional force caused by blood flow promotes emergence of blood stem cells during embryonic development. We are interested in how we might use this information in the laboratory to expand improved sources of these stem cells for treatment of hematologic disorders and cancers, such as bone marrow failure syndromes and leukemias. Complex signaling occurs in response to flow that poises stem cell potential, including activation of integrins, mechanosensitive ion channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.

In addition, we have found that frictional force in biomimetic microfluidic channels, and primary cilia (Fig. 1). In our primary research projects, we address how biomechanical force affects cell fate and behavior in bone marrow transplantation.
Translational cancer research aims to identify novel drug targets followed by the discovery and development of drug candidates as potential cancer therapeutics. The goal is to translate discoveries made in basic cancer research to potential drugs that could be tested in human patients. It relies on a plethora of information and data on cancer origin, progression, metastasis, drug-resistance, and disease relapse to uncover the driving mechanisms of tumor growth and invasion. Technologies such as next generation sequencing of DNA and RNA in cancer and non-cancer cells of tumor tissues, CRISPR screening, proteomics, imaging, patient-derived tumor models, drug candidate discovery, and bioinformatics are utilized to reveal drug targets and validate potential drug candidates.

The current research in the Center for Translational Cancer Research emphasizes several areas, including the application of cutting edge bioinformatic and experimental technologies to identify and validate novel drug targets in several major types of solid tumors, the discovery of specific molecules against the targets with a focus on antibody/protein-drug conjugates, the development of targeted contrast agents for disease visualization, and the study of proteome alterations to elucidate disease mechanism and discover biomarkers.

These efforts connect us with collaborators, such as physicians, pathologists, biologists, bioinformaticians, and bioengineers, across UTHealth, institutions within the Texas Medical Center, and across Texas to enhance basic, translational and clinical research. At the IMM, we have state-of-the-art mass spectrometers that provides in-depth proteomic analysis of cells, tissues or biological fluids, with the goals to discover novel targets and biomarkers to inform the development of therapeutic treatment and early detection of diseases. We combine critical data from cancer genetics, genomics and proteomics to identify drug targets, create targeted antibodies and peptides, and synthesize drug conjugates that are then evaluated in tumor models. We also have expertise in the development and application of novel antibody-based agents that have imaging implications in cancer as well as infectious diseases. Furthermore, the Center specializes in the development of multifunctional peptides that combine radioactive and fluorescent contrast to enable tumor identification before, during, and after surgery, thus introducing a precision surgery approach. In addition, we have an active probe development program that includes the development of new spacers and multi-functional nanoconjugates for targeting cancer and other diseases. We also have large-scale, multi-color, high resolution state-of-the-art 3D printers for both fast prototypes and finished production level models of new surgical tools and instruments or patient-specific organ models.

Our center houses several core facilities, including the Nanochemistry Service Center, 3D-printing Service Center and Clinical and Translational Proteomics Service Center, to support many research labs through service and collaborative efforts.

**Qingyun “Jim” Liu, PhD**
Professor
Janice Davis Gordon Chair for Bowel Cancer Research

**Investigation of normal and cancer stem cells for the discovery of cancer therapeutics**

Adult stem cells are specialized cells that can self-renew and give rise to all the other types of differentiated cells in the tissue where the stem cells reside. They are essential for the maintenance of tissues with high turnover rates, such as the gut and skin, and for tissue repair after injury. However, these cells are also believed to be the cells of origin for many types of cancer as they are programmed to divide indefinitely. Furthermore, tumor tissues are also heterogeneous in which only a subpopulation of cells can self-renew and provide daughter cells that make up the bulk of the tumor. These self-renewing cancer cells, designated cancer stem cells or tumor-initiating cells, often bear great similarity to normal stem cells in molecular profile and regulatory systems. Understanding of the mechanisms that govern the control of the self renewal and differentiation of normal and cancer stem cells will provide crucial knowledge to the discovery and development of novel therapeutics for regenerative medicine and cancer treatment.

