Summary:

The goal of this project is to determine the structure of a polyketide synthase (PKS) product that has yet to be identified. Polyketides represent a diverse class of secondary metabolites that have vast applications. Polyketide products have already been employed to combat bacterial and fungal infections, immune disorders, and to name a few.

Characterizing PKS through usual laboratory techniques is not always practical, often due to chemical properties of the products**.** One work around is to characterize them computationally. This is made possible thanks to the collinear relationship between the synthase and resulting polyketide. This colinearity is referring to the ability to determine the structure of the polyketide result from the PKS amino acid sequence and vice versa. Computational identification is possible thanks to the assembly style manufacturing process through which the PKS makes the polyketides. There are a limited number of specific enzymatic domains that the PKS employs. These individual domains perform specific reactions at defined regions of the polyketide as is determined by the location of the domain in the module, and in turn its location in the PKS.

The first step will be finding a previously characterized PKS with a large amount of diversity in its domains. Once a PKS is decided, a fragment of its amino acid sequence will be used to find an uncharacterized PKS that has a high degree of homology. The program clustermine360 and DoBISCUIT will be used to help find an initial PKS sequence in its entirety. The NCBI database will then be searched for similar proteins by performing a Blastp search on the initial sequence while excluding the PKS that it is from. This provides results for PKS that have a high degree of homology to the initial, and an uncharacterized one will be selected. The search sequence will then be submitted to AntiSMASH which is domain recognition software for natural product biosynthesis. The AntiSMASH results will then be combined with manual curation of the sequence to build the structure of the polyketide that is produced from the orphan PKS.