Austin Young Shull

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INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Presbyterian College Clinton, South Carolina	B.S. *(magna cum laude)*	2007-2011	Biology (with Honors)
Medical College of Georgia Augusta University Augusta, Georgia	Ph.D.	2011-2016 (expected)	Biochemistry & Cancer Biology

A. RESEARCH FOCUS

The encompassing theme of my research involves discovering novel therapeutic targets in cancers by interpreting the molecular profiles of malignancies using next-generation DNA sequencing and array technologies. Integration of this information is then used in preclinical cell models to determine therapeutic vulnerabilities of specific cancer types. This research strategy is carried out in my particular projects:

Examples:

- Determining the molecular response of targeted therapeutics (ex: BRD4i, JQ1; CDK7i, THZ1; mTORi, NVP-BEZ235) in chronic lymphocytic leukemia (CLL) cells by integrating ChIPseq, RNAseq, DNA Methylseq, and protein array analysis (Shull et al. *Oncotarget* 2015; Shull et al. *manuscript in preparation*).

- Discovering novel DNA methylation events that exist in breast cancer stem cells using 450K Methylation Bead arrays and determining the prognostic potential of a cancer stem cell-derived DNA methylation signature in clinical breast cancer datasets (*research in progress*).

My research expertise has also led me to begin developing education modules for undergraduates that integrate clinically relevant laboratory exercises for illustrating fundamental molecular biology principles.

Examples:

- Utilizing DNA methylation-specific PCR (MSP-PCR) to test the *MGMT* DNA methylation status of cancer cell lines. This module will be used to teach undergraduates how DNA methylation in promoter gene sequences affects gene expression and how non-classical nucleotide alterations (i.e. epigenetic modifications) correspond with certain diseases.

B. PROFESSIONAL EXPERIENCE

Research Experience

2013- Present — Graduate Research Assistant, Huidong Shi Laboratory, GRU Cancer Center and Department of Biochemistry & Molecular Biology, Medical College of Georgia, Augusta University, Augusta, GA

2011- 2013 — Graduate Research Assistant, Phillip Buckhaults Laboratory, GRU Cancer Center and Department of Biochemistry & Molecular Biology, Medical College of Georgia, Augusta University, Augusta, GA

2010-2011 — Research Assistant, Stuart Gordon Laboratory, Department of Biology, Presbyterian College, Clinton, SC

Mentoring Experience

2015 — Jordan Bauer, Summer Medical Fellow, Huidong Shi Laboratory
Project: *Therapeutic potential of CDK7 inhibition in CLL*

2015 — Toku Shi, Summer High School Student, Huidong Shi Laboratory
Project: *Inhibiting the spliceosome complex in CLL*

2014 — Brian Buckley, Summer Undergraduate Fellow, Huidong Shi Laboratory
Project: *Therapeutic potential of BRD4 inhibition in CLL*

Teaching Experience

2015	Guest Lecturer: Genetics 334, Department of Biology, Presbyterian College, Clinton, SC
2014	Laboratory Instructor, Department of Biological Sciences, Augusta University, Augusta, GA
2010-2011	Assistant Laboratory Instructor, Department of Biology, Presbyterian College, Clinton, SC

C. AWARDS & PROFESSIONAL ACTIVITIES

Honors & Awards

2015	Darrell Brann Alumni Scholarship, Augusta University
2015	Who's Who Among Students in American Universities and Colleges
2014	R. August Roesel Memorial Award in Biochemistry Research, Augusta University
2012	Travel Award, Southern Translational Educational & Research Conference (STaR)
2011	Outstanding Service Award from the Department of Biology, Presbyterian College
2011	Omicron Delta Kappa Leadership Honor Society
2011	Phi Alpha Theta Historical Honor Society
2010	Tri-Beta Biological Honor Society

