EXAMPLE 1

Title of Capstone project: Oxidative stress via inhibition of the mitochondrial electron transport and subsequent Nrf-2-mediated anti-oxidative response regulate the cytotoxic activity of plumbagin

- 1. Describe the scientific questions and goals of the capstone project. Include the major question being addressed. If your project is a part of a broader lab effort, please provide some background and clarify your role and contribution to this larger context.
 - Plumbagin is a natural product that has been shown to have anti-cancer activity. The goal of this project was to show the mechanism by which plumbagin induces cancer cell death. This project is part of a broader effort in the lab where we are testing the ability of some molecule agents to induce cancer cell death by increasing the level of oxygen radicals in the cancer cells. My role in the project was to conduct experiments such as Western Blotting, MTT, and cell culture to determine the molecular changes at the protein level that would occur in cancer cells after they were treated with plumbagin.
- **2.** Explain and provide an example of how the project has allowed you to develop problem-solving skills.
 - Initial assay prepared by me showed that when exposed to plumbagin, the viability of the cells was decreasing significantly. This was determined by analyzing MTT assays. The problem however was that we were not aware of the mechanism by which the cell viability was being affected. In order to understand the mechanism, I tested several different hypothesis and was ultimately able to show that plumbagin was causing apoptotic cell death.
- **3.** Explain how the project exposed you to <u>multidisciplinary</u> topics and approaches. A discipline is a branch of knowledge, not a list of techniques.
 - Working on this project gave me extensive knowledge of natural products and their effect on cancer cell biology and mitochondrial function. In addition to that, it also exposed me to knowledge on how to relate the structure of natural products to their several useful functions.
- **4.** Explain how the project has allowed you to develop teamwork and interpersonal skills, including the ability to communicate effectively to multiple audiences.
 - A key part of working in a research laboratory is to communicate effectively. In order to come up with a successful research paper, communication and team work skills are a must. This project has enabled me to conduct experiments individually as well as in a team. There were times when I would start an experiment and another student researcher would complete it and vice versa. Thus, communicating experimental procedures to other lab members is very important in a lab setting. Additionally, presenting and analyzing data in weekly lab meetings have helped me develop strong communication, time management and teamwork skills
- 5. Explain and describe (be specific) how the project has allowed you to develop skills in accessing and using information resources (e.g., electronic databases, library resources, national repositories).

In order to conduct successful research, it is extremely essential to look at any previous available

literature. For this project, I had the opportunity to perform several database searches for my PI to find any papers related to plumbagin and its effects. I used electronic databases such as PubMed/Medline and Web of Science.

6. Why is this research important? Explain how the project addressed larger societal, economic, ethical, scientific or professional issues.

Cancer is a major disease with very few effective treatments. Introduction of new, effective therapies would benefit the lives of many people. However, the therapy has to be economical in order to be accessed by everyone in society. Studies on molecules like plumbagin that are easily available and not very expensive will lead to therapies that have a far reaching impact on health of cancer patients globally. From an ethical point of view, it is very important to be truthful and honest about all data gathered while conducting research. There are several times results may not turn out as expected, however it is important to be professional and take into consideration ethical issues while performing research on cancer cells.

7. Describe and provide examples of how you have communicated or extended the capstone experience via written, oral, and/or multimedia reports.

While carrying out weekly experiments for this paper, I presented any significant results found at the weekly lab meetings, while discussing them with the other members of lab. Additionally, I have also gained experience with writing extensive grant applications about the research conducted in lab. Lastly, I have also reviewed and critiqued research papers before submission.

EXAMPLE 2

Title of Capstone project: Investigating Efficacy of Microlyte at Combating Various Biofilms

1. Describe the scientific questions and goals of the capstone project. Include the major question being addressed. If your project is a part of a broader lab effort, please provide some background and clarify your role and contribution to this larger context.

