Baylor College of Medicine

DEPARTMENT OF MOLECULAR & HUMAN GENETICS

ANNUAL REPORT 2019

Transforming Medicine Through the Practice and Science of Genetics

Message from the Chair

I am delighted to welcome you to our 2019 Annual Report. As we begin a new year, I'd like to briefly reflect on last year's accomplishments.

The Department of Molecular and Human Genetics at Baylor College of Medicine remains the No. 1 ranked genetics department in the country based on total National Institutes of Health funding and awarded grants.

We remain committed to the growth of Baylor Genetics, our diagnostic laboratory venture with Miraca Holdings, Inc. This jointly governed entity continues to support the academic mission and innovation of the Department while promising to extend the impact of genetic diagnostic testing worldwide.

On the global front, we continued our support in our partnership with the Chinese University of Hong Kong Center for Medical Genetics which held its 3rd annual BCM-CUHK-Fudan Joint Symposium in Clinical Genetics.

In addition, during these past few years, new and continuing consortia with the NIH 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

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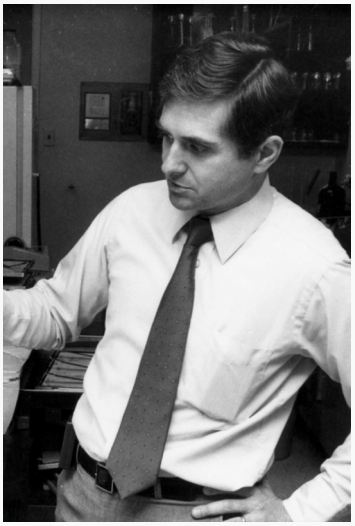
Making History

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







Research in genetics began at Baylor College of Medicine in 1971 when Dr. C. Thomas Caskey, 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 research team 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.

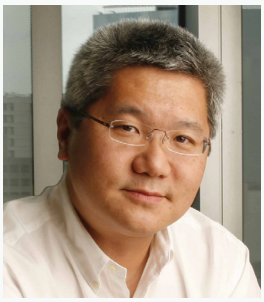
The Department's success reached new heights with the creation of the Human Genome Sequencing Center in 1996. The Center, led by Dr. Richard Gibbs, the Wofford Cain Chair and Professor of Molecular and Human Genetics at Baylor, was one of three sites (out of six pilot programs) to complete the Human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

In recent years, the Department has successfully provided comprehensive clinical care to patients worldwide. By assembling the largest clinical genetics program in the country, Baylor offers patients timely and expert assistance, as well as unparalleled treatment and counseling options through 14 specialized clinics.

In addition, the Department has expanded its reach to provide diagnostic genetic testing services to the broader medical genetics community through its laboratory, Baylor Genetics, a joint venture with Miraca Holdings. Baylor Genetics offers an expansive menu of genetic tests and provides leading service to practitioners worldwide.

The past almost 50 years have been an exciting time of growth and change. Initially focused on medical and pediatric genetics, the Department has since expanded its reach into diverse areas that include functional genomics, genome sequencing, cancer genetics and more. In the process, it has become the preeminent genetics department in the country, if not the world.

Department Leadership



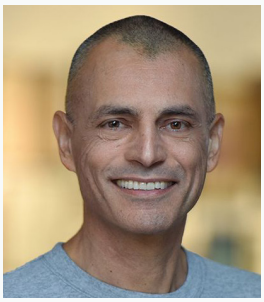
Brendan Lee, M.D., Ph.D.
Robert and Janice McNair Endowed Chair in Molecular and Human Genetics

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

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



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

Daniel Riconda, M.S., CGC
Vice Chair, Educational Affairs (Genetic Counseling Program)

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

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

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

We have more than **550 FACULTY, TRAINEES AND STAFF** who occupy **115,000 SQUARE FEET OF SPACE**. Faculty includes:

- **6** members of the National Academy of Medicine
- **3** Howard Hughes Medical Institute Investigators
- **9** Fellows of the American Association for the Advancement of Science
- **3** members of the National Academy of Sciences
- **2** members of the American Academy of Arts and Sciences

ASHG Lands in Houston

You know the saying "Everything is bigger in Texas" and this year's ASHG was just that...BIG! Thousands of genetics and genomics researchers, counselors, nurses and industry professionals from nearly 80 countries all descended upon the George R. Brown Convention Center in Houston where the American Society of Human Genetics held its 69th annual meeting this past October.

The Department of Molecular and Human Genetics at Baylor College of Medicine helped to kick off the five-day event by hosting a reception which saw around 500 people in attendance.

The society honored Dr. Huda Zoghbi, professor of pediatrics, molecular and human genetics, neurology and neuroscience at Baylor with the with its 2019 Victor A. McKusick Leadership Award.

The award, named in honor of the late Victor A. McKusick, M.D., recognizes individuals whose professional achievements have fostered and enriched the development of human genetics as well as its assimilation into the broader context of science, medicine and health.

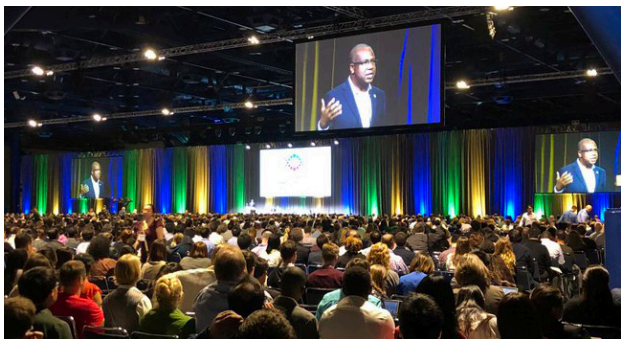
This is the third year in a row that a faculty member in Baylor's Department of Molecular and Human Genetics has received the honor.

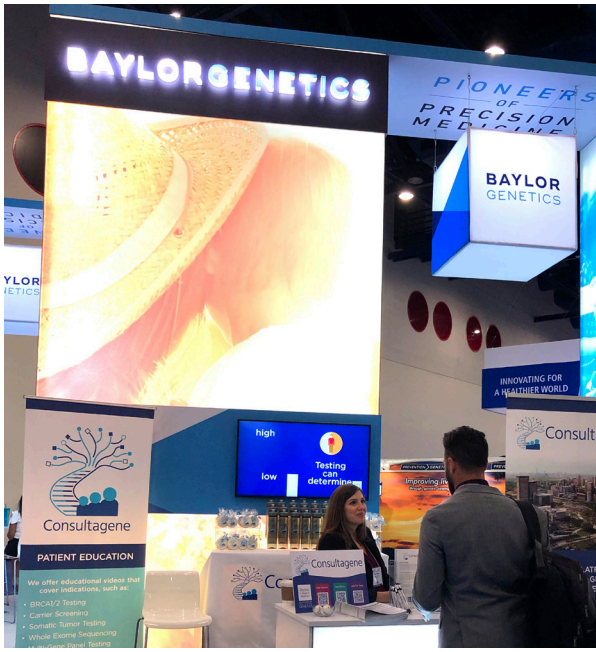
Zoghbi, who holds the Ralph D. Feigin, M.D., Endowed Chair at Baylor, is the director of the Jan and Dan Duncan Neurological Research Institute at Texas Children's Hospital, a Howard Hughes Medical Institute investigator and the world's leading expert on Rett syndrome.

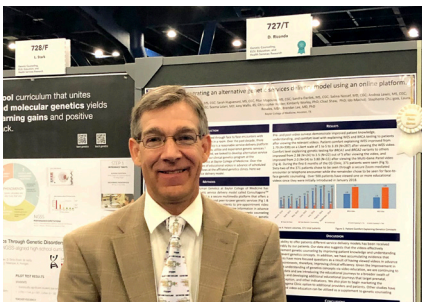
The Department also made its presence felt with the acceptance of over 100 abstracts including several that were recognized with a Reviewer's Choice award. Dr. Neil Hanchard, assistant professor of molecular and human genetics at Baylor College of Medicine, was one of the featured plenary speakers. Hanchard presented his work with the Human Health and Heredity in Africa (H3Africa) Consortium and their findings from sequencing the genomes of 426 individuals from 50 ethnolinguistic groups recruited from 13 different countries in Africa.

Manar Zaghlula, a graduate student in the Zoghbi laboratory, was selected as a trainee award finalist for his abstract, "The identification of post-translational regulators of MeCP2 levels as potential therapeutic targets for MECP2 duplication syndrome". Other trainee award finalists were Ning Liu for her work highlighting the importance of the use of metabolomics in improving the diagnosis rate of inborn errors of metabolism and Won-Seok Lee for his work in finding a pathway that regulates ATXN1, the protein that drives neurodegeneration in an inherited ataxia.

Baylor Genetics and Consultagene were also among the estimated 250 organizations who had exhibits at the meeting.







Consultagene Clinic Launches

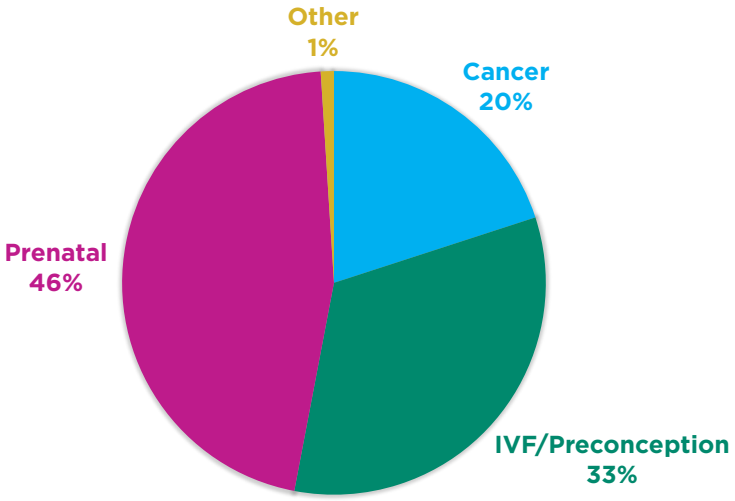
The Consultagene Clinic officially opened its doors in January of 2019. During its first year, a total of 642 patients were seen for genetic counseling.

Close to half of the patients were seen for a prenatal indication with the rest seen for cancer, IVF/preconception, and other indications. In January 2020, the clinic started to accept neurology referrals for indications of family history of Alzheimer's disease, Parkinson's disease, atypical dementia, parkinsonian conditions, ALS, and cerebellar ataxia.

