SESSION II: POSTER ABSTRACTS

In vitro Reconstitution of Fusilassin

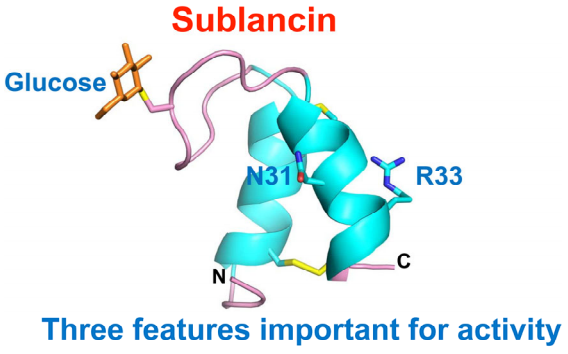
Adam J. Dicaprio and Douglas A. Mitchell

Lasso peptides are a class of ribosomally synthesized natural product which possess a unique, threaded lariat knot conformation. Lasso peptides with reported bioactivity often act as enzyme inhibitors or antagonists of cell-surface receptors. The low entropy threaded conformation of a lasso peptide endows them with considerable resistance to heat and proteolytic degradation, which are attractive properties for the development of peptide-based therapeutics. Despite their discovery nearly 30 years ago, the molecular mechanism underlying lasso peptide biosynthesis remains poorly characterized due to problematic characteristics of the purified biosynthetic enzymes. Here, we report the biosynthetic reconstitution of a lasso peptide derived from *Thermobifida fusca*, termed fusilassin, which demonstrates robust enzymatic activity *in vitro*. The improved biosynthetic capability of these enzymes, coupled with their desirably solubility and stability, is enabling a deeper look into the molecular mechanisms governing lasso peptide biosynthesis.

Structure activity relationships of the S-linked glycocin sublancin

Subhanip Biswas and Wilfred A. van der Donk

Sublancin is a 37-amino acid antimicrobial peptide belonging to the glycocin family of natural products. It contains two helices that are held together by two disulfide bonds as well as an unusual S-glucosidic linkage to a Cys in a loop connecting the helices. We report the reconstitution of the biosynthetic pathway to this natural product in *Escherichia coli*. This technology enabled the evaluation of the structure–activity relationships of the solvent-exposed residues in the helices. The biosynthetic machinery proved tolerant of changes in both helices, and the bioactivity studies of the resulting mutants show that two residues in helix B are important for bioactivity, Asn31 and Arg33.



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