REGIONAL CENTRE FOR BIOTECHNOLOGY

Seminar series

Rapid construction and high-throughput screening of novel combinatorial libraries to identify bioactive molecules

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Abstract

High-throughput screening (HTS) has emerged as an important technique to identify bioactive molecules. Conventionally, in high-throughput screening, a large collection of small molecules maintained in a central facility are tested against the target of interest using functional assays in 384- or 1,536-well microtiter plates. This screening technique requires an elaborate infrastructure of liquid handlers, plate readers and robotics and the large cost of the maintenance of the compound library makes it fairly expensive. The screening of one-bead one-compound (OBOC) combinatorial libraries on the solid phase is an attractive alternate approach. This bead-based screen on the solid phase is far less expensive than functional HTS and requires none of the infrastructure. For some compound classes, using combinatorial synthesis, millions of compounds can be constructed de novo in a few days for the bead-based screening purpose. Using this on bead screening technology, ligands of potential interest such as tool compounds, therapeutic leads and diagnostic reagents have been successfully discovered. In this talk, I will focus on the design and synthesis of chemically diverse and conformationally rigid OBOC libraries and discuss our screening efforts with these libraries to isolate bioactive compounds. The screening technology discussed here is a promising tool to accelerate ligand discovery process, which is one of the most important goal in chemical biology research.