Short stories in molecular recognition (of protein surfaces) and catalysis (of amide bonds)

Protein-protein complexes are difficult targets for inhibitor design, and therefore, offer a testing ground for new approaches. We are developing a rational design approach that begins by mimicry of protein interfaces by constrained peptides and peptidomimetics. However, direct mimicry of protein interfaces often leads to weak inhibitors. We overcome this inherent limitation by designing nonnatural side chain functionality. The first part of this presentation will discuss the application of our approach to the discovery of inhibitors for oncogenic Ras. The second part of the talk will focus on a rational design approach to develop catalysts for peptide bond formation. This work aims to address the significant challenge of excess reagent use in peptide synthesis.