Baylor College of Medicine

DEPARTMENT OF MOLECULAR & HUMAN GENETICS

ANNUAL REPORT 2021

Transforming Medicine Through the Practice and Science of Genetics

Message from the Chair

I am delighted to welcome you to our 2021 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.

Despite the challenges of the COVID-19 pandemic, the Department continues to excel in all aspects of its mission to transform medicine with the practice and science of genetics and genomics.

The Department remains a top-ranked genetics program, ranking first among other U.S. genetics departments in total awarded NIH funding and number of NIH grants.

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 including, most recently, for infectious diseases.

Our faculty continue to deliver our clinical, training and research missions at home and abroad through our ongoing partnership with the Chinese University of Hong Kong Center for Medical Genetics.

In addition, new and continuing consortia with the National Institutes of Health and industry are leading to new gene discoveries and advancements in the implementation of genetics and genomics.

As we take measure of the past year, let us also look forward. 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

Table of Contents

We have more than **530 FACULTY, TRAINEES AND STAFF** who occupy over **110,000 SQUARE FEET OF SPACE**. Faculty includes:

7 members of the National Academy of Medicine

3 members of the National Academy of Sciences

2 Howard Hughes Medical Institute Investigators

3 members of the American Academy of Arts and Sciences

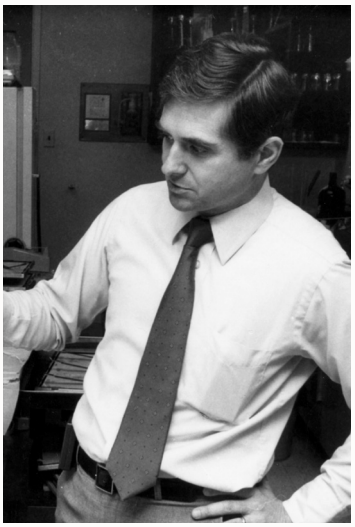
9 Fellows of the American Association for the Advancement of Science

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, professor of molecular and human genetics, 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.

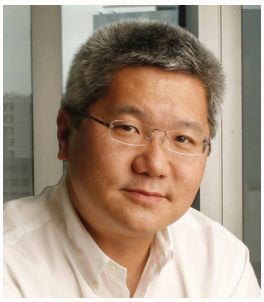
The Department's success reached new heights with the creation of the Human Genome Sequencing Center in 1996. Led by Dr. Richard Gibbs, the Wofford Cain Chair and Professor of Molecular and Human Genetics at Baylor, the HGSC at Baylor was one of three sites (out of six pilot programs) to complete the 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

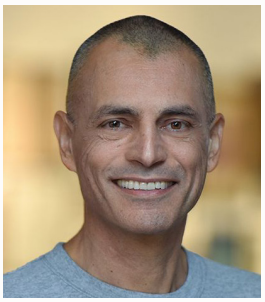


Brendan Lee, M.D., Ph.D.
Robert and Janice McNair Endowed Chair in Molecular and Human Genetics

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., CGC
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

Shashikant Kulkarni, M.S., Ph.D., F.A.C.M.G.
Vice Chair for Research Affairs (Baylor Genetics)

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

Susan Fernbach, R.N., B.S.N., Co-Director, Office of Community Engagement and Diversity

NIH award supports diverse researchers in *All of Us* Research Program

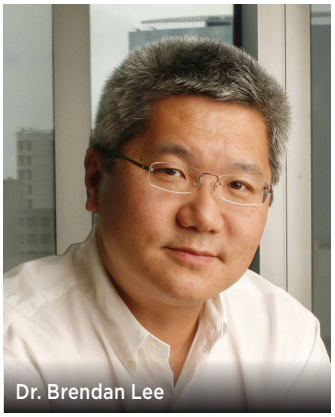
Baylor College of Medicine received more than $1 million in the first year of an up to five year grant from the National Institutes of Health to engage researchers from diverse backgrounds, including those from underrepresented groups, in utilizing the *All of Us* Research Program's data resources to advance precision medicine.

The NIH *All of Us* Research Program is a historic effort to collect data from 1 million or more people living in the United States to support a wide range of scientific discoveries. The goal of the program is to advance research that may lead to better health for all. The Baylor program aims to ensure that a diverse group of researchers uses *All of Us* data in their studies.

As part of the effort to engage biomedical researchers from diverse backgrounds, including those from underrepresented groups, Baylor will host *All of Us Evenings with Genetics* seminars, modeled after the highly successful *Evenings with Genetics* series, at universities across the country. Through this series, Baylor will introduce the *All of Us* Research Program and show how to use its data in a variety of fields, including medicine, psychology, nutrition and education.

"The *All of Us* Evenings with Genetics program will engage students who may not have considered research as a career," said Dr. Debra Murray, co-director of the Office of Community Engagement and Diversity, assistant professor of molecular and human genetics and co-investigator of the Baylor program. "We hope to inspire more students to use the *All of Us* data to work with faculty and engage in research earlier in their academic careers."

Baylor also will host an annual summit for early career faculty and senior postdoctoral fellows from diverse backgrounds, including those from underrepresented groups, to establish a framework of collaboration and training using the *All of Us* data platform. Summit participants will develop multidisciplinary research projects with a foundation in the *All of Us* Research Program and will be able to apply for seed awards and external pilot awards to fund additional collaborations and projects. These projects can serve as stepping stones to manuscripts and grant proposals.


Dr. Brendan Lee


Dr. Debra Murray


Susan Fernbach, R.N., B.S.N.


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

"This program embraces the diversity of participants of the *All of Us* Research Program by fostering the same diversity among the scientists who will lead us in the discoveries on this enormous dataset," said Dr. Brendan Lee, professor and chair of the Department, Robert and Janice McNair Endowed Chair in Molecular and Human Genetics at Baylor and principal investigator of the award.

Susan Fernbach, co-director of the Office of Community Engagement and Diversity and assistant professor of molecular and human genetics, and Laura Rosales, administrator in the Department, are co-investigators of the program at Baylor.

This work is supported under NIH funding award OT2 OD031932. *All of Us* is a service mark of the U.S. Department of Health and Human Services.

Medical Genomics Workshop Teaches Introduction to Genetics and Genomics

Genetics and genomics are increasingly incorporated into all areas of medical practice and play an important role not only in diagnosis, but also in the management of individuals with both rare and common diseases. Over the past three years, the Department has hosted a workshop entitled "Medical Genomics in the New Millennium."

The virtual workshop provided for healthcare professionals in China took place over the course of six Saturdays in March and April. The program was designed to provide an introductory educational experience across the breadth of genetics and genomics ranging from laboratory diagnostics to prenatal genetics, from inborn errors of metabolism to common genetic syndromes and from gene regulation to cancer genetics.

Students in this program have the opportunity to apply what they learned in hands-on, problem-solving sessions overseen by faculty experts in the field. Dr. Daryl Scott, associate professor, and Dr. Sau Wai Cheung, professor in the Department, are co-course directors of the program with over 15 faculty serving as lecturers.


Dr. Sau Wai Cheung


Dr. Daryl Scott

In 2021, about 100 people attended the workshop from all over China.

Baylor designated a NORD Center of Excellence

In November of 2021, the National Organization for Rare Disorders named Baylor College of Medicine one of its 31 Rare Disease Centers of Excellence.

NORD's Rare Disease Center of Excellence Program is the first-ever designation program dedicated to all rare diseases and the patients impacted by them.

Each Center for Excellence was selected by NORD as a result of a competitive application process in which institutions had to provide evidence of staffing of clinical experts across multiple specialties, exceptional facilities and significant contributions to rare disease patient education, physician training and research.

Through this nationwide network of centers, NORD aims to provide health equity to rare disease patients and ease their journey toward diagnosis and finding coordinated care by creating connections to new resources and qualified specialists across the country.

"We are pleased to have been designated a NORD Center of Excellence", said Dr. Reid Sutton, professor of molecular and human genetics and director of the NORD Center of Excellence at Baylor. "We are excited to be a part of NORD's initiative to address an unmet need for collaboration across the medical community that we hope will help fuel an era of faster diagnoses, new treatment guidelines, best practices and knowledge sharing."

Research and Discovery

Research in the Department of Molecular and Human Genetics at Baylor College of Medicine 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.

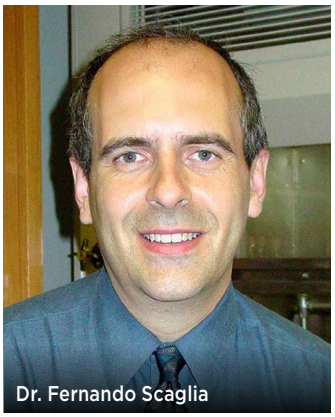
Aspirin reduces preeclampsia risk, affecting the gestation metabolic clock

A joint study conducted by Baylor College of Medicine and the Chinese University of Hong Kong discovered that the benefit of aspirin treatment in preventing preeclampsia is mediated through decelerating the metabolic clock of gestation.

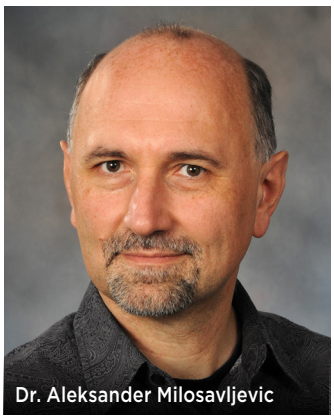
The researchers analyzed the blood samples collected from more than 100 high-risk pregnant women at 11 to 13 weeks and 20 to 24 weeks of their pregnancy and demonstrated that the preeclamptic or non-preeclamptic outcome in response to aspirin treatment was significantly associated with the level of internal aspirin exposure ascertained from metabolomic data.

The researchers also constructed a model of the metabolic clock of gestation and found that aspirin significantly decelerated metabolic gestational age by 1.27 weeks in mid gestation. One-fourth of the metabolites experienced a partial reversal of gestational age advancement, suggesting that aspirin treatment helps prevent preeclampsia by slowing down the metabolic clock of gestation. The study results are published in the journal Hypertension.

