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Srivastava, 2024-01-11 This Research Topic is part of a series with Multi targeted Natural Products as Cancer Therapeutics

Challenges and Opportunities Volume II Cancer remains a leading cause of disease related deaths worldwide despite recent

advances in our understanding of cancer initiation progression and metastasis Chemotherapy and radiotherapy have been

used as standard non surgical treatments of human cancer for decades however the survival rates of patients with cancer

especially those with advanced diseases are still very low due to the high toxicities of these treatments as well as the severe

side effects This fact has motivated researchers to discover new cancer therapeutics with minimum side effects which

intensively promotes the rapid development of single specific molecule targeted therapies SSMTT Many efforts have been

made in world wide cancer drug discovery research and several single molecule targeted therapies have been successfully

developed Unfortunately most of the investments failed because cancer is a genetic disease and always harbors multiple

alternations of molecules or genes at the genomic genetic and epigenetic levels The inhibition of a single molecule or

signaling pathway by SSMTT frequently results in a hyperactive compensation of other cancer related molecules and

signaling pathways as well as the subsequent development of drug resistance Therefore identifying multi targeted therapies i

e drugs that are able to target multiple cancer related genes proteins or signaling pathways is a more promising way to

success in developing new cancer therapeutics Natural products especially those from traditional Chinese medicine and folk

remedies in other countries are an extraordinarily important source for new drug discovery over the past decades Of note

many natural products have often been demonstrated to target several crucial genes or proteins in cancer related signaling networks and exert synergistic effects For example Japonicone A a dimeric sesquiterpenoid from the medicinal plant *Inula japonica* has been found to inhibit tumor growth and metastasis by dually targeting the TNF NF B and p53 MDM2 signaling pathways Traditionally researchers have believed that the multi targeting mechanisms of natural products have limited their use in cancer treatment due to the low specificity and potential side effects The growing interest in developing multi targeted cancer therapies may provide another golden opportunity to develop natural products as new cancer therapeutics Nevertheless critical investigations for a comprehensive understanding of the molecular mechanisms of natural products also mean more challenges Our long term goals are to fully understand the molecular targets and mechanisms of action of anticancer natural products and develop them as novel cancer preventive and therapeutic agents The specific goal of this Research Topic is to bring together the recent findings of newly identified anticancer natural products especially those with multiple molecular targets Papers Original Research articles or Reviews which discuss the in vitro and in vivo efficacy and pharmacological and toxicological properties of natural products are also welcome to be submitted Guidelines for the conception and review of submissions As many anticancer drugs working as cytotoxic compounds have non selective effects annihilating their potential therapeutic benefits manuscripts are advised to provide evidence of a significant selectivity towards cancer cells vs healthy cells Specifically if the studied anticancer drug or modality does not target an oncogenic pathway the authors should make every effort possible to prove that the cytotoxic or cytostatic effects they have identified exhibit selectivity for cancer cells ideally 1 log difference in EC50 or IC50 vs non malignant cells eg fibroblasts or primary culture of cells The authors should also demonstrate the applicability of their anticancer modalities on a minimum of two well authenticated cancer cell lines ideally originating from distinct organs tissues For manuscripts dealing with plant extracts or other natural substances compounds the composition and the stability of the study material must be described in sufficient detail In particular for extracts chromatograms with characterization of the dominating compound s are requested The level of purity must be proven and included Please refer to the Four Pillars of Best Practice in Ethnopharmacology a subset of which concerning general standards in natural product research are applied to all such studies in all sections of *Frontiers in Pharmacology*

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