Duke Center for Genomic and Computational Biology Newsletter: Spring 2018

Greetings from GCB!
We've had a busy start to 2018 with publications, new collaborations, and the formation of our fifth core facility. Meanwhile, the Sequencing & Genomic Technologies and Proteomics & Metabolomics shared resources have settled in to the Chesterfield and have started expanding their capabilities. Our two Bass Connections teams are hard at work gathering and analyzing data, and we've funded three new, exciting pilot projects that are well underway. We are excited to see what other research and successes 2018 will bring to our faculty, students and staff.
Sincerely,
Greg Wray

Research Roundup

Here are summaries of a selection of publications by GCB Faculty in 2018 :

Alzheimer's Disease:
Ornit Chiba-Falek and team propose a framework to address conflicting findings with the TOMM40 poly-T allele associations with late-onset Alzheimer's disease phenotypes and their functional effects.

Human Development:
Jenny Tung was part of a team highlighting key outstanding questions in developmental plasticity research along with suggestions for how to answer these questions.

Avshalom Caspi, Terrie Moffitt and collaborators investigated whether early-life victimization stress is associated with genome-wide DNA methylation. They determined that epigenetic effects of early-life stress do not support the hypothesis of major changes in DNA methylation in victimized young people.

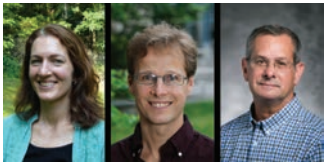
Biofabrication:
Lingchong You was part of a team contributing to the evolving field of biofabrication. Using E. coli, the team designed and optimized growth platforms to direct inorganic nanoparticle synthesis onto porous polycarbonate membranes. They also developed a proof-of-concept experiment to test the photocatalytic properties of their bacterial/ membrane composites.

New Methodologies:
Charlie Gersbach, Tim Reddy, Greg Crawford, and members of the Gersbach lab demonstrated the utility of CRISPR-Cas9-based epigenomic regulatory element screening (CERES) for improved high-throughput screening of regulatory elements in their native chromosomal context.

Amy Schmid, Tim Reddy and team collaborated to develop a methodology to cluster measurements of genomic features such as gene expression levels over time.

Bruce Donald and team developed BBK*, the first provable, ensemble-based computational protein design algorithm to run in time sublinear in the number of sequences. BBK* accelerates protein designs that are possible with previous provable algorithms and efficiently performs designs too large for previous methods.

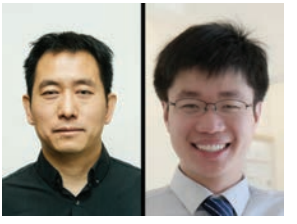
GCB Pilot Projects



Jennifer Wernegreen, Joel Meyer and Richard Di Guilio

Harnessing genomics for environmental toxicology: Exploring how a key anthropogenic pollutant impacts mitochondrial mutation in the model vertebrate, Atlantic Killifish

This project will investigate how chemical pollutants affect mutation rates in natural populations by studying the impacts of polycyclic aromatic hydrocarbons (PAHs) on the genomes of mitochondria (mtDNA) in Atlantic killifish living within and near the Elizabeth River estuary in Virginia.



Lingchong You and Junjie Yao

Listening to Gene Expression in Living Cells

This project will use photoacoustic microscopy (PAM), a hybrid imaging modality that acoustically detect the optical absorption contrast, to create the first prototype PAM system to image different proteins in living cells with high spatial resolution, high imaging speed and high spectral sensitivity. Once the team has developed the prototype, they will use the PAM system to study the dynamics of self-organized pattern formation in engineered bacteria.

Raluca Gordân and Hashim Al-Hashimi

The Impact of DNA Damage on Transcription Factor Binding

Gordan and Al-Hashimi labs will develop and use high-throughput assays and computational modeling to define the influence of DNA damage on transcription factor (TF) binding. The team will work to determine the effects of mismatch damage on TF-DNA binding and characterize the influence of UV damage on TF-DNA binding. Their approach will be applicable to other types of damage, such as RNA:DNA hybrids, cisplatin damage and smoking-induced damage and will provide a critical step forward in deciphering the interplay between transcriptional regulatory proteins and the DNA repair machinery.