Professional Activities

President	Biomedical Student Association, Augusta University (Term: 2015-'16)
Member	The Graduate School Student Council, Augusta University (Term: 2015-'16)
Member	American Society of Hematology, (2015-Present)
Vice President	GRU Cancer Center Postdoc & Grad Student Association [GRUCC-PGA] (Term: 2014-'16)
Member	American Association of Cancer Research (2014-present)

D. PEER-REVIEWED PUBLICATIONS (CHRONOLOGICAL ORDER)

1. Lee EJ, Rath P, Liu J, Ryu DS, Pei L, Noonepalle SK, **Shull AY**, Feng Q, Litofsky NS, Miller DC, Anthony DC, Kirk MD, Laterra JJ, Ryu DH, Choi JH, Shi H. *Identification of Global DNA Methylation Signature in Glioblastoma-derived Cancer Stem Cells.* J Genet Genomics 2015 July 7 Vol 42:7, 355-371
2. **Shull AY,** Noonepalle SK, Awan FT, Liu J, Pei L, Bollag RJ, Salman H, Ding Z, Shi H. *RPPA-based protein profiling reveals eIF4G overexpression and 4E-BP1 serine 65 hyperphosphorylation as molecular events that correspond with a pro-survival phenotype in chronic lymphocytic leukemia*. Oncotarget 2015 10;6(16):14632-45
3. Teng Y, Ren X, Li H, **Shull A**, Kim J, Cowell JK. *Mitochondrial ATAD3A combines with GRP78 to regulate WASF3 metastasis-promoting protein.* Oncogene 2015 Mar 30 doi:1038/onc.2015.86
4. **Shull AY,** Noonepalle SK, Lee EJ, Choi JH, Shi H. *Sequencing the Cancer Methylome.* Methods Mol. Biol., 2015; 1238:627-51 (Review)
5. **Shull AY**, Clendenning ML, Ghoshal-Gupta S, Farrell CL, Vangapandu HV, Dudas L, Wilkerson BJ, Buckhaults PJ. *Somatic Mutations, Allele Loss, and DNA Methylation of the Cub and Sushi Domains 1(CSMD1) Gene Reveals Association with Early Age of Diagnosis in Colorectal Cancer Patients.* PLoS One, 2013 8(3): e58731.
6. **Shull AY**, Latham-Schwark A, Ramasamy P, Leskoske K, Oroian D, Birtwistle MR, Buckhaults PJ. *Novel Somatic Mutations to PI3K Pathway Genes in Metastatic Melanoma*. PLoS One, 2012 7(8): e43369.

E. PRESENTATIONS & ACCEPTED ABSTRACTS

Presentations

1. **Shull AY**, Choi JH, Buckley B, Pei L, Awan FT, Salman H, Shi H, *Transcriptome analysis demonstrates the ability of the bromodomain inhibitor JQ1 to attenuate common oncogenes heterogeneously expressed among chronic lymphocytic leukemia subsets*. American Association of Cancer Research Annual Meeting, Philadelphia, Pennsylvania, 2015. (Poster)

2. **Shull AY,** Luo J, Choi JH, Pei L, Awan FT, Lee EJ, Liu J, Buckhaults PJ, Yan XJ, Chiorazzi N, Shi H. *Identifying differential gene expression and splicing events in chronic lymphocytic leukemia patients through whole transcriptome profiling*. American Association of Cancer Research (AACR) Annual Meeting, San Diego, California, 2014. (Poster)
3. **Shull AY**, Latham-Schwark A, Ramasamy P, Leskoske K, Oroian D, Birtwistle MR, Buckhaults PJ: *Novel Somatic Mutations to PI3K Pathway Genes in Metastatic Melanoma*. Southern Translational Education and Research (STaR) Conference, Augusta Georgia, 2012. (Poster)

Abstracts (excluding those as primary presenter)

