CLEMSON UNIVERSITY
CENTER FOR HUMAN GENETICS

The Transcript

Newsletter of the Center for Human Genetics at Clemson University
Fall, 2022

From the Director

Dr. Trudy F. C. Mackay, FRS, is the Self Family Endowed Chair of Human Genetics. She is a Fellow of the Royal Society of London, a member of the National Academy of Sciences of the USA, a member of the American Philosophical Society, and recipient of the 2016 Wolf Prize.

The year 2022 is a special year for genetics. It is the bicentennial year of Gregor Mendel, born 200 years ago on July 22. The Center for Human Genetics honored his legacy with a Mendel birthday party and a distinguished lecture by well-known Mendel historian Dr. Daniel Fairbanks, summarized in this issue of *The Transcript* by Bibhu Simkhada.

It has also been a special year for the Mackay-Anholt lab family. On August 5 and 6, former students and postdocs of the Mackay and Anholt laboratories organized a symposium in quantitative genetics at Clemson University in honor of their former mentors. This reunion brought former students, postdocs, and staff from the Mackay and Anholt laboratories together to reconnect and reminisce, and the symposium showcased their flourishing careers and impressive accomplishments. It also formed a bridge between the past and the future, introducing the current Mackay and Anholt students and postdocs to their successful predecessors.

The symposium also paid tribute to Dr. Richard Lyman, a stalwart of the laboratory for more than three decades, who currently serves as the director of the Drosophila core at the Center for Human Genetics. In addition to his numerous accomplishments, Dr. Lyman generated the Drosophila Genetic Reference Panel, a population of inbred wild-derived lines with complete genome sequences that many laboratories across the globe have used. This magnificent event is summarized in this issue of *The Transcript* by Spencer Hatfield and Rebecca MacPherson.

In May, the Center for Biomedical Research Excellence (COBRE) in Human Genetics organized its first annual summer symposium at the Arts Center in Greenwood. This highly successful event juxtaposed the genetics of rare diseases and common diseases with excellent lectures by leading scientists and a well-attended poster session by members of the Center for Human Genetics. A description of this symposium is presented by Debarati Majumdar and Monireh Mohammadpanah in this issue of *The Transcript*.

Congratulations to Dr. Fabio Morgante, the first project leader to rotate off our recently awarded Center for Biomedical Research Excellence in Human Genetics grant after obtaining his independent NIH R35 grant. Dr. Zhana Duren will take his place as project leader. Dr. Duren develops and applies novel computational approaches to uncover gene regulatory networks from single-cell multi-omic data.

The Center for Human Genetics says farewell to two outstanding technicians, Brian Kessler and Yu-Chen "Janet' Pan, who will pursue graduate studies at the University of South Carolina and the University of Washington, respectively. We also say farewell to M.S. student Edward Mabry. We wish them all much success in their academic careers.

We welcome our new technical staff members, Tori Gyorey and Katelynne Collins.

The Center for Human Genetics welcomes Dr. Qing Liu, who is joining Clemson's Department of Biological Sciences. Dr. Liu comes from Stanford University and uses human stem cell technology to study the relationships between transcription regulatory networks and metabolic changes in the cardiovascular system.

Several new graduate students are starting their academic careers in the Center for Human Genetics this Fall. We welcome Alp Ummet, Zeynab Tabrizi, Alexandra Randazza, Fengge Chang and Bhoomi Mirani. We also welcome visiting scholar Maryam Nasiri Aghdam.

The Fall semester offers a wide range of academic activities, including our weekly Advances in Human Genetics meetings, distinguished lectures by Aravinda Chakravarti, Vivian Cheung, and Evan Eichler, monthly lunch-and-learn sessions, and the annual COBRE retreat in early November.

I wish all of you a productive and successful Fall semester.

Gregor Mendel at the Bicentennial of his Birth:

The Life and Legacy of a Scientific Genius

by Bibhu Simkhada

The Clemson University Center for Human Genetics and the College of Science invited Dr. Daniel J. Fairbanks, Professor of Biology at Utah Valley University, for a special lecture on Gregor Mendel on September 2, 2022. After a brief introduction to Mendel's early life, the talk advanced into a wonderful description of his research that would ultimately address how traits are inherited, a question that had baffled philosophers, breeders, and biologists for a long time.

Dr. Daniel Fairbanks in Brno with Mendel's bust which he sculpted; photo by Mike Terry

Fairbanks was born into a family of artists. His appreciation for the arts and his devotion to learning about Mendel have given him a unique perspective on Mendel's history. Working closely with Dr. Anna Matalova, who is the Director of the Mendelianum Museum Moraviae at Brno, he has hosted a 20-piece art exhibition about Mendel's life history and recently published a book on Mendel's legacy, which has been his labor of love for over 30 years.

Unfortunately, much of Mendel's work was not recognized until after his death, so a lot of his history went unrecorded. However, evidence shows that he had a prodigious educational background. After completing his early education and working as a friar at the St. Thomas monastery for a few years, Mendel joined the University of Vienna to continue his educational journey. There, he worked with some of the most prominent scientists of the time, including Doppler, Kerner, Fenzl, and Unger.