Dr. Aleksandar Milosavljevic, Henry and Emma Meyer Professor in Molecular Genetics, Dr. Sarah Elsea, professor of molecular and human genetics, and Dr. Fernando Scaglia, professor of molecular and human genetics at Baylor and clinical director of the Joint Baylor-CUHK Center of Medical Genetics in Hong Kong, were co-authors of the study.


Dr. Fernando Scaglia


Dr. Sarah Elsea


Dr. Aleksander Milosavljevic

"These relevant findings showed that aspirin treatment resulted in a robust metabolomic signature, lending support to the hypothesis that the use of aspirin may delay the onset of preeclampsia," Scaglia said. "The fruits of this research may potentially impact the clinical care provided to women in high-risk pregnancies."

Early training delays symptom onset in mouse model of Rett syndrome

New scientific findings bring hope that early training during the presymptomatic phase could help individuals with Rett syndrome, a neurodevelopmental disorder. Researchers at Baylor College of Medicine and the Jan and Dan Duncan Neurological Research Institute (NRI) at Texas Children's Hospital reported in the journal *Nature* that, in a mouse model of Rett syndrome, intensive training beginning before symptoms appear dramatically improved the performance of specific motor and memory tasks and substantially delayed the appearance of symptoms.

The researchers propose that newborn genetic testing for Rett syndrome, followed by prompt intensive training in the skills that will be affected, such as gait/balance, manual dexterity and communication, may alter the progression of the condition in ways that would improve the patients' quality of life and prepare them for later therapies.

Dr. Huda Zoghbi, Ralph D. Feigin, M.D. Endowed Chair and professor of molecular and human genetics, pediatrics and neuroscience at Baylor and the director of the Duncan NRI, is corresponding author of the study. Her team worked with Rett mice, a mouse model of Rett syndrome in which females lack one of the two Mecp2 genes, testing the effect of intensive training in a motor coordination task – walking forward on a rotating rod – on Rett syndrome progression.


Dr. Huda Zoghbi

Their findings show that intensive behavior training in early life, before the onset of symptoms, significantly improved behavioral deficits in the mice when compared with mice that did not train. When the researchers provided early training on memory tasks, the mice showed improvement on those tasks. The early intense training also delayed the appearance of memory and learning difficulties in these mice.

HeartCare study IDs patients' genetic risk for cardiovascular disease

A person's genetics may hold the key to early intervention in cardiovascular disease, leading to better outcomes in patient care. Researchers at Baylor College of Medicine's Human Genome Sequencing Center and Baylor cardiologists conducted a pilot study to determine if providing genetic testing for patients in cardiovascular clinics would benefit clinical care as part of a precision medicine initiative. They found that the test results did have implications on the course of treatment for approximately one-third of participants. Their results are published in the journal *Genetics in Medicine*.

The researchers developed a HeartCare panel that provided DNA sequencing for 158 genes associated with medically actionable cardiovascular conditions along with a genetic risk score for developing cardiovascular disease and genetic data on drug interactions. 709 patients were enrolled at Baylor College of Medicine cardiology clinics and received a free HeartCare panel test as part of their routine care. Results were returned to the patient's physician and entered into their electronic medical record for ease of access.

After testing, 32% of participants received a genetic finding that impacted their clinical management. Of those participants, 11% were referred to a genetic specialist for further care. Out of all participants, 9% had an inherited pathogenic gene mutation associated with cardiovascular diseases like cardiomyopathy and high cholesterol, and 9% had a high overall genetic risk score for developing cardiovascular disease. High risk scores could be addressed with medication, diet and other lifestyle changes.

"This study shows that a large proportion of individuals in select ambulatory care clinics can benefit from genetic data," said Dr. Richard Gibbs, a senior author of the study, director of the Human Genome Sequencing Center and Wofford Cain Chair and professor of molecular and human genetics at Baylor. "There is tangible follow-up care for people who received a positive result, and in many cases for their family members."


Dr. Richard Gibbs

This research was funded by the St. Luke's Foundation.

Researchers identify genetic cause of endometriosis and reveal potential drug target

Research conducted by Baylor College of Medicine, the University of Oxford, the University of Wisconsin-Madison and Bayer AG, offers new insight into how to treat endometriosis, a painful, chronic condition in which tissue from the uterus inappropriately grows outside the uterus.


Dr. Jeffrey Rogers

The researchers performed genetic analyses of humans and rhesus macaques to identify a specific gene, NPSR1, that increases risk of suffering from endometriosis. The results reveal a potential new nonhormonal drug target that may lead to improved therapy. Their results are published in *Science Translational Medicine.*

The Oxford team, led by corresponding author Dr. Krina T. Zondervan, had previously found a genetic linkage to endometriosis on chromosome 7p13-15 by analyzing DNA from families containing at least three women diagnosed with endometriosis. The Baylor team, led by senior author and associate professor at the Human Genome Sequencing Center Dr. Jeffrey Rogers, verified this genetic linkage in the DNA of rhesus monkeys with spontaneous endometriosis at the Wisconsin National Primate Research Center at the University of Wisconsin-Madison. This validation justified further research through in-depth sequencing analysis of the endometriosis families at Oxford, which narrowed down the genetic cause to rare variants in the NPSR1 gene. Most of the women carrying these rare variants had stage III/IV disease. The Baylor researchers similarly sequenced rhesus monkeys and again showed suggestive evidence also in this species. Finally, an Oxford study of more than 11,000 women, including patients with endometriosis and healthy women, identified a specific common variant in the NPSR1 gene also associated with stage III/IV endometriosis.

The insights revealed in this genetic analysis point to a potential new drug target. As part of this collaboration, researchers at Bayer, in scientific partnership with Oxford University, used an NPSR1 inhibitor to block protein signaling of that gene in cellular assays and then in mouse models of endometriosis. They found this treatment led to reduced inflammation and abdominal pain, thus identifying a target for future research in treating endometriosis.

Research Administration

For the year 2021, a total of 380 grant proposals (including 116 proposal collaborations through other departments) were submitted to Baylor's Office of Research by the Department of Molecular and Human Genetics, resulting in over $212 million in competing and non-competing proposals.

This past year the MHG Research Administration Team developed resource materials and instituted a bi-monthly training series for administrative staff. The team also participated in the National Council of University Research Administrators (NCURA) Region V annual meeting in Fort Worth by serving as volunteers on the program committee and presenting two sessions.

Team members also passed certification exams this year. Courtney Gomez passed the Certified Research Administrators (CRA) exam. Sherri Weaver and Betty Fernandini passed the Certified Financial Research Administrators (CFRA) exam. Both Sherri and Betty have established and now oversee the first CFRA Exam Study Group with participants throughout the U.S.

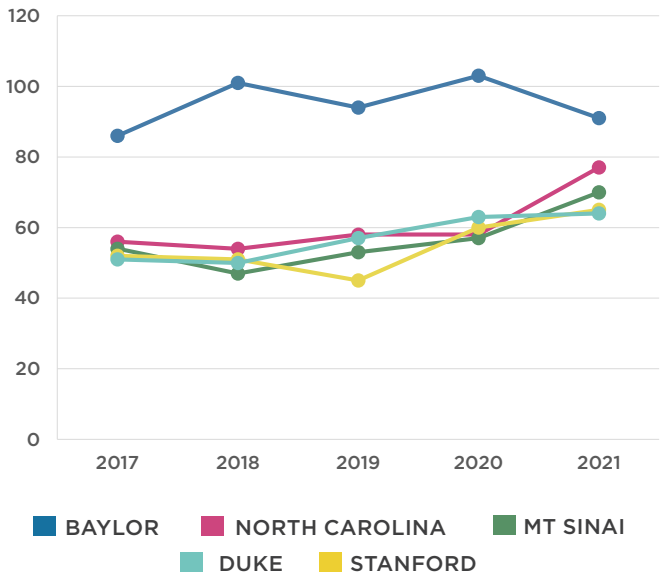
Grant Awards Continue to Drive Progress

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.

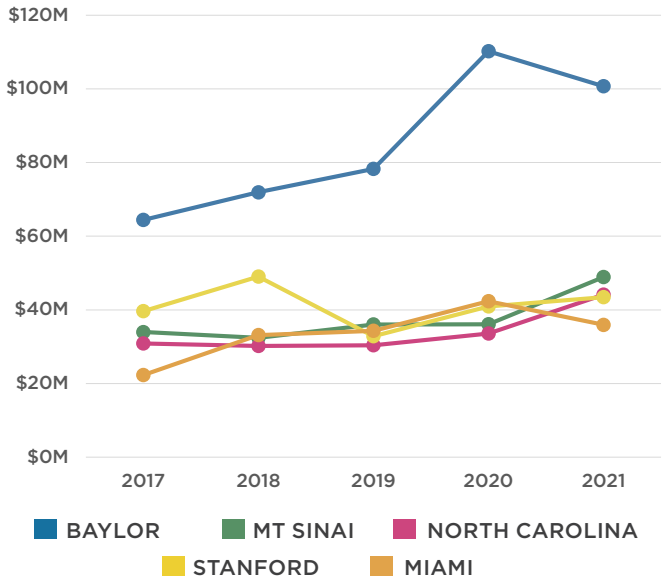
#1 ranked U.S. Genetics Department in NIH awarded grants and total funding for past 11 years

over **$100 million** total NIH funding in 2021

NIH Grants Awarded to Leading Genetics Departments



NIH Funding to Leading Genetics Departments



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

NIH-funded consortium focuses on advancing genome editing research

The Somatic Cell Genome Editing Consortium (SCGE), a massive research effort funded by the National Institutes of Health, aims to accelerate genome editing research and the development of new gene-editing related technologies and therapeutic approaches. The collaborative initiative includes 45 projects from 38 institutions and 72 principal investigators, including researchers from Baylor College of Medicine and Rice University. A collaborative manuscript published in *Nature* describes the overall organization, goals and planned activities.


Dr. Mary Dickinson


Dr. Jason Heaney

SCGE-funded groups are engaged in the development of new delivery systems for genome editing machinery, identification of new editing enzymes, assessing the risks of genome editing and generating reporter models for detecting editing events, as well as testing in small- and large-animal models to support these efforts.