Our research is focused on delineating the function and mechanism of a group of novel cell surface receptors called LGR4, LGR5, and LGR6 (LGR4-6) that play critical roles in the survival of normal stem cells and tumour cells. Previously, we discovered that LGR6-4 function as receptors of a group of stem cell factors called R-spondins (RSPRs) that are essential for the survival and growth of stem cells. We have now focused on understanding how RSPRs and LGRs work together to regulate the growth and migration of normal and cancer cells. We found that LGR6 and LGRs work through a different mechanism to control the survival and expansion of intestinal stem cells, which challenges a major current paradigm that LGR6 and LGRs work in an identical way in cell signaling. Meanwhile, we showed that drug conjugates of anti-LGR antibodies showed excellent anti-tumor efficacy in preclinical models of colon cancer. Recently, we have discovered a novel approach that can target all three LGR receptors for the treatment of cancers of the digestive system. We are not optimized this approach by protein engineering to increase its potency and efficacy in tumor models.
Intraoperative visualization of residual cancer following gross tumor resection under ambient light. This image shows the use of a molecular imaging probe to visualize residual cancer after surgery. The near-infrared fluorescence signal (NIR) highlights the areas of cancer, allowing for accurate assessment of tumor clearance.

**RESEARCH PROJECTS**
- Development of contrast agents for real-time surgical guidance.

**KEY PUBLICATIONS**
Deciphering proteome alterations associated with diseases

Our lab is focused on understanding the signaling programs underlying cancer progression and developing therapeutic strategies to prevent or treat metastasis. We wish to understand the events that lead tumor cells to become metastatic, whether through acquired mutations or epigenetic mechanisms. Our ultimate goal is to translate these findings into the clinic through the development of genomic biomarkers and repurposing of drugs. To do this, we use a range of approaches encompassing genomics, cell biology, and biochemistry; and use models including cell culture, mouse models, and clinical samples.

Our research program encompasses two broad and complementary areas of emphasis:

1. Breast cancer metastasis. It is estimated that up to 90% of cancer deaths are due to metastasis, in part because metastatic cells do not respond to traditional therapies. To address this problem, we have used computational approaches to characterize the metastatic state and to repurpose drugs to target cells that exhibit phenotypes that promote metastasis.

Through these studies, we have found that metastasis is driven in part by cells that acquire a stem-like state through deregulation of cholesterol trafficking in cancer stem cell differentiation, the epithelial-to-mesenchymal transition, and cancer metastasis.

2. Artificial intelligence for genomic analysis.

Many of our projects require the integration with bioinformatics to mine public data sets, develop hypotheses, or analyze results. To amplify our ability to do bioinformatics, we have developed an artificial intelligence, BETSY, that can automatically plan and execute these tasks, presenting us with finished results. It is a backwards-chaining expert system that leverages a knowledge base containing descriptions of common bioinformatics algorithms.

Proteins are essential functional biomolecules that are involved in all aspects of cellular physiological activities and have been important targets for drug development and early detection of diseases. Proteomics, especially quantitative proteomics, has been a valuable tool in basic, translational, and clinical research, providing a unique avenue to investigate disease-associated molecular alterations at a functional level. Proteome alterations that are associated with diseases may include changes in protein expression, sequence, post-translational modifications (PTMs) and protein interactions with other biomolecules, which may all lead to a malfunction of cellular processes. In our lab, mass spectrometry-based proteomic technologies are applied to study cancer and other diseases. These studies are carried out with various goals, such as aiming to better understand the molecular mechanisms underlying tumorigenesis, to investigate changes in PTM status associated with diseases, to identify disease-associated protein biomarkers or therapeutic targets, or to interrogate microbiome dysbiosis. The samples involved in our studies include a variety of research and clinical specimens, including tumor tissues, blood and other bodily fluids, as well as isolated cells from various clinical specimens. Currently, our major disease focuses are pancreatic cancer and other gastrointestinal malignancies, as well as neurological diseases. In addition, through collaborative efforts, our lab also supports proteomic studies of various diseases, including chronic inflammations, degenerative diseases, infectious diseases, and therapeutic drug development.

Mass spectrometry, bioinformatics, systems biology, and chemical biology are important components in our study.

