Identifying genes responsible for calcium induced Polymyxin-B resistance

Pseudomonas aeruginosa is an opportunistic pathogen that causes major illness on immunocompromised patients. Cystic Fibrosis (CF), for example, is a disorder that affects the respiratory system, and patients with CF are highly susceptible to infections caused by *P. aeruginosa*. Once a patient with CF acquires this infectious pathogen, it is nearly impossible to eliminate, which increases the morbidity of the patient about ten-fold. Treating *P. aeruginosa* infections is a major challenge because this microbe becomes resistant to a majority of antibiotics. Antibiotic resistance is caused by a variety of mechanisms including mutations, alteration in membrane permeability to antibiotics, acquisition of resistant genes on plasmids, or through changes in gene expression.

Calcium (Ca^{2+}) is an essential secondary signal. It is one of the most frequently found minerals in the body, and is very important for muscle function, nerve transmission, hormonal secretion, and many other purposes. Individuals with a compromised immune system have an imbalance in Ca^{2+} levels. For example, patients with CF, have elevated levels of calcium in their mucous and nasal secretion fluids. *P. aeruginosa* forms biofilms in the mucous filled airways of a CF patient. Our lab has identified that Ca^{2+} induces antibiotic resistance especially for the antibiotic Polymxin B (Pol-B). Pol-B binds and alters the structure of the bacterial cells, making the cell wall more permeable, which results in bacterial death. *P. aeruginosa* can overcome Pol-B toxicity with its ability to alter the membranes susceptibility. To identify the molecular mechanisms of Ca^{2+} induced resistance, my mentor PhD student has already performed random mutagenesis, antibiotic susceptibility assays, and sequencing for each of the mutants generated through the mutagenesis. The names for each mutant are PA2802, PA2803, PA2804, PA3237, PA3238, PA2890, and PA5317. My goal is to identify the genes responsible for Ca^{2+} induced Pol-B resistance. A polymerase chain reaction (PCR) will be conducted on the mutants lacking selected genes to confirm the presence of the disrupting transposon and to confirm the absence of the selected genes. After that, a growth analysis will identify any growth defects on the mutants. Then, antibiotic susceptibility assay will identify whether the targeted genes play role in Ca^{2+} induced Pol-B resistance. This research is important because finding the genes responsible for Pol-B resistance will help a better understanding of *P. aeruginosa* ability to become resistant. Knowing the molecular mechanisms for *P. aerguniosa* antibiotic resistance will enable the development of novel approaches for preventing and treating *Pseudomonas* infections.

Throughout my life, I've always had a strong passion for science, mostly biology. Learning about how tiny microscopic organisms highly impacts human life fascinates me. The human body is captivating in itself. It's amazing how humans, one of the most successful creatures on earth, can be threatened by something so small and what seems insignificant. My love and passion for science far exceeds the interest of an average individual. This is why my aspirations for becoming a medical doctor are so strong. The ideal image of me lies in the pursuit of science. When I become a doctor, not only do I want to save lives, but I want to make outstanding contributions to scientific research relating to medicine. Having my name published in renowned scientific journals and researching major diseases is a dream of mine. The sky is my limit and I have every opportunity to be the best version of myself. Researching *P. aeruginosa* will be a stepping stone for my long journey ahead on becoming a medical doctor with a PhD. Receiving this scholarship will motivate me in my studies to become an even greater researcher. It will help me in understanding what it is like to truly be a scientist