A Natural Solution to the Crisis of Pathogens

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Abstract

Bacteriophage therapy, a process in which viruses are used to kill bacteria, is an alternative method to antibiotic treatment. Viruses infect specific strains of pathogenic bacterial cells and are a safer option than antibiotics for the body's natural defense system. As a result of the large increase in drug-resistant bacteria, society is approaching a pre-antibiotics era. Bacteriophages are a potential solution to this problem because of their applications in medicine and in agriculture, which could be applied to the human population. The purpose of this paper is to provide the history, use, and future applications of phage therapy to prove that it is a rational solution to the growing problem of drug-resistant bacteria.

Background

History of Bacteria

When individuals mention the word bacteria people immediately attach a negative connotation to it. Bacteria are living organisms that are typically one-celled and can be found everywhere. From what we can touch, see and eat, there are millions of microbes around us. In order to view bacteria, a microscope needs to be used since they are invisible to the naked eye. Antony van Leeuwenhoek, a Dutch tradesman and scientist, was the first person to view bacteria with a microscope that he developed himself (A History of the Compound Microscope). Contrary to popular belief, not all bacteria are bad and harmful; there are bacteria that provide benefits. Probiotics, for example, are beneficial bacteria which are found within the human digestive system. They are a part of our body's natural defense system and help the process of digestion by decomposing organic materials that have been consumed. Bacteria that is harmful is referred to as being pathogenic. These pathogens can lead to the development of several infections that affect individuals worldwide.

Discovery of Antibiotics

A solution known as antibiotics has been developed in order to combat these troublesome pathogenic bacteria. Alexander Fleming discovered penicillin, the first form of antibiotics in 1928 while he was working in his laboratory in London. This discovery of antimicrobial drugs was one of the most significant achievements that occurred in the medical field in the 20th century. It also played a profound effect in World War II by helping to reduce the amount of deaths from bacterial infections as well as decreasing the number of amputations that needed to

occur. As a result of the powerful influence that this new phenomenon created in many people's lives, penicillin was considered as a wonder drug (Explorable).

Antibiotics work by being ingested through a capsule or can be given through an injection. Once it successfully goes through the body, it will attack the cell walls of bacteria, specifically the peptidoglycan, which is only found in bacterial cells. This attack helps the prevention of diseases and serious infections. Most antibiotics will start their effects within a couple of hours (Healthychildren). Antibiotics are used in the treatment and prevention of bacterial infections and can assist with the management of pathogenic bacteria.

Phage Therapy:

The use of bacteriophages, called phage therapy, was first discovered by English Bacteriologist Frederick Twort in 1915, and then backed by French Canadian Microbiologist Felix d'Herelle in 1917 (Sulakvelidze et al.). It started to become incorporated in treating patients with bacterial infections in France in 1919, and by 1930, it had been implemented throughout Europe and the United States of America. However, it lost a lot of interest when antibiotics were discovered for multiple factors. One of the factors was that scientists started having a skeptical outlook on using viruses for treating diseases. Consequently, interest was lost with the ease of using antibiotics, which did not pose the problem of regulation that viruses did from phage therapy **(**Summers**)**.

Antibiotic Threat

The issue with antibiotics is that their targets are not specific to individual bacterium; therefore, antibiotics can harm the bacteria that can provide beneficial use in the body. This harm

then, can lead to the compromise of an individual's body system due to the development of drug resistance in treatments. As a result, some of the infections can become highly difficult to treat. Due to the issue of drug-resistance, stronger antibiotics are used to combat the bacteria. This use of stronger bacteria will then cause those bacteria to become resistant to the stronger antibiotics ultimately leading to powerful drug-resistant bacteria that will require a more powerful antibiotic to treat it. Bacteria that form resistance to antibiotics are referred to as superbugs. Superbugs have become a fundamental threat to the health of society as they have been considered a bigger problem than cancer (McKenna). The decline of effectiveness from antibiotics poses both health and economic problems for society.