My research lab is currently developing a wound dressing called Microlyte, which is impregnated with silver nanoparticles. Currently, we are investigating the efficacy of Microlyte at inhibiting biofilm growth for several bacterial species, mainly Pseudomonas and Staphylococcus. Not only are we testing how effective Microlyte works at combating biofilms, but we are also comparing its effectiveness to several other wound dressings and current standard methods of treatment. I have been very involved with the testing of Microlyte over the past two years, much of which includes studies on swine and rodents. Much of my research involves surgical procedures on both of these species. Specifically, for our swine subjects, we will perform a surgical procedure that involves creating 1cm-sized wounds all along the animal's back, then infecting each wound with various bacteria species. Then, each wound is covered with a different treatment method (including Microlyte), which allows us to compare the effectiveness of various treatments. The biofilm is allowed to grow, which we then eventually harvest, dilute to various concentrations, and plate in order to determine how effectively each bacteria species survived against the various wound dressings used. We also grow much of our bacteria on mice, which I am also very involved with for surgical procedures. Similar to our pig subjects, we also create wounds on the backs of each mouse and infect them with various bacteria species for harvesting purposes. I am also involved with the

data analysis process, which we use the program Prism to track the healing of the wounds on our mice, as well as the ability of the harvested bacteria to grow in response to Microlyte.

2. Explain and provide an example of how the project has allowed you to develop problem-solving skills.

The past 2.5 years I have worked under Dr. McAnulty and Patty Kierski, which allowed me to continuously develop independent ideas and allow me to better understand the complexity of our research. For example, during Spring 2015 and Fall 2015, I began running my own independent project investigating how effective Zinc and Iron chelators are at inhibiting Pseudomonas and Staphylococcus biofilm growth. This required me to design and run my own independent experiment, which provided statistically significant results. I continued this research into the next year, in which I had another undergraduate student running the bacteria assays to see if my results could be replicated. As I became more accustomed to the laboratory, I began working more independently, which meant that if a problem arose with the bacteria assays or our research animals, I would have to deal with it without the direct supervision of our principal investigator.

3. Explain how the project exposed you to <u>multidisciplinary</u> topics and approaches. A discipline is a branch of knowledge, not a list of techniques.

Our development of Microlyte and my investigation regarding how various chelators affect biofilm growth has taught me how involved our lab not only is with veterinary medicine, but human medicine and engineering as well. While our research efforts obviously have many veterinary benefits, they also have human health applications as well. For example, when we research biofilm growth on mice, we suture a small ring to each side of their backs that surrounds the wounds. This allows the mice to heal like humans do, by preventing the natural twitching of their skin. Development of Microlyte has also involved extensive communication with engineers, which has allowed us to develop a wound dressing that adheres to the entire surface of the wound (instead of just sitting on top of it like traditional wound dressings), while still being strong enough to work with.

4. Explain how the project has allowed you to develop teamwork and interpersonal skills, including the ability to communicate effectively to multiple audiences.

Throughout my time at this lab, I have worked with professors, certified veterinary technicians, research veterinarians, PhD students, veterinary students, and undergraduates. I have learned to communicate my ideas with this entire audience, as well as develop meaningful work relationships with them. Two faculty from my laboratory even wrote me recommendation letters that attest to my research abilities and work ethic. I also was tasked with communicating my research involving chelators and biofilm to a group of undergraduate students that knew very little about biofilms and chelators, which presented a difficult and rewarding challenge. It required me to break my research down into easy-to-understand concepts in the hopes of getting an unfamiliar audience to understand the goals and results of my project.

5. Explain and describe (be specific) how the project has allowed you to develop skills in accessing and using information resources (e.g., electronic databases, library resources, national repositories).

Before the work in this laboratory began, I did extensive research regarding Dr. McAnulty's

publications in order to familiarize myself with past and current research efforts. All of these publications can be accessed through electronic databases, such as World of Science (which I have access via the library and my NetID). Furthermore, my past independent project required me to heavily use library resources and online databases. I scanned and read through countless online publications that the library gave me access to in order to determine which chelators would be the best choice for my project. I also extensively investigated the types of bacteria I would be using, including their composition, their ability to survive and produce biofilms, and how they behave in similar studies. The library was extremely helpful in acquiring articles from databases that they were not already subscribed to. Without using the online library resources such as its access to countless databases such as Web of Science, I would never have been able to read through so many scientific publications.

