

Baylor
College of
Medicine

DEPARTMENT OF
MOLECULAR & HUMAN
GENETICS



ANNUAL REPORT
2022

Transforming Medicine Through
the Science and Practice of
Genetics and Genomics



Message from the Chair

I am delighted to welcome you to our 2022 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 a top-ranked genetics program, ranking first among other U.S. genetics departments in total awarded funding and number of grants from the National Institutes of Health.

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.

Baylor was recognized on Gizmodo's Degrees of the Future 2022 list as one of the top genetics and genomics programs.

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

In addition, new and continuing consortia with the NIH and industry are leading to new gene discoveries and advancements in the implementation of genetics and genomics. We recently established the Baylor Undiagnosed Diseases Center to incorporate the work of Baylor's Undiagnosed Disease Network clinical site, DNA sequencing core and model organisms screening center.

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



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We have more than **540 FACULTY, TRAINEES AND STAFF** who occupy over **110,685 SQUARE FEET OF SPACE**. Faculty includes:



members of the National Academy of Medicine



members of the National Academy of Sciences



Howard Hughes Medical Institute Investigators



members of the American Academy of Arts and Sciences



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 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 and
Co-Director, Office
of Community
Engagement and
Diversity



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
Diversity



All of Us Evenings with Genetics Research Program Hosts First Annual Summit

In 2021, Baylor College of Medicine received funding from the National Institutes of Health for the *All of Us Evenings with Genetics* Research Program. The goal of the program is to engage underrepresented researchers in biomedical research to utilize the data collected from the NIH's *All of Us* Research Program. NIH's *All of Us* Research Program is an ambitious effort to gather biomedical data from one million or more individuals living in the United States, especially those that are traditionally excluded from biomedical research studies, to support scientific discoveries and advance precision medicine.

In May 2022, the *All of Us Evenings with Genetics* Research Program hosted its first annual Underrepresented Biomedical Researchers Faculty Summit in Houston. The purpose of the summit is to train early career faculty and

senior postdoctoral researchers around the NIH's *All of Us* Researcher Workbench. The Workbench is a cloud-based platform where registered researchers can access registered and controlled tier data. For the summit, a data science curriculum was created to instruct the participants on how to set up cohorts on the Workbench. In addition to the data science training, those who attended the summit took part in professional development sessions, learned of mentoring opportunities and formed research teams. Summit speakers included Dr. Karriem Watson, NIH's *All of Us* Chief Engagement Officer, Dr. Huda Zoghbi, Distinguished Service Professor at Baylor and the director of Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital, and Dr. Shayla Rivera, professor of practice in the College of Engineering and director of ENGR[x] at Texas A&M University.



Data science training (left) and Dr. Brendan Lee with Dr. Karriem Watson (middle). *All of Us Evenings with Genetics* Program Staff (top right) and attendees form research team with assistance from Dr. Steven Scherer, professor at the Human Genome Sequencing Center (bottom right).

Attendees included 34 researchers from 26 institutions. The researchers formed six research teams and each team developed a research project. Post summit, the researchers entered the *All of Us* UBR Scholars Program. In this program, the scholars will continue working on the projects developed at the summit for an additional 12 months. Each month, the program provides virtual professional development sessions with required research team updates. The scholars will also receive ongoing support from data science trainers and Baylor faculty

mentors, as well as funding through the Seed Award Program.

Due to the success of the summit and the usefulness of the data science curriculum, the *All of Us Evenings with Genetics* Research Program received additional funding for NIH's *All of Us* Researcher Workbench Support. Through this additional funding, Baylor faculty will provide weekly training and support for *All of Us* Community Engagement Partners.

Undiagnosed Diseases Center Evaluates Rare Genetic Conditions

Baylor's Undiagnosed Diseases Center (UDC), was formed in 2022 to incorporate and extend the work of its Undiagnosed Diseases Network (UDN) clinical site, DNA sequencing core and model organisms screening center by providing a path to evaluate individuals who remain undiagnosed despite extensive testing. A multidisciplinary team of Baylor faculty provides clinical services, genetic testing and analysis to assess patients who have not received a diagnosis for their condition.



Jill Mokry, M.S., C.G.C.

had long diagnostic odysseys," said center director Dr. Brendan Lee, Robert and Janice McNair Endowed Chair in Molecular and Human Genetics at Baylor.

Baylor also will expand services to patients outside the UDN through its Consultagene platform, an online portal that provides educational resources and genetics services. Patients can apply directly or be referred by their physician. Physicians also can connect with Baylor faculty directly for a consultation on their

cases. Consultagene offers options for telehealth appointments, which may eliminate the need for some patients to travel to Houston for clinic visits and genetic testing. Alternatively, after review by the UDC, additional clinical workup may be recommended either at their local provider or via referral to adult and pediatric specialties at Baylor Medicine and Texas Children's Hospital, respectively.

"At Baylor, we have a multidisciplinary team that has experience working together to solve these difficult cases," said Jill Mokry, center coordinator and associate professor of molecular and human genetics at Baylor. "It's possible that a person is undiagnosed because the condition isn't yet discovered by medicine. We have the genetic expertise and access to research tools that might help us make that discovery."

The UDN is a research study funded by the National Institutes of Health Common Fund aimed at bringing together clinical and research experts to solve the most challenging medical mysteries using advanced technologies. Although NIH Common Fund support of the UDN as it existed is ending, clinical sites across the country, including Baylor's site, will continue to provide services to existing UDN patients. New patients with rare, undiagnosed conditions may still be referred to Baylor's center through the UDN central coordinating center or they can be referred directly to the center via the Baylor UDC website.

"The UDN sites at Baylor and Texas Children's Hospital have been enormously successful in making new diagnoses in patients who have

The Texome Project

The Texome Project was established by physicians at Baylor College of Medicine and Texas Children’s Hospital to ameliorate genomic health inequity that exists due to financial, historical and systemic factors.

The project, co-led by Dr. Michael Wangler, assistant professor of molecular and human genetics at Baylor and Dr. Hugo Bellen, distinguished service professor of molecular and human genetics at Baylor and chair in neurogenetics at the Duncan NRI, provides exome sequencing to children and adults from underserved backgrounds who have undiagnosed diseases. Study participants receive a full genetic evaluation and genetic testing free of charge. Additionally, the Texome team follows up with participants over two years to collect additional information about their medical presentation. Participants also complete numerous surveys that provide insight into the perceptions, obstacles, and experiences associated with genomic medicine in underserved communities. The Texome Project is funded by the National Human Genome Research Institute and receives philanthropic support through the Jan and Dan Duncan Neurological Research Institute and Texas Children’s Hospital.



Dr. Michael Wangler



Dr. Hugo Bellen



already been enrolled. Most participants come from larger Texas cities such as Houston and San Antonio, although participants have been recruited from rural areas as well. About 49% of enrolled participants identify as Hispanic/Latino, 28% report White/European descent, 10% identify as Black/African American and the remaining 13% are of Asian or Native American descent.

Exome sequencing through the Texome project has identified a definitive genetic diagnosis in 44% of participants, in some cases ending decades-long diagnostic odysseys. The Texome team utilizes novel technology to reanalyze data of unsolved cases, and model organisms research is conducted to assess the functional consequences of candidate variants.

The Texome project enhances representation of minority and underserved populations in genetics research and is making great strides in closing the gap that exists in clinical genetics care for minority and underserved communities.

“The Texome Project is a win-win for all people involved. Families who are historically underserved receive access to crucial genomic care, and researchers are able to gain a better understanding of the needs, beliefs and experiences of underrepresented minority

populations when it comes to genetics and genomics. I look forward to analyzing our survey data as we continue to recruit participants and believe that our findings will have real-world implications for the equitable provision of

Project GIVE

There is a significant disparity in access to genomic care for low income families in the Rio Grande Valley where over 90% of the population is Hispanic and an estimated one-third is uninsured. To meet this need, Drs. Brendan Lee and Seema Lalani, professor of molecular and human genetics at Baylor received funding through the National Center for Advancing Translational Sciences (NCATS) to use genome sequencing and Consultagene for genetic services.

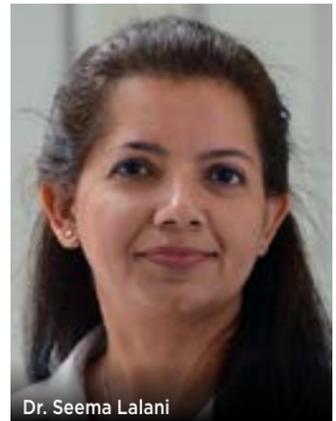
The study, called Project GIVE (Genetic Inclusion by Virtual Evaluation) aims to simplify patient pathways and reduce the time-to-diagnosis for clinical decision-making in this medically underserved pediatric population. Project GIVE utilizes Consultagene, a virtual online platform created by the Department of Molecular and Human Genetics at Baylor, to provide access to genetic evaluation, peer-to-peer consultation and genetic counseling. These services are

genomic care,” said Dr. Chaya Murali, assistant professor of molecular and human genetics at Baylor. Murali is a clinical geneticist and leads the survey arm of the Texome Project team.

packaged with multiple educational videos available in different languages, including Spanish.