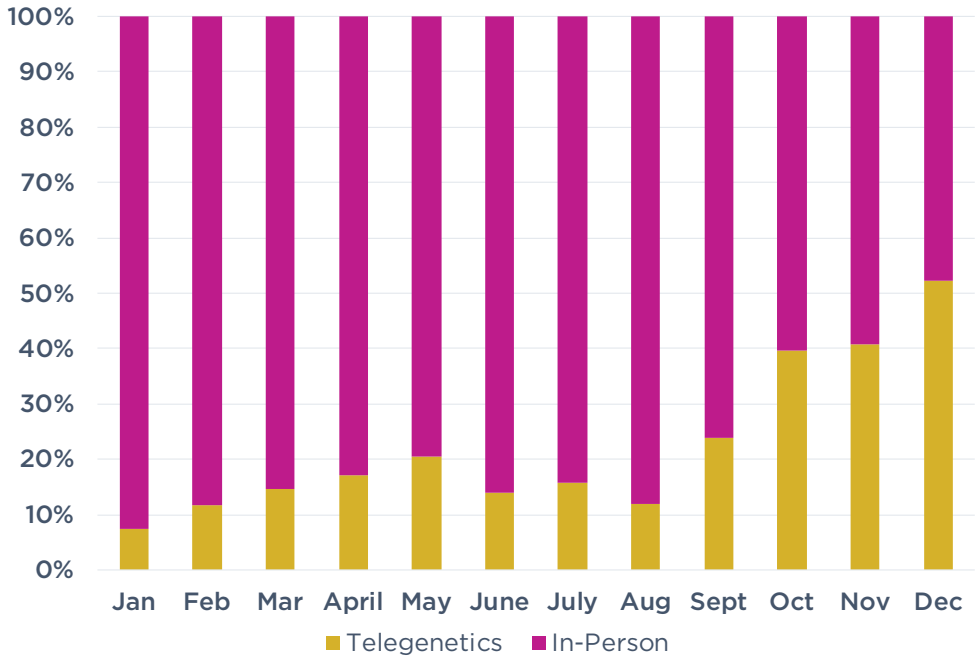
Patients of the clinic are offered the option of telegenetic or in-person consultation. Throughout most of 2019, less than a quarter of the patients were seen via telegenetic counseling. By the end of the year, the percentage of consults seen via telegenetic counseling increased to 50%.

Since July 2019, patients seen in the clinic were provided access to the Consultagene platform, allowing patients to watch educational videos, explore online resources, message with their provider and access documentation from their consultations. From the start of November 2019, patients were surveyed to gauge their Consultagene Clinic experience. All survey participants indicated that the genetic counseling met or exceeded their expectations and all of the patients who had telegenetic counseling agreed or strongly agreed that the consultation was equivalent to an in-person visit with a healthcare provider.

Consultations By Indication

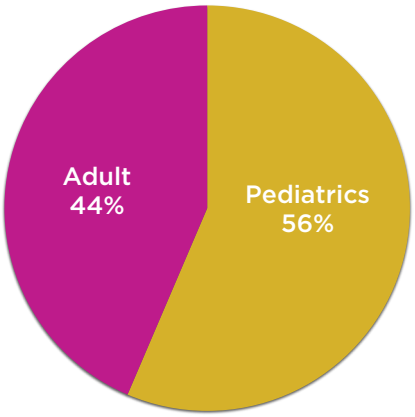


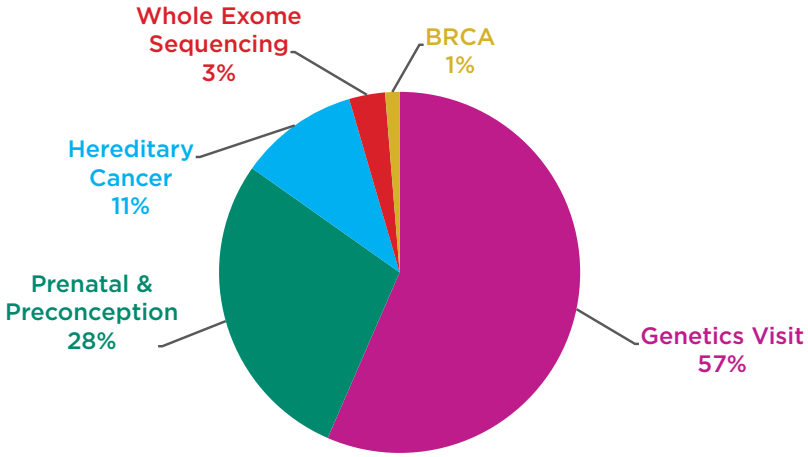
2019 Patient Consultations



Consultagene By The Numbers

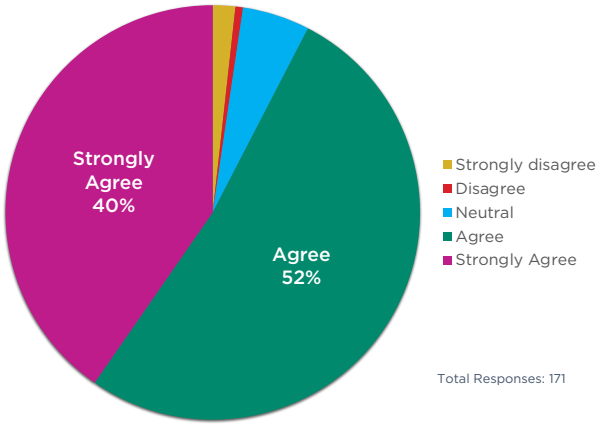
There were a total of 1244 referrals made to Consultagene in 2019.



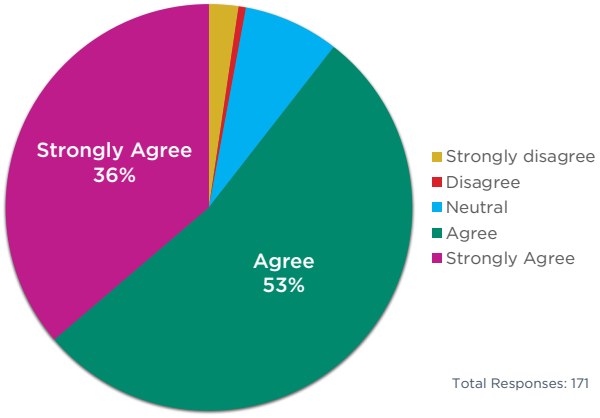


During a patient's journey in Consultagene, the patient is assigned videos to watch as part of the education designed to inform the patient about the indication. Patients were also asked to answer surveys that evaluated the effectiveness those videos.

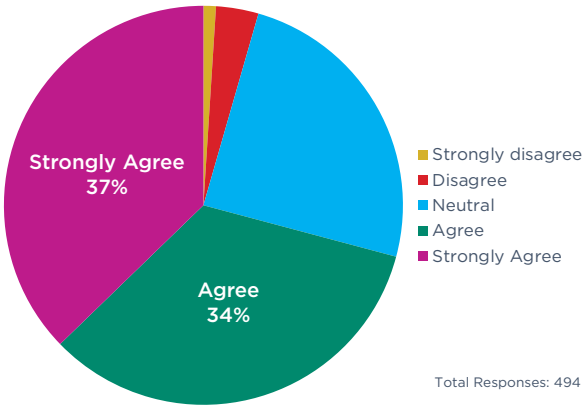
Videos were easy to understand



Videos were informative and helpful



Better Understanding of Indication After Watching the Assigned Videos



Baylor Genetics Launches Whole Genome Sequencing

In February 2019, Baylor Genetics launched clinical whole genome sequencing (WGS) for the diagnosis of rare genetic and inherited disorders.

One of the most comprehensive genetic testing methods for DNA-based mutations, WGS can cover a wide range of mutation types including single nucleotide variants and indels in both coding and noncoding regions, copy number variants, structural variants, regions of absence of heterozygosity, and repeat expansion variants.

The analysis and interpretation of these different mutation types are integrated, and thus diagnoses of more complicated nature may be revealed. Moreover, WGS offers additional depth of results compared to WES and CMA, for example, interpretation of variants in non-coding regions, and accessibility to breakpoint junction sequences of copy number variants from structural variation analysis.

"We have long-standing experience in clinically analyzing and interpreting each component in the spectrum of mutation types covered by whole genome sequencing," said Christine Eng, MD, Chief Medical Officer and Chief Quality Officer of Baylor Genetics, and professor and Vice Chair for Diagnostic Affairs in the Department of Molecular and Human Genetics at Baylor College of Medicine. "Our experts are also dedicating efforts to organically integrate the analysis and interpretation of different types of mutations potentially identified in whole genome sequencing, which we think is the key to exploit the full value of WGS."

While WGS currently offers several detection types including single nucleotide variants, indels, copy number, and structural variants, the company states the next phase will include the detection of trinucleotide repeats and mitochondria variants available later this year further challenging other WGS tests on the market.

Baylor Genetics and King Faisal Specialist Hospital Join Forces

In May 2019, Baylor Genetics (BG) and Riyadh-based Saudi Diagnostic Limited (SDL), a subsidiary of King Faisal Specialist Hospital International Holding Company (KFSHI) signed a Memorandum of Understanding (MOU) to work toward a Strategic Partnership agreement for all genetic testing and precision medicine in the Middle East and North Africa (MENA) regions.

As part of the partnership agreement, KFSHI-SDL will utilize BG as its exclusive laboratory partner for all genetic testing and precision medicine. Both institutions will work together to develop a bi-directional system for seamless ordering, reporting, and interpretation. BG will provide KFHSI-SDL with technical support, technology transfer and training services to further enhance its existing capabilities. Furthermore, both parties will make efforts to develop and commercialize testing for the Saudi Arabian population.

The mutual goal of this collaboration is to commercialize genetic testing in the MENA region, and for both institutions to work collaboratively on their research endeavors.

Kengo Takishima, BG President and CEO, stated, "This Strategic Partnership will bring together our genetic testing expertise with KFSHI-SDL, the premier healthcare provider in the region. We believe this collaboration positions both entities to further expand best-in-class genetic testing to the Kingdom of Saudi Arabia and surrounding regions, and increase access to expertise, support, training, and education."

Research and Discoveries

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 treatment. Here are four recent studies that are representative of the groundbreaking research in the department.

Reanalysis of molecular data yields new genetic diagnoses

A genomic strategy implemented by a team of researchers at Baylor College of Medicine can efficiently increase the molecular diagnostic rate of undiagnosed diseases.


Dr. Pengfei Liu

The research team, led Dr. Pengfei Liu, assistant professor of molecular and human genetics at Baylor and laboratory director of clinical research at Baylor Genetics, reported in the *New England Journal of Medicine* that reanalysis of preexisting molecular data, taking into consideration new disease-causing genes and other genetic knowledge that have been identified since the original analysis, resulted in an increase in the diagnostic yield of cases, nearly doubling it in one of the reanalysis cohorts.

Liu and his colleagues reanalyzed exome sequencing data, which refers to the pieces of a person's genomic DNA that contain instructions for making proteins, of two patient cohorts taking into account the genetic knowledge published between the date of the original analysis and December 2017.

The first cohort of 250 patients had been originally analyzed in 2012 and the second cohort of 2,000 patients in 2013. Manual reanalysis of the exome sequencing data of the first cohort nearly doubled the diagnostic yield – it increased from 25 to 47 percent.

The manual reanalysis was very labor intensive and time consuming. This prompted the team to design a computational pipeline that would semi-automate the process.

The team tested the new method by reanalyzing the sequencing data of the first cohort and found that it achieved a diagnostic sensitivity of 92 percent.

