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Special Issue Reprint

Topoisomerases as Targets for Novel Drug Discovery

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Topoisomerases play a crucial role in controlling DNA topology and have long been established as the therapeutic targets of several clinically successful antibacterial and anticancer drugs. Despite decades of clinical use, topoisomerase-targeting agents still face several limitations, including antibiotic resistance, off-target toxicity, the induction of secondary malignancies, cardiotoxicity, and limited tumor selectivity. These challenges have driven extensive research toward elucidating novel inhibitory mechanisms, designing more selective or multitarget topoisomerase inhibitors, and developing combination strategies that enhance therapeutic efficacy and reduce toxicity.

Topoisomerases as Targets for Novel Drug Discovery is a Reprint of the Special Issue in *Pharmaceuticals* and contains a collection of review and research articles highlighting recent progress made in overcoming these challenges. The contributions explore the discovery and development of new topoisomerase inhibitors, innovative strategies to improve therapeutic selectivity and safety, and novel insights into the management of chemotherapy-induced toxicities. Overall, these articles highlight emerging trends in topoisomerase research and emphasize the importance of interdisciplinary approaches that connect structural biology, chemistry, and pharmacology to advance the next generation of topoisomerase-targeting therapies.



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