Prioritizing equity and inclusion in healthcare, Baylor has partnered with pediatricians at the University of Texas Rio Grande Valley (UTRGV) to provide virtual clinical evaluation and genome sequencing for 100 hard-to-diagnose children with suspected genetic disorders over a period of two years. The frontline healthcare providers in the RGV refer children with various birth defects and suspected genetic diseases to Consultagene for evaluation. A multidisciplinary team that includes physicians and healthcare providers from both Baylor and UTRGV meet virtually every week to select patients most likely to benefit from testing. Once accepted, the patients are brought to the UTRGV Pediatric specialty clinic where a remote consultation is completed via a Consultagene kiosk placed at the facility. The kiosk helps to overcome the challenges participant patients face accessing digital technology. During their visit, samples are collected and sent to Baylor Genetics for analysis.

To date, the study has accepted 34 children from 30 families. Of these, 10 have received test results with a diagnostic yield of around 30%. Genetic counseling is provided to the families through Consultagene, with appropriate recommendations for management and follow up care. Subjects are also followed for 12 months after initial referral. Surveys are administered at three different points during the study to gauge patients’ and providers’ experiences. Patients who remain undiagnosed are then referred to



Dr. Seema Lalani



Consultagene kiosk at UTRGV

the Baylor's Undiagnosed Diseases Center for consideration for further research study.

Project GIVE also is designed to build genomic competency of frontline healthcare providers through use of facial recognition technology and education to expedite referral of pediatric patients with suspected rare diseases. This project provides a unique opportunity to transform the current clinical practice paradigm to integrate genetics evaluation in primary care

setting to reduce inequities in health outcomes for children with rare genetic disorders.

"Project GIVE gave my family and I not only hope but peace of mind. If it weren't for Project GIVE, I don't think we would be able to assist our son in getting the head start he needs to thrive and grow. I can't put into words how thankful we all are. The process was explained thoroughly, and it was simple. I would highly recommend Project GIVE to anyone in a similar situation," said a participant in the study.

Clinical Genome Resource receives global recognition

The Clinical Genome Resource (ClinGen) knowledge base is among the Global Core Biodata Resources (GCBRs) announced in 2022 by the Global Biodata Coalition (GBC), a forum for research funders to better coordinate and share approaches for the efficient management and growth of biodata resources worldwide. Baylor College of Medicine and Stanford University hold one of three National Institutes of Health grants that support the development of the ClinGen Resource.

The GBC recognizes these GCBRs as resources whose long-term funding and sustainability is critical to life science and biomedical research worldwide. The GCB notes that GCBRs represent the most crucial components or nodes within the global life science data infrastructure.

Baylor and Stanford have been participating in the NIH-funded ClinGen since its beginning in 2013. The goal is to build publicly available resources to support the growth of clinical genomics. ClinGen develops and implements standards and tools to support clinical classification, shares genomic and disease data between clinicians, researchers and patients, facilitates expert review of the clinical relevance of genes and variants, and disseminates resources to the broader community.

Dr. Sharon Plon, professor of pediatrics – hematology and oncology and molecular and human genetics, and Dr. Aleksandar Milosavljevic, Bioinformatics Research Laboratory director and Henry and Emma Meyer Chair in Molecular



Genetics, are principal investigators of the Baylor ClinGen project. The Baylor team has developed key elements of the ClinGen infrastructure, including Allele Registry, Evidence Repository, Criteria Specification Registry and Linked Data Hub.

Other Baylor team members involved in this project include Andrew R. Jackson, Kevin Riehle, Neethu Shah, Anton V. Kodochygov, Tierra R. Farris, Arturo Alejandro Zuniga, Keyang Yu, Matthew E. Roth, Deborah Ritter, Sheng-An Yang, Farid Ali, and William Craigen. Dr. Teri Klein is the principal investigator from Stanford University of the ClinGen project.



Dr. Sharon Plon



Dr. Aleksander Milosavljevic

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.

Circadian clock in heart failure

Disrupting circadian rhythms, which change naturally on a 24-hour cycle, has been implicated in heart disease, but it is unclear how it leads to the condition. A research team at Baylor College of Medicine and collaborating institutions investigated the function of the protein Rev-erb α/β , a key component of the circadian clock, on heart disease development in animal models and human patients.

The team reports in the journal *Circulation* that Rev-erb α/β in cardiomyocytes mediate a normal metabolic rhythm that enables the cells to prefer lipids as a source of energy during the animal's resting time, daytime for mice. Removing Rev-erb α/β disrupts this rhythm, reduces the cardiomyocytes' ability to use lipids in the resting time and leads to progressive dilated cardiomyopathy and lethal heart failure.

Dr. Lilei Zhang, assistant professor of molecular and human genetics and of molecular physiology and biophysics, and Dr. Zheng Sun, associate professor of medicine, section of endocrinology, diabetes and metabolism, and of molecular and cellular biology, are co-corresponding authors of the research.

Their team found that the metabolic defect that prevents the heart cells from using fatty acids as fuel causes the majority of the cardiac dysfunction seen in Rev-erb α/β knockout mice. Importantly, they also showed that correcting the metabolic defect can help improve the condition.



Dr. Lilei Zhang

The researchers explored the possibility of pharmacologically manipulating fatty acid and sugar metabolism to improve the condition. They found that while medications can help restore the altered metabolic pathways, it was important to give the drugs aligned with the internal circadian rhythm of the corresponding metabolic pathways. If the drugs were given out-of-sync with the pathway they were intended to restore, the treatment did not improve the cardiac condition. These findings highlight the importance of chronotherapy, the scheduling of medications according to the circadian rhythm.

Reduced inhibition of hippocampal neurons impairs long-term memory recall in Rett syndrome

A study by researchers in the laboratory of Dr. Huda Zoghbi, distinguished service professor at Baylor College of Medicine and director of the Jan and Dan Duncan Neurological Research Institute (Duncan NRI) at Texas Children's Hospital, has discovered that diminished memory recall in Rett syndrome mice can be restored by activating

specific inhibitory cells in the hippocampus. The findings are published in *Neuron*.

Rett syndrome is a neurodevelopmental disorder characterized by loss of acquired cognitive, motor, language and social skills after the first year of life as well as profound learning and memory impairments. Contextual memories that encode an event and the circumstances in

which the event was experienced are diminished in mouse models of Rett syndrome. Previous research has suggested that this results from disruptions in the finely tuned balance between excitatory and inhibitory synaptic inputs that constantly bombard hippocampal neurons.

Zoghbi's team hypothesized that disruptions in this balance may alter the size and composition of ensembles of hippocampal neurons needed to encode a contextual memory. They directly monitored these ensembles as mice recalled a fearful experience. They found that Rett mice have larger and more correlated ensembles of neurons than wild-type mice, suggesting that hippocampal pyramidal neurons are not receiving enough inhibition in Rett mice.

Next, the team recorded neuronal activity from cells in brain slices and found a significant reduction in connectivity between pyramidal cells and a subset of somatostatin-expressing (SOM) inhibitory neurons, the OLM cells. They found that these cells, which are normally recruited by hippocampal pyramidal neurons in healthy mice during memory recall, were poorly engaged in Rett mice.

This led the team to wonder if activating these inhibitory neurons during memory recall would help Rett mice remember better. To address this, they selectively enhanced the activity of somatostatin cells in the hippocampus using a chemical-genetic approach that allows for the

activation of a specific cell type. Incredibly, activating somatostatin-expressing cells in Rett mice restored contextual memory recall.

"This is the first study to demonstrate that upregulating the activity of SOM neurons can improve memory recall and retrieval capacity in Rett mice," said Zoghbi, Howard Hughes Medical Institute investigator. "It opens exciting areas of research to explore therapeutic possibilities that could improve contextual memory recall in individuals affected by Rett syndrome."

Lingjie He, postdoctoral associate in the Zoghbi lab, is first author of this research. Other authors are Matthew Caudill, Junzhan Jing, Wei Wang, Yaling Sun, Jianrong Tang and Xiaolong Jiang.

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.



Dr. Huda Zoghbi

Fruit fly study uncovers functional significance of gene mutations associated with autism

Research has shown that *de novo* DNA changes could be responsible for about 30% of autism spectrum disorder (ASD). However, which *de novo* variants play a role in causing ASD remains unknown.

In a multi-institutional study published in the journal *Cell Reports*, researchers at Baylor and Texas Children's applied sophisticated genetic strategies in laboratory fruit flies to determine the functional consequences of *de novo* variants identified in the Simons Simplex Collection (SSC), which includes approximately 2,600 families affected by autism spectrum disorder.

The team worked with the fruit fly lab model to determine the biological consequences of the ASD-associated variants. They selected 79 ASD variants in 74 genes identified in the SSC and studied the effect of each ASD-linked gene variant compared to the commonly found gene sequence (reference) as a control.

Altogether, the team generated more than 300 fly strains in which they conducted functional studies of human gene variants associated with ASD. Their screen elucidated 30 ASD-linked variants with functional differences compared to the reference gene, which was about 40% of the genes for which they were able to perform

a comparative functional assay. Their work also identified the gene *GLRA2* as the cause of a spectrum of neurodevelopmental phenotypes beyond ASD in 13 previously undiagnosed subjects.

Dr. Shinya Yamamoto, assistant professor of molecular and human genetics and of neuroscience, and Dr. Michael Wangler, assistant professor of molecular and human genetics, are co-corresponding authors of the study. Both also are investigators at the Jan and Dan Duncan Neurological Research Institute at Texas Children's. Dr. Paul Marcogliese, postdoctoral fellow in Dr. Hugo Bellen's lab,

Targeting TGF- β for treatment of osteogenesis imperfecta

A new study led by Baylor College of Medicine identifies an underlying mechanism of pathogenesis for osteogenesis imperfecta (OI) in human bone. The report, published in the *Journal of Clinical Investigation*, also shows the results of a Phase 1 clinical trial testing the safety and effectiveness of an antibody treatment targeting that pathway.