With the benefit of outstanding education, Mendel returned to the St. Thomas Monastery in 1853. At the time, Fenzl and Unger were debating whether there was a maternal contribution to inherited traits. This debate inspired Mendel to plan his hybridization experiments on peas, and he spent the next two years executing them. He initially looked at four traits: seed shape, seed color, seed coat color, and plant size; later, he added three more traits: pod shape, pod color, and flower position.

After a mere three generations of crosses, Mendel had collected enough evidence to refute Fenzl's argument of a strictly paternal mode of inheritance, and confirmed the equal contribution of both parents in inheritance. He presented this two-part work to the Brünn Society for Natural Science in February and March of 1865. Fairbanks holds up that this work published a year later as one of the finest pieces of scientific literature due to Mendel's keen observation, excellent record keeping, and sound reasoning.

It is widely known that Mendel owned a heavily annotated copy of Charles Darwin's "Origin of Species" which has led to much speculation over Darwin's influence on his work. While there is no direct evidence of communication between the two, Fairbanks' research has shown that Mendel's wording of some concepts in his writing is similar to Darwin's notion of adaptive evolution. Even though the truth of their relationship to each other will likely remain unknown, it is gratifying to know that both of these sharp minds existed at the same time, complimenting each other's work, together laying the scientific and mathematical foundations for modern-day genetics.

Bibhu Simkhada is a graduate student in the Center for Human Genetics at Clemson University.

The 2022 Symposium of the Clemson University Center for Biomedical Research Excellence in Human Genetics

by Debarati Majumdar and Monireh Mohammadpanah

The 2022 Symposium of the COBRE in Human Genetics was held on May 20 in the Arts Center of Greenwood, SC, focusing on the genetics of rare and common diseases. Rare diseases affect a small number of people, but collectively the 7,000 documented rare diseases affect over 30 million Americans.

The symposium began with a lecture by the Director of the Clemson Center for Human Genetics, Dr. Trudy Mackay, who presented elegant studies on *Drosophila melanogaster,* highlighting the prominence of non-additive gene-gene interactions (epistasis) as a central feature of the genetic architecture of complex traits. *Drosophila melanogaster* is a powerful model system to study fundamental principles of the genotype-phenotype relationship of quantitative traits, and many human disease genes have a Drosophila ortholog.

Whereas epistasis - the presence of modifier loci - is well recognized and appreciated in the community of medical geneticists who study and treat rare disorders, epistasis is often ignored in the interpretation of genome-wide association analyses of common diseases, primarily due to a lack of statistical power. Mackay's studies have taken advantage of the Drosophila Genetic Reference Panel (DGRP), a population of inbred wild-derived lines with well-annotated whole genome sequences, which was created in her laboratory and is publicly available as a resource to the Drosophila community.

Mackay's presentation set the stage for Dr. Clement Chow from the Department of Human Genetics at the University of Utah, who used the DGRP to identify genetic modifiers associated with phenotypic variation in a *Drosophila* model of NGLY1 deficiency. N-Glycanase 1 (NGLY1) is a cytoplasmic deglycosylating enzyme. Loss-of-function mutations in the *NGLY1* gene cause NGLY1 deficiency, characterized by developmental delay, seizures, and inability to produce sweat and tears. Chow identified a conserved ion transporter, which could be responsible for defects in secretory epithelium function when misregulated in NGLY1 deficiency patients.

Dr. Monica Justice from the Hospital for Sick Children at the University of Toronto gave an impressive account of her work on Rett syndrome, a rare genetic neurological and developmental disorder that affects brain development and results in progressive loss of motor skills and speech. It is an *X*-linked disorder caused by mutations in methyl CpG-binding protein 2 (MECP2). Justice used a *Mecp2*-mutant mouse model and large-scale genetic

screens. She found an accumulation of neutral lipids in alveolar epithelium cells, implicating enzymes associated with lipid metabolism in respiratory symptoms that occur in Rett syndrome patients.

Dr. Marcelo Nobrega from the University of Chicago explores how genetic variation increases the risk of common human diseases by trying to understand how noncoding genetic variants, most uncovered by genome-wide association studies, are associated with disease etiology. His laboratory has identified long-range *cis*-regulatory enhancers that can affect the FTO gene's temporal and spatial gene expression associated with obesity risk. Specifically, he showed that multiple variants from long, megabase distances could modify the regulatory properties of several enhancers of the *IRX3* and *IRX5* genes in this genomic region.

The final talk of the symposium was delivered by Dr. Nancy Cox from Vanderbilt University, who gave an inspirational presentation on the future of genomics in medicine with an emphasis on the large-scale integration of genomics with other "-omics" data and biobank and electronic medical records.

In addition to five excellent presentations, the symposium featured a lively poster session with 20 posters from students and postdoctoral fellows highlighting the diverse research programs at the Clemson University Center for Human Genetics.

