

Method of Rapidly Identifying Inhibitors of Topoisomerase DNA Religation

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Applications:

Infection, Oncology, Antibacterials, Antifungal, Antiviral, Drug Discovery and Development
High throughput screen for compounds that modulate topoisomerase activity

Topoisomerases play a central role in nucleic acid metabolism and are important in a variety of biological processes related to cell division, DNA replication, chromosome structure and gene expression. Compounds that act as effective cellular inhibitors of topoisomerases are expected to act as cytotoxic agents through the disruption of the normal cell division process. Such compounds can be effective and selective antibacterial, antifungal and antiviral agents. And because cell division is an important characteristic of cancers and other proliferative diseases, agents that inhibit topoisomerases are also useful as antineoplastic agents. The invention provides methods for identifying topoisomerase activity modulators in both solid and liquid phase formats. High throughput screening methods, compositions, kits and integrated systems for performing the assays are provided. The invention represents an improvement over existing technology in several ways. Through the use of different nucleic acid substrates, the assays can be adapted to screen for inhibitors of numerous different classes of topoisomerase enzymes and assay multiple different topoisomerase enzymes in a single reaction, thus enhancing throughput. The assays can be run in a parallel fashion such that multiple different topoisomerase enzymes and/or modulators are assayed simultaneously. The assays can be performed in the liquid or solid phase and each of the formats is readily amenable for automation and high throughput screening. Further, the assays are extremely sensitive relative to previous assay formats and only minimal quantities of reagents are required.

References:

Nucleic Acids Res 28(24):4884-92 (December 2000)

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