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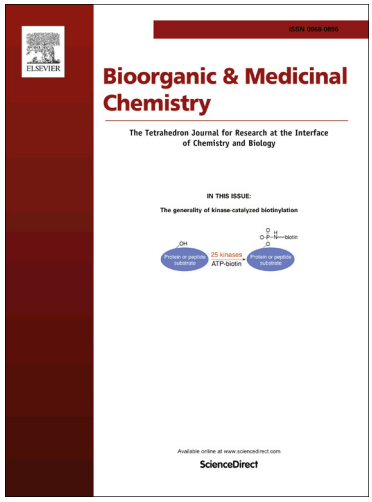

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Small molecules that target phosphorylation dependent protein-protein interaction

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ABSTRACT

Protein-protein interaction is one of the key events in the signal transduction pathway. The interaction changes the conformations, activities, localization and stabilities of the proteins, and transduces the signal to the next step. Frequently, this interaction occurs upon the protein phosphorylation. When upstream signals are stimulated, protein kinase(s) is/are activated and phosphorylate(s) their substrates, and induce the phosphorylation dependent protein-protein interaction. For this interaction, several domains in proteins are known to specifically recognize the phosphorylated residues of target proteins. These specific domains for interaction are important in the progression of the diseases caused by disordered signal transduction such as cancer. Thus small molecules that modulate this interaction are attractive lead compounds for the treatment of such diseases. In this review, we focused on three examples of phosphorylation dependent protein-protein interaction modules (14-3-3, polo box domain of Plk1 and F-box proteins in SCF ubiquitin ligases) and summarize small molecules that modulate their interaction. We also introduce our original screening system to identify such small molecules.