Debarati Majumdar and Monireh Mohammadpanah are graduate students at the Clemson University Center for Human Genetics.

Genomic Insights into the Developmental Origins of Behavioral Disorders

by Allen Wu

On February 25th, Dr. Daniel Weinberger from the Lieber Institute for Brain Development gave us an excellent presentation titled "Genomic insights into the developmental origins of behavioral disorders." Weinberger was the head of the Genes, Cognition, and Psychosis Program at the National Institute of Mental Health (NIMH). In 2011, he became the Director of the Lieber Institute for Brain Development. During his scientific career, he has received many honors and awards, such as the NIH's Director's Award, the K.J. Zulch Neuroscience Prize of the Max Planck Society in Germany, the Adolf Meyer Prize of the American Psychiatric Association, the William K. Warren Medical Research Institute Award, and the Lieber Prize of the National Alliance for Research on Schizophrenia and Affective Disorders. He has also been elected to the National Academy of Sciences Institute of Medicine.

Weinberger is renowned for his work on schizophrenia and related disorders. His laboratory documented the first genetic underpinnings for variation in human cognitive functions and the first specific genetic mechanism of risk for schizophrenia. In addition, he and his colleagues developed the first high-fidelity animal model of schizophrenia. In addition to schizophrenia, they have dedicated themselves to exploring the regulation of genes in the human placenta. They have been trying to understand how certain inborn features of human behavior might also be relevant to the emergence of major psychiatric disorders.

"Are genes associated with genetic risk for developmental disorders prominently expressed during prenatal life?" To look into how genes are processed and expressed in the human brain across the human lifespan, Weinberger showed us that genome-wide association studies, exome sequencing studies, and identification of chromosomal aberrations could generate a list of genes linked with developmental behavior disorders. By acquiring the sequenced transcriptomes from 72 prefrontal cortex samples across six life stages, 50,650 differentially expressed regions (DERs) associated with aging and development were identified. Their studies showed that these DERs associated with changes in neuronal phenotype related to differentiation and maturation have conserved molecular signatures of transcriptional dynamics across brain development, which have potential clinical relevance.

Weinberger also investigated the relationship between epigenetic state and gene regulation. His work suggests that genetic and environmental risk factors that affect the adult brain are principally related to early brain development and not to the tumultuous time of clinical diagnosis. He pointed out that schizophrenia is not a disorder caused by a single gene. There is no specific gene for mental illness. These are all polygenic conditions where many risk factors exist in different combinations that interact in different ways and individuals. Weinberger's group reported that the

Dr. Daniel Weinberger

intrauterine environment modulates risk for schizophrenia along with genomic risk assessed by polygenic risk scores.

Analyses of samples from different countries showed that the risk for schizophrenia, as estimated from polygenic risk scores, is more than five times higher in individuals who experienced early-life complications. The schizophrenia-risk genes which are sensitive to early-life complications are highly expressed in the placenta, with significant differential expression in placentae from complicated pregnancies. In infants with early-life complications due to placental stress, the high placental genomic risk for the later development of schizophrenia is related to early neurodevelopmental trajectories. In most individuals in which early brain development is compromised, "developmental canalization" restores healthy conditions due to rescuing genetic and environmental factors, but in some individuals, such genetic and environmental risk factors may result in "decanalization," which leads to the development of schizophrenia.

At the end of his seminar, Weinberger gave critical summaries and take-home messages. 1) Genes associated with developmental disorders tend to be preferentially expressed during fetal life. 2) Gene-environment interactions influencing placental biology may account for the higher incidence of schizophrenia in males than females. 3) Polygenic risk scores in environmentally sensitive genes that are dynamically regulated in the placenta may predict early brain and cognitive development, perhaps unique to schizophrenia. Thus, preserving prenatal health may be one effective way to prevent schizophrenia, especially in males with high genetic risk.

Allen Wu is a graduate student in the Center for Human Genetics at Clemson University.