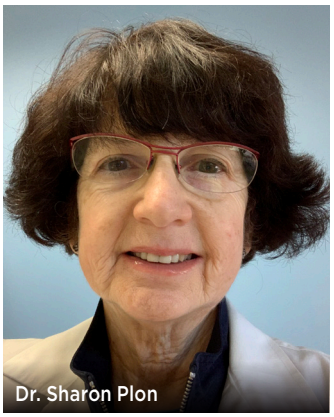
A Baylor team led by Dr. Jason Heaney, Dr. William Lagor and Dr. Mary Dickinson is one of two groups that serve as a small-animal testing center. They are responsible for developing new reporter mice to detect somatic genome editing events. The mouse models that are being developed by Heaney's lab allow for detection of genome editing events through activation of fluorescence and luminescent reporter genes. The new models can detect different types of genome editing events, including small insertion and deletion mutations, homology directed repair and off-target editing.

Dickinson's lab will coordinate research activities for the grant, including developing and applying new imaging modalities to quantify genome editing. Lagor's lab serves as the genome editing testing core, which is tasked with validation of the newly generated reporter mice. This includes delivery of genome editing enzymes such as the CRISPR/Cas9 system. As part of the SCGE, the small-animal testing centers also provide independent validation for teams developing new delivery systems. Results from experiments in the SCGE will become part of a publicly available toolkit that will allow researchers from around the world to benefit from these cutting-edge technologies.

Baylor awarded NIH funding for Clinical Genome Resource

Baylor College of Medicine and Stanford University received an award for more than $25 million over five years from the National Institutes of Health to continue building the Clinical Genome (ClinGen) Resource, an effort to create expert curated knowledge about clinically relevant genes and genomic variants for use in precision medicine. The award is one of three NIH grants totaling $73.2 million over five years for the project.

The National Human Genome Research Institute established the ClinGen consortium in 2013 to fill the need for organized information about which genes and genomic variants are relevant to human disease. The consortium works to identify which genes are associated with disease and which variants in those genes are


Dr. Sharon Plon


Dr. Aleksander Milosavljevic

disease-causing. Then, they work to standardize the way researchers and clinicians share this information for broad use. A multidisciplinary team from Baylor and Stanford has led one of the consortium awards since 2013 and is now working on phase 3 of the project.

The work at Baylor focuses on developing software infrastructure and computational approaches to enable researchers to scale up the current work, expand the number of genes in the resource and facilitate integration into healthcare delivery. This award will also fund research into cancer disease genes and expanding the use of ancestry and diversity in genetic research.

Dr. Sharon Plon and Dr. Aleksandar Milosavljevic are co-principal investigators of the Baylor ClinGen project.

NIH funding supports genetic single-gene disorder research

The National Institutes of Health has awarded nearly $80 million to establish the Genomics Research to Elucidate the Genetics of Rare Diseases (GREGoR) Consortium and the development of novel methods and approaches that help researchers identify the genetic causes of single-gene diseases. Baylor College of Medicine is one of five clinical sites included in the consortium, which is funded by the National Human Genome Research Institute.

More than 400 million people worldwide have been diagnosed with one of about 7,000 Mendelian diseases, which are disorders generally thought to be caused by mutations in a single gene. The consortium's goal is to significantly increase the number of Mendelian disorders for which the genetic cause is known. Researchers will explore and find innovative methods to increase the rate at which the genes responsible for all Mendelian diseases can be identified.

The central vision of BCM-GREGoR is to translate these discoveries to precision molecular diagnostics in the clinic. The team's goal is to define all Mendelian diseases and to catalog the human health impacts of genetic changes in the approximately 20,000 protein-coding genes. In order to drive this knowledge to the front lines of medical care, the Baylor team will continue to strengthen partnerships with genetic and genomic diagnostic laboratories and further develop tools to empower clinicians across all specialties to use genetic information in patient care.

"Over the past 15 years, we have made tremendous strides in the field of genomic medicine and rare disease research," said Dr. Jennifer Posey, assistant professor of molecular and human genetics at Baylor and one of the principal investigators of the Baylor site, with Dr. Richard Gibbs and Dr. James Lupski. "Despite this, about two-thirds of rare disease families still remain without an identified genetic cause of their condition. We now have the opportunity to address this challenge head-on by harnessing new approaches to study families with rare diseases."


Dr. Jennifer Posey


Dr. Richard Gibbs


Dr. James Lupski

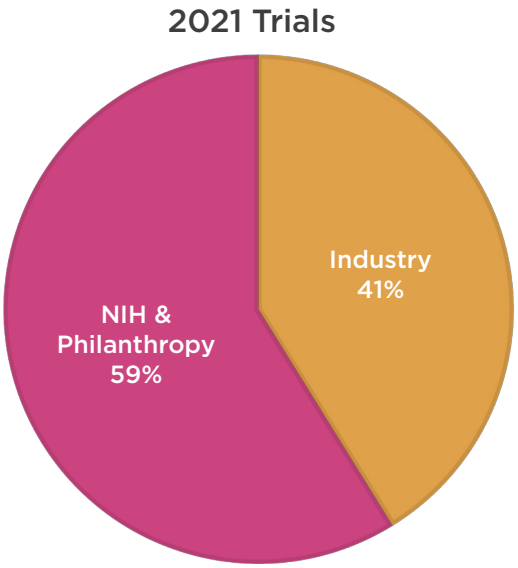
Clinical Research

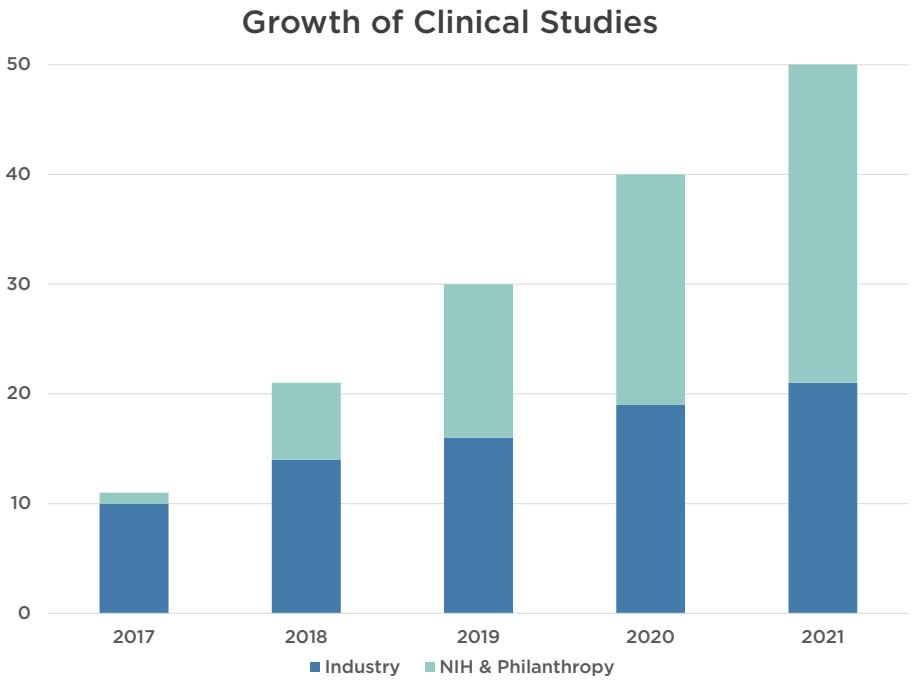
The Clinical Research Division of the Department of Molecular and Human Genetics at Baylor College of Medicine facilitates the implementation and conduct of many clinical studies in rare disorders.

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 2021, the division, led by Dr. Sandesh Nagamani, associate professor of molecular and human genetics at Baylor College of Medicine, 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 Congenital Disorders of Glycosylation. Baylor's sites for the NIH Undiagnosed Diseases Network, 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.





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.

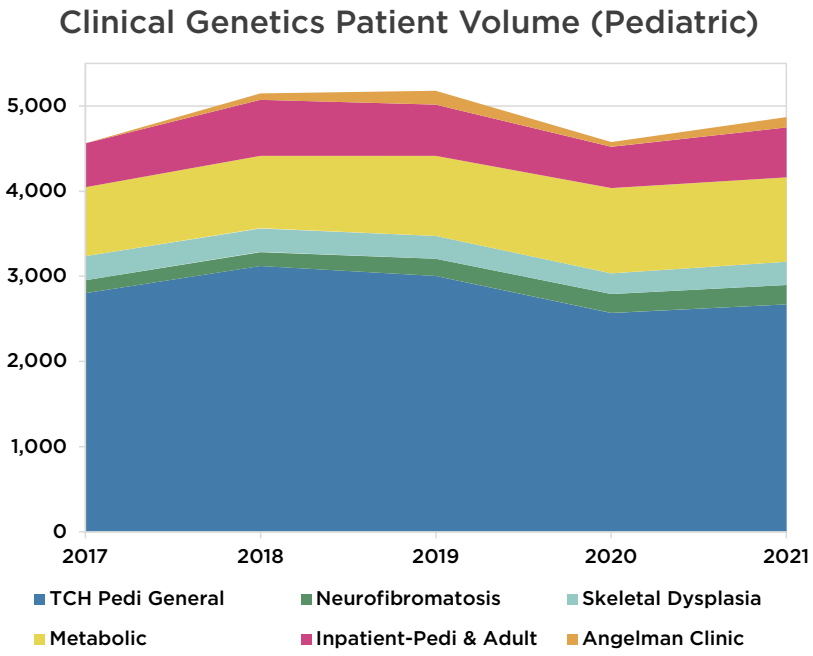
Pediatric Genetics

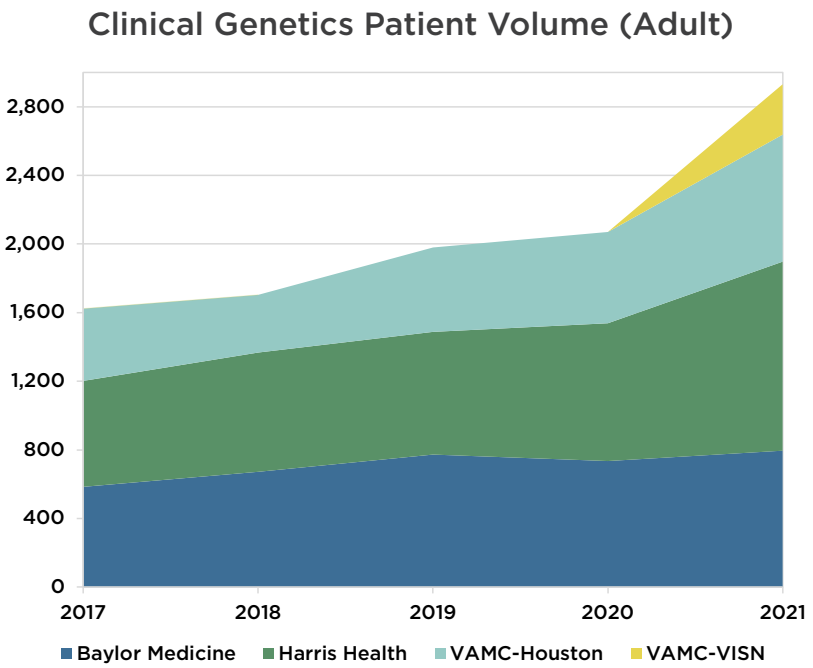
Our pediatric genetics service provides inpatient and outpatient care to patients with complex conditions and those who are critically ill. We have clinics located at Texas Children's Hospital and several other hospitals within the Texas Medical Center and outside of it (TCH West Campus and The Woodlands Texas Children's Hospital). Physicians at the Texas Children's Genetics Clinic see more than 5,000 patients each year.