Osteogenesis imperfecta is the most common skeletal dysplasia and causes bone fragility in children and adults. There is no FDA-approved treatment for OI. Previous research conducted at Baylor has shown that a protein called transforming growth factor - beta (TGF- β) is upregulated in bones and connective tissues of mouse models of common forms of OI, suggesting a common signaling pathway in OI and a potential therapeutic target.

In this study conducted through the Brittle Bone Disorders Consortium, a part of the NIH-funded Rare Diseases Clinical Research Network, Baylor researchers examined human bone samples from OI patients at consortium sites at Baylor/Texas Children's Hospital and the University of Nebraska Medical Center. A multiomic approach analyzing RNA and protein expression revealed that TGF- β was upregulated when compared to non-OI bone.

Dr. Jonathan Andrews, postdoctoral fellow in Wangler's lab, and Samantha Deal and Michael Harnish, both graduate students in Yamamoto's lab at the time of research, are co-first authors of the study. Dr. Ronit Marom, assistant professor of molecular and human genetics, is lead clinician of the study.



Dr. Shinya Yamamoto



Dr. Brendan Lee

To translate these findings to the clinic, the Baylor team tested fresolimumab, a monoclonal antibody therapy that neutralizes TGF- β in a Phase 1 clinical trial conducted at BBDC sites at Baylor and Oregon Health & Science University. Eight adults with moderate to severe

OI received a single infusion of fresolimumab provided by Sanofi. Patients with moderate forms of OI showed a significant increase in bone density at 3 and 6 months.

Sanofi is leading a larger Phase 1b clinical trial to test safety, tolerability and impact on bone density (NCT05231668).

Dr. Brendan Lee, Robert and Janice McNair Endowed Chair in Molecular and Human Genetics, is corresponding author of the study. Dr. I-Wen Song, research associate in the Lee Lab, and Dr. Sandesh Nagamani, associate professor of molecular and human genetics, are co-first authors.

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.

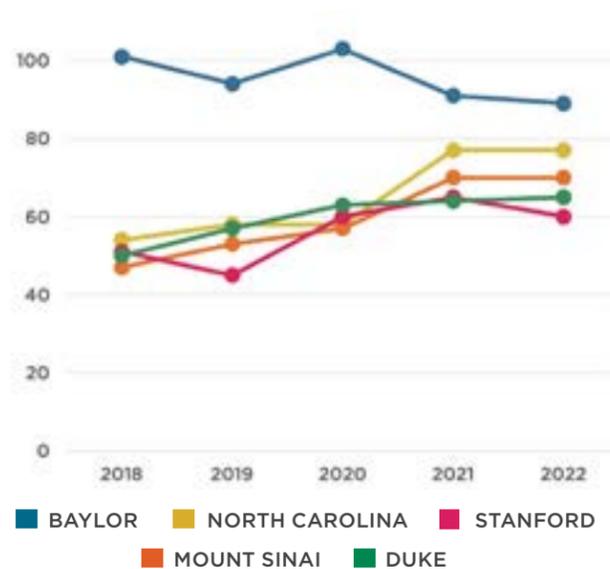
#1 ranked U.S. Genetics Department in NIH awarded grants and total funding for past 12 years

over **\$92 million** total NIH funding in 2022

Total NIH Funding to Leading Genetics Departments



Number of NIH Grants Awarded 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 Association
- Autism Speaks



Baylor receives NIH funding to study neuronal anatomy of the knee joint

Baylor College of Medicine has been named a site for the Restoring Joint Health and Function to Reduce Pain (RE-JOIN) Consortium, part of the National Institutes of Health's Helping to End Addiction Long-term® (HEAL) Initiative. Baylor researchers will be awarded up to \$12 million over five years to map and characterize the neurons that supply the tissues forming the knee joint and mediate the sensation of pain.

"We need a better understanding of neuronal inputs to the joint and how those inputs change with chronic diseases, like osteoarthritis, physical impact and aging," said Dr. Brendan Lee, principal investigator and Robert and Janice McNair Endowed Chair in Molecular and Human Genetics at Baylor.

The Baylor team will create a neuronal connectivity and molecular map of the neurons that innervate the knee joint in mouse models of osteoarthritis, which will help identify molecular signatures that can be targeted for therapy. The research will include mouse models of different ages and of both sexes and test joint effects after exercise and after gene therapy that delivers an



Dr. Brendan Lee



Dr. Benjamin Arenkiel

experimental osteoarthritis medication directly to the joint.

Dr. Benjamin Arenkiel, professor of molecular and human genetics and neuroscience and McNair Scholar, Dr. Russell Ray, associate professor of neuroscience, molecular physiology and biophysics and biochemistry and molecular biology and McNair Scholar, and Dr. Joshua Wythe, associate professor of integrative physiology and neurosurgery, are co-principal investigators. Dr. Rui Chen, professor of molecular and human genetics, is a co-investigator. Baylor also will lead the consortium-wide administrative core for all five sites of the consortium.

This research is funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases.

Research Administration

For the year 2022, a total of 324 grant proposals were submitted to Baylor's Office of Research by the Department of Molecular and Human Genetics, resulting in over \$80,277,956 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) Annual Meeting in

Washington D.C., and in the Region V annual meeting in Sugar Land, Texas by serving as volunteers on the program committee and presenting sessions.

New team members also passed certification exams this year. Francoise Caro and LaTonya Beavers both passed the Certified Research Administrators (CRA) exam. The Department now has a total of 8 CRAs. In addition, Betty Fernandini passed the Certified Pre-Award Administrators (CPRA) exam.

Clinical Research

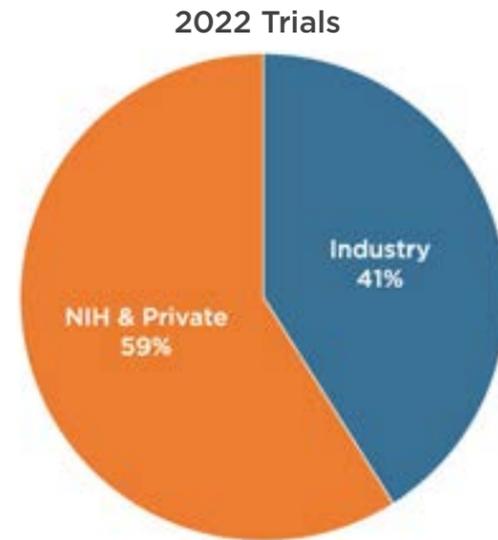
The Clinical Research Division of the Department of Molecular and Human Genetics at Baylor College of Medicine facilitates the planning, implementation and conduct of many clinical studies in rare disorders.

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.

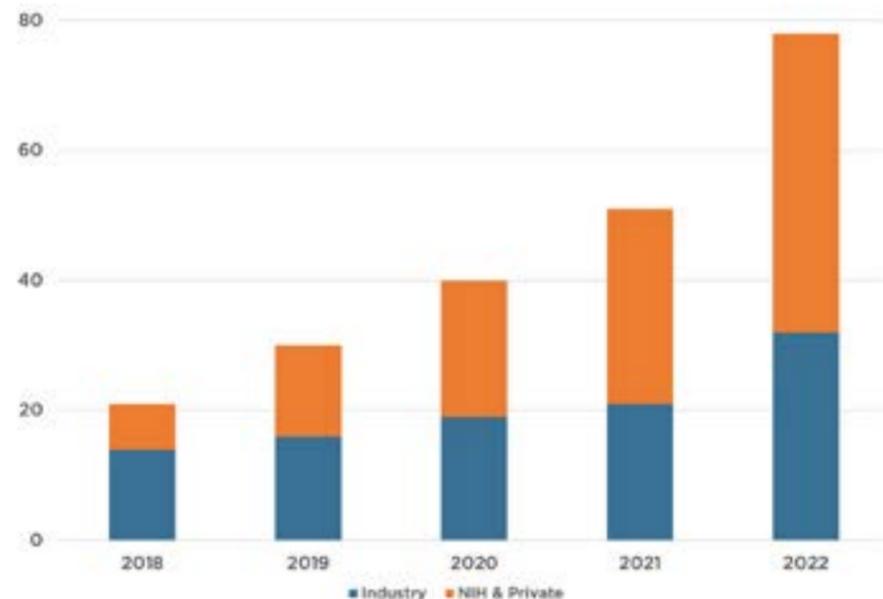
In 2022, the division, led by Dr. Sandesh Nagamani, professor of molecular and human genetics at Baylor, had more than 75 ongoing studies. These studies consisted of investigator-initiated studies where department faculty are sponsors, industry-sponsored studies and studies that are conducted within 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

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

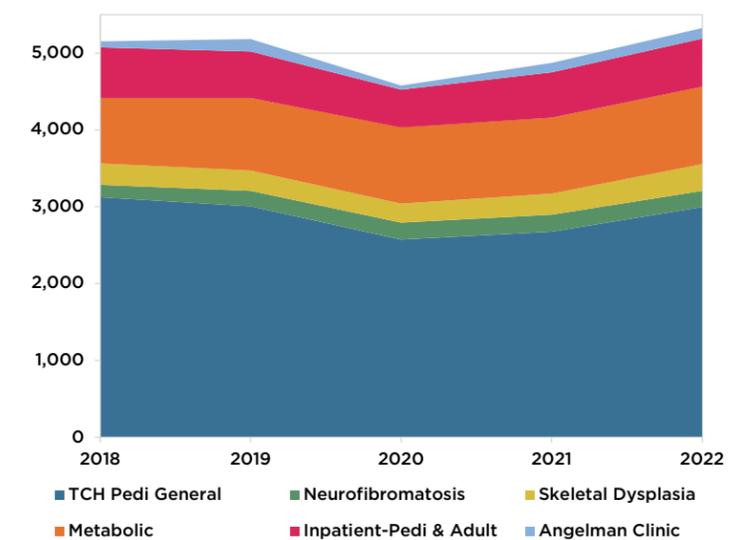
The pediatric genetics service provides inpatient and outpatient care to patients with complex conditions and those who are critically ill. Clinics are located at Texas Children's Hospital and several other hospitals within and outside of the Texas Medical Center (TCH West Campus and The Woodlands Texas 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 clinic, neurofibromatosis clinic, skeletal dysplasia clinic and the cancer genetics clinic. There are also multidisciplinary team clinics like the Angelman Syndrome Clinic, the Center for Genetic Disorders of Obesity, Mitochondrial Medicine Clinic and the Gender Medicine Program. Clinical genetics physicians and genetic counselors from Baylor also staff joint clinics with other departments, such as otolaryngology (otogenetics) and neurology (neurogenetics/tuberous sclerosis).