An Icon of Human Genetics

by Rebecca Bishop

Dr. James R. Lupski

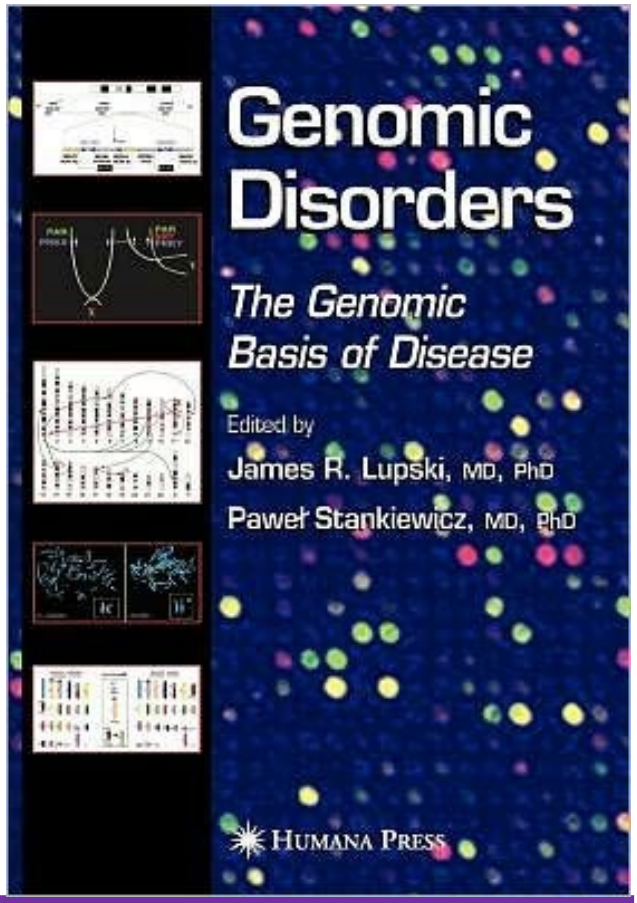
On February 4, 2022, Dr. James Lupski, Cullen Endowed Chair in Molecular Genetics and a Professor in the Department of Pediatrics at Baylor College of Medicine, presented a memorable lecture titled “Biology in balance: human diploid genome integrity, gene dosage, and genomic medicine.” Early in his life, Lupski was diagnosed with a rare genetic disorder, Charcot Marie Tooth Disease (CMT). Given this life-long disability, his contributions to the scientific and medical communities are genuinely remarkable. Lupski has achieved a rare feat, turning a hereditary neuropathy into a prolific scientific career that has inspired and benefited many students, scholars, and patients alike.

After completing his MD/Ph.D. studies at New York University Medical School, he joined the Baylor College of Medicine faculty, where he became close friends with Dr. Richard Gibbs, director of the Baylor Human Genome Sequencing Center. The first individual human genomes that were sequenced were those of James Watson and James Lupski. Lupski identified the variant that led to his CMT condition, which he published on March 10, 2010, in the New England Journal of Medicine.

During his seminar, Lupski provided an impressive kaleidoscope of the number and breadth of his studies on human genomics. His research led to advances in understanding copy number variants, DNA repair, genomic disorders, clan genomics, and genetic architectures of Mendelian diseases. Perhaps, his most impactful research has been in medical diagnostics through variant calls. A major focus of his work was determining the underlying genetic mutations leading to CMT. He uncovered a rare mutational variant impacting vitamin cofactor processing within CMT patients. His contribution revealed the PMP22 gene mutation, which contributes to around 70% of overall CMT cases and sheds light on the involvement of periaxin (PRX), EGR2, and SH3TC2. The latter is the mutational variant responsible for Lupski’s CMT.

Lupski is a role model for young scientists and an iconic personality in the history of human genomics. He received many accolades for his work. In 1993, he received the Distinguished Research Award for Outstanding Contributions to Understanding the Genetics of Charcot-Marie-Tooth Disorders from the Charcot-Marie-Tooth Association. He was elected to the National Academy of Medicine in 2002. That same year he received the Curt Stern Award from the American Society for Human Genetics, and in 2018 he received the Society’s prestigious Victor A. McKusick Leadership Award. In 2011, he received an honorary doctorate from the Watson School of Biological Sciences at the Cold Spring Harbor Laboratory, where he had worked as a summer intern during his undergraduate years at New York University.

Lupski has been a pioneer in genomic medicine. The Clemson University Center for Human Genetics was fortunate to host this inspirational scientist.



Rebecca Bishop is a graduate student at the Clemson University Center for Human Genetics.

Partnering with Communities in Genomic Research

by Kristin Bussey

On April 15th, 2022, Dr. Wylie Burke, Professor Emerita and former Chair of the Department of Bioethics and Humanities and Professor of Medicine in the Division of Medical Genetics at the University of Washington, gave a seminar as part of the Clemson University's Center of Human Genetics distinguished speaker series. The title of the talk, "Partnering with Communities in Genomic Research," delved into the fascinating topic of ethical and policy implications when genetic information is used in research, public health, and clinical care.

Burke received her Ph.D. in Genetics and an M.D. from the University of Washington. Afterward, she completed a residency at the University of Washington and was also a Medical Genetics Fellow. Burke is also a former president of the American Society of Human Genetics (ASHG). She co-directs the Northwest-Alaska Pharmacogenomics Research Network, a partnership involving universities and tribal communities across multiple states, including Montana and Washington. In 2021, Burke was awarded the prestigious Victor A. McKusick Leadership Award in recognition of her dedication to improving ethical and political discourse surrounding the use of genetic information in research, clinical care, and public health, with a focus on impacts on underserved communities.

