Baylor
College of
Medicine

DEPARTMENT OF
MOLECULAR & HUMAN
GENETICS

ANNUAL REPORT
2023

Transforming Medicine
Through the Science and
Practice of Genetics

Message from the Chair

I am delighted to welcome you to our 2023 Department of Molecular and Human Genetics Annual Report. As we begin a new year, I'd like to briefly reflect on last year's accomplishments.

The Department continues to excel in all aspects of its mission to transform medicine with the science and practice of genetics and genomics.

The Department remains the top-ranked genetics program, ranking first among all U.S. genetic departments in total awarded funding and number of grants from the National Institutes of Health for over thirteen years.

We continue to lead in the diagnostic testing arena with Baylor Genetics, our joint venture with H.U. Group Holdings, Inc. This jointly governed laboratory supports the academic mission and innovation of the Department while promising to extend the impact of genetic diagnostic testing worldwide.

Our faculty continue to deliver our clinical, training and research missions at home and abroad through our ongoing global partnerships.

In addition, new and continuing consortia with the NIH and industry, such as the *All of Us* program, GREGoR: Genomic Research to Elucidate the Genetics of Rare disease, the Knockout Mouse Phenotyping Program, and the Center for Precision Medicine Models, are leading to new gene discoveries and advancements in the implementation of genetics and genomics in medicine.

Our Baylor Undiagnosed Diseases Center houses our NIH Undiagnosed Diseases Network clinical site and provides clinical services, testing and analysis to assess patients who have not received a diagnosis for their condition. The NIH-supported Project GIVE study has also advanced in its mission to address disparity in access to genomic care for underserved families in the Rio Grande Valley and in west Texas. Both the Undiagnosed Diseases Center (UDC) and Project GIVE utilize the Consultagene platform to provide access to genetic evaluation, peer-to-peer consultation and genetic counseling.

Baylor's *All of Us Evenings with Genetics* Research Scholar Program is now in its third year and has completed two successful Biomedical Researcher Faculty Summits.

The future holds much promise due to the talent and dedication of our renowned faculty, trainees and staff. I consider myself privileged to be a part of this exciting and vital effort.

Warm regards,

Brendan Lee, M.D., Ph.D.
Robert and Janice McNair Endowed Chair
Professor and Chairman
Department of Molecular and Human Genetics

Our Team

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Making History

History of the Department of Molecular and Human Genetics at Baylor College of Medicine

Research in genetics began at Baylor College of Medicine in 1971 when Dr. C. Thomas Caskey and, soon thereafter, Dr. Arthur Beaudet, were recruited from the NIH to lead Baylor's entry into that field. Operating initially within the Departments of Internal Medicine and Pediatrics, the pair created a clinical training program in 1976 to educate and train a group of top investigators in genomics and biomedical research.

As the team of researchers grew in size, scope and ambition, a centralized organization was needed to fuse together the disparate lines of effort. For that reason, in 1985, the Institute of Molecular Genetics was created, thereby placing Baylor on the map as a genetics powerhouse. By leveraging its ability to recruit the best and brightest physicians and scientists in the field, the Institute grew substantially and in 1994, the decision was made to make the Institute a full department.

The Department's success reached new heights with its selection as one of the six pilot programs for the Human Genome Project in 1996. The Human Genome Sequencing Center at Baylor College of Medicine, led by Dr. Richard Gibbs, the Wofford Cain Chair and Professor of Molecular and Human Genetics at Baylor, later became one of three sites to complete the Human Genome Project. In 2000, scientists triumphantly announced they had deciphered the human genome—the blueprint for human life.

The Department has since successfully provided comprehensive clinical care to patients worldwide. Through its position as the largest clinical genetics program in the country, Baylor can offer patients timely and expert assistance, as well as unparalleled treatment and counseling options.

The Department has also expanded its reach by providing diagnostic genetic testing services to the broader medical genetics community through its laboratory, Baylor Genetics, a joint venture with H.U. Group Holdings. Baylor Genetics offers an expansive menu of genetic tests and provides leading service to practitioners worldwide.

The past 50 years have been an exciting time of growth and change. Focused initially on medical and pediatric genetics, the Department has since diversified into functional genomics, genome sequencing, cancer genetics and more, cementing its spot as the preeminent genetics department in the country, if not the world.

Department Leadership

Brendan Lee, M.D., Ph.D.
Robert and Janice
McNair Endowed Chair
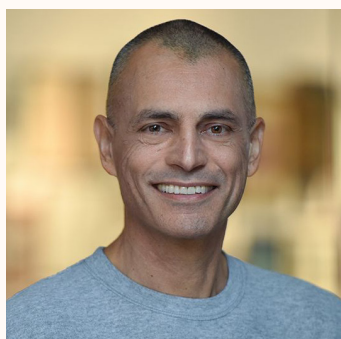in Molecular and Human
Genetics

Laura Rosales, Ed.D.,
M.B.A.
Administrator

Carlos Bacino, M.D.
Vice Chair, Clinical Affairs

Christine Eng, M.D.
Vice Chair, Diagnostic
Laboratory Affairs

Gad Shaulsky, Ph.D.
Vice Chair, Educational
Affairs (Graduate
Education)

Lorraine Potocki, M.D.
Vice Chair for Educational
Affairs (Undergraduate
Medical Education)

V. Reid Sutton, M.D.
Vice Chair for Educational
Affairs (Graduate Medical
Education)

Daniel Riconda, M.S., C.G.C.
Vice Chair for Educational
Affairs (Genetic Counseling
Program)

Kim C. Worley, Ph.D.
Vice Chair for Research
Affairs - Basic and
Translational

Sandesh C. Sreenath
Nagamani, M.B.B.S., M.D.
Vice Chair for Research
Affairs - Clinical

Debra Murray, Ph.D.
Co-Director, Office of
Community Engagement
and Equity

Gladys Pryor, B.S.
Co-Director, Office of
Community Engagement
and Equity

Building a Legacy of Undiagnosed Diseases Research

Over the decades, the Department of Molecular and Human Genetics has been at the forefront of the treatment and research of undiagnosed diseases. Here, we spotlight a few of the key projects that have contributed to the legacy of leadership in this field.

"Researching undiagnosed, rare genetic diseases has been a part of our department's fabric for five decades," said Dr. Brendan Lee, professor and chair of the Department and Robert and Janice McNair Endowed Chair of Molecular and Human Genetics. "We have a long history of landmark genetic discoveries, including in Rett syndrome, Angelman syndrome, Fragile X, spinal cerebellar ataxia, muscular dystrophy, brittle bone diseases and transcription disorders."

The Department's history of undiagnosed diseases research dates back to its founding in the 1970s with Drs. Arthur Beaudet and C. Thomas Caskey leading diagnostic activities like chromosome analysis and cytogenetics. Early investment in research of gene discovery put the Department on a trajectory to become a national and international leader in rare diseases research and clinical diagnosis.

When the National Institutes of Health Common Fund established the Undiagnosed Diseases Network in 2014, Baylor was chosen to serve as one of two sequencing centers for the network, the primary clinical site in the southwest and the lead model organism screening center. The establishment of Baylor's UDN sites brought together the Department's strengths – patient care, state-of-the-art genomic sequencing and functional studies in model organisms to help understand the consequences of genetic variation. Ten years later, as the UDN transitioned from the NIH Common Fund, Baylor established the Undiagnosed Diseases Center to continue providing care to UDN patients and to help other patients with rare undiagnosed diseases.

"Baylor's leadership in multiple aspects of the UDN has allowed for discovery, both in uncovering previously unidentified genetic diseases and in exploring new technologies to be utilized in genetic diagnosis," said Jill Mokry, UDC coordinator and associate professor of molecular and human genetics. "This work is being translated from the study into the clinic, with tests like whole genome sequencing and, and soon, RNA sequencing becoming clinically available tests at Baylor Genetics in collaboration with the Department's newly established Multi-omic Medical Genetics Laboratory (MMGL). With the establishment of Baylor's UDC, a hybrid clinical/research program, we look forward to continuing to bring the lessons learned in the UDN into the clinic for improved patient care and diagnosis."

Leveraging the infrastructure and achievements of the UDN and UDC, Baylor and Texas Children's Hospital have launched a new clinical genomic sequencing program to help patients with an undiagnosed condition. This transformational project is made possible by a grant from the Chan Zuckerberg Initiative and is an extension of national collaborative initiatives such as the UDN and the Genomics Research to Elucidate the Genetic of Rare Diseases programs (GREGoR). Dr. Hugo Bellen, Dr. Katherine King and Dr. Richard Gibbs are leading the program, which provides genomic sequencing for patients with severe conditions such as structural defects or dysfunction in organs including the immune system, heart, lungs and liver.

Baylor also has been a leader in expanding access to genetic testing to underserved populations. The National Human Genome Research Institute (NHGRI)-funded TEXOME Project, led by Dr. Michael Wangler and Dr. Hugo Bellen, leverages Baylor's expertise in clinical research, whole exome sequencing (WES) technology, innovative bioinformatics analysis and functional assays to find answers for underserved patients with undiagnosed diseases across Texas. The Department also has partnered with the University of Texas Rio Grande Valley to provide genetic evaluation and genomic sequencing for

underserved children with suspected genetic disorders living along the Texas-Mexico border. Led by Drs. Seema Lalani and Brendan Lee, the National Center for Advancing Translational

Dr. Brendan Lee opening ASHG 2023 with his presidential address

Dr. Olivier Lichtarge (middle) and Dr. Kim Worley (right) at the department's reception at ASHG 2023

Sciences (NCATS)-funded Project GIVE (Genetic Inclusion by Virtual Evaluation) leverages the Department's Consultagene virtual genetics service delivery platform that was launched in 2018. Using Consultagene, Baylor geneticists can provide virtual genetics consultation to physicians in distant clinics, expanding access to patients who do not live near a clinic that provides genetics services. Next, the Department is working to expand genomic medicine access to underserved neonatal intensive care units across Texas and the broader underserved adult population in rural Texas.

As undiagnosed diseases research continues to grow at Baylor, projects like these support the Department's mission to deliver on the promise of precision medicine for all patients.

Baylor at ASHG 75

For the American Society of Human Genetics, 2023 was a year to celebrate. The society, founded in 1948 to lead research, education and service in human genetics marked its 75th anniversary with a meeting at the Walter E. Washington Convention Center in Washington D.C., this past October. Over 8,000 genetics and genomics researchers, counselors, nurses and industry professionals from nearly 80 countries attended the five-day meeting and presented their research findings in invited, plenary, platform and poster sessions.

The society honored Dr. Jennifer Posey, professor of pediatrics, molecular and human genetics, neurology and neuroscience at Baylor with the with its 2023 ASHG Early Career Award. The award recognizes scientists who are in the early stages of their career as independent investigators.

The Department of Molecular and Human Genetics helped to kick off the festivities by hosting a reception, which saw around 500 people in attendance.

During the event, the Department co-hosted a booth with Baylor Genetics where attendees were able to meet and get more information from representatives of the department's training and

research programs such as Baylor's *All of Us Evenings with Genetics* Research Program, the Center for Precision Medicine Models and TEXOME.

Baylor investigators contributed to over 135 poster abstracts with 12 of those abstracts receiving a Reviewer's Choice Award. Dr. Sairam Behera, postdoctoral associate in the Human Genome Sequencing Center, Jill Mokry, associate professor of molecular and human genetics at Baylor, Dr. Lindsay Burrage, associate professor of molecular and human genetics at Baylor, and Dr. Matthew Chau, an ACGME Laboratory Genetics and Genomics Fellow at Baylor, were first authors on four of the abstracts that received a Reviewer's Choice Award. Baylor investigators also contributed to over twenty platform abstracts.

Dr. Brendan Lee, the 2023 president of ASHG, hosted a Presidential Symposium entitled, "Delivering on the Promise and Future of Genetic

Dr. Stacey Lloyd, Dr. Sandesh Nagamani, and Dr. Debra Murray at the booth at ASHG 2023

and Genomic Medicine, Not a Sisyphean Task." The symposium featured talks by Dr. Donald Kohn from the University of California Los Angeles David Geffen School of Medicine, Dr. Dennis Lo from the Chinese University of Hong Kong and Dr. Olufunmilayo Olopade from the Center for Clinical Cancer Genetics and Global Health at the University of Chicago Medicine. The goal of the symposium was to highlight the enormous research advances of genetics and genomics research in the past two decades, examples of successful clinical implementation, and the continuing challenges of health access disparity.

A special closing reception at the ASHG 2023 Annual Meeting honoring the Society's 75th anniversary was held on the final night at the Ronald Reagan Building and International Trade Center. Themed "One Humanity, Many Genomes™" the event spotlighted 75 years of innovation in the field and how genetics and genomics research is generating benefits for people everywhere. The evening included live music from Ethidium Spill featuring ASHG members Dr. Francis Collins, Dr. Anthony Antonellis, and Dr. Elliott Margulies.
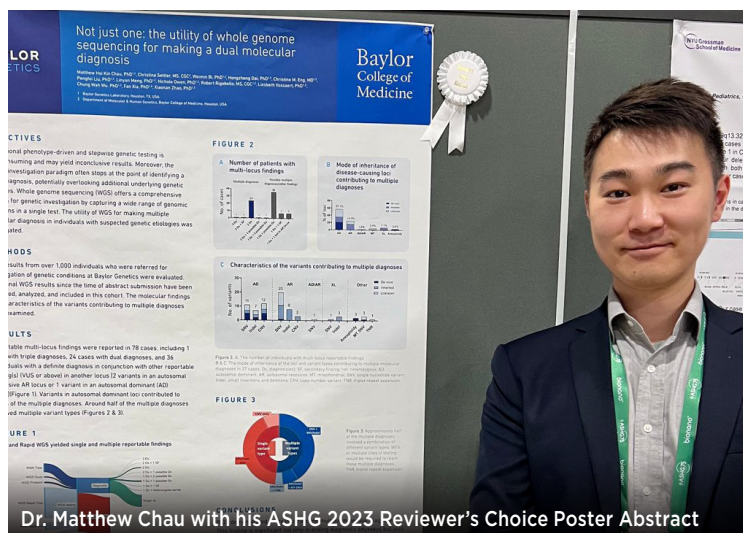
Dr. Matthew Chau with his ASHG 2023 Reviewer's Choice Poster Abstract

Fourth BCM-CUHK-NUS Joint Symposium in Clinical Genetics

In September, the fourth BCM-CUHK-NUS Joint Symposium in Clinical Genetics convened at the MAX Atria in Singapore. The two-day medical convention on clinical genetics and birth defects was jointly organized by the Department of Molecular and Human Genetics at Baylor College of Medicine, Department of Obstetrics & Gynaecology and Department of Paediatrics at the Chinese University of Hong Kong, Department of

Obstetrics & Gynaecology, and Department of Paediatrics at the National University of Singapore.

Nominal sponsors for the event were the National University Centre for Women and Children (NUWoC), College of Obstetricians and Gynaecologists Singapore, College of Paediatrics and Child Health Singapore, Obstetrical and Gynaecological Society of Singapore, College of Clinician Scientists, and the Singapore Paediatric Society.

The symposum began with pre-congress workshops on ultrasound and genetics, bioinformatics and genetic counseling. The first official day of the symposium had opening addresses from Dr. Mahesh Choolani, Dr. Leung Tak-Yeung, Dr. Brendan Lee, and guest of honor, Dr. Kenneth Mak, the director of general health in Singapore. These opening remarks were followed with a plenary session that touched on subjects such as artificial Intelligence in the practice of fetal medicine, new therapies in skeletal dysplasias and the neonatal gut microbiome.

Sessions took place for the rest of first day and continued into the second day of the symposium. These sessions covered topics such as prenatal exome and genome sequencing, advances in genetic diagnosis, prenatal testing and therapy, inborn errors of metabolism, reproductive health, advance pediatric therapies, mosaicism and subspecialty genetics. Baylor faculty speakers

Dr. Ignatia Van den Veyver speaking at the 4th BCM-CUHK-NUS Joint Symposium in Clinical Genetics

included Dr. Carlos Bacino, professor of molecular and human genetics, Dr. Pengfei Liu, associate professor of molecular and human genetics, Dr. Fernando Scaglia, professor of molecular and human genetics, and Ignatia Van den Veyver, professor of molecular and human genetics and obstetrics and gynecology.

Closing the symposium were talks by Dr. Bacino ("Angelman Syndrome: A Journey through Clinical Care, Gene Discovery, Research Studies and Application"); Dr. Richard Choy ("Towards Comprehensive Identification and Interpreation of Pathogenic Structural Variation") and Baylor alumnus, Dr. Cornelius Boerkoel ("Clinical Applications of Long Read Sequencing").

Invited speakers and attendees of the 4th BCM-CUHK-NUS Joint Symposium in Clinical Genetics

Research and Discovery

Research in the Department of Molecular and Human Genetics has led to important discoveries that increase understanding of disease and guide potential new treatments. Here are four recent studies that are representative of the groundbreaking research in the department.