Researchers then applied the computational pipeline to reanalyze the data of the second cohort of 2,000 patients. Once again, the diagnostic rate increased from 25 percent to 37 percent.

Liu and the team then sent the updated sequencing results to the corresponding physicians of the patients in the cohorts. They also requested feedback from the physicians in the first cohort whose patients' reanalysis had produced a new molecular diagnosis. About 40 percent of the physicians responded. They reported that 75 percent of their patients received genetic counseling for the updated findings, and about half of those patients had their clinical management changed as a consequence of the new results. The patients who did not receive genetic counseling about their updated results had moved, died or did not keep their follow-up appointment.

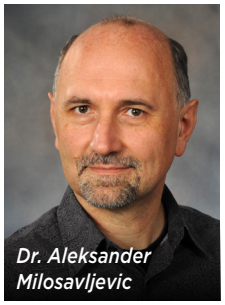
"Our work suggests that periodic reanalysis may benefit patients, their families and the physicians caring for them," said co-author Dr. James R. Lupski, Cullen Professor of Molecular and Human Genetics at Baylor, principal investigator at the Baylor Hopkins Center for Mendelian Genomics and faculty with the Baylor genetics and genomics graduate training program. "Drs. Liu, Yang and colleagues provide a computational process that demonstrates the feasibility of reducing the work-load involved in reanalysis. We hope that other genetic labs, physicians and patients will benefit from this strategy."

Research improves understanding of cell-cell communication

Scientists have improved their understanding of a new form of cell-cell communication that is based on extracellular RNA (exRNA). RNA, a molecule that was thought to only exist inside cells, now is known to also exist outside cells and participate in a cell-cell communication system that delivers messages throughout the body.

To better understand this system, the National Institutes of Health Common Funds Extracellular RNA Communication Consortium, which includes researchers from Baylor College of Medicine, created the exRNA Atlas resource, the first detailed catalog of human exRNAs in bodily fluids. They also developed web-accessible computational tools other researchers can use to analyze exRNAs from their own data. The study, published in the journal *Cell*, contributes the first 'map of the terrain' that will enable scientists to study the potential roles exRNA plays in health and disease.

Dr. Aleksander Milosavljevic, who holds the Henry and Emma Meyer Professorship in molecular and human genetics, and his lab worked with other members of the Extracellular RNA Communication Consortium to analyze human exRNAs from 19 studies. They soon realized that the system was significantly more complex than initially assumed. Due to unanticipated complexity, existing laboratory methods failed to reproducibly isolate exRNAs and their carriers. To help create the first map of this complex system of communication, Milosavljevic and his colleagues used computational tools to deconvolute the complex experimental data. Deconvolution refers to a mathematical process that is used to separate complex information into components that are easier to interpret.


Dr. Aleksander Milosavljevic

"Using computational deconvolution, we discovered six major types of exRNA cargo and their carriers that can be detected in bodily fluids, including serum, plasma, cerebrospinal fluid, saliva and urine," said co-first author Oscar D. Murillo, a graduate student in Baylor's Genetics & Genomics Graduate Program working in the Milosavljevic lab. These carriers act like molecular vessels moving their RNA cargo throughout the body.

The researchers found that the computational method helps reveal biological signals that could not be previously detected in individual studies due to the naturally complex variation of the biological system. For example, in an exercise challenge study their computational approach revealed differences before and after exercise in the proportions of the exRNA-cargo in HDL particles and vesicles in human plasma.

"Exercise increased a proportion of RNA molecules involved in regulating metabolism and muscle function, suggesting adaptive response of the organism to exercise challenge," Milosavljevic said. "This finding opens the possibility that in other conditions, both in health or disease, the computational method might identify signals that could have physiological and clinical relevance."

To help researchers around the world with their analyses, Murillo, Milosavljevic and their colleagues have made the computational tool available online.

"We anticipate that it will take a combination of scientific knowledge, enhanced experimental techniques to isolate cargo and carriers in bodily fluids, and advanced computational methods to deconvolute and interpret the complexity of the exRNA communication system," Murillo said.

Bacteria help discover human cancer-causing proteins

A team led by researchers at Baylor College of Medicine and the University of Texas at Austin has applied an unconventional approach that used bacteria to discover human proteins that can lead to DNA damage and promote cancer. Reported in the journal *Cell*, the study also proposes biological mechanisms by which these proteins can cause damage to DNA, opening possibilities for future cancer treatments.

Mutations that cause cancer can be the result of DNA damage. External factors such as tobacco smoke and sunlight can damage DNA, but most DNA damage seems to result from events that occur within cells and is mediated by cellular components, including proteins. Despite the importance of these events, they have not been studied extensively.

The overproduction of proteins is a frequent cellular event and one cause of DNA damage. In this study, Dr. Susan M. Rosenberg, Ben F. Love Chair in Cancer Research and professor of molecular and human genetics, molecular virology and microbiology and biochemistry and molecular biology at Baylor, and her colleagues set out to uncover proteins that, when overproduced by the cell, cause damage to DNA in ways that can lead to cancer.


Dr. Susan Rosenberg

Rosenberg, who also leads the Cancer Evolvability Program at the Dan L Duncan Comprehensive Cancer Center at Baylor, and the rest of the team began the search for proteins that promote DNA

damage in human cells by looking at proteins that, when overproduced, would cause DNA damage in the bacterium *E. coli.*

"This was a wild idea," Rosenberg said, and was possible because of funding from two sources aimed at trying high-risk strategies that, if successful, would have high impact: a National Institutes of Health Director's Pioneer Award and a gift from the W.M. Keck Foundation, among many other grants to the 16-lab team.

The researchers genetically modified bacteria so they would fluoresce red when DNA was damaged. Then, they overexpressed each of the 4,000 genes present in E coli individually and determined which ones made bacteria glow red.

They discovered an extensive and varied network of proteins that, when overproduced, altered cells in ways that lead to DNA damage. Surprisingly the researchers discovered that most of the proteins uncovered are not directly connected to processing DNA. For example, some of the proteins participate in the transport of molecules across the cell membrane.

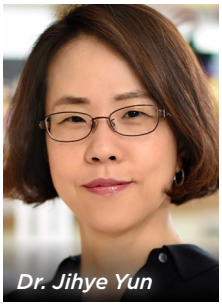
When the researchers looked for human protein relatives of the DNA "damage-up" proteins they had found in bacteria, they identified 284. Interestingly, they determined that these human proteins are linked to cancer more often than random sets of proteins. In addition, the proteins' RNAs, an indicator of protein production, predicted mutagenesis in tumors and poor patient prognosis. When the researchers overproduced these proteins in human cells in the lab, half of the proteins triggered DNA damage and mutation.

"We showed that E. coli can help to identify DNA damage-up proteins and mechanisms of action in human cells quickly and inexpensively. Some of the proteins and their mechanisms were known to be involved in cancer, but many others were not suspected of being in the cancer-causing list," said co-corresponding author Dr. Christophe Herman, professor of molecular and human genetics and molecular virology and microbiology at Baylor College of Medicine and member of the Dan L Duncan Comprehensive Cancer Center.

"Our work has significant implications both in basic biological fields and in clinical research," Rosenberg said. "We provide a previously unknown understanding of the diverse mechanisms that can generate DNA damage leading to cancer. In the future, this finding may lead to new ways to identify people who are likely to develop cancer so that strategies to prevent it, slow it down or catch it early can be used."

The study's two co-first authors were students earning their doctorates: Dr. Jun Xia at Baylor College of Medicine and Dr. Liya Chiu at the University of Texas at Austin.

High-fructose corn syrup promotes intestinal tumors in mice


Dr. Jihye Yun

A study published in *Science* and led by researchers at Baylor College of Medicine and Weill Cornell Medicine showed that consuming a daily modest amount of high-fructose corn syrup – the equivalent of people drinking about 12 ounces of a sugar-sweetened beverage daily – accelerates the growth of intestinal tumors in mouse models of colon cancer, independently of obesity. The team also discovered the mechanism by which the consumption of sugary drinks can directly feed cancer growth, suggesting potential novel therapeutic strategies.

"An increasing number of observational studies have raised awareness of the association between consuming sugary drinks, obesity and the risk of colorectal cancer," said co-corresponding author Dr. Jihye Yun, assistant professor of molecular and human genetics at Baylor and Cancer Prevention and Research Institute of Texas (CPRIT) scholar. "The current thought is that sugar is harmful to our health mainly because consuming too much can lead to obesity. We know that obesity increases the risk of many types of cancer including colorectal cancer; however, we were uncertain whether a direct and causal link existed between sugar consumption and cancer. Therefore, I decided to address this important question when I was a postdoc in the Dr. Lewis Cantley lab at Weill Cornell Medicine.

First, Yun and her colleagues generated a mouse model of early-stage colon cancer where APC gene is deleted. "APC is a gatekeeper in colorectal cancer," Yun said. "Without it, normal intestinal cells neither stop growing nor die, forming early stage tumors called polyps. More than 90 percent of colorectal cancer patients have this type of APC mutation."

Using this mouse model of the disease, the team tested the effect of consuming sugar-sweetened

water on tumor development. The sweetened water was 25 percent high-fructose corn syrup, which is the main sweetener of sugary drinks people consume. High-fructose corn syrup consists of glucose and fructose at a 45:55 ratio.

When the researchers provided the sugary drink in the water bottle for the APC-model mice to drink at their will, the mice rapidly gained weight in a month. To prevent the mice from being obese and mimic humans' daily consumption of one can of soda, the researchers gave the mice a moderate amount of sugary water orally with a special syringe once a day. After two months, the model mice receiving sugary water did not become obese, but developed tumors that were larger and of higher-grade than those in model mice treated with regular water.

"These results suggest that when the animals have early stage of tumors in the intestines – which can occur in many young adult humans by chance and without notice – consuming even modest amounts of high-fructose corn syrup in liquid form can boost tumor growth and progression independently of obesity," Yun said. "Further research is needed to translate these discoveries to people; however, our findings in animal models suggest that chronic consumption of sugary drinks can shorten the time it takes cancer to develop."

The team then investigated the mechanism by which this sugar promoted tumor growth. They discovered that the APC-model mice receiving modest high-fructose corn syrup had high amounts of fructose in their colons. "We observed that sugary drinks increased the levels of fructose and glucose in the colon and blood, respectively, and that tumors could efficiently take up both fructose and glucose via different routes."

Using cutting-edge technologies to trace the fate of glucose and fructose in tumor tissues, the team showed that fructose was first chemically altered and this process then enabled it to efficiently promote the production of fatty acids, which ultimately contribute to tumor growth.

"Most previous studies used either glucose or fructose alone to study the effect of sugar in animals or cell lines. We thought that this approach did not reflect how people actually consume sugary drinks because neither drinks nor foods have only glucose or fructose. They have both glucose and fructose together in similar amounts," Yun said. "Our findings suggest that the role of fructose in tumors is to enhance glucose's role of directing fatty acids synthesis. The resulting abundance of fatty acids can be potentially used by cancer cells to form cellular membranes and signaling molecules, to grow or to influence inflammation."