I had the pleasure of speaking with Dr. Burke before her lecture. Our conversation quickly turned to the topic of difficulties in obtaining genetic information from typically underserved communities like the Alaska native tribes due to a history of mistrust and unethical practices. For example, she noted the Havasupai case, which had legal repercussions since researchers used data collected from members of the tribe without appropriately informed consent. She spoke about initiatives to improve relations between tribes and researchers, some of which include speaking at length with the tribal leaders to ensure every step of the project is explicitly understood. These efforts also ensure that at minimum one researcher hails from the tribe under study and can advocate for their people. The conversation shifted to polygenic risk scores and how best to convey information on risk scores to patients. Burke places a great emphasis on the care with which the results of a polygenic risk score are delivered to avoid unnecessary stress being placed on patients.

Burke's interests lie in the ethical and policy implications of the genetic information used in research, clinical care, and public health. The overarching question she is concerned with is: does clinical utility suffer as researchers focus more on phenotypes with variable penetrance and genetic risk profiles? When someone arrives for clinical genetic testing, what genetic information is classified as useful, and how does this affect the patient? Furthermore, when medical intervention becomes available, is it available to all or only a select few who can benefit from it?

Dr. Wylie Burke

There is a fundamental lack of diversity when it comes to genomics data. A large proportion of genomic data is collected from those of European descent with a limited representation of Asian and African populations and almost no indigenous representation. Lack of genomic diversity can have consequences for those underserved communities who are more likely to have reduced efficacy in clinical and health care. Burke recalls a poignant example highlighting this issue with breast cancer. A study conducting a genetic test for women with breast cancer returned a higher percentage of Variants of Unknown Significance (VUS) in Black and Asian patients versus Caucasian patients. While the possibility of a higher VUS rate in non-European ancestry groups cannot be ruled out, the underrepresentation in genetic databases for variant interpretation cannot help.

Wylie Burke continues in her mission to bridge the gap between underrepresented communities and the scientific community at large. The importance of interdisciplinary open dialogue to combat the current weaknesses in both ethical and clinical settings is necessary for enhancing how vital genetic information is defined, obtained, and used for the future of public healthcare.

Kristin Bussey is a graduate student in the Center for Human Genetics at Clemson University.

A Conversation with Lela Lackey

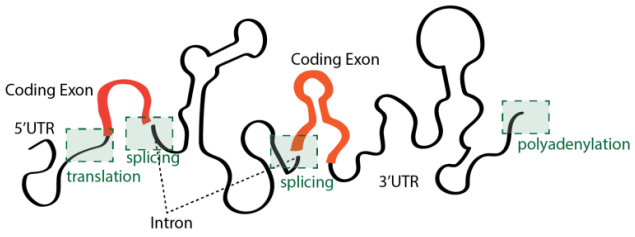
What brought you to the Clemson Center for Human Genetics?

I discovered my love for RNA biology as an undergraduate at North Carolina State University, where I worked in the laboratory of Dr. Stuart Maxwell. Dr. Maxwell's laboratory studied small nucleolar RNAs, so I had an early introduction to RNA. Then, during graduate school in Dr. Reuben Harris's lab at the University of Minnesota, I became interested in somatic mutation and how human variation affects molecular and cellular biology. My postdoctoral work combined these two interests, where I studied the impact of genetic variation on RNA structure and the influence of RNA structure on gene expression.

When I was looking for an independent position, the Clemson Center for Human Genetics stood out. I was immediately drawn to the diversity of research in the Department of Genetics and Biochemistry and the team of scientists at the Center for Human Genetics. The Center for Human Genetics has been a fantastic place to continue my work on the influence of RNA structure on biological pathways and how human variants can alter functional RNA structures.

Could you briefly describe the goals and impact of your research program?

My research program focuses on how RNA structure influences gene expression. One of the main projects in my laboratory concerns the impact of RNA structure on splicing. When precursor RNAs are transcribed from DNA, they contain long sequences called introns that are usually removed during splicing. Splicing involves hundreds of proteins and accessory RNAs that recognize the ends of the intron (splice sites) and process intron removal.



When splicing goes wrong, it has a domino effect on downstream RNA pathways and can lead to RNA degradation or altered protein isoforms. We are particularly interested in the impact of RNA structure on the recognition of splice sites. Splicing is altered in many human diseases, including cancer. We hope that characterizing the structures surrounding splice sites will advance our understanding of how splice sites are recognized and why splice sites are altered in human disease. Functional RNA structures have many additional roles in RNA processing and regulation, including regulation of RNA polyadenylation and protein translation.

What do you consider the most pressing unresolved issue in Human Genetics?

One of the most pressing issues in Human Genetics is our lack of understanding of regulatory biology. For example, we know very little about how noncoding genome regions contribute to human traits, yet we know that many human variants fall in regulatory areas. One of the reasons my laboratory is interested in RNA biology, specifically RNA structure, is that the RNA stage of a gene is often tightly controlled and has significant effects on biological pathways. A better fundamental understanding of regulatory biology will give us a much better picture of the impact of human variation.

How do you see the impact of genetics on the future of medicine?

