CLEMSON UNIVERSITY
CENTER FOR HUMAN GENETICS

The Transcript

Newsletter of the Center for Human Genetics at Clemson University
Fall, 2025

From the Director

The last six months have been a turbulent period for the scientific community. There is considerable concern that the administration's "war on science" will have long lasting detrimental consequences, especially for young investigators. Despite this disconcerting reality, there is cause for optimism. Members of the Center for Human Genetics have been extraordinarily productive with 74 publications since the last issue of *The Transcript*, more than two papers per faculty over a six-month period. There is no reason to doubt that research progress in our Center will continue vigorously. The Clemson University administration has handled the current situation with foresight, and Clemson University is better positioned to deal with - hopefully temporary - adversity than many other institutions.

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, the National Academy of Medicine, and the American Philosophical Society, and recipient of the 2016 Wolf Prize.

The Fall semester will be exciting, with distinguished lectures by Andrew Clark from Cornell University, Fernando Pardo Manuel de Villena from UNC Chapel Hill, and Elissa Chesler from the Jackson Laboratory. Jonathan Losos from Washington University at St. Louis will deliver a Discover Science Lecture about the evolution of cats, certain to draw all cat lovers.

Spencer Hatfield, a recent PhD graduate from the Center for Human Genetics, has taken a position at 10x Genomics. We wish him well in his new career. We welcome Mille Elsborg, a new research technician in the Mackay-Anholt laboratory. Originally from Denmark, Mille graduated from Lander University in Greenwood with a B.S. degree in Biology. We also welcome two new graduate students, Arunima and Devin Keane, and postdoctoral fellow Robin Singleton.

Despite threats to funding biomedical research, I am proud to note that members of the Center for Human Genetics continue to make groundbreaking discoveries.

In a paper published in *Genetics*, Fabio Morgante with his postdoctoral fellow Kushi Goda and collaborator Francesco Tiezzi from the University of Florence in Italy used data from more than 100,000 adults in the UK BioBank to assess whether information on lifestyle could improve accuracy of disease risk prediction. They looked at the effects of 27 lifestyle factors on systolic and diastolic blood pressure. They showed that lifestyle traits that have a genetic component, like alcohol use, can be a confounding factor in predicting disease risk. When these variables were adjusted, prediction accuracy improved, an important insight for integrating lifestyle and genetic factors to predict risk for cardiovascular disease.

Miriam Konkel contributed her expertise in transposable elements to the Human Genome Variation Consortium with two groundbreaking papers in *Nature*, the complete telomere to telomere sequencing of six species of apes, providing a new baseline for studies on the evolution of primate genomes, and complete pangenomes of 65 individuals, the most in-depth analysis to date of human genetic variation from telomere to telomere.

In the Mackay-Anholt laboratory, Anurag Chaturvedi and colleagues used Drosophila to analyze the genomic response to neurotoxic effects of chronic arsenic exposure at single cell resolution. Arsenic remains the most prevalent environmental toxin in many countries in Asia and some regions in the United States. In a paper published in *Frontiers in Toxicology* the team reports sexual dimorphism and sexual antagonism in gene expression changes after exposure to arsenic with differential gene expression in females being biased toward neuronal cell populations and in males toward glia. They identified arsenic responsive biological processes and genetic interaction networks that could be translated to human gene networks.

Renee Cottle and her group continue to advance gene therapy for metabolic liver diseases. Using CRISPR-Cas9 technology, they corrected genetic defects in hepatocytes from a mouse model for hereditary tyrosenemia type 1 *in vitro* and then returned the modified hepatocytes back into the recipients. This *ex vivo* transplantation approach holds great promise for applied gene therapy in human patients.

Finally, using long-read sequencing methodologies, Gavin Arno, a member of the Center for Human Genetics based at the Greenwood Genetic Center, has identified numerous new genes that contribute risk for retinal disorders. Each new gene can be a potential therapeutic target for the treatment of retinal disorders and prevention of blindness.

These discoveries underscore the benefits of basic biomedical research. At a time that global scientific leadership of the United States is in peril, it is my hope that our representatives in Washington will realize the importance of strong support for the National Institutes of Health.

I wish you a successful Fall semester, and Go Tigers!

Summer Symposium 2025: Advances in Ancient DNA Research

by Gauri Bhide and Alexandra Randazza

The 2025 Summer Symposium of the Center for Human Genetics was organized on May 16th at The Arts Center, Greenwood. The theme for this year was *"Evolutionary genetics in human health and disease".* The event lineup had four plenary lectures from distinguished scientists, eight 5-minute talks from select graduate students and postdocs and 26 poster presentations, each displaying innovative research on how evolutionary genetics can be utilized to better our understanding of human health and diseases.

The first speaker was Dr. Antonio Capra from the University of California at San Francisco, who presented his research on utilizing ancient DNA, population-scale genetic databases and machine learning to investigate ancient hominin traits and the phenotypic influence of Neanderthal ancestry in modern human populations. Various genes inherited from Neanderthals shape traits such as metabolism, disease susceptibility, circadian rhythm and skin color and contribute to our modern adaptation as well as gene regulation. Machine learning models can now be used to predict the molecular phenotypes of ancient genomes and identify divergence in gene expression, splicing, and genome folding between ancient hominins and modern humans. Some of these introgressed variants are predicted to contribute to diseases, but it does not mean that they cause the disease. So, ultimately, you need not run to the doctor solely because you have Neanderthal genes!