Specialty clinics within the Texas Children's Genetics Clinic include the metabolic, neurofibromatosis, skeletal dysplasia and cancer genetics clinics. We also have multidisciplinary team clinics like the Angelman Syndrome Clinic, the Center for Genetic Disorders of Obesity, Mitochondrial Medicine Clinic, and the Gender Medicine Program. Genetics physicians and counselors from Baylor also staff joint clinics with other departments, such as otolaryngology (otogenetics), neurology (neurogenetics/tuberous sclerosis) and plastic surgery (craniofacial/craniosynostosis clinics).

Adult Genetics

Our adult genetics service is one of the largest in the country providing inpatient and outpatient care and genetic counseling exclusively for adult patients at four different locations: Baylor Medicine, Harris Health, the Michael E. DeBakey VA Medical Center





and through our virtual Consultagene Clinic. We see patients for a wide variety of indications including, but not limited to, intellectual disability, neurological conditions, cardiovascular conditions, connective tissue disorders and personal or family history of cancer.

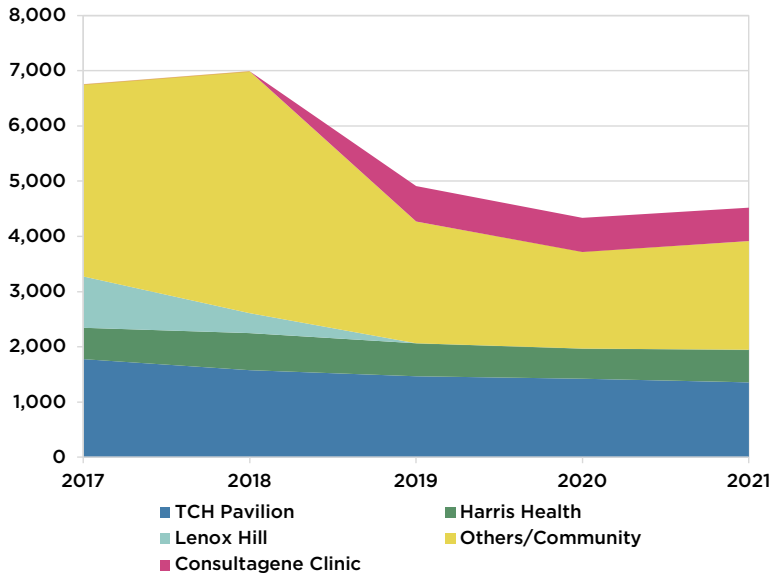
In addition to the general genetics clinics, we also have a Metabolic and Genetic Disorders of the Bone Clinic and a Cardiomyopathy Clinic.

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 and its five 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)



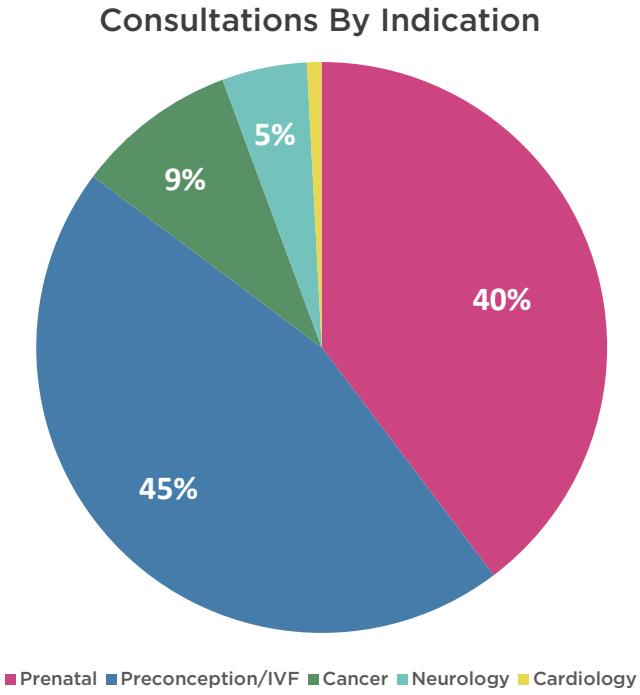
The Consultagene Clinic

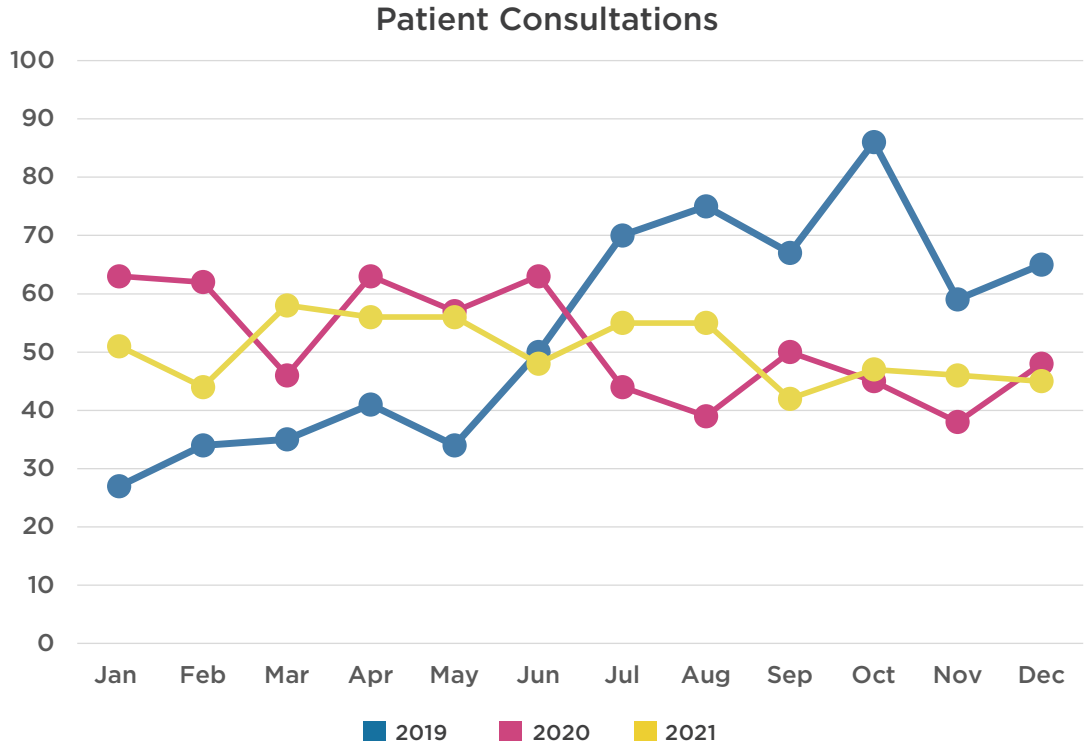
In its third year of operation, the decision was made that the Consultagene Clinic would remain a fully virtual clinic. The clinic maintained its overall patient numbers and saw a total of 603 patients in 2021.

The clinic's volume for neurology referrals, for indications such as family history of Alzheimer's disease, Parkinson's disease, atypical dementia, parkinsonian conditions, ALS and cerebellar ataxia, grew 37% in 2021. This year, most patients (45%) were seen for a IVF/preconception indication while 40% were seen for a prenatal indication, 9% were seen for cancer, 5% for neurology and 1% for cardiology.

Since its inception in 2019, patients seen in the clinic have been 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. In September 2021, the Consultagene platform was redesigned with focuses on user experience, modular workflow and security.

Patients have also been surveyed to gauge their Consultagene Clinic experience. Of the 111 patients who participated in the survey since its update in March, 77% used the resources provided in the patient portal and all indicated that the telegenetic counseling experience met or exceeded their expectations.





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 research 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.

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 since expanded its research focus into new and exciting areas.

The Baylor HGSC employs more than 180 staff and occupies more than 36,000 square feet of space in the Margaret M. and Albert B. Alkek Building at Baylor College of Medicine 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 in order to direct therapeutic strategies. This pathway from "bench to bedside" is the foundation of the new national initiative in Precision Medicine.

Dr. Richard Gibbs in Baylor's Human Genome Sequencing Center

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 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 (NRI) at Texas Children's Hospital

Jan and Dan Duncan Neurological Research Institute

In December of 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 United States 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 Alzheimer's, Parkinson's, bipolar disorder, eating disorders and addiction.

The NRI, under the astute direction of Dr. Huda Zoghbi, the Ralph D. Feigin professor of pediatrics, molecular and human genetics, neurology, and neuroscience at Baylor and Howard Hughes Medical Institute investigator, fosters a one-of-a-kind research environment uniquely designed to impact the future of neurological disease. About 30 investigators from around the world and their research teams, all experts in diverse disciplines – such as genetics, neurobiology, physics, mathematics, bioinformatics and engineering

– work in specially designed "collaboratories." These open labs facilitate the free exchange of ideas, information and resources.

