PROJECT REPORT

An Authentic Course-Based Research Experience in Antibiotic Resistance and Microbial Genomics

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Abstract

We have designed and implemented a novel microbiology elective course "Microbiology of Urban Spaces" to provide students with a transformative education in microbial ecology and genomics. It champions the values of general education while making sure students are well equipped for their future careers. Infusing my personal research into the course allowed me the time and resources needed to advance my own research, while allowing the students to tackle an authentic and real-world problem that they can be passionate about. Several students who were engaged in the research course developed their own research projects during the summer, based upon their own ideas and questions. These students have taken the first steps towards developing the mindset and confidence in themselves that will enable them to succeed in their future scientific endeavors. Though still in its infancy, this course shows great promise to promote SENCER ideals at Mercy College and beyond.

Introduction

A Capacious and Civic Issue

Bacteria residing in the environment can act as reservoirs for resistance, having been exposed to many antimicrobials such as disinfectants, heavy metals, and antibiotics

(He et al. 2014). Frequently encountered in the environment are the Staphylococci, many species of which are human pathogens. Especially problematic are the coagulase negative staphylococci, as they are among the most resistant, the most prevalent in environmental settings, and frequently the source of hospital-acquired infections of immunocompromised patients (Becker et al. 2014).

One of the most recognized and worrying antibiotic-resistant bacteria is a form of *Staphylococcus aureus* called MRSA or Methicillin Resistant *Staphylococcus aureus*. MRSA is recognized as a serious threat by the CDC, causing 80,000 infections and 11,000 deaths annually (CDC 2013). About one in three people carry Staphylococci asymptomatically in their noses. Several different mechanisms of transmission have been described for MRSA and it is frequently isolated from the environment (Smith et al. 2010). The recent emergence of community-associated MRSA or CA-MRSA has had a huge impact on the field, as the bacteria are acquired by people with no known risk factors. What is known about transmission of MRSA (Smith et al. 2010), particularly in the built environment, has generated many questions that can be of interest to our students. Such questions can include the following: Is the choice of material used in construction important in how long bacteria can adhere to a surface? Are some types of staphylococci better able to adhere to surfaces than others? Can some surfaces facilitate colonization by bacteria more readily than others?

Many Mercy students are studying to be healthcare professionals, such as nurses and veterinary technologists. As such, they are usually familiar with antibiotic-resistant bacteria. Thus, my goal is to help students understand the role of human activity, particularly the role they themselves can play, in driving or tackling this problem. Antibiotic resistance is now being recognized as a global threat (Nathan and Cars 2014). Over the past ten years, the Infectious Diseases Society of America, the Centers for Disease Control and Prevention, the World Health Organization (WHO), and the World Economic Forum have placed antibiotic-resistant bacteria at center stage. The WHO exclaimed in April 2014 (WHO 2014) that the problem "threatens the achievements of modern medicine. A post-antibiotic era—in which common infections and minor injuries can kill—is a very real possibility for the 21st century." The Obama administration released a National Action Plan for Combating Antibiotic-Resistant Bacteria in March 2015 (The White House 2015a). The 2016 federal budget almost doubled the amount of federal funding for combating and preventing antibiotic resistance to more than $1.2 billion (The White House 2015b). Our success or failure in the coming years will depend upon continued support for these initiatives and having a well-educated workforce, ready and prepared to tackle this capacious problem.

