

Areas of research expertise

Transcription | Chromatin Structure and Function | Genomics | Molecular Biology | Systems Biology

Introduction

I have a long-term research goal to understand how regulatory DNA sequences and transcription factors modulate gene expression, influence molecular and cellular phenotypes, and lead to variability in disease progression and treatments. My key contribution to science has been defining the rules by which transcription factors determine where to bind in the genome and characterizing how transcription factors discriminate between genes to regulate. I have a strong technical background in molecular biology, biochemistry, genomics, and computational biology—my group integrates these disciplines to study mechanisms of transcription regulation. As a colleague at UVA and UConn Health, I collaborated with many groups within and outside my department. Together we have used different disease models to study transcription, such as type-I diabetes, coronary artery disease, cancer biology, and viral latency/activation. I am primarily involved in the design of molecular genomics experiments and analyses of genomic data for these projects.

My role as the leader of a lab is to provide the major questions, direction, technical expertise, and training to a talented, collaborative, and congenial group of undergraduate students, graduate students, and postdoctoral fellows. I continue to devote time at the bench and within the Terminal to develop and adopt the latest methods to study transcription factor function. My group members bring their own insights, drive, skepticism, and technical skills to complement one another and I am continually reevaluating their training and development plans as they mature and become more independent. I lead my group by defining important questions in transcription, delving into the classic and contemporary literature, and then designing and implementing hypothesis-neutral experiments, molecular surveys, and statistical analyses to impartially inform on the biology. I will continue to initiate collaborations and interactions with colleagues at UConn to contribute to the research and teaching environment at UConn Health.

Professional

I am requesting tenure within the Investigator professional category. I ask to be considered within the context of the “independent leg.” I began as an Assistant Professor in the fall of 2015 and I have published 10 corresponding author papers since. Each publication was a research article that was independent from my postdoc advisor. These publications are within reputable journals in my field: *Genes and Development*, *Nucleic Acids Research*, *Nucleic Acids Research Genomics and Bioinformatics*, *Genome Biology*, *Genome Research*, *Communications Biology*, *PLoS Genetics*, and *Bioinformatics*. These peer-reviewed publications are within respectable journals, but the perceived impact of a journal does not inform on the influence of any individual article published within the journal. As a testament to the impact of the research itself, these corresponding author publications have amassed over 342 citations in total even though the earliest publication was less than 7 years ago. In addition, I have sustained publications in refereed journals that result from collaborations with the following labs: Dennis Thiele Lab, Duke University; Andrew Holding Lab, University of York; Lea Sistonen Lab, Åbo Akademi; David Gross Lab, Louisiana State University; Anindya Dutta Lab, University of Alabama Birmingham; and Chongzhi Zang Lab, University of Virginia. I have published with each of these labs over the past 6 years (see **Appendix C**), although the collaborations precede publication by many years. In each of these collaborations I analyzed genomic transcription factor binding or RNA expression data and directly contributed to analyses and figures in the publications. In the case of the collaboration with Dr. Andrew Holding, I led the project and I was the first author of the publication as an Assistant Professor.

Since becoming an Assistant Professor in 2015, I have given nine talks at conferences within my field and I organized the symposium “Mechanisms of Transcription” in Ithaca, NY. I have also been invited as an external seminar speaker from the following institutions: University of Utah (2024), Cornell University (2023), University of Iowa (2023), Universidad de Puerto Rico Río Piedras (2022), National Cancer Institute (2020), Northwestern University (2020), University of Houston (2020), Penn State University (2020), Harvard University (2018&2022), and Brown University (2017), and Virginia Commonwealth University (2017).