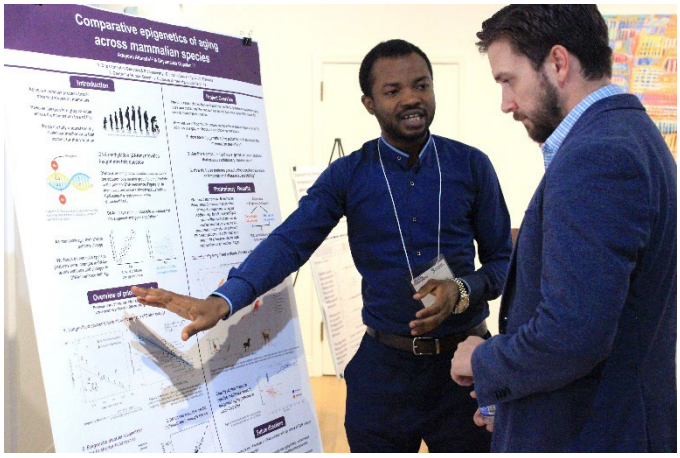
Next up was Dr. John Lindo from Emory University, who shared his fascinating work using genome-wide selection scans to uncover adaptations in two human populations. His work in the Lipan Apache tribe in southwest North America was quite peculiar as it integrated genomics and oral history to understand the population history. In the Lipan Apache, positive selection was detected in *MAPK23* and *UGT2B7. MAPK23* is associated with construction of narrative memories while *UGT2B7* is associated with the removal of toxins from plants and fungi. This corresponds with the dense oral history and diet in the Lipan Apache ancestral and contemporary populations. The second population Dr. Lindo studied was 14th century Europe before and after the Black Death and the evolution of immune genes associated with the disease. *Yersinia pestis* killed a third of Europe's population acting as a strong force of selective pressure on innate immune and epithelial pathways. This selection is predicted to have contributed to persistence of alleles associated with cystic fibrosis pathophysiology.

Starting the third session, Dr. Megan Dennis from the University of California at Davis presented her research using the complete telomere-to-telomere genome sequence to identify novel, human-specific gene families resulting from genomic duplications and their evolutionary significance. She used long-read sequencing to reveal signatures of selection in a subset of genes that are likely functional in human brain development. She then used zebrafish models to characterize the functions of the genes of interest. To investigate noncoding regulatory features, such as chromatin interactions and *cis* regulation in these human-specific duplications, her laboratory devised a genomic approach combining chromatin-conformation capture with HiFi long-read sequencing. Through utilizing all these methods, new insights about the interplay of genomic expansion and human evolution and disease can be studied.

The final keynote speaker was Dr. Scott Williams from Case Western University, who talked about his research on host-pathogen co-evolution and its contribution to disease susceptibility and severity. *Helicobacter pylori* and

From left to right: Robert Anholt, Trudy Mackay, Megan Dennis, John Lindo, Scott Williams, Antonio Capra, Richard Steet

Mycobacterium tuberculosis were used as case studies for pathogens that have likely co-evolved with humans. Ultimately, the susceptibility and severity of disease from both bacteria depend on host ancestry and pathogen strain.



The poster sessions showcased an extensive collection of research, extending well beyond the main theme of the symposium. They showcased scientific innovations at the Center for Human Genetics, which led to many engaging and insightful discussions. The research posters of these young enthusiastic scientists offered a glimpse into the future of genetic research.

Photo credits – Katelynne Collins

Shannon Lattimore, Administrative Coordinator of the Center for Human Genetics, was the well-deserved recipient of the Center's Award for Excellence for going above and beyond in her role.

This event was made possible due to our sponsors, Illumina, Inc., Thomas Scientific, Zymo Research and PacBio, who presented information about their products at their respective booths. The exhibitors presented informative insights about their products that facilitate our research and, of course, fun goodies to take home.

Gauri Bhide and Alexandra Randazza are graduate students in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University.

Diving into the Wet Lab

by Kaitlyn Williams

The Clemson University Center for Human Genetics (CHG) hosted its first Greenwood campus hands-on wet lab workshop "NEBNext UltraExpress RNA Workshop". The workshop was presented in collaboration with the Clemson University Genomics and Bioinformatics Facility (CUGBF) and took place over two days, March 18th and March 19th. Participants attended the retreat free of charge due to the generous sponsorship of New England Biolabs.

The workshop had 7 attendees, all from the Clemson Center for Human Genetics. Attendees were a mix of graduate students and staff scientists.

The workshop provided participants with hands-on experience in RNA library preparation, covering all steps from rRNA depletion to library quality control. Each participant successfully produced two high-quality libraries from reference RNA.

New England Biolabs graciously provided all materials for the workshop. We hosted a NEB Field Application Scientist and a NEB Application Scientist who primarily led the workshop.

Additional instructors under the direction of Dr. Trudy Mackay (CHG; Kaitlyn Williams and Sidney Angner) and Dr. Christopher Parkinson (CUGBF; Dr. Maslyn Greene), and Dr. Lela Lackey (CHG; Abigail Hatfield) assisted with teaching.

We plan to offer other genomic workshops and seminars throughout the year annually.

One participant notes: "I would absolutely recommend this workshop to other individuals at Clemson who work in research".

The CHG Genomics Core

Upcoming events for Fall 2025

Lunch and Learn sessions

- Thomas Scientific & Corning Lunch and Learn on August 19th at 12:00 pm
- Agilent Lunch and Learn on September 3rd at 11:30 am
- 10X Genomics Lunch and Learn on September 24th at 10:30 am

Wet Lab Workshops - Dates To Be Decided

- Agilent DNA Library Prep Workshop
- Oxford Nanopore Technologies Long Read DNA Workshop

Collaborative Bioinformatics and Genomics Workshop – Date To Be Decided

- Single Cell Sequencing Workshop

Kaitlyn Williams is the director of the Genomics Core Facility at the Center for Human Genetics at Clemson University.

For information about events she can be contacted at kaitly6@clemson.edu

Trudy Mackay Receives the Darwin-Wallace Medal from the Linnean Society

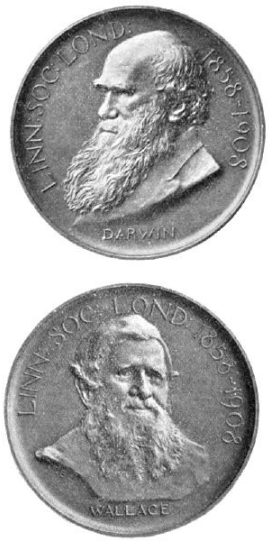
Trudy Mackay, Director of the Center for Human Genetics, received the Darwin-Wallace Medal from the Linnean Society during a ceremony at Burlington House in London, UK, on May 22, 2025. Founded in 1788 and named after the Swedish naturalist Carl Linnaeus, the Linnean Society is the oldest learned society devoted to the study of natural history.

