

Title: **Natural Chemical Selection – The evolution of bioactive molecules**

Abstract:

Natural products and the specialized metabolism that leads to them emerged as evolutionary advantages to the producing hosts. Nature has inherently selected for molecules and structural motifs that are biologically active and perturb the surrounding ecological microcosm to impart evolutionary fitness. Natural products have thus become a great resource for drug discovery and the elucidation of disease mechanisms. However, as the low-hanging fruit of extant natural product discovery rapidly approaches depletion, it can be useful to predict the past and future of natural product evolution to expand our understanding of how Nature uses chemistry as a functional tool.

The bipyrrrolic natural products are an archetype for the dynamic and convergent evolution of biologically active chemical structures. Using bioinformatics and examining key metabolic enzymes we were able to reconstruct a timeline for the evolution of the bipyrrrolic natural products and suggest what they may look like in the future under certain ecological contexts. The analysis pipeline discussed herein could be a benchmark for unlocking the full potential of natural products and the enzymes that construct them.

