

Title: Cyclotides, a New Molecular Scaffold to Target Protein-Protein Interactions

Cyclotides are a new emerging family of large plant-derived backbone-cyclized polypeptides ($\approx 28-37$ amino acids long) that share a disulfide-stabilized core (3 disulfide bonds) characterized by an unusual knotted. Cyclotides contrast with other circular polypeptides in that they have a well-defined three-dimensional structure, and despite their small size, can be considered as microproteins. The main features of cyclotides are a remarkable stability due to the cystine knot, a small size making them readily accessible to chemical synthesis, and an excellent tolerance to sequence variations. Cyclotides thus appear as promising leads or frameworks for design of peptide-based diagnostic and therapeutic compounds. I will present new data on the biosynthesis of cyclotides using bacterial and yeast expression systems for the generation of large -based libraries for rapid screening of cyclotides with novel biological activities. We will also report the design and biosynthesis of cyclotides able to target protein-protein interactions *in vivo*, as well as modified cyclotides with improved pharmacokinetic and cellular uptake properties.