Genome guided approaches towards uncovering the hidden biosynthetic potential of marine proteobacteria

Bacteria have proven to be an abundant source of antibiotics and other medicinal compounds that have been essential tools for modern medicine. However, since approximately 1960 bioactivity-guided antibiotic discovery pipelines have only uncovered a handful of truly novel antibiotic scaffolds from easily culturable bacteria. The drought of new antibiotics has led to the question: have we already discovered all the bioactive small molecules that nature has to offer?

The science of genomics has allowed for an answer to this question. It has become clear from metagenomic analysis that only a very small number of bacteria that exist in the environment have been successfully cultured in the lab. Additionally, the genomes of many bacteria contain "silent" biosynthetic genes are likely capable of synthesizing compounds that have not been identified in conventional laboratory cultures. It is therefore likely that nature contains a huge untapped potential for new bioactive compounds that have yet to be characterized.

In this talk I will detail a number of attempts to access unknown natural product chemistry from marine proteobacteria through various means. Firstly, I will discuss the awakening of "silent" biosynthesis pathways through culturing marine proteobacteria of the genus *Pseudoalteromonas* in media that promotes biofilm formation. I will also discuss attempts to awaken a silent biosynthetic gene cluster from the difficult-to-culture bacterium *P. luteoviolacea* by targeted cloning of very large biosynthetic gene clusters using CRISPR-Cas9 technology and expressing the gene cluster in a more amenable organism. Finally, I will discuss my investigations into the biosynthesis of a very uncommon natural product produced by an oil-degrading marine proteobacterium *Marinobacter nauticus,* the aryl-sulfonic acid siderophore petrobactin.