DHX9 Variations Underly Wide Spectrum of Human Neurodevelopmental Disorders

A group of 20 patients with undiagnosed neurodevelopmental disorders ranging from severe to mild has received a genetic diagnosis thanks to an international team of researchers at the GREGoR Research Center at Baylor College of Medicine, the Chinese University of Hong Kong, the German Mouse Clinic and collaborating institutions.

The team analyzed the patients' genes and conducted family studies to detect genetic mutations related to their condition. They discovered that the patients had mutations of the gene *DHX9*, which disrupted the gene's normal function. This is the first time that this gene has been associated with a human disease. Studies in animal models showed a connection between defective variations of the gene and neurodevelopmental problems. Altogether, the findings support that those variations of *DHX9* underlie human neurodevelopment disorders and neuropathy. The study appears in the *American Journal of Human Genetics*.

"Our study started with two patients with remarkably different neurologic conditions for which they did not have a diagnosis despite extensive testing," said first author Dr. Daniel Calame, instructor of pediatric neurology and developmental neurosciences and part of the GREGoR Research Center at Baylor. "In the beginning, we did not have any reason to believe that these patients had a genetic diagnosis in common. It was after we analyzed the results of their genome sequencing that we realized that each had a distinct unusual variant of gene *DHX9*. This motivated us to expand our efforts

to find more cases, ultimately the 20 we came upon."

One of the surprising aspects of this study is that the patients' conditions are remarkably diverse, ranging from severe intellectual disability and seizures to nerve degeneration and neuropathy.

"This is an amazing story of international collaborative science, the global nature of human genetics research and the insights that can be gleaned by the study of neurological disease from a gene and genomic

Dr. James Lupski

variation viewpoint – and achievements possible by the joining of scientific forces from two of my favorite cities: Hong Kong and Houston," said Dr. James R. Lupski, the Cullen Foundation Endowed Chair in Molecular Genetics and professor of pediatrics and molecular and human genetics. Lupski is co-corresponding author of this work and a principal investigator at GREGoR Research Center.

Drug Decelerates Bacterial Race to Antibiotic Resistance

A team of researchers led by Dr. Susan M. Rosenberg, Ben F. Love Chair in Cancer Research, is gaining ground in their search for solutions to the global problem of bacterial antibiotic resistance.

In a study published in *Science Advances*, the team reports on a drug that, in laboratory cultures

and animal models, significantly reduces the ability of bacteria to develop antibiotic resistance, which might prolong antibiotic effectiveness. The drug, called dequalinium chloride (DEQ), is a proof-of-concept for evolution-slowing drugs.

"Most people with bacterial infections get better after completing antibiotic treatment, but there are also many cases in which people decline because the bacteria develop resistance to the antibiotic, which then can no longer kill the bacteria," said Rosenberg, corresponding author

Dr. Susan Rosenberg

and professor of molecular and human genetics, biochemistry and molecular biology and molecular virology and microbiology at Baylor.

The team looked for drugs that could prevent or slow down *E. coli* bacteria from developing resistance to two antibiotics when exposed to a third antibiotic, ciprofloxacin (cipro), the second most prescribed antibiotic in the U.S. and one associated with high bacterial resistance rates. The resistance is caused by new gene mutations that occur in the bacteria during infection. The drug DEQ reduces the speed at which new mutations are formed in bacteria, the team finds.

This study is the first to show that in animal infections treated with cipro, the bacteria activate a known stress-induced genetic mutational process. Cipro resistance occurs mostly by the bacteria developing new mutations, both clinically and in the laboratory, rather than by acquiring genes that confer antibiotic resistance from other bacteria.

The researchers screened 1,120 drugs approved for human use for their ability to dial down the master bacterial stress response, which they showed counters the emergence of resistance mutations. They wanted "stealth" drugs that would not slow bacterial proliferation, which would confer a growth advantage to any

bacterial mutants that resist the mutation-slowing drug itself.

"We found that DEQ fulfilled both requirements. Given together with cipro, DEQ reduced the development of mutations that confer antibiotic resistance, both in laboratory cultures and in animal models of infection, and bacteria did not develop resistance to DEQ," said first author Yin Zhai, a postdoctoral associate in the Rosenberg lab.

Variants of MRTFB Gene Linked to Novel Neurodevelopmental Disorder

Researchers at Baylor College of Medicine have linked specific variants or mutations of the gene myocardin-related transcription factor B (MRTFB) with a novel neurodevelopmental disorder. The team reports in the journal *Genetics in Medicine* that they found variants in this gene in patients whose neurodevelopment disorders had previously gone undiagnosed. The research also revealed that the mutations disrupt the way the MRTFB protein controls other genes in the cell and this cascades to affect hundreds of other genes.

"We identified two patients with this novel neurodevelopmental disorder through the Undiagnosed Diseases Network (UDN). The patients have intellectual disability, difficulty speaking, impulse control issues, movement impairments and altered facial features," said first author Dr. Jonathan Andrews, postdoctoral associate of molecular and human genetics in Dr. Michael Wangler's lab. "Both patients have mutations in the *MRTFB* gene, which until now had not been associated with a genetic condition. We decided to investigate how these mutations affected the function of the MRTFB protein to try to understand how the changes in the patient's gene might lead to their medical condition."

The MRTFB protein is an important transcriptional regulator, meaning it normally promotes the activity of approximately 300 other genes, including genes involved in making the structure of the cell and communication

between brain cells. MRTFB is thought to be particularly important during early development in shaping the heart, lungs, liver and brain.

"While additional research is necessary to demonstrate that the patients' *MRTFB* variants affect neurological development, it is plausible that the lack of regulation present in these variants may be sufficient to alter normal patterns of neuronal growth and development," said

Dr. Michael Wangler

Wangler, associate professor of molecular and human genetics and corresponding author of the work. "The findings are important because they open new avenues to investigate mechanisms that lead to this disorder, offering ideas toward a future treatment for the disease."

Novel Biomarker and Potential Improved Therapy for MS and Related Disorders

Degeneration of myelin, an insulating sheath required for rapid communication between nerve cells, is a notable hallmark of multiple sclerosis (MS) and related neurodegenerative disorders such as Alzheimer's disease or Huntington's disease.

A team led by researchers at Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute (Duncan NRI) at Texas Children's Hospital report in the journal *Cell Metabolism* that myelin breakdown results in an accumulation of very long-chain fatty acids (VLCFA) and their intermediates, which triggers an autoimmune response that damages brain cells. Furthermore, reducing the levels of VLCFA using approved drugs bezafibrate and fingolimod had a synergistic beneficial effect on MS in an animal model, suggesting a potential more effective treatment for MS patients.

Dr. Hyunglok Chung, a former postdoctoral fellow in Dr. Hugo Bellen's lab who also is the

first and co-corresponding author of this study, had previously reported that excess VLCFA is harmful to nerve cells in fruit flies. In the first part of this study, Chung and his colleagues show, also in fruit flies, that accumulation of S1P, a key product of VLCFA degradation, causes inflammation in nerve cells and potentially damages them.

The team then collaborated with the lab of Dr. Hyun Kyoung Lee, associate professor of pediatrics – neurology and co-corresponding author, to explore the role of S1P in MS progression in a mouse model. The team found that pre-symptomatic treatment of these mice with bezafibrate, a lipid-lowering drug that inhibits the synthesis of VLCFA, slowed the progression of this debilitating disorder by reducing myelin loss, neuronal damage and infiltration of immune cells into the brain. They also tested the potential therapeutic effect of lowering VLCFA and S1P on MS and saw a synergistic improvement in paralysis and motor performance, and in myelin and neuronal loss.

"We are very excited by the potential clinical implications of this study not just in the treatment of MS but also for other neurodegenerative conditions that are associated with myelin loss, disruptions in lipid metabolism and neuroinflammation," said Bellen, Distinguished Service Professor in molecular and human

Dr. Hugo Bellen

genetics and a co-corresponding author of this study.

Path-breaking Research Reveals New Possibilities to Improve Treatment of Endometrial Carcinoma

Endometrial carcinoma, a cancer of the lining of the uterus, is the most common gynecologic malignancy in developed nations. A study published in the journal *Cancer Cell* and led by Dr. Bing Zhang, professor in the Lester and Sue Smith

Breast Center and the Department of Molecular and Human Genetics and a McNair Scholar at Baylor, used 10 genomics and proteomics platforms to identify biological markers and pathways that could be used to develop improved therapies for this condition.

The findings provided functional validation of previously described effects of frequently observed gene mutations, protein markers of clinical and genomic tumor subgroups and the impact of defects in antigen presentation, an important step in triggering an immune response, on patterns of immune infiltrates in some tumors.

"Importantly, our current study also expands our previous work in endometrial cancer in several ways, including the exploration of additional protein types such as glycoproteins, contributing further insights into endometrial cancer biology," said co-first author Dr. Yongchao Dou, postdoctoral associate in Zhang's lab at the Lester and Sue Smith Breast Center. "We also developed targeted mass spectrometry-based assays, which provide a path to the development of clinical assays."

The researchers explored in detail the role of mutations called in-frame indels in the PIK3R1-AKT pathway that have been associated with worse cancer outcomes. The researchers hypothesized that in-frame indels eliminate PIK3R1's ability to suppress cancer progression. PIK3R1 is thought to suppress cancer progression by preventing AKT1 phosphorylation, the addition of a phosphate chemical group to the enzyme AKT1. Phosphorylated AKT1 is thought to activate pathways that help cancer grow.
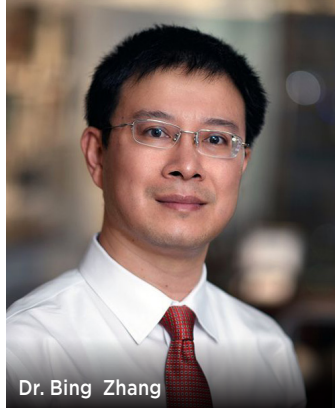
Dr. Bing Zhang

The Zhang lab collaborated with Dr. Yi Li, professor of molecular and cellular biology and of molecular virology and microbiology, to gain more evidence supporting their observation of the potential role PIK3R1 proteins with in-frame indels in promoting AKT phosphorylation.

"Altogether, our findings suggest that PIK3R1 in-frame indel mutations are potential markers of the AKT inhibition response and might be used to identify patients who could respond to AKT inhibitors, moving a step toward future improved clinical applications," said co-corresponding author Zhang. "We have generated a list of potential therapeutic targets for the scientific community to test for their potential clinical value.

Grant Awards Continue to Drive Progress

The National Institutes of Health is the primary governmental agency responsible for biomedical and health-related research in the United States. A department's ability to consistently obtain NIH grants, which are awarded through a competitive peer review process, demonstrates the strength of its research and training programs. On that basis alone, the Department of Molecular and Human Genetics at Baylor College of Medicine continues to distinguish itself.

#1 ranked U.S. Genetics Department in NIH awarded grants and total funding for past 13 years

Total NIH Funding to Leading Genetics Departments for 2023

Number of NIH Grants Awarded to Leading Genetics Departments
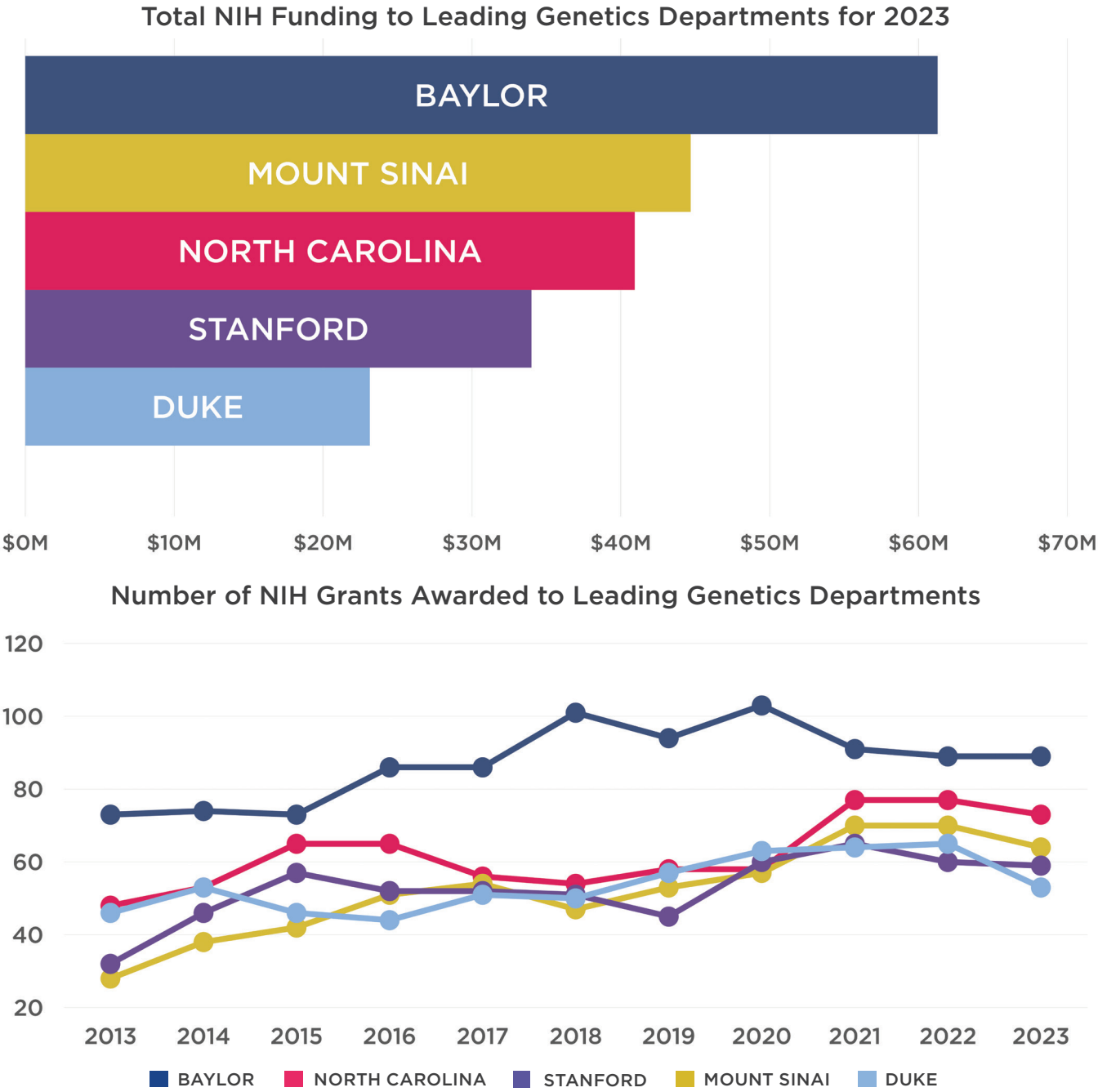
Baylor Receives NIH Funding to Study Somatic Mosaicism

As part of a new National Institutes of Health Common Fund program called the Somatic Mosaicism across Human Tissues (SMaHT) Network, Baylor College of Medicine researchers received three grants totaling more than $17.8 million over five years to develop state-of-the-art tools to catalog the extent of somatic mosaicism in different cell types, tissues and

Dr. Richard Gibbs

life stages, to better understand how much somatic mosaicism influences human biology and disease.

"This important program will comprehensively assess the role of somatic mutations in normal human development," said Dr. Richard Gibbs, founding director of the Human Genome Sequencing Center and Wofford Cain Chair and Professor in Molecular and Human Genetics at Baylor. "It will be foundational for fully understanding the role of somatic variation in all aspects of human disease."

One of Baylor's grants will establish a genome characterization center at Baylor's Human Genome Sequencing Center. Gibbs serves as co-principal investigator of the project, along with Dr. Harsha Doddapaneni, associate professor at the Human Genome Sequencing Center, and Dr. Rui Chen, professor of molecular and human genetics. The center will characterize somatic variation in 550 of the SMaHT program's 2,250 tissue samples. Sample tissues will come from approximately 150 human donors from diverse ancestry backgrounds and stages of life and will represent different tissue types, including brain, blood, skin, muscle, colon, spleen, uterus, vas deferens, ovaries and testis.

Along with the large-scale profiling endeavors from SMaHT Centers in the network, new methods for accurate detection of somatic mosaicism, especially at single-cell resolution, are greatly needed. To address this issue, 14 projects in the network, including two at Baylor, will focus on developing new methods.

A project led by principal investigator Dr. Chenghang (Chuck) Zong, assistant professor of molecular and human genetics and a McNair Scholar, will develop a new single-cell whole-genome amplification chemistry that allows high-accuracy and high-coverage detection of somatic mutations in single cells.

A project led by principal investigator Dr. Fritz Sedlazeck, associate professor at the Human Genome Sequencing Center, will focus on developing novel computational methods for studying somatic structural variation based on long-read sequencing that use new algorithmic and machine learning approaches.

