CENTER FOR COMBINATORIAL GENE REGULATION

Alejandro Ochoa, Assistant Prof. Biostatistics and Bioinformatics, Duke University

Duke | SCHOOL *of* MEDICINE
PRATT SCHOOL *of* ENGINEERING
TRINITY COLLEGE *of* ARTS & SCIENCES

Duke Center for Statistical Genetics and Genomics

GCB Duke Center for Genomic and Computational Biology

CAGT CENTER *for* ADVANCED GENOMIC TECHNOLOGIES

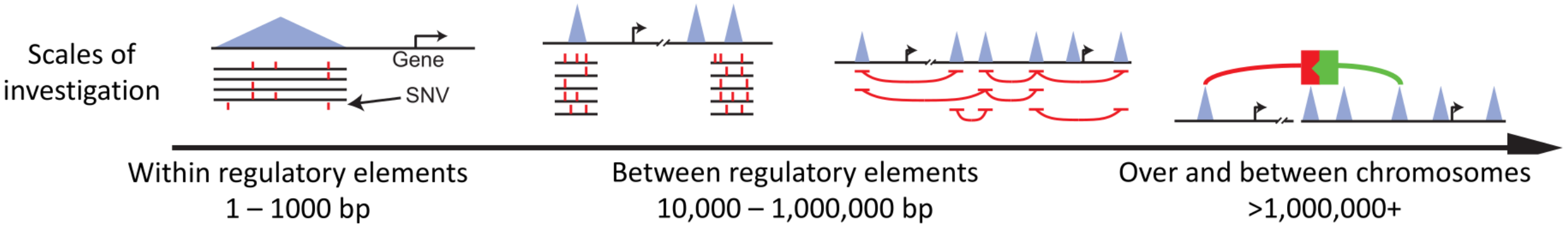
COLUMBIA | COLUMBIA UNIVERSITY IRVING MEDICAL CENTER

UNC SCHOOL OF MEDICINE

https://biostat.duke.edu/research/center-combinatorial-gene-regulation

The goal of the Center for Combinatorial Gene Regulation is to make combinatorial studies of noncoding variants routine

- **Noncoding variants** act in combinations to impact health and disease.
- We are developing **technologies** and **study designs** to model such combinations across a wide range of **genomic scales**:



The goal of the Center for Combinatorial Gene Regulation is to make combinatorial studies of noncoding variants routine

We have established a multidisciplinary team focused on:

- Developing **technologies** to study combinations of noncoding variants
- Realizing **translational** possibilities from understanding combinations of genetic variants in patients
- **Disseminating data** in ways that make results from complex genomics assays usable for the broad biomedical research community

Leadership Team

Wet lab technologies

Statistical and evolutionary technologies

Greg Crawford, PhD
Pediatrics,
Molecular Genetics &
Microbiology

Charlie Gersbach, PhD
Biomedical Engineering,
Surgery

Tim Reddy, PhD
Biostatistics &
Bioinformatics,
Biomedical Engineering,
Molecular Genetics &
Microbiology

Greg Wray, PhD
Biology,
Biostatistics &
Bioinformatics

Raluca Gordân, PhD
Biostatistics &
Bioinformatics,
Computer Science

Andrew Allen, PhD
Biostatistics &
Bioinformatics

Alex Ochoa, PhD
Biostatistics &
Bioinformatics

Bill Majoros, PhD
Biostatistics &
Bioinformatics

Clinical:

Vandana Shashi, MD
Pediatrics
Genome sequencing clinic

Priya Kishnani, MD
Pediatrics
Pompe/GSDs

Khoon Tan, MD, PhD
Pediatrics
Genome sequencing clinic

Informatics:

Warren Kibbe, PhD
Biostatistics &
Bioinformatics

Schizophrenia Collaborations:

Ali Ghavari, MD
Institute for Genomic Med
Columbia University

Patrick Sullivan, MD
Psychiatry and Genetics
UNC-CH

Project Management:

