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Merideth Krevosky and Jeffery Bowen



INTRODUCTION

Upon arrival at Bridgewater State College, most students have little to no idea of what they want to do when they graduate four or more years away. Students often choose their majors with little more input or insight. For example, Biology faculty often hear that students want to do what “those people do on Crime Scene Investigations” (CSI) or similar shows.

Certainly, with a rare exception or two, students are not thinking about research and the impact it may have on their futures, let alone about graduate school and earning a doctorate.

The story of how many BSC Biology faculty members went from small undergraduate programs into graduate studies has been mirrored in our own students' experiences. Like our students, some of us were the first in our families to go to college, and we certainly didn't know anything about academia or how to enter its “hallowed” halls. Fortunately, something along the way provided us with a glimmer of what the possibilities were; a small crack in the proverbial door to our futures. For us in the sciences, that epiphany to pursue an advanced degree is often stimulated by the experience of undergraduate research. An interesting and common theme is that most of the BSC Biology faculty attended primarily undergraduate institutions, and/or had direct contact with professors who profoundly shaped our lives and served as valuable mentors.

Biology faculty members are not concerned that our undergraduate research students make profoundly significant breakthroughs in the field, such as discovering a gene to cure an illness or forging that critical compound that cures cancer. That isn't our goal, although we'd take it. Our goal here at BSC is to take that spark for biology and add fuel to it, thereby igniting a passion for doing science that will serve our students well throughout their lives and impact the lives of people they touch. In addition, we want to generate confidence in our students and to open their eyes to the possibilities of what they can become. Students must also realize that ‘just wanting’ to do or become something isn't enough.

For some of our students, those who came to Bridgewater with talent and clear goals, success was almost a certainty. However, the research experience and close personal interactions with faculty members

has also improved the students' confidence. Karen Debalsi (BSC 2005), for example, had worked for over fifteen years as an occupational therapist. Unhappy with her career choice, Karen returned to school to pursue her degree in biology and chemistry with the ultimate goal of attaining a position in research. In collaboration with Dr. Edward Brush in Chemistry, Karen focused her efforts on the biological effects of a novel compound she created with Dr. Brush, writing and defending an Honors Thesis which could rival many dissertations in depth and thoroughness. Karen has since joined the Program in Cell and Molecular Biology at Duke University where she is pursuing a doctorate.

Another non-traditional student, Betsy Powers (BSC 2008), had been a tax accountant for more than thirty years when she returned to BSC to complete her science coursework in preparation for veterinary school. While Betsy only planned on taking the necessary courses to enter veterinary school, she became involved in, and enthralled by, research. She never looked back. Betsy's dedication to her project focusing on the role of intercellular signaling in apoptosis was unparalleled, and after presenting her work to admissions counselors during her veterinary interview process, she learned that her work helped to solidify her acceptance into the program at Ross University where she is now a second year veterinary student.

Two of our other research students arrived at BSC with clear goals in mind, knowing that they wanted to be veterinarians or doctors, and embarked upon this goal from day one as biology majors. Karyn O'Connell (BSC 2005), matriculated in Tufts School of Veterinary Medicine where she received her Masters in Science degree. Her involvement in research during her studies at BSC helped to shape Karyn's long term goal, which is to serve as a faculty member at a veterinary school where she can continue to do research as well as teach. Brian Agbor-Etang (BSC 2008), is working toward his dream of becoming a physician as a second year medical student at Meharry Medical College. While Brian always knew his future was as a clinician, his research experience enhanced his medical school application, helping him to gain entry to medical school directly

upon graduation from BSC, a rare accomplishment. For each of these students, involvement in research was instrumental in allowing them to learn to think critically and to arrive at their destinations a little more easily.