There are resistant bacterial infections that affect humans worldwide. For example, *Methicillin-Resistant Staphylococcus Aureus* (MRSA) can be seriously life threatening and is the most frequently occurring antibiotic-resistant threat. MRSA has shown to be a versatile pathogen, spreading over different areas, from hospitals to animals in agricultural settings (Ventola**)**. By using the phage lysate the host's immune system is stimulated, which clears the pathogenic bacteria. An example of where phage therapy is used is in the major medical school in the country of Georgia. The surgeons are trained to manage infections by using phages as key elements. Specifically, pyophages are used by incorporating them into a bandage composed of phages and other ingredients so that when it is applied to a wound, the phages can be released over a period of time after application. This thoroughly cleans and allows the wound to heal properly (Abedon).

Another example is *Vancomycin-Resistant Enterococci* (VRE), which can cause a diverse amount of illnesses. This pathogen exists mostly in hospitals as well as other health care settings.

These infections are caused by the *Enterococcus faecium* and *Enterococcus faecilis* species. VRE has less of an impact worldwide when compared to MRSA and there are few antimicrobial treatments for it. The antibiotics used against VRE are linezolid and quinupristin, but they remain a major threat as bacteria are always forming a stronger resistance (Ventola**)**. Phage therapy was used on mice infected with VRE via lytic activity where they were given isolates of VRE. A single injection of the phage strain rescued 100% of the mice. This was a result of the nonspecific effect that phages have on the immune system (Biswas).

Another form of bacteria is *Streptococcus pneumonia* (*S.pneumoniae*) which is a major cause of pneumonia, meningitis and bloodstream infections. A majority of these cases have resulted from resistant clones spreading through gene transfer events. A majority of deaths occur in adults over the age of 50 and that rate increases exponentially after the age of 65. The infected human bodies are resistant to antibiotic drugs such as amoxicillin and azithromycin. Phage lytic enzymes have been successfully used in order to destroy the cell wall of *S.pneumoniae,* which has made it an alternative strategy to combat antibiotic resistance (Ventola**)**.

Mycobacterium Tuberculosis is a bacterial infection that is spread through the air. Infections caused by this bacteria can potentially occur anywhere in the body, however they mostly appear in the lungs. Mycobacterium Tuberculosis cases are a serious threat worldwide and are treatable by commonly prescribed first-line drugs, such as isoniazid. In some cases, they can be resistant to the first-line drugs that require more complex, stronger drugs that result in side effects. There are two categories for classifying resistant bacteria which are extensively-drug resistant TB(XDR TB) and totally-drug resistant (TDR) strains. There has been an interest in using Mycobacteriophages, viruses that can infect the mycobacterial hosts. For instance, using

phages to target the pathogenic bacteria in the upper respiratory tract where the phages could then infect and kill those M. tuberculosis cells (Hatfull).

Process

The mechanism of bacteriophages is that they essentially parasitize bacteria by infecting it and then reproducing in it. The scientific process of this begins when the bacteriophages bind to the target bacteria and punctures the cell wall of the bacterium. The phages inject their DNA via their tail into the host cell. Then, the phage directs the host cell to produce progeny phages at an exponential growth rate. After, the newly produced bacteriophages will end up bursting from the host cell. This kills the pathogens and infects others nearby until all the bacteria has been treated. In addition, bacteriophages are strain specific meaning that they will not harm other cells or good bacteria in the body, only the pathogenic bacteria (Sulakvelidze et al.)