Shannon Clarke
Biostatistics &
Bioinformatics

Emphasis on CEGS Outreach Efforts

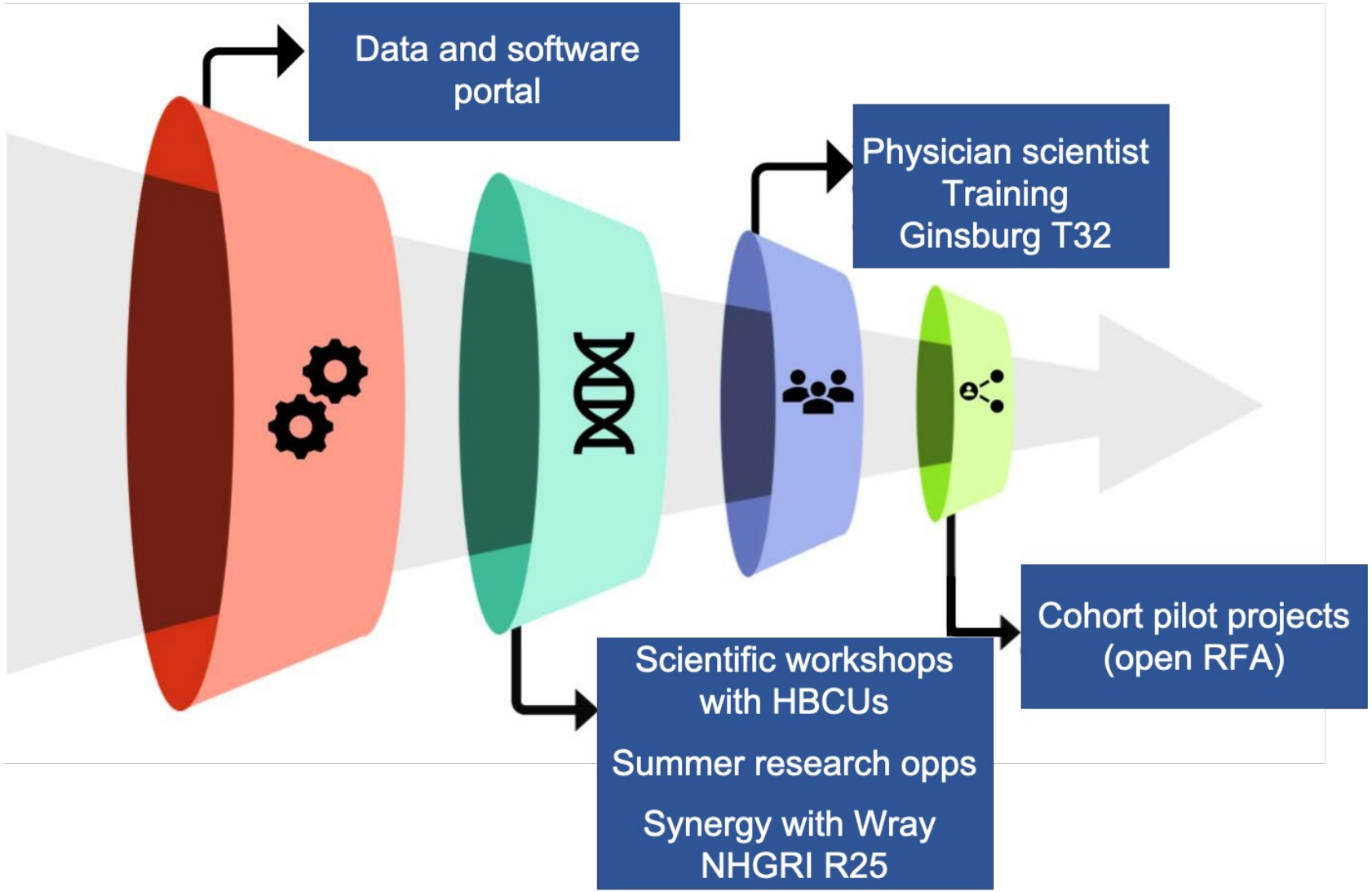
- Partnership with the Genome Technology Development Coordinating Center (Genome TDCC), the Jackson Laboratory, and NHGRI CEGS leadership
- Planned this outreach-specific CEGS meeting!
- Goal to leverage outreach efforts across CEGS sites and also encourage a focus on these critical initiatives