Other Baylor researchers contributing to this work include Donna Muzny and Drs. Marie-Claude Gingras, Elizabeth Atkinson and Tao Wu.
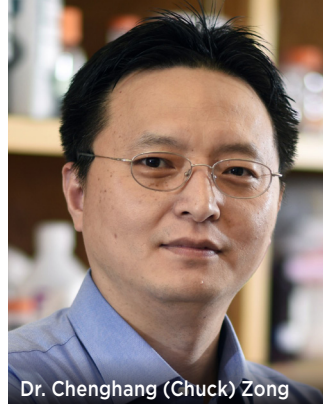
Dr. Chenghang (Chuck) Zong   Dr. Fritz Sedlazeck

Boeynaems Awarded CPRIT Grant to Study Stress Response in Cells

Dr. Steven Boeynaems, assistant professor of molecular and human genetics, was awarded a Cancer Prevention and Research Institute of Texas (CPRIT) grant to continue his work studying how cells and organisms respond to stress.

"Any cell, in nature or in our bodies, during its existence, will have to deal with some conditions

that deviate from its ideal environment," Boeynaems said. "The key issue that all cells face in such conditions is that they can no longer properly fold their proteins, and that leads to the abnormal clumping of proteins into aggregates. We have seen such aggregates occur in many species and under a variety of stress-related conditions, whether it is in a plant dealing with drought or in a human patient with aging-related Alzheimer's disease."

It appears that when cells undergo stress, the proteins tend to aggregate. However, Boeynaems says that does not appear to be the full story and there is still much to learn.

"It is becoming increasingly evident that under stressful conditions, our cells are not completely defenseless. Nature has evolved innovative mechanisms for organisms to protect their cells. For instance, instead of forming toxic clumps, some proteins form liquid droplets, which we think act in a protective manner. This is a very important cellular process that will help us understand how these diseases develop," he said. "For example, in the past few years we have seen that defects in these liquid protein droplets can underlie diseases like ALS."

He said that figuring out how to maintain proteins in their non-aggregated state in these liquid droplets is a part of potentially preventing, treating or slowing the progression of certain illnesses. While Boeynaems will continue his work on neurogenerative disease, his lab will now also study the role of cellular stress in brain cancer.

"We have studied protein droplets not only in humans but also in stress-tolerant organisms such as plants and bacteria for years now. We propose to build and leverage on that knowledge to come up with innovative new treatments for cancer patients," Boeynaems said.

Dr. Steven Boeynaems
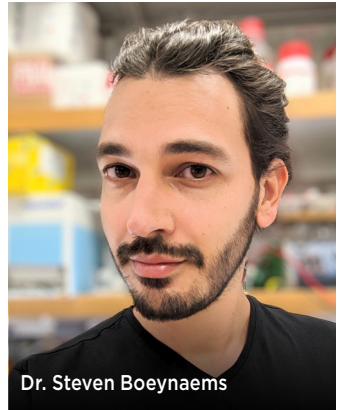
Other Grants/Awards

The Department is proud to receive generous funding from many agencies and foundations, some of which are listed below:

The Howard Hughes Medical Institute
The Robert and Janice McNair Foundation
The Cancer Prevention and Research Institute of Texas
The Welch Foundation
The Simons Foundation
The Huffington Foundation
The Doris Duke Foundation
The American Heart Assocation
Autism Speaks

Clinical Research

The Clinical Research Division of the Department of Molecular and Human Genetics at Baylor College of Medicine facilitates the planning, implementation and conduct of many clinical studies in rare disorders.

Our department's clinical research consists of studies that aid in the discovery of new genes as causes for human diseases and genetic traits, natural history studies, proof-of-concept studies that help translate research findings from the bench to bedside and clinical trials of novel therapies for genetic disorders.

In 2023, the division, led by Dr. Sandesh Nagamani, professor of molecular and human genetics at Baylor, had more than 50 ongoing studies. These studies consisted of investigator-initiated studies where department faculty are sponsors, industry-sponsored studies and studies that are conducted within the context of large, multicenter consortia and networks.

We are a primary or a lead site for many consortia of the NIH Rare Diseases Clinical Research Network including Urea Cycle Disorders Consortium, Brittle Bone Disorders Consortium, North American Mitochondrial Disease Consortium, Global Leukodystrophy Initiative Clinical Trials Network and Frontiers in

2023 Trials
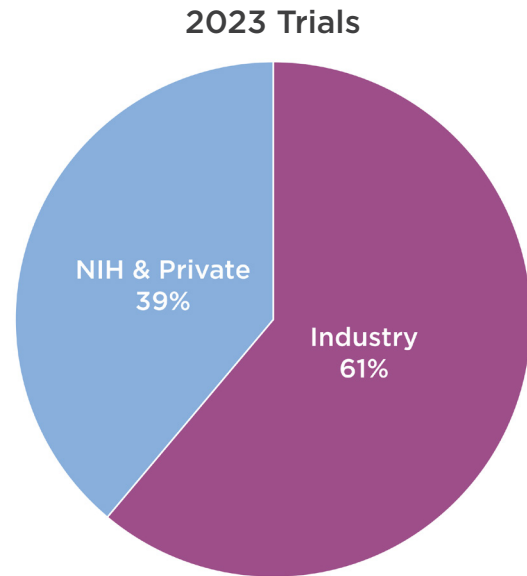
Congenital Disorders of Glycosylation. Baylor's Undiagnosed Diseases Center, Center for Precision Medicine Models, GREGoR Consortium and the Intellectual and Developmental Disabilities Research Center leverage the facilities available within the Division of Clinical Research.

Growth of Clinical Studies
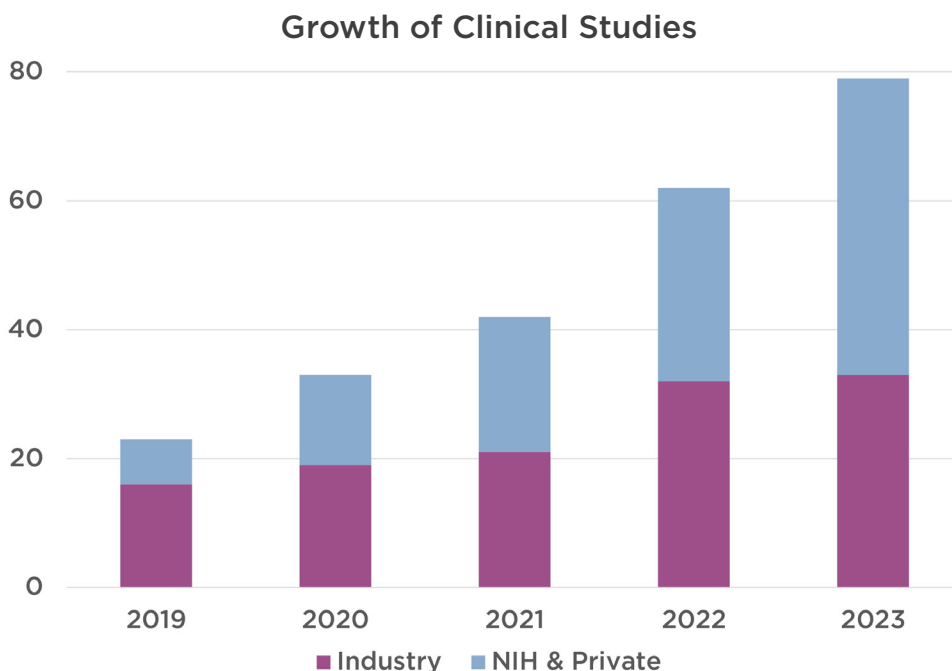
Genetics Clinics

Improving Patients' Lives with Unmatched Clinical Services

Baylor College of Medicine's clinical genetics program is the largest program of its kind in the country, with clinics spanning across multiple genetics-based disciplines. The clinical program takes a collaborative approach that provides patients with the highest quality, individualized care available. Clinical activities take place across several sites.
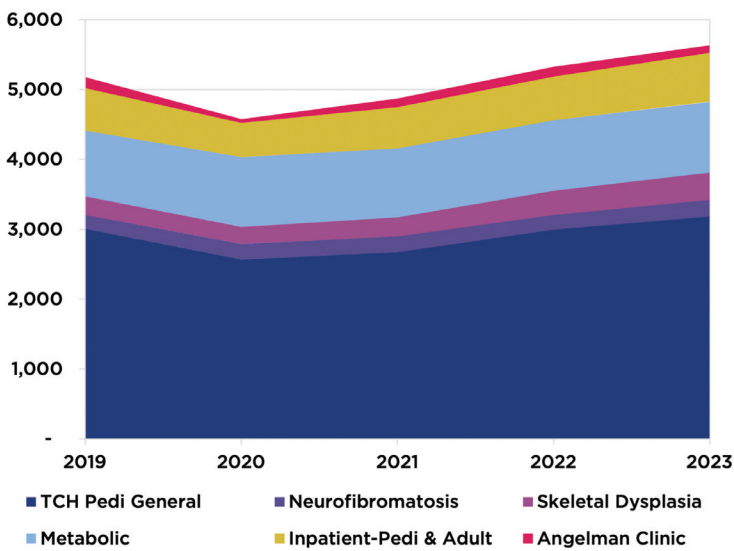
Pediatric Genetics

The pediatric genetics clinical service provides inpatient care to complex and/or critically ill patients at Texas Children's Hospital and several other hospitals within the Texas Medical Center and outside (TCH West Campus and The Woodlands Texas Children's Hospital). The outpatient pediatric genetics clinics are among the largest genetics clinics in the country and see over 5,000 patients annually.

Specialty clinics within the Texas Children's Genetics Clinic include the metabolic clinic, neurofibromatosis clinic, and the skeletal dysplasia clinic. We also have many multidisciplinary team clinics like the Angelman Syndrome Clinic, the Center for Genetic Disorders of Obesity, Mitochondrial Medicine Clinic, and the Gender Medicine Program. The Department of Molecular and Human Genetics clinical and genetic counseling faculty also staff joint clinics with other departments such as oncology (cancer genetics), otolarynogology (otogenetics) and neurology (neurogenetics/ tuberous sclerosis).
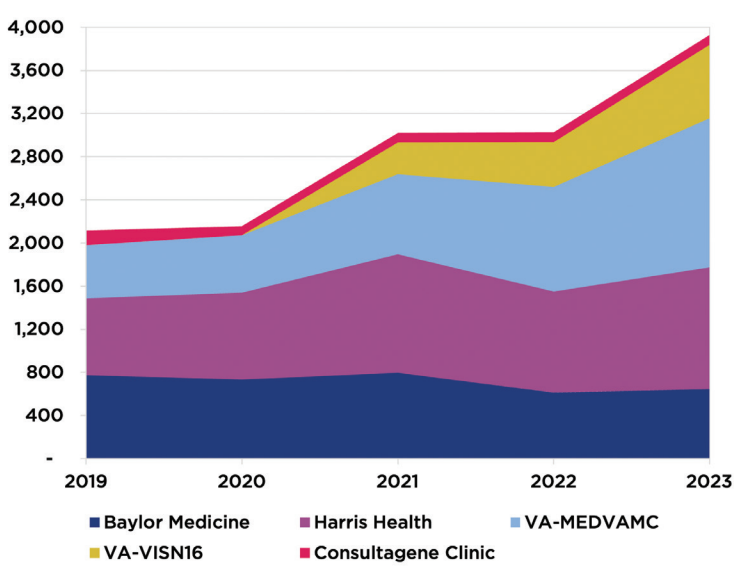
Adult Genetics

The Department's adult genetics clinical service is one of the largest in the country, providing inpatient and outpatient care and genetic counseling exclusively for adult patients at Baylor Medicine, Harris Health, the U.S. Department of Veterans Affairs (VA), and through its virtual Consultagene Clinic. The service at the VA includes the Michael E. DeBakey VA Medical Center and as well as local community based outpatient clinics. In addition, the service sees patients via telemedicine throughout Veteran Integrated Service Network 16 (VISN16). The

Clinical Genetics Patient Volume (Pediatric)

Legend: TCH Pedi General, Neurofibromatosis, Skeletal Dysplasia, Metabolic, Inpatient-Pedi & Adult, Angelman Clinic

Clinical Genetics Patient Volume (Adult)

Legend: Baylor Medicine, Harris Health, VA-MEDVAMC, VA-VISN16, Consultagene Clinic

U.S. is divided into 18 VISNs that provide care for veterans. VISN16 includes eight veterans affairs medical centers (VAMCS) and community clinics in the Southeast U.S.

This service sees patients for a wide variety of indications including, but not limited to, intellectual disability, neurological conditions, cardiovascular conditions, connective tissue disorders and for a personal or family history of cancer.

In addition to our general genetics clinic, we have specialty clinics such as the Metabolic and Genetic Disorders of the Bone Clinic, Cancer Genetics Clinic, Neurogenetics Clinic, Cardiovascular Genetics Clinic and Mitochondrial Medicine Clinic.

Prenatal Genetics

As the largest of its kind in the U.S., the Baylor Prenatal and Reproductive Genetics Clinic at Texas Children's Pavilion for Women with its seven associated Texas Children's community maternal-fetal medicine clinics is comprised of physicians and genetic counselors that specialize in prenatal and reproductive genetic risk assessment and the latest genetic testing technologies. Through its partnership with the Department and the Texas Children's Fetal Center, the clinic offers world renowned clinical and research expertise in prenatal and reproductive genetic screening, diagnostic testing and counseling.

Prenatal and reproductive genetic services and counseling are also offered at Ben Taub Tower specialty clinics and virtually through the Consultagene Clinic.

Clinical Genetics Patient Volume (Prenatal)


19
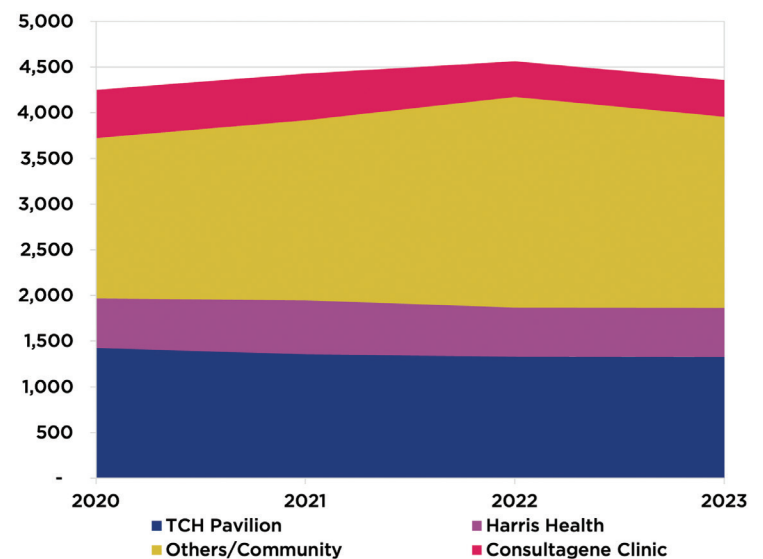
The Consultagene Clinic

The Consultagene Clinic is now in its fourth year of operation and remains a fully virtual genetic counseling clinic. In 2023, a total of 495 patients were seen. Since its launch in 2019, a total of 2,844 patients have received genetic counseling through the Consultagene Clinic.

Preconception/IVF referrals continue to make up the majority of referrals seen, making up 62% of referrals in 2023. Neurology and cardiology referrals continue to increase due to the use of Consultagene for results disclosure by the PDGene study and the Cardiometabolic study. The clinic also saw a 52% increase in requests for genetic counseling from patients outside of Texas. To address the increase in interest, expand its reach and make genetic counseling more accessible, the clinic now has genetic counselors licensed in Alabama, Arkansas, California, Illinois, Louisiana, New Mexico, Oklahoma and Washington. The clinic has continued outreach to IVF practices in these states and states without genetic counseling licensure. Consultagene had a booth at the 2023 American Society for Reproductive Medicine (ASRM) Scientific Congress & Expo due to the clinic's expertise in reproductive genetic counseling.

Patients seen in the clinic are provided access to the Consultagene platform, allowing patients to watch educational videos, explore online resources, communicate with their provider and access documentation from their consultations. For 2023, the platform saw another change through the incorporation of DocuSign.

Patients are asked to participate in a survey to gauge their experience with the clinic and the platform. Of the 99 patients who participated in the survey this past year, 44% used the resources provided in the patient portal; 99% said the genetic counseling met or exceeded their

2023 Consultations By Indication

Legend: Preconception/IVF, Prenatal, Cancer, Neurology, Cardiology
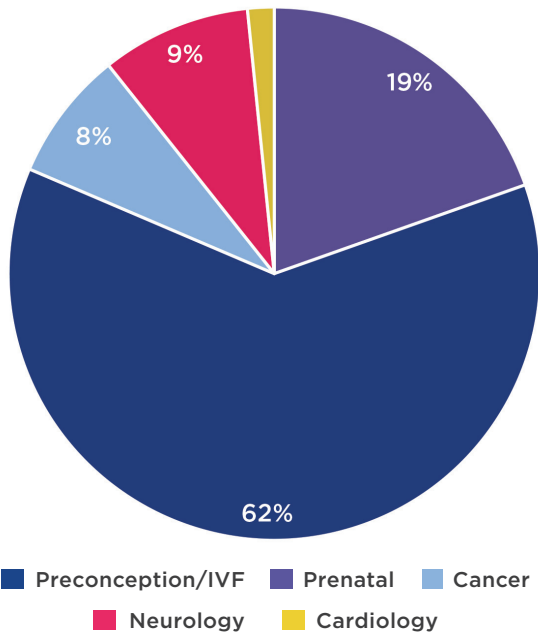
expectations; 99% agreed or strongly agreed that virtual genetic counseling was equivalent to an in-person appointment; and 95% would recommend virtual genetic counseling.