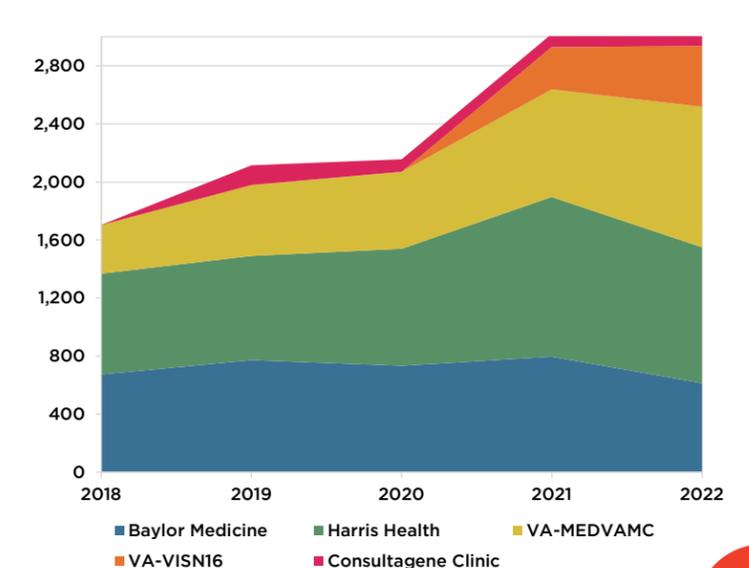
Adult Genetics

The Department's adult genetics service is one of the largest in the country, providing inpatient and outpatient care and genetic counseling 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

Clinical Genetics Patient Volume (Pediatric)



Clinical Genetics Patient Volume (Adult)



16 (VISN16). The 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.

The 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.

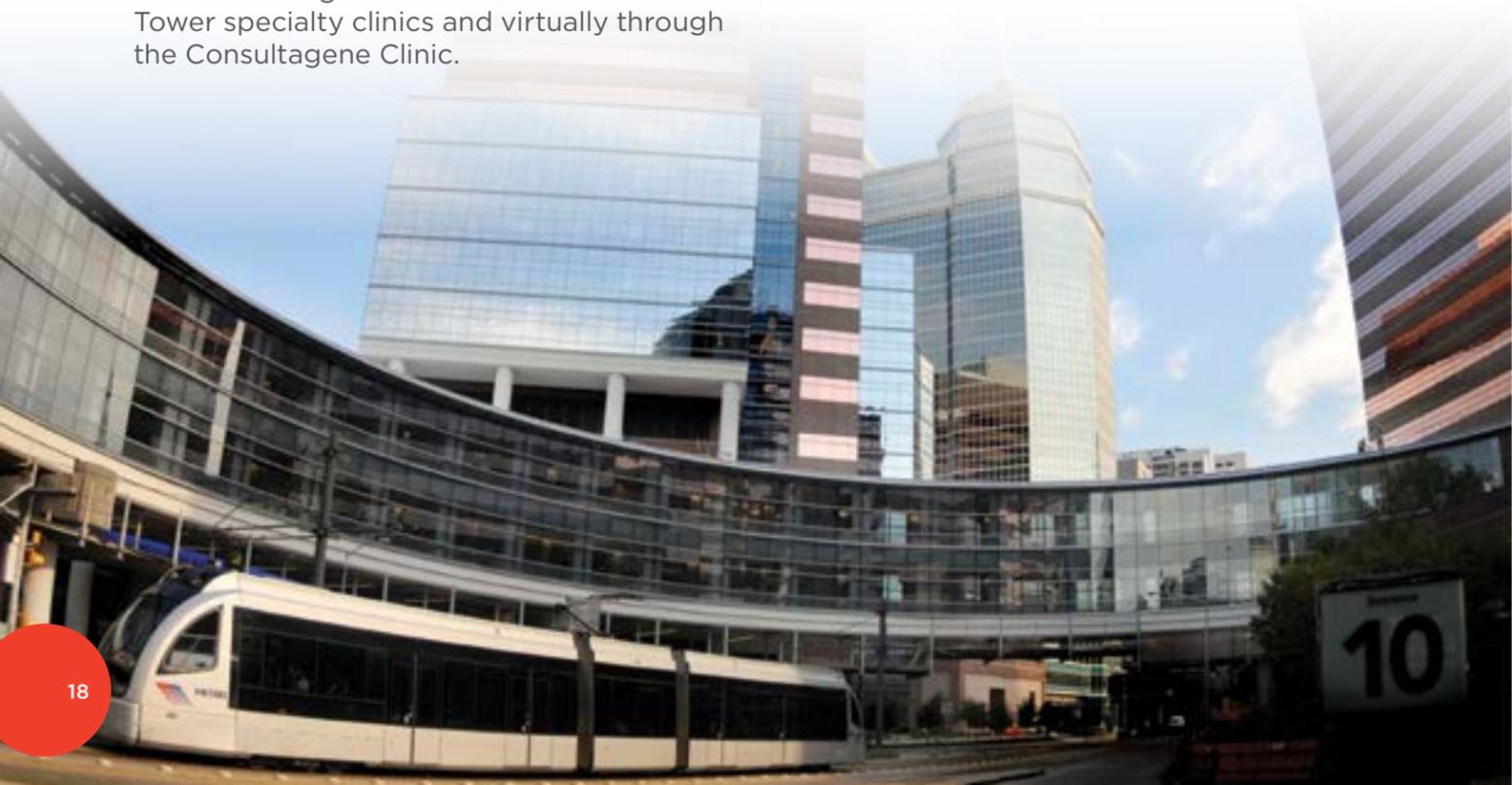
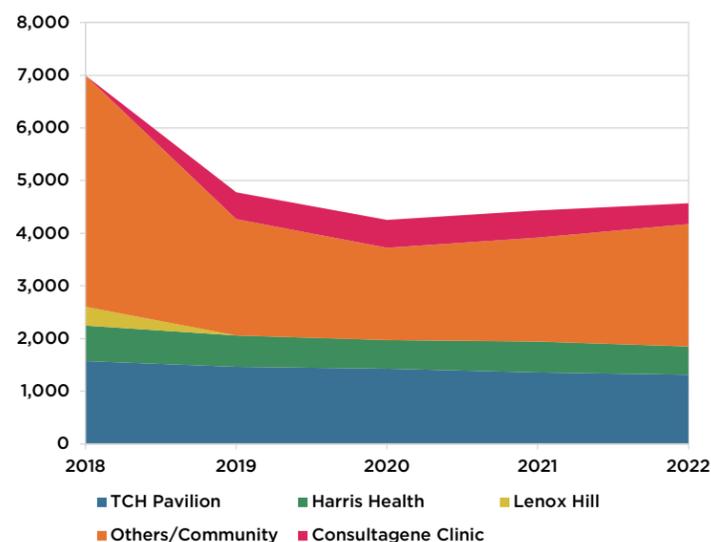
In addition to our general genetics clinic, we have specialty clinics such as the Metabolic and Genetic Disorders of the Bone Clinic, Cancer Genetics Clinic, Neurogenetics Clinic, Cardiovascular Genetics Clinic and Mitochondrial Medicine Clinic.

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)

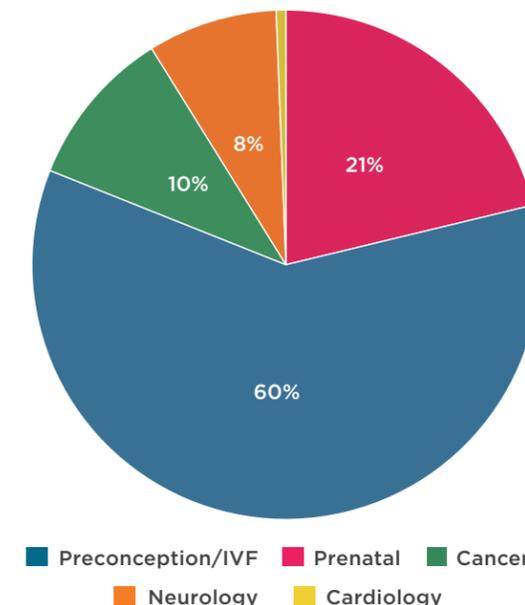


The Consultagene Clinic

The Consultagene Clinic is now in its fourth year of operation and remains a fully virtual genetic counseling clinic. In 2022, a total of 485 patients were seen for a total of 2,349 patients receiving genetic counseling through the Consultagene Clinic since its launch in 2019.