Results and Discussion

Students As Researchers

Incorporating research into the classroom, be it the lecture or the laboratory, affords all students an opportunity to be included in and exposed to research, which their economic means, schedule, or background may prevent them from otherwise experiencing (Bangera and Brownell 2014; Gasper and Gardner 2013). Engaging students in undergraduate research can promote retention and career readiness and increase enrollment in graduate studies. It can improve their critical thinking and problem solving abilities as well as their independence (Auchincloss et al. 2014; Harrison et al. 2011; Jordan et al. 2014; Lopatto et al. 2008). Thus, the aim of this ongoing project is to design, implement, and improve upon a novel course-based undergraduate research experience that investigates the prevalence and persistence of antibiotic-resistant staphylococcal bacteria in the environment. By participating in this course, students engage with the literature and keep pace with new developments in antibiotic resistance research; they learn about government-driven and global efforts to combat resistance; and finally, they present their work in a public forum. They begin to understand the dual roles that research and education play in tackling this capacious problem. The course involves isolating and characterizing specific antibiotic-resistant staphylococci colonizing the campus, using a range of classical and next-generation techniques and correlating these findings with metagenetics, a novel technology that allows the researcher to sample all DNA at a site (Blow 2008). This new course called "Microbiology of Urban Spaces" directly ties into my own research agenda and expertise and helps me to recruit and retain a team willing and ready to tackle the problem. Student learning outcomes

are presented in Box 1 and specific activities in Box 2. The data generated as part of this project are used as a foundation for further student projects in the summer and have served as preliminary data for federal grant proposals and to obtain funding to support and sustain the course.

Briefly, students isolate individual bacteria using media selective for antibiotic and heavy metal resistance and characterize them phenotypically and genotypically over the course of the semester. They use a BSL2 lab that was recently refurbished for the purpose of microbiological research. The students are then encouraged to design their own phenotypic-based experiments (antibiograms, biofilms, adherence) to be conducted over the summer, and to develop their own research questions while continuing to harness the technologies and techniques learned in the course. The course is designed such that the metagenetic data are available for analysis towards the end, allowing time to expose the students to other characteristics and mechanisms leveraged by environmental staphylococci. The metagenetic component (swabbing, isolating DNA, and sequencing) is entirely at the discretion and choice of the students. In the first meeting of the course, students are introduced to my research questions and the work that my students and I have completed to date. They then brainstorm what sites would be of interest to target for sampling in view of my research and considering their own research questions. Once they have discussed and planned, the students, working as a team, sample various sites on campus. In Spring 2016, we targeted the new residence hall and sites such as elevator buttons, door handles, and handrails, and in Fall 2016, we targeted various water bodies in the vicinity of Mercy, including the Hudson and East Rivers and the Old Croton Aqueduct. The data we generated in Spring 2016 revealed the impact of human presence on newly colonized buildings at Mercy, and we have begun to design experiments targeting the specific organisms we have isolated and identified on surfaces there. While my original target was antibiotic-resistant staphylococci, we have also used metagenetics to identify the presence of Acinetobacter, Pseudomonas and Streptococcus on surfaces, many species and strains of which are also resistant to antibiotics. We shall adapt and modify our screening in future semesters.

How the Students Are Evaluated

Microbiology of Urban Spaces is designed not only to improve students' knowledge and understanding of research and antibiotic resistance, but also to train them to be 21st-century citizens. Students are expected to work in teams and build their communication skills. In this digital age we use instant messenger and group chats to facilitate communication. Dropbox is used to store course materials, protocols, and data in shared folders. Digital lab books are used (viewable to all team members) to ensure notes are updated regularly. Students are expected to be able to use and develop their quantitative reasoning skills and develop mastery of basic microbiology techniques such as dilutions, conversions, and basic computational tools and to generate a properly formatted bibliography. Above all else, the course encourages critical thinking and teamwork; students are able to choose their own sampling sites, interpret their findings, and learn from their mistakes. Repetition and iteration ensure mastery. Students are graded on the basis of their participating in lab meetings and lab activities, their detailed lab books, their final papers, and the generation of a scholarly poster. In addition, a survey based upon the SENCER SALG is administered at the beginning and end of the course, as well as the standard Mercy College End of Course surveys.