Patient Consultations

Legend: 2019, 2020, 2021, 2022, 2023
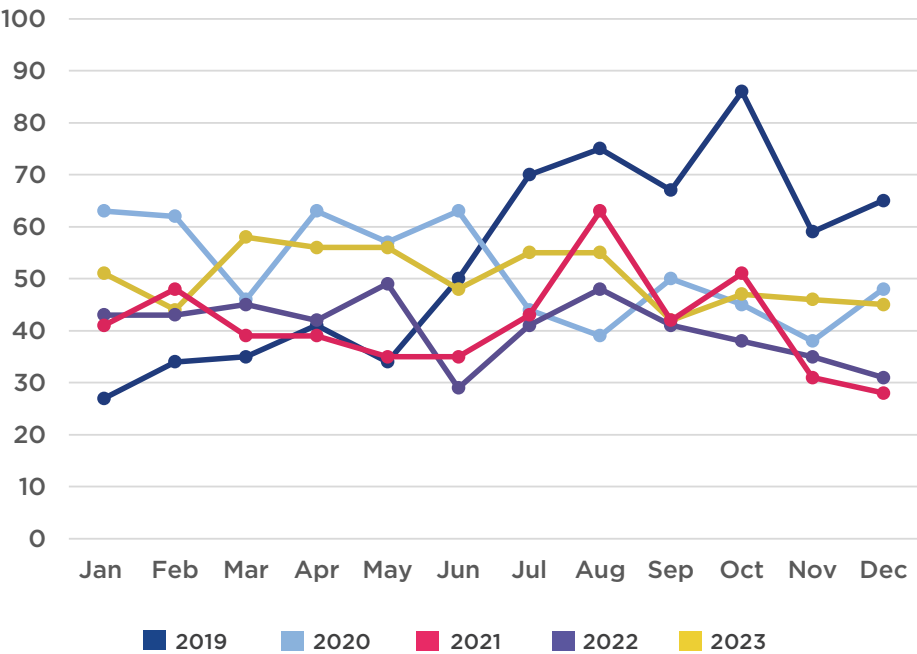
Research Centers

Baylor College of Medicine is home to one of the largest biomedical research programs in the nation. The Department of Molecular and Human Genetics is proud to work hand-in-hand with the following centers, each of which focuses on specialized areas of medical research. These centers are led by primary faculty of the Department and, together, advance the current boundaries of scientific knowledge.

New Center Provides Resources to Develop, Test New Genome Editing Technologies

Researchers at Baylor and Rice University received a grant for more than $3.9 million over five years from the NIH's Office of Research Infrastructure Programs to establish the Baylor/Rice Genome Editing Testing Center (GETC). The new center will assist investigators from across the country with somatic cell genome editing experiments in mouse models.

Somatic cell genome editing, the ability to edit DNA within the body's non-reproductive cells, is a promising potential treatment for the most severe human diseases. Over the last decade, significant effort has gone into developing more effective genome editing systems and methods of delivery to specific cells and organs. However, many of these new technologies do not progress to use in humans because there is insufficient evidence from animal models supporting their effectiveness.

"Our center will provide mouse model resources and genome editing testing pipelines to researchers who are developing new genome editing and delivery technologies, but need assistance with conducting preclinical animal studies," said Dr. Jason Heaney, co-principal investigator and associate professor of molecular and human genetics. "Our goal is to help generate the animal model data needed to demonstrate the therapeutic potential of these cutting-edge technologies."

The center will offer paid services, including use of somatic genome editing testing pipelines and mouse models for *in vivo* testing, to investigators across the country.

Dr. William Lagor, professor of integrative physiology, and Dr. Christopher Walkey, instructor of integrative physiology, are co-principal investigators. Dr. Denise Lanza, assistant professor of molecular and human genetics, will lead mouse resource management. Dr. Cecilia Ljungberg, assistant professor of pediatrics and director of the RNA In Situ Hybridization Core, will supervise and support quantitative tissue imaging. Dr. Uma Ramamurthy, associate professor of pediatrics and executive director of research information technology in the Office of Research, will assist with informatics. Dr. Gang Bao, department chair and Foyt Family Professor of Bioengineering at Rice, will lead the efforts in the GETC to determine the efficiency, specificity and safety of genome editing systems in disease models.

Human Genome Sequencing Center

The Baylor College of Medicine Human Genome Sequencing Center (Baylor HGSC), led by Dr. Richard Gibbs, has been operational for more than 20 years. Originally established in 1996 to participate in, and eventually help complete, the Human Genome Project, the HGSC has grown and achieved international recognition as a large-scale DNA sequencing and analysis center. Currently a Center for Complex Disease Genomics supported by the NIH and the National Human Genome Research Institute (NHGRI), the Baylor HGSC has expanded its research focus into new and exciting areas.

The Baylor HGSC employs more than 180 staff members, and occupies more than 36,000 square feet of space in the Margaret M. and Albert B. Alkek Building at Baylor located in

the heart of the Texas Medical Center, the world's largest medical complex.

The major activity of the Baylor HGSC is high-throughput DNA sequence generation and the accompanying analysis. The center currently operates multiple sequencing platforms: Illumina, Pacific Biosciences, Oxford Nanopore and Sanger. The sequence data generated by these machines is analyzed in a complex bioinformatics pipeline, and the data are deposited regularly in the public databases at the National Center for Biotechnology Information (NCBI) or cloud partners for secure data sharing. This ensures that the worldwide research community has timely access to the data.

A major focus of the Baylor HGSC is the deciphering of the genetic architecture of common complex diseases. These include cardiovascular disease, neurodegeneration and cancer predisposition – all major causes of adult death with strong heritable components. Understanding the genetic architecture of these disorders is the key to identifying gene changes that directly cause the diseases and then developing therapeutic strategies. This pathway from "bench to bedside" is the foundation of the national initiative in precision medicine.

In direct response to this new era, the Baylor HGSC has launched the HGSC Clinical Lab (HGSC-CL), which has a complete infrastructure to support large-scale sequencing and genomics projects. With its sophisticated informatics core and pipeline and state-of-the-art technology development core, the CAP accredited/CLIA-certified HGSC-CL can deliver clinical test grade data for returning results to diagnosing physicians.

In addition to studying genetic datasets, the Baylor HGSC places great emphasis on integrating other omic data into genetic analyses.

In support of this effort, the Baylor HGSC routinely generates RNA-Seq data to look at expression patterns across samples and time
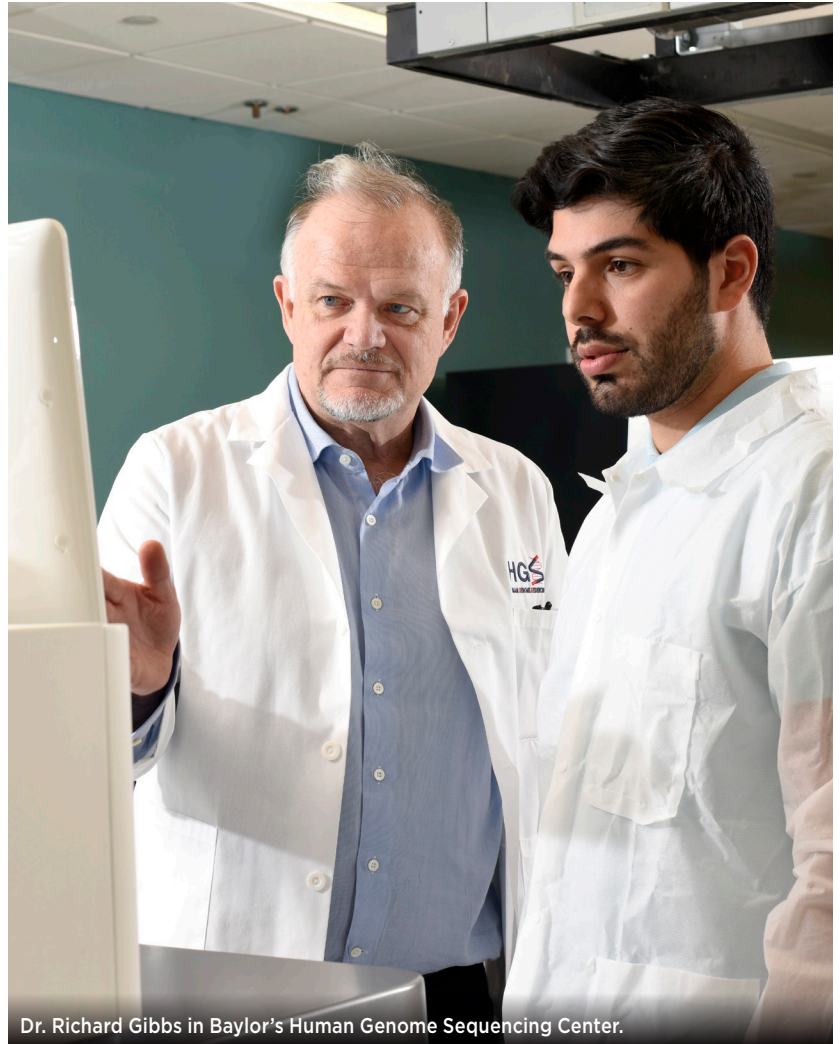
Dr. Richard Gibbs in Baylor's Human Genome Sequencing Center.

points. Additionally, the Baylor HGSC regularly evaluates metabolomic and methylation profiles across samples. The Baylor HGSC also works in close partnership with the Alkek Center for Metagenomics and Microbiome Research (CMMR) to assess how the microbiome impacts human health.

Developing new technologies and applications is a major objective for the Baylor HGSC. These development steps, which produce laboratory innovations and enhancement to analyses, are made possible by a dedicated R&D team. The Baylor HGSC regularly serves as a beta test site for new technologies and provides feedback to companies on performance. This arrangement allows the Baylor HGSC to have early access to the latest improvements available.

Jan and Dan Duncan Neurological Research Institute

In December 2010, the Jan and Dan Duncan Neurological Research Institute (NRI) at Texas Children's Hospital opened and was the first facility of its kind in the U.S. with a multidisciplinary research approach dedicated to pediatric brain disorders. Since then, NRI researchers have published more than 1,000 scientific studies in top-tier journals, discovered 72 disease-causing genetic mutations, completed one successful clinical trial for an intractable epilepsy and have six additional clinical trials in development. The reach of these discoveries extends beyond the pediatric world, impacting critical understanding of a wide spectrum of neurological and psychiatric diseases including

Jan and Dan Duncan Neurological Research Institute (NRI) at Texas Children's Hospital

Alzheimer's, Parkinson's, bipolar disorder, eating disorders and addiction.

The NRI, under the astute direction of Dr. Huda Zoghbi, a Distinguished Service Professor at Baylor and Howard Hughes Medical Institute investigator, fosters a one-of-a-kind research environment designed to affect the future of neurological disease. About 30 investigators from around the world and their research teams, all experts in diverse disciplines – genetics, neurobiology, physics, mathematics, bioinformatics and engineering – work in specially designed "collaboratories." These open labs facilitate the free exchange of ideas, information and resources.

Huffington Center on Aging

Recognized as one of the premier aging centers in the world, the Roy M. and Phyllis Gough Huffington Center on Aging, led by Dr. Hui Zheng, Huffington Foundation Endowed Chair in Aging and professor of molecular and human genetics and neuroscience, spearheads breakthrough research and is committed to translating basic research discoveries into applications that promote healthy aging and combat age-associated disorders.

The center facilitates and coordinates interdepartmental research and initiates its own research studies to address questions that are important to the biology, pathophysiology and diseases of aging. Major research topics include cell and molecular biology of aging, adrenal cell biology, DHEA, aging of the skin, the aging cardiovascular system, healthcare outcomes research and ethical issues in acute and long-term care settings.

Through close alignment with the Section of Geriatrics and Palliative Medicine in the Department of Medicine, the HCOA also provides medical education and training and delivers healthcare through affiliated hospitals.

The HCOA was formed in 1988 with the generosity of the late Roy M. and Phyllis Gough Huffington, Houston philanthropists who foresaw the need for an academic entity devoted to studying aging,

providing care for older people and teaching future health professionals and researchers about geriatrics and gerontology.

## Computational and Integrative Biomedical Research Center

The Computational and Integrative Biomedical Research (CIBR) Center is directed by Dr. Olivier Lichtarge, Cullen Chair and professor of molecular and human genetics at Baylor.

The CIBR Center is comprised of more than 100 affiliate faculty members from different Houston institutions. The CIBR Center helps the College bridge the translational gap from data to models, and from models to drug discovery and personalized therapy by fostering collaborations among scientists and developing original quantitative approaches to biological and clinical problems.

To assist students and faculty, the CIBR Center provides the resources to help address the broad range of analytical problems posed by the complexity of high throughput biological datasets. The center organizes the Current Topics in Computational Biomedicine Course where students keep abreast of active quantitative research among the CIBR faculty. To date, the Current Topics course has hosted more than 160 seminars and approximately 40 journal clubs.

In addition to the Current Topics course, the CIBR Center coordinates workshops and access to cluster computing for its faculty members. The center provides site licenses to scientific software (Mathworks MATLAB and Wolfram Mathematica) and regular consultation on data organization and analysis through its Data Clinics (16 sessions per year).

Intellectual and Developmental Disabilities Research Center

Dr. Hui Zheng, director of the Roy M. and Phyllis Gough Huffington Center on Aging
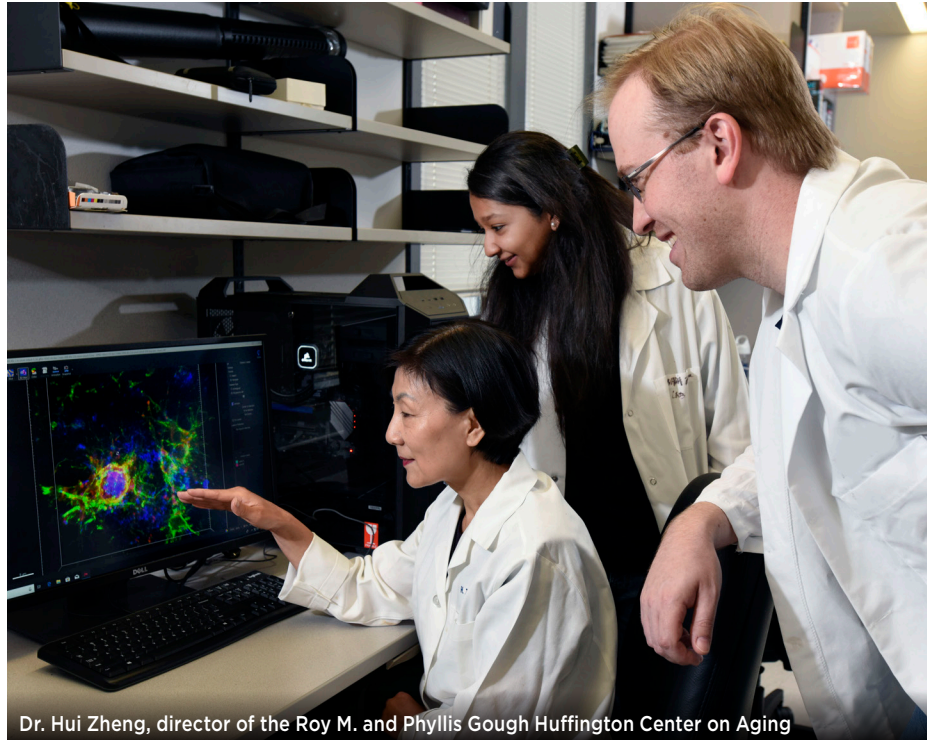
The Intellectual and Developmental Disabilities Research Center (IDDRC) at Baylor, led by Dr. Huda Zoghbi with assistance from Dr. David Nelson, the Cullen Foundation Professor of Molecular Genetics at Baylor, and Dr. Sandesh Nagamani, professor of molecular and human genetics at Baylor, is one of 14 centers across the country funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development. The core facilities of the center support some 75 investigators engaged in basic, translational and clinical studies of intellectual and developmental disabilities (IDDs). NIH funding was renewed in 2020, supporting cores and a research project aimed at solving challenges facing clinical trials in IDD research. The Center has been continuously funded since 1988.

The IDDRC's core facilities play a pivotal role in advancing basic science discoveries "at the bench" into preclinical and eventual clinical trials in humans. Facilities include the Clinical Translational Research Core, the Cell and Tissue Pathogenesis Core, the Molecular and Expression Analysis Core, the Circuit Analysis and Modulation Core and the Preclinical and Clinical Outcomes Core.

