Lasso Peptides as Building Blocks: Unthreading, Switching, and Synthesis

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Abstract

Lasso peptides are a diverse class of bacterially-derived natural products defined by a slipknot-like structure. The slipknot is established via an isopeptide bond formed between the N-terminus of the peptide and a glutamate or aspartate residues 7-9 amino acids away. The C-terminal portion of the peptide threads through the isopeptide-bonded ring, generating a [1]rotaxane structure. In this talk I will introduce the structural and functional features of lasso peptides and describe our work on the kinetics and energetic of lasso peptide unthreading. I will also describe recent work on a lasso peptide that exhibits switching between two distinct threaded states upon thermal activation. Finally, I will describe our work in using lasso peptides as building blocks for peptide catenanes.

Biography

James Link grew up in Massachusetts. He attended Princeton University as an undergraduate, earning a Bachelor's of Science in Engineering in Chemical Engineering with High Honors in 2000. He then moved to the California Institute of Technology (Caltech) in Fall 2000 to begin his PhD in the lab of David Tirrell as an NSF Graduate Research Fellow. During his PhD, Prof. Link worked on azide-bearing unnatural amino acids with applications in protein engineering and proteomics. Prof. Link moved to the University of Texas at Austin for an NIH postdoctoral fellowship with George Georgiou. In 2007, Prof. Link moved back to Princeton as an assistant professor in the department of Chemical Engineering, now named the department of Chemical and Biological Engineering. He was promoted to associate professor in 2013. Prof. Link's work at Princeton has been recognized with awards including an NSF CAREER award, a DuPont Young Professor Award, and a Sloan Fellowship in Chemistry.