STUDENTS AS RESEARCHERS

There are several key elements available on our campus that have opened doors to the future for our students, and have allowed them to see their potential and a wide range of opportunities that they had never envisioned. These opportunities include participating in our seminar series, conducting undergraduate research and working with world renowned scientists at the Woods Hole Oceanographic Institute. Importantly, many of our students participate in as many opportunities as they can. They realize that as these doors start to open, and the challenges are presented to them, they can rise to the occasion and use these opportunities to better themselves and brighten their futures.

Over the last ten years, the Department of Biological Sciences has adopted a philosophy that encourages undergraduate research. Research is something that faculty and students talk about and share. It is common to find one of our faculty members in the Biology Museum discussing some aspect of research with our students. Even more remarkably, it is now part of the departmental culture to see groups of students discussing their research!

Part of the reason is the Friday Informal Seminar Hour, or FISH. The concept of FISH was brought to our campus by Dr. Kevin Curry who 'caught' the idea while on sabbatical at Dalhousie University. FISH is a seminar series that allows our undergraduates to talk about their research and hear about the research of others in a casual, informal setting. We began using this concept of FISH with our undergraduate research students in 2003 when we concentrated on reading and discussing scientific literature related to our field of research, cancer biology. Not long after that we expanded the concept of FISH to include the entire department. It is now firmly entrenched in the departmental psyche. Students now have a forum to share their data, talk about the problems they encounter in their work and to define possible solutions with insight from others.



The 2008–2009 Apoptosis Research Group with (left to right) Allison Galanis (BSC 2010), Anna Grodecki (BSC 2009), Janelle Mapes (BSC 2009; now in the doctoral program at the University of Illinois, Champaign-Urbana), and Ryan Bagley (BSC 2009, now at Zeiss, Inc.).

Photograph provided by A. Galanis.

Students are given many opportunities to discuss their research progress so that once they are ready to begin to present their research outside of BSC, whether at conferences or during interviews for jobs or graduate schools, they are quite comfortable talking about their projects and can even describe them to a layperson. The change in confidence in our students who participate in FISH is often striking. One such student who benefitted from presenting her work at departmental seminars for

faculty and students was Courtney Calabria nee Tanzi (BSC 2001). The first time she spoke in public about her research her voice was barely above a whisper, and she rarely looked at the audience. Each time she presented there was marked improvement. The Courtney we saw at her last presentation as a BSC student was clearly not the same person. Her confidence had grown tremendously and paralleled the skills she had developed in the laboratory. Courtney went on to receive her Masters in Biotechnology at UMass Boston and is now at Tufts Veterinary School. This story is not uncommon. Biology alumni often remark on the impact that FISH has had on them. They join research labs and feel that they are ahead of the learning curve because they already know how to critically read scientific papers and talk about their data. In short, our students have begun to see themselves as contributing members of a scientific community.

The Office of Undergraduate Research (OUR) and the Adrian Tinsley Program (ATP) have also had major impacts on our students. Under the directorship of Dr. Lee Torda, OUR and ATP provide our students with opportunities to write competitive grants based on their research and to present their findings at a year-end symposium. The value added to their growth, development and marketability is immeasurable. It is very rare for students applying for jobs, graduate school, or professional school to have this type of experience. Additionally, OUR and ATP allow students to present their findings at meetings both on campus through the annual Undergraduate Research Symposium at BSC, and off-campus at regional, national, or international conferences.

We have seen several students "change course" during their studies. This is especially the case for those who

have worked in our lab and been exposed to the conduct of serious research. For example, Megan Dobro (BSC 2006), aspired to become a high school biology teacher. After engaging in research as an undergraduate her focus changed. Her desire to pursue her graduate studies in biology became so strong that she turned down the opportunity to enter a doctoral program at Harvard in order to expand her personal and professional horizons by attending the California Institute of Technology. There, Megan has traveled extensively as part of her graduate work, and has been privileged to meet several Nobel Laureates, including James Watson, who discovered the three dimensional structure of DNA. Megan credits the personal attention she received from the faculty in biology at BSC for influencing her path, leading her to her true passion.