Student Success, Course Limitations, and Reflections

Since the pilot, I have been able to recruit eight students to participate each semester, and the course has gone through three iterations. Each section has been a success, with students reporting their enjoyment, self-satisfaction with their learning, and demonstrating their improvement in knowledge and skills over the span of the semester. Many had never generated a poster, worked with computational tools, or used molecular biology techniques except in class (if at all). Two students registered to take the course for a second time. Feedback from the End of Course and SALG surveys was positive as indicated in Box 3 and 4 (though not all students responded). In Spring 2016, when asked on the End of Course survey "if they would recommend a course to their friends and why," students answered, "Sure, opens your eyes to the world of research and looks great when applying to any grad

BOX 1
STUDENT LEARNING OUTCOMES:

1. Students will gain experience in reading, interpreting, and critiquing primary research articles.
2. Students will be trained in the use of microbiological and molecular lab equipment, methods, and standard operating procedures of the instructor.
3. Students will utilize classical and next-generation microbiology techniques to identify, quantify, and isolate organisms.
4. Students will gain experience in the formulation of hypotheses and the design of a research plan.
5. Students will learn how to document their findings and maintain an online laboratory notebook.
6. Students will learn how to generate a literature review and to maintain a bibliography in Zotero.
7. Students will have the opportunity to gather, interpret, and present their own data, in oral and written form.
8. By participating in grading of peer presentations and reports, students will gain an insight into both sides of the peer-review process.
9. Students will gain insights into the essential roles that bacteria play in ecosystems, their ubiquity in nature, and the impact of perturbing microbial populations.
10. Students will gain insights into the role of human activity in the evolution of bacterial antibiotic and antimicrobial resistance.

BOX 2
STUDENT ACTIVITIES:

- Swabbing surfaces and isolating DNA from the swabs
- Basic laboratory techniques and practices (dilutions, media preparation, sterilization)
- Environmental surface sampling using contact agar plates
- Colony purification and presumptive identification
- DNA isolation and electrophoresis
- PCR and sequencing
- SCCmec typing
- Metagenetic Sequencing, BLAST, and Data Analysis

BOX 3
END OF SEMESTER SURVEY RESPONSES (SPRING AND FALL 2016, N=5 STUDENT RESPONDENTS):

What activity or aspect of the course was most effective?

- Hands-on experience
- Research and hands-on experience
- The collecting of bacteria from our designated sites.
- The freedom to practice and experience a research project
- Performing different processes such as extraction and isolation of DNA using detailed procedures

What activity or aspect of the course was least effective?

- None
- Lecture (?)
- This course required more equipment that the school couldn't provide or provided late.
- We only meet once a week officially

Any additional comments?

- Very rewarding experience
- Class provides a wide variety of research opportunities for us students. But like I mentioned before, not enough support from the school financially. Learned a lot from this course and enjoyed every minute of it. Felt limited because we didn't have enough equipment the course asked for.
- Great course! Learned a lot and the Professor seemed prepared for every unexpected situation
- Prof. Smyth is a wonderful mentor, and the best professor I ever had. Her passion for biology inspires me. Her constant support helped me to achieve my goals.

schools," and "Yes, I personally learned a lot more about microbiology research and improved my skills." Limitations and student concerns were also noted in the end of semester surveys, where a student revealed that they didn't enjoy the lectures. Interestingly, student frustration with backordered/missing lab supplies also manifested itself on the end of semester surveys, indicating that they were indeed having an authentic experience. The minimal budget and modest lab facilities limit some of what can be done at Mercy. Students also learned that working in the lab is frequently frustrating and not always for reasons under our control.

BOX 4
END OF SPRING 2017 – SALG SURVEY (N=4 RESPONDENTS)

Q1. Please comment on how THE WAY THIS CLASS WAS TAUGHT helps you REMEMBER key ideas.

- "Hands-on learning puts into practice what I read about (i.e. PCR'ing, antibiogram, gel electrophoresis)."
- "I liked the hands-on stuff—it helped me remember what we talked about "
- "Well, Dr. Smyth was great at explaining things to us, even if we didn't quite get it the first time. Reading research papers on pubmed forced me to really delve into the subject matter, which made me understand the concepts better. "
- "I learn well through application of knowledge, therefore, this class was an applied reinforcement of what I learned in Microbiology lecture."