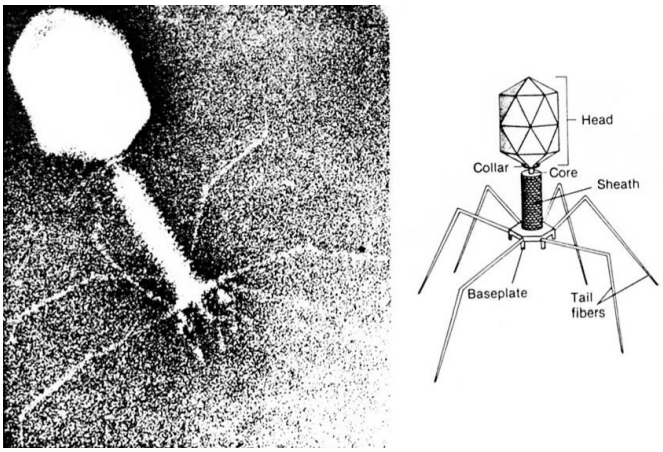

Figure 1: Left. Electron Micrograph of bacteriophage T4. Right. Model of bacteriophage T4 particle, which is among the largest of phages at 90 nm wide and 200 nm long, also it encodes approximately two-hundred genes. The head contains DNA or RNA. The collar, helical sheath and tail grant the virus the

ability to be able to bind to the surface of the target bacterium. These are used extensively for molecular biology research (Todar).

Potential Use of Phages to Treat Bacterial Infections

Current Use and Future application of phages. The FDA (Food & Drug Administration) has allowed the use of bacteriophages in factories and agriculture. By incorporating the use of bacteriophages into agriculture, it allows the reduction of the amount of pathogenic bacteria in livestock as well as other food sources that have been contaminated with antibiotic use in animals. This promotes the consumers health and adds extra value for the produce since it is free of antibiotics. It can also apply to factory and hospital settings by appropriately being able to sanitize equipment. Equipment could be considered sanitized, but may not actually be since bacteria can develop resistance to the cleaning supplies. This is critically dangerous to society because if hospital equipment is not being cleaned adequately it can lead to the spread of dangerous pathogens and infection to others in the hospital that may already be sick and have weak body systems. These patients would be unable to combat the infection that is at hand, resulting in rapid spreading throughout hospitals and the infecting of patients (Potera).

Advantages of Phages over Antibiotics

When comparing bacteriophages and antibiotics, there are many advantages that lean towards bacteriophages being a better treatment option. For one, there are no known side effects when using bacteriophages; whereas antibiotics can cause many side effects, from allergies to secondary infections. In addition, it is easier to select and develop new treatments with phages because of the high specificity that phages possess; whereas antibiotics do not target any

bacterial strain specifically (Pirisi). This is also a rational solution because there is a ratio of about ten viruses for every one bacterium, which increases the chances for successful virus based treatments. As a result, the United States interest has reappeared in bacteriophage therapy (Viertel).

Conclusion

The continuous use of antibiotics will cause severe negative impacts on society. For one, by the year 2050, a report from the Wall Street Journal predicts that there will be around 10 million deaths per year caused by drug resistant bacteria. Moreover, it will cost the United States about $100 trillion dealing with circumstances created by the superbugs. For the people who are currently using antibiotics, their immune systems will be severely compromised. Humans have reached this crisis because of the misuse of antibiotics. About half of the prescriptions written for antibiotics by doctors in the United States provide no benefit at all, instead they make the pathogenic bacteria even stronger. The prescription of antibiotics should be accompanied by a clear explanation and instructions of use. It should include the importance of finishing the course of treatment because often times people will not finish their course of medication because they feel prematurely better. By not finishing the complete treatment period and stopping the antibiotics before the prescribed course is over, the pathogenic bacteria is not being fully treated, making the resistance worse **(**Naik).

Looking into the future of fighting drug-resistant pathogenic bacteria, the use of bacteriophage therapy provides an alternative treatment when compared to the use of antibiotics. Bacteriophages have a lot of characteristics that would make them a better alternative as a therapeutic agent. They are very specific to the bacteria they infect, but they can also have very

broad applications from medical to agricultural use. Actions need to be taken in order to provide the best care possible, which phage therapy is able to provide. If phages are able to be used in treatment plans for pathogenic bacterial infections, the issue of antibiotic resistance may be able to be combated. The use of bacteriophage therapy will allow society to take back control of their bodies in this ongoing war of drug-resistance.