GCB Adds a Fifth Core

GCB is excited to announce the creation of its fifth core facility. The Microbiome Shared Resource (MSR) will serve as a centralized hub to enhance existing interactions with the Duke Microbiome Center, the Duke Cancer Institute and the Genomic Analysis and Bioinformatics shared resource to address the role of microbial systems in human healthcare, food production and environmental restoration. MSR will provide access to a variety of services that enable researchers the ability to focus on microbial communities (bacteria, fungi and virus), immune oncology, cancer research and infectious disease.

“We are excited to provide the research community a comprehensive range of services that will help enhance microbiome research from the onset of experimental design through data analysis support,” said director Holly Dressman.

GCB Hosts Open House at the Chesterfield

On February 2, GCB hosted an open house at the newly remodeled Chesterfield Building to celebrate the new laboratory spaces for two of its core facilities: The Sequencing & Genomic Technologies Shared Resource (SGT) and the Proteomics & Metabolomics Share Resource (DPMSR).

The Duke research community had the opportunity to tour the new state-of-the-art lab spaces for the two core facilities and learn more about the cores and the research the cores have helped others at Duke conduct. Representatives from Agilent Technologies, Illumina, Waters Corporation and Thermo Fisher Scientific educated guests about their equipment and capabilities.

Raphael Valdivia, Vice Dean of Basic Science, gave the opening remarks, noting that Duke's presence at the Chesterfield will help allow world-class science to flourish at Duke. SGT and DPMSR's expansion at the Chesterfield will create more space for both planned and unplanned collisions and interactions both within the other Duke labs and with outside industries located in the Chesterfield building.

Four Duke faculty gave brief presentations to describe how theirresearch has been positively impacted by SGT and DPMSR. Their research spanned a large array of topics:

- Utilizing PacBio's Single Molecule Real-Time (SMRT) technology for targeted gene sequencing to investigate the effects of transcription on stability of the underlying DNA.
- Using RNA sequencing technology to sequence whole blood samples from patients infected with malaria to help investigate clock control of malarial diseases.
- Using proteomics to predict the sustained viral response in high-risk patients with HIV/HCV co-infection and discover proteomic biomarkers in HIV and HCV to help improve patient diagnosis and treatment plans using a combined pharmacogenomics/ proteomic approach.
- Utilizingl abel free quantitative mass spectrometry services to discover novel proteins enriched in inhibitory synapses in vivo.

The cores also presented vouchers to 12 lab groups to help cover costs associated with using the cores.

GCB and Sequencing Core host students from NC School of Science & Math

On February 20, Sequencing and Genomic Technologies Shared Resource (SGT) Director Nico Devos and postdoc Devjanee Swain hosted students taking a human evolutionary genomics course at the NC School of Science and Math. Students listened to a short lecture and then toured the SGT facilities at the Chesterfield.

Top: Nico Devos talking to students from NC School of Science and Math; Bottom Left: Postdoc Devjanee Swain from the Wray lab presents a leture on genomics and human evolution to students; Bottom Right: Devos demos the Illumina HiSeq 4000.

Spotlight on Anna Lowegard

Anna Lowegard was born in Sweden and grew up outside of Dallas, Texas. She received her B.S. from the University of Texas at Austin and double majored in Mathematics and Computational Biology.

What drew you to GCB's program?
I really enjoyed the sense of community, especially because Duke was one of the few places that really encouraged grad students to hang out with other students in the program. Durham's affordability was also a huge draw.

What is your primary area of research?
I work in computational structure-based protein design in the Donald Lab. Most of my research is focused on using and developing tools for it.

What excites you about your work?
Considering how much guesswork protein design involves, it's exciting when we can create a protein that works the way we intended. We're not in a place where the process is automated, but I think we can definitely get there.

What are your next steps?
I plan to go to Sweden as a post-doc for a couple of years. I still have family there. I'll probably continue doing protein design, but in a different way.

Is there anything else you would like to tell us?
I have two corgis, Olive and Juneau. My least favorite question is "What is your favorite movie?" because I'm a firm believer in not having favorites – why pick one?

Undergrads Aim to Shape Future of Health and Medicine

GCB teamed up with the Center for Applied Genomics and Precision Medicine (CAGPM) on the inaugural Bass Connections project team, Enabling Precision Health and Medicine.

Thirteen undergraduate students, led by GCB Director Greg Wray, GCB Assistant Director Greg Crawford, CAGPM Director Geoff Ginsburg, and Associate Professor Susanne Haga, have been investigating two issues facing precision health and medicine: family health history and infectious disease.

