OMB No. 0925-0001 and 0925-0002 (Rev. 03/2020 Approved Through 02/28/2023)

BIOGRAPHICAL SKETCH

NAME: Boone, David N

eRA COMMONS USER NAME: davidnboone

POSITION TITLE: Assistant Professor of Biomedical Informatics

EDUCATION/TRAINING:

| INSTITUTION AND LOCATION | DEGREE  (if applicable) | Completion Date  MM/YYYY | FIELD OF STUDY |
| --- | --- | --- | --- |
| The Pennsylvania State University | B.Sc. | 05/2003 | Biology/Genetics |
| Vanderbilt University | Ph.D. | 05/2011 | Cell and Molecular Biology |
| University of Pittsburgh | Postdoc | 5/2015 | Breast cancer |
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# PERSONAL STATEMENT

The mission of the Hillman Cancer Center Academy is to provide authentic and mentored, cutting-edge biomedical cancer research and academic preparatory experiences to high school and undergraduate students from underrepresented and disadvantaged (URM/DA) backgrounds. The long-term goal is to leverage our strengths in training and research to increase both the number and diversity of the students prepared to be active members of the biomedical research workforce. If funded, we will do this by welcoming new cohorts of students over the next two years while prioritizing fundraising to endow the Hillman Academy so that we can excite and inspire minoritized students for years to come. I have the expertise, training, and passion on how to teach, train, and mentor pre-doctoral students that is necessary for my role as Director of the Hillman Academy and Vice-Chair of the Cancer Research Career Enhancement Committee.

My current position is tailored to broadening participation and teaching and training the next generation of scientists especially those from URM/DA backgrounds. I have been the acting Director of the NCI R25- and Doris Duke Charitable Foundation-funded Hillman Academy for the past 8 years. The Hillman Academy was named as one of the top global 100 educational innovations in 2019 for our work with Black, Latina/o, low income, first-gen, and Deaf and Hard of Hearing students. For the past 17 years, I have served as a mentor, instructor, and designer of high school and undergraduate summer programming at the University of Pittsburgh and Vanderbilt. I am also the Director of outreach for the Department of Biomedical Informatics including the formerly NIH- (BD2K R25 supplement; co-PI), NLM- (T15), and PA Department of Health-funded Internship in Biomedical Research, Informatics, and Computer Science (iBRIC) program. iBRIC aimed to build a foundation for a career in biomedical data science for URM/DAundergraduate. For iBRIC, I worked directly with faculty from minority serving institutions at the University of Puerto Rico–Rio Piedras, Lincoln University, Howard University and others to recruit and train ~15 students during summer internships at Pitt and CMU. Through these grants, I developed curriculum in cancer genomics that is actively used in a Biochemistry course at Lincoln University. Likewise, I helped to develop and deliver a workshop on causal modeling of breast cancer TCGA data that was taught at UPR and Pitt. Currently, I am co-I on 2 additional R25s that 1) partners with Gallaudet University to provide AI research experiences to the Deaf and Hard of Hearing and 2) develops and creates curriculum with partner teachers to deploy in classrooms in Pittsburgh. I was co-PI on an NSF INCLUDES Design and Development Launch Pilot, entitled “Diversifying Access to Urban Universities for Students in STEM Fields,” and currently am a co-PI on an NSF INLCUDES Alliance that has created a nationwide network improvement community of precollege STEM programs. For this work, there are currently 40 precollege STEM programs involved from 10 urban areas (Pittsburgh, New York, Chicago, San Francisco, Cleveland, New Jersey, Arizona, Colorado, Los Angeles, and Florida). I was also a co-I on an NLM T15 supplement to develop a data science module in RNAseq analysis in a Jupyter Notebook of TCGA data for graduate students. Finally, I am an active member in Pitt’s local Center for the Integration of Research, Teaching and Learning (CIRTL), co-chair of the Hillman Cancer Center’s Education committee, a member of the local Intermediate Unit’s Math Science Collaborative Resource Partners, and a member of Remake Learning demonstrating my commitment to education and connections with the broader Pittsburgh community.