In 2022, there was a shift in patient referral indications. The majority of patients (60%) we saw were for an IVF/preconception indication. There also was a growing number of neurology referrals due to the PDGene study and a decline in prenatal referrals. The clinic also saw an increased number of requests for genetic counseling from patients outside of the state of Texas. To address the increase in interest, expand its reach and make genetic counseling more accessible, the clinic now has licensed counselors in Louisiana, California, Arkansas, Washington, Alabama and Illinois, with licensure pending in Oklahoma and New Mexico. The clinic has started outreach to IVF practices in these states and states without genetic counseling licensure due to the clinic’s expertise in reproductive genetic counseling.

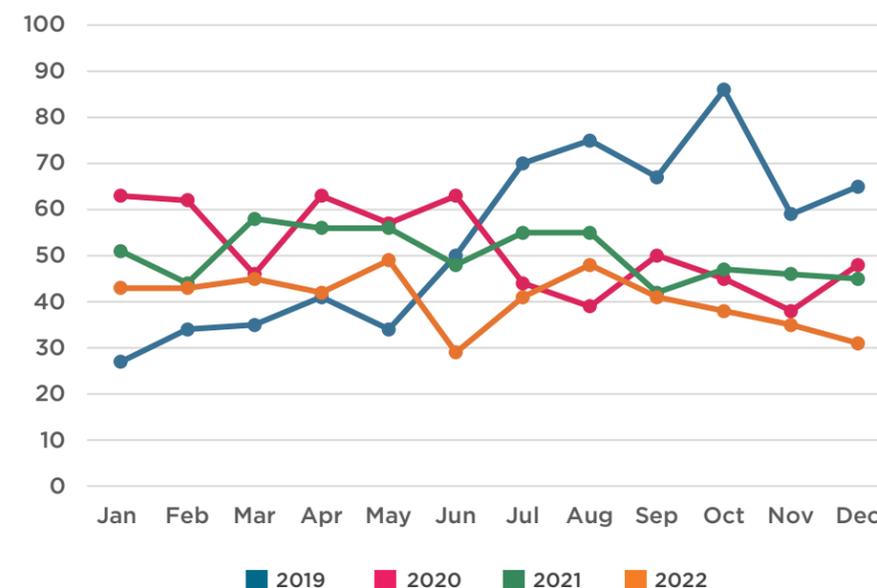
2022 Consultations By Indication



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. For 2022, the platform saw some extensive upgrades: the peer-to-peer experience was redesigned and self-referral functionality was added.

Patients also have been surveyed to gauge their Consultagene Clinic experience. Of the 460 patients who participated in the survey, 68% used the resources provided in the patient portal, 99% said the genetic counseling met or exceeded their expectations, 92% agreed or strongly agreed that virtual genetic counseling was equivalent to an in-person appointment and 97% would recommend virtual genetic counseling.

Patient Consultations



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 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 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.

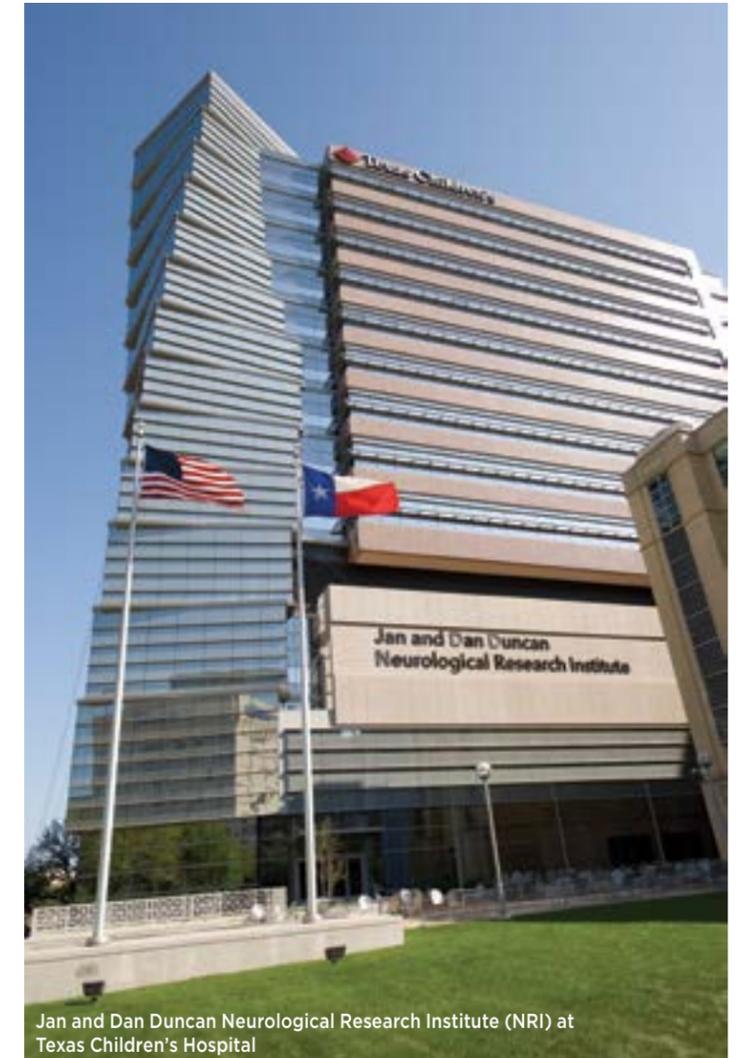
In addition to studying genetic datasets, the Baylor HGSC places great emphasis on integrating other omic data into genetic analyses.

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

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



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

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, a Distinguished Service Professor 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.”

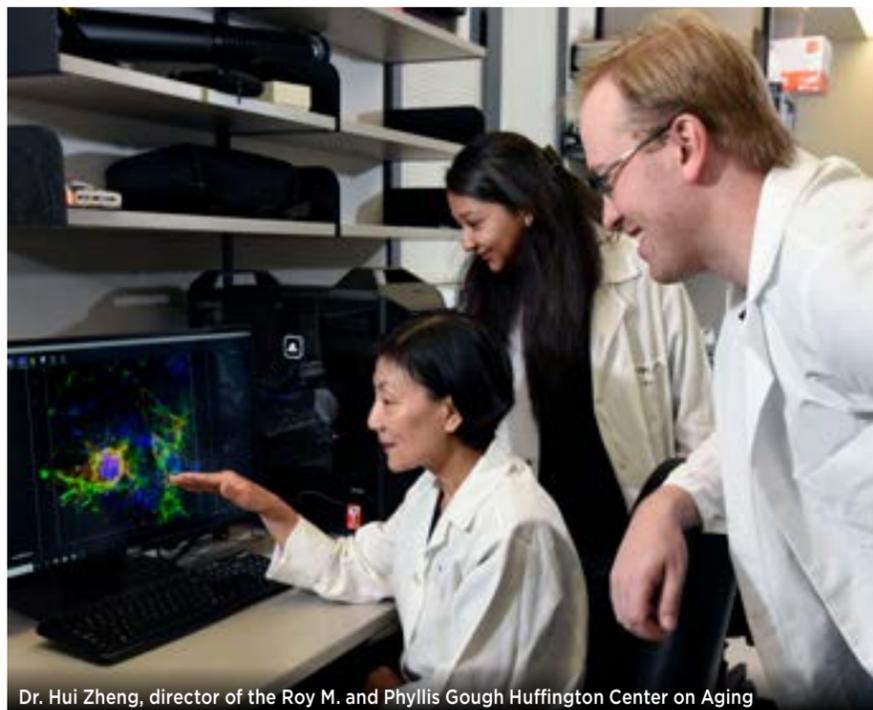
These open labs facilitate the free exchange of ideas, information and resources.

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.

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.



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

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, 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 of crucial importance 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 by 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.

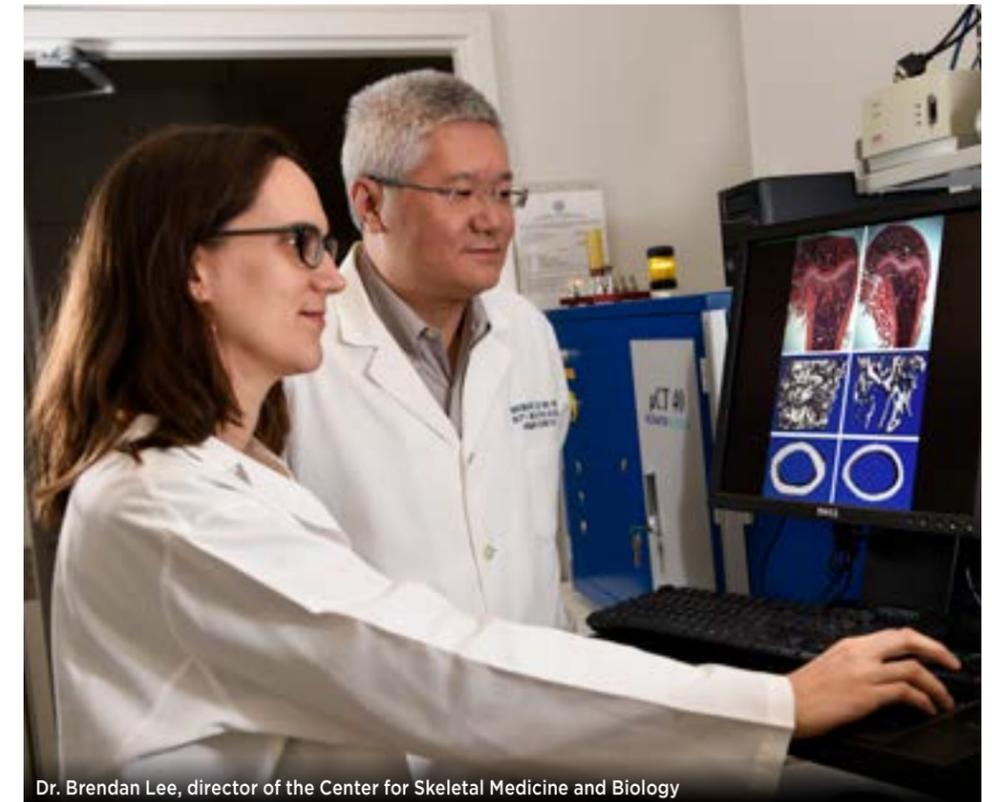
Center for Skeletal Medicine and Biology

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.