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Christian Aguirre is a fourth year Sociology major and political science minor at UC Merced. Christian originates from the fifth biggest city in California, Fresno. During his spare time, Christian enjoys listening to music, attending music festivals, going out with friends, and catching up on his television shows. Christian is a proud comic book enthusiast and prides himself on his knowledge of the Flash and Green Lantern. Christian chose to become an editor because he has always felt inkling towards writing. Writing offers an individual an avenue to express himself or herself, and as an editor Christian hopes to help students express their research in the best possible way. In the future, Christian hopes to attend medical school and become a cardio-thoracic surgeon. In his spare time, he hopes to have enough time to start his own non-profit organization focusing on helping underprivileged children advance professionally.

Arely Macias ’18 grew up in Modesto California graduated from Merced Junior College at Merced, with a Degree in Associates in Arts Social and Behavioral Science. Arely was the Secretary of History Club at Merced College. She also participated in sports and competed in Track and Field. At UCM, Arely plans to pursue a major in Sociology. She is a member of the University California Merced Undergraduate Research Journal Team and hopes to publish her own research. After graduating Arely plans to attend law school and pursue a career in family law.

My name is Alma Bogarin and I was born and raised in Escondido, California specifically from the Southern region of California in San Diego County. My major is in Sociology and my interest vary on a large spectrum of different hobbies I enjoy such as yoga, dance, and exploring new places. I wanted to be a UCM Undergraduate Research Journal editor because I want to achieve a new style of writing and an understanding of what kind of research is happening on campus. I want to develop a new form of writing in order to have a greater knowledge of the different kinds of writing that are available. My future goals are to create my own nonprofit organization that will focus on providing homes for the homeless youth and provide them any assistance they need in order to get out of the situation they are living in such as workshops that will help them get a job.

My name is Meghan Christopherson and I grew up in Fresno,California with a large family of 10 kids. Ever since high school I've had a competitive interest in academics, which is how I ended up at UC Merced. I am a Human Biology major (Pre-Med) and a Professional Writing Minor. My plan is to get a Master's degree in Science Writing and then attend medical school to become a Pediatric Oncologist. When I'm not in school, I enjoy traveling and going to concerts. I joined the URJ because I wanted to explore journal production in preparation for my Master's degree.

Katherine Cervantes is a 3rd year is a Management and Business Economics major whom is interested in public policy in the public sector, with a concentration in public education. Katherine is a strong advocate for underrepresented communities and collaborates with organizations locally to increase awareness on issues pertinent to students. She was born in San Diego, CA and speaks fluent Spanish. She currently serves on the Executive board of The Prodigy as Social Media Manager and as staff writer. She is also affiliated with ASUCM's External Office and Lobby Corps that partakes in lobbying efforts at the local, state, and national level. As well as being involved in media and advocacy work, Katherine is also the Spring 2017 senior editor for the UC Merced Research Journal. She has a strong passion for writing and would like to continue working closely in the writing field for the years to come.

Jocelyne Fadiga is a fifth-year chemical sciences major, minoring in applied mathematics and writing. She is graduating on May 13th, 2017. She transferred to UC Merced 2 and half years ago after attending a community college in the Bay Area. She is passionate about spirituality, science and social justice, and she hopes to use her passions to promote equality and equity in education. She is also interested in promoting healthcare access for underserved communities. When she is not fighting inequalities, she enjoys connecting with family and friends, traveling and adventure, food, music and long impromptu conversations. In the workplace, she has had experience in academia, but has also worked in non-academic environments. She has held positions ranging from tutoring and peer instructing at community colleges to conducting and presenting scientific research at conferences and symposia. However, she has also been a babysitter, a caregiver, and a barista. She joined the URJ team compelled by her love for writing and research. Furthermore, she hopes to gain experience in editing and publishing.