6. Why is this research important? Explain how the project addressed larger societal, economic, ethical, scientific or professional issues.

As bacteria species continue to evolve, the need to more advanced treatment methods becomes increasingly necessary. While current wound dressings that incorporate silver exist, Microlyte has the unique ability to adhere to the entire surface of a wound. Since biofilm is the property of bacteria that is most difficult to combat (and what often leads to resistance), it is essential that an effective anti-biofilm dressing is created. In today's society, we have seen increased bacteria resistance and even resurgence of diseases that were thought to be eradicated. It is therefore essential that we develop new and effective treatment methods to combat the resistant bacteria, which is exactly what my laboratory is working to accomplish.

7. Describe and provide examples of how you have communicated or extended the capstone experience via written, oral, and/or multimedia reports.

As previously described, I have been required to present my individual research efforts to a group of unfamiliar undergraduates. I did so by creating a PowerPoint presentation. I also wrote an entire scientific paper (unpublished) about my independent project, which was overseen by my principal investigator back in Spring 2015. More recently, I have had to orally communicate my research with various interviewers for veterinary schools, requiring me to be both concise and detailed with how I present the last 2.5 years of my research experience. During all of these experiences, I have exemplified the significance of the capstone experience, as all of my communication efforts have emphasized how interconnected my research is to veterinary medicine, human medicine, and engineering. Furthermore, I have emphasized how significant my research is in terms of current scientific issues, such as the constant problem of dealing with bacteria evolving to convey more and more resistance.

EXAMPLE 3

Title of Capstone project: Insect specific flavivirus infection in *Aedes albopictus*

1. Describe the scientific questions and goals of the capstone project. Include the major question being addressed. If your project is a part of a broader lab effort, please provide some background and clarify your role and contribution to this larger context.

Aedes albopictus is a mosquito species invasive to the Midwest and capable of transmitting epidemiologically important viruses such as Zika, Dengue, and Chikungunya. Insect specific flaviviruses (only capable of infecting mosquitoes of a particular genus) are generally harmelss to the mosquito, but may enhance or suppress the mosquito-to-human transmission of the abovementioned viruses in co-infected mosquitoes. The objectives of my capstone project are to establish and maintain a laboratory colony of Ae. albopictus from eggs collected in Southern Illinois and to ultimately screen them for insect specific flavivirus infection using various molecular biology techniques. I also aimed to screen the two previously established laboratory colonies of Ae. albopictus – from Missouri and Panama. Because these viruses are thought to have a high rate of vertical transmission (mother to offspring), if the mosquitoes in the wild are infected, the infection would carry over to subsequent generations. This project is part of the Upper Midwestern Regional Center of Excellence for Vector-Borne Disease effort on vector surveillance.

2. Explain and provide an example of how the project has allowed you to develop problem-solving skills.

Projects of this nature require quite a bit of troubleshooting. When it came to the molecular biology side of the projects, I ran into obstacles that led to me back tracing my steps and figuring out where I went wrong. For example, in an attempt to save time by using RT-PCR, I discovered that with the nature of my samples I had to go the longer route and run the RT and PCR reaction separately. This also induced more persistence in me as a student, and taught me that science requires patience – a key component of being a good problem solver.

Another issue I ran into was successfully cultivating field caught mosquitoes in a controlled laboratory setting. Mosquitoes from the wild sometimes have trouble adjusting to this environment and often face issues with feeding and staying alive. As a student, I had to find alternative ways to try and start a colony.

3. Explain how the project exposed you to <u>multidisciplinary</u> topics and approaches. A discipline is a branch of knowledge, not a list of techniques.