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



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

Cullen Foundation Professor of Molecular and Human 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 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 United States 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 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 unique 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.



Dr. Joshua Shulman, co-director of the Duncan NRI and director of the Center for Alzheimer’s and Neurodegenerative Diseases

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

Award	Student Name(s)	Organization
BP America Biomedical Scholarship	Emily Busse	BP America Endowment
2nd place platform speaker, Baylor College of Medicine 2022 Graduate School of Biomedical Sciences Symposium	Catherine Bradley	Baylor College of Medicine Graduate School of Biomedical Sciences
2nd place poster presentation, Baylor College of Medicine 2022 Graduate School of Biomedical Sciences Symposium	Harini Tirumala	Baylor College of Medicine Graduate School of Biomedical Sciences
Outstanding Teaching Assistant for Genetics & Genomics	Shelley Gibson	Baylor College of Medicine Graduate School of Biomedical Sciences
John J. Trentin Scholarship	Brandon Garcia; Alexandra Garza; Nikhita Gogate; Gwendolynn Hummel; Suhasini Lulla; Matthew McAlister; Apoorva Thatavarty; Rebekah Townsley	Baylor College of Medicine Graduate School of Biomedical Sciences
Post Award for Research Relevant to Contraceptive Research and Development	Katarzyna Kent	Gates Foundation
Ruth L. Kirschstein NRSA for Individual Predoctoral Fellows (F31) for “Investigating the role of CRAT as a driver of triple negative breast cancer chemoresistance”	Katherine Pendleton	National Institutes of Health, National Cancer Institute
Ruth L. Kirschstein NRSA for Individual Predoctoral Fellows (F31) for “Investigating the Role of the Cytoskeleton”	Morgan Stephens	National Institutes of Health, National Institute of Neurological Disorders and Stroke

2022 Dissertations

Student Name	Title	Preceptor/Advisor
Amrita A. Iyer	Transcription factors ATOH1, GF11 and POU4F3 have age-dependent reprogramming potentials in the maturing mouse cochlea	Andrew K. Groves, Ph.D.
Chaofan Zhang	Novel pathogenic variants, quantitative phenotypic analyses, and functional assessment of Robinow syndrome	James R. Lupski, M.D. Ph.D.
Stephanie L. Coffin	The role of the transcription factor Capicua in spinocerebellar ataxia type 1 and female specific weight gain	Huda Y. Zoghbi, M.D.
Rocco D. Lucero	Contributions to Endocrine and Paracrine Extracellular RNA Communication	Aleksandar Milosavljevic, Ph.D.
Celina Y. Jones	C-circles form in telomerase positive human cells with abnormally long telomeres	Alison A. Bertuch, M.D. Ph.D.
Saumya D. Sisoudiya	Alteration of the USP9X deubiquitinase by germline mutation, somatic mutation and misexpression in childhood B-cell acute lymphoblastic leukemia	Sharon E. Plon, M.D. Ph.D.
Emily LaPlante	Deconvoluting heterotypic and cell-intrinsic interactions within the tumor microenvironment and a refined map of extracellular RNA communication in humans	Aleksandar Milosavljevic, Ph.D.
Haowei Du	Family-based Genomics and Improved Genomic Data Visualization Allow Further Characterization of Copy Number Variation in Human Disease	James R. Lupski, M.D., Ph.D.
Catherine (Cathy) Bradley	RNA polymerase inaccuracy underlies SARS-CoV-2 variants and vaccine heterogeneity	Christophe Herman, Ph.D.
Varuna Chander	Addressing Challenges and Complex Etiologies in Mendelian Disease Genetics Using Computational and Functional Genomic Approaches	Benjamin R. Arenkiel, Ph.D.
Jaime Reyes	Integrating Multiomics Approaches to Investigate DNMT3A- and Aging-Dependent Transcriptional Control of Stem Cell Function	Margaret A. Goodell, Ph.D.
Jessica Swanson	From Appetite to Aversion: The Role of Basal Forebrain-to-Lateral Habenula Projections in Modulating Opposing Behaviors	Benjamin R. Arenkiel, Ph.D.

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. 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 inextricably 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 College of Medicine's genetics diagnostic laboratory, Baylor Genetics, for 24 months.

The Department also offers a one-year Medical Biochemical Genetics Fellowship training 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

2022 MHG Trainee Awards



Yishay Ben Moshe, M.D.
Clinical Resident Award



Maria Vladoiu, Ph.D.
Laboratory Fellow Award

2022 Graduating Class of Residents and Fellows



Yoel Gofin, M.D.
Medical Genetics Residency



Matthew Snyder, M.D.
Pediatrics/Medical Genetics Residency



Runjun Kumar, M.D., Ph.D.
Pediatrics/Medical Genetics Residency



Eran Tallis, M.D.
Medical Biochemical Genetics Fellowship



Laura Mackay, M.D., M.P.H.
Medical Biochemical Genetics Fellowship



Scott Ward, M.D.
Pediatrics/Medical Genetics Residency



John "JD" Odom, M.D.
Medical Biochemical Genetics Fellowship



Roni Zemet Lazar, M.D.
Medical Genetics Residency

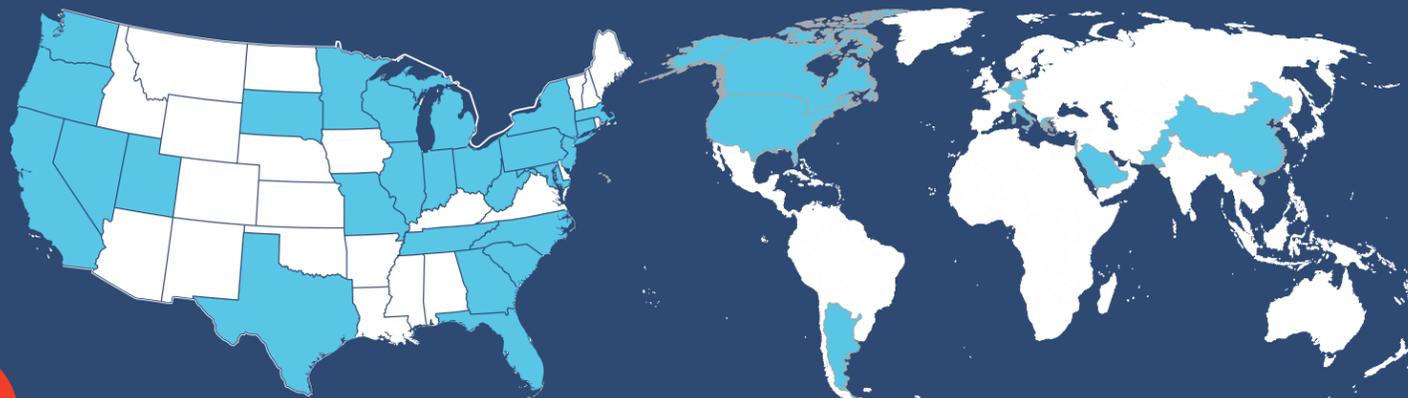


Katharina Schulze, Ph.D.
Laboratory Genetics and Genomics Fellowship



Xiaonan Zhao, Ph.D.
Laboratory Genetics and Genomics Fellowship

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 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 of 2021. The program currently has a total of 18 trainees and plans to welcome 9 new students in July of 2023.

"The program has been even more rewarding than I expected. With so many clinical sites in the TMC, 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 with current and graduating students

Genetic Counseling Program Class of 2022

Alexa Badalamenti
Malia Bauder
Raymond Belanger Deloge
Shannon Bonner
Brianna Cadalzo

Dina El Achi
Chandra Perez-Gill
Julie Stefka
Blake Vuocolo

Distinguished Lectures

Jeanette Oshman Efron Lecture in Molecular Genetics

Jeanette Oshman Efron, who passed away in 2009 at the age of 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 to Baylor to present seminars on important developments in genetics. This year, Dr. Ardem Patapoutian was the featured speaker. The title of his talk was "How Do You Feel? The Molecules That Sense Touch."

After completing his doctoral work on transcription at Cal Tech, Patapoutian continued his training as a postdoc at UCSF where he began to explore how our cells register the experiences of cold and noxious stimuli. As an assistant professor at the Scripps Research Institute, Patapoutian and his team investigated the mysteries of touch. They identified cells that are responsive to various sorts of mechanical pressure and found the genes whose expression increased after mechanical stimulation. Knocking down these genes one by one, they pinpointed a channel they named Piezo (from a Greek word for "pressure") that mediates mechanical activation. Patapoutian and his team laid the groundwork for a new field of study by proving that Piezo

1 and 2 enable mechanotransduction in a wide variety of cells, from Merkel cells in the skin that sense texture to proprioceptors that sense the positions of our bodily parts in space, even when our eyes are closed. Piezo channels are active in endothelial cells, red blood cells, airway stretch cells, interoceptors (which sense pressure within organs such as the bladder and intestine) and the neuronal sensors of blood pressure. Patapoutian also has discovered completely unexpected functions for Piezo ion channels, such as their ability to help red blood cells adjust their volume to ward off infection with the parasite that causes malaria.