Charles Darwin and Alfred Russell Wallace joint paper *"On the Tendency of Species to Form Varieties; and the Perpetuation of Varieties and Species by Natural Means of Selection"* was read at the Linnean Society on 1 July 1858.

The first Darwin-Wallace Medal was awarded to Alfred Russell Wallace in 1908 along with six other distinguished scientists. Thereafter Darwin-Wallace Medals were awarded every fifty years, in 1958 and 2008. From 2010 onward, medals were awarded annually. Previous recipients include historical luminaries of evolutionary biology, like Francis Galton, Ronald Fischer, J.B.S. Haldane, Ernst Mayr, and contemporary scientists Peter and Rosemary Grant, Brian Charlesworth, and Nobel laureate Svante Paäbo.

Mackay was recognized for her "essential and groundbreaking contributions to the analysis of quantitative traits."

On receiving the Darwin-Wallace Medal, Mackay said: "*I was surprised and delighted to learn that I am the recipient of the 2025 Darwin–Wallace Medal. It is a great honor to join the ranks of the celebrated evolutionary biologists who are recent and past recipients of this prestigious award."*



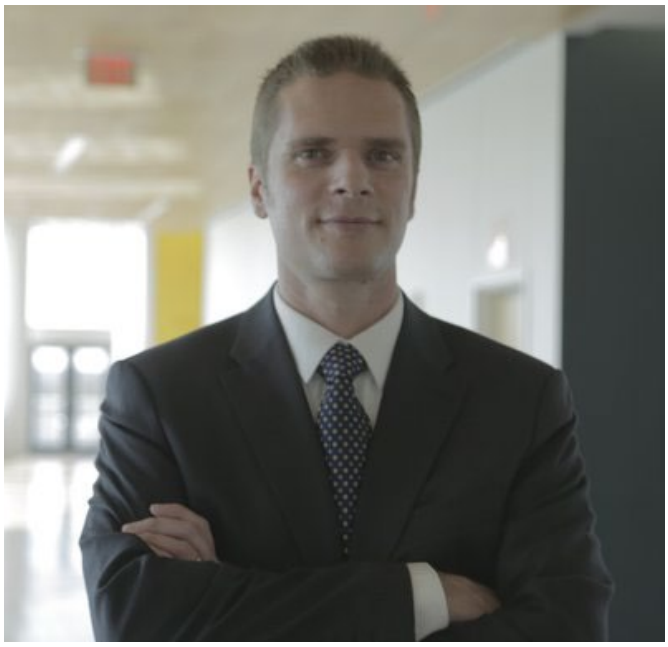
DARWIN-WALLACE MEDAL
1st July, 1908.

CRISPR on the Move

by Austin Herbert

On Friday, January 24th, 2025, Dr. Rodolphe Barrangou, Todd R. Klaenhammer Distinguished Professor in the Genetics and Food, Bioprocessing and Nutrition Sciences program at North Carolina State University presented a seminar titled *"Applications and implications of genome editing technologies"*. Since 2005, Barrangou has held positions at both industrial and academic institutions including Dupont, Pennsylvania State University, and most recently, North Carolina State University. He is a recipient of the prestigious Canada Gairdner International Award, the National Academy of Sciences award for microbiology (2017), and a member of the US National Academies of Sciences and Inventors (2018, 2019). Barrangou also serves as the editor-in-chief for the CRISPR Journal.

In the early 2000s, Barrangou published the genetic characterization and genome sequencing of bacteriophages and bacteria essential to industrial processes like fermentation. This included the elucidation of the life cycle of bacteriophages isolated from sauerkraut fermentations, and whole-genome sequencing of *Lactobacillus acidophilus NCFM*, a lactic acid bacterium commonly used in probiotics. These studies proved essential for improving fermentation processes and generating novel probiotic strains.



Dr. Rodolphe Barrangou

Just as humans are susceptible to virus infection bacteria are susceptible to bacteriophages. These phages function in a similar manner to viruses that infect humans, they penetrate cell membranes and hijack the host replication machinery to replicate and thrive. Though the function and mechanism of phages had been well known through the late 1900s, bacterial immune pathways utilized to resist and counter bacteriophage infections were not well characterized until much later. This is thanks to the advent of whole-genome sequencing technology. In 2007, in collaboration with Nobel laureate Dr. Jennifer Doudna, Barrangou and collaborators published the first paper identifying and characterizing clustered regularly interspaced short palindromic repeats and associated *cas* proteins, better known as the CRISPR/CAS system, from *Streptococcus thermophilus*. The CRISPR/CAS system is regarded as an adaptive immune system utilized by prokaryotes to combat bacteriophage infections. Upon infection by a bacteriophage, bacterial host machinery will chop up the phage genome and integrate those pieces into its own as CRISPR elements. Then, the next time the host is infected, *cas* proteins utilize CRISPR sequences homologous to the infecting phage to find and degrade the intruder. Thus, CRISPRs serve as a "memory" of phages that the host knows as dangerous and the *cas* proteins utilize those memories to provide resistance to future infections.

When investigating the *S. thermophilus* genome, Barrangou discovered that these CRISPR elements contained high sequence homology to pieces of previously identified phages. Furthermore, he identified CRISPR elements as a contributor of sequence variation between strains of *S. thermophilus*. This prompted the hypothesis that CRISPR elements served as a genetic memory of previous phage infections, and that variation in CRISPR elements among strains is due to exposure to different phages. To assess this hypothesis, Barrangou utilized a phage sensitive strain of *S. thermophilus*, a bacterium widely used in the dairy industry, and two phages isolated from yogurt cultures. By continuously exposing this bacterium to the two phages, he was able to create novel *S. thermophilus* strains with resistance to one or both infectious phages. Sequence analysis of the phage resistant mutant *S. thermophilus* strains revealed expansion of the CRISPR loci by inclusion of sequences from the phages they were challenged with.