I have received two independent NIH grants since I became an Assistant Professor and the renewal of the R35 is pending. I was one of two Principal Investigators (PI) on an R21 entitled “*Functional Characterization of Coronary Artery Disease Loci*”, in which we were awarded \$150,000 total direct costs. I also received an R35 entitled “*Mechanisms of coordinate gene regulation by transcription factors*”, in which I am the sole PI. The R35 is a relatively new mechanism of funding. An R35 provides support for an investigator’s research program, as opposed to funding a specific project. This award totaled \$1,250,000 in direct costs over the five year period of the award. The renewal funding is not official until council meets, but the renewal received an impact score of 29. Based on NIGMS data (<https://loop.nigms.nih.gov/2023/04/application-and-funding-trends-in-fiscal-year-2022/>), this application will likely be renewed. Note that unfunded applications with very low (good) overall impact scores are often unfunded because they are declined due to restrictions associated with the R35 mechanism. I requested \$1,681,200 total direct costs requested over years 6-10 (see **Appendix B**). In addition to these independent grants, I have provided collaborative support for many colleagues that have submitted grants and four colleagues have received grants that funded a portion of my salary. I contributed to the design and analysis of molecular genomics experiments to support these four projects.

Teaching and education

Teaching and training students is a highlight of my job. As soon as I decided to come to UConn, I developed the class MEDS5420: Molecular Genomics Practicum. The four linked PDF documents highlight my initial work that was the basis of the molecular genomics curriculum:

- 1) http://guertinlab.org/wp-content/uploads/2019/09/Genomic_ChIP_RNA-seq_analysis.pdf
- 2) http://guertinlab.org/wp-content/uploads/2019/09/Genomic_PRO-seq_analysis.pdf
- 3) https://github.com/stefbekir/bioc8145/raw/master/Guertin_week4/vignette.pdf
- 4) http://guertinlab.org/wp-content/uploads/2019/09/Genomic_ATAC-seq_analysis_190912.pdf

These course materials that I developed have been adopted by others. Associate Professor Richard Meisel of the University of Houston has used the ChIP-seq vignette that I developed for the past 5 years in his course “Genomic Data Analysis.” The ChIP-seq and RNA-seq vignettes linked above were used to establish ChIP-seq and RNA-seq data-analyses at Åbo Akademi University in Finland.

MEDS5420 introduces students with no computational background to the command line and gradually builds upon concepts and skills so that students are capable of building workflows to process and analyze high throughput sequencing data. After basic concepts and command line competency are established, the course focuses on the analysis of ChIP-seq, RNA-seq, and ATAC-seq data. Students learn to use many common genomics software packages to perform such tasks as genome alignment, peak calling, motif analysis, and differential expression analysis. Students are introduced to the statistical computing language R and perform analyses and visualization using an R interface. I offered this class in 2022 and 2023, each time the class was oversubscribed. I capped the class at 12 (2022) and 16 (2023) students, but this summer I streamlined the content (<https://github.com/guertinlab/meds5420>) and I will admit 20 students in the spring of 2024. Students evaluations indicate that this class is well-organized and informative (**Appendix A**).

I taught a grant writing course for 3 years at UVA and students within my section submitted the final product of the class and many were awarded F30 grants. I was the course director for the CMB

training grant research in progress and the last two years two of the trainees who participated in this course received F30 grants. Since I arrived at UConn Health, I have served as a faculty advisor for MD/PhD scientific writing students, I provide in depth feedback for 3-5 students per semester who are submitting F30 grants. Dr. Kimberly Dodge-Kafka organizes the ad hoc workshops and we train students to develop a competitive research proposal. Students submit F30 proposals at the conclusion. I have also given lectures in MEDS6501 (2022 and 2023) and serve as a discussion and topic leader in Foundations of Biomedical Sciences I (2021 and 2023).

In addition to training students and being adopted by others, these teaching materials have directly influenced peer-reviewed publications. These course materials were the basis of the ChIP-seq analyses for Dr. Anniina Vihervaara's 2017 Nature Communications paper entitled: "Transcriptional response to stress is pre-wired by promoter and enhancer architecture" article. The RNA-seq vignette was used by Ashley Bolte and Dr. John Lukens in their 2020 Nature Communication paper entitled: "Meningeal lymphatic dysfunction exacerbates traumatic brain injury pathogenesis." Upon taking my course, Ashley realized that they were analyzing RNA-seq data in an incorrect manner; Ashley modified her manuscript when it was in the revision stage to correct the RNA-seq analysis error.