To determine whether fructose metabolism or increased fatty acid production was responsible for sugar-induced tumor growth, the researchers modified APC-model mice to lack genes coding for enzymes involved in either fructose metabolism or fatty acid synthesis. One group of mice lacked the enzyme KHK, which is involved in fructose metabolism, and another group lacked the enzyme FASN, which participates in fatty acid synthesis. They found that mice lacking either of these genes did not develop larger tumors, unlike APC-model mice, when fed the same modest amounts of high-fructose corn syrup.

"This study revealed the surprising result that colorectal cancers utilize high-fructose corn syrup, the major ingredient in most sugary sodas and many other processed foods, as a fuel to increase rates of tumor growth," Cantley said. "While many studies have correlated increased rates of colorectal cancer with diet, this study shows a direct molecular mechanism for the correlation between consumption of sugar and colorectal cancer."

"Our findings also open new possibilities for treatment," Yun said. "Unlike glucose, fructose is not essential for the survival and growth of normal cells, which suggests that therapies targeting fructose metabolism are worth exploring. Alternatively, avoiding consuming sugary drinks as much as possible instead of relying on drugs would significantly reduce the availability of sugar in the colon."

While further studies in humans are necessary, Yun and colleagues hope this research will help to raise public awareness about the potentially harmful consequences consuming sugary drinks has on human health and contribute to reducing the risk and mortality of colorectal cancer worldwide.

Grant Awards Continue to Drive Progress

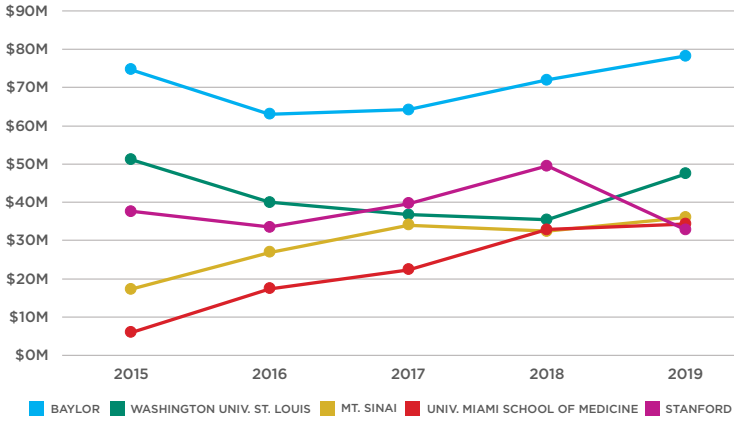
The Department of Molecular and Human Genetics continues to be ranked No. 1 in NIH funding

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.

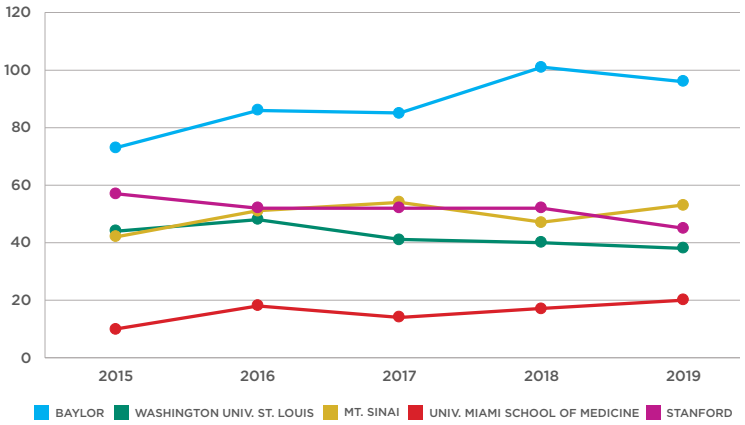
For nine years running, the Department remains the No. 1 ranked U.S. genetics department, as measured by the number of NIH-awarded grants and total funding received. For 2019, the amount in funding dollars from NIH awards totaled more than $78 million (source Blueridge rankings).

The Department is excited to receive this funding, and has put this support to excellent use. Through the funding of the Undiagnosed Disease Network Center, the Center for Mendelian Genomics, the Knockout Mouse Project, and many other investigator-initiated grants, the Department is finding answers to science's most pressing questions. In the process, the Department is improving the well-being of patients across the world.

NIH Funding to Leading Genetics Departments



NIH Grants Awarded to Leading Genetics Departments



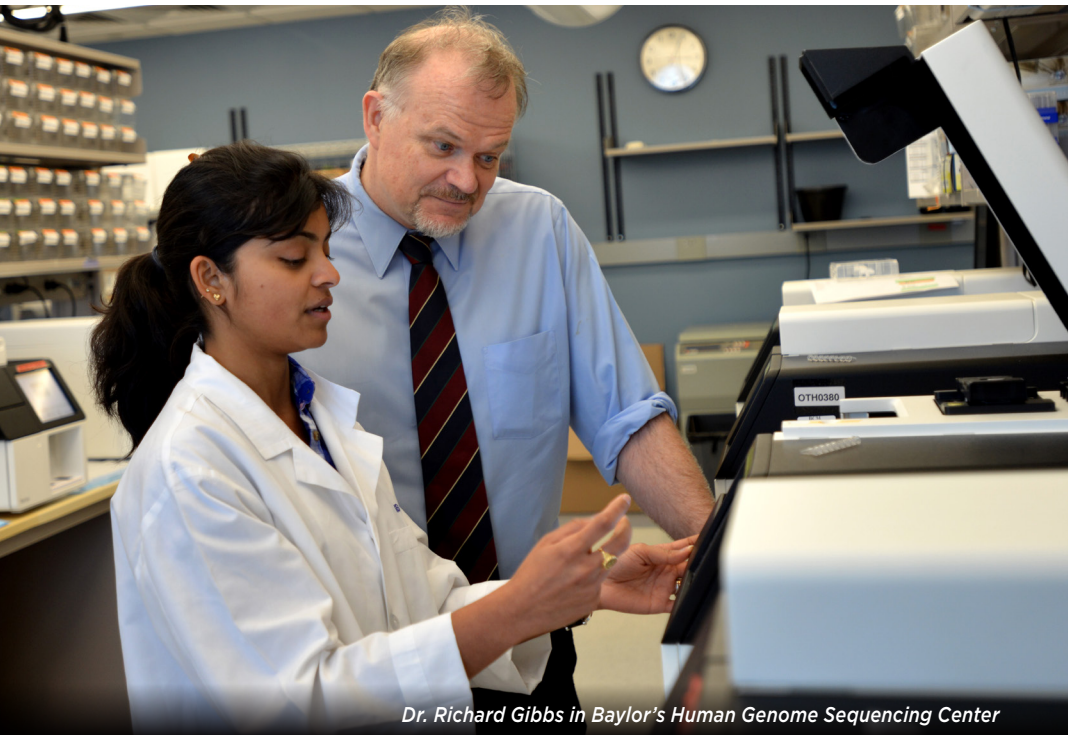
Other Grants/Awards

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 Doris Duke Foundation
W. M. Keck Foundation
The March of Dimes
The Angelman Syndrome Foundation
The American Heart Assocation
Autism Speaks

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 six 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.



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

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 (CVD), 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.

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

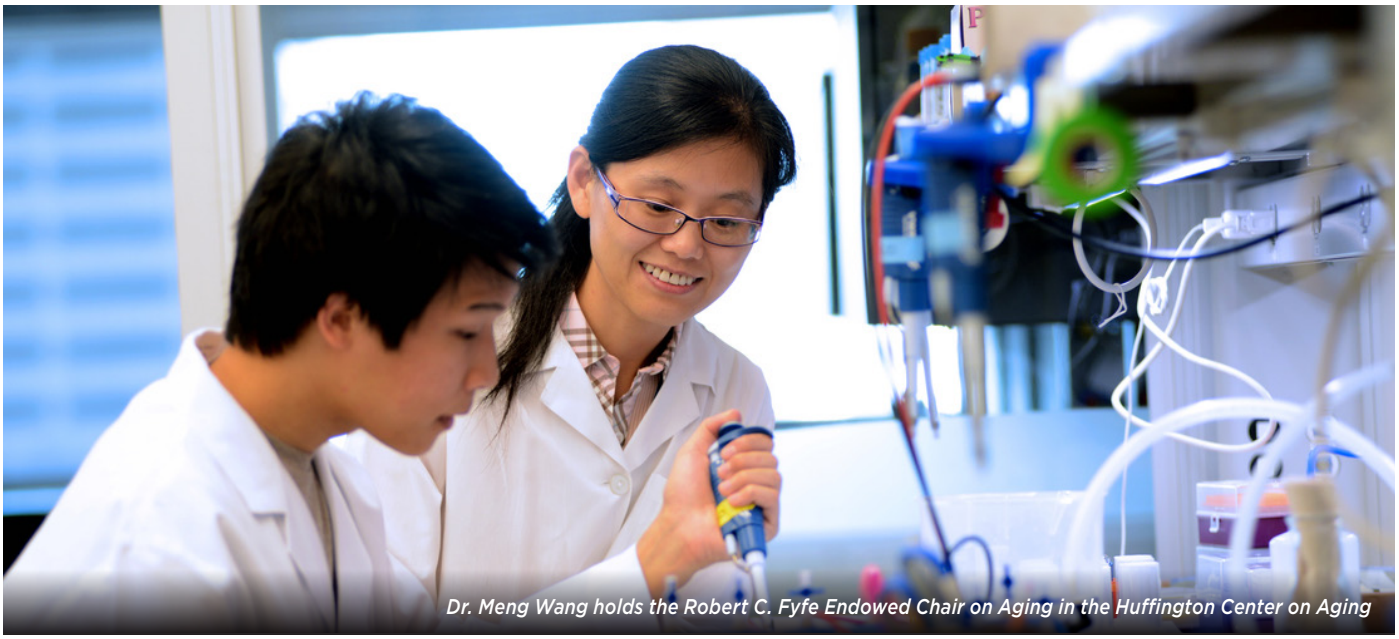
Jan and Dan Duncan Neurological Research Institute

During the past year, investigators at the Jan and Dan Duncan Neurological Research Institute (NRI) at Texas Children's Hospital have made many discoveries that enhance our understanding the pathogenesis of neurological disorders. The following are a few examples:

Researchers in the laboratory of Dr. Hugo Bellen, a professor of molecular and human genetics and HHMI investigator at Baylor College of Medicine, identified a potential therapeutic strategy for ALS through clearing cellular waste in Drosophila models of the disease. This discovery may also prove helpful treating fronto-temporal dementia.

A collaborative study between the laboratory of Dr. Huda Zoghbi, the director of the NRI, and Mass General revealed that the ATAXIN-1 gene, responsible for spinocerebellar ataxia type 1, is genetically and functionally associated with amyloid plaque formation, revealing a new therapeutic approach to prevent Alzheimer's disease. Additional Alzheimer's research, led by Dr. Joshua Shulman, identified a new molecular cause for neurodegeneration in Alzheimer's disease. Integrating data from human brain autopsies and Drosophila, Shulman's group discovered a novel mechanistic link between RNA splicing alterations and neurodegeneration.