Barrangou's research opened a new world of biotechnology with extensive applications in agriculture and medicine. Since 2007, Barrangou has become Co-Founder and CEO of CRISPR Biotechnologies, Co-Founder and CSO of Ancilia Biosciences, Co-Founder, President and CSO of TreeCo, and Co-Founder and scientific advisory board member of Intellia Therapeutics. CRISPR gene editing has found a wide range of applications. For example, traditional breeding for favorable traits like cold tolerance in trees usually takes several decades. However, Barrangou's company TreeCo employs CRISPR gene editing to improve economically important traits in a matter of months. In another case, Intellia Therapeutics harnesses CRISPR gene editing to modify T cells to recognize antigens on normally immuno-evasive cancers. The highly cell-type specific targeting of these modified T cell therapies has the potential to replace non-specific chemotherapies often accompanied by adverse side-effects. Moving forward, Barrangou continues to lead his laboratory at North Carolina State University profiling differences in CRISPR/CAS systems among prokaryotes to develop novel gene editing technologies.

Austin Herbert is a graduate student in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University.

Learning the Biology of Genes a Few at a Time

by Alp Ummet

On March 3, 2025, the Clemson University Center for Human Genetics hosted Dr. Nancy Cox, the Mary Phillips Edmonds Gray Professor of Genetics at Vanderbilt University Medical Center, as part of the Distinguished Lectures in Human Genetics series. Her seminar, titled *"Learning the biology of genes a few at a time - easier and more powerful than one at a time!"* provided a thoughtful and engaging look at how studying groups of genes - rather than one at a time - can reveal much more about the complexity of human disease.

Cox is a leading expert in quantitative human genetics. Her work focuses on integrating large-scale genomic data with real-world clinical outcomes, particularly for common complex diseases. After completing her Ph.D. in Human Genetics at Yale University, she conducted postdoctoral research in psychiatric and diabetes genetics before joining the faculty at Vanderbilt in 2015. She also plays an active role in the Vanderbilt Alzheimer's Disease Research Center.

She began her talk by reflecting on how far the field has come, from struggling to identify even a handful of associated variants decades ago to now being able to map thousands across the genome. Yet, she emphasized, many of these variants lie outside coding regions, and understanding how they influence disease requires following their impact through layers of regulation and gene expression.

One of the cornerstones of Cox's work is Vanderbilt's vast electronic health record (EHR) system. It includes data from nearly 4 million individuals, with over 330,000 enrolled in a biobank that links clinical records with genomic data. More than 150,000 of those individuals have already been genotyped. This offers a unique opportunity to study the effects of genetic variation over time, often across decades of health data, enabling her team to explore how genes influence not just isolated conditions, but patterns of disease progression.

Using this resource, Cox and her team focus on genetically predicted gene expression and its relationship with the "medical phenome"—the broad landscape of health traits, conditions, and outcomes present in patients' records. Rather than isolating genes one by one, her approach looks at how sets of related genes behave together and how that translates into real-world biology.

A major example in her presentation centered on the GLP1R pathway, targeted by a class of drugs known as GLP-1 receptor agonists. These medications were originally designed to help regulate blood sugar in people with type 2 diabetes, primarily by slowing gastric emptying and stimulating insulin production. But Cox pointed out that much of their real-world impact appears to go far beyond what was initially expected.

In practice, GLP-1 receptor agonists often lead to substantial weight loss, not just because of digestive effects but due to changes in the brain's reward system. These drugs reduce food craving and influence behaviors linked to addiction, such as alcohol use, gambling, and compulsive shopping. They also significantly lower the risk of cardiovascular and kidney disease and even reduce overall mortality in long-term studies.

Dr. Nancy Cox

The GLP1R pathway is large, involving roughly 47 genes with numerous feedback loops and branches. When Cox's team studied the predicted expression of these genes as a group, they found strong associations with a wide range of traits: diabetes, obesity, heart disease, and more. These associations help explain why GLP-1 agonists seem to affect so many systems at once.

To navigate this complexity, her team now studies smaller subsets of the pathway, just a few genes at a time, to better understand which ones are tied to specific effects. For example, one subset might show stronger links to reward-related behaviors, while another is more involved in inflammation or cardiovascular traits. This modular approach helps pinpoint what parts of the pathway are driving which outcomes, making it easier to connect genetic data with drug response or disease risk.

In closing, Cox reminded the audience that while it is tempting to treat genetic discoveries like a checklist - one gene, one disease - the truth is rarely that simple. Diseases arise from networks of interacting genes, each contributing in small but meaningful ways. And when we shift our focus from isolated signals to the broader architecture of gene function, we can begin to make more accurate and useful predictions.

Her talk was a reminder that deeper understanding in genetics does not always come from more data; it comes from asking the right kinds of questions. By studying genes in their biological context and thinking in terms of systems and pathways, Cox's work opens new doors for translating genetic research into human health.

Alp Ummet is a graduate student in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University.

Turning Unexpected Test Results into Life-Saving Diagnoses

by Bibhu Simkhada

As a part of the ongoing Distinguished Lectures in Human Genetics, the Clemson University Center for Human Genetics hosted Dr. Diana W. Bianchi on March 31st, 2025. At the time of the lecture, Dr. Bianchi was the director of the National Institute of Child Health and Development (NICHD). Previously, she has also served as a member of the board of directors of the American Society for Human Genetics, council member at the American Pediatric Society and the president of the International Society for Prenatal Diagnosis. Her lecture featured an excellent synopsis of the work that she has built over the years, where she uses the non-reportable results from the cell-free DNA (cfDNA) as a biomarker for early detection of maternal cancer.

The use of cfDNA sequencing in the early 2000s revolutionized the pre-natal testing for many disorders that arise from karyotype abnormalities including trisomy 13, 18 and 21. Over the years, cfDNA has been established as a gold-standard for prenatal testing, and an economic alternative for the more costly and laborious biochemical assays. However, in rare cases, the results from cfDNA sequences are non-reportable. This can be due to several factors such as fetal/placental mosaicism, co-twin demise, chromosomal copy number variants, organ transplant and occult malignancy. Occult malignancy generally refers to a type of malignant tumor whose primary site cannot be identified in preemptive evaluations. This is detectable in cfDNA as DNA fragments from tumor necrosis and apoptosis are released and can travel to placental regions.