Hello! My name is Amri Milan Gray. I am a Public Health major with a minor in writing that is mostly emphasized towards creative writing. I am from Berkeley, CA. I'm very interested in getting to know people and figuring out ways to help them when they need it because I want to be a therapist after college. I'm also interested in writing and am always looking to enhance my writing skills in any way. I wanted to be a UCM URJ editor because for a while I was interested in becoming a journalist as a possible career, but I had no idea where to start researching the job. I added the class hoping to get an introduction on journalism and to my surprise I actually get to go through the process of being a journalist

I am from a small town called Goleta, which is in close proximity to Santa Barbara. I am a management and business economics major with a proposed minor in professional writing. My interests consist of the following: dancing, writing, music, socializing, photography, and drawing. Being a UCMRJ editor meant, exposure to a field in which I have interest in, yet never explored. I found this to be an opportunity to further my understanding of the writing and editorial field since, I want to eventually publish a book. This is a way for me to make connections and expand my horizon. For my future goals, I aspire to graduate from the University of California, Merced in 2019, follow up by attaining a masters degree, and gain a multitude of work experience through the way. After graduate school, I desire to become a manager of a corporation and eventually own a business.

Wen W. Li, a senior student at the University of California, Merced with a major in psychology. He is a transfer student from the college of Alameda. He will graduate in May 2017 and is currently almost finished all his major requirement. He has taken many classes in psychology, and he has high interests in child development, health psychology, and clinical psychology because he wants to know how environmental influences one's personality. He also speaks four languages: Cantonese, Mandarin, Japanese, and English. He also loves to travel in a different place, that he already had been to Hong Kong, Macau, and Guangzhou in China. He also interests in visiting the Yosemite National Park and Lake Tahoe for skiing. He is one of a University of California Merced Undergraduate Research Journal (UCMURJ) editors for Spring 2017. Because he always loves to read and interested to read other's views of the world, become a part of the UCMURJ provide him more opportunity to work with other and read research papers from the different major department. His future goals are work in the field of psychology, become a social worker, or work for an organization that could help people.

My name is Karla Lopez and I am from Hawthorne, CA, which is small town in the Southbay of Southern California. I am a fourth year Management major with a Psychology minor. On campus, I am apart of Delta Sigma Pi which is a professional fraternity dedicated to business majors. Some of my interests include digital design, makeup artistry, DIY projects, and traveling. This semester in the Undergraduate Research Journal, I took on the role of the treasurer. I essentially managed the financial side of the events and coordinated the purchases. I wanted to be an editor of the URJ because I wanted to meet new people and become more aware of the research my colleagues are working on. I have also considered a career in journalism, so I thought this course was a great way to get hands on experience. In the future, I would like to attend art school for graphic design. I would also like to go into marketing with a company like Sephora.

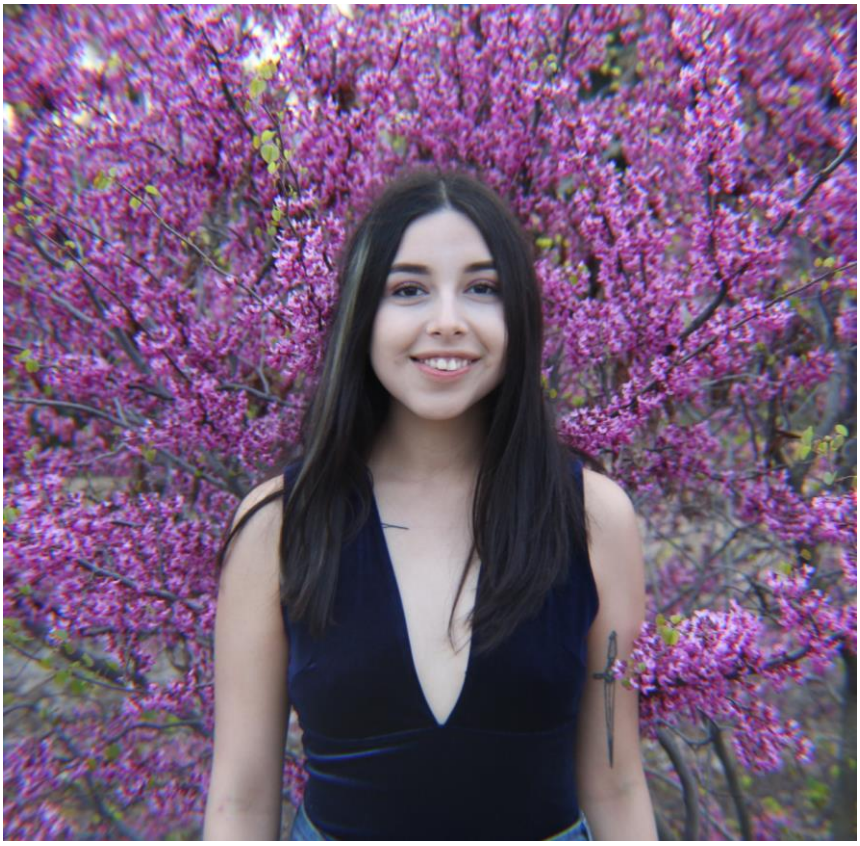
I, Emily (theBobcat) Ochoa, is currently studying both Sociology and Political Science here at UC Merced. Along with my two majors, I am also working on a creative writing minor. I enjoy writing (duh), as well as making art and music, running marathons, climbing, skating, being at the beach, laying on grass, petting dogs, and eating. I hope to continue enjoying dogs and the beach and art when I'm working for community outreach programs after I graduate.