An Angelman syndrome clinical trial, based on work from multiple NRI labs, will begin enrolling participants in spring 2020. The Zoghbi lab, with clinical collaborators, has commenced clinical readiness studies on MECP2 duplication syndrome



Dr. Meng Wang holds the Robert C. Fyfe Endowed Chair on Aging in the Huffington Center on Aging

with Ionis Pharmaceuticals. A clinical trial on juvenile Batten disease, based in large part on work from the Ballabio and Sardiello labs, is poised to start early 2020.

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. 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, neuroscience, and molecular and cellular biology, is committed to addressing the needs of an aging population through basic and clinical science research.

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

Current research projects of the HCOA include: (1) determining the factors that regulate lifespan and healthspan in model systems, (2) investigating the role of protein turnover and cellular clearance in stem cells and aging, (3) prevention and treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's disease, (4) understanding and preventing age-related disorders such as cancer, diabetes, and liver diseases, (5) maintaining and improving cardiovascular health, (6) cellular restoration and regeneration in auditory and nervous systems, (7) understanding the molecular

and genetic basis of development, (8) aging, (9) minimizing frailty in older people.

Intellectual and Developmental Disabilities Research Center

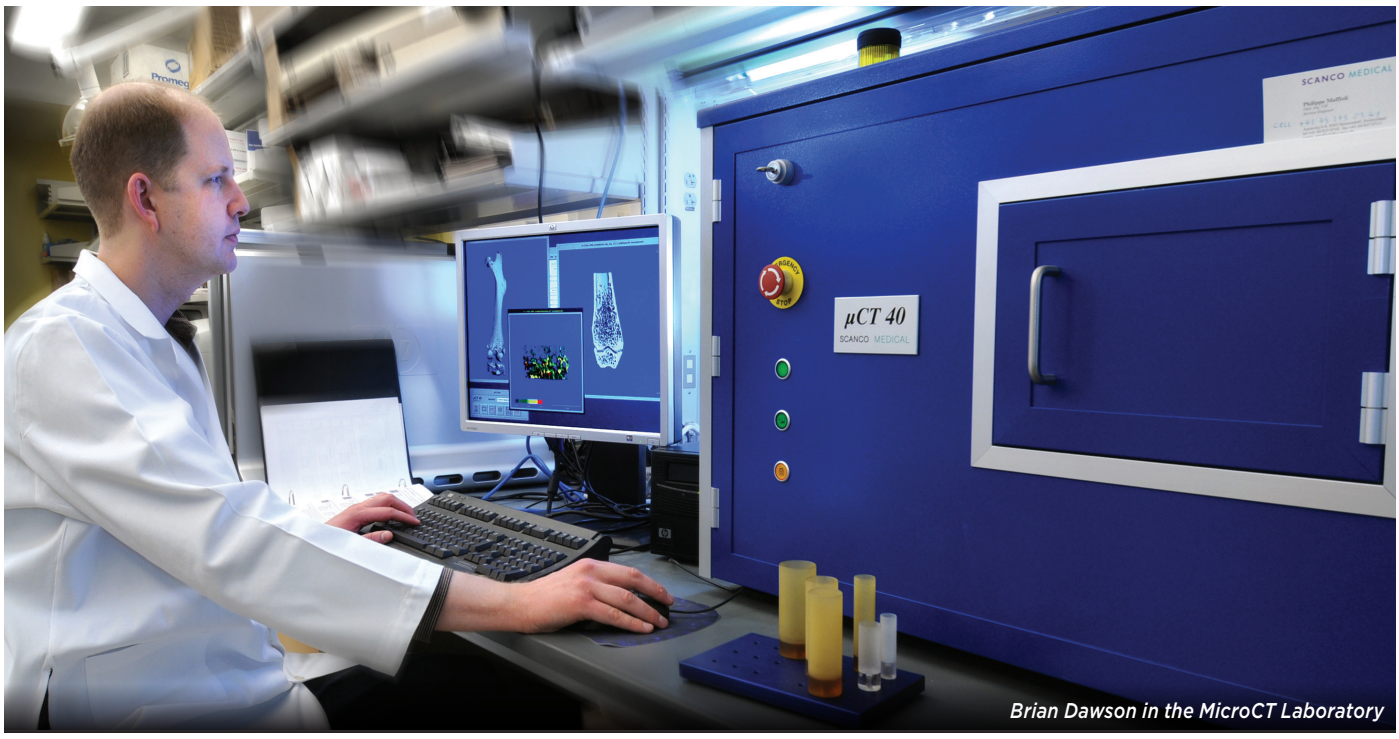
The Eunice Kennedy Shriver Intellectual and Developmental Disabilities Research Center (IDDRC) at Baylor, led by Dr. Huda Zoghbi and co-led by Dr. David Nelson, the Cullen Foundation Professor of Molecular and Human Genetics at Baylor, and Dr. Rodney Samaco, an assistant professor of molecular and human genetics at Baylor, is one of 14 centers across the country supporting 57 investigators engaged in basic, translational and clinical studies of intellectual and developmental disabilities (IDDs).

Housed in the Department of Molecular and Human Genetics, the IDDRC's Core Facilities play a pivotal role in moving novel basic science discoveries 'at the bench' into preclinical and eventual clinical trials in humans. The facilities include the Clinical Translational Research Core led by Dr. Sandesh Nagamani, an associate professor of molecular and human genetics at Baylor, with Dr. Eric Storch, the Neuropathology Core led by Dr. Roy Sillitoe with Drs. Cecilia Ljungberg and Dinghui Yu, the Neuroconnectivity Core led by Dr. Benjamin Arenkiel, associate professor of molecular and human genetics and neuroscience and McNair Scholar at Baylor, with Drs. Jennifer Seleve and Jianrong Tang, and the Neurobehavioral Core led by Dr. Rodney Samaco with Dr. Surabi Veeraragavan, an assistant professor in molecular and human genetics at Baylor.

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 College of Medicine, and Dr. Florent Elefteriou, associate professor of molecular and human genetics and orthopedics at Baylor College of Medicine, 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 collaboration of Baylor College of Medicine, 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 BCM investigators a number of specialized tools for musculoskeletal investigations and opportunities for faculty interested in musculoskeletal research to interact and share expertise through the monthly "Bone Club" for faculty and the T-Bone seminar for trainees of the Bone Disease Program. Both avenues aim at promoting interactions and cross-institutions collaborative research in bone and cartilage research.



Brian Dawson in the MicroCT Laboratory

Genetics Clinics

Improving Patients' Lives with Unmatched Clinical Services

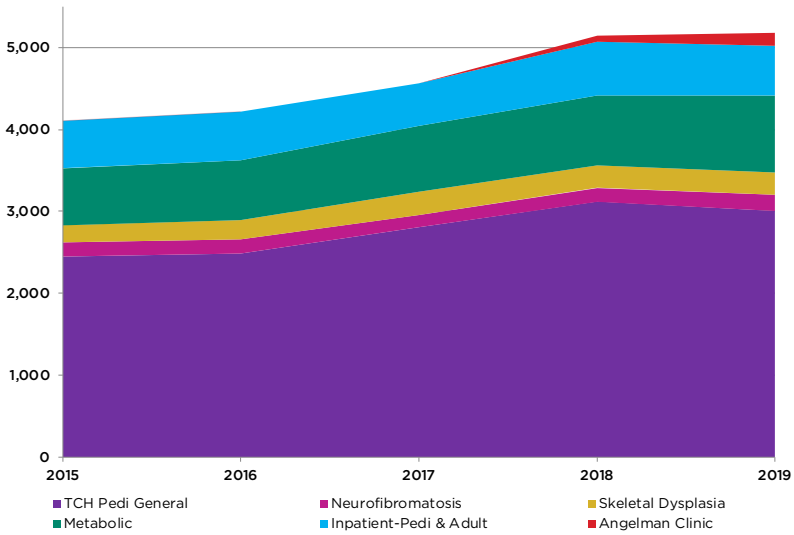
Baylor College of Medicine's clinical genetics program is the largest program of its kind in the country, with 14 clinics spanning across multiple genetics-based disciplines. The clinical program takes a collaborative approach that provides patients with the highest quality, individualized care available. Clinical activities take place across several sites.

Pediatric Genetics

Our pediatric genetics service provides genetic counseling and inpatient and outpatient care to complex and/or critically ill at Texas Children's Hospital and several other hospitals within the Texas Medical Center and beyond, including Texas Children's Hospital West Campus and Texas Children's Hospital The Woodlands. Physicians at the Texas Children's Genetics Clinic see more than 3,000 families 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, and the Gender Medicine Program. Genetics physicians and counselors from Baylor also staff joint clinics with other departments, such as otolaryngology (otogenetics) and neurology (neurogenetics/tuberous sclerosis), and plastic surgery (Craniofacial/Craniosynostosis clinics).

Clinical Genetics Patient Volume (Pediatric)

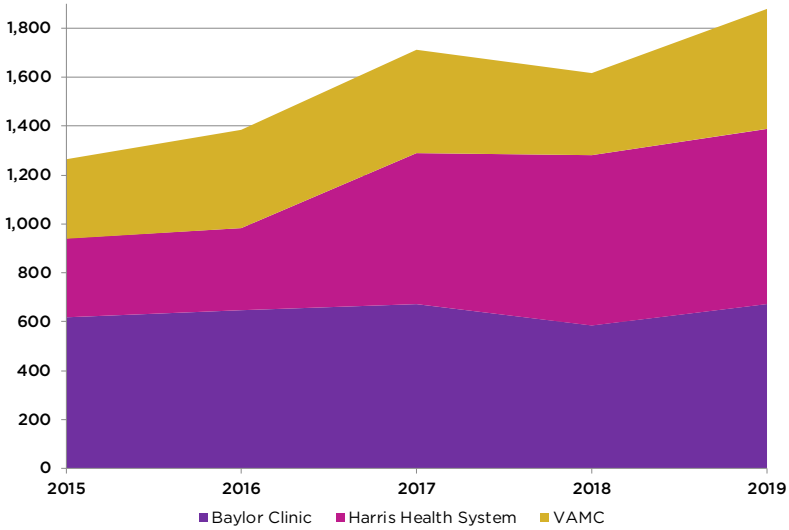


Adult Genetics

The Adult Genetics Clinic is one of the largest genetics clinics in the country providing inpatient and outpatient care and genetic counseling exclusively for adult patients at 3 different locations: Baylor Medicine at the McNair Campus, the Harris Health System's Smith Clinic, and the Michael E. DeBakey Veterans Affairs Medical Center. We see 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 the general genetics clinics, we also have a specialized Ehlers Danlos Syndrome Clinic, a Metabolic and Genetic Disorders of the Bone Clinic and a Cardiomyopathy clinic.