Ongoing projects that I would like to highlight:

**5R25CA236620-03**

Boone (PI)

09/13/2019 – 04/30/2026

University of Pittsburgh Medical Center Hillman Cancer Center Academy

**Doris Duke Charitable Foundation 2016146**

Boone (PI)

01/01/2024 – 12/31/2026

Clinical Research Continuum: High School to College for Students from Underrepresented Groups

**NSF1930990**

Boone/Legg/Allen/Iriti/Morrison (MPI)

09/30/1019 – 08/31/2024

NSF INCLUDES Alliance: STEM PUSH (Pathways for Underrepresented Students to Higher Education Network)

**1R25LM014208-01**

Boyce (PI), Boone (coI)

09/01/2022 – 08/31/2027

Building Accessible and Inclusive Paths for Students in Biomedical Informatics and Data Science

**1R25AI180989-01**

Cooper (PI), Boone (co-I)

04/01/2023 – 03/31/2028

EvolvingSTEM: authentic classroom research curriculum to enhance inclusion and agency in modern life

Citations:

1. Ayoob, J. C., Boyce, R. D., Livshits, S., Bruno, T. C., Delgoffe, G. M., Galson, D. L., ... & **Boone, D. N**. Getting to YES: The Evolution of the University of Pittsburgh Medical Center Hillman Cancer Center Youth Enjoy Science (YES) Academy. Journal of STEM Outreach, *5*(2), 1-15. 2022.
2. Delale-O'Connor L, Allen A, Ball M, **Boone DN**, Gonda R, Iriti J, Legg AS. Broadening equity through recruitment: Pre-college STEM program recruitment in literature and practice. Connect Sci Learn. 2021 Nov-Dec;3(6). PMID: 35295872; PMCID: PMC8923047.
3. Fung, Frey, Valmont..., **Boone DN**. Success of Distance Learning During 2020 COVID-19 Restrictions: Report from Five STEM Traning Programs for Underrepresented High School and Undergraduate Learners. JSO. 4(3) 2021
4. Allen, A., M. Ball, D. Bild, **D.N. Boone**, D. Briggs, D. Davis, L. Delale-O’Connor, R. Gonda, J. Iriti, A. Slinskey Legg, C. Long, C. Matthis, J. Zoltners Sherer, and T. Stol. 2020. Leveraging out-of-school STEM programs during COVID-19. Connected Science Learning 2 (4).
5. King A, Fisher A, Becich M, and **Boone DN**. Computer Science, Biology, and Biomedical Informatics Academy: outcomes from five years of immersing high school students into informatics research. J Pathol Inform. 2017 Feb 28;8:2. doi: 10.4103/2153-3539.201110. eCollection 2017. PMCID: PMC5359992.

# B. POSITIONS, SCIENTIFIC APPOINTMENTS, AND HONORS

**Positions and Scientific Appointments**

2017- Director, Hillman Academy and Doris Duke Charitable Foundation Undergraduate Internship

2015- Director of CoSBBI and iBRIC programs

2015- Assistant Professor, Department of Biomedical Informatics, *University of Pittsburgh*, Pittsburgh

2015-2017 Executive Director, UPCI Academy

2012 Part-time Teaching Faculty, *Robert Morris University*, Pittsburgh, PA

2011-2015 Susan G. Komen Postdoctoral Fellow, *University of Pittsburgh*, Pittsburgh, PA

2008-2011 NSF Science Teaching Fellow, *Vanderbilt University*, Nashville, TN

2005-2011 Graduate Student, *Vanderbilt University*, Nashville, TN

2004 Biochemist/Production Technician, *Aalto Scientific Ltd.*, San Diego, CA

2002-2003 Teaching Assistant/Tutor, *Pennsylvania State University*, State College, PA

2001-2003 Research Assistant/NSF-REU Fellow, *Pennsylvania State University*, State College, PA

1998,1999 Research Assistant/Intern, *West Virginia University,* Morgantown, WV

**HONORS/AWARDS/FELLOWSHIPS**

2021- Editorial Board – Journal of STEM Outreach

2019 Hillman Academy named as a top-100 global educational innovation

2018 - Member- Center for Causal Modeling Executive Board

2017- Vice-Chair UPCI Education and Training Committee

2017 NIH YES R25 Study Section x 2

2016 Session chair – Great Lakes Breast Cancer Conference

2015 Associate Level Certification in Teaching the STEM Disciplines – Center for the Integration of Research, Teaching and Learning (CIRTL)