Dr. Brendan Lee with Dr. Ardem Patapoutian

For this ground-breaking work, Ardem received the Kavli Prize of Neuroscience in 2020 and the Nobel Prize in Physiology or Medicine in 2021, both with David Julius, who discovered temperature-sensing receptors. Patapoutian is a professor of neuroscience and a Howard Hughes Medical Institute Investigator at Scripps. He is also a member of the American Academy of Arts and Sciences and the National Academy of Sciences.

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 eligible 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



Dr. Huda Zoghbi, Dr. Hugo Bellen, Dr. Arthur L. Beaudet and Dr. Brendan Lee at the 2022 Arthur L. Beaudet Lecture

speak or host an annual lecture. This year the recognition went to Dr. Hugo Bellen. The topic of his lecture was "Fly neurobiology: accomplishments and highlights of talented mentees."

Fernbach Lecture for Humanism in Genetics

In July 2022, after almost 40 years of service, Susan Fernbach, former co-director of the Office of Community Outreach and Diversity retired full time. Susan founded the Evenings with Genetics Seminar Series and served as a role model to many in the department. To honor her service and her community outreach efforts within the department and for the genetics community at large, an annual lecture was established.

The first annual Fernbach Lecture for Humanism in Genetics took place in October 2022. The guest speaker was Taylor Harris, author of "This Boy We Made."

"The first annual Fernbach lecture was well-received, and I look forward to continuing this annual tradition of honoring humanism in the work that we do as geneticists," said Dr. Chaya Murali, assistant professor of molecular and human genetics at Baylor.



Dr. Chaya Murali, Susan Fernbach, and Taylor Harris

Community Engagement and Diversity

The Department of Molecular and Human Genetics Office of Community Engagement and Diversity is co-directed by Laura Rosales, Ed.D., M.B.A., administrator for the Department, and Dr. Debra Murray, associate professor of molecular and human genetics. Under their leadership, additional diversity inclusion activities were introduced. The MHG Diversity and Inclusion Committee was instrumental in identifying speakers for the Tuesday seminars (Dr. Charles Rotimi, National Human Genome Research Institute, Dr. Fuki Hisama, University of Washington, and Dr. Folami Ideraabdullah, University of North Carolina School of Medicine), and organizing departmental volunteer outings at the Houston Food Bank, Project C.U.R.E., and Habitat for Humanity Restore.

Evenings with Genetics is a free virtual seminar series hosted by the Department and Texas Children’s Hospital and open to the community-at-large. Each seminar in the series features a

genetics faculty speaker paired with faculty from another specialty area plus a parent speaker. This year the webinar series had over 250 attendees and featured topics such as genetics and autism and genetic associated cardiac issues in adults and children.

For its 16th anniversary in February 2022, 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 first speaker, Vence L. Bonham, Jr., J.D., acting deputy director at the National Human Genome Research Institute, discussed precision and genomic medicine and health equity in genomics, whether new knowledge and new technology will benefit everyone. His group looked at how the American Journal of Human Genetics described populations over a 70-year period and found that the words ‘ancestry’ and



Front of the Roy and Lillie Cullen Building lit up for NORD Rare Disease Day



Dr. Vence L. Bonham Jr.



Dr. Fatimah Jackson

‘ethnicity’ are increasing in use in genetic studies, and ‘race’ is decreasing. These constructs are not discreet biological groups and change over time based on social context about how people think about them. The second guest speaker, Dr. Fatimah Jackson, professor and former director of the Cobb Institute at Howard University, stated that as we understand more about the genome and multiple factors influencing gene expression patterns and phenotype, we still retain certain concepts, such as race, even in the face of significant conflicts to those concepts. She presented results from a study that demonstrated an example of the persistence of genomic bias, showing that 64.2% of an African American woman’s genome is unassigned. She gave data on the complexity of the indigenous African origins, the heterogeneity of Africa, the substructure of the different groups brought to America and the complexity of African Americans. Jackson presented a case study using *APOL1*-mediated end stage renal disease to demonstrate how connecting the ancestral foundations increases our ability to detect patterns that could lead to early interventions that are initiated in infancy, rather than waiting for the disease to express itself. Lastly, Dr. Cherilyn Shadding, associate dean of the graduate school of biomedical sciences at UTHealth Houston, spoke about her experience being a parent and advocate for her 8-year-old son diagnosed with mild to moderate autism.

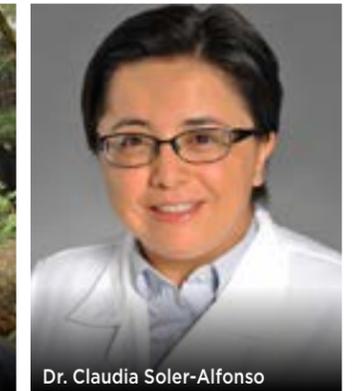
The inaugural webinar of virtual series “Celebrando Hispanic Heritage: What is in our genes?” was held in October of 2022. The series looks at the genetic history of Latin America, exploring the need for genetic testing and to understand diseases that impact the Latino/ community. The first speaker, Dr. Janitza Montalvo, assistant professor of psychiatry at Yale School of Medicine, introduced the history of Latin America. She discussed geography, language and population history to illustrate a picture of the Latin culture giving way to genetic admixture. Next, Dr. Paola Giusti-Rodriguez, assistant professor of psychiatry at the University of Florida, shared what the scientific community knows about the Latino population’s lack of data compared to other communities and made the case why more information and data are needed to identify and diagnose disease, improve healthcare and create targeted therapies and cures. Lastly, Dr. Claudia Soler-Alfonso, assistant professor in the Department, presented information about TANGO 2 and its effects on children. She spoke



Dr. Paola Giusti-Rodriguez



Dr. Janitza Montalvo



Dr. Claudia Soler-Alfonso

about the real-world example of identifying the genes responsible and how they impacted the population in Mexico. She shared data on how Latin America is represented in scientific research and the need for more testing to see what other diseases and disorders impact the community.

The From Stress to Strength program for parents of individuals with intellectual and developmental disabilities and autism returned to in-person attendance in October 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.

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. A total of 368 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.

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 Whitecoat and Genes: The Life of a Medical Geneticist," hosted 63 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 85 attendees. During the summer, a first-year medical student from Meharry Medical College interned with the Clinical Research Education Training Program. In November, the office hosted



Brandy Thibodeaux, Laura Rosales, and Gladys Pryor at the 36th Annual Hispanic Association of Colleges and Universities Conference in San Diego, California

the "Understanding Genetic Variation: Answers from African Ancestry" session at the Annual Biomedical Research Conference for Minoritized Students in Anaheim, California. The session, with speakers Dr. Neil Hanchard, senior investigator at the National Institutes of Health's Center for Precision Health Research, and Dr. Melissa Davis, an associate professor of surgery at Weill Cornell Medicine, was held to a standing-room-only crowd.

The Let's Learn About One Another series continued this summer with a focus on the Hispanic/Latin/a/o American experience. This session featured Dr. Maria Elena Zavala, professor of biology at California State University-Northridge, along with faculty members of our department.



"Understanding Genetic Variation: Answers from African Ancestry" Session at the 2023 ABRCMS Conference in Anaheim, California

Faculty Awards and Recognitions

Dr. David Nelson receives ASHG leadership award

The American Society of Human Genetics (ASHG) named Dr. David L. Nelson, professor of molecular and human genetics and holder of the Cullen Foundation Professorship in Molecular Genetics at Baylor, as the 2022 recipient of the Victor A. McKusick Leadership Award.

The award, which includes a \$10,000 prize, is named in honor of the late Dr. Victor A. McKusick and is bestowed upon an individual who has exhibited exemplary leadership and vision in advancing the ASHG mission through the promotion and successful assimilation of genetics and genomics knowledge into the broader scientific community.

"It's a great honor to receive ASHG's leadership award named for Victor McKusick. Dr. McKusick was a giant in our field of human genetics; he coined the term genomics. I am humbled to be associated with him," said Nelson, who also is director of the graduate programs in cancer and cell biology and integrative molecular and biomedical sciences at Baylor and co-director of the BCM Michigan Emory Fragile X Research Center and the Baylor Intellectual and Developmental Disabilities Research Center.

Nelson is a scientific leader and co-discovered the mutation that causes Fragile X syndrome as an expansion of a trinucleotide repeat in the *FMR1* gene by applying polymerase chain reaction (PCR), a technique that allows rapid gene mapping and isolation of specific chromosomal regions. His contributions led to the description of mutations in genes causing Lowe syndrome, Incontinentia Pigmenti and FRAXE syndrome. Additionally, he was an early contributor to methods used to map and sequence the human genome, beginning as a graduate student using selectable genes to enhance somatic cell genetic mapping.



2022 ASHG President, Dr. Charles Rotimi presenting the Victor A. McKusick Award to Dr. David Nelson

Dr. Christophe Herman elected 2021 AAAS Fellow

Dr. Christophe Herman, professor of molecular and human genetics and molecular virology and microbiology, was among two Baylor faculty members elected to the 2021 class of American Association for the Advancement of Science (AAAS) Fellows.