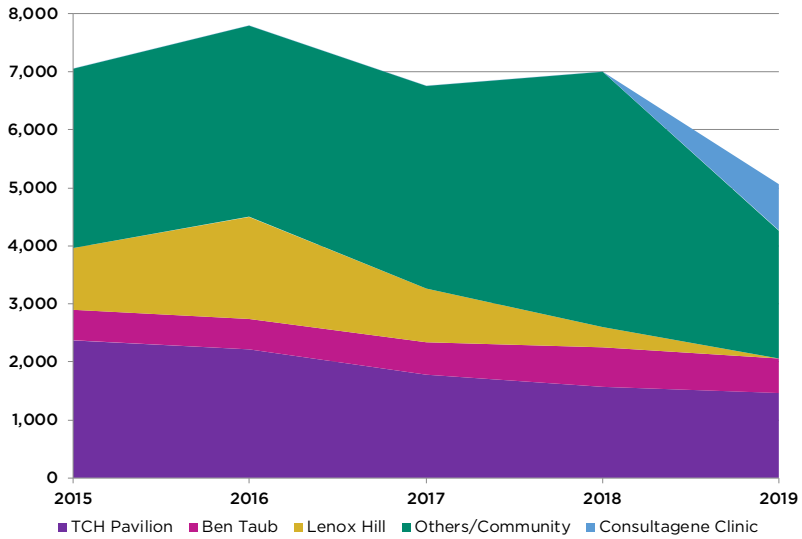
Clinical Genetics Patient Volume (Adult)



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 and diagnostic testing, and counseling.

Clinical Genetics Patient Volume (Prenatal)



Genetic counseling is offered to couples who have an increased chance of having a child with a genetic condition or birth defect, women who will be over 35 years of age at the time of delivery, couples who have had multiple miscarriages, couples who are carriers of a genetic condition, and couples who have had abnormal genetic or prenatal screening tests.

Graduate Program

Rigorous Training is Essential for Tomorrow's Genetic Discoveries

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. The inaugural class of the program matriculated in 2019. Currently there are 89 students enrolled in the program.

Dr. Gad Shaulsky in his laboratory

Students are trained by first-class researchers in an unmatched collaborative environment. "Collaborations between different types of researchers prepare our trainees for the challenges of modern biomedical research," said Dr. Gad Shaulsky, professor of molecular and human genetics and the director of the program. "These collaborations are greatly facilitated by easy access to large genome sequencing and diagnostic datasets that are not available to graduate students elsewhere."

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

Catherine Bradley, a McNair M.D./Ph.D. Student Scholar, was honored with the Kathy Crawford Service Award from the Medical Student Training Program at Baylor College of Medicine

Stephanie Coffin received a F31 Fellowship from the National Institute of Neurological Disorders and Strokes

Varuna Chandler received a Training Program in Biomedical Informatics and Data Science Fellowship from the National Library of Medicine of the National Institutes of Health

Christopher Grochowski took home 3rd Place for his poster at the Graduate School of Biomedical Sciences 2019 Symposium

Patrick Hunt received a 2020 AHA Predoctoral Fellowship from the American Heart Association

Amrita Iyer won the Elevator Pitch Award at Baylor's Graduate School of Biomedical Sciences 2019 Symposium

Jordan Lee received a Graduate Student Scholarship from the MD Anderson Foundation

Kristen Meyer Panthagani received the International Society for Microbial Ecology (ISME) Young Investigator Award

Thomas Ravenscroft was awarded 2nd Place for his poster at Baylor's Graduate School of Biomedical Sciences 2019 Symposium

Hadley Sheppard was awarded the Predoctoral Individual National Research Service Award from the National Cancer Institute at the NIH

Brian St. Hilaire received a Gilliam Fellowship for Advanced Study from the Howard Hughes Medical Institute

Xueyin (Alice) Wen was named a McNair M.D./Ph.D. Student Scholar by the Robert and Janice McNair Foundation/McNair Medical Institute M.D./Ph.D. Scholars Program

Genetic Counseling Program

Promoting excellence in the practice of genetic counseling

The mission of this program is to provide a genomic medicine education promoting excellence in the science of genetics and the practice of genetic counseling across the continuum of care. The interdisciplinary team of clinical, laboratory and research faculty at Baylor College of Medicine provide experiences that empower graduates to become empathic professionals with effective critical thinking skills.

In July 2019, the Baylor College of Medicine Genetic Counseling Program welcomed its second class. In 2019, the total number of applications the program for its second class came close to tripling the number received for the first class. The program received 180 applications and accepted 8 students. All of the second year students selected thesis projects and obtained required IRB approvals or waivers as needed. Both classes engaged in various community activities including serving as volunteers at Rare Disease Day events, school career fairs, and volunteering with local advocacy groups.

Genetic Counseling Program Class of 2021

Awards and Special Recognition for Genetic Counseling Program Students

Hannah Helber continues as president of the class of 2020

Farah Ladha was elected as class president to the Class of 2021.

Abigail Yesso was one of ten students, and the only genetic counseling student, selected to the Texas Society of Allied Health Professions Student Leadership Development Program.

Medical Genetics and Genomics Training Programs

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

The programs enjoy preeminence in the genetics community and are approved by the Accreditation Council for Graduate Medical Education. The following programs are also supported by a training grant from the National Institute of General Medical Sciences: two-year Medical Genetics and Genomics, four-year Combined Pediatrics and Medical Genetics and Genomics, and four-year Combined Internal Medicine and Medical Genetics and Genomics.

Resident Fellowships

The Department also offers two fellowship programs to residents: the four-year combined fellowship in maternal-fetal medicine and medical genetics and genomics, which consists of 18 months of clinical medical genetics training, 18 months of clinical maternal-fetal medicine training and 12 months of research, and the one-year Medical Biochemical Genetics Fellowship, which is meant to provide specialized training in the diagnosis and management of inborn errors of metabolism.

Clinical Laboratory Fellowships

The clinical laboratory fellowship programs provide postdoctoral physician-scientists opportunities to conduct and interpret laboratory analyses useful to the diagnosis and management of human genetic diseases.

Genetics fellows train at Baylor College of Medicine's genetics diagnostic laboratory, Baylor Genetics, for 24 months. After that period, they are eligible for board certification by the American Board of Medical Genetics and Genomics. Fellowships are offered in the following areas:

Laboratory Genetics and Genomics is a newly-designed specialty that incorporates training in both molecular and cytogenetic techniques and interpretations into a single program. The specialty will integrate training in the laboratory assessment of aneuploidies, copy number variants, single nucleotide variants, absence of heterozygosity and abnormal methylation for both constitutional disorders as well as cancers.

Clinical Biochemical Genetics is a specialty where trainees spend three months learning each of the following methods: tandem mass spectrometry, gas chromatography/mass spectrometry, high-pressure liquid chromatography (amino acid analysis) and enzyme analysis. Each day, the trainee participates in writing interpretations for all tests with one of the laboratory directors. The remainder of the training is spent developing new diagnostic tests or methodologies for the laboratory or working on a research project.

2019 Graduating Class of Residents and Fellows

Anjali Aggarwal, M.D. (Medical Biochemical Genetics)

Nurit Assia Batzir, M.D. (Medical Genetics)

Blake Atwood, Ph.D. (Laboratory Genetics and Genomics)

Rebecca Burke, M.D., Ph.D. (Medical Genetics)

Ye Cao, M.B.B.S., Ph.D. (Laboratory Genetics and Genomics)

Diana Carrasco, M.D. (Pediatrics/Medical Genetics)

Rajarshi Ghosh, Ph.D. (Laboratory Genetics and Genomics)

Kevin Glinton, M.D., Ph.D. (Medical Genetics)

Shen Gu, Ph.D. (Clinical Molecular Genetics and Genomics & Clinical Cytogenetics)

Jason Laufman, M.D. (Pediatrics/Medical Genetics)

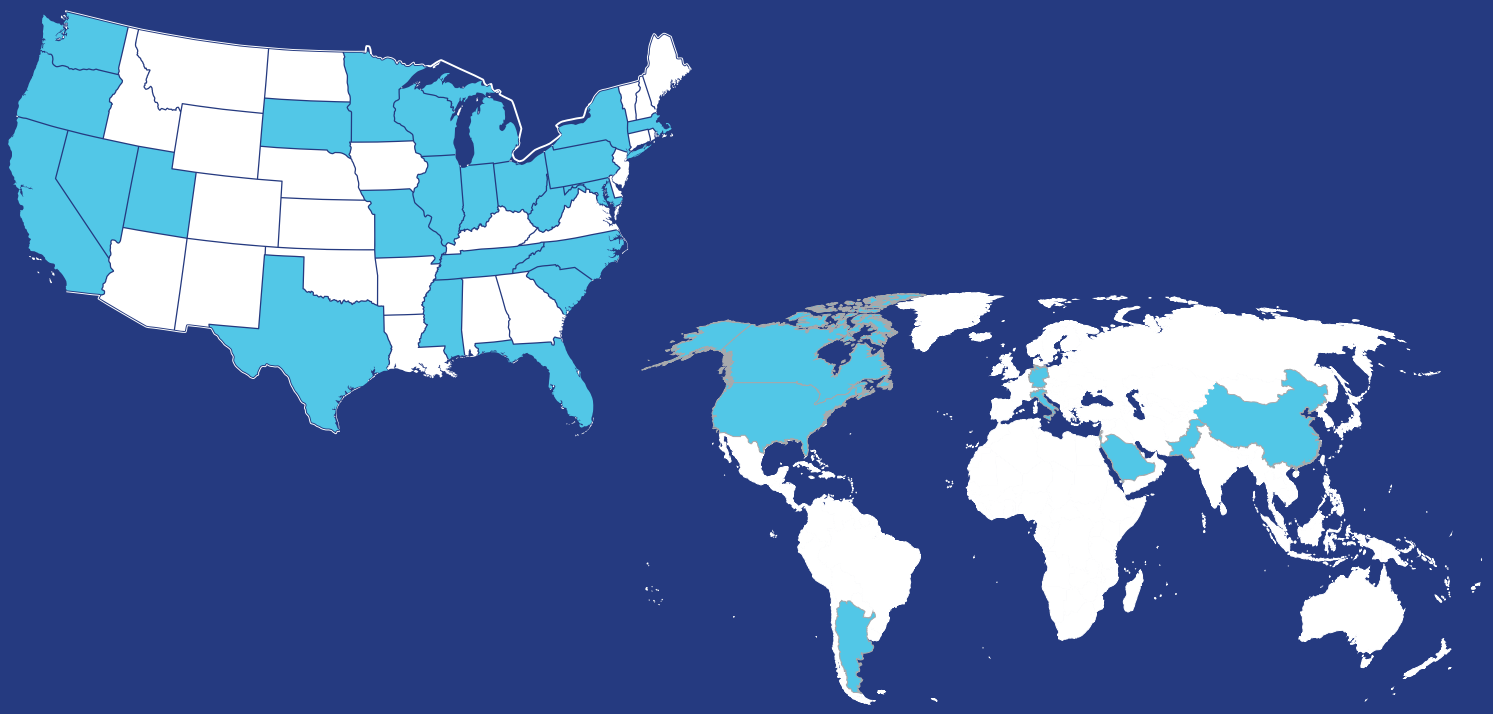
Ning Liu, Ph.D. (Clinical Biochemical Genetics)

Nishitha Pillai, M.B.B.S. (Medical Biochemical Genetics)

Brian Shayota, M.D., M.P.H. (Medical Genetics)

Current and graduating residents and fellows in the Medical Genetics Training Programs sitting with Drs. Brendan Lee and Reid Sutton

Locations of Former Medical Genetics Trainees



Frank Greenberg Memorial Lectureship marks 20th Anniversary

This lectureship was established in memory of Dr. Frank Greenberg, a faculty member in the Department of Molecular and Human Genetics and the Department of Pediatrics at Baylor College of Medicine from 1981 until his retirement in 1994.