Across the US, 12 laboratories perform prenatal screening using the cfDNA. When different laboratories analyze the cfDNA data, their proprietary algorithms either do not report cancer detection, or if detected, patients are often reassured by the lack of symptoms. Bianchi followed up with individuals to potentially use these non-reportable results as a method for actionable early detection of cancers. Recruitment for the study required the participants to be over 18 years, asymptomatic of cancer, and have a healthy fetus. The study design constituted several well-devised medical screenings, including one with a genetic counselor and an oncologist, along with hematological, biochemical, and genomic testing to detect known tumor signatures, followed by whole-body radiographic imaging. Contrary to the differences introduced by laboratory-specific protocols, her study design introduced a uniform and standardized cancer screening checklist.

After a 5-year follow up, 52 out of the 107 (48.6%) assessed individuals developed cancer. Among those with positive diagnosis, ~60% had lymphoma, ~17% had colorectal cancer, ~8% had breast cancer, and ~15% had other rare cancers. A closer look at their non-invasive prenatal testing (NIPT) plot revealed an aberrant distribution in all 52 individuals. Bianchi also observed that normal tests generally recommended in the literature were not helpful with cancer detection; however, cfDNA-seq, whole genome sequencing and MRI imaging together revealed several distinct (and strong) patterns for cancer detection.

Although these biomarkers can be strong indicators for early cancer diagnosis, Bianchi expresses concern that positive diagnosis might ruin pregnancy experiences, especially for

Dr. Diana Bianchi

first time mothers. However, directly quoting some patients, she indicated that most patients valued receiving these results despite the added stress of cancer diagnosis during pregnancy. Patients were especially appreciative when medical providers were direct, objective and transparent with the results, and established a follow-up plan. Furthermore, she argued that pregnancy alone should not be a reason to delay further management or treatment for a disease with grave consequences. She also added that in her initial assessment, 11 participants with stage 2, 3, or 4 cancers were eligible for potentially curative treatments.

During a meeting with students, Bianchi shared some strong motivators behind her work. She spoke about the loss of a close family member to malignant carcinoma early in her career which deeply highlighted to her a need for early cancer detection. Additionally, having worked with a mentor with a child with Down syndrome made her aware of the importance of non-invasive prenatal testing. These experiences, along with the increasing accessibility of sequencing technologies allowed her to explore the idea of using non-invasive prenatal testing for cancer detection. Finally, she encouraged students to pursue their ambitions and concluded the meeting with a simple yet powerful reminder “The hardest part is to get started.”

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

Drosophila Models of Human Degenerative Disease

by Kathryn Howe

On April 7th, Dr. Nancy Bonini, the Florence R.C. Murray Professor of Biology at the University of Pennsylvania, delivered a Distinguished Lecture in Human Genetics titled *"Insights into the brain from Drosophila models of human degenerative disease."* Bonini is a member of the National Academy of Sciences and the National Academy of Medicine. She received the March of Dimes Basil O'Connor Award, the NIH Outstanding Investigator R35 award and the Glenn Award for Research in the Biological Mechanisms of Aging, among many other honors. While she has covered many areas in her career, her lecture focused on the impact of molecular chaperones in neurodegeneration.

Drosophila melanogaster is a well-established model organism for genetic studies because of its rapid life cycle, it's easy genetic manipulation, the ability to control genetic backgrounds and environmental exposures. In addition, the Drosophila genome contains many genes that are shared with humans. In Bonini's work, the fruit fly enabled studies on the mechanisms by which orthologous genes contribute to neurodegenerative diseases.

To start with, Bonini introduced polyglutamine (polyQ) proteins, which contain long repeats of the amino acid glutamine and are associated with various neurodegenerative diseases. When Spinocerebellar type 3 (SCA3) protein, a polyQ protein, is expressed in the fly eye severe degeneration is observed. However, co-expression of a chaperone protein, Hsp-70, prevented the neurodegeneration. Further studies showed that the expression levels of the disease protein and chaperone proteins determined the extent of neurodegeneration. When there were low levels of SCA3 alone, the eye appeared normal, but when Hsp-70 was added, the neurodegeneration observed was severe. Bonini also demonstrated that polymorphisms of *Hsp-70* were a risk factor for Parkinson's disease.

To further describe the versatile advantages of fruit flies, Bonini presented her work on other neurodegenerative disorders, including amyotrophic lateral sclerosis and traumatic brain injury. Flies enable studies on behaviors, genetic interactions, lifespan, and protein interactions. They can also serve as tools for the development of potential therapeutics.

Bonini modeled traumatic brain injury in the Drosophila brain with a piezoelectric actuator that delivers a force to the head of a fly to simulate a traumatic brain injury. The fly would then exhibit uneven locomotion and behavioral defects like those observed in humans after traumatic brain injury. Traumatic brain injury is a substantial risk factor for the accelerated development and progression of neurodegenerative diseases. After successfully modeling traumatic brain injury in flies, Bonini attempted to uncover the mechanisms that lead to neurodegeneration by studying the effect of traumatic brain injury on gene expression in the brain.

Bonini discovered that traumatic brain injury results in upregulation of heat shock proteins. Next, she used RNA-seq analysis to examine the transcriptional response to traumatic brain injuries in greater detail.

Dr. Nancy Bonini

The RNA-seq results showed that from one hour to one day after the injury, there was a significant difference in up- or down-regulated genes. She identified that the AP1 motif, a binding site for a conserved transcription factor critical for glial recovery, could be found in 30-40% of upregulated genes, no matter the time point. AP1 helps to protect the brain. When AP1 expression is knocked down, rapid and dramatic brain degeneration is observed. However, after traumatic brain injury, AP1 is chronically upregulated, and this increased expression persists for decades in people after traumatic brain injury.

After establishing the impact of traumatic brain injury on long-term upregulation of AP1, Bonini hypothesized that AP1 might also play a role in brain aging. She evaluated RNA-seq data to compare transcripts that were upregulated during aging versus those differentially enriched after traumatic brain injury and found that AP1 levels are increased with age. These results were confirmed when she compared whole mount brains from aged flies and flies that received traumatic brain injury treatment and saw a similar pattern of AP1 response in both brains that was not observed in controls.

