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Abstract

Diversity-Oriented Synthesis and Chemical Genetics of Peptidomimetics to Address Lead Discovery of Anti-Infective Agents †

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Modern advances in Chemical Biology include the improvement of screening methods, the introduction of bioinformatic methods to unravel biological pathways, and the generation of high-quality chemical libraries. Diversity-Oriented Synthesis (DOS) has gathered interest to systematically explore the chemical space by generating high-quality small-molecule collections as probes to investigate biological pathways. DOS consists of generating structurally diverse compounds from a complexity-generating reaction followed by cyclization steps and appendage diversity. Also, chemical genetics emerged as a tool in chemical biology due to its role in selecting small molecules capable of inducing a biological phenotype or interacting with a gene product. Our efforts in this field are focused on the generation of diversity-oriented molecules of peptidomimetic nature as tool addressing protein—protein interactions, taking advantage of amino acid- and sugar-derived polyfunctional building blocks to be applied in couple-pair synthetic approaches. Also, we are applying peptidomimetic scaffolds to biological evaluation using cell growth as a phenotypic screening on yeast deletant strains to identify hit compounds in the discovery of novel antifungal and anticancer agents, and to dissect their mode of action.

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