1. Wu J, Pei L, Lee EJ, **Shull AY,** Awan FT, Xu W, Fan, L, Li J, Munn DH, Shi H. *Genome-wide DNA methylation analysis identifies aberrant epigenetic changes in CD8+ T cells from Chronic Lymphocytic Leukemia Patients.* American Society of Hematology (ASH) Annual Meeting, San Francisco, California, 2014.
2. Noonepalle SK, Lee EJ, Ouzounova M, Kim J, Choi JH, **Shull AY**, Pei L, Kohle R, Hsu PY, Naigireddy P, Huang TH, Sreekumar A, Korkaya HS, Munn DH, Shi H. *Promoter methylation regulates interferon-gamma induced indoleamine 2,3-dioxygenase expression in breast cancer*. American Association of Cancer Research (AACR) Annual Meeting, Philadelphia, Pennsylvania, 2015.
3. Noonepalle SK, **Shull AY**, Pei L, Awan FT, Ding Z, Shi H. *Profiling the signaling pathways in chronic lymphocytic leukemia using reverse-phase protein array (RPPA)*. American Association of Cancer Research (AACR) Annual Meeting, San Diego, California, 2014.
4. Luo J, Pei L, Choi JH, Liu J, Lee EJ, **Shull AY**, Wilson JM, Awan FT, Buckhaults PJ, Shi H. *Analysis of DNA Methylation Profiles in Chronic Lymphocytic Leukemia Reveals Differences between Molecular Subgroups*. NIH Roadmap Epigenomics Program Investigator's Meeting, 2012

TEACHING PHILOSOPHY

"*If I have seen further, it is by standing on the shoulders of giants*."
-Isaac Newton

I believe the foundational spirit of education is easily summarized by this classic quote commonly attributed to Sir Isaac Newton in a letter of response to fellow Renaissance Period scientist Robert Hooke. Though this quote may come across as too poetic or abstract to have any concrete implication in education, I do believe this simple metaphor depicted within Newton's letter greatly highlights the overarching aim of higher education, which is to provide the shoulders that furthers a student's understanding of the world.

Now, if I infer from Newton's mantra that the aim of education is to further a student's comprehension and knowledge, the next logical question then becomes "why should I be motivated to pursue such an aim?" Ultimately, I believe the fundamental motivation that drives an educator in shaping a student's intellectual understanding is based on the exciting, yet sobering, reality that educators are charged with the task of equipping students with an educational foundation that will serve society. Educators must be in constant reminder that they teach in the presence of future physicians, lawyers, scientists, businessmen, teachers, and many other future professionals who will use their molded talents to properly serve the work of their discipline that, in turn, serves the needs of society. Thus, it becomes evident that the information an educator presents, how an educator presents said information, and how an educator teaches their students to process the presented information will ultimately have resonating effects in how students serve society within their future careers. To rely again on the analogy provided by Newton, we must allow students to stand on the shoulders of their teachers in order for them to further see the coming needs of their community and best determine how to meet them. These reasons are why I believe it is imperative for teachers to have a desire for furthering the intellectual capabilities of students who will then use their educational foundation to serve the society that they will one day inherit.

So, if Newton's response to Robert Hooke illustrates the fundamental aim of an educator's role for their respective students, we as educators must then determine the best means for enabling students to "see further." The means of providing proper educational development has recently been a point of discussion and concern among academicians within the life and physical sciences. The American Association for the Advancement of Science (AAAS) and the National Science Foundation (NSF) have recently complied a report known as "Vision and Change in Undergraduate Biology Education: A Call to Action," in which the editors of the report greatly stress the need for better assimilating the foundational scientific principles within an undergraduate environment. Based on personal reflection of my experiences as a student, an instructor, a lab mentor, and a biomedical researcher, I believe the educational process within the undergraduate sciences can be best approached through a multi-faceted, yet intertwining process. My personal interpretation of this process can be characterized through three divisions: (**1) defining scientific principles for students, (2) integrating scientific principles for students, (3) applying scientific principles for students.**