Sheng Pan, PhD
Associate Professor / Director, the Clinical and Translational Proteomics Service Center
Rochelle and Max Levit Chair in the Neurosciences


Sheng Pan, PhD
Associate Professor / Director, the Clinical and Translational Proteomics Service Center
Rochelle and Max Levit Chair in the Neurosciences

Deciphering proteome alterations associated with diseases

Jeffrey Chang, PhD
Associate Professor
CPRIT Scholar in Cancer Research

Deciphering proteome alterations associated with diseases

Our research program encompasses two broad and complementary areas of emphasis:

1. Breast cancer metastasis. It is estimated that up to 90% of cancer deaths are due to metastasis, in part because metastatic cells do not respond to traditional therapies. To address this problem, we have used computational approaches to characterize the metastatic state and to repurpose drugs to target cells that exhibit phenotypes that promote metastasis.

Through these studies, we have found that metastasis is driven in part by cells that acquire a stem-like state through deregulation of cholesterol trafficking in cancer stem cell differentiation, the epithelial-to-mesenchymal transition, and cancer metastasis.

2. Artificial intelligence for genomic analysis.

Many of our projects require the integration with bioinformatics to mine public data sets, develop hypotheses, or analyze results. To amplify our ability to do bioinformatics, we have developed an artificial intelligence, BETSY, that can automatically plan and execute these tasks, presenting us with finished results. It is a backwards-chaining expert system that leverages a knowledge base containing descriptions of common bioinformatics algorithms.
The focus of my lab is to develop targeting agents and smart particles that attack cancer or infectious organisms, such as tuberculosis. Current treatments are often ineffective or create harsh side effects for patients. We use modified DNA linked to drug-like or protein-like attachments (X-aptamers). X-aptamers can be used alone or as complex particles containing anti-cancer agents to act as a one-two punch. Such particles also can be loaded into larger silicon particles for a sustained release of the disease-fighting particles.

**Aptamer Development** - In recent years we have developed DNA aptamers targeting breast and ovarian cancer. Such DNA can reduce cancer in a dose-dependent manner. However, DNA aptamers are even more effective when used in combination therapy together with chemotherapeutic agents such as siRNA or drugs like Paclitaxel. We have shown that our aptamer-targeted approach reduces tumor size and more importantly, the spread of metastatic disease. Furthermore, we have also shown our method is safe in preclinical testing. Our recent aptamer-related research has shown the following:

**Key Publications**

- **Development of smart particles to attack breast and ovarian cancers.**

- **Developing new X-aptamers targeting other diseases.**

**Research Projects**

- **Development of smart particles to attack breast and ovarian cancers.**

- **Developing new X-aptamers targeting other diseases.**

**Software Development**

- **Software Development**

**Associate Professor**

**David Volk, PhD**


**The focus of my lab is to develop targeting agents and smart particles that attack cancer or infectious organisms, such as tuberculosis. Current treatments are often ineffective or create harsh side effects for patients. We use modified DNA linked to drug-like or protein-like attachments (X-aptamers). X-aptamers can be used alone or as complex particles containing anti-cancer agents to act as a one-two punch. Such particles also can be loaded into larger silicon particles for a sustained release of the disease-fighting particles.**

**Aptamer Development** - In recent years we have developed DNA aptamers targeting breast and ovarian cancer. Such DNA can reduce cancer in a dose-dependent manner. However, DNA aptamers are even more effective when used in combination therapy together with chemotherapeutic agents such as siRNA or drugs like Paclitaxel. We have shown that our aptamer-targeted approach reduces tumor size and more importantly, the spread of metastatic disease. Furthermore, we have also shown our method is safe in preclinical testing. Our recent aptamer-related research has shown the following:

**Key Publications**

- **Development of smart particles to attack breast and ovarian cancers.**

- **Developing new X-aptamers targeting other diseases.**

**Research Projects**

- **Development of smart particles to attack breast and ovarian cancers.**

- **Developing new X-aptamers targeting other diseases.**

**Software Development**

- **Software Development**

**Associate Professor**

**David Volk, PhD**

The Texas Therapeutics Institute (TTI-IMM) was established in 2010 with funding from the Texas Emerging Technology Fund, The University of Texas System, and The University of Texas Health Science Center at Houston. TTI-IMM was created to develop, and commercialize, of therapeutic agents and diagnostic tools. Research conducted at the center focuses on the establishment of proof-of-principle for therapeutics and the identification and validation of drug targets.