This past year, Drs. Michael Wangler and Hugo Bellen, both professors of molecular and human genetics at Baylor College of Medicine and members of the NRI, initiated the Texome Project, a community-wide genomics effort to expand access to state-of-the-art genetic testing to low-income families without private medical insurance or other financial means to cover these expensive tests. Funded by the NIH and NRI, the Texome Project offers free exome sequencing to individuals with undiagnosed medical conditions or developmental delays, ultimately providing accurate diagnoses and potential treatments.

2021 was another year full of discoveries. The lab of Dr. Huda Zoghbi identified novel interactions of MeCP2. Published in *Proceedings of the National Academy of Sciences of the United States of America*, the work provides insight into the mechanisms involved in the pathogenesis of neurodevelopmental disorders. Also in *PNAS*, the Bellen lab demonstrated that gene variants associated with Alzheimer's disease disturb the brain's natural protective mechanism and that certain alterations can be restored.

A study from the Botas lab revealed that the brain downregulates glial genes involved in synaptic assembly and maintenance to protect itself against Huntington's disease. The study, published in *eLife*, highlights the critical and often overlooked roles played by glial cells in protecting against neuronal loss.

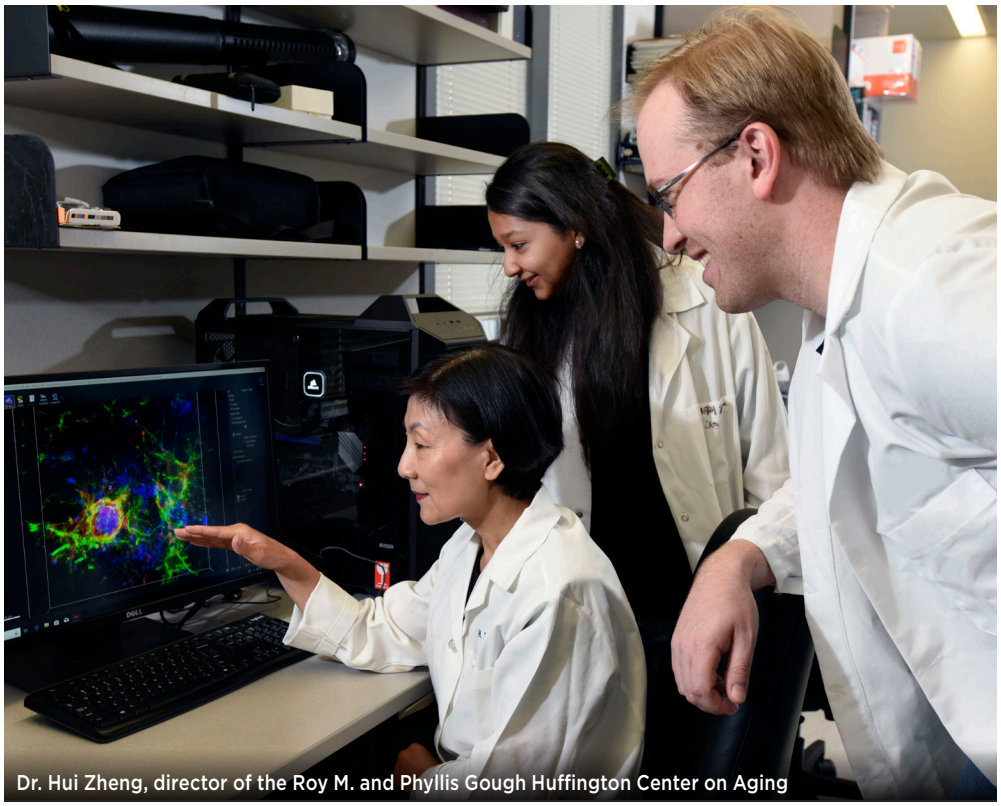
The Yamamoto lab identified a new role for the TM2D gene family in regulating neuronal survival and degeneration. The study, published in *PloS Genetics*, built on earlier work in Alzheimer's disease by Drs. Yamamoto, Bellen and Shulman.

Finally, an Undiagnosed Diseases Network study led by Dr. Bellen found that mutations in the transportin-2 gene was the underlying cause of a novel neurodevelopmental disorder. Published in the *American Journal of Human Genetics*, the team combined in-depth clinical tests, genome sequencing and functional studies in fruit flies to definitively diagnose the disorder.

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 over 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.



Dr. Hui Zheng, director of the Roy M. and Phyllis Gough Huffington Center on Aging

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 over 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 also 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).

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 is committed to cutting edge research in aging and age-related diseases.

The center facilitates and coordinates interdepartmental research and initiates its own research studies that 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.

Despite the challenges and uncertainties brought by the COVID-19 pandemic, the Center was successful in recruiting new faculty. Dr. Hongjie Li was recruited from Stanford University and started in January 2021 with a primary appointment in the Department of Molecular and Human Genetics. Li did his postdoc work with Dr. Liqun Luo at Stanford working on neuronal wiring in *Drosophila*. He is the recipient of a NIH Pathway to Independence Award from the National Institute of Aging and a CPRIT Scholar award.

Center faculty received various grants. Dr. Zheng and Dr. Jin Wang, CPRIT Scholar and professor of pharmacology and chemical biology, were awarded a five-year cooperative agreement drug development grant from the NIA aimed at developing small molecule inhibitors targeting neuroinflammation as potential Alzheimer's disease therapy.

In addition, Dr. Zheng led a team effort with Dr. Meng Wang, professor of molecular and human genetics at Baylor and Howard Hughes Medical Institute investigator, Dr. Nicolas Young, professor of biochemistry and molecular biology at Baylor, Dr. Joanna Jankowsky, professor of neuroscience at Baylor, and Dr. Marco Sardiello, professor of Pediatrics at Washington University School of Medicine as key investigators, to secure a five-year Program Project Grant from the NIA aimed at understanding the role of the lysosome in aging and Alzheimer's disease.

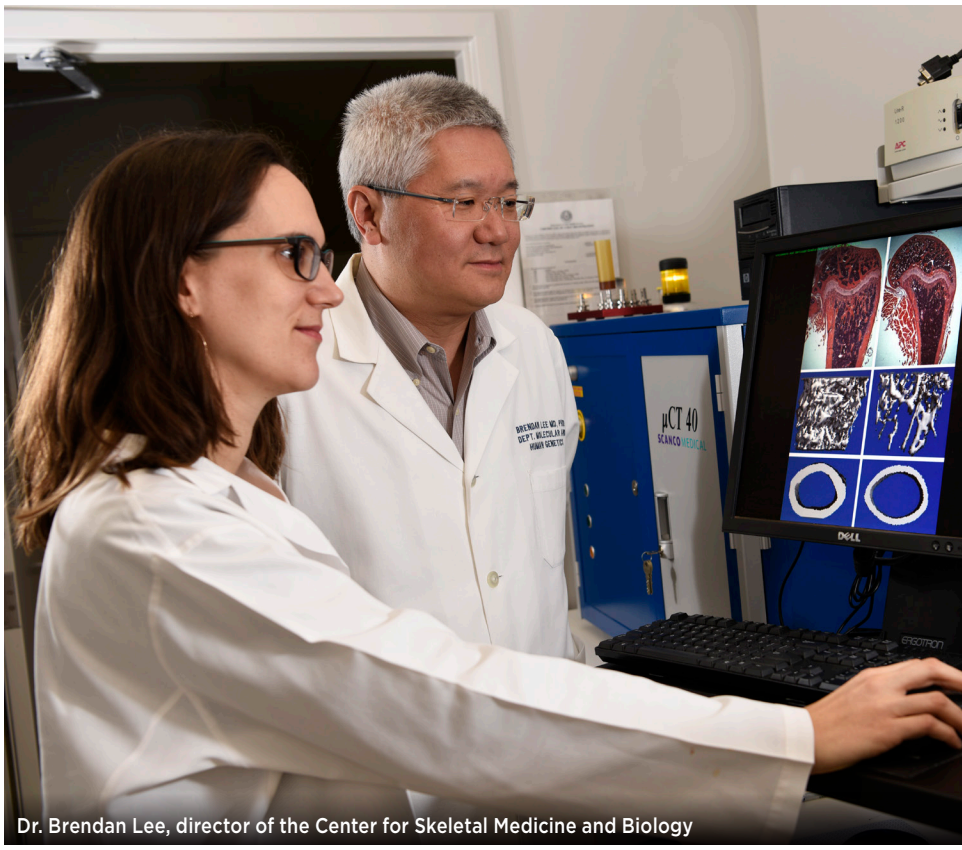
Intellectual and Developmental Disabilities Research Center

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 and Human Genetics at Baylor, and Dr. Rodney Samaco, assistant professor of molecular and human genetics in the Duncan Neurological Research Institute, 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 published nearly 2000 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.

Basic understanding of neural cells and circuits has provided pathways for preclinical studies and design of interventions for treating IDDs, and the IDDRC-supported Signature Project helmed by Dr. Mirjana Maletic-Savatic, assistant professor of molecular and human genetics, and Dr. Matthew McGinley, assistant professor of molecular and human genetics, is designed to further our understanding and treatment of gene dosage-dependent disorders.



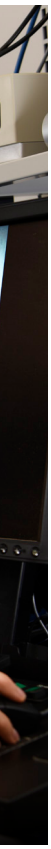
Dr. Brendan Lee, director of the Center for Skeletal Medicine and Biology

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 Rolanette and Berdon Lawrence 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.

In 2021, Flexion Therapeutics, which licensed our development of helper-dependent adenovirus gene therapy for osteoarthritis, reported on preliminary studies of their phase I clinical trial. The treatment was in general well tolerated with early signal of clinical activity in the low-dose cohort, with two of the five patients treated reporting pain relief.



Graduate Program.