1. Defining scientific principles

I believe one of the first and major hurdles in promoting scientific development within the undergraduate setting is the issue of vocabulary. To put it frankly, a language barrier exists for students regarding scientific nomenclature. It's been reported that students are expected to learn more new words in an introductory biology course (~1400 words) than required in an introductory foreign language course (~800-1000 words). I have experienced this firsthand as both a classroom instructor as well as a researcher mentoring students who have little understanding of the nomenclature in my specific scientific field. My personal solution to this language barrier was to provide general experiences as analogies for seemingly complex scientific concepts. A specific example of how I overcame the language barrier for students is when I compared the complexities of

polymerase chain reactions (PCR) with the abilities of a copying machine to my introductory biology lab. As the end goal for a copying machine is to make replicas of the scanned document, so is the goal of making replicas of a DNA product through PCR. With parallels such as DNA template acting as the original document, the needed nucleotides acting as the ink, and the Taq polymerase acting as the copier scanner, my freshman biology class was able to overcome the language barrier that originally existed and comprehend a very detailed molecular biology principle. From my experiences, simple measures like the example provided to my introductory biology class have personally helped alleviate many of the frustrations and confusions brought forth by a simple issue of language.

2. Integrating scientific principles

I believe one of the more insidious issues that arise when teaching students scientific principles is the segregation of a student's scientific knowledge with the real-world implications of the knowledge they temporarily retained for the current semester. Though this method of rote memorization provides temporary success within the classroom for a student, failure in understanding the full implications of scientific principles will potentially leave an unneeded void in a student's educational development in science. My specific solution to this subtle issue has been to integrate biological issues we face as a culture and demonstrate how these issues are consequence of biological principles. For example, as Darwin's finches serve as a great example for demonstrating the principle of natural selection, I also supplement the illustration of antibiotic-resistant bacterial strains and chemo-resistant tumors as an ever-occurring implication of natural selection within human health. By illustrating the constant real-world implications of scientific principles, students will then be able to learn how to define other scientific principles played out before them as they progress through their career and overall life.

3. Applying scientific principles

The further I progress in my scientific career, the more I begin to realize that science can not be fully understood when learned in a vacuum. In order to fully comprehend the scientific principles being taught within a classroom, a student must actively participate in applying such principles. This reason is why I believe hypothesis-driven and outcomes-based laboratory exercises provide a more fruitful learning experience for undergraduate students. Not only do students get to participate in the primary objective of the hypothesis-driven laboratory exercise, but they also get to participate in the underlying objective of learning to form, test, and interpret the most foundational element in science; their hypothesis. I believe a learning experience driven by hypothesis brings better clarity to the realization that these seemingly abstract scientific principles taught in lecture have true and meaningful application in life. The basis of this approach is also extended to undergraduate research, which allows students to experience a prideful ownership in applying their scientific capabilities towards advancing the information we have concerning life.

Through the integration of these approaches, my goal is for undergraduate students to appreciate the sciences as a multi-faceted, approachable, and ultimately worthy field of study. As Newton humbly claimed that he could see further in his scientific endeavors because of the shoulders he stood upon, my desire is to for students to be able to see the vast beauty of the scientific process because of the shoulders they were provided. Thus, by seeing the immense worth of the sciences, they can then go forth and better serve society through it.

RESEARCH PLAN

Since the completion of the Human Genome Project in 2001, the philosophy of determining proper therapies for human diseases has exponentially evolved. In the advent of genomic-driven biomedicine, therapies using non-specific mechanisms of actions and causing adverse effects in patients are no longer the desired treatment option. This reality is especially true for human malignancies. Because of the information we now extract using genomic technologies, we have been able to understand a great deal more about the precise molecular alterations that promote the progression of specific types of cancer. We are then able to use these newfound understandings to reverse the cancer-associated molecular events. This type of biomedical discipline is referred as **targeted molecular therapeutics**.