Since 2014, investigators supported by the IDDRC have published nearly 2,000 studies, with many in high-impact journals. Numerous studies reported discovery of genes and mutations involved in intellectual disability, autism, epilepsy and other developmental disabilities, as well as mechanistic studies of previously described genes.

Center for Skeletal Medicine and Biology

The Center for Skeletal Medicine and Biology (CSMB), co-directed by Dr. Brendan Lee, professor and chair of molecular and human genetics at Baylor, and Dr. Florent Elefteriou, professor of molecular and human genetics and orthopedic surgery at Baylor, seeks to improve the understanding, prevention and treatment of congenital and degenerative diseases of the skeleton, including skeletal dysplasias, osteoporosis, osteoarthritis, low back pain and bone cancers.

The CSMB at Baylor leverages the Lawrence Family Bone Disease Program of Texas, a contractual collaboration of Baylor College of Medicine, the University of Texas MD Anderson Cancer Center and the University of Texas Health Science Center at Houston, to cultivate teamwork between clinicians, clinical researchers and basic scientists of the Texas Medical Center. The center offers Baylor investigators a number of specialized tools for musculoskeletal investigations and provides avenues for faculty and trainees interested in musculoskeletal research to interact and share expertise.

Center for Precision Medicine Models

The introduction of clinical exome sequencing, whole genome sequencing, RNA sequencing and metabolomics has transformed our ability to diagnose patients with suspected genetic disease. With the introduction of these technologies, a potential molecular DNA lesion can be identified in 30-40% of patients with a suspected genetic diagnosis. These technologies have also led to the discovery of hundreds of new disease genes and to phenotypic expansion within known genetic diagnoses. This continued discovery of new disease genes leads to structure, function and mechanistic discoveries that assist personalized approaches for management and therapy. However, 60-70% of patients with suspected genetic disease remain undiagnosed likely because their disease-causing variant(s) has yet to be discovered or the clinical significance of identified variants remains unclear. Precision model organisms are important tools aiding in the interpretation of these variants of uncertain clinical significance and are critical for testing therapeutic paradigms.

The Center for Precision Medicine Models (CPMM), directed by Dr. Jason Heaney, associate professor of molecular
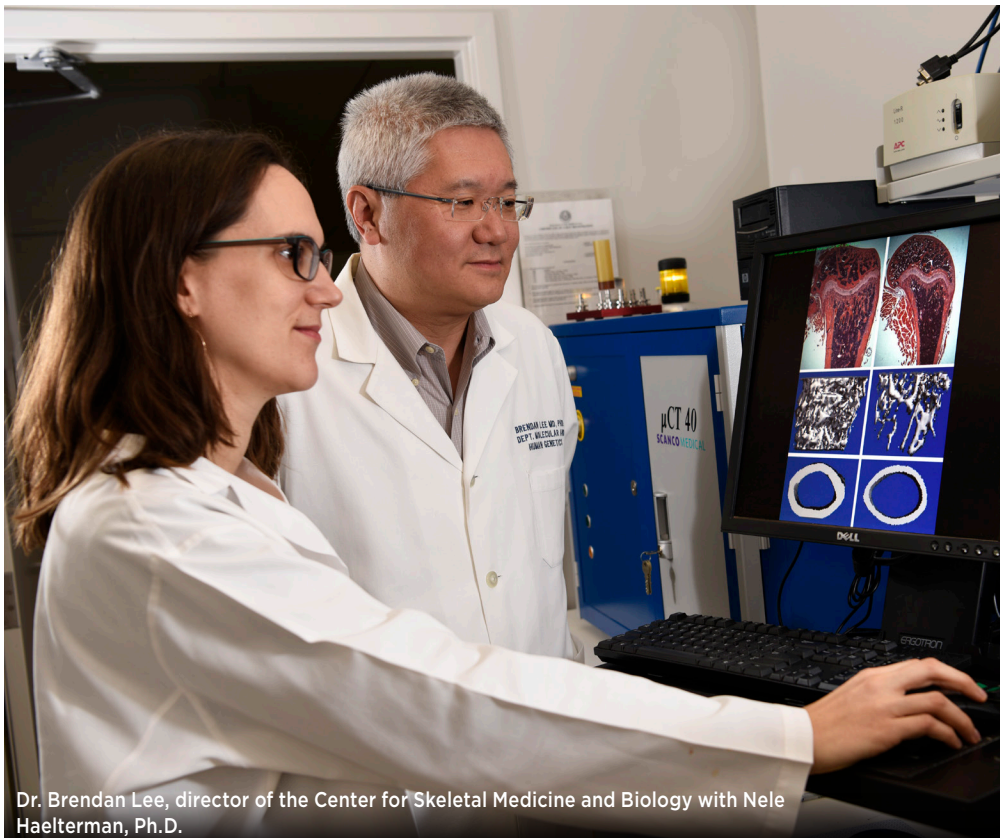
Dr. Brendan Lee, director of the Center for Skeletal Medicine and Biology with Nele Haelterman, Ph.D.

and human genetics, was founded in 2020. CPMM is funded by the NIH with a mission to aid researchers, clinicians, genetic counselors, patients and support organizations in the development and study of precision animal models of human-disease-associated genetic variation. To date CPMM has received 83 nominations for disease modeling, encompassing 131 genetic variants. Currently, 35 nominations, involving 71 gene variants, have been accepted for modeling with 19 projects using mouse models, eight using fly models and three using both fly and mouse models. Half of CPMM's projects support new disease gene discovery and the other half investigate new disorders caused by known disease genes or treatment strategies for known rare diseases.

The Department of Molecular and Human Genetics has a unique concentration of medical genetics, rare disease gene discovery, animal modeling and bioinformatics programs. By uniting the capabilities of these programs, CPMM will help to end the diagnostic odyssey of patients with undiagnosed, rare and Mendelian diseases and to develop personalized medicine approaches.

Center for Alzheimer's and Neurodegenerative Diseases

Neurodegenerative diseases, including Alzheimer's, Parkinson's and Lou Gehrig's disease, are a family of incurable conditions characterized by the progressive deterioration of neurons, cells in the brain and nervous system that are vital for cognitive, motor and other functions. More than 400,000 Texans and nearly 6 million Americans currently suffer from Alzheimer's. At least 50,000 in Texas and 1 million in the U.S. have Parkinson's disease. As our population grows older, the prevalence of these and related neurodegenerative conditions are anticipated to swell unless effective treatments or preventive approaches are developed.

The Center for Alzheimer's and Neurodegenerative Diseases (CAND), directed by Dr. Joshua Shulman, co-director of the Duncan NRI and professor of neurology, molecular and human genetics, and neuroscience, integrates cross-disciplinary clinical research and educational programs to advance precision diagnosis and personalized therapies for
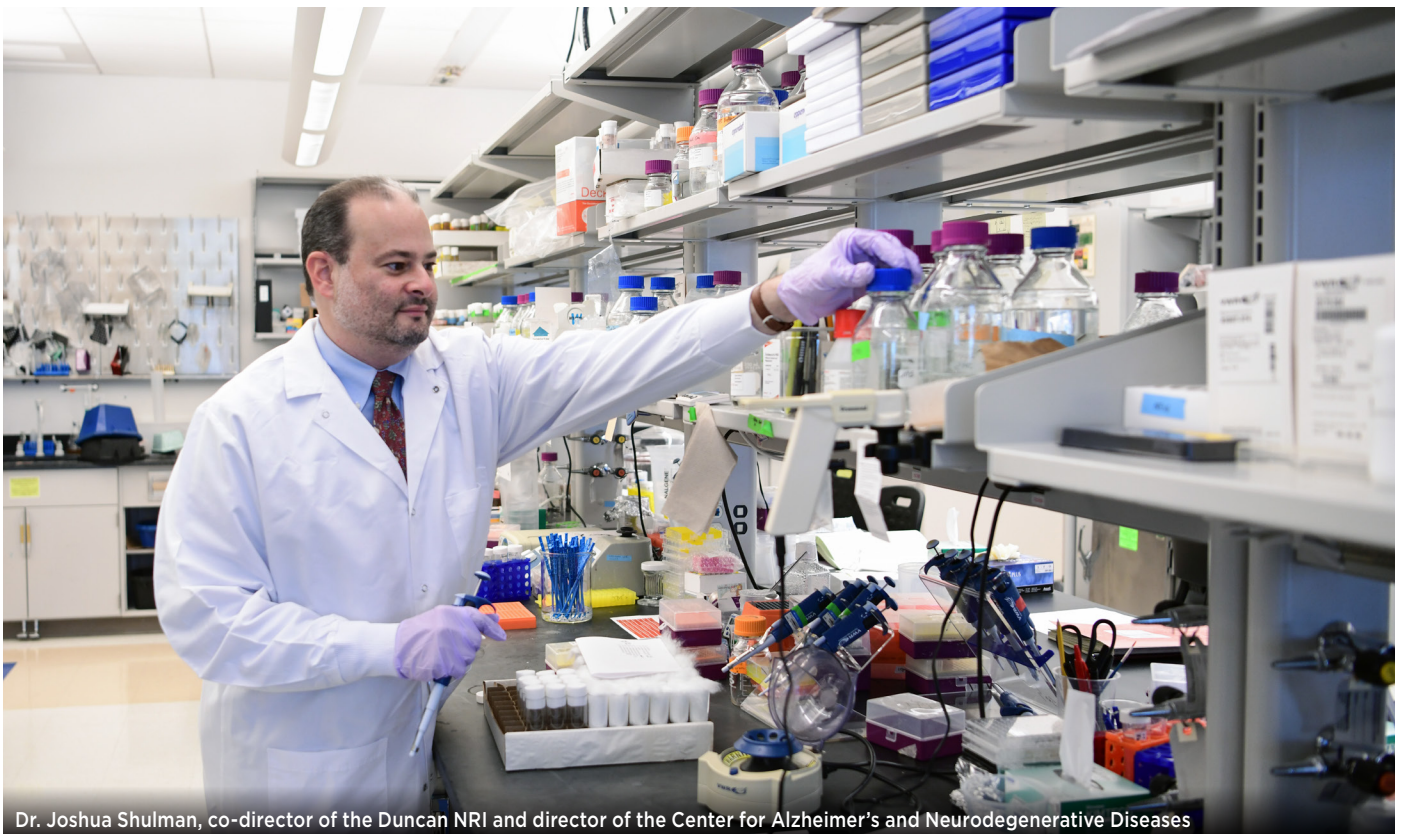
Dr. Joshua Shulman, co-director of the Duncan NRI and director of the Center for Alzheimer's and Neurodegenerative Diseases

Alzheimer's disease, Parkinson's disease and other neurodegenerative conditions.

The challenge of neurodegeneration requires innovative strategies informed by multiple scientific and medical disciplines. CAND's mission is to dissect the interactions between genes, lifestyle and other factors that trigger Alzheimer's and other forms of neurodegeneration in each person. These insights promise groundbreaking improvements for risk prediction and more personalized, targeted therapies.

The Texas Medical Center has a large and diverse patient population, excellence in clinical care, cutting-edge research and training programs, and expertise in genetics, neuroscience, aging and bioinformatics. CAND is uniquely positioned to eliminate barriers for cross-disciplinary collaboration in Houston. CAND will unite top minds to make Alzheimer's and related neurodegenerative diseases a distant memory.

Bioinformatics Research Laboratory

The Bioinformatics Research Laboratory, directed by Dr. Aleksander Milosavljevic, Henry and Emma Meyer professor in molecular and human genetics at Baylor, develops new data-intensive methods and advances computational methods to advance genomic research, open new roads to discovery and catalyze the advance of genomic medicine. The laboratory is engaged in collaborative projects with more than a dozen collaborators in the areas of genomics, epigenomics, extracellular RNA (exRNA) communication, brain, heart and tumor biology. One strength of the laboratory is a team of dozen software engineers that pioneer application of new web and computing technologies. Another strength is the development of innovative information-theoretic methodologies for the analysis of biological networks, deconvolution of omic profiles of complex tissues and identification of pathogenic variants.

As part of the NIH Roadmap Epigenomics Program, the laboratory constructed the Human Epigenome Atlas that maps cell-type specific epigenetic programs and identifies markers of cellular identity. This information is currently being applied in conjunction with computational deconvolution and single-cell omic profiling to decipher the pathological processes in Alzheimer's brain, heart failure, and in cancer progression.

The laboratory pioneered the use of allelic imbalances in the epigenome to decipher cis-effects of gene regulatory variants. These efforts produced a unifying model that links sequence-dependent allelic imbalances of the epigenome, stochastic switching at gene regulatory loci and disease-associated genetic variation. Based on the model, as part of the NIH Common Fund Ecosystem project, the laboratory is leading the development of analytical methods and computational infrastructure to enable discovery of disease-causing gene regulatory variants from whole genome sequencing.

The laboratory developed core informatics infrastructure for the FDA-recognized Clinical Genome Resource (ClinGen) based on an innovative API-centric microservice architectural design. Some of the laboratory products, including the ClinGen Allele Registry, Criteria Specification Registry and Evidence Repository are used globally via web UIs and APIs and have significantly contributed toward the formal recognition of ClinGen as the Global Core Biodata Resource.

As part of the NIH Extracellular RNA Communication Consortium, the laboratory constructed the exRNA Atlas, a map of extracellular RNA species and their vesicular, lipoprotein and protein carriers in human biofluids. Most recently, the laboratory refined the map by identifying extracellular RNA-Binding Proteins (exRBPs) and their exRNA cargo in bodily fluids. Exploring the biology of exRNA communication in cancer progression, the laboratory discovered that transfer of the miR-9-5p from glioblastoma cancer cells into endothelial cells promotes vascularization in glioblastoma by a growth-factor independent pathway. These findings explain the failure of anti-VEGF therapies in glioblastoma and establish a model for deciphering the role of exRNA communication in cancer and other pathological processes.

Graduate Program

The Genetics and Genomics Graduate Program provides outstanding educational opportunities for students who wish to pursue a career in the broad and exciting field of genetics. Students are trained by first-class researchers in an unmatched collaborative environment. In addition to their work in genetics, graduate students receive rigorous training in modern biology, bioinformatics, DNA replication and repair and other diverse fields. They also participate in cutting-edge research and publish their work in the most respected peer-reviewed scientific journals in the world.

Awards and Special Recognitions for Genomics & Graduate Program Students

Baylor Research Advocates for Student Scientists (BRASS) Scholar

Baylor Research Advocates for Student Scientists is a volunteer organization that supports Baylor's Graduate School of Biomedical Sciences by providing scholarships and research funding. Each year, the organization selects four first-year students to be BRASS Scholars. In 2023, English Laserna was selected.

Dean's Award of Excellence

The Graduate School of Biomedical Sciences offers the one-time, $3,000 Dean's Award of Excellence to graduate school students, postdoctoral fellows and postdoctoral associates who receive an eligible fellowship award. This year, Kevin Ho, Janel Peterson and Andrew Yang were among the recipients.

Professor John J. Trentin Scholarship Award

The Graduate School of Biomedical Sciences awards scholarships to graduate school students for their academic excellence. This year, several genetics and genomics students received the award: William Bauer, Shaghayegh Beheshti, Emily Busse, Jacob Chamblee, Jen-Yun Chang, Haley Dostalik, Gwynna Fuller, Gwendolynn Hummel, Pragati Kore, Yi-Sian Lin, Chloe Munderloh, Shahil Pema and Christiana Wang.
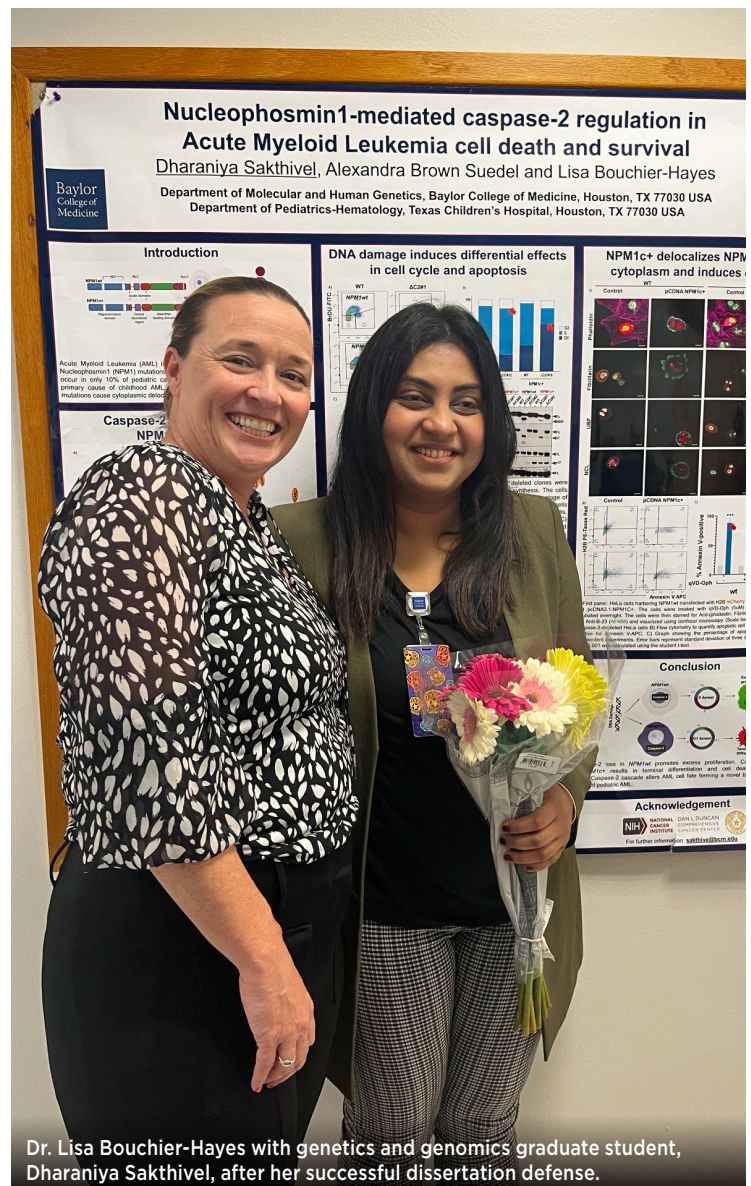
Dr. Lisa Bouchier-Hayes with genetics and genomics graduate student, Dharaniya Sakthivel, after her successful dissertation defense.