TTI-IMM investigators have brought in significant funding from biopharmaceutical companies, such as Merck, and from government organizations, including the National Institutes of Health, the Cancer Prevention and Research Institute of Texas, and the Department of Defense. These investigators have made significant scientific discoveries in the areas of cancer biology, fungal natural products, and antibody drug development.

Current research activities at TTI-IMM include: 1) signaling mechanisms of receptors and enzymes that have critical roles in human diseases; 2) discovery of biologics and natural products that modulate the activity of these targets as potential lead molecules for drug discovery; and 3) characterization of antibodies from animals and humans in response to viral infections and experimental vaccines.

In addition to basic and translational research programs, TTI has built a major drug discovery platform for therapeutic monoclonal antibody drug discovery optimization and development. Over the last 10 years, TTI established a network of collaborators from institutions across Texas and the nation. TTI has more than 30 active drug discovery projects targeting cancer, metabolic diseases, neurodegenerative diseases, spinal cord injury, fibrosis, acute drug induced liver injury, and viral infections. Six TTI inventions have been licensed to biotech companies for drug development. Three antibody-based therapeutics discovered by TTI scientists are currently in human clinical trials. In response to the COVID-19 pandemic, TTI scientists quickly discovered neutralizing antibodies targeting the SARS-CoV-2 virus. These antibodies in development as potential therapies for the treatment of COVID-19. Licensing deals resulted in significant upfront payments, potential milestone payments, and royalties. The Texas Therapeutics Institute is recognized as the drug discovery engine of McGovern Medical School and UTHealth.

Zhiquiang An, PhD
Professor & Center Director
Robert A. Welch Distinguished University Chair in Chemistry

Discovery and development of therapeutic antibodies


Our group focuses on the discovery and development of therapeutic antibodies against human diseases. Currently, we have three major research areas.

RESEARCH PROJECTS

- Antibody response to viral infections and vaccination. Identification of highly immunogenic vaccines that induce neutralizing antibodies against a broad range of viral isolates is one approach to developing effective viral vaccines. We have an ongoing project to aid the design of HCMV and dengue vaccines by profiling antibody response to the experimental vaccines in murine and human.

- Cancer antibody drug resistance mechanisms. Immune suppression is recognized as a hallmark of cancer. Our recent studies have demonstrated a new mechanism of cancer suppressors of immunity. This mechanism involves a requirement of antibody effector function mediated by proteolytic enzymes in the tumor microenvironment.

- Cancer therapeutics. Monoclonal antibody drug discovery. Our group has built a comprehensive antibody drug discovery platform with a focus on antibody lead optimization technologies such as antibody phage display, deep sequencing of antibody encoding genes from individual antibodies expressing B cells, affinity maturation, and humanization. Currently, we have multiple collaborative antibody drug discovery projects targeting various cancer types.

KEY PUBLICATIONS


Zhiquiang An, PhD
Professor and Co-Director of the Texas Therapeutics Institute
Robert A. Welch Distinguished University Chair in Chemistry

Discovery and development of therapeutic antibodies


Our group focuses on the discovery and development of therapeutic antibodies against human diseases. Currently, we have three major research areas.

RESEARCH PROJECTS

- Antibody response to viral infections and vaccination. Identification of highly immunogenic vaccines that induce neutralizing antibodies against a broad range of viral isolates is one approach to developing effective viral vaccines. We have an ongoing project to aid the design of HCMV and dengue vaccines by profiling antibody response to the experimental vaccines in murine and human.

- Cancer antibody drug resistance mechanisms. Immune suppression is recognized as a hallmark of cancer. Our recent studies have demonstrated a new mechanism of cancer suppressors of immunity. This mechanism involves a requirement of antibody effector function mediated by proteolytic enzymes in the tumor microenvironment.

- Cancer therapeutics. Monoclonal antibody drug discovery. Our group has built a comprehensive antibody drug discovery platform with a focus on antibody lead optimization technologies such as antibody phage display, deep sequencing of antibody encoding genes from individual antibodies expressing B cells, affinity maturation, and humanization. Currently, we have multiple collaborative antibody drug discovery projects targeting various cancer types.