My name is Manuel Ortiz Jr and I am from Fresno, CA. I am majoring in Sociology and aiming for a minor in writing. I was originally going to major in biology but I soon realized I did not have the patience nor dedication I thought I once had. Sociology stood out to me because I am fascinated by human interaction/behavior. I like analyzing social situations and breaking them down to their core. My interests include running because I feel like I am free from troubles even if it may be temporary. I also enjoy grabbing a couple of drinks with my close friends, we always have a good time when we are together. I recently got into photography but just simply admiring others' work. Another interest of mine is watching UFC which can be a gruesome sport. Two people are locked in a cage for three to five rounds and literally rip their heads off, it can be very entertaining to say the least. I wanted to become a UCMURJ editor because I wanted to add some more experience to my resume. I also enjoy reaching out to students and becoming involved with student lead events and I thought this would be a perfect opportunity. My future goals include becoming something in life that I can be proud of. I want to be able to spoil my mother and sisters because they mean the world to me and I want to make them proud. As far as my career goes, I want to help troubled kids so possibly becoming a social worker or guidance counselor.

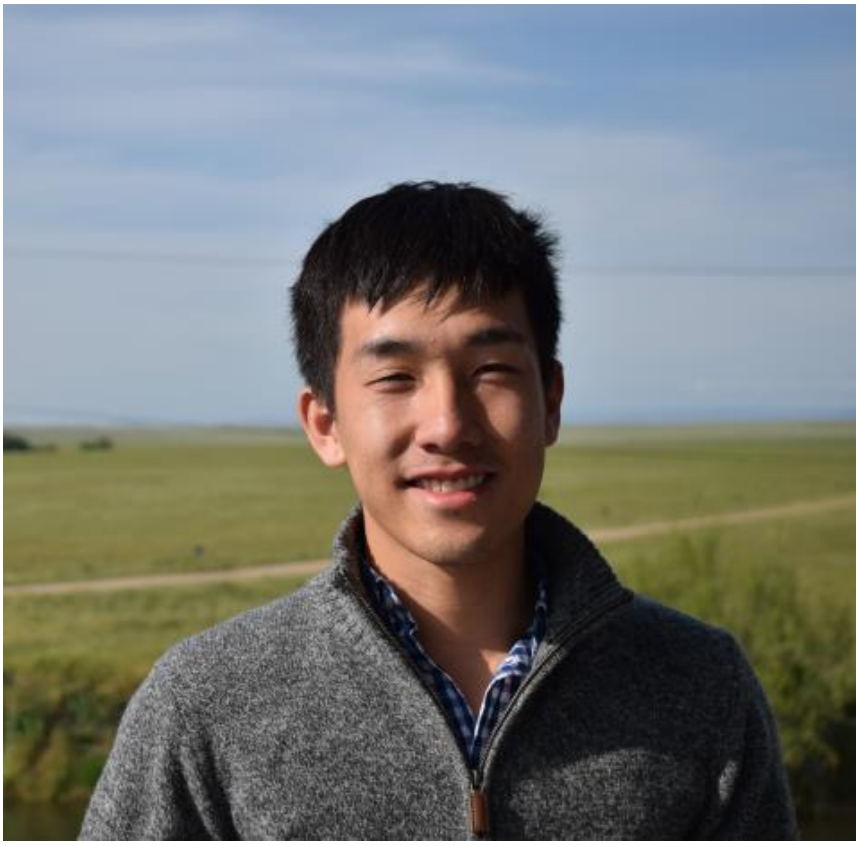
Jared Palma was born in Santa Clara, CA on July 14th 1996 and has since moved out to the Stockton area. Jared Palma is currently a third year attending the University of California, Merced. He is pursuing a B.S in Management & Business Economics and a minor is Sociology. He currently holds the position of " Social Media Director" for the the Undergraduate Research Journal along with his Co-Chair. Once he graduates from the University he plans to locate a job in either accounting or financial marketing and maintain that job for a year. If he decides that he is not happy with his job, he plans to pursue a degree in law (specifically in business law) in an attempt to further grasp ideas and concepts that his undergraduate career did not present.