Greenberg published more than 100 articles in all areas of clinical genetics and established himself as an expert in contiguous gene deletion syndromes. He contributed to the clinical delineation of a number of congenital chromosomal abnormalities including Prader-Willi, Williams, DiGeorge and Smith-Magenis syndromes. Greenberg was instrumental in the founding of the Williams Syndrome Professional Symposium that brought scientific presentations to the parental support organization of the Williams Syndrome Association National Convention. Greenberg proposed the creation of diagnostic criteria for Williams syndrome, which allowed better assessment of the clinical phenotype.

Through his involvement in the Medical Genetics Training Program at Baylor, Greenberg's extraordinary abilities in dysmorphology and clinical evaluation contributed to the education of numerous clinical geneticists throughout the world. Greenberg introduced innovative teaching methods, including the use of video to capture physical features, minor anomalies and behavioral characteristics of patients seen during clinical consultations. He will be remembered as a gifted educator, mentor, talented dysmorphologist and an empathetic and caring physician.

Dr. James Lupski was the featured lecturer at the 20th annual Frank Greenberg Memorial Lectureship, which took place in late March of 2019. The title of his presentation was "Molecular Mechanisms for Genomic and Chromosomal Rearrangements."

Lupski's research focuses on understanding mutational mechanisms and linking specific mutations and genes to human disease. Lupski started his laboratory at Baylor in 1989, where he still resides. His most significant contributions to genomics are centered on conceptualizing and understanding the mechanisms underlying genomic disorders, which is seen through his studies of Charcot-Marie Tooth (CMT) disease – specifically, duplication of

Dr. James Lupski

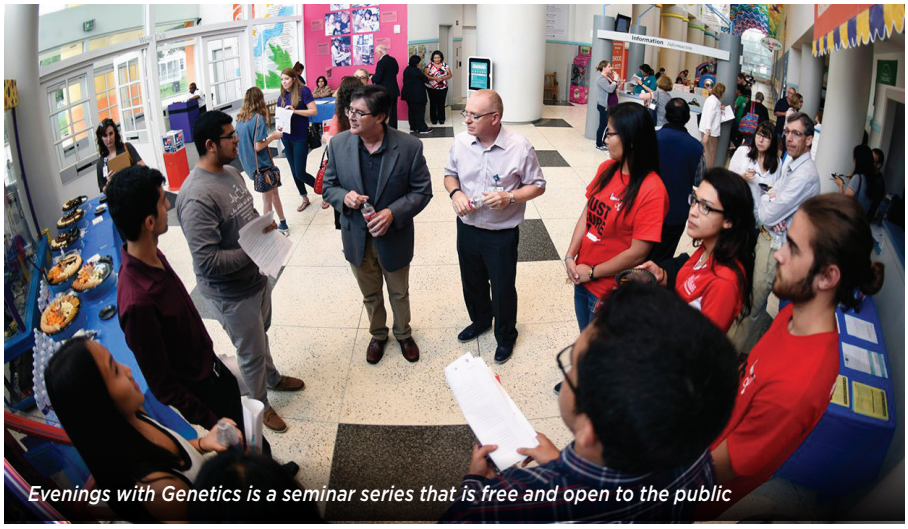
the CMT1A gene. In 1991, Lupski showed that CMT1A copy number variation and gene dosage are causes of CMT-related peripheral nerve dysfunction. In 2014, Lupski and colleagues found that the presence of three copies of CMT1A on one chromosome 17, a phenomenon known as triplication, causes a more severe form of CMT. His group was also the first to describe non-allelic homologous recombination as a mechanism for copy number variation formation and chromosomal aberrations.

Lupski received an honorary doctorate in 2011 from the Watson School of Biological Science at the Cold Spring Harbor Laboratory. Lupski has coauthored more than 700 scientific publications, including 88 in The American Journal of Human Genetics, and is a co-inventor on more than a dozen molecular diagnostic patents.

Community Engagement and Diversity

Evenings with Genetics

Since 2006, Baylor College of Medicine's Department of Molecular and Human Genetics and Texas Children's Hospital have partnered to host Evenings with Genetics, a free seminar series open to the public. The expertise of a genetics faculty member paired with faculty from another specialty area plus a parent expert speaker are highlighted at each seminar. Topics covered in 2019 include Cystic Fibrosis, Autism Spectrum Disorders, developmental disabilities, hearing loss, and Williams syndrome with around 500 family, caregiver and student attendees. In February, Rare Disease Day events were held at 2 locations: the TCH Auxiliary Bridge for patients and healthcare providers as well as an event open to the community at The Health Museum, where more than 35 rare disease organizations and scientists involved in rare disease research hosted booths. The event also held an "Ask the Expert" session and an educational presentation about the importance of rare diseases in human health.



Evenings with Genetics is a seminar series that is free and open to the public

Statewide genetic outreach, in collaboration with the UT Texas Center for Disability Studies and the Texas Department of State Health Services, has included half-day genetic conference and resource fairs in five underserved communities. These community events, in partnership with 22 local organizations, showcased 83 exhibitors and were attended by more than 300 people. Subsequently, geneticists have been invited to speak at regional medical/nursing conferences. Seven genetic webinars for healthcare providers offered continuing education for physicians, nurses, social workers and early childhood intervention providers with over 200 attending the live webinars and 1200 viewing the archived series.

Office of Community Outreach and Diversity

Along with Baylor's Office of Institutional Diversity, Inclusion and Equity, the Department's own Office of Diversity and Community Engagement, directed by Susan Fernbach, assistant professor of molecular and human genetics at Baylor, hosted a booth at the 2019 Biology Undergraduate Research Symposium at Prairie A&M University.

In March, The Department also hosted Dr. Hannah Valantine, NIH's first permanent Chief Officer for Scientific Workforce Diversity, to speak at the 2nd annual Women in Excellence Awards at Baylor College of Medicine.

In July, the first annual Lunch and Learn with summer interns in the department was held to discuss genetic/genomic careers and featured the following speakers: Dr. Huda Zoghbi, Dr. Lindsay Burrage, assistant professor of molecular and human genetics at Baylor, Dr. Debra Murray, assistant professor in the Human Genome Sequencing Center at Baylor, and Baylor genetic counselor, Haley Streff.

At the Annual Biomedical Research Conference for Minority Students that took place in Anaheim, California this past November, a scientific session entitled "Can Genetic Variation improve human conditions/diseases?" was presented by Dr. Neil Hanchard, assistant professor of molecular and human genetics at Baylor and Dr. Cristina de Guzman Strong from Washington University. The session was moderated by Dr. Debra Murray.

Since the field of genetics and genomics is growing rapidly, there is an urgent need for more medical geneticists in the United States. To address this need, this office established the Medical Genetics Diversity Visiting Students Program to reach out and recruit underrepresented medical students into the fields of medical genetics and genomics.

Faculty Awards and Recognitions

Symposiums honor Beaudet and Wong

Alumni scientific symposiums hosted by the Department of Molecular and Human Genetics at Baylor College of Medicine were held this year in honor of Dr. Arthur Beaudet and Dr. Lee-Jun Wong.

Dr. Brendan Lee, Dr. Arthur Beaudet, and Dr. Huda Zoghbi

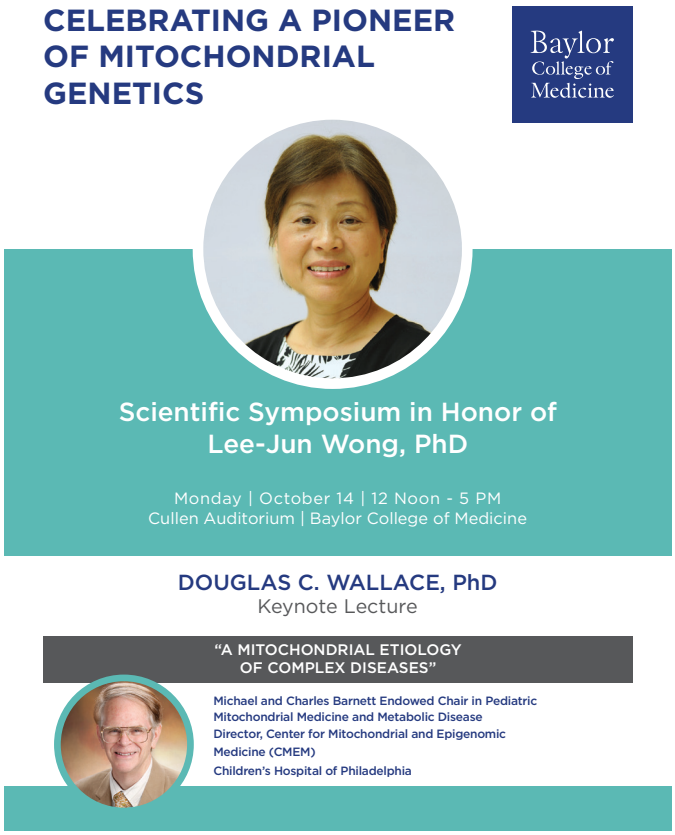
In January 2019, Dr. Arthur Beaudet, former chair and professor of molecular and human genetics at Baylor was celebrated with a day-long alumni scientific symposium which saw former colleagues, lab members, and students in attendance. Dr. Huda Zoghbi, Dr. Allan Bradley of the Wellcome MRC Cambridge Stem Cell Institute, Dr. Avi Orr-Urtreger director of the Genetic Institute at Tel Aviv Sourasky Medical Center (TASMC), Dr. Nicola Brunetti, associate investigator with the Telethon Institute of Genetics and Medicine, Hope Northrup, director of the Division of Medical Genetics in the Department of Pediatrics at McGovern Medical School at The University of Texas Health Science Center at Houston (UTHealth), and Dr. Christie Ballantyne, vice chair of research and professor of medicine at Baylor were some of the many who spoke at the event.

In the 1980s, Beaudet and colleagues were the first to document uniparental disomy, a phenomenon in which a person receives two copies of a chromosome from one parent and zero from the other. In the following years, they drew an important distinction between genetic and epigenetic diseases that both lead to altered expression of the same genes and identified ways to study these and better understand the conditions they caused. His research also touched on neuronal carnitine deficiency as a risk factor for autism; the role of genomic imprinting in diseases such as Prader-Willi syndrome, Angelman syndrome and autism; and prenatal genetic diagnosis based on fetal cells isolated from maternal blood.