The Genetics & 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 Recognition for Genomics & Graduate Program Students

Varuna Chander was awarded third place in Baylor College of Medicine's Three Minute Thesis Competition

Dharaniya Sakthivel, **Moez Dawood** and **Andrew Yang** all received CPRIT Predoctoral Training Grants from the Cancer Prevention & Research Institute of Texas

Timothy Abreo received a Predoctoral Research Fellowship from the American Epilepsy Society

Venkatasubramaniam Sundaramurthy was awarded a Predoctoral Fellowship by the American Heart Association

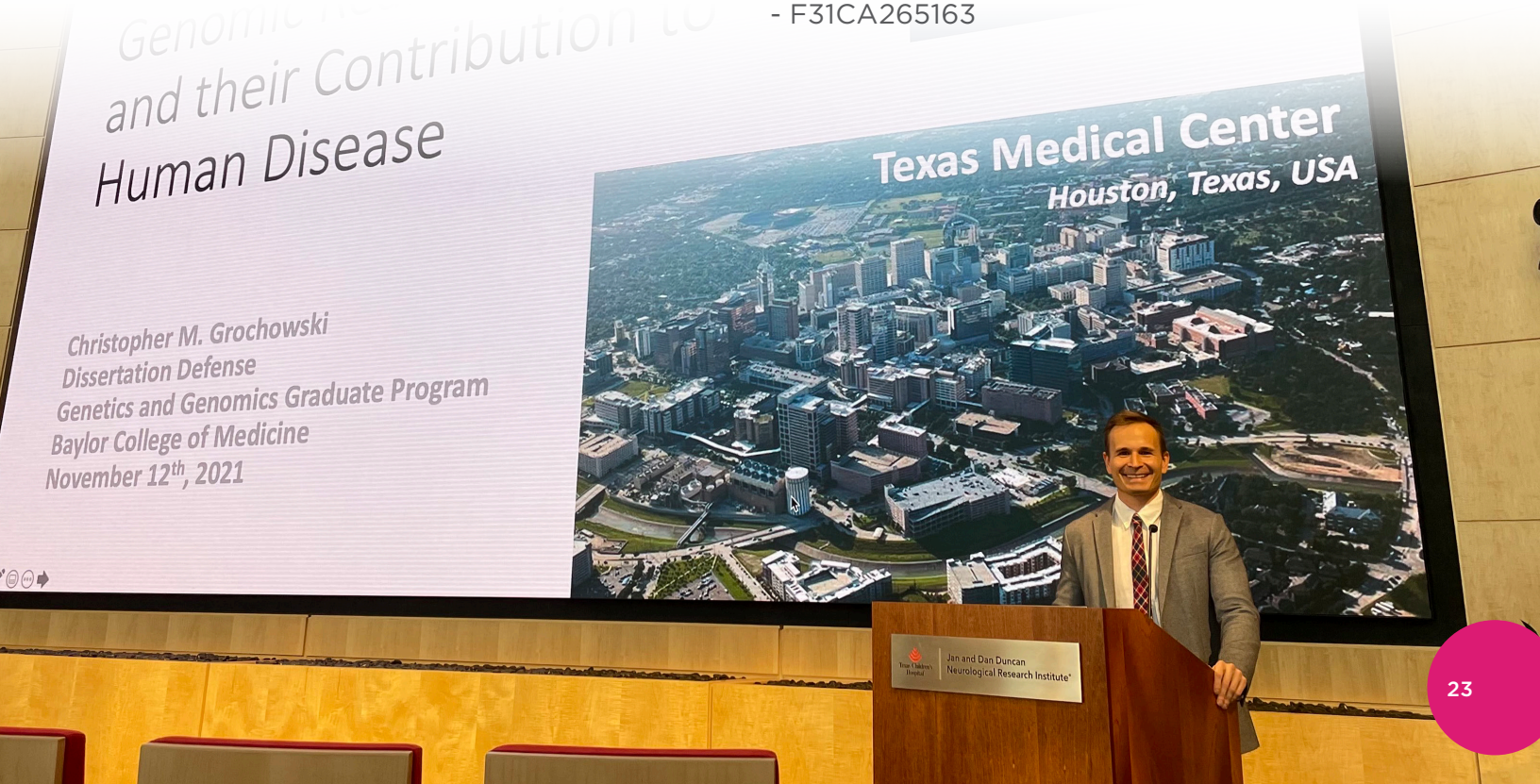
Cathy Bradley was awarded first place for her oral presentation at the 2021 BCM Medical Scientist Training Program Symposium

C. Grant Mangleburg was awarded third place for his oral presentation at the 2021 BCM Medical Scientist Training Program Symposium

Varuna Chander was named a semifinalist for the Charles J. Epstein Trainee Award for Excellence in Human Genetics at the 2021 American Society of Human Genetics

Adam Weinstein received an Honorable Mention for his oral presentation at the 2021 Dan L Duncan Comprehensive Cancer Center Symposium

Owen Hirschi was awarded a Ruth L. Kirschstein NRSA for Individual Predoctoral Fellows (F31) Fellowship by the National Cancer Institute for "Germline Structural Variant Identification and Functional Determination in Childhood Cancer" - F31CA265163



2021 Dissertations

Student Name	Title	Preceptor/Advisor
Raghu Chandramohan	Bioinformatics Solutions to Derive Clinically Relevant Copy Number Variants from Targeted Sequencing Data	Dr. Donald Will Parsons
Sean Dooling	The Gut-Microbiota-Brain Axis in Complex Behaviors	Dr. Mauro Costa-Mattioli
Christopher Grochowski	Deciphering Complex Genomic Rearrangements and their Contribution to Human Disease	Dr. James Lupski
Mike J. Harnish	Integrating Drosophila and rare disease matchmaking: studying the contribution of rare variants to genetic disease both rare and common	Dr. Shinya Yamamoto
Patrick Hunt	Acetylcholine and GABA Co-transmitting neurons in the lateral septal nucleus exhibit features of neurotransmitter switching	Dr. Benjamin Arenkiel
Angad Jolly	Functional Integration of Family Based Genomics, Biology of Disease, and Disease Trait Clinical Phenotyping	Dr. James Lupski
Michael Khayat	Beyond a Molecular Diagnosis: Current and Future Challenges in Variant Interpretation and Detection	Dr. Richard Gibbs
Jingjing Liu	DNA damage at sites of aborted transcription	Dr. Susan Rosenberg
Grant Mangleburg	Systems biology dissection of causal events in Alzheimer's disease	Dr. Joshua M. Shulman
Lauren Straker Manley	Computational analyses of structured and unstructured data guide studies showing that p21 (Cdc42/Rac) activated kinases phosphorylate and negatively regulate p53	Dr. Olivier Lichtarge
Woojun (Dan) Park	Evaluating the Therapeutic Potential of CDK7 in Multiple Myeloma	Dr. Charles Y. Lin
Varduhi Petrosyan	Computational Deconvolution and Network Modeling of Breast Cancer Tumors and Patient-Derived Xenograft Mouse Models	Dr. Aleksandar Milosavljevic
Thomas Ravenscroft	Identification of spike initiation zones in Drosophila	Dr. Hugo Bellen
Jose Salazar	TM2D genes regulate Notch signaling and neuronal function in Drosophila	Dr. Shinya Yamamoto

Residency Programs and Clinical Laboratory Fellowships

Throughout the evolution of the Department of Molecular and Human Genetics, there has been a strong emphasis on training and education. Our residency and clinical lab fellowship programs began in 1987, and we have had hundreds of trainees graduate from our programs. There has been no higher priority in the department. The growth and development of the department and clinical enterprises are inextricably linked to the excellence of the trainees and our training programs.

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.

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

Trainees in our clinical laboratory fellowship programs train at Baylor College of Medicine's genetics diagnostic laboratory, Baylor Genetics, for 24 months.

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

After the completion of all programs, trainees are eligible for American Board of Medical Genetics and Genomics certification.

Residencies:

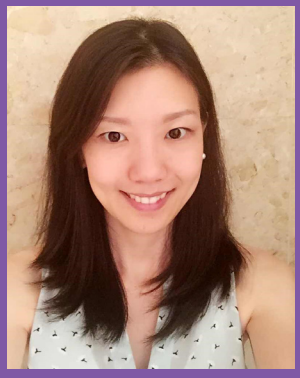
- Medical Genetics and Genomics
- Pediatrics/Medical Genetics and Genomics
- Internal Medicine/Medical Genetics and Genomics
- Maternal-Fetal Medicine/Medical Genetics and Genomics Fellowship

Clinical Laboratory Fellowships:

- Laboratory Genetics and Genomics
- Clinical Biochemical Genetics

2021 MHG Trainee Awards

Scott Ward, M.D.
Clinical Resident Award



Xiaonan Zhao, Ph.D.
Laboratory Fellow Award

2021 Graduating Class of Residents and Fellows

Monika Weisz Hubshman, M.D., Ph.D.
Medical Genetics Residency

Erica Lay, M.D..
Pediatrics/Medical Genetics Residency

Laura Mackay, M.D., M.P.H.
Pediatrics/Medical Genetics Residency

Yehoshua "Josh" Manor, M.D.
Medical Biochemical Genetics Fellowship

Rebecca Markovitz, M.D., Ph.D.
Pediatrics/Medical Genetics Residency

Annarita Nicosia, M.D.
Medical Genetics Residency

John "JD" Odom, M.D.
Medical Genetics Residency

Volkan Okur, M.D.
Laboratory Genetics and Genomics Fellowship

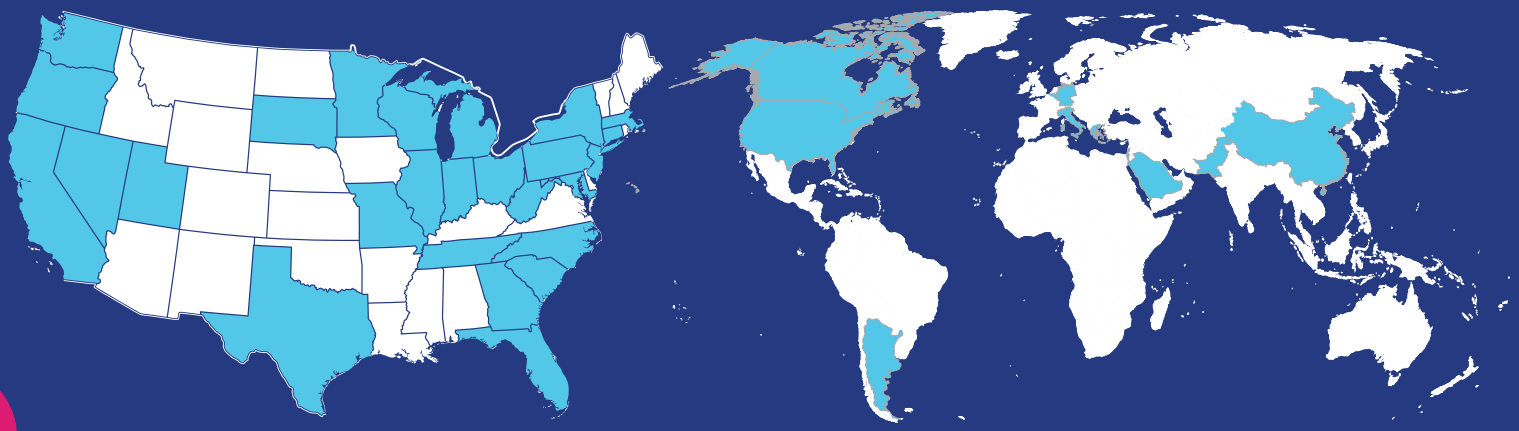
Eran Tallis, M.D.
Medical Genetics Residency

Liesbeth Vossaert, Ph.D.
Laboratory Genetics and Genomics Fellowship

Chung Wah "Wilson" Wu, Ph.D.
Laboratory Genetics and Genomics Fellowship

Jing Xiao, Ph.D.
Clinical Biochemical Genetics

Locations of Former Medical Genetics Trainees



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 a transformative education in genomic medicine and the practice of genetic counseling.