KEY PUBLICATIONS


Zhiquiang An, PhD
Professor and Co-Director of the Texas Therapeutics Institute
Robert A. Welch Distinguished University Chair in Chemistry

Discovery and development of therapeutic antibodies


Our group focuses on the discovery and development of therapeutic antibodies against human diseases. Currently, we have three major research areas.

RESEARCH PROJECTS

- Antibody response to viral infections and vaccination. Identification of highly immunogenic vaccines that induce neutralizing antibodies against a broad range of viral isolates is one approach to developing effective viral vaccines. We have an ongoing project to aid the design of HCMV and dengue vaccines by profiling antibody response to the experimental vaccines in murine and human.

- Cancer antibody drug resistance mechanisms. Immune suppression is recognized as a hallmark of cancer. Our recent studies have demonstrated a new mechanism of cancer suppressors of immunity. This mechanism involves a requirement of antibody effector function mediated by proteolytic enzymes in the tumor microenvironment.

- Cancer therapeutics. Monoclonal antibody drug discovery. Our group has built a comprehensive antibody drug discovery platform with a focus on antibody lead optimization technologies such as antibody phage display, deep sequencing of antibody encoding genes from individual antibodies expressing B cells, affinity maturation, and humanization. Currently, we have multiple collaborative antibody drug discovery projects targeting various cancer types.

KEY PUBLICATIONS

Genome mining, biosynthesis, and discovery of microbial metabolites for infectious diseases and cancer therapies

Microorganisms have produced many of our most important drugs. Their high biodiversity and genetic capacity for synthesis of organic molecules continue to add breakthrough molecules for investigations in human diseases. Multidisciplinary microbial biomedical research at the Texas Therapeutics Institute and the Institute of Molecular Medicine brings together members of our lab and collaborators from the Texas Therapeutics Institute and the Multidisciplinary microbial biomedical research. Our research involves testing microbial natural products for therapeutic applications, making natural products through fermentation to support medicinal chemistry synthesis, and elucidating biosynthetic pathways of bioactive natural products. We seek to test various hypotheses that natural product-producing microorganisms harbor biosynthetic gene clusters and novel biosynthetic mechanisms that can be harnessed to generate new bioactive chemistry useful in intervention in infectious diseases and cancers. In parallel, we use pathway genetics and genomic manipulation in the producing organisms to aid in supplying large quantities of these natural products to support synthesis of new derivatives. Our lab employs genomics to interpret and predict genetically encoded chemical diversity of microorganisms using filamentous fungi as model organisms, especially for biosynthetic families relevant for pharmaceutical intervention in human diseases. For example, we have characterized biosynthetic pathways responsible for the family of echinocandins antifungal drugs, including pentamidins B1, the starting molecule for the antifungal drug CANDIGEN. We have in-programmed pentamidine biosynthesis to produce new strains with improved product purity and new analogs with increased potency. In parallel, we use pathway genetics and genomic manipulation in the producing organisms to aid in supplying large quantities of these new products to support synthesis of new derivatives and overproduce drug precursor molecules.

We also carry out fundamental discovery of new bioactive natural products that inhibit growth of human pathogens, including Cryptococcus neoformans, a yeast causing Cryptococcosis meningitis and cryptococcosis. Extracts of fermented fungi are evaluated for useful biological effects using an assortment of assays directed at finding molecules that affect human pathogens. After preliminary chromatography, such as flash or columns chromatography, active fractions of the extracts are identified through our bioassays against the target pathogens. More refined chromatographic techniques, e.g., preparative HPLC and bioautography, guide us to the activity-causing natural products. These extracts are available through collaborations with other academic and industrial laboratories.

RESEARCH PROJECTS
• Biosynthesis of natural products and pathway engineering for improved antagonists.
• Development of methods for reprogramming transcription of biosynthetic genes of fungi to discover or overproduce natural products useful for treating human diseases.
• Discovery of new antagonists and other therapeutic agents.