Q2. Please comment on how has this class CHANGED YOUR ATTITUDES toward this subject.

- "I need more time in the subject area to feel more confident. It was amazing to talk about what I was doing even if I didn't understand everything. "
- "Before this class, I wasn't very well versed in Microbiology, even though I took the class. In terms of the practical stuff we did in class, I was very intimidated and felt like there was no way I was going to be doing all that! However, I have mastered using a pipette, I was able to load those tiny gels, and I definitely feel more confident around a laboratory. Because I know more about antibiotic resistance now, my interest in the topic as a whole has increased. "
- "My attitude has changed towards feeling the urgency of being knowledgeable of and acting upon bacterial resistance. "

Q3. Please comment on what SKILLS you have gained as a result of this class.

- "Presenting our poster forced me out of my comfort zone, but having confidence in the work we did helped me push past it. "
- "DNA extractions, swabbing sample sites, PCR and gel electrophoresis, making and presenting a poster, explaining my work to other scientists, using Zotero, writing a scientific paper"
- "I have greatly improved my lab etiquette skills and my research skills."

Q4. What will you CARRY WITH YOU into other classes or other aspects of your life?

- "While learning about the subject matter, I was able to apply it to my other classes."
- "Washing my hands a whole lot more. Practicing aseptic techniques, and being more calculated and precise in my measurements. Not using Purell or other hand sanitizers as a replacement for washing hands. Being more cognizant of the cleaning materials I use."
- "I will carry the knowledge and applications that I was able to acquire through this class. These factors will prove to be useful in my later studies."

Several of the students who were in the Spring 2016 pilot continued to work on their projects over the summer and developed their own areas of research such as prevalence of enterotoxin genes, detection of bacteria in the gym, natural antimicrobials, and using antimicrobials in building products. At the end of both Spring semesters, students in the class presented their work at a local conference, the Westchester Undergraduate Research conference. In addition, students who continued their Spring 2016 projects into the summer presented their own independent research projects at national and international meetings such as CSTEP (Collegiate Science and Technology Entry Program), ABRCMS (Annual Biomedical Research Conference for Minority Students) and Microbe (the American Society for Microbiology Annual Meeting). On the basis of their abstracts, one student was awarded a partial travel grant to attend ABRCMS and received an honorary mention for her poster at CSTEP. Another student was awarded an ASM Capstone award to attend and present at Microbe 2017.

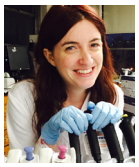
One of the most useful aspects of the course was using digital tools to facilitate teamwork and continual feedback. The use of Dropbox to store the digital lab books, though simple, was a successful social experience, as the students and I were able to engage with one another and make comments on each other's work; it was particularly useful since many of the students had jobs and commuted to school. The students could also make use of pictures and notes taken in class shared via Dropbox to ensure that their own lab books were up to date and not missing details. The groups used WhatsApp to connect with one another and to stay in contact throughout the course. This meant that students truly behaved as if they were on a team and worked as a unit throughout. When working on their poster in Spring 2017, the students took it upon themselves to book a conference room and displayed

the poster on the screen as they worked together in order to ensure that their poster was generated collaboratively and collectively.

Summary and Future Directions

Undergraduate research experiences can greatly enhance the career development and readiness of all students in STEM fields, and they have shown substantial impact on the retention of students in STEM disciplines. By integrating my research into a classroom-based research experience, I have enabled students to gain exposure to research while enhancing their critical thinking, communication, quantitative reasoning, and teamwork skills. For three semesters, I have had eight students register and the feedback has been positive. Working with the students has also rewarded me: useful and intriguing data were generated, which now inform my research and further student projects in the lab. In the coming semesters, I will continue to improve upon and modify this course so that it exemplifies a SENCER Model Course and provides a truly transformative and successful experience for our students.

About the Author



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