Duke Center for Genomic and Computational Biology Newsletter: September 2017

Greetings from GCB! With the help of this newsletter, we hope to keep you updated with the latest news from the Center.

We've added four new Duke faculty to our membership in the past year: **Andrew Allen** (Biostatistics and Bioinformatics), **Bruce Donald** (Computer Science), **Tom Mitchell-Olds** (Biology), and **John Rawls** (Molecular Genetics and Microbiology). We expect to add several more people to our ranks in the next year.

All four of our core facilities continue to grow. Two core facilities, **Sequencing and Genomic Technologies Shared Resource** and **Proteomics and Metabolomics Shared Resourc**e have expanded their capabilities and are relocating to state-of-the-art lab spaces in the newly renovated Chesterfield building in downtown Durham.

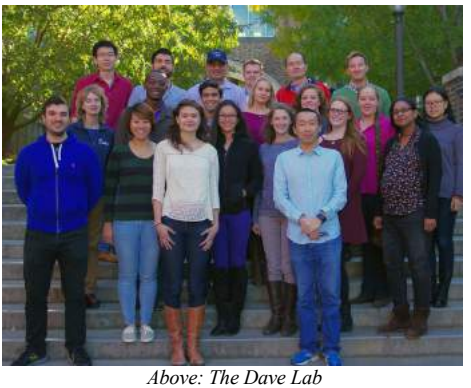
We had 13 students graduate from the CBB program last academic year and have accepted six new students for the 2017 – 2018 school year. We've been collaborating with the **Center for Applied Genomics and Precision Medicine (CAGPM)** on several new educational initiatives as well. This year will be our first involvement with the **Bass Connections** program, and we successfully completed our third annual **Summer Scholars** program.

We have a lot to look forward to in the coming year. I encourage you to visit our website to stay apprised of the latest research, education, and outreach efforts happening in GCB at genome.duke.edu.

Sincerely,
Greg Wray
GCB Center Director

GCB Research Highlights

The **Dave Lab** has taken a cohort of 1,000 patients from around the world with a single type of lymphoma, collected samples from them and turned the samples into DNA and RNA sequencing libraries. After applying next-generation sequencing and analyzing all the data, his lab could see which patients benefitted from the standard therapy and which patients gained virtually no benefit from treatment. Results will be published later this year.



Above: The Dave Lab

The **Chiba-Falek** lab researches the genomic loci associated with neurodegenerative diseases such as Parkinson's and Alzheimer's. Specifically, it examines non-coding structural variants, such as indels and short tandem repeats and their effect on disease risk. Dr. Chiba-Falek's research seeks to understand how changes in gene expression due to these structural variants result in alterations to biological pathways. Her lab utilizes state-of-the-art technologies such as Laser Capture Microdissection, NanoString nCounter Single Cell gene expression, and genome editing (CRISPR/Cas9). The Chiba-Falek lab also uses a variety of model-system approaches such as disease-affected and normal human brain tissues, luciferase reporter system, and the humanized mouse model.

Left: Postdoctoral Associate Lidia Taliafierro works in the Chiba-Falek lab

The **Shen lab** investigates colon cancer metastasis, epigenetic drivers of stem cell differentiation, and the enteric nervous system. Dr. Shen's cancer research focuses on non-coding RNA regulation and metabolism to determine how colon cancer cells are reprogrammed when they metastasize to a new organ. He is collaborating with David Hsu from GCB, as well as Guofang Zhang and Mark Herman from the Duke Molecular Physiology Institute. The Shen lab is also collaborating with GCB faculty Charlie Gersbach and Greg Crawford to study regulatory elements that drive stem cell differentiation and lineage commitment. Dr. Shen's other primary research focus investigates how the nervous system in the gut communicates with the brain and responds to gut bacteria, inflammation, and other stimuli. He is collaborating with Lawrence David in GCB and Diego Bohorquez from the Department of Medicine.

Chesterfield Building Brings New Opportunities for GCB

Since its founding in 2014, GCB has grown into a powerhouse for cross-discipline collaborations and research. We have 26 faculty and counting, many of whom have been recognized both inside and outside of Duke for their scientific contributions, and our core facilities have experienced substantial growth in demand and clients.

To continue improving our operations and better serving Duke clients and researchers, GCB is expanding and establishing a strong presence in Duke's downtown campus in the newly renovated Chesterfield building. Our custom-built, state-of-the-art labs and office space will allow two of our core facilities to expand our staff, boost overall sample capacity, reduce turn-around time, and continue to add cutting-edge technology and instruments.

The Sequencing and Genomic Technologies Shared Resource (SGT) moved into their new lab space in July The Duke Proteomics and Metabolomics Shared Resource (DPMSR) will move later this fall. These state-of-the-art labs will allow us to provide the best possible sequencing, proteomics and metabolomics resources for researchers at Duke and around the world. We expect to continue adding new instruments and technologies to both core facilities in the coming years to respond to the needs of Duke researchers, boost overall sample capacity, and reduce turn-around time.

GCB's presence in the Chesterfield will open new doors for collaboration both with Duke researchers and researchers around the world. Duke is leasing 100,000 square feet of space in the 286,000-square foot building. SGT and DPMSR will be joined by labs in the Duke School of Medicine, the Pratt

School of Engineering, and the Nicolas School of the Environment. In addition, Nutanix, a California-based digital storage software firm, and Biolab, a shared space model for start-ups and growing life sciences companies, will also reside in the Chesterfield.

The Chesterfield, located in Durham's Innovation District, will become a new center of gravity in the life science and technology ecosystem, according to Wexford, the building's developers. This expansion will allow GCB to foster, nurture, and expand interdisciplinary research conducted by our faculty and students, and it will help us become a leader in genomic research.