As we continue to sequence patients and identify causative variants, we will be able to understand the specific mechanisms underlying individual diseases. This will allow us to provide patients with knowledgeable advice and the most effective medicine. There is still much work ahead to deliver precision medicine at this level. Still, with our advanced technological capabilities, including sequencing and RNA structure methodology, I think precision medicine is possible and has great hope for the future.

What advice can you give students who aspire to academic careers in research?

Don't burn yourself out. Academic careers require effort and dedication. Sometimes you need to work extra hard for short periods, but you need to find a way to do so that you can maintain for years. Much scientific success is not giving up. There are steps to getting an academic career in research, and you can make it if you persevere. I think this advice applies to students interested in other scientific careers like industry or teaching.

How do you spend your time away from the lab?

I spend most of my free time with my family, husband, and three kids. We enjoy exploring the upstate area of South Carolina. We like hikes to the local waterfalls and biking on the Swamp Rabbit trail in Greenville. My hobbies are a bit of a paradox: I enjoy baking desserts and competing in triathlons! I'm working my way up to an Olympic distance triathlon.

Lela Lackey is an assistant professor in the Center for Human Genetics at Clemson University.

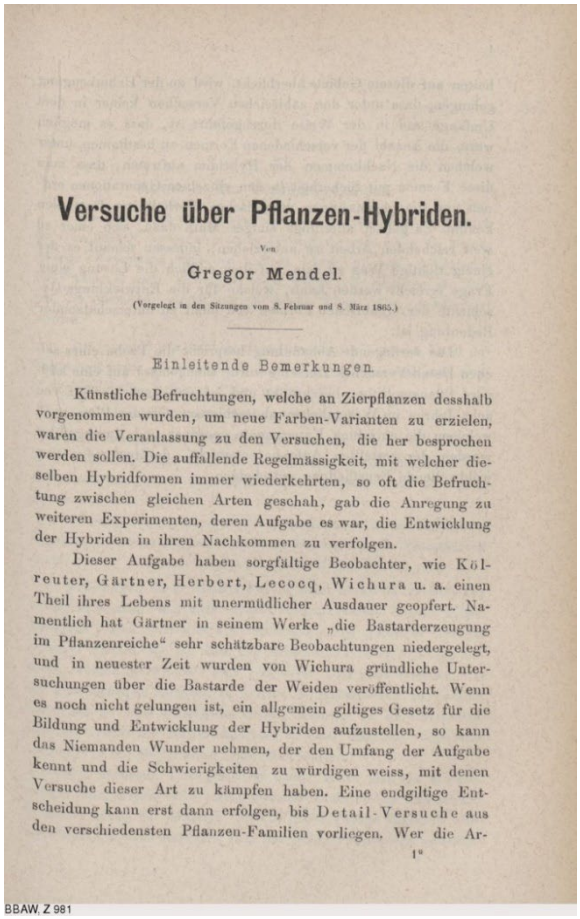
Viewpoint

The Impact of a Single Paper

by Robert Anholt

In 1865 a humble Austrian friar, Gregor Johann Mendel, presented his observations on segregating characters of the garden pea, *Pisum sativum*, to the Natural History Society of Brno in Moravia. His experiments, documented in *Versuche über Pflanzen-Hybriden*, formulated the Laws of Segregation and Independent Assortment that became foundational principles of genetics. His findings were published in the *Verhandlungen des naturforschenden Vereines in Brünn.* They made little impact at the time. It was not until 1900 that Hugo de Vries and Carl Correns rediscovered Mendel's work and recognized the profound significance of his contributions.

Throughout his experiments, Mendel corresponded with the Swiss botanist Carl Nägeli, whom he greatly admired. The correspondence with Nägeli and the 44 pages of the *Versuche* reveal a brilliant scientist who conducted carefully controlled experiments on large samples of plants and, with meticulous care, derived from his data principles that founded an entirely new field of science, genetics. If the Nobel prize existed in those days, Mendel and Darwin would have shared it.



Versuche über Pflanzen-Hybriden.

Von

Gregor Mendel.

(Vorgelegt in den Sitzungen vom 8. Februar und 8. März 1865.)

Einleitende Bemerkungen.

Künstliche Befruchtungen, welche an Zierpflanzen desshalb vorgenommen wurden, um neue Farben-Varianten zu erzielen, waren die Veranlassung zu den Versuchen, die her besprochen werden sollen. Die auffallende Regelmässigkeit, mit welcher dieselben Hybridformen immer wiederkehrten, so oft die Befruchtung zwischen gleichen Arten geschah, gab die Anregung zu weiteren Experimenten, deren Aufgabe es war, die Entwicklung der Hybriden in ihren Nachkommen zu verfolgen.

