Editorial

Recent Trends in Anticancer Drug Development: Challenges and Opportunities

Cancer is caused by the uncontrolled growth of cells and is a major cause of death throughout the world. Various strategies employed for the treatment of cancer include surgery, chemotherapy and radiation therapy used either alone or in combination that can significantly impact tumor growth. Conventional strategies for the complete eradication of the cancer cells have proved to be ineffective. Targeted chemotherapy was successful in certain malignancies, however, the effectiveness has often been limited by drug resistance and side effects on normal tissues and cells. The biggest challenge for the chemotherapeutic agents is acquiring multidrug resistance by the cancer cells. One drug one target approach for the treatment of cancer is not successful and may be responsible for the development of multidrug resistance. Hence the attention is shifting towards the development of single drug that can simultaneously bind to multi-targets. The advantage of one drug multi-target approach is that the drug can simultaneously target more than one pathway and increase its effectiveness even against multi-drug resistance cancer cell lines. Since the last few years, many promising drug targets have been identified for the effective treatment of cancer. Computer based rational drug designing, targeted drug delivery, combination therapy and targeting cancer stem cells are some of the recent strategies being explored for the development of potent drug candidates for the complete eradication of the cancer cell population with no possibility of relapse. In the review article, we have highlighted some promising anticancer drug targets that include kinases, tubulin, cancer stem cells, monoclonal antibodies and vascular targeting agents. A number of potential drug candidates in various phases of clinical trials were also discussed.

Sun Choi's research group reported the importance of computational approaches in expediting the anticancer drug discovery and development. The design and development of anticancer drugs is an intricate, expensive, and time-consuming process. To overcome these limitations and manage large amounts of emerging data, computer-aided drug discovery/design methods have been developed. Computational methods can be employed to help and design experiments, and more importantly, elucidate structure-activity relationships to drive drug discovery leading optimization methods. The integration of experimental and computational approaches holds great promise in the rapid discovery of novel anticancer therapeutics. The article also highlighted some latest advancements in the computational approaches for anticancer drug development.

Natural products like taxanes, vinca alkaloids and podophyllotoxin were found to be potent against different types of tumors. Marine natural products and their synthetic analogs have also been explored for number of bioactivities including anticancer activity. Fedorov *et al.* in their article reported structure-activity relationship studies on the anticancer activity of recently isolated marine compounds and their synthetic analogs. A number of compounds belonging to different chemical classes such as terpenes, glycosides, alkaloids and steroids with anticancer activities were described.

Chemoresistance is one of the major challenge in the effective treatment of cancer patients. Drug resistance in chemotherapy may develop due to decreased uptake of hydrophilic drugs, increase in energy dependent efflux, alteration of the redox state, alteration of apoptotic pathways, and modification of the tumor microenvironment. Nanoparticles are being explored as vehicle for the target based drug delivery to overcome multidrug resistance. Trotta *et al*. described various mechanisms involved in multidrug resistance and the nanoparticle based drug delivery systems to target specific aspects of this phenomenon.

Selective drug delivery to the cancer cells is a highly desired condition in the effective treatment of cancer. Kos *et al.* explored the role of nanoparticles in selectively delivering protease inhibitors to the cancer cells. Proteases play a crucial role in cancer cell migration, invasion and metastasis. Systemic delivery of protease inhibitors can reduce proteolytic activity in normal tissue leading to severe side effects. The problem can be addressed by target delivery of drugs to cancer cells.

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Cancer is a complex and multifactorial disease state and many novel targets are being explored for its effective treatment. G-quadruplexes is a family of nucleic acid four-stranded structures formed by sequences containing repetitive guanine-rich tracks. Interaction of G-quadruplexes with the small molecules can modulate oncogene expression in cancer cells. Thus, G-quadruplexes have been proposed as a novel target for the anticancer drug development. Paulo *et al.* reviewed the role of various G-quadruplexes interactive small molecules as novel anticancer agents.

G. M. Verkhivker described the allosteric regulatory mechanisms of protein kinases in the development of novel anticancer agents. Allosteric regulation of protein kinases can combat cancer mutants and is one of the frontier areas in cancer research. The article describes structural, biochemical and computational studies of kinases and discusses dimerization-dependent mechanisms of their regulation. These studies can further help in the design and discovery of kinase inhibitors and allosteric modulators for kinase activation.

Similarly, photodynamic therapy is a novel approach in targeted cancer therapy. Photoactivated chemotherapy is based on the use of inactive prodrugs whose biological activity is significantly increased upon exposure to light. This technique is a promising approach to selectively activate cytotoxic drugs at their site of action and thus to improve the tolerability and safety of chemotherapy. Szymanski *et al*. provided deep insight into the current state of photoactivated cancer therapy and to identify its challenges and opportunities. The role of photodynamic chemotherapy has been explored in various cytotoxic metal complexes and organic compounds.

Cancer cells develop multiple and complex mechanisms to evade the drug induced cytotoxicity and multi-drug resistance, therefore, represent a significant impediment to successful cancer therapy. A better understanding of various cell signalling pathways in the development and progression of cancer and mechanistic insight into the resistance mechanisms are crucial for the management and complete eradication of different types of cancers.

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