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 |

# PERSONAL STATEMENT

I am a breast cancer researcher deeply invested in education, training, and equity. This makes me uniquely qualified to participate in the training activities of the Hillman Cancer Center. I am the Vice-Chair of the Cancer Research Career Enhancement Committee at the Hillman Cancer Center. I am also the Director and PI of the NCI R25 YES Hillman Cancer Center Academy. 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 students from underrepresented and disadvantaged backgrounds. The long-term goal is to leverage our strengths in training and cancer research to increase both the number and diversity of the students prepared to be active members of the biomedical cancer research workforce.

I have been involved in education and training programs nearly my entire life. I credit my current faculty position to a high school internship program that I participated in as a junior and senior in high school and to the NSF-REU program that I completed as an undergraduate. During my graduate student career at Vanderbilt 20% of my effort for my final three years was dedicated to the other side of these programs—teaching and mentoring in two nationally recognized NSF-GK12 and NIH-SEPA funded outreach programs. As a postdoc, I gained further experience on curriculum development, training program organization, lecturing, mentoring, and exposing young students to science careers through various roles including site Leader of the Women’s Cancer Research Center site of the NIH-CURE funded UPCI Academy. My current faculty position is tailored to mentoring and teaching. In addition to being the Director of the Hillman Academy, I am also the Director of the Computer Science, Biology, and Biomedical Informatics (CoSBBI) Academy, and the Director of the NIH (R25 supplement/T15 supplement) and previously PA Department of Health funded Internship in Biomedical Research, Informatics, and Computer Science (iBRIC). All are research-intensive outreach programs for URM/DA high school and undergraduate students. Each also involves curriculum development. For example, through the iBRIC program I developed a module on cancer informatics that is now part of a Biochemistry course at the HBCU, Lincoln University. Finally, I am also a co-PI on an NSF-INCLUDES award aimed at creating a nationwide network of precollege programs aimed at changing how URM/DA students are evaluated during college admissions. From this work, my colleagues and I formed the Broadening Equity in STEM (BE STEM) Center at Pitt that has amassed community partners deeply embedded in Communities of Color throughout the city of Pittsburgh.

Finally, I am a breast cancer investigator. For the past decade my research has focused on cancer biology, from very basic studies on oncogenes and tumor suppressors to translational studies using sequencing and other –omics data. Combined my experience in outreach, education, and cancer research makes me uniquely qualified to be part of the training core of the breast cancer SPORE.

# B. POSITIONS AND EMPLOYMENT

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

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

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

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

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

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

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

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

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

2015-2017 Executive Director, UPCI Academy

2015- Director of CoSBBI and iBRIC programs

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

**HONORS/AWARDS/FELLOWSHIPS**

1999 High School Valedictorian

1999 Allegheny Energy academic and service excellence scholarship

1999 National Society of Collegiate Scholars

2000 Golden Key International Honor Society

2001 Phi Beta Kappa academic honor society

2002 Eberly College of Science Scholar

2002 Edward C. Hammond Jr. Memorial Scholarship

2002-2003 NSF-REU Fellowship

2003 Evan-Pugh Scholar Award

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

2007 Travel award from NIH-VNAC training grant

2009,2010 Travel award from Vanderbilt University Graduate School

2008-2011 NSF GK12 Science Teaching Fellowship

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

2012-2015 Susan G. Komen Postdoctoral Fellowship

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

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

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

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

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

2016 Session chair – Great Lakes Breast Cancer Conference

2017- Vice-Chair UPCI Education and Training Committee

2017 NIH YES R25 Study Section x 2

2018 - Member- Center for Causal Modeling Executive Board

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

**PROFESSIONAL AFFILIATIONS**

2010-2011 American Society for Cell Biology

2011- American Association for Cancer Research

2012- Society for Science & the Public

2014-2016 Endocrinology Society

2014- Center for the Integration of Research, Teaching and Learning

2016- American Medical Informatics Association

# 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>

# D. RESEARCH SUPPORT

**ACTIVE**

**NIH R25 (Boone/Bakkenist coPIs; Boone corresponding)** 04/01/2019 – 03/31/2024

**3.4 months** $2,500,000

University of Pittsburgh Medical Center Hillman Cancer Center Academy

The Hillman Academy at the University of Pittsburgh Medical Center will train 24 underrepresented minority and disadvantaged youth per year from Pittsburgh and surrounding areas by providing authentic cancer research experiences, didactic training from a tailored curriculum, and professional and academic development to prepare them for careers in cancer research and care. The Academy will also impact our local communities through outreach events facilitated by our long-standing community partners. The Hillman Academy will build from the strengths of our institution and past successes in working with emerging scientists from underserved backgrounds to broaden participation and expand diversity in the cancer workforce, which will produce more effective research and help decrease health disparities in cancer.