Dieser Aufgabe haben sorgfältige Beobachter, wie Köl-reuter, Gärtner, Herbert, Lecocq, Wichura u. a. einen Theil ihres Lebens mit unermüdlicher Ausdauer geopfert. Namentlich hat Gärtner in seinem Werke „die Bastarderzeugung im Pflanzenreiche" sehr schätzbare Beobachtungen niedergelegt, und in neuester Zeit wurden von Wichura gründliche Untersuchungen über die Bastarde der Weiden veröffentlicht. Wenn es noch nicht gelungen ist, ein allgemein giltiges Gesetz für die Bildung und Entwicklung der Hybriden aufzustellen, so kann das Niemanden Wunder nehmen, der den Umfang der Aufgabe kennt und die Schwierigkeiten zu würdigen weiss, mit denen Versuche dieser Art zu kämpfen haben. Eine endgiltige Entscheidung kann erst dann erfolgen, bis Detail-Versuche aus den verschiedensten Pflanzen-Familien vorliegen. Wer die Ar-

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Today's world of science is dramatically different. Mendel did not have to worry about funding from NIH or NSF. Nor was he concerned about peer pressure or academic competition. Although Darwin and Mendel were contemporaries, the two never met and Darwin was unaware of Mendel's work. And, as a friar in the monastery, Mendel had *de facto* tenure.

Today, much emphasis is placed on the number of publications, impact factors, and success in obtaining extramural funding. This is not necessarily inappropriate, given the current conditions of academia. It is, however, sobering to reflect on Gregor Johann Mendel, whose work was driven solely by scientific curiosity and meticulous dedication and whose paper on the study of plant hybrids was not published in a journal with a high impact factor. Yet, the impact of his *Versuche über Pflanzen-Hybriden* has been monumental. What Mendel can teach us today is that we should judge our peers on the impact of their work rather than the number of publications or the dollars they generate.

Robert Anholt is the Provost's Distinguished Professor of Genetics and Biochemistry and Director of Faculty Excellence in the College of Science at Clemson University.

The Clemson Symposium on Quantitative Genetics

by J. Spencer Hatfield and Rebecca MacPherson

The 2022 Clemson Symposium on Quantitative Genetics, held on August 5-6 at the Clemson University Madren Center, highlighted the prolific scientific careers of two Center for Human Genetics (CHG) faculty members: Drs. Trudy F. C. Mackay and Robert R. H. Anholt. Trudy Mackay is the Director of the CHG and Self Family Endowed Professor in the Department of Genetics and Biochemistry, while Robert Anholt is the Provost's Distinguished Professor of Genetics and Biochemistry and Director of Faculty Excellence for the College of Science.

The scientific careers of Mackay and Anholt have been intertwined for over thirty years. However, the story of how they met has little to do with science and much to do with their mutual love of horses. In the late 1980s, Mackay and Anholt held professorships at North Carolina State University and Duke University, respectively. The two scientists both attended a cross-country horseback riding event in Rougemont, North Carolina, as members of the local hunt club. At the opening meeting of the hunt, Anholt's horse was lame, and he could not ride. Instead, he presented glasses of champagne, the stirrup cups, to the riders, and it was there that he met Trudy Mackay. Not long after they married, Trudy convinced Robert of the benefits of the fruit fly model system, and the two developed behavioral assays on flies at their kitchen table. Their fondness of horses continues to this day with weekend carriage rides.

Mackay and Anholt were already prominent quantitative genetics and neurobiology scholars, respectively. However, the integration of these fields laid the groundwork for the Clemson University CHG. Before Clemson, both scientists held faculty positions at North Carolina State University. Throughout their careers at NC State, they trained, mentored, and prepared many young scientists, many of whom now have faculty positions. A group of these former students organized the Clemson Quantitative Genetics Symposium in honor of Mackay and Anholt.

The symposium began with a keynote by Mackay, describing her impressive career journey from Dalhousie University in Halifax to the Clemson CHG. Throughout her career, she has led the field of quantitative genetics. One of her most significant accomplishments is the invention of the *Drosophila melanogaster* Genetic Reference Panel, a population of inbred fruit fly lines with complete DNA sequences that are used around the globe for investigating the genetic underpinnings of complex traits.

The symposium was filled with scientific presentations from Mackay and Anholt's former lab members, ranging across precision medicine, medical writing, bioinformatics, biomanufacturing, and systems genetics. In addition to keynotes delivered by Mackay and Anholt, current CHG members that spoke include Dr. Fabio Morgante, postdoctoral scholar Dr. Nestor Octavio Nazario-Yepiz, and Ph.D. students Kristin Bussey, J. Spencer Hatfield, and Rebecca MacPherson.

Anholt gave the final talk of the symposium – a sensational and heartwarming auto-biographical drama of his scientific life before and after meeting Trudy Mackay. It was clear that both Mackay and Anholt have produced both world-class discoveries and world-class scientists throughout their illustrious careers. After Anholt's talk, Mackay and Anholt presented Dr. Richard Lyman, Director of the CHG Drosophila Core and longtime Mackay-lab member, with gifts to recognize his efforts and many contributions to the Mackay and Anholt labs for nearly 34 years (and counting).