Tucker Putz is a 4th year Psychology major at the University of California, Merced. Tucker's hometown is Sutter Creek, California, which is a small gold mining town about 150 miles north of Merced located in between Sacramento and Lake Tahoe. Tucker began his academic career at UC Merced as a Human Biology major, and 2 majors later he found his calling as a Psychology major. After he graduates from UC Merced, he plans to join the US Air Force. Although school is his main priority while attending UC Merced, one of his favorite hobbies is cars. In his free time, he enjoys working on his 2007 Ford Mustang GT. For the past two years he has actively participated in the newly formed Automotive Club at UC Merced. Tucker was also elected as the club's treasurer and is in charge of the club's social media sites for the current and past academic year.

My name is Christian Rivera and I am from Sacramento, CA. My major is Management and Business Economics, and the things that drew me into this field of my undergraduate study is the ability to eventually create and operate a business on my own. Even though I am not sure what kind of business yet exactly, I know I want to own a business one day. I am also minoring in Writing and Political Science, so I have contemplated in running my own law firm or even run a buffet of lawyers in my hometown of Sacramento. I feel this would incorporate all the areas of my undergraduate study.



My name is Angelica Soza and I am the Undergraduate Research Journal's class presentation manager. I am currently a sophomore on campus with a double major in cognitive science and psychology and a minor in creative writing. I hope to pursue a career in linguistics and I hope to further augment cognition along with our lexicon systems of language within any discourse (i.e. art, publications, etc). When I'm not editing papers I can be found working in my linguistics lab, painting, cooking vegan meals, or spinning records. I am also the secretary of Alliance with Animals, an animal rights club on campus and I'm also an active member of the Cognitive Science Student Association. I am currently creating my own non-profit organization that aims to reduce food waste in the central valley to ultimately combat obesity and spread healthy eating habits in this low SES community.



My name is Danny Wu and I'm from San Francisco, California. I'm currently pursuing a bachelor degree in Mechanical Engineer at UC Merced, in hopes of someday I could work in the solar industry to help benefit the world economically and environmentally. During my free time, I would take the chance to travel different parts of California like Marin County and hopefully Yosemite National Park next. I wanted to be an UCMURJ editor since I wanted to enhance and learn ways to evaluate research paper/journal,so that later on I would have an idea of how my research should be layered out and written. My long-term goal, meanwhile, is relatively either to work in the engineering field to help develop better solar applications or California's federal or state energy department that's focused on Sustainable or Renewable Energy, Energy Analyst, or Energy Assessment.