KEY PUBLICATIONS

LAB MEMBERS
Post doctoral Fellow: Dr. Xin Lan, Dr. Bruce Perotti, Dr. Zhao Zhang

Our laboratory studies intracellular signaling associated with second messenger cAMP, a major stress signal exploited in the development of human diseases. We apply multiplexed approaches, coupling biochemistry, biophysics, and cell biology with pharmacology and chemical biology, to understand the structure and function of a family of CAMP sensors: exchange proteins directly activated by CAMP (EPAC). Our goal is to understand the signaling intricacies of EPAC proteins and to design pathway specific modulators for these important signaling molecules so that their functions can be exploited and controlled pharmacologically to the treatment of human diseases. We have developed first-in-class EPAC selective inhibitors and EPAC knockout mouse models to study the physiological functions and disease relevance of this family of important signaling molecules. Recently, we have identified a potential use of nuclear receptor, and are developing second-generation isoform specific EPAC inhibitors in the prevention and treatment of polyneuropathy. Currently, we are developing second-generation isoform specific EPAC inhibitors and agonists and in exploring their potential uses in various human diseases including cardiovascular diseases and chronic pain.

RESEARCH PROJECTS
• Structural and functional analyses of the exchange proteins directly activated by CAMP (EPAC).
• Examines the role of EPAC proteins in major human diseases such as chronic pain and polyneuropathic vascular diseases using EPAC knockout mouse models and pharmacological inhibitors.
• Preclinical development of novel drug candidates targeting EPAC for the treatment of microbial infections caused by bee and tick-borne bacteria Robertsii.

KEY PUBLICATIONS

LAB MEMBERS

Xiaodong Cheng, PhD
Assistant Professor


RESEARCH PROJECTS
• Structural and functional analyses of the exchange proteins directly activated by CAMP (EPAC).
• Examines the role of EPAC proteins in major human diseases such as chronic pain and polyneuropathic vascular diseases using EPAC knockout mouse models and pharmacological inhibitors.
• Preclinical development of novel drug candidates targeting EPAC for the treatment of microbial infections caused by bee and tick-borne bacteria Robertsii.

KEY PUBLICATIONS
Our research programs are (1) to obtain critical new knowledge of cancer metastasis and drug resistance of human cancer cells, and (2) to identify new biomarkers and drug targets for the development of better therapeutics for human cancers.

Cancer metastasis, the spread of tumor to other parts of patient's body, is responsible for over 90% of cancer deaths. However, cancer metastasis is still poorly understood and the current approaches to prevent or treat human metastatic cancers are mostly unsuccessful. Therefore, there is a huge unmet medical need to better understand cancer metastasis and to develop new therapies against cancer metastasis. Through genomics, RNAi and CRISPR functional screens, our lab has identified several novel crucial but previously unknown regulators for cancer metastasis. Some of the novel regulators control epithelial-mesenchymal transition (EMT), while some others are essential for survival and proliferation of highly metastatic cancer cells (i.e., essential genes). EMT, a developmental process, is believed to play a key role in cancer cell invasiveness, drug resistance, organ metastases, and stem cell phenotypes. Essential genes for metastatic cancer cells may be the key to understand colonization, the site-limiting step of cancer metastasis. Signaling pathways and molecular mechanisms of these novel regulators are under investigation with nucleo- luric, cellular, biochemical, genetic, proteomic approaches, and mouse models. These studies are yielding critical new insights for cancer metastasis and facilitating the development of new therapeutics and biomarkers. Another research topic in our lab is to study the mechanisms of cancer cell plasticity and drug resistance. In particular, we study how prostate cancers become resistant to a new generation of androgen receptor pathway inhibitor (ARPI), and how non-small cell lung cancers (NSCLC) become resistant to EGFR inhibitors. The common theme in this topic is to be better understood and to target a process called neoplastic differentiation (ND).

**Key Publications**


**Lab Members**

Post-doctoral fellow: Zhong Wang
Student: Gaolin Zhang, Sanrui Nadenezh-

**Research Assistant:** Han Yang

**Research Projects**

- Mechanisms of action for novel regulators of NED, cellular plasticity and drug resistance, especially the roles and mechanisms of action of several novel epigenetic regulators.