2023 Dissertations

Student Name	Title	Preceptor/Advisor
Dharaniya Sakthivel	The Role of Nucleophosmin-1 Mediated Caspase-2 Activation in Acute Myeloid Leukemia	Lisa Bouchier-Hayes, Ph.D.
Denice Palmos	Investigating the genetic differences between pediatric endemic and genomic Burkitt lymphoma	Donald Williams Parsons, M.D., Ph.D.
Ruizhi (Vince) Duan	Deciphering human diploid genome integrity, instability and variability via large-scale family-based multimodal genome analyses in rare Mendelian traits	James R. Lupski, M.D., Ph.D., D.Sc. (hon)
Timothy Wu	Cross-species dissection of brain gene expression in Alzheimer's disease	Joshua Shulman, M.D., Ph.D.
Dillon Shapiro	Integrating evolutionary knowledge and machine learning for the study of functional genome-wide associations	Olivier Lichtarge, M.D., Ph.D.
Xuwen Li	Developing Novel Sequencing Methods for DNA Methylation Profiling at Single-Base Resolution	Tao Wu, Ph.D.
Daniel Sutton	Exploring parallels in auditory function between Drosophila and humans	Andrew Groves, Ph.D.
Hilary Chester	ABCC10: a novel modulator of tau pathology and protein levels	Juan Botas, Ph.D.
Per A. Adastra	The Development of Pathogen Orientated Low-cost Assembly & Resequencing (POLAR), A Sequencing-based in vitro Diagnostic Platform	Erez Lieberman Aiden, Ph.D.
Brandon Pekarek	Oxytocin signaling is necessary for synaptic maturation of adult-born neurons	Benjamin R. Arenkiel, Ph.D.
Pamela Lurie	Long read sequencing of the beta-globin locus in African populations with sickle cell disease revealed novel variations and additional insights into the population structure	Neil Hanchard, Ph.D.
Yichi Niu	Development of Two Novel Single-Cell-Omics Methods and Their Applications in Biological Studies	Chenghang Zong, Ph.D.
Jaime Reyes	Integrating multiomics approaches to investigate dnmt3a- and aging-dependent transcriptional control of stem cell function	Margaret Goodell, Ph.D.
Jessica Swanson	From appetite to aversion: The role of basal forebrain-to-lateral habenula projections in modulationg opposing behaviors	Benjamin R. Arenkiel, Ph.D.

Residency and Clinical Laboratory Fellowship Programs

Throughout the evolution of the Department of Molecular and Human Genetics, there has been a strong emphasis on training and education. The residency and clinical lab fellowship programs began in 1987 and are among the Department's highest priorities. The growth and development of the Department and its clinical enterprises are linked to the excellence of the training programs and its trainees.

The Medical Genetics and Genomics Residency Programs at Baylor College of Medicine are designed to prepare individuals for an academic career by providing an integrated experience in both clinical and experimental genetics. Training activities in clinical genetics and research are coordinated through the Department of Molecular and Human Genetics. The programs prepare trainees to care for both pediatric and adult patients with cytogenetic, biochemical and developmental diseases. Residents also gain laboratory experience in a chosen area of medical genetics and genomics.

The Department's residency programs enjoy preeminence in the genetics community. They are approved by the Accreditation Council for Graduate Medical Education and supported by a training grant from the National Institute of General Medical Sciences.

Trainees in the Department's clinical laboratory fellowship programs train at Baylor's genetics diagnostic laboratory, Baylor Genetics, for 24 months.

The Department also offers a one-year Medical Biochemical Genetics Fellowship program that provides additional training in the diagnosis and management of inborn errors of metabolism.

After completion of these programs, trainees are eligible for American Board of Medical Genetics and Genomics certification.
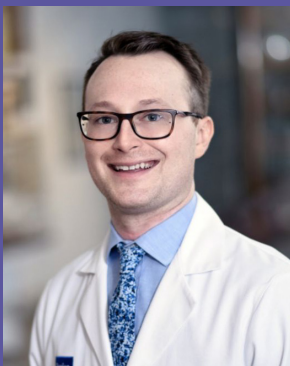
Residencies:

- Medical Genetics and Genomics
- Pediatrics/Medical Genetics and Genomics
- Internal Medicine/Medical Genetics and Genomics
- Maternal-Fetal Medicine/Medical Genetics and Genomics Fellowship

Clinical Laboratory Fellowships:

- Laboratory Genetics and Genomics
- Clinical Biochemical Genetics

2023 MHG Trainee Awards

Matthew Shanahan M.D.
Clinical Resident Award

Matthew Hoi Kin Chau, Ph.D.
Laboratory Fellow Award

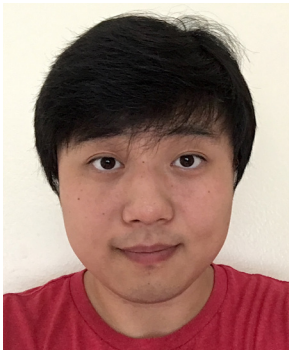## 2023 Graduating Class of Residents and Fellows

Yishay Ben Moshe, M.D.
Medical Genetics Residency

Raiza Exantus, M.D.
Medical Genetics Residency

Charul Gijavanekar, Ph.D.
Clinical Biochemical Genetics

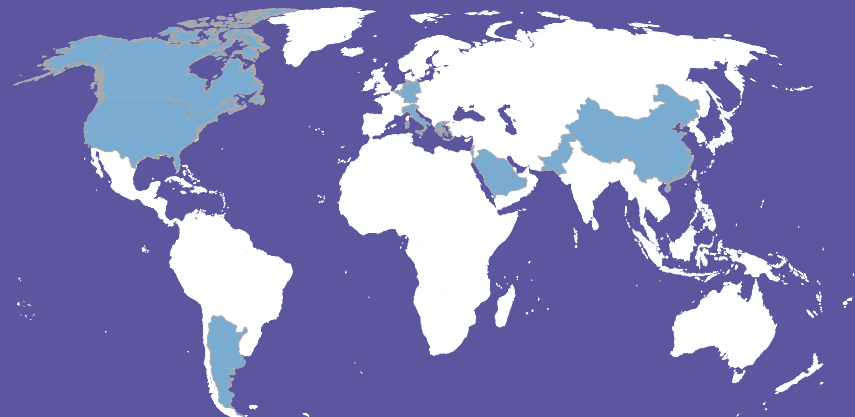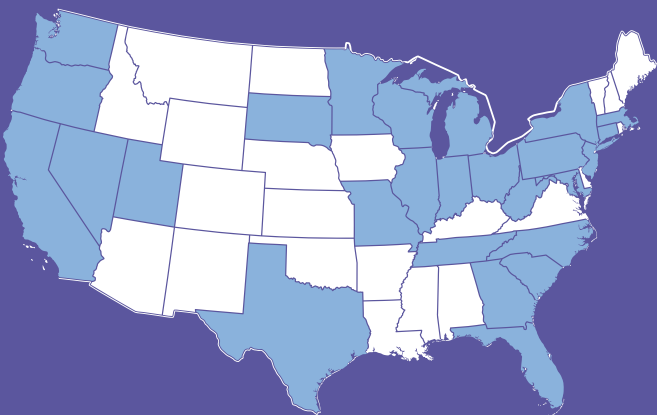**Xi Luo, Ph.D.**
Laboratory Genetics and
Genomics Fellowship

Matthew Snyder, M.D.
Medical Biochemical Genetics
Fellowship

Maria Vladoiu, Ph.D.
Laboratory Genetics and
Genomics Fellowship

Locations of Medical Genetics Alumni

Genetic Counseling Program

Under the School of Health Professions, the Baylor College of Medicine Genetic Counseling Program was established with the financial and logistical support of the Department of Molecular and Human Genetics. The 22-month Master of Science degree program provides students with a transformative education in genomic medicine and the practice of genetic counseling.

The program initially received "Recognized New Program" accreditation status in 2018 and was granted full accreditation for eight years by the Accreditation Council for Genetic Counseling in December 2021. The program currently has a total of 18 trainees and plans to welcome nine new students in July 2024.

"The program has been even more rewarding than I expected. With so many clinical sites in the Texas Medical Center, we had the opportunity to take what we learn in the classroom right into the clinic, where we serve a diverse patient population," said Hannah Helber, program alumna.

Genetic counseling program faculty and students visiting the state capitol in Austin in April 2023 to attend the March of Dimes Lobby Day.

2023 Graduating Class

Jana Heady

Nhi Ho

Emily Huth

Kari Johnston

Nicole Kelly

Fatima Khan

Stephanie Middleton

Welcome to the Genetic Counseling Program Class of 2025: Zoe Epstein, Ryan German, Claudia Cerezo, Sonja Singelstad, Lane McCormick, Aeran Melancon, Julia Volpi, McKay Shumway, and Ashley Ray.

Distinguished Lectures

Jeanette Oshman Efron Lecture in Molecular Genetics

Jeanette Oshman Efron, who died in 2009 at 98, was an ardent supporter of science and the arts and a generous friend to Baylor College of Medicine. The Oshman Lectureship in Molecular Genetics was established at Baylor in 1989 by her daughters, Marilyn Oshman and Judy Margolis, and her grandchildren, Karen Desenberg, Gary Gerson, Jay Gerson and Andrew Lubetkin, to honor Jeanette's passion and commitment to the advancement of medical education and biomedical research.

This lecture series, which is held once every two years, brings internationally renowned scientists

Dr. Leslie B. Vosshall delivers the Oshman Lecture in the Blue Bird Circle Auditorium in the Jan and Dan Duncan NRI in the Texas Medical Center.

to Baylor to present seminars on important developments in genetics. This year, Dr. Leslie B. Vosshall was the featured speaker. The title was "The Unbreakable Attraction of Mosquitoes to Humans."

Dr. Brendan Lee with Dr. Leslie B. Vosshall, Dr. Huda Zoghbi and members of the Oshman family.

Dr. Vosshall is the Robin Chemers Neustein professor and head of the Laboratory of Neurogenetics and Behavior at The Rockefeller University. She is the vice president and chief scientific officer of the Howard Hughes Medical Institute.

Dr. Vosshall's laboratory studies how complex behaviors are controlled by cues from the environment and modulated by the internal physiological state. Working with the yellow fever and Zika vector mosquito, *Aedes aegypti*, Vosshall's research has yielded new knowledge

about how sensory stimuli are perceived and processed.

Arthur L. Beaudet Lecture for Outstanding Mentorship

In 2019, Dr. Huda Zoghbi established an endowment in the Department of Molecular and Human Genetics to recognize outstanding mentorship at Baylor College of Medicine.

The award is open to any outstanding faculty mentor from any discipline and all academic ranks. An elligible candidate must have demonstrated a sustained career of exemplary mentorship at the graduate, postdoctoral, residency, fellowship or junior faculty level across the educational, clinical and research missions of the College. The award is named after its first recipient, Dr. Arthur L. Beaudet.

The awardee receives a plaque and a monetary award of $10,000 and is invited to speak or host an annual lecture. This year, the recognition went to two people, Dr. Malcolm K. Brenner and Dr. Mary Estes.

Brenner is the founding director of the Center for Cell and Gene Therapy and the Fayez Sarofim Distinguished Service Professor at Baylor in the Departments of Medicine, Pediatrics and Molecular and Human Genetics. Brenner's clinical research interests span many aspects of stem cell transplantation, using genetic manipulation of cultured cells to obtain therapeutic effects. Efforts in his laboratory to analyze the cell of origin when relapse occurs in patients with acute myelogenous leukemia led Brenner's team to be the first to label autologous bone marrow cells genetically after purging, prior to being reintroduced to the patient. He is now studying the use of gene-modified T lymphocytes for prevention and treatment of Hodgkin and non-Hodgkin lymphoma, lung cancer, nasopharyngeal cancer and neuroblastoma, and has developed
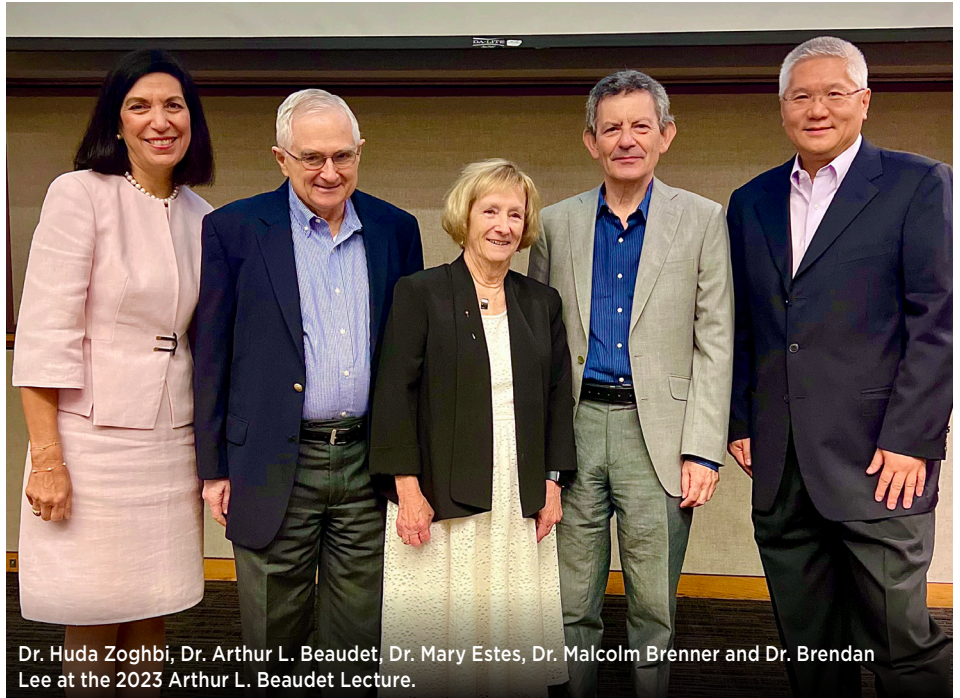
Dr. Huda Zoghbi, Dr. Arthur L. Beaudet, Dr. Mary Estes, Dr. Malcolm Brenner and Dr. Brendan Lee at the 2023 Arthur L. Beaudet Lecture.

and clinically-tested safety switches to reduce the toxicity of these cells.

The title of Brenner's talk was "My Mentoring 'Event Horizon' and Other Views."

Estes holds the Cullen Foundation Endowed Chair of Molecular and Human Virology and is a Distinguished Service Professor in the Departments of Molecular Virology and Microbiology and Medicine. Her research is focused on understanding viral (rotavirus and norovirus) infections of the gastrointestinal tract; her lab dissects basic mechanisms that control virus replication, virus-host interactions and pathogenesis. Groundbreaking research in her laboratory discovered the first viral enterotoxin that is a novel calcium agonist, developed virus-like particle (VLP) vaccines for both viruses and cultivated human noroviruses in human intestinal stem-cell derived organoids.

The title of Estes's lecture was "Advancing Gastrointestinal Biology and Scientific Mysteries with Viruses, Mini-guts, and Mentees."

Community Engagement and Equity

The Department of Molecular and Human Genetics Office of Community Engagement and Equity, co-directed by Dr. Debra Murray, associate professor of molecular and human genetics, and Gladys Pryor, works alongside Baylor's Office of Community Engagement and Health Equity to promote an environment that fosters inclusion, education and understanding for faculty, trainees, staff and the community-at-large. The office's engagement and equity committee have created educational programs for its faculty and staff that address equity in education, research and medicine, as well as genetics outreach programs for the general public.

This year, the office invited Dr. Elba Serrano, New Mexico State University Regent's Professor, to speak during Hispanic Heritage Month. Dr. Serrano's talk, "Developing Pathways to Success for Latine Women in STEM" illuminated her research history and insights for improving the success of young people in science. Volunteer outings for the department to promote workplace culture included the Houston Food Bank, Project C.U.R.E., and Habitat for Humanity Restore.

