



**CALIFORNIA STATE SCIENCE FAIR
2016 PROJECT SUMMARY**

Name(s) Abheer Singh	Project Number S1525
Project Title Inhibition of Bacterial Mutagenesis through Polyubiquitination: A Solution to Antibiotic Drug Resistance	
<p style="text-align: center;">Abstract</p> <p>Objectives/Goals Bacterial cells can have DNA damage due to transcriptional error, or through the effect of an antibiotic. The SOS response is a bacterial cell program for coping with DNA damage, in which the cell cycle is arrested, and DNA repair is induced. The repairs have high probability in leading to mutagenesis in the bacteria, which can lead to antibiotic resistance. The RecA protein in bacteria is responsible for the activation of the SOS response; therefore, making it a target for inhibition. Developing a method to degrade RecA in bacteria, can inhibit SOS response related mutations, preventing antibiotic drug resistance.</p> <p>Methods/Materials The ubiquitination system was elected as a means of targeted degradation of the RecA protein in bacteria prone to mutations. Polyubiquitination of misfolded proteins leads to the breaking down of the protein with the aid of proteasomes. Using random forest-predictors, a statistically high likelihood of ubiquitination of the RecA protein in high risk bacterial infections, such as MRSA and TB, was determined. It was hypothesized that ubiquitin-tagging on RecA could be fostered by forcing the protein to misfold. Chaperones are proteins which interact with each other to prevent proteins from misfolding. CHIP (C terminus of HSC70-Interacting Protein) is a biomolecule that inhibits interactions between the chaperones of RecA. Adding CHIP, ubiquitin, and proteasomes into the bacterial system, theoretically leads to the degradation of the RecA protein. This was tested by conducting an assay for monitoring CHIP-mediated ubiquitination.</p> <p>Results Analysis was conducted on the assay using SDS-Page gel electrophoresis, and Western-blotting. The resulting data showed signs of polyubiquitination on the RecA protein, with chains of five or more ubiquitin, showing high drug potential.</p> <p>Conclusions/Discussion Adding an antibody drug conjugate, containing all the necessary components of a CHIP-mediated ubiquitination reaction, to common antibiotics can lead to the inhibition of bacterial mutagenesis, and higher antibiotic drug potency.</p>	
Summary Statement My project tests the possibility of polyubiquitinating the RecA protein, as a method of inhibiting bacterial mutations, to fight antibiotic drug resistance.	
Help Received The experimentation involved in my project was conducted at Dx-Sys, a lab in Mountain View. I received assistance from the staff there in using the equipment, and analyzing my data.	