2015 Session Chair – Endocrinology Annual Meeting, San Diego, CA

2014 Statement of Accomplishment – An Introduction to Evidence-Based Undergraduate STEM Teaching

2014 “Best Oral Presentation” – Women’s Cancer Research Center Retreat

2013-2015 Session Chair – Women’s Cancer Research Center Retreat

2012-2015 Susan G. Komen Postdoctoral Fellowship

2012,15,18 Grand Awards Judge – INTEL International Science and Engineering Fair

2008-2011 NSF GK12 Science Teaching Fellowship

2009,2010 Travel award from Vanderbilt University Graduate School

2007 Travel award from NIH-VNAC training grant

2005-2007 Ruth L. Kirschstein National Research Service Award Training Grant

2003 Evan-Pugh Scholar Award

2002-2003 NSF-REU Fellowship

2002 Edward C. Hammond Jr. Memorial Scholarship

2002 Eberly College of Science Scholar

2001 Phi Beta Kappa academic honor society

2000 Golden Key International Honor Society

1999 National Society of Collegiate Scholars

1999 Allegheny Energy academic and service excellence scholarship

# C. CONTRIBUTIONS TO SCIENCE

**1) lncRNAs and IGF1 in breast cancer**

Insulin-like growth factor 1 (IGF1) signaling is involved in the initiation and progression of a subset of human breast cancers by inducing cell proliferation and survival. Although the signaling cascade following IGF1 receptor activation has been well studied, the key elements of the robust transcriptional response and the molecular mechanisms governing IGF1’s actions are not well understood. ENCODE recently revealed that the majority of the genome is transcribed and that there are more long non-coding RNAs (lncRNAs) than protein coding genes. Several of these are dysegulated in human cancer. However, the studies to determine the mechanisms of how these lncRNAs are regulated and function are in their infancy. In this study we demonstrated with RNAseq that IGF1 stimulation of a breast cancer cell line causes significant changes in the expressions of putative lncRNAs. Two of the top five most highly expressed and consistently regulated lncRNAs are SNHG7 and SNHG15, which are members of the small nucleolar host gene family. Interestingly, while we show that SNHG15 expression is induced by IGF1 signaling, we demonstrate that IGF1 signaling decreases SNHG7 expression by a post-transcriptional mechanism through the MAPK pathway. We further demonstrate that SNHG7 is necessary for proliferation of breast cancer cell lines in a dose-dependent manner. We observed that silencing SNHG7 expression stimulates cell cycle arrest in G0/G1 by altering the expression of many of the same genes as IGF1 signaling and by directly regulating the expression of a significant proportion of IGF1 signaling molecules. Finally, we show with TCGA data that SNHG7 is overexpressed in the tumor cells of a subset of breast cancer patients and that these patients have lower disease-free survival than patients without elevated SNHG7 expression. Therefore, we propose that SNHG7 is a putative lncRNA oncogene that is controlled by growth factor signaling in a feedback mechanism to prevent hyperproliferation, and that this regulation can be lost in the development or progression of breast cancer.

1. **Boone DN** and Lee AV. SNHG7 is a lncRNA oncogene controlled by Insulin-like Growth Factor Signaling Through a Negative Feedback Loop to Tightly Regulate Proliferation. Sci Rep. 2020 May 22. 10(1):8583. PMCID: PMC7244715

b) Chen J, Nagle AM, Wang YF, **Boone DN**, Lee AV. Controlled dimerization of insulin-like growth factor-1 and insulin receptors reveal shared and distinct activities of holo and hybrid receptors. J Biol Chem. 2018 Jan 12. pii: jbc.M117.789503. doi: 10.1074/jbc.M117.789503.PubMed PMID: 29330302.PMCID:PMC5846141

c) Warburton AJ & **Boone DN**. Insights of Global Analyses of Long Noncoding RNAs in Breast Cancer. Curr Pathobiol Rep.2017. Jan 23, 2017. doi:10.1007/s40139-017-0122-1 PMCID: PMC5467540.

d) Farabaugh SM, **Boone DN**, and Lee AV. Role of IGF1R in breast cancer subtypes, stemness, and lineage differentiation.Frontiers in Endocrinology. 2015 PMCID: PMC4408912.

e) **Boone DN** and Lee AV. Targeting the Insulin-like Growth Factor Receptor: Developing Biomarkers from Gene Expression Profiling. Critical Reviews in Oncogenesis. 2012;17(2):161-73 PMCID: PMC3926653