Another such example is Janelle Mapes (BSC 2009), who was exposed to research during her freshman year. As a student in Dr. Bowen's general biology course, Janelle found the course much less challenging than many of her peers did, so she was challenged to read a scientific research article to engage her further in the subject. Janelle took the bait and became more and more curious about the opportunities of research. She was subsequently recruited to join our research team, and ultimately was accepted into three graduate programs. She chose to matriculate into the Cell and Developmental Biology Program at University of Illinois at Champaign-Urbana beginning in the summer of 2009.

Finally, several of our students have been able to take advantage of off-campus opportunities presented to them. For example, we have a long standing relationship with the world-renowned Marine Biological Laboratory (MBL) in Woods Hole, Massachusetts. During the summer, MBL hosts for professors, post-doctoral fellows, and graduate students a number of special courses that are focused on very specific scientific topics. These courses are taught by the leading world experts in their fields, including several Nobel Laureates. In fact, fifty six Nobel Laureates have been affiliated with MBL, including three of the 2009 Nobel Laureates.

Our students have worked for various courses as Course Assistants and Course Coordinators. Beyond their routine responsibilities such as making photocopies, setting up audio-video equipment and preparing and cleaning the labs, students also attend lectures and are often invited to participate in cutting-edge lab exercises. Along the way, students become well acquainted with the various instructors and lecturers, and become very close to the course participants. The amazing result of

this interaction is that our students come to see something of themselves in many of the course participants. They get to see the instructors and students as real people who are much like them in terms of background and experience. By the time our students are done working for these courses, their confidence in their potential is dramatically improved. Regardless of their level of activity, the students have always been extremely dedicated and very hard working, traits that have resulted in the directors inviting BSC students to return as course assistants year after year. In fact, most of our students have been heavily recruited to apply to graduate school at a number of institutions. Most recently, Ryan Bagley (BSC 2009), had the opportunity to work as a course assistant at MBL, a position in which he performed admirably. Over the course of his experience Ryan grew in confidence in, and understanding of, microscopy. As a result, he was recruited to an internship with Zeiss (the Mercedes Benz of microscopes), an experience which served as a springboard and an opportunity to be hired full time upon graduation.

REAL STUDENTS DOING REAL RESEARCH

Thanks to the successes of our students, BSC is becoming known as an outstanding institution for training and preparing undergraduate students in the sciences for technical jobs, graduate school, and professional school. We were able to use that reputation along with a novel research problem to attain the prestigious National Institutes of Health Academic Research Enhancement Award (NIH-AREA) to study the cell biology of retinoblastoma tumors. (Please see the accompanying sidebar to learn some of the specifics of this retinoblastoma research project.) This important work, and the first grant of its kind at Bridgewater State College, will further our understanding of this devastating childhood disease. Equally important, this grant will help advance the training of qualified undergraduates at Bridgewater State College and expose these future scientists to the exciting field of research.

We have seen an explosion of student interest in post-graduate careers, and of their dedication to the task of comprehending some pretty complicated thoughts and ideas. In all, we have had the great fortune of having nearly thirty students come through our lab, and we hope that we have inspired them as much as they have inspired us. Even better, we hope these students will someday mentor and inspire others to reach new heights.

—Merideth Krevosky is Associate Professor and Jeffery Bowen is Professor in the Department of Biological Sciences.

EYE RESEARCH PROVIDES VISION FOR THE FUTURE

While relatively rare, retinoblastoma is the most common ocular tumor in children, which can be life-threatening and may result in loss of vision. As such, it is an important clinical problem facing ocular oncologists. Current treatments for retinoblastoma most often employ a strategy known as chemoreduction which uses chemotherapeutic agents to reduce the size of the tumor prior to radiation treatment. The goal of these treatments is to kill the tumor cells while sparing normal cells. However, one of the major problems facing patients and physicians is that cancer cells can be resistant to chemotherapy drugs and radiation. This is often because tumor cells find ways in which to avoid a process of cell suicide known as apoptosis. Apoptosis, from the Greek *apo* meaning "away" and *ptosis* meaning "falling off" as in leaves from a tree, is a fundamental biological process by which over abundant and redundant cells are eliminated during development. Additionally, damaged or potentially harmful cells can be destroyed with this process, often with the help of a person's immune system.