Anu Sharma shows off a TV studio at Duke.

The Family Health History team launched their study of assessing students' and staff attitudes about family health history. As part of the study, they gathered opinions about two types of educational interventions the team has developed: a video and a print-based resource. Senior Sarina Madhavan and master's student Emily Bullis led the team and filmed the educational video with the assistance of Duke Media Services. Their project focused on assessing public understanding of family history, which will inform the expansion of the MeTree™ application, a patient-facing web-based family health history-driven risk assessment application developed at Duke.

"I was drawn to this team in particular for its intellectual diversity," undergraduate student Chris Zhou said. "We have students spanning a wide range of programs and a mentor network consisting of teaching faculty, practicing physicians, and genetic counselors."

The Infectious Disease team identified genetic markers that can distinguish pathogenic from benign bacteria in Burkholderia and developed a rapid and robust diagnostic assay around these markers. Burkholderia is a pathogen usually causing infection to immunocompromised or hospitalized patients. It is also associated with infections in patients with underlying lung diseases like cystic fibrosis. The team conducted bioinformatics analyses and have identified a few interesting candidate genes. They are are now working on PCR protocols to test their candidates. Their goal is to provide assay results to physicians in the Duke Health System so they can tailor antimicrobial therapy for critically ill transplant patients.

"It's exciting to know that we may be able to develop a practical product for clinical application," undergraduate student Noelle Garbaccio said.

Exploring Duke's Microbiome

GCB has teamed up with CAGPM, Pratt and the Department of Molecular Genetics and Microbiology (MGM) on the Blue Devil Resistome Bass Connections project.

Fourteen undergraduates, led by Lingchong You, Ph.D., are mapping the distribution of antibiotic resistant bacteria on Duke Campus.

The undergraduate students were split into an experimental team, led by third-year MGM graduate student Jonathan Bethke, and a computational team, led by fourth-year biomedical engineering graduate student Carolyn Zhang. "We are evaluating the microbiome of Duke and how resistance spreads and fluctuates in the environment," Bethke said. The experimental team has been collecting samples from buildings, printers, garden benches, the gym, and a host of other locations. They selected a diverse set of sites but also sites that they could easily compare. "We could look at the men's bathroom versus the women's bathroom, or the inside of the bathroom door handle versus the outside," Bethke said.

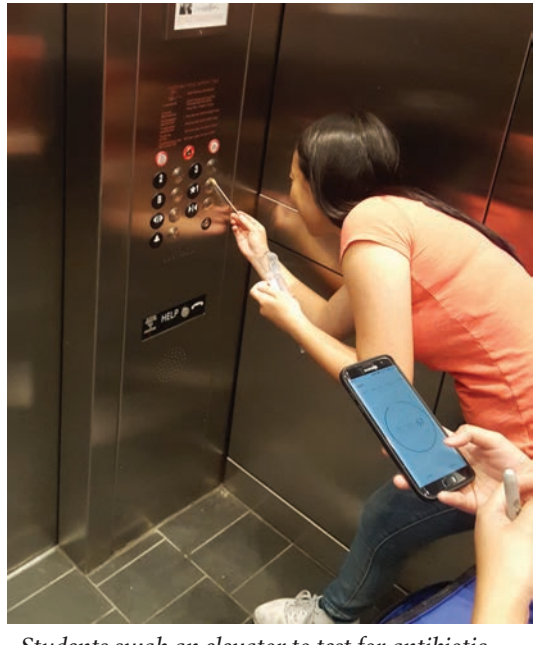
The team is analyzing their data and have found some interesting results: The lowest proportions of antibiotic-resistant bacteria were found in a women's bathroom and West Union; conversely, a bench in the Duke Gardens has consistently had the highest proportion of antibiotic resistant bacteria of all of their sampling sites.

"We would expect a relatively high microbial load on regions outside and closer to the garden," Bethke said. "We did not expect such a high proportion of antibiotic resistance in a more natural environment, though."

However, such results must be taken with a grain of salt--it's hard to attribute these findings to anything in particular. They stressed the importance of long-term measurements to establish a consistent baseline for each site.

The computational team released the data to the public through a database they've created. "We have interactive maps users can look at over time and examine different growth conditions," Carolyn Zhang said.

As antibiotic resistance continues to grow globally, they hope greater awareness of the good and bad microbes around us will facilitate measures aimed to prevent infection.



Students swab an elevator to test for antibiotic-resistant bacteria

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