Bonini's career and use of the Drosophila model to study different neurodegenerative diseases have furthered the understanding of key proteins and genes involved in human neurodegenerative disease processes. Her work showcases the versatility and genetic power of the fruit fly for modeling human diseases. It was an honor to have her share her work with the students and staff of the Center for Human Genetics.

Kathryn Howe is a graduate student in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University.

A Conversation with Shyamalika Gopalan

Can you briefly describe the scope of your research program?

I am interested in deciphering how a person's unique genetics and environmental circumstances influence their traits. To this end, I use computationally-intensive simulations to better understand how evolutionary history has shaped our genetic predispositions to certain phenotypes. I also believe it is critically important to understand how these genetic backgrounds interact with the environments that humans experience in the present day, which are often vastly different than they were for the majority of our history. For this reason, my lab also works on developing trait prediction models that account for environmental variation.

What do you consider the most important question today in population genetics?

I think the most important question we should be asking today is: how can we use population genetic tools to better understand genetic and phenotypic variation in real-world populations? For most of the history of the field, building truly realistic models has been out of reach because representing non-neutral processes, like selection, is very challenging. But with modern computational capabilities, it has become much easier to directly model how features like complex population structure and genotype-phenotype maps can shape the evolutionary process. This has many practical applications, from improving disease prediction in clinical settings to aiding in wildlife conservation and management.

How does your work impact human health?

Most of the traits that we think of as being relevant to human health are complex, since they are significantly influenced by a person's genetics and by their environment. For example, to truly understand a person's lifetime risk of being diagnosed with cancer, we would need to know if they carry cancer-promoting genetic variants as well as their carcinogen exposure levels. I work on building models that are capable of accounting for both types of factors, rather than genetics alone.

What is the most rewarding part of your research in population genetics?

I find it very rewarding to be able to connect a pattern that I have observed in population genetic data with something that happened in the past. Studying human population genetics gives us a way to understand how ancient events have shaped us and connects us to a broader human story. We are still constantly learning new things in this field, which makes the research very exciting.

If you could have dinner with any scientist, either alive or from the past, who would it be and what would you talk about?

Definitely Richard Lewontin. Not only was he a hugely influential theoretician, he was also a fearless science communicator with a passion for social justice. Over dinner, I would love to hear his thoughts on how scientists can effectively engage with the public about human genetic research, particularly in the fast-paced, algorithm-driven age of social media.

What advice would you give young investigators at a time when support for basic research is declining?

My advice would be to think outside the box. There are many non-traditional sources of funding available that can be easier to win because they are not as widely known. Identifying these opportunities does take extra time and effort, but it can be worth it. I also encourage my students to apply for their own funding, especially for fellowships and conference travel. Winning an award of any size provides a morale boost and can help stretch a lab start-up that much further.

What activities do you enjoy when you are not working in the lab?

I love to cook, bake, and spend time in my garden.

Shyamalika Gopalan is an Assistant Professor in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University.

Viewpoint

US Science – The End of an Era

by Robert Anholt

About 50 years ago, cancer was considered a death sentence. Today, many cancers are treatable. The first titanium dental implant was performed in 1965, setting a new gold standard for endodontics. The use of lasers in surgery started in the 1960s and blossomed in the 1980s. When AIDS first emerged as a new infectious disease, it was a fatal condition, but new pharmaceutical developments enable HIV patients to survive and lead normal lives. Advances in anesthesiology resulted in drugs that allow comfortable recovery from anesthesia without nausea. Genomic advances have led to the discovery of variants in *BRCA1* that predispose to breast and ovarian cancer enabling life-saving preventive measures. These advances and many more all depended on years of previous sustained biomedical research, funded largely by the National Institutes of Health.

Advances emanating from biomedical research resulted not only in improved healthcare, but were accompanied by economic developments, including new biotechnology companies and patient healthcare facilities, and the education of the next generation of scientists and clinicians trained to implement research advances to improve the human condition. It has been estimated that each dollar spent for NIH-funded research results in a $2.46 return, a result on investment that would delight any Wall Street broker. Strong bipartisan support for funding of the NIH has served as an economic driver and positioned the United States as a global leader in biomedical technology.

Given this history of success, it is baffling that the current administration has decided to wage a war on science and make deep funding cuts in biomedical research which will result in long-term irreversible damage to the scientific infrastructure of the United States. This policy is either based on the short-sighted misconception that funding biomedical research is an expense rather than an investment, or simply on irrational animosity toward science to appeal to an uneducated segment of the population that harbors a distrust for science and scientists and does not realize that every aspect of their lives is touched by science. It is noteworthy that concerns about the "Big Beautiful Bill" focused on Medicaid, border control and the deficit. Disastrous cuts to the NSF and NIH were not mentioned. The politicization of the biomedical research endeavor, in which organizations that promote diversity, equity and inclusiveness (when did these concepts become dirty words?) are stripped of funding is an ominous intrusion on academic freedom and a not so subtle attempt to disenfranchise vulnerable populations that are already experiencing health care disparities and economic and social hurdles to obtain an education that will enable them to participate in developing future healthcare improvements.

The steep reductions in funding, the attacks on elite universities and academic freedom, the aggressive anti-immigrant policies, and hostility toward foreign students have made the United States an unwelcoming country for talented aspiring young scientists from other countries, which are such an important component of a healthy university community. The word has gone out: the lights of the "shining city on the hill" have been extinguished.

> *Two things are infinite: The universe and human stupidity; and I'm not sure about the universe….*
>
> *Albert Einstein*

European countries and China are jumping at the opportunity to siphon off scientific talent from the United States, providing incentives to recruit senior research scientists away from the US and to attract promising young investigators. The United States' global leadership position in science and technology has already been slipping, while China is investing heavily in developing research capacity. China is poised to take leadership in AI, electric vehicles and renewable energy, and making inroads in genomic science and pharmaceuticals. My advice to students or postdocs who have a passion for pursuing a career in basic biomedical research: learn German or Mandarin.