The program initially received accreditation status in 2018 and was granted full accreditation for eight years by the Accreditation Council for Genetic Counseling in December of 2021. The program currently has a total of 18 trainees and plans to welcome 9 new students in July of 2022.

“The program has been even more rewarding than I expected. With so many clinical sites in the TMC, we have 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.

Program directors, Salma Nassef, M.S., C.G.C. (second from left) and Dan Riconda, M.S., C.G.C. with current and graduating students

Genetic Counseling Program Class of 2021

Abigail (Abby) Yesso
Lisa Saba
Olivia Thompson
Mikaela Francisco
Adasia (Daisy) Ritenour
Farah Ladha
Ashley Spector
Emily Soludczyk

Community Engagement and Diversity

The Department of Molecular and Human Genetics' Office of Community Engagement and Diversity is co-directed by Susan Fernbach, an assistant professor of molecular and human genetics, and Dr. Debra Murray, an assistant professor of molecular and human genetics. Under their leadership, the MHG Diversity and Inclusion committee and the virtual diversity and inclusion library (articles, statistics on systemic health, educational equity issues) has grown.

Evenings with Genetics is a free community seminar series hosted by the department and Texas Children's Hospital. The series features a genetics faculty speaker paired with faculty from another specialty area plus a parent speaker at each seminar.

The webinar format expanded its national and global reach this year with over 740 attendees and topics such as new insights and directions for TANGO2, current management, treatment and resources for achondroplasia, pharmacogenomics, CRISPR and genome editing, and the genetics and care for inherited renal disorders. The webinars were recorded and are available on our website.

To celebrate Rare Disease Day in February, a virtual event was held in collaboration with the Texas Rare Action Network of the National Organization for Rare Disorders. The event had over 70 in attendance.

The virtual From Stress to Strength program was held in February and July with parallel tracks in English and Spanish. The event was led by faculty and trainees from the department, the Baylor Medicine Transition Medicine Clinic, psychologists with the Texas Children's Autism Center and parent co-facilitators for parent participants from around the state.

In collaboration with the UT Texas Center for Disability Studies and the Texas Department of State Health Services, statewide genetic

Dr. Brendan Lee, Dr. Debra Murray, Dr. Reid Sutton, and Dr. Lindsay Burrage with 2021 Clinical Research Education Training Program interns

outreach included webinars in English and in Spanish with a total of 57 attendees. One-page fact sheets and short animated videos were developed and made available on our website to accompany each recorded webinar. Five webinars for healthcare professionals were also held with a total of 315 attending.

The annual virtual Careers in Genetics and Genomics was presented to Baylor summer interns and underrepresented high school and college students from across the state. The series featured a medical geneticist, basic scientist, genetic counselor and trainee speaker with 65 attendees.

This year the office increased efforts to educate medical students about clinical research careers in genetics and genomics. In February, the first "Everything You Want to Know About Medical Genetics" virtual series was held for first year medical students at Meharry Medical College. In March, a Town Hall "A Whitecoat and Genes: The Life of a Medical Geneticist" was held for 3rd and 4th year medical students with 54 attendees from across the U.S. In May, the inaugural short-term summer Clinical Research Education Training Program trained its two interns, first-year medical students, one from Meharry Medical College and the other from the University of Texas-Rio Grande Valley School of Medicine.

The Let's Learn About One Another series continued this summer with a focus on the Asian American experience and was held in collaboration with the Department of Neuroscience. This featured national speakers, Dr. David Asai, senior director for science education at the Howard Hughes Medical Institute, along with members of our department with over 65 people in attendance.

Evenings with Genetics addresses race, genetics and the future of precision medicine

In 2021, for the 15th anniversary of the Evenings with Genetics webinar series and in honor of Black History Month, two webinars were held on Race and Genetics: Perspectives on Precision Medicine. The goals of the series were to look at the history of race and genetics and to understand that the construct of race is independent from genetics and ancestry. More than 400 attendees from across the country attended this two-part series, which was moderated by Dr. Charmaine Royal, professor of African & African American studies, biology, global health and family medicine & community health at Duke University.


Shawneequa Callier, M.A., J.D.


Dr. Clayton Yates


Dr. Charmaine Royal

On February 9th, Shawneequa Callier, associate professor in the Department of Clinical Research and Leadership at the George Washington University School of Medicine and Health Sciences, focused on issues at the intersection of bioethics, law and emerging technologies related to precision medicine. Discussing research and health disparities, the lack of diversity and inclusion in genomic research, which includes participants, researchers and the research questions asked, she highlighted the ongoing need to develop frameworks in bioethics to assess the role of race and racism in research and precision medicine while understanding that race is a social, not biological construct.

The second speaker, Dr. Clayton Yates, professor in the Department of Biology and Center for Cancer at Tuskegee University, presented his research with minority

populations demonstrating that changes in the epigenome could be contributing to gene expression differences. Yates showed one example highlighting the gene KAISO, where high expression levels in African American patients cause more aggressive prostate or breast cancers, and he explained how this knowledge can be essential in developing the patient's precise treatment plan.

The March 9th webinar featured Dr. Chanita Hughes-Halbert, professor in the Department of Psychiatry and Behavioral Sciences and associate dean of Assessment, Evaluation, and Quality Improvement at the College of Medicine at Medical University of South Carolina. Her genetic counseling and testing research has provided a model of culturally tailored strategies for cancer prevention and control among racial minorities. She discussed research looking at social determinants in minority health and cancer health disparities, with data indicating the cumulative life stressors in minority men may also have predictive effects, as the stressors can affect biological function at a cellular level, disease processes and outcomes.


Dr. Chanita Hughes-Halbert


Dr. Rick Kittles


J.H. Jones

Next, Dr. Rick Kittles, professor and founding director of the Division of Health Equities within the Department of Population Sciences at the City of Hope (COH), and associate director of Health Equities of COH Comprehensive Cancer Center, spoke about the high genetic diversity in the African American population due to diverse ancestry from multiple countries across Africa. He emphasized that the term "race" does not provide insight biologically but is a sociocultural concept. He gave an example of a new study with Naltrexone, a more effective drug in white and western African populations, but not those with ancestry from other countries in Africa. Currently, precision medicine may increase health disparities as most of the information is based on people of European ancestry studies.

Lastly, J. H. Jones, a self-described "sickle cell elder," shared her journey as an advocate. Jones said she fears precision medicine will be years away for the African American community as it is expensive, and few African Americans are participants in studies. She feels that participating in clinical trials is the only way to improve care, but she stressed that providers need to do a better job of the informed consent process. She discussed how minority communities want researchers to understand the importance of including the community in deciding the research questions. The community values long-term relationships with researchers and wants to be informed of study progress, or lack of progress.

Faculty Awards and Recognitions

Arenkiel recognized by TAMEST for breakthrough findings

Dr. Benjamin Arenkiel, associate professor of molecular and human genetics and neuroscience, was awarded the prestigious 2021 Edith and Peter O'Donnell Award in Medicine from the Academy of Medicine, Engineering and Science of Texas (TAMEST). He was recognized for his breakthrough identification of the brain's neural pathways that are connected to eating disorders, addiction and other neuropsychiatric disorders, leading to a better understanding of the makeup of neural circuits and how they talk to each other.

He and his team identified a convergent brain circuit that combines sensory perceptions and motivational state. They found that when the circuit is disrupted, it leads to behaviors ranging from anxiety, anorexia, addiction and more.

Arenkiel, who also is a McNair Scholar at Baylor, showed how scientists might use this knowledge to treat severe eating disorders, obesity and addictive behaviors by manipulating the acetylcholine signals initiating such behavior in the basal forebrain. His research shows how replacing or rerouting information around the "bad spots" of the brain can allow the restoration of normal cell function.

Arenkiel is one of four Texas-based scientists who received the TAMEST 2021 Edith and Peter O'Donnell Award for their individual contributions addressing the essential role that science and technology play in society, and whose work meets the highest standards of exemplary professional performance, creativity and resourcefulness.

More Awards and Recognitions for MHG Faculty

Pilar Magoulas, M.S., CGC was the 2021 recipient of the Heart of Genetic Counseling Award presented by the National Society of Genetic Counselors and Invitae

Dr. Brendan Lee was elected president of the American Society of Human Genetics

Dr. Hugo Bellen was recognized by Baylor College of Medicine with the Barbara and Corbin J. Robertson, Jr. Presidential Award for Excellence in Education

Dr. Reid Sutton was recognized by Baylor College of Medicine with a Master Clinician Faculty Award for Excellence in Patient Care

More Awards and Recognitions for MHG Faculty (cont.)