**Key Publications**


4. **Li, W.,** Molecular links between neuroendocrine differentiation and angiogenesis in prostate cancer progression. Frontiers in Endocrinology, 2020 Jan 21;9:1489. *Corresponding author*


**Lab Members**

Post-doctoral fellow: Zhong Wang
Student: Gaolin Zhang, Sanrui Nadenezh-

**Research Assistant:** Han Yang

**Research Projects**

- Mechanisms of action for novel regulators of NED, cellular plasticity and drug resistance, especially the roles and mechanisms of action of several novel epigenetic regulators.

**Key Publications**


4. **Li, W.,** Molecular links between neuroendocrine differentiation and angiogenesis in prostate cancer progression. Frontiers in Endocrinology, 2020 Jan 21;9:1489. *Corresponding author*


**Lab Members**

Post-doctoral fellow: Zhong Wang
Student: Gaolin Zhang, Sanrui Nadene-

**Research Assistant:** Han Yang

**Research Projects**

- Mechanisms of action for novel regulators of NED, cellular plasticity and drug resistance, especially the roles and mechanisms of action of several novel epigenetic regulators.
Monoclonal antibodies are becoming a major drug modality for cancer treatment and have shown clinical successes for treatment of various types of cancer. Tumor targeting monoclonal antibodies, such as trastuzumab against HER2 and bevacizumab targeting tumor angiogenesis factor VEGF, have been successfully used for treatment of many types of cancer. However, similar to many targeted cancer therapies, both innate and acquired resistance to these therapeutic antibodies are widely reported. Understanding the mechanism of cancer resistance to therapeutic antibodies is of paramount importance for improvement of efficacy of these cancer targeted therapies to benefit more cancer patients. Our current research programs are centered on better understanding of tumor microenvironment and cellular immunity and to identify key molecular targets for development of effective anti-cancer immunotherapies.

**RESEARCH PROJECTS**

- Underestimated mechanisms of cancer immunity suppression.
- Develop platform technologies for discovery of therapeutic antibodies.

**KEY PUBLICATIONS**


Ningyan Zhang, PhD
Associate Professor

**Cancer resistance mechanisms to therapeutic antibodies and modulation of anticancer immunity**

State-of-the-art technologies are used in our studies such as high content fluorescence imaging, mass spectrometry, fluorescence activated cell sorting (FACS), and single cell cloning of antibodies. We have established a monoclonal antibody platform technology to discover and select novel anticancer antibodies for functional evaluation and preclinical development. The long-term goal of my research is to understand mechanisms of cancer evasion of antibody and cellular immunity and to identify key molecular targets for development of effective anti-cancer immunotherapies.
Flow Cytometry Service Center
Flow cytometry is a single-cell analysis technology used for cell counting and fluorescent marker detection. It allows high-speed identification, and even isolation, of specific subsets within mixtures of cells. The fluorescence can be measured to determine cellular properties like relative size, complexity, cell type, and response to specific stimuli, such as drugs and genetic manipulations.

These specialized multicolor cell analysis instruments allow researchers to evaluate a large number of samples in a short time frame and gather information on very rare populations of cells and additionally isolate cell populations to be sorted. The current instrumentation allows simultaneous acquisition of more than 10 fluorescent signals from thousands of individual cells per second.

The Flow Cytometry Service Center offers FACS acquisition and analysis, cell sorting, user training, and consultation for experimental design, interpretation, and troubleshooting.

Our instruments are available on a fee-for-service charge to all research investigators from UTHealth and external organizations.

Transgenic and Stem Cell Service Center
Our Immunology and Autoimmune Diseases Center operates a Transgenic and Stem Cells service center, which was established in 1998. It has generated over 800 new transgenic and knock-out mouse animal models for all research investigators from UTHealth and external organizations on a fee-for-service basis.

The stem cell lines that have been derived in the laboratory are highly effective for the generation of knock-out/knock-in mice and for cell differentiation studies. In addition to the production, cryopreservation, and re-derivation of genetically-engineered mice and rats, the services of the facility also include gene targeting, CRISPR/Cas9 genome editing, derivation of new cell lines, and intellectual/technical support in different aspects of microsurgery, cell culture, and stem cell research.