Evenings with Genetics

Evenings with Genetics is a free virtual seminar series hosted by the Department and Texas Children's Hospital which is open to the public. Each seminar in the series features a genetics faculty speaker paired with faculty from another specialty and a parent speaker. This year the webinar series had more than 250 attendees for topics like genetics and autism and genetic-associated cardiac issues in adults and children.

For its 18th anniversary in February 2023, Evenings with Genetics honored Black History Month with its second annual Race and Genetics: Perspectives on Precision Medicine. This webinar series looks at the history of race and genetics, understanding that the construct of race is independent of genetics and ancestry. The event featured two distinguished speakers, Dr. Constance Hilliard and Dr. Chester Brown.

Dr. Constance Hilliard   Dr. Chester Brown

Hilliard, who is known for her groundbreaking research in African evolutionary history, highlighted the ecological niche to which the ancestors of Black Americans were genetically adapted. Hillard's work questions existing medical literature paradoxes related to diseases prevalent among Black populations, such as hypertension, kidney failure, certain cancers, and childbirth mortality.

Dr. Chester Brown, the St. Jude Chair of Excellence in Genetics and professor at the University of Tennessee Health Science Center, challenged the use of racial classifications in medical science. He argued against the one-size-fits-all paradigm in precision medicine, emphasizing its limitations and proposing an alternative approach.

The discussions addressed ongoing social issues in the U.S., emphasizing the need to revisit genetic concepts related to race. Criticisms were raised against the current genomic standards based on European genomics, as it tends to overlook the genetic diversity among non-European populations, ultimately impacting minorities and people of color.

Challenges in genetic research were highlighted, including the reliance on outdated genomic standards, as illustrated by a case of sickle cell anemia. The speakers stressed the urgency to move away from "color blindness" and racial

classifications in medical science to better tailor treatments, taking into consideration diverse genetic and nutritional needs.

The event placed importance of representing all populations in genomic research, pointing to initiatives like Human Heredity & Health in Africa (H3 Africa) and private sector involvement to address disparities in data generation. As sequencing becomes more accessible, there is a growing recognition of the need to improve representing different populations in genetic research efforts. The discussions called for a shift in the current genomic research landscape toward a more equitable inclusion of all people to maximize the benefits of human genetics and genomics.

National DNA Day

National DNA Day commemorates the successful completion of the Human Genome Project in 2003. This year was the 20th anniversary of the project's completion. The Department celebrated National DNA Day by arranging tours of 11 research laboratories. Forty-two visitors were made up of high school students from Bellaire High School and college students from the University of Houston-Downtown and Houston Community College.

Statewide Genetic Outreach

Statewide genetic outreach, in collaboration with the UT Texas Center for Disability Studies and the Texas Department of State Health Services, included webinars for health professionals and community outreach. More than 300 health professionals including nurses, social workers, early childhood development providers and special educators from around the world registered to attend the webinars and receive continuing education units.

These efforts also included in-person genetic conferences and resource fairs across Texas. These conferences bring geneticists and genetic counselors to areas with little-to-no
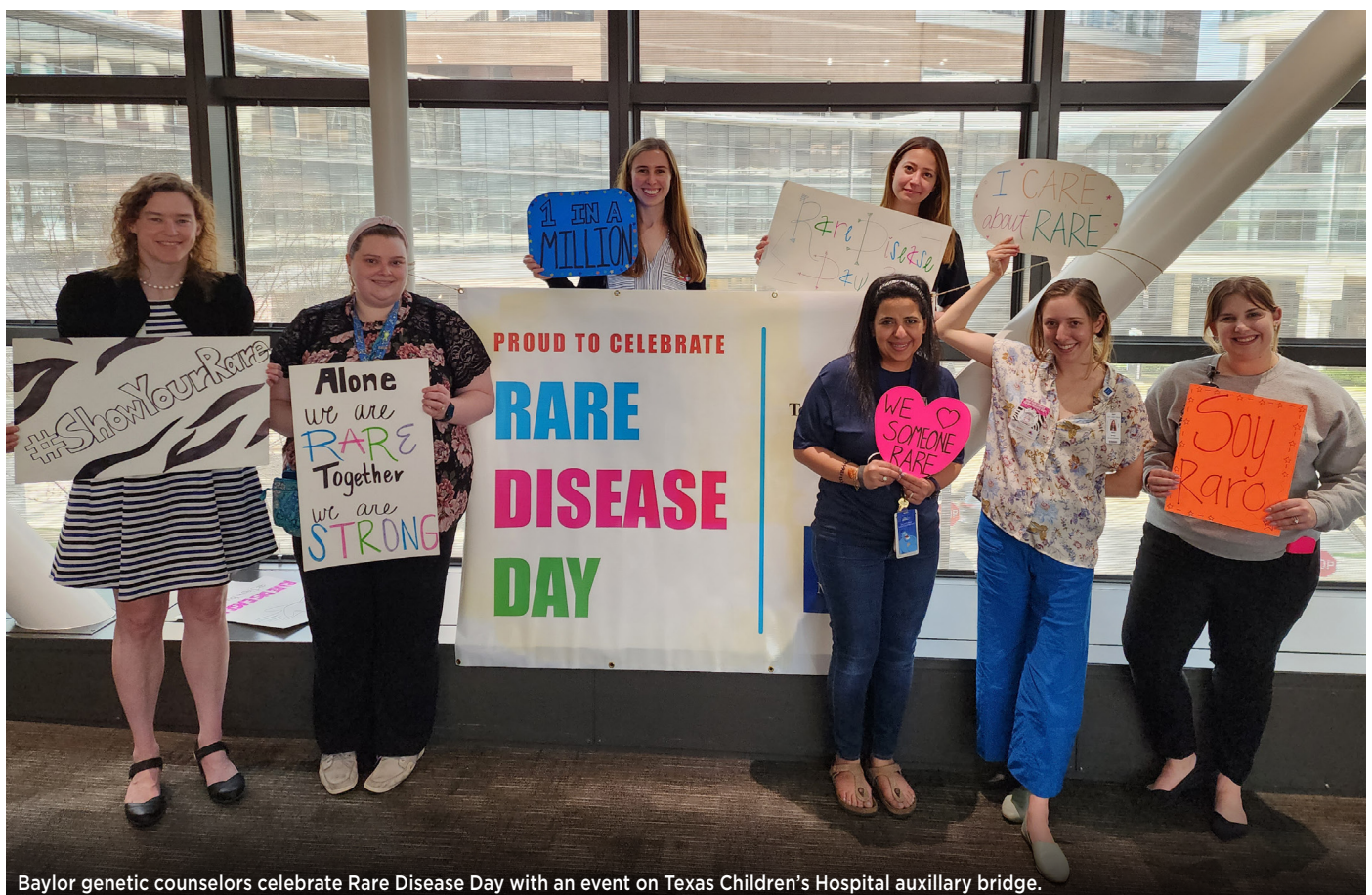
Baylor genetic counselors celebrate Rare Disease Day with an event on Texas Children's Hospital auxillary bridge.

Volunteers from the Department at a Rare Disease Day event in Sugar Land, Texas.

access to genetic resources. Resource fairs with representation from local government agencies, nonprofits, and health organizations were held in conjunction with these conferences to aid families in finding resources.

In April 2023, the Area Health Education Center (AHEC) helped organize the Genetic Conference and Resource and Information Fair in Laredo. Dr. Daryl Scott, professor of molecular and human genetics at Baylor, and local health professionals presented to more than 120 families about the influence genetics can have on behavior.

The office partnered with Texas Parent to Parent to host the second annual West Texas Parent Conference in El Paso in November. Over 80 families attended to learn about genetic testing, resources and caring for children with disabilities. Dr. Seema Lalani, professor of molecular and human genetics at Baylor, presented on genetic testing and programs such as Project GIVE that could assist families searching for answers regarding an undiagnosed disease.

Rare Disease Day

Rare Disease Day is a globally coordinated movement on rare diseases, working towards equity in social opportunity, healthcare, and access to diagnosis and therapies for people who live with a rare disease. Rare Disease Day is celebrated Feb. 29, the rarest day of the year. When it is not a leap year, Rare Disease Day is celebrated Feb. 28.

The office partnered with the National Organization for Rare Disease (NORD) to host two awareness events for Rare Disease Day. The first event was held at Brazos River Park in Sugar Land, Texas. More than 100 families enjoyed finger painting, bounce houses, snacks and bubble machines while they visited local healthcare agencies and nonprofit organizations' tables. The second event was held at the auxiliary bridge at Texas Children's Hospital. Baylor and TCH clinics and research programs hosted tables for those visiting the hospital. Hundreds of passersby stopped for treats and information at booths that lined the bridge.

Local Outreach and Educational Initiatives

In September, the office presented at the 33rd Annual Houston Chinese Community Health Fair. The event, organized by the Health Education of Asians League of Houston, was held at the Culture Center of Taipei Economic and Cultural Office in Houston and had over 300 people in attendance. Dr. Fernando Scaglia, professor of molecular and human genetics at Baylor, shared information on the services that Baylor provides through its clinical sites including Texas Children's Hospital, Harris Health, and Baylor St. Luke's Medical Center.

The office continues efforts to educate high school, undergraduate and medical students about genetics and genomics and careers in medical genetics. In March and September, the town hall series, "A White Coat and Genes: The Life of a Medical Geneticist" hosted 30 attendees from across the U.S. In July, the Careers in Genetics and Genomics series introduced a medical geneticist, basic scientist, genetic counselor and trainee to 75 attendees.

In November, the office hosted the "Understanding Genetic Variation: A Matter of Taste from Individual and Community Level Perspectives" session at the Annual Biomedical Research Conference for Minoritized Scientists in Phoenix. Speakers included Dr. Paule V. Joseph, chief of the Section of Sensory Science and Metabolism in Division of Intramural Clinical and Biological Research at the National Institute on Alcohol Abuse and Alcoholism with a joint appointment at National Institute of Nursing Research, and Dr. Krystal Tsosie, the first indigenous human geneticist-bioethicist and assistant professor in the School of Life Sciences at Arizona State University.

The "Let's Learn About One Another" series continued with a focus on the woman's experience in academia. This session was led by Dr. Sarah Elsea, professor of molecular and

Furjen Deng, chairwoman of the Health Education of Asians League of Houston with Dr. Fernando Scaglia, Alyssa Tran, and Gladys Pryor at the 33rd Annual Houston Chinese Community Health Fair.

human genetics at Baylor, Dr. Debra Murray and Dr. Janice Smith, associate professor of molecular and human genetics at Baylor.

All of Us Evenings with Genetics Research Program

NIH's *All of Us* Research Program is an ambitious effort to gather biomedical data from 1 million or more individuals living in the U.S., especially those who are traditionally excluded from biomedical research studies, to support scientific discoveries and advance precision medicine.

The *All of Us Evenings with Genetics* Research Program held its second annual Biomedical Researcher Faculty Summit in Houston. Dr. Melissa Davis, associate professor of cell and developmental biology research in surgery at Weill Cornell Medicine and the Georgia Research Alliance Distinguished Investigator at the

Morehouse School of Medicine, delivered the keynote address.

The purpose of the summit is to train early career faculty and senior postdoctoral researchers around the NIH's *All of Us* Researcher Workbench. During the summit, participants form teams around a common research question, receive data science training on how to set up cohorts on the workbench and professional development. Two types of mentors are present: invited distinguished faculty for one-on-one sessions, and Baylor research faculty for guidance with projects. The program conducted a mini-training session for the Department and began offering office hours for assistance with the workbench.

Dr. Melissa Davis at the second annual Biomedical Researcher Faculty Summit.

The second annual Biomedical Researcher Faculty Summit Research scholars.

Faculty Awards and Recognitions

Dr. Jennifer Posey Receives 2023 ASHG Early Career Award

The American Society of Human Genetics named Dr. Jennifer Posey, assistant professor of molecular and human genetics, a 2023 recipient of the ASHG Early Career Award. She is one of two award recipients in 2023. This award recognizes scientists who are in the early stages of their career as independent investigators; it includes a $5,000 prize.

"ASHG applauds Dr. Posey's accomplishments in such a short period of time," said Dr. Brendan Lee, 2023 ASHG president, and Robert and Janice McNair Endowed Chair and professor of molecular and human genetics at Baylor. "Her leadership and drive have already resulted in an impressive array of successes in genomic medicine. We are excited to award her with the ASHG Early Career Award and eagerly await what is to come in future years."

Posey has forged her own path to create an immediate and lasting impact. In residency, she created her a training path to gain experience in the clinical evaluation of adult patients in medical genetics, and later, chose not to follow the typical progression from a K08 to R01-level grant and instead took on the lead role in an NIH/NHGRI-supported U01 program. Under her leadership, the Baylor College of Medicine site for the Genomics Research to Elucidate the Genetics of Rare diseases (GREGoR) research consortium has supported discoveries published in 20 peer-reviewed scientific manuscripts. As one of only a small number of clinical geneticists involved in the Rare and Atypical Diabetes Network (RADIANT) consortium, her success in the rare disease research space quickly led to her holding leadership positions for two of the key working groups of the RADIANT program. This consortium seeks to identify and characterize individuals with atypical diabetes.
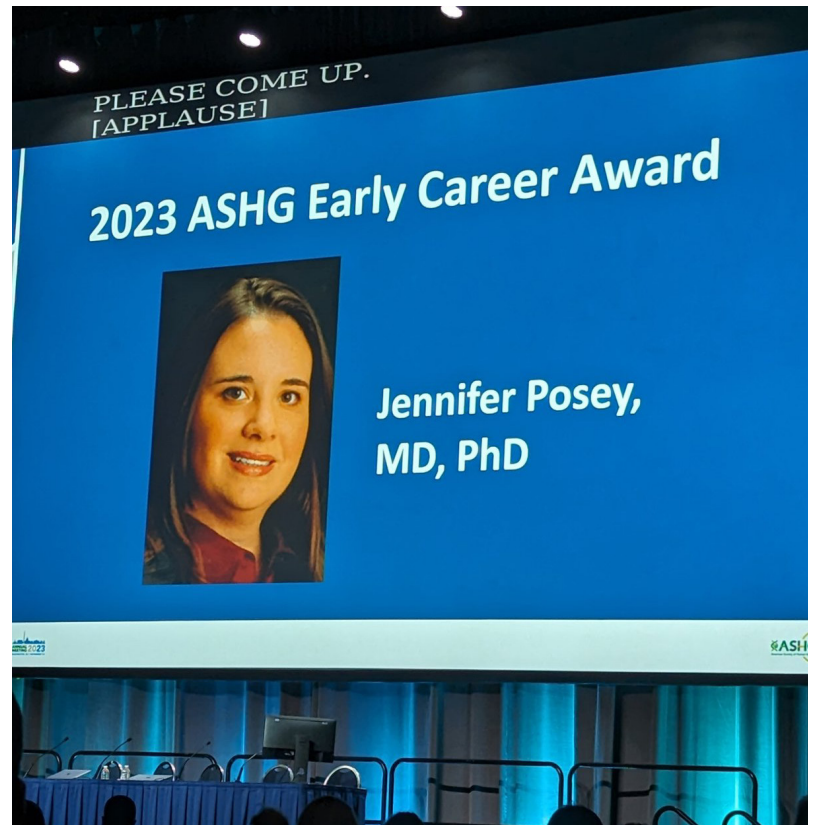
Her leadership has led to assessments of more than 100 participants in the last two years and has united specialists' findings across eight clinical sites around the U.S.

Four Genetics Faculty Receive 2023 Michael E. DeBakey Excellence in Research Award

Drs. Olivier Lichtarge, Daisuke Nakada, Fritz Sedlazeck and Jeffrey Rogers were among the 2023 recipients of the Michael E. DeBakey Excellence in Research Award. On Sept. 18, they were honored at a ceremony at Baylor where they each presented a talk about their research.

Dr. Olivier Lichtarge, Cullen chair and professor of molecular and human genetics, focuses on research combining computer analyses with experiments to understand the molecular evolution of genes and pathways. Using this innovative approach, he has identified genes

and molecular pathways linked to autism, cancer and Alzheimer's disease.

Dr. Daisuke Nakada, professor of molecular and human genetics, focuses on the molecular and cellular mechanisms that regulate the biology of hematopoietic stem cells (HSCs), the parent cells of blood cells. His research examines how these cells give rise to leukemia and how identifying vulnerabilities could improve treatment.

Dr. Fritz Sedlazeck, associate professor of molecular and human genetics and in the Human Genome Sequencing Center, focuses on the understanding of genome instability and complex variations and their impact on evolution and disease. His research has advanced the understanding of complex cardiovascular, neurological and Mendelian diseases.

Dr. Jeffrey Rogers, associate professor of molecular and human genetics and in the Human Genome Sequencing Center, focuses on the genetics and genomics of nonhuman primates. He researches genetic variation within nonhuman primate species that are used as models of human disease. His research also focuses on identifying new fundamental information on primate genomics.