Over his nearly 50 years at Baylor, Beaudet helped to build the largest genetics department in the world. Beaudet chaired the department for close to 20 years. He has trained several Ph.D. students and physician scientists and more than 60 postdocs. He has also published more than 350 articles in scientific literature.

Beaudet served as President of the American Society of Human Genetics in 1998. He also received the Society's William Allan Award in 2007 and the Victor A. McKusick Leadership Awards in 2017. He was also awarded the Texas Genetics Society Barbara H. Bowman Award in 1999 and the March of Dimes' Colonel Harland Sanders Award for Lifetime Achievement in Genetic Research and Education in 2002. He was inducted into the Institute of Medicine in 1995 and into the National Academy of Sciences in 2011.

In October, another symposium was held in honor of Dr. Lee-Jun Wong, professor of molecular and human genetics at Baylor. Wong received her training in



medical genetics at Baylor. She was the Director of the Molecular Diagnostic Laboratory at Children's Hospital Los Angeles and Georgetown University in Washington D.C. for 10 years before rejoining Baylor College of Medicine as a tenured full professor at the Department of Molecular and Human Genetics in 2005.

Dr. Wong has published over 290 peer-reviewed articles, 13 book chapters, and edited 3 books. Her research interest is in the area of mitochondrial genetics and function in disease, aging, and cancer. She has been applying novel technologies including the custom designed exon targeted, high density MitoMet oligonucleotide array and the innovative next generation sequencing approaches for simultaneous detection of SNVs and CNVs to clinical molecular diagnoses of human genetic disorders. She has been known as "Mitochondrial Queen" in the mitochondrial disease diagnostic field. Recently, she has developed the innovative cell free DNA testing technologies that include NIPT and liquid biopsies for monitoring cancer progression and therapeutic strategies. Her basic research interest focuses on the investigation of dual genome cross-talk mechanisms in diseases and energy metabolism in cancers.

Dr. Christophe Herman receives NIH Pioneer Award


Dr. Christophe Herman

Dr. Christophe Herman, professor of molecular and human genetics and molecular virology and microbiology at Baylor College of Medicine, has been awarded the National Institutes of Health Director's Pioneer Award. The award supports scientists with outstanding records of creativity pursuing new research directions to develop pioneering approaches to major challenges in science. The $3.5 million award will fund his work to overcome growing resistance to antibiotics and to develop a genetically engineered antimicrobial platform.

"The discovery of antibiotics has saved many millions of people. We all take antibiotics. The problem is that we are abusing the system. Bacteria are very smart and they can very quickly evolve and become resistant," said Herman, a member of the Dan L Duncan Comprehensive Cancer Center at Baylor. "I wondered, could you hijack the function bacteria use to protect themselves from invading viruses and evolve resistance to do the opposite and kill them?"

Herman will work to create a non-antibiotic platform to treat bacterial infections by engineering antimicrobial bacteria to attack pathogens. He will harness bacterial sex, the process that drives antibiotic resistance, to deliver toxic CRISPR nucleases to selectively destroy pathogenic bacterial DNA. The main bottleneck is to tame bacterial sex to deliver the deadly CRISPR toxin and make sure the system is contained to infected people. He will develop a universal method to transfer this engineered DNA from a harmless bacterial carrier to pathogenic bacteria and engineer a way to control the curing-bacteria, preventing it from spreading to the wild.

This new antimicrobial method, called the Cas system, will provide another benefit over antibiotics. Herman said his strategy would be more selective in the bacteria it kills. The Cas system can target specific genetic variations found only in pathogens, leading the genetically engineered bacteria to seek out bad bacteria, and leave the helpful bacteria alone.

"Right now when you take antibiotics, it kills everything. It's not specific. You kill bad bacteria but you also kill the good ones. That's a problem," Herman said. "A lot of bacteria are there to protect us. This new method may be better because it can specifically target bad bacteria.

"Dr. Herman's work is not only innovative, it has the potential to address one of the greatest health challenges of our work, that of infection and antibiotic resistance. Receiving a Pioneer Award is one of the highest recognition by the NIH," said Dr. Brendan Lee, professor and chair of molecular and human genetics at Baylor.

Lichtarge and Wang named AAAS Fellows

In November, the American Association for the Advancement of Science elected two Baylor Researchers to their 2019 class of fellows. Fellows are elected each year by their peers who sit on the Council of AAAS. Scientists are selected for their distinguished efforts toward advancing science applications that are deemed scientifically or socially distinguished.

Dr. Meng Wang, the Robert C. Fyfe Endowed Chair on Aging in the Huffington Center on Aging, Howard Hughes Medical Institute Investigator and professor of Molecular and Human Genetics at Baylor, was elected in the section of of biological sciences for pioneering contributions to the field of molecular genetics, particularly mechanisms underlying diseases of aging in the *C. elegans* model system relevant to human health.

Dr. Olivier Lichtarge, Cullen Foundation Endowed Professor of molecular and human genetics and professor of biochemistry and molecular biology and pharmacology at Baylor, was elected in the section of biological sciences for distinguished contributions to field of computational biology through an evolutionary trace approach to protein engineering and genomic medicine.

"It is my great honor to be named as an AAAS Fellow this year," said Wang, member of the Dan L Duncan Comprehensive Cancer Center at Baylor. "AAAS has been speaking out for science and advocating innovation throughout the world for nearly 170 years. I truly value its mission to advance science for the benefit of all people."

"This honor acknowledges the work of so many graduate students and postdoctoral researchers in my lab," said Lichtarge, director of the Computational and Integrative Biomedical Research Center and member of the Dan L Duncan Comprehensive Cancer Center at Baylor. "We mix evolution with math and physics to understand complex diseases, and to our excitement, the practical applications are becoming apparent. There still is so much more to do."

APPOINTMENTS

Assistant Professor, non-tenure

Alessia Calcagni
Neva Durand
Jamie Fong
Bo Yuan

Assistant Professor, tenure-track

Hsiao-Tuan Chao (McNair Scholar)
April Adams

Instructor

Maria de Haro
Rachel Franciskovich
Denise Lanza
Ning Liu
Shigenori Hirosi
Shamika Ketkar

Adjunct Instructor

Melissa Hsu

PROMOTIONS

Professor, tenured

Chad Shaw

Associate Professor, tenured

Jason Heaney
Daisuke Nakada
Marco Sardiello

Associate Professor, tenure-track

Benny Kaipparettu

Associate Professor, non-tenure

Przemyslaw Szafranski
Matt Roth

Assistant Professor, non-tenure

Ronak Patel
Laurie Robak
Surabi Veeraragavan

More Awards and Recognitions for MHG Faculty

Dr. Lindsay C. Burrage, assistant professor of molecular and human genetics, was selected as a recipient of the 2019 Young Physician-Scientist Award from the American Society of Clinical Investigation

Dr. Hsiao-Tuan Chao, assistant professor of pediatrics and molecular and human genetics at Baylor College of Medicine, has been named the newest McNair Scholar at Baylor.

Dr. Jason Heaney, associate professor of molecular and human genetics at Baylor, was a recipient of the Norton Rose Fulbright Faculty Excellence Award for Teaching and Evaluation 2019

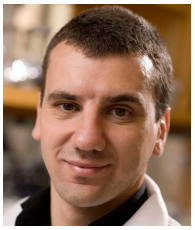
Dr. Hamed Jafar-Nejad, associate professor of molecular and human genetics at Baylor, was given the Alagille Syndrome Accelerator Award by The Medical Foundation at HRiA

Dr. Seema Lalani, associate professor of molecular and human genetics at Baylor, was a recipient of a Norton Rose Fulbright award for development of enduring educational materials

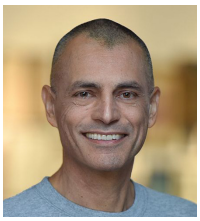
Dr. Aleksander Milosavljevic was named the Henry and Emma Meyer Professorship in Molecular Genetics and selected as a recipient of the 2019 Michael E. DeBakey Excellence in Research Award given by Baylor College of Medicine

Dr. Jennifer E. Posey, assistant professor of molecular and human genetics at Baylor, was selected as a recipient of the 2019 Young Physician-Scientist Award from the American Society of Clinical Investigation

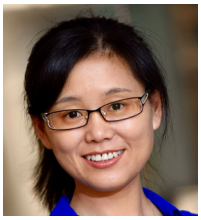
Dr. Susan Rosenberg was awarded a NIH NIGMS MIRA (R35) Award (Maximizing Investigators' Research Award) and asked to give the keynote lecture at the Center for Molecular Carcinogenesis and Toxicology Symposium held at the University of Texas at Austin



Dr. Marco Sardiello, professor of molecular and human genetics at Baylor, was selected as one of the five recipients of the 2019 Michael E. DeBakey Excellence in Research Award given by Baylor College of Medicine



Dr. Gad Shaulsky received the 2019 Kenneth Scott Graduate Mentor Award



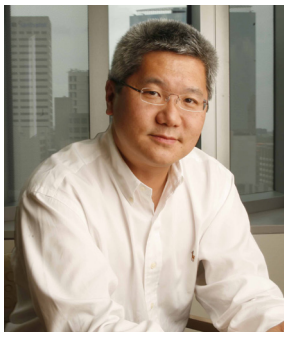
Dr. Meng Wang was recognized with the Lifetime Achievement Award, Society of Chinese Bioscientists in America

Dr. Jihye Yun received the V Scholar Cancer Research Award from the V Foundation and was a Finalist for the 2019 Rosalind Franklin Young Investigator Award receiving an Honorary Mention

Dr. Huda Zoghbi was elected to the National Academy of Inventors, received the Norman J. Siegel Award from the American Pediatric Society, and the Victor A. McKusick Leadership Award from the American Society of Human Genetics

Department Clinical Faculty Awards

Best Metabolic Attending
Dr. William Craigen



Best Research Mentor
Dr. Brendan Lee

Best Pediatric Attending
Dr. Seema Lalani

Best Subspecialty Attending
Dr. Allison Bertuch

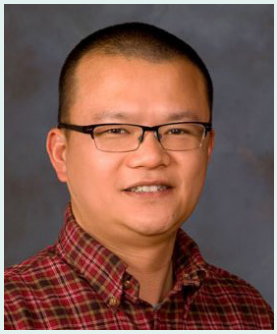
Best Adult Attending
Dr. Shweta Dhar

Best Genetic Counselor
Amanda Gerard, MS, CGC,

Best Educator
Dr. Lindsay Burrage

Baylor Genetics Service Award

Dr. Linyan Meng



Dr. Zhao Chen

Graduate Teaching Award

Dr. Jason Heaney

Graduate Program Bravo Awards

Christopher Grochowski
Angad Jolly

Clinical Resident Award

Dr. Linda Rossetti

Baylor College of Medicine

DEPARTMENT OF
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GENETICS

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