2) **Methylation in breast cancer biology and cell-type deconvolution**

As part of a team of researchers at University of Pittsburgh, Baylor School of Medicine, and Raindance Technologies, I examined the role of methylation in breast cancer and the utilization of methylation for cell-type deconvolution. Tumor phenotypes result from interactions between diverse cell types. Yet it is currently not possible to measure epigenomic and transcriptomic states of constituent cell types without physically isolating them from their microenvironment, which perturbs their interactions and internal states. To gain insights into cancer-related processes within epigenomically defined subpopulations of breast tumor cells within their native microenvironment, we developed Epigenomic Deconvolution (EDec), a two-stage computational method that makes use of cell-type marker loci inferred from IHEC reference epigenomes. The first stage utilizes methylation profiles of tumor samples as an input and outputs average methylation profiles and relative proportions of each constituent cell type in each sample of interest. In the second stage, EDec takes gene expression profiles of the same samples as an input and estimates average gene expression profiles of constituent cell types. When applied to 1184 breast tumor methylation profiles from the TCGA collection the method infers methylation profiles of constituent cell types that closely match the reference methylation profiles of cell types known to constitute breast tumors. The inferred cell type proportions are highly concordant with pathologist’s estimates based on H&E staining. We detected strong association between immune cell proportion and longer survival for triple negative breast cancer patients. Lastly, by analyzing gene expression changes specific to epithelial cells of basal-like breast cancers, we identified gene expression changes in numerous SP1 regulated genes, including mir200 and CDH1. Such changes are consistent with the down-regulation of SP1 that is also identified specifically in epithelial cells of basal-like breast cancers. Notably, down-regulation of SP1 is consistent with *SP1* single copy deletions present in nearly 60% of basal-like breast cancers, but rarely detected in other breast cancer subtypes. Despite not being previously reported, the basal-like breast cancer specific down-regulation of SP1 and deregulation of its targets is highly consistent with the more aggressive and EMT-like phenotype of basal-like breast cancer and the basal-specific effectiveness of mir200 therapy. We show that these cancer cell perturbations could not be detected without EDec because of signal averaging across diverse cell types within complex tumor tissue. These results suggest that EDec in conjunction with newly available reference epigenomes provides a unique approach to gaining new insights into the biology of tumor cells in their native microenvironment.

a) Onuchic V, Hartmaier RJ, **Boone DN**, Samuels ML, Patel RY, White WM, Garovic VD, Oesterreich S, Roth ME, Lee AV, Milosavljevic A. Epigenomic Deconvolution of Breast Tumors Reveals Metabolic Coupling between Constituent Cell Types. Cell Rep. 2016 Nov 15;17(8):2075-2086. PMCID: PMC5115176.

b) Nayak S, Harrington E, **Boone DN**, Hartmaier R, Pathiraja, T, Cooper K, Fine J, Sanfilippo J, Davidson N, Lee AV, Dabbs D, and Oesterreich S. A Role for Histone H2B Variants in Endocrine Resistant Breast Cancer. Hormones and Cancer. 2015 PMCID: PMC4408912.

**3) The transcriptional and biological regulation of c-Myc by the cofactors ARF and NPM.**

The transcription factor c-Myc is essential for proliferation and is one of the most frequently activated oncogenes in human cancer. Although deregulated c-Myc leads to tumor growth, it also triggers apoptosis in partnership with tumor suppressors such as ARF and p53. Apoptosis induced by c-Myc is a critical fail-safe mechanism for the cell to protect against unrestrained proliferation. Despite the plethora of information on c-Myc, the molecular mechanism of how c-Myc induces both transformation and apoptosis is unclear. The goal of these studies was to investigate the molecular mechanisms whereby cofactors (ARF and NPM) are able to selectively and differentially regulate c-Myc-induced transcription and biology. Specifically, we found that ARF directly interacts with c-Myc, which causes the upregulation of Egr1 and the induction of p53-independent apoptosis. I designed, performed, and analyzed the experiments for this project and wrote the two manuscripts for publication. I was the first-author on both papers. I am also a coauthor on a paper that explores the transcriptional and biological consequences of ARF-mediated alterations of post-translational modifications of Myc. Additionally, we discovered that the interaction of NPM with Myc enhances induction of canonical Myc target genes resulting in enhanced hyperproliferation and transformation. I designed, performed, and analyzed experiments for this project. Specifically, I focused on the transcriptional aspect of the project.

a) Zhang Q, Spears E, **Boone DN**, Li Z, Gregory M, and Hann S. Domain specific c-Myc ubiquitylation controls c-Myc transcriptional and apoptotic activitys. PNAS. 2012; 110(3):978-83 PMCID: PMC3549076.

b) **Boone DN** and Hann SR. The Myc-ARF-Egr1 Pathway: Unleashing Myc’s Apoptotic Powe*r.* Cell Cycle. 2011 Jul1;10(13):2043-4 PMCID: PMCID: PMC3234342.

c) **Boone DN**, Qi Y, Li Z, and Hann S. Egr1 mediates p53-independent c-Myc-induced apoptosis via a noncanonical ARF-dependent transcriptional mechanism. PNAS. 2011 Jan 11;108(2):632-7. PMCID:

PMC3021028.

d) Zhaoliang Li, **Boone D**, and Hann S. Nucleophosmin interacts directly with c-Myc and controls c-Myc-induced hyperproliferation and transformation. PNAS, Proceedings of the National Academy of Sciences, 2008. Ed: Vogt PK. Dec 2;105(48):18794-9. PMCID:PMC2596228

**Complete List of Published Work in My Bibliography:**

<http://www.ncbi.nlm.nih.gov/sites/myncbi/1Tilst6dx7o/bibliography/41249134/public/?sort=date&direction=ascending>