My capstone project allowed me to tie together the fields of virology, entomology, and molecular biology. During my initial literature review, I learned about the *Flaviviridae* family, viral transmission, and insect-specific flaviviruses as a whole. Then, I got hands-on experience on the entomology side of the project. As we received the field samples of eggs, I played a role in hatching them and then identifying the species under a microscope while the mosquito was still a larva. Because in the wild there isn't just one type of mosquito, we had to seek out the smallest anatomical differences between species in order to identify them. I also got additional experience in keeping the lab colony going by maintaining the mosquitoes through different life stages. Lastly, I took adult mosquitoes from my samples and performed RNA extractions, a reverse transcriptase reaction, and a polymerase chain reaction using primers designed to see if our virus of interest is present. Having worked in this lab for 2 years, this project really allowed me to put together everything I have learned and solidify my skillset.

4. Explain how the project has allowed you to develop teamwork and interpersonal skills, including the ability to communicate effectively to multiple audiences.

Throughout this project, I had the opportunity to collaborate with multiple individuals from different laboratories. This has helped me become more of a team player than I previously was, as

communication was crucial to the success of the project. Within my lab I was guided by a graduate student who introduced me to the molecular biology and virology side of things and my PI who facilitated the project and had endless ideas. I also worked with entomologists from the Paskewitz lab, who were a very valuable asset to the project, not only in collecting the field samples, but also teaching me how to identify the larvae based on minute morphological differences.

5. Explain and describe (be specific) how the project has allowed you to develop skills in accessing and using information resources (e.g., electronic databases, library resources, national repositories).

When I first started working on this project, I spent a lot of time on background research. I mostly used electronic databases, such as PubMed and Web of Science. I developed more critical reading skills and became more adept at evaluating information and interpreting charts and graphs. I also had the opportunity to attend the American Society for Virology annual meeting, where I visited a poster session to learn more about current research involving insect-specific flaviviruses.

6. Why is this research important? Explain how the project addressed larger societal, economic, ethical, scientific or professional issues.

Detection of insect specific flaviviruses in field collected mosquitoes may impact the transmission of human pathogenic flaviviruses and has applications in global health as well as laboratory experiments. This is also part of a surveillance study to monitor invasive species in the Midwest. Additionally, insect-specific flaviviruses are not as well studied as the human pathogenic flaviviruses, so it is important to acquire new information on how they play a role in our lives.

7. Describe and provide examples of how you have communicated or extended the capstone experience via written, oral, and/or multimedia reports.

I have put together a PowerPoint presentation to present my findings, which I can provide to CALS. In it I cover background and methods used, present data, and provide future work and applications of the project.

EXAMPLE 4

Title of Capstone project: Novel Epigenetic Modifying Agents Increase Tumor Associated Antigen Expression in Prostate Cancer

1. Describe the scientific questions and goals of the capstone project. Include the major question being addressed. If your project is a part of a broader lab effort, please provide some background and clarify your role and contribution to this larger context.

Epigenetic modifications including histone deacetylation and hypermethylation can affect gene expression. Previous and ongoing work in our lab has shown that it is likely that epigenetic modifications have occurred at regions in the genome which lead to defects in antigen presentation machinery. In my capstone project, we aimed to return antigen presentation machinery to normal levels of expression in prostate cancer cell lines through a novel hypomethylating agent, SGI-110, and histone deacetylase inhibitor Entinostat.

2. Explain and provide an example of how the project has allowed you to develop problem-solving skills.

Before I began my project, I performed pilot studies to solve the problem of what drug concentration and treatment regimen we would use for the main experiment. Higher drug concentrations and increased frequency of treatment typically induced higher levels of gene expression. However, higher drug concentrations and increased frequency of treatment also typically induce cell death. Therefore, we had to run pilot studies with multiple combinations of drug concentrations and treatment regimens in order to determine the concentration and treatment schedule which balanced drug toxicity (cell death) with effectiveness (gene expression induction). After each pilot study, I analyzed the expression of key genes involved in antigen presentation—HLA-A, HLA-B, and Beta-2-microglobulin (B2M) and compared gene expression induction relative to cell yield. I ultimately selected a moderately high concentration of SGI-110 (1uM) but only one day of treatment which minimized cell death.