Nano 3D Printing Service Center
Nano 3D Printing Service Center provides state-of-the-art 3D printing services. We provide 3D printed models of human and laboratory animal organs, novel surgical tools, and custom-made laboratory supplies, in prototype or final production models.

We have both traditional FDM (Fortus 450mc) thermoplastic as well as multi-color, resin-based, high-resolution Stratasys J750 (14 micron) 3D printers with large print beds. A wide range of materials with varying Shore A values (hardness) is available. STL files, SolidWorks, or medical imaging files can be used to produce the 3D models.

We are located on the 3rd floor of the Fayez S. Sarofim Research Building.
**IMM Extramural Funding Inception to Date**

- Federal Government: 78.5%
- State Government: 12.6%
- Foundations: 3.5%
- Industry: 0.3%
- Other: 3.5%

**$189,707,325**

**IMM Commercial Outcomes Inception to Date**

- U.S. Patents Issued: **54**
- License & Option Agreements Executed: **71**
- Startup Companies Formed: **18**
- Income Generated from Intellectual Property: **$17,869,290**

---

**Institute of Molecular Medicine Endowments**

- Becker Family Foundation Professorship in Diabetes Research
- Harry E. Bovay Lecture Series in Molecular Medicine
- The Harry E. Bovay, Jr. Distinguished University Chair in Metabolic Disease Research
- Cullen Chair in Molecular Medicine
- John S. Dunn Research Scholars
- The Laurence and Johanna Favrot Distinguished Professorship in Cardiology
- Linda and Ronny Finger Foundation Distinguished Chair in Neuroimmunologic Disorders
- Kay and Ben Fortson Distinguished Chair in Neurodegenerative Disease Research
- Janice Davis Gordon Chair for Bowel Cancer Research
- Annie and Bob Graham Distinguished Chair in Stem Cell Biology
- George and Mary Josephine Hamman Foundation Distinguished Professorship in Cardiovascular Research
- Mary Elizabeth Holdsworth Distinguished University Chair in Metabolic and Inflammatory Disease Research
- IMM General Endowment
- Jerold B. Katz Distinguished Professorship in Stem Cell Research
- The Carolyn Frost Keenan Professorship in Cardiovascular Disease Research
- William S. Kilroy, Sr. Distinguished University Chair in Pulmonary Disease
- Nancy and Rich Kinder Distinguished Chair in Cardiovascular Disease Research
- Kozmetsky Family Chair in Human Genetics
- Rochelle and Max Levit Chair in the Neurosciences
- George and Cynthia Mitchell Distinguished Chair in Neurosciences
- Muller-Eberhard Memorial Lecture Series
- Hans J. Muller-Eberhard, MD, PhD and Irma Gigli, MD Distinguished Chair in Immunology
- D. Dudley and Judy White Oldham Research Fund
- Marjorie B. Poyner and Herbert F. Poyner, Jr. Endowment for Medical Research in the Institute of Molecular Medicine for Prevention of Human Diseases
- Dr. Edward Randall, Jr. Memorial Fund
- Shavonnah Roberts Schreiber Women’s Health Endowment
- The Jerry and Maury Rubenstein Foundation Distinguished Professorship in Heart Disease Research
- Pierce Runnells Memorial Research Fund
- Rodney J. Sands New Initiatives Stem Cell Research Endowment Fund
- C. Harold and Lorine G. Wallace Distinguished University Chair
- Walter and Mary Mischer Distinguished Professorship in Molecular Medicine
- Robert A. Welch Distinguished University Chair in Chemistry
- The Welch Foundation Endowment in Chemistry and Related Sciences
- James T. Willerson Distinguished Chair in Cardiovascular Research in Tribute from the Ewing Halsell Foundation
- Nina and Michael Zilkha Distinguished Chair in Neurodegenerative Disease Research

---

**Thank you to our donors,**

**WHO THROUGH THE ESTABLISHMENT OF THESE ENDOWMENTS, ENABLE THE IMM TO RECRUIT AND RETAIN TOP SCIENTISTS FROM AROUND THE WORLD.**