CALIFORNIA STATE SCIENCE FAIR
2017 PROJECT SUMMARY

Name(s)

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Project Number

S0510

Project Title

Analyzing Proteins of the BCL-2 Domain: Exploring the Potential of Protein Mimetics in Cancer Immunotherapy

Abstract

Objectives/Goals

Cancer has been a pervasive and deadly problem for many years. So far, no treatments have been developed that specifically destroy cancer cells while sparing healthy cells. Our goal is to use a knob-socket analysis of protein quaternary packing structure to map the key protein interactions between a cancer protein and its ligand. This mapping allows us to identify the quaternary amino acid interactions that define ligand specificity and binding strength. From this analysis, an artificial protein mimetic of the binding helix can be developed which is specific for cancer cells, leaving normal healthy cells to thrive.

Methods/Materials

Using the protein-modeling program, Chimera, and PDB files 2PQK, 3KJO, 2VM6, and 2XAO, I recorded the knobs and sockets of each of the four interactions. I then used the information to create two-dimensional models using Adobe Illustrator. This allowed me to easily see interactions that might be important.

Results

Protein mimetics have a similar domain structure, and can bind with pro-apoptotic activators to help destroy cancer cells. In the knob-socket mapped protein-ligand interactions, the helix ligand possesses between 8 to 10 residues that specifically interact with 4 helices on the binding protein: the N terminus of helix 2, the main bodies of helix 3 and helix 4 and the C terminus of helix 5. Among all of the interactions that were analyzed, there were three amino acids from the ligand, glycine, leucine, and isoleucine, that always packed into the binding protein helices in the hydrophobic groove, which is key for ligand recognition.

Conclusions/Discussion

Identifying the key amino acids important for binding can contribute to the design of a mimetic that can be used as a treatment for cancers. Further analysis involving mapping the important residue interactions can help with the development of mimetics that are more effective as treatments.

Summary Statement

I discovered that the three amino acids, glycine, leucine, and isoleucine, are potentially key to creating a mimetic BH3 protein that can bind to the BCL-2 proteins and act as a cancer treatment by helping to induce apoptosis.

Help Received

I conducted research at the University of Pacific, under the guidance of Professor Jerry Tsai. He provided research papers so that I could learn and understand the previous work that had been done. This enabled me to conduct my own project. Zaina Chaban provided feedback and helped guide the poster design.