NIH National Human Genome Research Institute

GENOME TDCC

The Jackson Laboratory

Outreach strategy



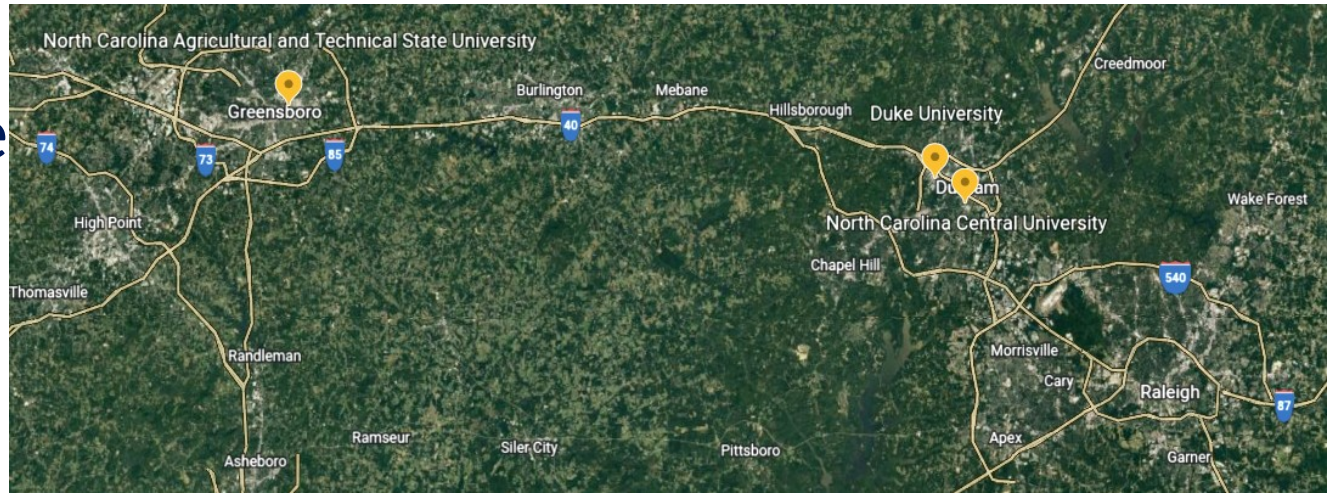
Development of Genomic Resource Modules for a Diverse Workforce

- Alejandro Ochoa, Yuncheng Duan, Revathy Venukuttan, Shannon Clarke, Timothy Reddy
- Mission: To contribute to building a diverse genetics and genomics workforce
  - Teach use of **public resources** to advance their research
- Examples:
  - Predicting the effects of genetic variants on gene regulation
  - Predicting how changes in gene regulation contribute to disease

Development of Genomic Resource Modules for a Diverse Workforce

Target audience, partnerships:

- Researchers from greater Raleigh/Durham interested in genetics/genomics, wanting to use existing data.
- Focus on historically marginalized communities
  - Duke BioCoRE
  - Local HBCUs: NCCU, NC A&T
- Students with limited programming experience



DID YOU KNOW...

People of African ancestry are 4 times more likely to develop kidney disease than Caucasians.

People of African ancestry have a high risk of kidney disease because of changes in the apolipoprotein L1 (APOL1) gene.

However, not all carriers of APOL1 gene changes will develop kidney disease.

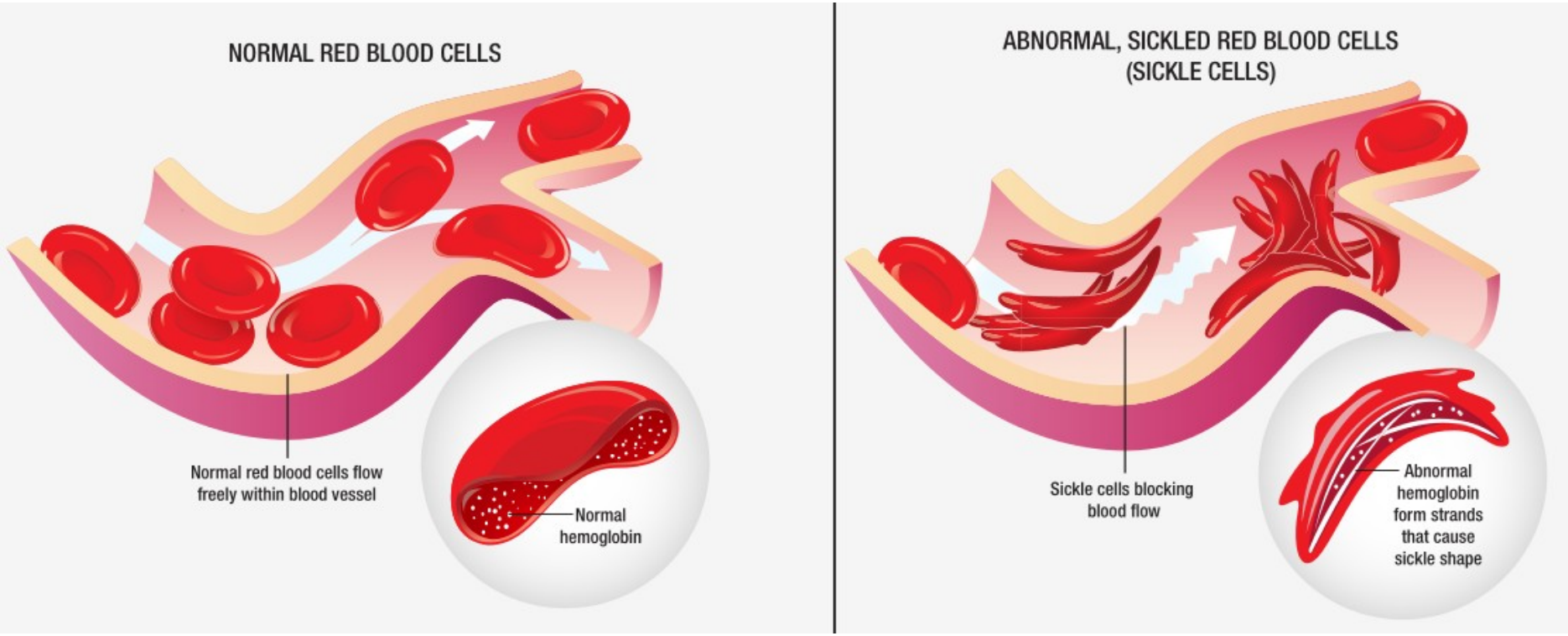
In the U.S., 13% of Blacks carry APOL1 gene changes that cause kidney disease. 70% of Blacks with diagnosis of focal segmental glomerulosclerosis (FSGS) carry these APOL1 gene changes.