I currently mentor 2 MD/PhD students, 3 PhD students, and an in-residence Assistant Professor. I have previously mentored four postdoctoral fellows, a Fulbright Master's student, and many undergraduate students. I was student-nominated for the UVA "Dean's excellence in Teaching award" for recognition of my teaching and mentoring in 2020.

Local, regional, and national presence

My research is recognized locally, regionally, and nationally beyond just the speaking opportunities at invited seminars and conferences. I contributed to the NCI's Stimulating Innovation in Breast Cancer Genetic Epidemiology Challenge and co-authored an editorial with my colleagues. I led a research team of scientists from UVA and VCU in the NCI's initiative to stimulate innovation in breast cancer genetic epidemiology and my team won 2nd place in the competition. I have served as an ad hoc reviewer for United States-Israel Binational Science Foundation (February 2022), Worldwide Cancer Research (September 2019), and Cancer Research UK (January 2018). I am an active member of the Cell Stress Society International professional society (2019-current) and the American Society of Biochemistry and Molecular Biology (2022-current). I have peer reviewed for many journals, including *BBA-Gene Regulatory Mechanisms*, *Bioinformatics*, *Cell*, *Cell Reports*, *Communications Biology*, *Developmental Biology*, *Developmental Cell*, *EMBO Journal*, *eLife*, *Epigenetics and Chromatin*, *FEBS Letters*, *Genome Biology*, *Genome Research*, *JCI Insight*, *Molecular and Cellular Biology*, *Molecular Cell*, *Nature*, *Nature Communications*, *Nature Genetics*, *Nucleic Acids Research*, *PLOS Biology*, *PLOS Genetics*, *PLOS ONE*, *PNAS*, *RNA*, *Science Advances*, and *Scientific Reports*.

I also served as the external thesis committee member for Colin Waters (graduated from Dr. Martha Bulyk's lab at Harvard in June 2018) and Emily Kaye (graduated from Dr. Erica Larschan's lab at Brown in July 2017).

I am currently an instructor for a 3-week CSHL summer course on Chromatin, Epigenetics and Transcription (2023 - current). My role as an instructor is to teach the students how to perform ChIP-seq and ATAC-seq experiments and analyze the data. The other 3 co-instructors and I organize the invited seminars of 16 leading scientists in the field over this 3 week period.

Conclusion and additional service

I have contributed to the UConn Health and the University of Virginia in many ways, but I would like to highlight my efforts to positively affect the culture and environment at my institution. As a faculty member, I view inclusion and diversity through three overlapping lenses: mentorship, policy, and culture. Most summers I mentor students as a part of an R25 or UConn Health Research Mentor Match to provide research opportunities to underrepresented students. I directly mentor these students over the summer as they develop in their careers as scientists. I facilitate the recruitment of a diverse

student population by attending conferences such as SACNAS and ABRCMS, which offer career development opportunities for individuals from demographic groups that are under-represented in science. My outreach at these conferences is aimed to increase representation of people of color and underserved populations in STEM through engagement and encouragement of students. To this end, I am involved in shaping graduate student recruitment, admissions, and training. I was a member of the biomedical sciences admissions committee at UVA, I ran the Cell and Molecular Biology Training Grant research in progress seminars, and was the course director for the biomedical sciences student journal club. Within my department at UVA, I successfully advocated for changes to reimbursement policies for graduate student travel, conference registration, and accommodations. I continue these activities as a faculty member at UConn. I am on the biomedical sciences admissions committee for incoming PhD students, I developed a bioinformatics course that is required for Genomics T32 students, and I attend conferences to increase representation and recruitment of underrepresented students at UConn Health.

Culture is the most challenging issue to address from a diversity and inclusion perspective. There is a critical mass of faculty and students at UConn Health who realize the importance of having a diverse workplace that is also inclusive. An effective way to encourage a more inclusive culture is exposure. In order to facilitate a more inclusive culture, I will continue to encourage colleagues to ensure that invited speakers, faculty candidates, and prospective students are diverse and representative.

I continue to join with colleagues at UConn Health to grow my research program and contribute to the successes of my colleagues, students, and professional trainees.