Throughout the symposium, gratitude and admiration for Mackay and Anholt were consistently on display. Some stories highlighted how dedicated Trudy and Robert are to their students, whether volunteering to complete lab work for their students during the holidays or diving into the statistical code to perform troubleshooting. One former student said their effort "was unlike all other professors." Other colleagues highlighted the scientific accomplishments of Trudy and Robert, mentioning that they "do science the correct way," are detail-oriented, and stimulate collaborations and ideas between colleagues. Furthermore, Mackay was considered a "scientific idol," as one former student recounted how her writings directly shaped her work in academia and industry. As director of the Keck Center for Behavioral Biology at NCSU, Anholt developed careers, facilitated funding opportunities, and brought world-class speakers for the seminar series.

Not only were Mackay and Anholt commended for their scientific accomplishments, but also their friendly personalities. "Family" was used to describe the Mackay and Anholt labs. Trudy and Robert have opened their home monthly for a casual scientific conversation with "slightly better than average wine." This family-like atmosphere was emphasized by the laughter and genuine joy that filled the lobby between talks as symposium attendees reminisced and caught up with one another. Attendees heard multiple stories of lab members returning to the Mackay and Anholt labs for a second stint after an internship or graduate school due in part to how much they enjoyed the laboratory atmosphere (in addition to the scientific training). Going so far as to serve as surrogate parents for one of their lab members on her wedding day, it is clear that Trudy and Robert are "good scientists and good people." We are privileged that Mackay and Anholt are at the Clemson University CHG!

J. Spencer Hatfield and Rebecca MacPherson are graduate students in the Center for Human Genetics at Clemson University.

Grants

Trudy Mackay and **Robert Anholt** received a five-year $2,476,880 grant from the National Institute on Drug Abuse to study the genetics of cocaine sensitivity in Drosophila.

Trudy Mackay and **Robert Anholt** received a five-year $2,438,650 grant from the National Institute on Ageing to study the genetic basis of lifespan and health span extension by ACE inhibition in Drosophila. This includes a subcontract with Dr. Maria de Luca at the University of Alabama at Birmingham, AL.

Fabio Morgante received a five-year $1,801,825 Maximizing Investigator Research Award from the National Institute of General Medical Sciences for studies aimed at understanding and using gene-by-context interactions in human complex trait genetics.

Seminars

On Friday, **September 16**, at 2:30pm **Dr. Aravinda Chakravarti**, Muriel G. and George W. Singer Professor of Neuroscience and Physiology, and Director of the Center for Human Genetics and Genomics at the New York University Grossman School of Medicine, will present a seminar titled "Transcriptional enhancers and their phenotypic effects."

On Friday, **October 7**, at 2:30 pm **Dr. Vivian Cheung**, Frederick G.L. Huetwell Professor in the Department of Pediatrics, Division of Neurology, and Professor in the Department of Human Genetics at the University of Michigan School of Medicine, will present a seminar titled "An enhancer RNA that modifies susceptibility to Alzheimer's Disease."

On Friday, **November 11**, at 2:30 pm **Dr. Evan Eichler**, Professor of Genome Sciences at the University of Washington, will present a seminar titled "Complex structural variation in a complete human genome"

Publications

(affiliates of the Center for Human Genetics are in bold font)

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Gene Machine

A science and music lecture with Nobel laureate Venki Ramakrishnan

Working at the MRC Laboratory of Molecular Biology in Cambridge, Venki Ramakrishnan, Ph.D., received the Nobel Prize in chemistry for elucidating the structure of the ribosome, the organelle which translates genetic information into proteins.

He was knighted by Queen Elizabeth and has served as president of the Royal Society of London. His book, "Gene Machine," describes the history of the field — and the personalities involved — which led to the discovery of the mechanisms that translate our genetic blueprint into a functioning individual.

Venki Ramakrishnan's lecture will be preceded and followed by musical performances by his son, renowned cellist Raman Ramakrishnan, and concert pianist and conductor Benjamin Hochman.

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— The New York Times, about Hochman

Raman Ramakrishnan

Benjamin Hochman

There will be an open reception with the speaker and artists immediately following the performance

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Cellist Raman Ramakrishnan has performed around the world. He was a member of the Horszowski Trio and a founding member of the Daedalus Quartet. Ramakrishnan has given numerous solo recitals, performed as guest principal cellist with the Saint Paul Chamber Orchestra and was a guest member of Yo Yo Ma's Silk Road Ensemble. Ramakrishnan is currently an artist member of the Boston Chamber Music Society and a faculty member at Bard College.

Pianist Benjamin Hochman has enjoyed an international performing career ever since his Carnegie Hall debut as soloist with the Israel Philharmonic under Pinchas Zukerman, appearing as soloist with the New York, Los Angeles and Prague philharmonic orchestras, and the Chicago, Pittsburgh, San Francisco and Jerusalem symphony orchestras. He has conducted the English Chamber Orchestra, The Orchestra Now at Bard Music Festival and the Juilliard Orchestra, among others.

"Classical music doesn't get better than this..." — *The New York Times, about Hochman*

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