All cells are born with a program that dictates their longevity. Long-lived cells will remain with an organism from birth until death and include cells such as cardiac and skeletal muscle cells, neurons, and cells in the lens of the eye. Other cells in the body have to be replaced more rapidly, such as the cells of the skin, within the digestive tract, and even bone cells which allow the skeleton to be replenished once every seven to ten years. When the lifespan of a given cell has expired, the cell needs to be removed in a way that is not harmful to the body. Apoptosis is that cell suicide process which allows the safe removal of cells that are programmed to die. However, defects in apoptotic cell death underlie a wide spectrum of diseases, including cancer, wherein many tumor cells acquire genetic mutations that make them resistant to death by apoptosis. "To die or not to die," that is the question that we are attempting to answer using retinoblastoma tumor cells. Understanding how retinoblastoma cells can evade apoptosis is the hallmark of this study.

While this concept seems relatively straight forward, unfortunately, there are hundreds of genes that are involved in the process of apoptosis. Cancer can result when genes that promote apoptosis are inactivated or when genes that inhibit apoptosis are activated. Both paths provide tumors with a selective growth advantage and play a critical role in the initiation and progression of cancer. Unfortunately, some genes that prevent apoptosis also render tumors resistant to chemotherapy and radiation therapy, a major problem that limits the effectiveness of current cancer treatments.

Consequently, a better understanding of the molecular mechanisms of cancer cell death can lead to improved therapies.

One way in which cells can avert apoptosis is to increase the expression of protective stress proteins inside the cell. One family of stress-related proteins are the heat shock proteins, so named because these proteins were first shown to increase in cells exposed to heat in order to protect the cell. Heat shock proteins function as molecular chaperones that ensure that other proteins are made correctly and maintain their proper shape when exposed to stressful conditions that can disrupt proper protein structure. Rather ironically, chemotherapy and radiation therapy induce stress within cells, leading the cell to make heat shock proteins to protect itself. Thus, heat shock proteins prevent cancer cells from undergoing apoptosis, the very thing treatments aim to promote. Consequently, the role of heat shock proteins is likely to be key in understanding how cancer cells become chemoresistant.

Until recently, very little was known about how heat shock proteins inhibit apoptosis. We now know that heat shock proteins interfere with the "cell death machinery" to prevent the cell from undergoing apoptosis. One such heat shock protein is called alphaB-crystallin, which is found normally in a wide variety of cells, including cells that are very long-lived such as neurons and cardiac and skeletal muscle cells. Importantly, in the study of the eye, alphaB-crystallin is found in the cells that make up the lens of the eye. In fact, crystallins were named for their translucent nature and are solely responsible for keeping the cells of the lens viable for up to 100 years! AlphaB-Crystallin has recently been detected in diverse tumors and has been linked to one of the more invasive types of breast cancer. Given these findings, it is our premise that retinoblastoma cells may fail to die and become resistant to chemotherapy and radiation because they express this specialized protein.

The experiments currently being done by our research students use cells derived from patient tumors that are maintained using *in vitro* cell culture techniques, and are the first to explore the role of alphaB-crystallin in tumors of the eye. Hopefully, with the support of the NIH-AREA grant, the Office of Undergraduate Research, the Biology Department, and Bridgewater State College, our students will identify new markers in retinoblastoma that can be targeted to improve treatment. We may discover novel treatment strategies that target alphaB-crystallin and other small heat shock proteins that could help save the lives and the eyesight of children suffering from retinoblastoma. For more information go to <http://webhost.bridgew.edu/jbowen/research.htm>