3. Explain how the project exposed you to <u>multidisciplinary</u> topics and approaches. A discipline is a branch of knowledge, not a list of techniques.

This project required knowledge of molecular, biochemical, physical, statistical, and computational processes. To design the experiment, I needed to understand the molecular mechanisms behind epigenetic modifications and their effects on gene expression. I also needed to understand the biochemical interactions between our drugs, SGI-110 and Entinostat, and the enzymes DNA methyltransferase and histone deacetylase to rationalize the mechanism of action behind our drugs. I learned about the physical properties of cell culture flasks and selected flasks with different protein coatings for different cell lines based on the adhesion needs for each cell line. I learned how to interpret the results from a qPCR output and determine statistical significance of gene induction through one-way ANOVA through the programs Excel and GraphPad Prism. I also needed to develop my computational skills to learn how to graph the results of our study with GraphPad Prism. Each step of this project integrated multiple branches of knowledge, from biological to chemical to physical to mathematical, to produce results.

4. Explain how the project has allowed you to develop teamwork and interpersonal skills, including the ability to communicate effectively to multiple audiences.

This project relied heavily on collaboration between team members. I designed the project under the guidance of my scientific advisor and with an experienced undergraduate student. I worked with both of these team members throughout the project on cell culture, gene expression analyses, and data representation. We also gained two new undergraduate team members partway through the semester who I trained for 4-6 hours per week. Teaching these students allowed me to practice communication of our laboratory techniques, the biological rationale behind our experiments, and interpretation of our results. I also attended lab meetings where I observed how other members of the lab presented and interpreted their research which I now mimic when presenting any sort of research project. Outside of the lab, I have also learned how to discuss my project with other people who are educated but not experts in my field. For example: I studied how new drugs can make cancer cells visible to immune cells which can then attack and kill the cancer. While an oversimplification of my study, this short-and-sweet summary often serves as a nice

explanation of my project which I can communicate effectively to all levels of audiences.

5. Explain and describe (be specific) how the project has allowed you to develop skills in accessing and using information resources (e.g., electronic databases, library resources, national repositories).

I relied heavily on literature that I found through the database PubMed to learn about the role of epigenetic modifying agents in prostate cancer treatment. I also used similar studies to determine the range of drug concentrations and treatment regimens which I tested in pilot studies. While searching for literature during this project, I learned how to send in a library request for access to a journal article which UW-Madison had lacked access to. Within a few weeks and some correspondence with UW librarians, I gained access to the journal article and used information from the article to tweak my experimental design. I also learned how to use Web of Science to find articles which cited an older article which helped me to find additional useful articles once I had already found one. Finally, I learned how to use the NCBI database to search for information related to primers which served useful when we began to work with a mouse model that we needed to genotype.

6. Why is this research important? Explain how the project addressed larger societal, economic, ethical, scientific or professional issues.

The results from this project have been passed along to a collaborator who is looking for new drugs to use in clinical trials for patients with prostate cancer. So, if the drugs and treatment regimen lead to tumor reduction in patients during clinical trials, these drugs could potentially go on the market as a new targeted therapy for prostate cancer. Targeted therapies tend to have lower toxicity and side effects than traditional treatments for prostate cancer such as surgery and chemotherapy which can lead to issues with morbidity and mortality. Therefore, our research is a step toward the discovery of less toxic and damaging drugs which could treat prostate cancer in a human patient.

7. Describe and provide examples of how you have communicated or extended the capstone experience via written, oral, and/or multimedia reports.

I have not yet presented my project, but I am confirmed to present this project at the Undergraduate Research Seminar in Spring 2018. I am also looking at scholarships and grants which would permit me to travel and present this project at other universities outside of Madison and potentially even outside of the state or country.