Herman was awarded for distinguished contributions in the field of bacterial genetics, physiology and biochemistry, particularly for showing that transient errors in transcription can cause permanent and heritable phenotypic change in a clonal cell population. Herman received his Ph.D. from the Université Libre de Bruxelles. He was a postdoctoral fellow at the Massachusetts Institute of Technology and a Human Frontier Fellow at the University of

California San Francisco, prior to moving to Baylor in 2004. His early work on transcription errors was supported by an Human Frontier Science Program award. More recently, his lab made the groundbreaking discovery that transcription fidelity comes at the expense of DNA repair. He has received the Michael E. DeBakey Excellence in Research Award from Baylor and a NIH Director's Pioneer Award. He also is a member of the Dan L Duncan Comprehensive Cancer Center at Baylor.



Dr. Christophe Herman

"It is my greatest privilege and honor to receive the Michael S. Watson Genetic and Genomic Medicine Innovation Award from the ACMG Foundation," Liu said. "The last 10 years have been a period of dramatic innovation in our field of human and medical genetics. I feel so fortunate to have received my training and started my career during this time. I am excited to continue this journey to translate cutting-edge technologies to clinical implementation and to improve the utilization of diagnostic big data."

Liu is the director of the ACGME-accredited Laboratory Genetics and Genomics Fellowship Training Program at Baylor and an associate clinical director at the Baylor Genetics diagnostic laboratory. His scientific contributions include using clinical diagnostic big data to generate knowledge that advances genomic science, as well as developing novel approaches to improve the implementation of genomic medicine.

Dr. Huda Zoghbi named the 2022 Kavli Prize Laureate in neuroscience

Dr. Huda Zoghbi, a Distinguished Service Professor at Baylor, director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's and Howard Hughes Medical Institute investigator, was awarded the prestigious 2022 Kavli Prize in the field of neuroscience. She was recognized for two discoveries - first, of the gene responsible for spinocerebellar ataxia 1 (SCA1), a progressive and often deadly disease in which neurons in the cerebellum and brain stem degenerate, causing loss of balance and coordination as well as swallowing difficulties. Second, for her discovery of the *MECP2* gene responsible for Rett syndrome, a developmental disorder that strikes children, mostly girls, causing regression and disability.

Zoghbi is one of 11 scientists from across the globe being named a Kavli Prize Laureate. The Kavli Prize is a partnership among the Norwegian Academy of Science and Letters, the Norwegian Ministry of Education and Research and the Kavli Foundation to recognize scientists in astrophysics, nanoscience and neuroscience for

Dr. Pengfei Liu receives 2022 Dr. Michael S. Watson Genetic and Genomic Medicine Innovation Award

Dr. Pengfei Liu, assistant professor of molecular and human genetics, is the recipient of the ACMG Foundation for Genetic and Genomic Medicine's 2022 Dr. Michael S. Watson Genetic and Genomic Medicine Innovation Award. The "Watson Award" is named for the American College of Medical Genetics and Genomics, first and longstanding executive director, Dr. Michael Watson. It recognizes those who have demonstrated innovation in their work and developed or implemented a new concept, method or idea that has had significant impact on genetic and genomic medicine.



Dr. Pengfei Liu

breakthroughs that transform our understanding of the big, the small and the complex.

Her longtime collaborator and colleague Dr. Harry T. Orr, professor in the Department of Laboratory Medicine and Pathology at the University of Minnesota, also received the same honor. He and Zoghbi independently discovered the gene known as *ATAXIN1*, which is responsible for SCA1. Working together, Orr and Zoghbi discovered that a repeat expansion causes SCA1 and discovered that the mutation caused proteins to misfold and accumulate, eventually leading to neuronal dysfunction and death. The Zoghbi and Orr teams have elucidated the disease mechanism and identified paths that can be pursued for therapeutic interventions.

Dr. Brendan Lee receives the ASBMR William F. Neuman Award

In 2022, Dr. Brendan Lee, was recognized by the American Society for Bone and Mineral Research with the William F. Neuman Award for his contributions to the field of bone science.

Dr. Lee's first two major contributions included identifying the first genetic cause of human chondrodysplasia - type II collagen mutations in spondyloepiphyseal dysplasia and cloning and linking the Fibrillin gene to Marfan Syndrome. Many of Dr. Lee's scientific discoveries have been complemented and extended by scientists and have formed the foundation of many outstanding discoveries in skeletal development, cell differentiation, and cell fate and function.



2022 Kavli Prize in Neuroscience Winners: Dr. Christopher Walsh, Dr. Jean-Louis Mandel, Dr. Harry Orr and Dr. Huda Zoghbi

In addition to Dr. Lee's stellar research efforts, he has been an inspiring leader in genetics and rare bone disorders. He has also been responsible for creating an environment that has paved and encouraged the careers of many clinicians and researchers in the field of skeletal medicine. Dr. Lee's work is truly translational and has led to new therapies that have changed clinical practice and the lives of millions of his patients.

"I want to thank the ASBMR for this great honor. I am humbled to have been considered in the same vein as previous awardees. However, I would not have been able to achieve such without the creativity, hard work, and collaboration of the over 100 outstanding trainees whom I have had the privilege and honor to mentor. I also have been the beneficiary of great fortune, having grown up in human genetics where studying rare phenotypes has evolved into the most powerful approach to discovering disease mechanisms and treatments, and having the privilege to do so in the best genetics department in the U.S.," Lee said.



Dr. Brendan Lee

More Awards and Recognitions for MHG Faculty



Dr. Carlos Bacino received the Rolanette and Berndon Lawrence Family Achievement Award in Genetics.



Dr. Richard Lewis received the Rolanette and Berndon Lawrence Family Achievement Award in Genetics.



Dr. Lindsay Burrage was recognized by Baylor College of Medicine with a Woman of Excellence Award.



Dr. Lorraine Potocki received the Baylor College of Medicine Master Clinician Lifetime Award.



Dr. Hsiao Tuan Chao was recognized on Spectrum News' "40 under 40" list of global autism researchers and inducted into the Society for Pediatric Research.



Dr. Susan Rosenberg was elected to the American Association for the Advancement of Science (AAAS) Board of Directors (2022-2026).



Dr. Shweta Dhar was named National Program Executive Director for Genomics for the U.S. Department of Veterans Affairs.



Dr. Shinya Yamamoto received the Marc Dresden Excellence in Graduate Education Award from the Graduate School of Biomedical Sciences, Baylor College of Medicine.



Dr. Hamed Jafar-Nejad was named Chair of the NIH Maximizing Investigators' Research Award D (MRAD) Study Section.



Dr. Lilei Zhang received the Ron Konopka Memorial Junior Faculty Award from the Texas Society for Circadian Biology and Medicine.

Department Faculty Awards

Best Metabolic Attending
Dr. William Craigen

Best Adult Genetics Teaching
Dr. Sandesh Nagamani

Best Pediatric Attending
Dr. Chaya Murali
Dr. Keren Machol

Baylor Genetics Laboratory Service Awards
Dr. Nichole Owen and Dr. Liesbeth Vossaert

Best Adult Attending
Dr. Reza Bekheirnia

Outstanding Graduate Teaching Awards
Dr. Benjamin Arenkiel (Faculty)
Shelley Gibson (Teaching Assistant)
"Human Genetics" directed by Dr. Daryl Scott (Best Course)

Best Clinical Educators
Dr. Sandesh Nagamani (Adult)
Dr. Ronit Marom (Metabolic)
Dr. Claudia Soler Alfonso (Metabolic)
Dr. Seema Lalani (Pediatric)
Dr. Daryl Scott (Pediatric)

Shan and Lee-Jun Wong Fellowship
Debdeep Dutta, Ph.D.

Best Mentor
Dr. Lindsay Burrage

New Faculty

Primary Research

In 2022, the Department of Molecular and Human Genetics welcomed a new tenure-track primary research faculty member, Dr. Steven Boeynaems.



Boeynaems received his Ph.D. from Katholieke Universiteit Leuven and trained as a postdoc in the Gitler lab at Stanford University before joining the Department and the Duncan NRI as an investigator.

The work of the Boeynaems lab focuses on understanding how cells and organisms regulate their proteome as a way to sense and respond to cellular stress, which has led the lab to study a variety of stress paradigms in physiology and disease with an emphasis on the role of tandem repeats, intrinsically disordered proteins and biomolecular condensates. Their goal is to create biosynthetic and mimetic tools for synthetic biology and to translate fundamental biological insights into novel therapeutic approaches for human diseases.

Diagnostic Laboratory



Katharina Schulze, Ph.D.
Assistant Professor



Xiaonan Zhao, Ph.D.
Assistant Professor

Genetic Counseling



Emily Magness M.S., C.G.C.
Instructor

PROMOTIONS

Professor, tenured

Chonghui Cheng
Shweta Dhar
Sandesh Nagamani
Daryl Scott

Associate Professor, tenured

Lindsay Burrage

Associate Professor, non-tenure

Jill Mokry
Debra Murray
Bo Yuan

Assistant Professor, non-tenure

Kwanghyuk (Danny) Lee
David Marciano

NEW NON-TENURE RESEARCH FACULTY

Nele Haelterman, Ph.D.
Assistant Professor

Zixue Jin, Ph.D.
Assistant Professor

I-Wen Song, BPharm, Ph.D.
Instructor

Jun Wang, Ph.D.
Instructor

Baylor
College of
Medicine

DEPARTMENT OF
MOLECULAR & HUMAN
GENETICS

One Baylor Plaza
Houston, Texas 77030

bcm.edu/genetics
twitter: @bcmgenetics
instagram: @bcmgenetics