Dr. Debra Murray was recognized by Baylor College of Medicine with a Norton Rose Fulbright Faculty Excellence Award for Educational Leadership

Tanya Eble, M.S., C.G.C. was recognized by Baylor College of Medicine with a Norton Rose Fulbright Faculty Excellence Award for Teaching & Evaluation

Dr. Lindsay Burrage was recognized by Baylor College of Medicine with a Norton Rose Fulbright Faculty Excellence Award for Teaching & Evaluation

Dr. Sandesh C.S. Nagamani was recognized by Baylor College of Medicine with a Norton Rose Fulbright Faculty Excellence Award for Development of Enduring Educational Materials

Dr. Susan Rosenberg was named to the executive committee of the new American Association of Cancer Research Cancer Evolution Working Group.

Dr. Richard Lewis was selected to the International Choroideremia Research Advisory Committee, of the Choroideremia Research Foundation

Dr. Pengfei Liu was a recipient of a 2021 National Human Genome Research Institute Genomic Innovator Award

Department Faculty Awards

Best Metabolic Attending
Dr. Lindsay Burrage

Best Pediatric Attending
Dr. Chaya Murali

Best Adult Attending
Dr. Shweta Dhar

Best Clinical Educator
Dr. Reid Sutton

Best Clinical Research Mentors
Dr. Seema Lalani

Best Subspecialty Attendings
Dr. Surya Rednam
Dr. Ignatia Van den Veyver

Best Genetic Counselors
Lisa Saba, M.S., C.G.C.
Adasia Ritenour, M.S., C.G.C.

Baylor Genetics Laboratory Service Awards
Dr. Nichole Owen and Dr. Linyan Meng

Outstanding Graduate Teaching Awards
Dr. Daryl Scott (Faculty)
Shelley Gibson (Teaching Assistant)

Kenneth Scott Graduate Mentor Award
Dr. Herman Dierick

Shan and Lee-Jun Wong Fellowship
Jun Hyoung Park, Ph.D.

New Faculty

In 2021, we recruited three new tenure-track primary research faculty: Nicholas Tran, Elizabeth Atkinson, and Anthony Zoghbi.

Nicholas Tran, Ph.D.

Dr. Nicholas Tran studied biology at the University of Virginia and from there went to Washington University in St. Louis where he got his doctorate in molecular genetics and genomics. Tran's research focuses on understanding what happens to different neuronal populations in neurodegenerative conditions using cutting edge single-cell genomic approaches. Tran's lab uses the retina to study blinding disorders like glaucoma and basic mechanisms of degeneration. Tran's ultimate mission is to identify better targets for therapies that protect neurons from degeneration and stimulate axon regeneration.

Elizabeth Atkinson, Ph.D.

Dr. Elizabeth Atkinson studied biology at Williams College and from then went to Washington University in St. Louis where she got her doctorate in evolution, ecology, and population biology. She then went on to complete a postdoctoral research fellowship in the Analytical and Translational Genetics Unit at Massachusetts General Hospital and the Broad Institute working in the lab of Mark Daly. Atkinson's research is centered around neuropsychiatric traits with particular focus on admixed American populations and groups of African descent, though the tools her lab builds are broadly applicable giving them the potential for widespread impact on human health. The primary goal of her lab is to reduce the disparity in genomics research across ancestries through leveraging global genomic datasets and cutting-edge computational techniques to build and apply resources for the improved statistical genetic study of diverse human populations that genomics has so far underserved.

Anthony Zoghbi, M.D.

Dr. Anthony Zoghbi studied philosophy, neuroscience and psychology at Washington University in St. Louis. He then went on to get his doctorate in medicine at Baylor College of Medicine. He completed his residency at Columbia University Department of Psychiatry and New York State Psychiatric Institute. He has made it back to Baylor as the Beth K. And Stuart C. Yudofsky Scholar and chief of psychiatric genetics in the Menninger Department of Psychiatry and Behavorial Sciences. His lab's primary research goal is currently focused on studying rare genetic variation in severe forms of schizophrenia and obsessive-compulsive disorder, though he intends to apply similar strategies across neuropsychiatric disorders.

PROMOTIONS

Professor, tenured

Benjamin Arenkiel
Hamed Nejad-Jafar
Joshua Shulman

Associate Professor, non-tenure

Tanya Eble

Assistant Professor, non-tenure

Laura Ellis
Yanghong Gu
Denise Lanza
Andrea Moon
Samantha Stover
Lauren Westerfield

Instructor

Saima Ali
Dianne Bauri
Katie Chan
Amanda Gerard
Elizabeth Mizerik
Ralf Nehring

In Memoriam

Dr. Lee-Jun Wong

Dr. Lee-Jun C. Wong passed away on April 29, 2021. Wong was a professor of molecular and human genetics at Baylor College of Medicine where she made seminal and groundbreaking contributions to the field of mitochondrial genetics.

Wong received her undergraduate degree in biochemistry from the National Taiwan University. She earned her doctorate in biochemistry from the Department of Chemistry at Ohio State University under the mentorship of the National Academy of Sciences member Dr. Perry A. Frey. Wong followed her doctorate with research training in the labs of the Nobel Laureate Dr. Irwin Rose at the Institute for Cancer Research in Philadelphia, Dr. Bruce Alberts at Princeton University and Dr. George Marzluf at Ohio State University. After her time at Ohio State, she took a faculty position in the Department of Biological Sciences at the University of Massachusetts-Lowell, where she earned tenure.

After 14 years, Wong came to Baylor for fellowship training in biochemical genetics with Dr. William O'Brien. During that period, she also published with Dr. C. Thomas Caskey on the recently discovered triple repeat disorder, myotonic dystrophy. Upon completion of her fellowship, she earned board certification in biochemical genetics and took a faculty position as the Director of the Molecular Diagnostic Laboratory at the University of Southern California School of Medicine.

Wong's interest in mitochondrial disorders began when she published papers on the then recently described MELAS and Kearns-Sayre syndromes. She pioneered techniques for the detection of mitochondrial DNA (mtDNA) mutations, in addition to developing assays for prenatal testing of Mendelian disorders. In 1997, she became the Director of the Molecular Genetics Laboratory within the Institute for Molecular and Human Genetics at Georgetown University Medical Center. There she developed state-of-the-art molecular diagnostic testing, and at the same time began a long-term research focus on the role of mitochondrial dysfunction in cancer biology.

Wong returned to Baylor in 2005, establishing and becoming the Director of the Mitochondrial Diagnostic Laboratory. During this time, she developed the now gold standard diagnostic test for mtDNA using long range PCR and the pipeline for massively parallel next generation mtDNA sequencing. Over the years, she kept improving bioinformatic tools and computational criteria to validate novel pathogenic variants.

Wong's scientific accomplishments and relentless enthusiasm have led to the discovery of many novel variants. The depth of her contributions on accurate clinical diagnostic testing and genetic counseling has had a significant impact on the classification of these mitochondrial disorders and the lives of our patients with mitochondrial disease. Wong trained and mentored a large number of laboratory diagnosticians who now are directors of diagnostic laboratories around the world. With great generosity she endowed the Shan and Lee-Jun Wong Fellowship which is awarded competitively at Baylor College of Medicine to a trainee or early career faculty focused on translational studies in medical genetics. Throughout her career, she published over 400 peer-reviewed manuscripts and edited four books, while directing an NIH-funded research laboratory. Wong was a role model of integrity, leadership and mentorship. She was an exemplary scientist and leader who passionately contributed to the field of mitochondrial disease and she will be missed.

Dr. C. Thomas Caskey

In January 2022, Dr. C. Thomas Caskey, a pioneer in genetics and genomics and a professor of molecular and human genetics at Baylor College of Medicine passed at the age of 83. Caskey built the genetics program at Baylor from the ground up, founding what is known today as the Department of Molecular and Human Genetics and growing the department into a national leader in genetics. He is remembered for his contributions to genetic research and his dedication to mentoring and developing the next generation of scientists and physicians.

Caskey began his research career at Duke University, studying de novo purine allosteric regulation with Dr. James B. Wyngaarden. At the National Institutes of Health, under Dr. Marshall Nirenberg, he defined the 'universality' of the genetic code and discovered codon-specific proteins controlling translation termination. In 1971, he moved to Baylor College of Medicine and established the Institute of Molecular and Human Genetics. "Dr. Caskey was a visionary human geneticist who made landmark discoveries that helped accelerate the field of genomic medicine," said Dr. Brendan Lee, Robert and Janice McNair Endowed Chair in Molecular and Human Genetics and professor and chair of the Department of Molecular and Human Genetics at Baylor. "As the founder of genetics activities at Baylor, he laid the groundwork for what has become the leading, most integrated genetics department in the world."

Caskey was a national leader in genetic research. He was influential at the earliest meetings about the Human Genome Project, a massive, worldwide effort to sequence the entire human genome. His genetic research identified the genetic basis of 25 major inheritable diseases and clarified the understanding of "anticipation" in triplet repeat diseases, Fragile X and myotonic muscular dystrophy. His personal identification patent is the basis of worldwide application for forensic science, and he also was a consultant to the FBI in forensic science.

In 1994, Caskey went on to become senior vice president of Human Genetics and Vaccines Discovery at Merck Research Laboratories. Later, he returned to Houston and became the CEO of the Brown Foundation Institute of Molecular Medicine at the University of Texas

Health Science Center at Houston. In 2011, he came back to Baylor as a professor to continue the work in the department he helped build.

His recent publications addressed the utility of genome-wide sequencing to prevent adult-onset diseases, and his research focused on the application of whole genome sequencing and metabolomics of individuals to understand disease risk and its prevention.

Throughout his career, Caskey received numerous academic and industry honors, including the William Allan Award from the American Society of Human Genetics in 2021 and the William G. Anlyan, M.D., Lifetime Achievement Award from the Duke University Medical Alumni Association in 2015. He was a member of the National Academy of Sciences, the National Academy of Medicine (serving as chair of the Board of Health Sciences Policy) and the Royal Society of Canada. He was a past president of the American Society of Human Genetics, the Human Genome Organization and the Texas Academy of Medicine, Engineering and Science.

"Dr. Caskey was a true pioneer in medical genetics," said Dr. Mary Dickinson, senior vice president and dean of research at Baylor. "He charted a path for many to follow through his research and education, and he set the standards for those who came after him. There are so many that will remember him fondly and will carry his legacy through their own work and actions. We have lost a true pillar of our academic community and he will be missed."

Baylor College of Medicine

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