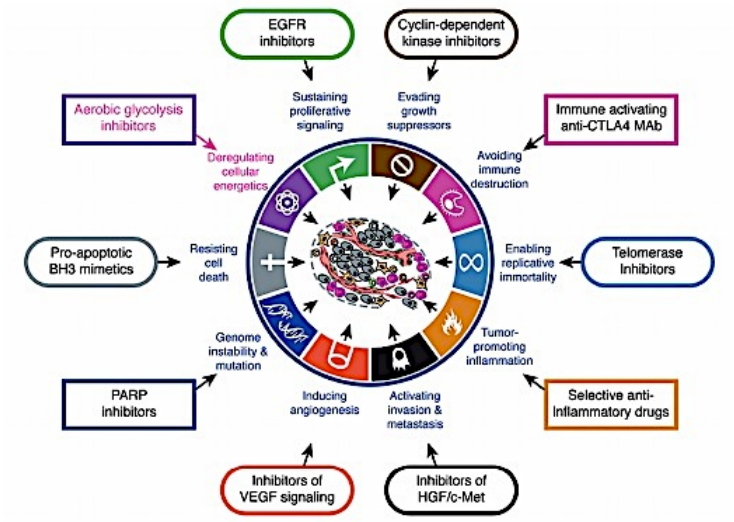

Figure 1. Hallmarks of Cancer. Hanahan & Weinberg, *Cell* 2013

Many of these molecular mechanisms targeted in cancer can be categorized into 10 categories or "hallmarks" of cancer (Figure 1). By understanding how genomic alterations attribute to these molecular hallmarks, researchers can then unlock critical information regarding the reversing of these cancer hallmarks. This concise philosophy of genomic-driven strategies for precision therapies helps illustrate the intentions of my connected research strategies:

Strategy #1: Analyzing the molecular patterns of cancer genomes using clinically available datasets

Through the inception of The Cancer Genome Atlas (TCGA) initiative, cancer researchers are now available to access hundreds of publically available datasets pertaining to genomic information of de-identified cancer patients. Such information is immensely valuable in determining precise molecular targets within subtypes of cancers. My strategy involves using the computational information provided by databases like TCGA to determine how certain molecular alterations statistically correlate with clinical parameters such as survival status, disease subtype status, age of diagnosis, and relapse status. Technical methodologies that will be used in this strategy include:

-Genomic mapping and variant identification using available sequencing platforms (i.e. Galaxy, GenePattern)
-Statistical comparisons of genomic alterations between disease types (i.e. CLC, Graphpad, GENE-E)
-Visualizing genomic alterations using publically available software (i.e. IGV Viewer, UCSC Browser)

Strategy #2: Determining the molecular consequences of discovered genomic alterations

Based on the analyzed information provided by the genomic profiling of cancer subtypes, the candidate events speculated to be involved in cancer progression can then be further investigated through *in vitro* cancer cell lines that model the disease phenotype in question. To best determine the specific effects of the candidate event, two experimental strategies are employed for determining its molecular role in malignant progression.

-Genetic manipulation: By using experimental methods such as siRNA-mediated gene suppression, gene overexpression plasmids, and CRISPR/Cas9-mediated genome engineering, we can determine whether certain molecular events are necessary for cancer cell growth and survival. The phenotypic effects of these manipulations can be studied using methods such as proliferation, viability, and apoptosis assays. The intrinsic molecular consequences can then be studied through techniques such as PCRs, ELISAs, Western blots, imummostaining, nucleotide microarrays, and sequencing analysis.

-Targeted chemical inhibition: Through use of chemical inhibitors that specifically counteract the discovered molecular alteration, we can determine whether this therapeutic inhibitor in question mimics the specific phenotype seen by genetic manipulation in the *in vitro* cancer cell lines. We can then propose both a novel mechanism involved in cancer progression as well as a potential therapeutic strategy for the caner phenotype in question by implementing this research strategy.