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FURSCA Summer 2023

End of Summer Report

Cancer is the uncontrolled cell growth within the body. The cancer drug asciminib targets a specific enzyme, BCR-ABL, which is a cause of uncontrolled cell growth, halting those processes. Azo compounds are compounds with nitrogen-nitrogen double bonds. These bonds can be photo-switchable, meaning they change shape with UV light. Shape is key to a drug’s function, and this property can be used as a light activated “on/off” switch for asciminib. Many side effects of these drugs are caused by off-target enzyme binding, in other words, when the drug binds its target outside of cancerous cells. These enzymes are found throughout the body making side effects very common. By adding an azo bond with the properties already described, it is possible to selectively bind the enzyme in only cancerous cells using UV light in order to avoid these side effects. For my project this summer, I designed and carried out a chemical synthesis pathway that places an azo bond into the asciminb drug, in order to give this drug photo-switchable properties and limit the side effects on the body.

While I came into this project with a laid out plan of how to synthesize this molecule, that original plan needed to be reworked. To start, a chemical synthesis pathway is a sort of road map in order to plan out the chemical reactions necessary to build the target molecule. This is necessary because it is impossible to just change the existing molecule immediately to the target molecule, we must start from scratch. Furthermore, this molecule has never been synthesized before, which makes buying this molecule from a chemical supplier impossible as well. As I began on the first synthesis pathway, I approached a roadblock at just step 2. In other words, this reaction failed. While I attempted this reaction under many different conditions, the molecule I was attempting to synthesize was too different from the previous literature I was basing this plan off of and it became clear that this pathway needed to be altered. Therefore I researched other possible reactions/pathways that could yield the product I wanted. I tried these reactions, and failed again. Ultimately I redesigned three synthesis pathways throughout the summer after approaching several different roadblocks. However towards the end of the summer I began having success on the third redesign. This new synthesis consists of six consecutive steps, of which I completed four upon the end of the FURSCA summer program.

For each completed step in this synthesis pathway, I have NMR (Nuclear Magnetic Resonance) data in my laboratory notebook confirming that the intended product was indeed what was produced during the chemical reaction carried out. All of my products made during the summer are being stored in order to continue this project at a later date.

This project has given me the opportunity to develop invaluable skills in the laboratory and an experience that will greatly increase my future opportunities in education post-undergrad. I will be continuing this project throughout my time at Albion College, with the hope of completing the synthesis of azo-asciminib, carrying out biological and UV testing, and ultimately publishing this research. I plan on presenting this research next year at the Elkin Isaac Research Symposium and hopefully at national research conferences such as ACS. This experience has taught me the importance of failure during a project and how to persevere through it in order to reach your goals. I will be forever grateful for this opportunity that has been afforded to me to learn and grow this past summer, and would like to thank all of those who made this possible. A special thanks goes to the donors who fund the FURSCA department, without this funding I would not have been able to pursue this project and I greatly appreciate their support.