Right now, there is no treatment for APOL1-associated kidney disease, and doctors don't have a way to screen for people with APOL1 gene changes who are likely to develop kidney disease.

Dr. Opeyemi Olabisi and
Dr. Rasheed Gbadegesin

https://dmpi.duke.edu/studies/apol1-study

Sickle Cell Disease



sicklecell.nhlbi.nih.gov

Dr. Allison Ashley-Koch

Disease allele found in gene *HBB*

BCL11A modulates disease severity: a TF with variants that turn on fetal hemoglobin!

Development of Genomic Resource Modules for a Diverse Workforce

Mode of Delivery:

- Taught annually, in person or virtually
- Built upon Data Carpentry platform
    - Day divided into focused modules
    - Substantial time on hands-on practice
    - Common thread: focus on two genetic disease/treatment loci in African ancestry (*HBB*/*BCL11A* and *APOL1*).
    - Workshop leaders take “Data Carpentry for Genomics” course

Development of Genomic Resource Modules for a Diverse Workforce

Day	Type	Topic	Leader
1	Lecture	Clinical motivation: FSGS and SCD	Rasheed Gbadegesin
1	Exercise	Intro to genome browsers	Revathy Venukuttan
1	Lecture	Gene structure: central dogma, splicing	Bill Majoros
1	Exercise	Gene expression tracks	Revathy Venukuttan
2	Lecture	Genetic association for common disease	Alex Ochoa
2	Exercise	Genotype data, simulated phenotypes	Yuncheng Duan
2	Lecture	Consequences of genetic variation	Bill Majoros
2	Exercise	Intersect seq data with databases	Apoorva Iyengar
3	Lecture	Analyses using high-throughput seq data	Tim Reddy
3	Exercise	Use and download data from ENCODE portal	Apoorva Iyengar
3	Lecture	Clinical interpretation and current uses/room for growth	Makenzie Beaman
3	Exercise	Navigating dbGaP	Shannon Clarke
3	Lecture	Bridging data generation, analyses, clinical interpretation	Allison Ashley-Koch
3	Exercise	Pitch research questions	Alex Ochoa
3	Lecture	Closing thoughts: FSGS, APOL1	Opeyemi Olabisi

Development of Genomic Resource Modules for a Diverse Workforce

Other Key Components:

- Highlight career pathways
  - Clinical and basic science endpoints, various levels of education
- Identify mentors also from historically marginalized communities
- Network of researchers, internships, rotations
- Partnering with NCCU/Duke Communication Summer Internship program to recruit interns

Development of Genomic Resource Modules for a Diverse Workforce

- Individuals will leave with:
  - Foundational knowledge of key genomic data resources and clinical motivation for analyzing these datasets
  - Methods for analyzing SNP and GWAS data
  - Individual research questions to be explored
  - Identified datasets and next steps for these research questions
  - Opportunities to:
    - Partner with CCGR investigators and collaborators
    - Contribute to future module offerings and recruitment

Next Steps

- Launch modules with offering(s) to Duke BioCoRE scholars
    - Explore opportunities to involve scholars in future offerings and/or networking components
- Design and implement marketing and communication strategy in partnership with departmental communications team and communications intern
    - Visual and graphic materials dissemination
    - Execution of social media campaign
    - In-person presentations at regional schools
- Expand collaborations with regional schools and explore opportunities to incorporate collaborators into module program and/or career pathway offerings