Nelson Barrientos

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Education

Johns Hopkins University — **Baltimore, MD**
School of Medicine, Department of Genetic Medicine — July 2021 - Present
Doctor of Philosophy, Human Genetics

University of Virginia — **Charlottesville, VA**
School of Medicine, Department of Public Health — Graduated in May 2020
Master of Science, Clinical Research

University of Virginia — **Charlottesville, VA**
School of Engineering and Applied Sciences — Graduated in May 2017
Bachelor of Science, Biomedical Engineering

Northern Virginia Community College — **Annandale, VA**
Mathematics and Science — Transferred out in May 2014

Colegio Salesiano Santa Cecilia — **Santa Tecla, El Salvador**
High School Diploma — Graduated in October 2010

Publications

Ma, W. F., Hodonsky, C. J., Turner, A. W., Wong, D., Song, Y., Mosquera, J. V., Ligay, A. v., Slenders, L., Gancayco, C., Pan, H., **Barrientos, N. B**., Mai, D., Alencar, G. F., Owsiany, K., Owens, G. K., Reilly, M. P., Li, M., Pasterkamp, G., Mokry, M., … Miller, C. L. (2022). Enhanced single-cell RNA-seq workflow reveals coronary artery disease cellular cross-talk and candidate drug targets. *Atherosclerosis*, *340*, 12–22. https://doi.org/10.1016/j.atherosclerosis.2021.11.025

Hodonsky, C. J., Turner, A., Khan, M. D., López, N. G., Wong, D., **Barrientos, N.**, Kovacic, J. C., Leeper, N. J., Björkegren, J. L. M., & Miller, C. (2021). Ancestrally diverse study populations benefit eQTL discovery and characterization in coronary artery tissue. Atherosclerosis, 331, e215. https://doi.org/10.1016/j.atherosclerosis.2021.06.659

Ma, W. F., Hodonsky, C., Turner, A., Wong, D., Song, Y., **Barrientos, N.**, Verdezoto Mosquera, J., & Miller, C. (2021).). Single-cell RNA-seq analysis of human coronary arteries using an enhanced workflow reveals SMC transitions and candidate drug targets. BioRxiv. https://doi.org/https://doi.org/10.1101/2020.10.27.357715

Research Experience

McCallion Lab **Baltimore, MD**
Johns Hopkins University School of Medicine November 2021 – Present
Department of Genetic Medicine
Graduate Student
Professor: Dr. Andrew McCallion, Ph.D.

Thesis Research Plan:

My thesis will help elucidate the biological relevance of functional noncoding variation in the context of Parkinson disease (PD) and their impact in disease risk and progression. This will be accomplished by integrating genomic, computational, and experimental strategies. We will use as our model, human induced pluripotent stem cell-derived dopaminergic (hiPSC-DA) neurons with and without α-syn preformed fibril (PFF) treatment. DA neurons on the midbrain are preferentially vulnerable to insults driving PD risk. PFF treatment induces a recognized spectrum of PD-relevant pathological processes in these cells e.g., DA neuron cell death, aberrant mitochondrial function and oxidative stress, and Lewy bodies (LB) pathology.

First, we will catalog the open chromatin regions (OCRs) in these cells/states via ATAC-seq. OCRs are regions that frequently represent gene regulatory sequences, so the integration of these assays with this cellular model are likely to be biologically informative. We will pair this data with transcriptional signatures (RNA-seq), so we know how gene activities are being modulated. Next, we will apply our machine learning (ML) classifier (gkm-SVM/SVR) on the hiPSC-DA neuron OCR data to identify sequence motifs that confer DA neuron regulatory control and specify enhancer function under PD-relevant stress. Evaluation of transcription factor binding sequences will be done by transcription factor (TF) footprinting and correlation with RNA-seq from hiPSC-DA neurons.

We will functionally test selected OCRs harboring PD-associated variation or in PD associated intervals using a lentiviral massively parallel reporter assay (lentiMPRA). These assays will highlight sequences that are active in these cells, allowing us to prioritize enhancer sequences that harbor PD-variation for allele dependent assay. Similarly, I may include variation predicted to impact function, as a further test and refinement of the machine learning algorithm. I can enrich for active sequences by further prioritizing sequences marked by the H3K27Ac histone modification. I will establish a lentiMPRA library to evaluate the effects of disease-associated (or synthetic variants) within validated enhancers. With this, we will assay the pathological relevance of PD-implicated variation and facilitating refinement of the ML classifier predictions.

Lastly, we will test the function and necessity for OCRs harboring PD-associated variants. In contrast to previous aims, here we will use hiPSC-DA neurons from a PD patient in which SNCA is amplified, sensitizing the system to less significant perturbations. Testing will be accomplished by performing CRISPR/Cas deletions of ≥2 identified midbrain enhancer OCRs. Prioritization of OCRs for deletion will be done by integrating ATAC-seq, fine-mapping, promoter capture HiC (performed in parallel by others in the lab), and lentiMPRA data. Subsequently, the risk or non-risk alleles of disease-associated SNPs within one validated enhancer OCR will be reinserted to determine allele-specific effects on cognate genes.

