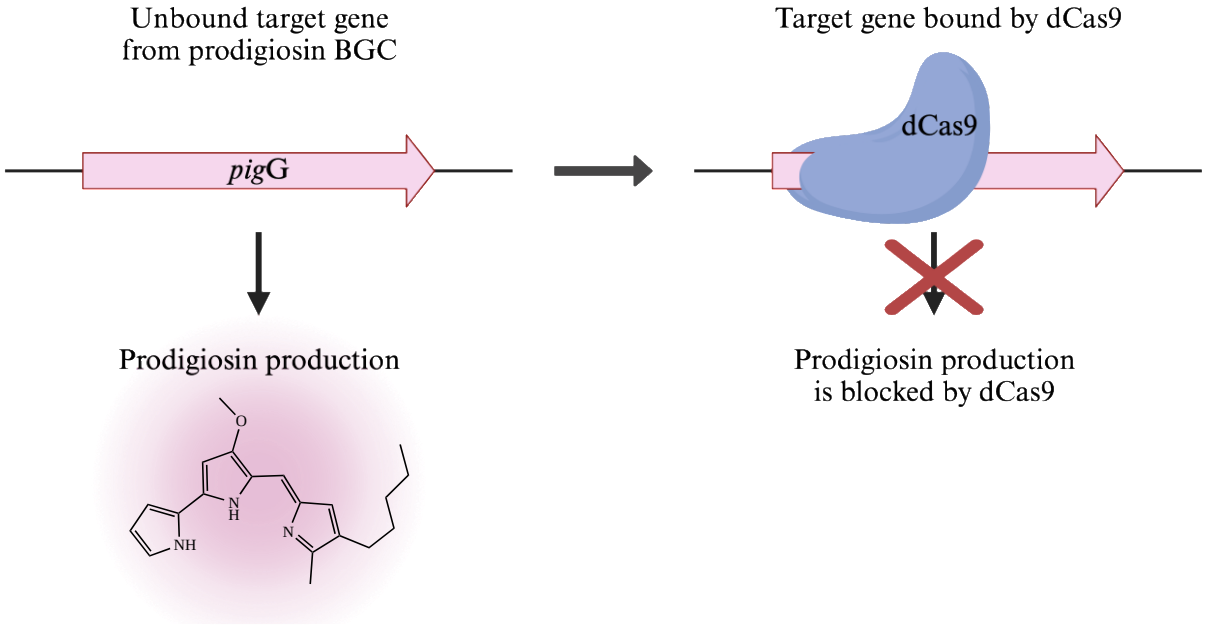
Title: Stimulating Natural Product production in *Pseudoalteromonas rubra* with CRISPR-dCas9



Natural products (NPs) have been a source of inspiration for more than half the pharmaceutical drugs currently in clinical use, including antibiotics and anti-cancer agents. However, the effectiveness of many antibiotics and anti-cancer agents has diminished partly due to over-usage, resulting in antibiotic/drug resistance. Adding to the issue, the discovery rates of new drugs have declined since the 1990s, resulting in a "discovery void" period. The decrease in discovery rates was mainly caused by the overexploitation of terrestrial bacteria and fungi, the most lucrative sources of many NPs. Fortunately, there is a relatively untapped resource of NPs in marine bacteria. These bacteria, such as those belonging in to the Pseudoalteromonas genus, produce secondary metabolites (i.e. NPs) with diverse and complex structures, encoded by biosynthetic gene clusters. Genome-mining studies have revealed numerous "silent" biosynthetic gene clusters in various Pseudoalteromonas species, suggesting significant untapped structural potential.

During my PhD studies, I have focused on exploring ways to uncover NPs from Pseudoalteromonas. I have been involved in four major projects: investigating the influence of cotton on Pseudoalteromonas, elucidating the structure of a molecule with a mass of 984 m/z, using CRISPR-dCas9 to knock down prodigiosin production, and developing a high-throughput method in collaboration with the Oleschuk group. Among these projects, the one that excites me most is the CRISPR-dCas9 project. The goal is to use dCas9 to bind to the open reading frame of a gene in the prodigiosin biosynthetic gene cluster of Pseudoalteromonas rubra DSM6842. By doing so, I aim to diminish the production of prodigiosin and explore the possibility of discovering new NPs.