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Establishment of biophysical methods for fragment screening

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Fragment-Base drug discovery (FBDD) has emerged as an important means generating lead compounds. FBDD identifies low-molecular-weight ligands (less than 300 Da) that bind to biologically important macromolecular targets. The application of sensitive biophysical techniques to capture these weak binding molecules is paramount to the success of FBDD. Herein we describe the set up of a cascade biophysical method to detect fragment binding. Fragment screening against Ftsz (an antimicrobial target) and NS2B-NS3 (Dengue protease) is discussed.

Filametous temperature-sensitive Protein Z (FtsZ): The essential cytosketal protein FtsZ is a well validated target for developing antibacterial drugs. FtsZ is an essential cell-division protein that polymerizes in a GTP-dependent manner, forming a Z ring at the septum site. The inactivation of FtsZ or alteration of FtsZ assembly results in the inhibition of Z-ring and septum formation, impairing bacterial cell division.

NS2B-NS3 protease: The serine protease NS2B-NS3 is a target for the development of drugs against Dengue virus infections. NS2B-NS3 is involved in posttranslational processing of polyproteins, and thus plays a vital role for life cycle sustenance and replication in viruses.

Biography

Guo-Ying Chen achieved his PhD in Organic Chemistry at National University of Singapore in 2012. Now he is doing his Postdoctoral research at Experimental Therapeutic Center, A.STAR, Singapore. His research interest is in fragment based drug discovery.

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