

Discovery and Characterization of RiPP Natural Products

A. James Link

Princeton University, Department of Chemical and Biological Engineering

The posttranslational modifications (PTMs) in RiPPs (ribosomally synthesized and post-translationally modified peptides) dictate their 3D structure and their bioactivity. An underlying structural feature of many RiPPs is macrocyclization, installed by a growing number of different enzymatic strategies. Another common class of PTM in RiPPs is backbone modification, such as the formation of thiazol(in)es and oxazol(in)es. Our group has recently been interested in aspartimidylation, a backbone modification occurring at Asp residues that installs a metastable succinimide moiety into several different RiPPs. This talk will focus on recent work on the O-methyltransferase enzymes that install aspartimide in lasso peptides, graspetides, and a new class of peptides, the imiditides. The surprising stability of these aspartimide moieties will also be discussed within a kinetic framework. Finally, the talk will discuss potential chemical and biological ramifications of the aspartimide moiety in RiPPs.

Brief Bio

A. James (Jamie) Link is professor of chemical and biological engineering at Princeton University. He also holds appointments in the departments of chemistry and molecular biology as well as the Andlinger Institute for Energy and the Environment and the Omenn-Darling Bioengineering Institute. Jamie grew up in Newburyport, Massachusetts and earned his BSE in chemical engineering from Princeton University. Jamie completed his PhD at Caltech under the supervision of David Tirrell. Following postdoctoral work at the University of Texas at Austin in George Georgiou's lab, Jamie started his independent career at Princeton in 2007. Work in the Link laboratory has been recognized with awards such as the NSF CAREER award and a Sloan Fellowship in chemistry.