**Doris Duke Charitable Foundation 2016146 (Boone)** 01/01/2020 – 12/31/2022

**1.8 months** $400,000

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

This grant aims to broaden participation in biomedical research by providing authentic and mentored research and career development experiences to underrperresented minority and disadvantaged youth. Students from this program will work closely with Hillman Academy students.

**DOD (Roy**) role – CoI 9/1/19-8/31/21

**0.6 months** $250,000

Profilin 1 as a novel target in patients with renal cancer

**NSF1930990** (Boone/Legg/Allen/Iriti/Morrison) 09/30/1019 – 08/31/2024

**3.96 calendar months**  $10,000,000

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

This work intends to create a nationwide network of precollege STEM programs and an accreditation process to strengthen STEM programs and increase the number of underrepresented students into and through higher education.

**NIH Cancer Center Support Grant** 08/01/2020-07/31/2025

**1.2 months** $120,424

**COMPLETED**

**NIH U54 HG008540 (Cooper)** role Co-I 09/29/2014-08/31/2019

**1.2 months** $11,401,540

Center for Causal Modeling and Discovery of Biomedical Knowledge from Big Data

This center of excellence is developing, implementing, and evaluating an integrated set of tools that support causal modeling and discovery (CMD) of biomedical knowledge from very large and complex biomedical data. The approaches and products emanating from this Center are likely to have a significant positive impact on our understanding of health and disease, and thereby on the improvement of human health.

**NIH U54 HG008540-03S1 (Cooper)** role Co-I 12/01/2016-8/31/2019

**2.4 months** $590,122

Center for Causal Modeling and Discovery of Biomedical Knowledge from Big Data (supplemental)

This supplement will provide funding to establish programs at Pitt that will enhance the diversity of the BD2K program. Working together through the existing CCD at Pitt and the R25 at UPR-RP, this proposed R25 Supplement will leverage strengths and synergize efforts at both sites to rise to the challenge of training, equipping, and supporting a biomedical workforce that will be able to tackle the Big Data challenges of today and help guide the continuing discovery process in this emerging science. Training opportunities will leverage the strengths of both institutions to prepare a diverse workforce to utilize the tools and approaches being developed within and beyond the CCD.

**NSF Includes** **DDLP 1744446** (**Boone – CoPI**; Legg corresponding PI) 01/01/2018-12/31/2019

**1.5 months** $300,000

Diversifying Access to Urban Universities for Students in Stem Fields

This NSF INCLUDES Design and Development Launch Pilot seeks to address the gap between precollege STEM program participation and admissions offices by developing and testing credentialing and processes for four STEM precollege programs. This was the precursor to the NSF INCLUDES Alliance.

**NLM T15 Supplement (Hochheiser)** role Co-I09/01/2018 – 6/30/19

**1 month** $100,000

Internship in Biomedical Research Informatics, and Computer Science

Continue collaborations with UPR-RP and Lincoln University to provide summer research internships and mentorship to minority students from those institutions.

**Doris Duke Charitable Foundation (Boone)** 11/01/2018-06/01/2019

**0.4 months** $35,566

Clinical Research Continuum: High School to College Annual Directors Meeting 

Use human-centered design to increase the impact of DDCF-sponsored clinical internships, both at the individual program level and collectively, on broadening participation.

**PA DOH 4100070287 (Cooper)** role Co-I06/01/15-05/31/19

**1.2 months** $5,042,791

Big Data for Better Health (BD4BH) in Pennsylvania

Supported partnership with Lincoln University in order to train underrepresented minority students in the analysis of Big Data and develop curriculum to be used at Lincoln to broaden our reach.

**NLM T15 Supplement LM007059-31S1 (Hochheiser)** role Co-I09/01/2017 – 6/30/18 **1.44 months**

Pittsburgh Biomedical Informatics Training Program Data Science Curriculum Development

This supplement aims to develop hands-on curricular modules in various areas of data science using Jupyter Notebook or RStudio and R Markdown. My role is to develop a module of how to analyze gene expression data from The Cancer Genome Atlas.