CALIFORNIA SCIENCE & ENGINEERING FAIR
2019 PROJECT SUMMARY

Name(s)

Alexander Guh-Siesel

Project Number

S0510

Project Title

A Method for Treating Celiac Disease: Synthesis of Small Molecule Inhibitors of the HLA-DQ2 Receptor

Abstract

Objectives

My project aims to synthesize small molecules that prevent the HLA-DQ2 receptor from binding to alpha-2-gliadin proteins found in gluten, thus preventing the autoimmune response associated with Celiac Disease.

Methods

To synthesize my small molecule inhibitors, I developed a six-step synthesis that include a few different types of reactions such as: peptide coupling, heat-induced cyclization, Boc and Cbz protection and deprotection, and introduction of the alpha-keto sidechain derived from diethyl tartrate.

Results

Based on the data I have collected so far (proton NMR and TLC), my synthesis has been successful. I have also confirmed the identities of all of my intermediates throughout the process by interpreting the proton NMR data. This sets the stage for me to test the binding potential of my small molecule inhibitors on the HLA-DQ2 receptor.

Conclusions

I have successfully conducted my synthesis and I will send out purified samples of my small molecule inhibitors for binding assays at Stanford University Chemistry Department in the coming weeks. Those results will determine the effectiveness of my compound expanding the knowledge surrounding HLA-DQ2 Receptor inhibitors, and hopefully pave the way as an effective new treatment for Celiac patients. My work will hopefully lead to the synthesis of additional derivatives in an iterative fashion to ultimately discover a new class of compounds as therapeutics for patients with Celiac Disease.

Summary Statement

I synthesized small molecule inhibitors that competitively inhibit the HLA-DQ2 receptor from binding to proteins found in gluten, thus preventing the autoimmune response associated with Celiac Disease that leads to inflammation.

Help Received

I would discuss some of my reactions with my advisor, Mr. Darren Dressen, who would help me decide on which reactions were feasible. I also got some of my NMR data from Dr. David Brooks at SJSU, where I would send him my purified compounds and I would get back data to confirm it's identity.