It takes many decades to educate and train a scientist to an independent biomedical researcher. Most scientists obtain their first assistant professor position in their thirties. Students today are hesitant to embark on a basic research career steeped in uncertainty, choosing alternative careers instead. The pipeline for future scientists will be depleted. This will not only impact the research workforce at universities, but also the biotechnology and pharmaceutical industries which rely on universities as educational resources for recruitment of future employees. The damage to the country will not be immediately evident, but will become painfully apparent five or ten years from now, when it will be blamed on a different administration. Then, there will be no quick fix.

It is easy to take the past medical advances for granted, but what would have happened without postwar NIH support? Cancer might still be a death sentence, dental implant technology would be primitive and without a deep understanding in virology we would not be able to rapidly track new forms of viral infectious diseases, like COVID.

Today, we face new challenges: antibiotic resistance, the emergence of new infectious diseases, obesity, and a variety of medical conditions due to environmental pollution. Building on past successes and facing looming future health challenges should motivate a vigorous investment in biomedical research. Leading a war on science is counterproductive, irresponsible, and a betrayal of the nation.

Robert Anholt is Provost Distinguished Professor in the Department of Genetics and Biochemistry and the Center for Human Genetics at Clemson University. The opinions expressed in this article are his own.

Grants

Anurag Chaturvedi and John Poole received a one-year $25,000 Clemson University Research Foundation Technology Maturation grant to develop high-throughput screening of drugs using Drosophila.

David Feliciano received a two-year $297,000 grant from the American Cancer Society to study neuron control of tumor growth. He also received a $20,000 grant from the Tuberous Sclerosis Complex Alliance for a subependymal giant cell astrocytoma atlas “confirmation”, and an SBIR grant from the Department of Defense to study dexamethasone nanotherapeutics for traumatic brain injury.

Miriam Konkel is co-lead with Dr. Shaun Mahony at Pennsylvania State University of the transposable element working group, which received a two-year grant from the U.S. National Science Foundation National Synthesis Center for Emergence in the Molecular and Cellular Sciences (NCEMS) to study the role of transposable elements in gene regulation.

Jessica Larsen received a one-year $310,834 grant from the National Institute of Neurological Disorder and Stroke to study noninvasive nanoparticle-directed therapy to the peripheral nervous system. She also received a three-year $1,323,950 grant from the National Institute of Neurological Disorder and Stroke for studies on transporting stable RNA across the blood-brain barrier for on-demand translation.

Xinyi Li received an 18-month $30,615 SPARK grant from the South Carolina Alzheimer’s Disease Research Center, SPARK Grant to investigate interpretable statistical and machine learning for precision medicine with abundant features in Alzheimer’s disease.

Qing Liu received a six-month $40,000 SPARK-South Carolina Alzheimer’s Disease Research Center (ARDC) pilot grant to study the Interplay between Alzheimer's disease and cardiac dysfunction through Apolipoprotein E mutation.

Alexis Stamatikos received a five-year $1,906,250 grant from the National Heart Lung and Blood Institute to identify novel atheroprotective mechanisms.

Patents

Andrei Alexandrov, **Rui Che**, **Bhoomi Mirani** and **Monireh Mohammadpanah** filed a patent application, titled “Bacteria-free approach for expressing nucleic acids and proteins in eukaryotic cells.” In: US Patent App. 18/949,053.

Alex Feltus filed a non-provisional patent application with the U.S. Patent and Trademark Office, titled “DNA biomarker panel for the detection of autism spectrum disorder.”

Seminars

On Monday, **September 22**, at 1:00-5:00 pm, the College of Science will hold its annual **Rising Star Symposium** featuring new assistant professors from across the College of Science. The symposium will be in Life Sciences Building 142.

On Friday, **October 3**, at 2:30 pm, **Dr. Jonathan Losos**, William H. Danforth Distinguished University Professor at Washington University in St. Louis, will present a College-wide Discover Science seminar titled “The cat’s meow: how cats evolved from the savannah to your sofa.” The seminar will be via Zoom, https://clemson.zoom.us/j/99081232717.

On Monday, **October 6**, at 2:00 pm, **Dr. Andrew Clark**, Jacob Gould Schurman Professor and Nancy and Peter Family Investigator of the Department of Molecular Biology and Genetics and Chair of Computational Biology at Cornell University, will present a seminar titled “Exploring the genetic architecture of fitness in wild populations”. The seminar will be via Zoom, https://clemson.zoom.us/j/96034570631.

On Monday, **October 27**, at 2:00 pm, **Dr. Fernando Pardo Manuel de Villena**, Professor and Chair of the Department of Genetics at the University of North Carolina at Chapel Hill, will present a seminar titled “The Murine Leukemia Virus is undergoing a massive expansion by retrotransposition in the Collaborative Cross: implications for genetic and phenotypic stability of a key mouse resource”. The seminar will be via Zoom, https://clemson.zoom.us/j/99709281596.

On Monday, **November 17**, at 2:00 pm, **Dr. Elissa Chesler**, Professor at the Jackson Laboratory, Ann Watson Symington Chair in Addiction Research, and Senior Director of Integrative Data Science, will present a seminar titled “Systems genetics and multi-species integrative genomics of substance use disorders”. The seminar will be via Zoom, https://clemson.zoom.us/j/99992829825

Publications

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

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Out and About

Emil Alexov was elected Fellow of the American Institute for Medical and Biological Engineering and has been named College of Science Dean's Distinguished Professor.

Robert Anholt joined the Advisory Board of the Blackland Charity Initiative, Ghana. He presented a Workshop on "Dazzle 'Em with Style: The Art of Oral Scientific Presentation (Presentation Skills)" and was a Panel Member of a grant review writing session "Interpreting Reviews and how to get a good grant review" at the 2025 SC INBRE Career Development Workshop, USC School of Medicine, Columbia, SC. He also presented a virtual presentation skills workshop for graduate students in the Department of Neuroscience at the University of Chile, Santiago, Chile. He also served on the NIH Special Emphasis Panel/Scientific Review Group for Program Projects: Centers of Biomedical Research Excellence (COBRE) Phase 1.