Gersbach named Allen Distinguished Investigator

Charlie Gersbach has been named an Allen Distinguished Investigator by the Paul G. Allen Frontiers Group. The award comes with $1.5 million over three years to conduct pioneering research in epigenetics.

While the various cell types in the body have the same DNA, they come in hundreds of different types and perform vastly different functions. Epigenetics describes the chemical and structural modification of that DNA that programs this diversity.

Imprecise epigenetic regulation, however, is the primary mechanism by which cells malfunction in diseases including autoimmune, metabolic and neurological disorders. It is also a big part of how cells respond to drugs and other environmental cues.

Gersbach and team have developed several tools based on the gene editing technology CRISPR for untangling this complex web of gene regulation. They have demonstrated the ability to control gene expression by writing epigenetic marks onto the genetic code and have used related techniques to control cell type determination by targeting "master switches" in the genome. More recently, they have developed high-throughput versions of these technologies to map the gene regulatory function of the "dark matter of the genome" that exists between genes.

With the new award, Gersbach and his colleagues plan to build on these proof-of-principle results to take their research to the next level.

Over the next three years, they will develop a robust toolkit that can edit epigenetic marks with precise spatial and temporal control. Their goal is to establish a technology to program any arbitrary epigenetic state that can then be applied to disease modeling, drug discovery and regenerative medicine. They will also manipulate the epigenome of neurons in live animals as a method to better understand the root causes of many complex behavioral functions and pathological states, such as drug response, addiction, learning and memory.

Summer Scholars Program

GCB partnered with the Center for Applied Genomics and Precision Medicine (CAGPM) to design this year's Genome Sciences and Medicine Summer Scholars program aimed at first- and second- year Duke Undergraduate students. The program allows students to work with faculty to develop a passion for research. Students engage in ongoing projects and gain an appreciation for the values of open-ended, student-initiated research.

For many, Summer Scholars gives students their first lab experience and offers an interactive and collaborative experience.

"I have learned not only how to master the pipet, but also to analyze conceptual ideas such as DNA translation and CRISPR in the lab," first-year student Jeffrey Gu said.

Students work with faculty mentors to develop a passion for research. This year's mentors were Ashley Chi, Charlie Gersbach, Xiling Shen, Deepak Voora and Arthur Moseley.

Projects cover a wide range of topics including cancer research, muscular degeneration, proteomic analysis, neurodegenerative diseases and prognostic biomarkers of aspirin responses in patients.

"I've been able to experience the famed 'highs and lows of research,'" Summer Scholar Ammara Aqeel said. "The summer project gave me a sense of how amazing it feels when you produce spotless data and how frustrating it is when you just don't understand what went gone wrong."

Some Summer Scholars, like Jennifer Huh, will continue working with their Summer Scholar mentors into the academic year. "This summer, I was inspired to ask specific questions that have never been investigated," Huh said. "I learned how to construct research questions and investigate them." Huh will continue to research the function of DDRT and RIPK3 in mitotsis of recurrent breast cancer cells. "My Summer Scholars experience has proven to me the importance of pursuing rigorous scientific inquiry and making this my lifelong endeavor," she said.

Back row: Ashish Vankara, Austin Zhang, Jeffrey Gu; Front row: Jennifer Huh, Christopher Lin, Ammara Aqeel

GCB joins forces with Bass Connections

Bass Connections is an interdisciplinary initiative that encourages collaboration among students and professors to research the multi-faceted problems of the 21st century. This program integrates traditional coursework, independent study and community involvement to connect Duke's many institutes and departments.

GCB, in collaboration with the Duke Center for Applied Genomics and Precision Medicine (CAGPM), is involved in two Bass Connections projects: "Blue Devil Resistome" and "Enabling Precision Health and Medicine." Through these projects, researchers at GCB are analyzing big data in innovative ways.

Blue Devil Resistome

The Blue Devil Resistome project aims to analyze the microbial environments around Duke University. Researchers will use samples to assess the extent of bacterial resistance near the medical center, map different bacterial species using geographic information systems (GIS), and develop computational tools to analyze and distribute the genomic information.

GCB Connections: Lingchong You and Susanne Haga
Timing: Summer 2017 - Spring 2018

Enabling Precision Health and Medicine

Precision medicine uses genomic information to diagnose and treat health problems. This Bass Connections team will work toward developing a diagnostic test from genomics and other technologies to meet the real-world needs of patients in the Duke Health System.

GCB Connections; Greg Wray, Greg Crawford and Susanne Haga
Timing: Fall 2017 - Spring 2018

Learn more about Bass Connections: https://bassconnections.duke.edu/.

Spotlight on: Lanie Happ

Hometown: Fort Lauderdale, Fla., and San Jose, Calif.
CBB Starting Year: Fall 2015
Lab Affiliation: Dave Lab
What is your favorite thing about working in the Dave Lab? The people make it a great community to be around. Every day there's a whole bay of computational biologists and wet lab people. It's a really fun group to work with.

What are your research interests? The Dave lab has done a lot of bulk experiments with RNA and whole genome sequencing. The results have made it increasingly clear that the cancers we study are coming from a specific cell type, so understanding the biology of that cell type could help identify novel therapeutics. I want to bring single cell technologies into the lab and use them to handle single cell data. I hope this will eventually connect cancer subtypes to their cell of origin.
What advice do you have for the new CBB students? When it comes to joining a lab, I would recommend thinking a lot more about the people and environment you're going to be around, because grad school is much easier when you're happy.

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