In conclusion, my thesis work will aid in the identification of noncoding disease-risk variants in PD and in illuminating their biological relevance. The impact of this work will extend across common disease and contribute to a better understanding of the consequences of regulatory variation.

Florea Lab **Baltimore, MD**
Johns Hopkins University School of Medicine July 2021 – October 2021
Department of Genetic Medicine
Rotation Graduate Student
Professor: Dr. Liliana Florea, Ph.D.

- Mapping splice QTLs in 467 lymphoblastoid cell lines from the GEUVADIS and 1000 Genomes Projects using sQTLseekeR2.

Miller Lab **Charlottesville, VA**
University of Virginia School of Medicine August 2019 – June 2021
Center for Public Health Genomics
Graduate Research Assistant
Professor: Dr. Clint Miller, Ph.D.

- Differential splicing analysis and mapping splice QTLs in CAD using RNAseq data from 149 samples and the software LeafCutter.

Druzgal Lab **Charlottesville, VA**
University of Virginia School of Medicine August 2016 – May 2017
Department of Radiology and Medical Imaging
Biomedical Engineering Capstone Student
Professor: Dr. Jason Druzgal, M.D., Ph.D.

- Imaging genetics using multimodal MRI and PET scans to create statistical correlations of external medical imaging data with brain genetic information from the Allen Human Brain Atlas.

Shin Lab **Charlottesville, VA**
University of Virginia School of Medicine May 2015 – May 2016
Department of Neuroscience
Undergraduate Research Assistant
Professor: Dr. Jung-Bum Shin, Ph.D.

- Conducted an independent research project to generate knock-in mice for a detailed biochemical characterization of the mechanotransduction complex in the stereocilia of hair cells.

Conferences and Meetings

The Jackson Laboratory **Bar Harbor, ME**
Human and Mammalian Genetics and Genomics: July 2022
The 63rd McKusick Short Course

American Society of Human Genetics **Remote -** October 2020
Session: Improving our understanding of the causes and consequences of cardiometabolic dysfunction.
Abstract and Presentation Title: Differential splicing analysis and mapping splicing quantitative trait loci in coronary artery disease.
Presenter: Nelson Barrientos

Teaching Experience

Emergency Training Solutions, LLC **Charlottesville, VA**
Assistant EMT Instructor October 2017 – December 2019
- Assisted with teaching and mentorship of EMT students.
- Provided workshops for new EMT students to practice their skills.

BME Teaching Fellowship – University of Virginia **Charlottesville, VA**
Teaching Assistant Spring 2017
- Assisted Dr. William Guilford, Ph.D. in teaching the BME Design and Discovery class that is divided in modules where students learn to use machine shop equipment appropriately. Other skills taught include electromechanics with Arduino, CAD for 3D printing and laser cutting, vacuum press, soldering, etc.

Technical Knowledge

Laboratory Skills
- Tissue culture, cell transfection and transformation
- CRISPR/Cas editing and differentiation of human induced pluripotent stem cells
- Gateway BP and LR recombination cloning
- Next Generation Sequencing with Oxford Nanopore technology
- Functional genomics

Computer and Software Skills
- Operating Systems: Windows, IOS, Unix, Linux
- Software: RStudio and R, Python, GitHub, MATLAB, Microsoft Office, CAD

Language
- Spanish: Native
- English: Fluent

Other Work and Volunteer Service

Charlottesville-Albemarle Rescue Squad **Charlottesville, VA**
Basic and Advance Emergency Medical Technician October 2016 – January 2020
- Provided pre-hospital care and transport to patients in need for urgent and emergent medical attention.
- Task included emergency care, scribing, ambulance driving under pressure, training and teaching new EMTs.

University of Virginia Health Center **Charlottesville, VA**
Rehabilitation Services Technician August 2017 – July 2019
- Assisted physical, occupational, and speech language pathology therapists with their in-clinical duties.

Madison House – University of Virginia **Charlottesville, VA**
Student Volunteer Fall 2015 – Spring 2016
- Greeted and assisted patients and their family members to find their destinations inside UVA Health Center.
- Provided indoor transportation to patients and their family members with UVA Health Center's golf cart.
- Assisted patients to get to their vehicles upon discharge.

Academic References

Dr. Andrew McCallion, Ph.D.
Assistant Director, Human Genetics Graduate Program
Professor of Genetic Medicine
Address: 733 N. Broadway, 515 Baltimore, MD 21205
Telephone: 410-502-7533
Email: andy@jhmi.edu

Dr. Liliana Florea, Ph.D.
Associate Professor of Genetic Medicine
Address: 733 N. Broadway, 515 Baltimore, MD 21205
Email: florea@jhu.edu

Dr. Clint Miller, Ph.D.
Assistant Professor of Public Health Sciences
Address: PO Box 800717, Center for Public Health Genomics, MSB 3231 Charlottesville, VA 22908
Telephone: 434-982-0502
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