Faculty Mentor: Professor Barbachyn

Other Professor Involved: Professor Blankespoor

Lab Partners: Hyeong Gyu Jang, Matthew Vander Wal, and Michael Moentmann

By: Anna Essenburg

Design and Synthesis of Novel Antibacterial Agents Targeting Bacterial Topoisomerases

This summer, our group worked on synthesizing new antibiotics, specifically targeting DNA gyrase and topoisomerase IV in gram negative bacteria. Gram negative bacteria are called such because they have two membranes- an outer membrane that is hydrophilic and an inner membrane that is hydrophobic (Figure 1). Due to the two membranes with opposite characteristics, it is hard to find compounds that will get through both layers. Bacteria are quickly becoming resistant to many of the antibiotics currently on the market today. We are getting around some of the current resistance by having our compounds interact with a slightly different part of the DNA gyrase in bacteria. We are trying to inhibit DNA gyrase and topoisomerase IV because they are involved in DNA replication, and if the cell's DNA cannot replicate, then the bacteria will die. The antibiotics that we worked on are part of a class called the fluoroquinolones.

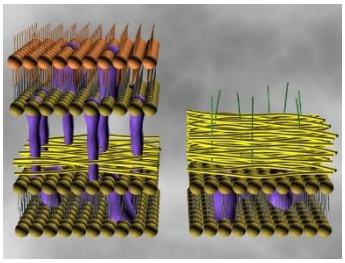

Figure 1: Gram negative vs. Gram Positive Bacteria

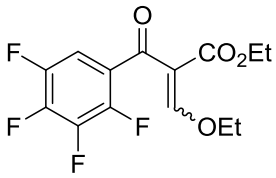

Figure 2: Common starting material

Most of my summer was spent running various reactions, purifying the products through filtration and chromatography, and verifying that the right product was made using the NMR. It also involved some literature searches to get myself more familiar with antibiotics, more specifically, the fluoroquinolones. We all started with the same starting material, but added different compounds to it to make our own compounds. We each lead our compounds through a series of reactions starting with the enol ether (Figure 2), then making an enamine and doing a cyclization reaction. Next, I did the hydrolysis to the quinolone acid, and added the piperazine or 1-methylpiperazine to make the final compound. I made four potential new antibiotics. One of which is seen in figure 3.

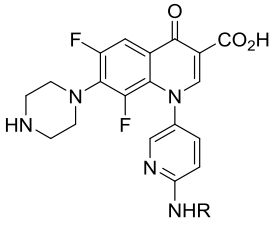

Figure 3: Synthesized compound

The work that our group has completed this summer is only part of an ongoing project. These antibiotics are in a class called the fluoroquinolones. The compounds that we synthesized will be sent off to Walter Reed Army Institute of Research to be tested against different kinds of bacteria to determine their usefulness. Overall, our hope is that we will synthesize a new antibiotic that will be effective against antibiotic resistant bacteria.

I am grateful to have been a part of this research project at Calvin College. Through this research experience, you get to catch a glimpse of what chemistry actually is and what it is that

chemists actually do. I learned that a lot of science is trying new things and knowing when to give up on parts of the project that are failing. It also involves reading the literature. Perhaps the most important thing I learned was to think for myself and know when to speak up. Sometimes the literature will have typos and lead you astray, but it'll be ok. Overall, summer research at Calvin and working for Professor Barbachyn has been a valuable experience for me.