Dr. Erez Lieberman Aiden Receives 2023 Edith and Peter O'Donnell Award in Physical Sciences from TAMEST

Dr. Erez Lieberman Aiden, associate professor of molecular and human genetics at Baylor was awarded the 2023 Edith and Peter O'Donnell Award in Physical Sciences from the Texas Academy of Medicine, Engineering, Science & Technology (TAMEST).

He was among five other Texas-based researchers recognized for their groundbreaking work. Annually, the Edith and Peter O'Donnell Awards are given to rising Texas researchers who are address the essential role that science and technology play in society and whose work meets the highest standards of exemplary professional performance, creativity and resourcefulness.

2023 Michael E. Debakey Research Award Winners: Dr. Fritz Sedlazeck, Dr. Yong Xu, Dr. François St-Pierre, Dr. Jeffrey Rogers, Dr. Daisuke Nakada, and Dr. Olivier Lichtarge with Dr. Paul Klotman and Dr. Mary Dickinson (fourth and fifth from left)

Aiden was chosen for dramatically impacting the understanding of genomic 3D structures and the role and processes of the human genome.

Aiden's research looks at the physical architecture of the human genome, which is over two meters long and folds to fit inside a microscopic cell nucleus, and studies how the folding process is tied to governing gene regulation and how cells function.

Edith and Peter O'Donnell Award Winners (from left) Dr. Jennifer Wargo, Dr. Jamie Padgett, Dr. James J. Collins III, Dr. Erez Lieberman Aiden, and Dr. Chengbo Li. Image courtesy of TAMEST

The human body holds approximately 20,000 genes for the proteins that direct all the processes that make up the human body. However, the majority of the genome is made up of "dark matter," matter without protein-code information, where loops and folds are hidden that can control the expression of genes. Aiden and his collaborators have created a series of methods to map and modify the looping and folding of the genome which allows him to explore and alter how genes are turned on and off.

By understanding how the genome folds and functions, and how its dark matter can be manipulated, he is providing insight into all elements of life processes. His team is currently working at Baylor to determine how this work can be applied to genome sequences in clinical settings and the hope is that it will eventually be used to target dark matter in the body to treat disease.

"Dr. Aiden's research has been no less than transformative, and his multidisciplinary approach to science has been key to his discoveries," said Dr. Brendan Lee, nominator and TAMEST 2023 Board President. "He doesn't just use genetics; he uses computation, physics and other specialties to tackle these big questions of how the human genome folds and fits inside a single cell nucleus and how manipulating that process leads to potential clinical application. The impact of this work is just unbelievable."

Lalani and Nagamani receive the Paragon Award for Research Excellence

Dr. Seema Lalani, professor of molecular and human genetics at Baylor, and Dr. Sandesh C.S. Nagamani, professor of molecular and human genetics at Baylor, received the Paragon Award for Research Excellence from the Doris Duke Foundation. Lalani and Nagamani, along with 23 others who had all been previously awarded the Doris Duke Clinical Scientist Development Award, were recognized in a ceremony in New York in October that celebrated 25 years of support by the foundation for physician scientists and clinical research.

The Paragon Award for Research Excellence is a one-time recognition that celebrates physician

Dr. Seema Lalani

Dr. Sandesh Nagamani

scientists who have, according to the foundation, "significantly advanced knowledge toward the prevention, diagnosis and treatment of human disease or who have, through their professional contributions, improved health outcomes of patients today."

Honorees are selected based on their proven accomplishments in one of the following categories: outstanding contributions to their field of study; impactful developments in disease diagnosis, treatment or prevention; and innovative improvements to clinical care or healthcare delivery.

Lalani and Nagamani were both awarded for impactful developments in disease diagnosis, treatment, or prevention. They will receive a grant of $10,000 to support their research.

This year, Nagamani also received a Clark Faculty Service Award from Baylor College of Medicine. Recipients of this prestigious award represent their professions and Baylor's mission, vision and values at the highest level. Award recipients consistently demonstrate service contributions through a single endeavor or multiple activities.

Dr. Elizabeth Atkinson, assistant professor of molecular and human genetics at Baylor, received the Pamela Sklar Innovation Award on behalf of the Latin American Genomics Consortium at the 2023 World Congress of Psychiatric Genetics Awards.

Dr. Steven Boeynaems, assistant professor of molecular and human genetics at Baylor, received a 2023 Frick Foundation Starting Grant in ALS Basic Research.
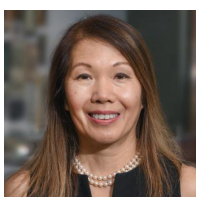
Dr. Christine Eng, professor of molecular and human genetics at Baylor, was elected to the ASHG Board of Directors.

Dr. Benny Kaipparettu, professor of molecular and human genetics at Baylor, received a Norton Rose Fulbrignt Faculty Excellence Award in the category of Teaching and Evaluation from Baylor College of Medicine.
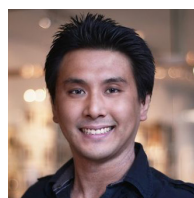
Dr. Richard Lewis, professor of molecular and human genetics, ophthalmology, medicine and pediatrics, was recognized in December for his leadership to the National Ophthalmic Diseases Genotyping Network, or eyeGENE, and was renewed as chair of the eyeGENE Steering Committee, marking 18 years of service to the organization.

Salma Nassef, M.S., C.G.C., assistant professor of molecular and human genetics at Baylor, was recently elected secretary and treasurer-elect for the National Society of Genetic Counselors.

Dr. Pawel Stankiewicz, professor of molecular and human genetics at Baylor, was the recipient of the 2023 Owen McKinnon Lecture Award presented at the University of California, San Francisco's 16th International Conference on Neonatal & Childhood Pulmonary Vascular Disease.

Dr. Shinya Yamamoto, assistant professor of molecular and human genetics at Baylor, received the 2023 Young Alumnus Award from the Alumni Executive Committee at Baylor College of Medicine.
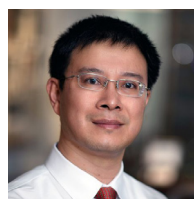
Dr. Bing Zhang, professor of molecular and human genetics at Baylor and McNair Scholar, received the 2023 Gilbert S. Omenn Computational Proteomics Award from the U.S. Human Proteome Organization.

Dr. Huda Zoghbi, a Distinguished Service Professor of molecular and human genetics at Baylor, was inducted to the Texas Women's Hall of Fame. Texas Women's Hall of Fame, recognizes women for significant achievements in arts, community service, education, health, science and business. Dr. Zoghbi also received an honorary doctorate from KU Leuven.

Graduate School of Biomedical Sciences Awards

Best Course in Development Disease Models & Therapeutics
Neural Development; Director: Dr. Benjamin Arenkiel

Best Course in Genetics and Genomics
Mammalian Genetics; Director: Dr. Jason Heaney

Outstanding Lecturer in Genetics and Genomics
Dr. Daryl Scott

Outstanding Lecturer in GSBS Interdisciplinary
Dr. Herman Dierick

Department Awards

Best Metabolic Attending
Dr. Claudia Soler-Alfonso

Best Pediatric Attending
Dr. Chaya Murali

Best Adult Attending
Dr. Mir Reza Bekheirnia
Dr. Kevin Glinton

Best Reproductive Genetics Attending
Dr. April Adams

Best Metabolic Dietician
Brandy Rawls-Castillo

Best Clinical Research Mentor
Dr. Fernando Scaglia

Best Teacher/Educator
Dr. Lindsay Burrage

Best Genetic Counselor
Emily Magness, M.S., C.G.C.

Baylor Genetics Laboratory Service Awards
Dr. Weimin Bi and Dr. Yue Wang

Rolanette and Berdon Lawrence Awards
Dr. Seema Lalani (Faculty)
Janel Peterson (Trainee)
Demetria Dalco (Administration)

Kenneth Scott Graduate Mentor Award
Dr. Christophe Herman

Faculty Appointments

Primary Research Tenure Track

In 2023, the Department welcomed four new tenure-track primary research faculty members, Dr. Graham Erwin, Dr. Ronit Marom, Dr. Fritz Sedlazeck, and Dr. Qian Zhu.

Dr. Graham Erwin is a molecular, chemical, and genome biologist elucidating the functional role of tandem repeat (TR) DNA sequences. This work is guiding the design of new therapeutics and diagnostics for human disease. He is currently supported by an NIH Pathway to Independence Award (K99/R00) and funding from CPRIT.

Erwin received his Ph.D. in biochemistry from the University of Wisconsin–Madison where he was a co-inventor of synthetic transcription factors to treat neurodegenerative diseases. An analog of the prototype molecule, Syn-TEF1, is currently in clinical trials.

Prior to joining Baylor, he was a Stanford Cancer Institute Postdoctoral Fellow in the Department of Genetics at Stanford University.

Dr. Ronit Marom is an American Board of Medical Genetics and Genomics (ABMGG) certified clinical geneticist and medical-biochemical geneticist. She received her M.D./Ph.D. from Tel Aviv University with a yearlong research visit to the NIH. She completed her pediatrics training at Tel Aviv Medical Center, followed by a medical genetics residency and medical biochemical genetics fellowship at Baylor College of Medicine.

Marom's research focus is on secretory pathway defects. This group of disorders can affect many organ systems, but skeletal development and neurodevelopment are most impacted. She uses a variety of laboratory methods to study the changes that are induced by secretory pathway defects in bone and cartilage. In addition, through the Undiagnosed Diseases Network and other collaborative clinical research efforts, she is involved in projects that identify and characterize new genetic syndromes.
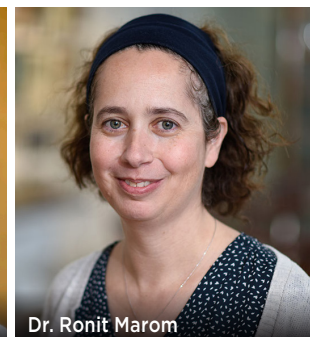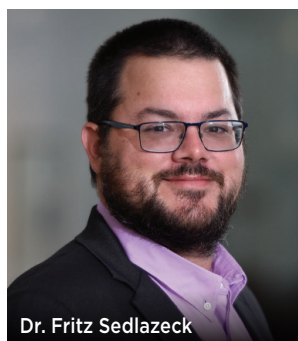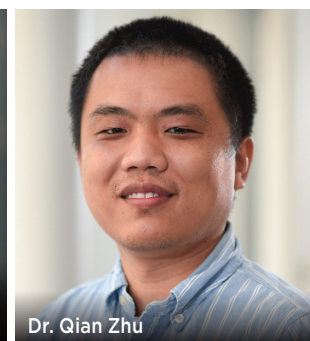

Dr. Graham Erwin
Dr. Ronit Marom
Dr. Fritz Sedlazeck
Dr. Qian Zhu

Dr. Fritz Sedlazeck earned his Ph.D. in Bioinformatics from the University of Vienna where he designed algorithms to investigate genomic variability of model and non-model organisms through the alignment of short reads. Sedlazeck is intrigued by genomic variability and the impact of such variability. He has collaborated and initiated efforts to determine which technologies or methodologies are most appropriate to discover variations of different forms, as well as the biases that they contain. His work recently led to novel insights in structural variations and their genotypic and phenotypic impact on cardiovascular, mendelian and neurological diseases and other organisms.

Dr. Qian Zhu is interested in the development of computational methods for genomic technologies that are being applied in cancer research. He received his Ph.D. from Princeton University and completed his postdoctoral training at the Dana-Farber Cancer Institute in Massachusetts. He is also supported by funding from CPRIT.

Zhu's previous works include: smfishHMRF, a hidden-Markov random field model for single-molecule FISH; Giotto, a comprehensive package for spatial transcriptomic analyses; CUT&RUNTools, a tool for CUT&RUN data processing and motif footprinting prediction.

Zhu has developed a range of computational tools that are currently being used to better understand the sources of intra-tumor heterogeneity, tumor-immune cross-talk. The tools reveal novel image-based and genomic biomarkers that are predictive of clinical outcomes. He works closely with experimental collaborators to understand mechanisms underlying tumor progression and therapy resistance.

Currently, Zhu is interested in developing methods in the area of spatial transcriptomics, and working on improving the integration of machine learning algorithms in histopathology imaging analyses. He is interested in large-scale data visualization approaches and developing databases/portals to improve the access of genomics information for patients and clinicians.

Appointments

Research Division

Ashutosh Pandey, Ph.D.
Assistant Professor, non-tenure-track

Jennifer Asmussen, Ph.D.
Instructor

Dimos Gkountaroulis, Ph.D.
Instructor

Clinical Division

Roni Zemet-Lazar, Ph.D.
Assistant Professor

Diagnostic Division

Jun Chen
Assistant Professor, non-tenure-track

Xiaoyan Ge
Assistant Professor, non-tenure-track

Xi Luo
Assistant Professor, non-tenure-track

Chung Wah "Wilson" Wu
Assistant Professor, non-tenure-track

Promotions

Benny Kaipparettu, Ph.D.
Associate Professor, tenured

Pengfei Liu, Ph.D.
Associate Professor, tenured

Pamela Luna, Ph.D.
Assistant Professor, non-tenure-track

Linyan Meng, Ph.D.
Associate Professor, non-tenured

Daisuke Nakada, Ph.D.
Professor, tenured

Haley Streff, M.S., C.G.C.
Assistant Professor, non-tenure-track

Michael Wangler, M.D.,
Associate Professor, tenured

Lilei Zhang, M.D., Ph.D.
Associate Professor, tenured

William E. "Bill" O'Brien

August 23, 1943 - August 15, 2023

Dr. William E. O'Brien was born Aug. 23, 1943, in Christiansburg, Virginia, to Robert Emmett and Margaret Moon O'Brien. At an early age, he moved with his family to Belzoni, Mississippi, where he met his wife, Edie, and graduated from Belzoni High School in 1961. He attended the University of Mississippi for two years before transferring to Mississippi State University after discovering his love of microbiology. O'Brien received a B.S. and M.S. in Microbiology from Mississippi State University and a Ph.D. in Biochemistry in 1971, from University of Georgia, Athens.
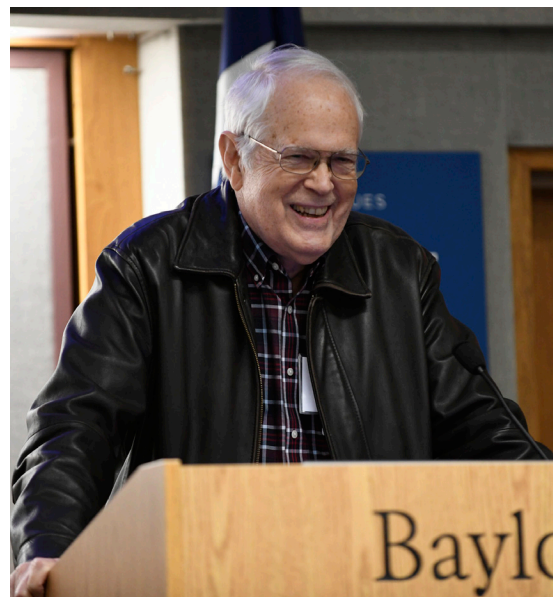
In 1975, following a postdoctoral research position at Case Western Reserve University in Cleveland. O'Brien began his professional career in genetics at Cleveland Metropolitan Hospital. He then joined Baylor College of Medicine as an assistant professor in pediatrics and genetics in 1978. Upon his arrival at Baylor, he founded the Biochemical Genetics Laboratory and served as director until his retirement in 2012.

O'Brien played a leadership role in the commercial development of the Medical Genetics Laboratory at Baylor as it grew to be a globally prominent genetic lab providing services and research in biochemical genetics, cytogenetics, and molecular genetics. He was part of a small group of faculty that went on to become the Department of Molecular and Human Genetics where O'Brien was instrumental in the department's growth over many decades. His support and guidance combined with scientific expertise created an environment of curiosity, focus and purpose that he imparted on former trainees, facilitating their contributions to advancements in medical genetics.

He will be remembered fondly by family and friends, particularly for his enthusiasm for birding, dancing, dining, travel, photography and lively conversation.
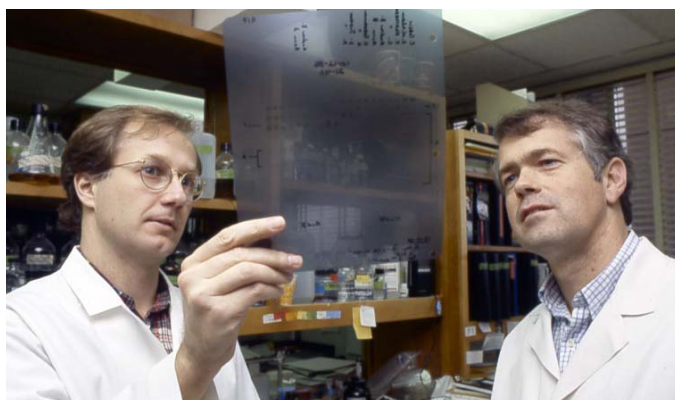
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