Anurag Chaturvedi gave an oral presentation, titled "Unravelling toxicogenomics: From single cell to populations" as part of a workshop at the Drosophila Research Conference in San Diego.

Rui (Jerry) Che gave an oral presentation, titled "Identification of human pathways acting on nuclear non-coding RNAs using the Mirror forward genetic approach" at the 30th annual meeting of the RNA Society in San Diego, CA. He also presented a poster, titled "Two proteins control processing of the bulk of human RNA via a switch in RPP14/HTD2 mRNA isoforms" at the 15th Cold Spring Harbor meeting on Eukaryotic mRNA Processing.

Renee Cottle gave a lecture titled "Cell therapy combining *ex vivo* gene editing with hepatocyte transplantation for inherited metabolic liver diseases" as part of the Miltenyi Mindshare Seminar Series, Miltenyi Biotec. She also gave an invited presentation titled "Cell therapy combining *ex vivo* gene editing with hepatocyte transplantation for inherited metabolic liver diseases" as part of the Department of Biomedical Sciences Seminar Series, New York Institute of Technology, College of Osteopathic Medicine, Old Westbury, NY. Her laboratory presented five posters at the SC INBRE 16th Annual Science Symposium in Columbia, SC, on cell-based genome editing for the treatment of familial hypercholesterolemia, comparison of electroporation systems for CRISPR-Cas9 mediated gene-editing in primary hepatocytes for the correction of hereditary tyrosinemia type 1, *ex vivo* lipid nanoparticle-mediated delivery of CRISPR-Cas9 mRNA into hepatocytes for treatment of familial hypercholesterolemia, and, with **Alexis Stamatikos**' laboratory, gene editing combined with APAP diet-mediated selection in LDLR-/- mouse model of familial hypercholesterolemia, and *ex vivo* multiplex knockdown of ANGPTL3 and CYPOR in hepatocytes as a novel cell therapy for familial hypercholesterolemia. Her laboratory also presented posters at the 20th Annual Focus on Creative Inquiry Forum at Clemson University, and together with the laboratory of **Alexis Stamatikos**, a poster at the Biomarkers of Aging Consortium 2024 Biomarkers of Aging Conference in Boston, MA, and oral and poster presentations at the Southeastern Medical Scientists Symposium 2024 in Nashville, TN.

Tara Doucet-O' Hare, **Kathryn Howe** and **John McCoy** are contributing two chapters in a textbook titled "Transposable

Elements in Health and Disease" by Springer Nature. The chapter titles are "Transposable elements and therapeutics" and "The role of transposable elements in development". They also attended the Inaugural 2025 Carolina Symposium on Genome Integrity and Chromatin Regulation at the University of North Carolina at Charlotte. Tara gave a presentation, titled "The SWI/SNF pathway regulates transposable element expression and provides a new therapeutic opportunity for pediatric tumors".

David Feliciano was an invited speaker and panelist at the 2025 TSC International Research Conference Tuberous Sclerosis Complex in Bethesda, MD.

Laura Finzi was appointed Dr. Waenard L. Miller, Jr. '69 and Sheila M. Miller Endowed Chair in Medical Biophysics. She gave invited presentations at the Physics Department of the Catholic University of America in Washington DC, the American Physics Society Joint March & April Meeting: Global Physics Summit 2025 - Focus Session "DNA mechanics and gene expression," the Single Molecule Biophysics Winter Conference, titled "Macromolecular crowding and DNA condensation", in Aspen, CO, the Single Molecule Biophysics (C-Trap microscopy) Meeting, titled "Macromolecular crowders: Influencers of DNA Structure and Topology" at the Rockefeller University, New York, NY, and the American Chemical Society Fall Meeting, titled "Transcription and its regulation studied with complementary single-molecule methods," in Denver, CO.

Miriam Konkel presented a seminar at the Department of Genetics at the University of Georgia.

Xinyi Li was appointed to the Institute of Mathematical Statistics (IMS) Thelma and Marvin Zelen Emerging Women Leaders in Data Science Award Committee and the IMS Lawrence D. Brown PhD Student Award Committee. She gave presentations at the 2025 Joint Statistical Meetings, Nashville, TN on linear regression using Hilbert-space valued covariates with unknown reproducing kernel, the virtual ASA NSF@75 Conference on empowering precision medicine through interpretable statistical learning: innovations enabled by NSF support, and the 2025 Summer Research Conference of the Southern Regional Council on Statistics on Jekyll Island, GA on nonparametric learning for 3D point cloud data".

Trudy Mackay received the Darwin-Wallace Medal from the Linnean Society in London, UK. Together with **Robert Anholt**, she attended the biannual meeting of the American Philosophical Society in Philadelphia, PA.

Aaron Masino was elected to Sigma Xi, the Scientific Research Honor Society. He also served on NIH Special Emphasis Panel/Scientific Review Group 2025/10 ZRG1 MGG-J (40) P. He presented an invited lecture on artificial intelligence for phenotype discovery and recognition in support of rare disease research and diagnosis at the South Carolina Genetic Counseling Society's 2024 Annual Education Meeting, and an invited lecture on continuous monitoring artificial intelligence for early detection of acute inpatient conditions at the 2024 Neuro Impact Conference. He gave a poster presentation, titled "artificial intelligence for unsupervised population phenotyping to uplift disease genotype to phenotype association discovery" at the American Society for Human Genetics' 2024 Annual Meeting. He has also been appointed to the editorial board of *BMC Digital Health*.

Fabio Morgante gave an invited presentation, titled "variational empirical Bayes approach to multivariate multiple regression, with applications to polygenic prediction" at the CM Statistics 2024 conference in London, UK. He also presented a seminar on exploiting complexity to improve phenotype prediction in the medical biophysics seminar series at Clemson University.

Bibhu Simkhada attended the summer course on Neurobiology of Drosophila at the Cold Spring Harbor Laboratories. He also won second place in the Clemson iGRADS video competition ($2000) and the people's choice award ($250) for his video on Sanfilippo disease.

Alexis Stamatikos was elected Fellow of the American Heart Association and named Discovery Chamber representative for the American Heart Association South Carolina Upstate Region.