Identification of anti-cancer compounds from natural products

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Natural products serve as abundant resources with diversity of chemical structures, which has been widely explored for the pharmacological researches and drug discovery [1,2]. They are generally isolated from microorganisms, plants, marine organisms, etc., with multifarious pharmacological activities [3]. To date, natural products and their derivatives have been extensively used for the treatment of various diseases, such as malarial, immune-related diseases and cancer [4,5]. According to a statistical data from 1946 to September 2019, there are 13.5% and 25.1% of approved anti-cancer drugs originating from natural products and natural product derivatives, respectively [1], indicating the essential role of natural products in anti-cancer drug development.

The global morbidity and mortality of cancer are still rapidly increasing, which is regarded as a prominence health issue worldwide [6]. Natural products trigger anti-cancer effects on different processes of cancer, through various potential mechanisms [7]. To date, the phenotypes of cancer cells, including inducing cell death, restraining cell proliferation, and inhibiting cell mobility, etc. [8]. For instance, natural product-originated paclitaxel and camptothecin are both famous clinical chemotherapeutic drugs for cancer treatment, which are identified with their cytotoxic effect [9]. Additionally, some natural products could directly or indirectly inhibit cancer-driver targets or signal pathways to exhibit anti-cancer effects [10]. Meanwhile, some of them enhance the anti-cancer effect or overcome the drug resistance of clinical anti-cancer agents [11,12]. Moreover, the successful development of immunotherapy provides a novel strategy for anti-cancer drug development from natural products. Currently, natural products have been reported with the effect on the regulation of immune checkpoints and the modulation of immune cells like myeloid-derived suppressor cells, which indicates their adjustment functions on anti-cancer immunity and shows potential combination strategies with immunotherapeutic agents [13,14]. Besides, gut microbiota is associated with the progression of various cancer types including colorectal cancer, which has been demonstrated to promote the proliferation of cancer cells, modulate immune cells and induce drug resistance, etc. [15]. Natural products are capable to modulate cancer-related gut microbiota to prevent tumorigenesis [16], which offers a new avenue for anti-cancer drug discovery from natural products in the future.

Five research articles about the investigation on the anti-cancer effect of natural products have been organized in this issue of Chinese Journal of Natural Medicines. Fan et al. [17] reported that the ethyl acetate extraction of *Pileostegia tomentella* Hand. Mazz (ZLTE) exerted anti-cancer effect on cancer cells via inducing canonical apoptosis. ZLTE significantly increased the expression of cleaved-poly (ADPribos)e polymerase and decreased pro-caspase-3/7/8 on cancer cells. Meanwhile, ZLTE-induced apoptosis was mediated by reactive oxygen species generation, which could be partially reversed by N-acetyl cysteine. Yang et al. found that JNK2 played an important role in drug resistance induced by adriamycin and the high expression of JNK2 activated protective autophagy in Hep G2-DOXR cells. GL-V9, a new synthesized flavonoid derivative with anti-cancer effects, reversed adriamycin resistance by blocking the JNK2-related protective autophagy in hepatocellular carcinoma cells [18]. Jing et al. [19] reported that cucurbitacin E (CuE) exhibited potential anti-cancer effect against lung cancer cells by interfering with the EGFR/mitogen-activated protein kinase signaling pathway. Treatment with CuE triggered apoptosis by increasing cleaved caspase-3/9 and induced G1/G0 cell cycle arrest on cancer cells. Consequently, the results of molecular simulation indicated the potential interaction between CuE and EGFR. Chen et al. [20] reported that nagilactone E (NLE), a natural product with anti-cancer potential, up-regulated the expression of PD-L1 via activation of c-Jun N-terminal kinases-c-Jun axis in lung cancer cells. Furthermore, NLE promoted the binding of programmed cell death protein 1 on the cell surface of NCI-H460 cells. Therefore, NLE has the potential to induce enhanced anti-cancer effect by combining with the immunotherapy antibodies. Chen et al. [21] reported the preventive effect of *Panax notoginseng saponins* (PNS)
on colitis-associated colorectal cancer development pertinent to the role of gut microbiota. PNS significantly relieved the disease activity index scores and colon tumor loads in azoxymethane/dextran sulfate sodium mouse model. The abundance of Akkermansia spp. in rat feces was negatively associated with the development of colorectal cancer, which could be restored by PNS.

To date, natural products have been attracting lots of research attentions in the field of anti-cancer drug development. The biological cognition of cancer progression and the development of modern technologies will promote the exploration of natural products. As the research move along, natural products are not only identified with their conventional cytotoxic effects, but also with the potentials to regulate cancer-driver signals, as well as to modulate cancer microenvironment. Meanwhile, more and more cancer-related factors have been studied and they also provide different ideals for drug screening from natural products. Collectively, we believe that natural product is an important resource for anti-cancer drug discovery and would make more contributions to cancer treatment in the future.

References


Dr. LU Jin-Jian is now an Associate Professor of Pharmacology in University of Macau. He mainly focuses on screening of natural compounds with anti-cancer potential and exploration of the molecular mechanisms. He is also interested in studying the new targets and strategies for cancer therapy. To present, Dr. Lu has published more than 150 scientific papers in the SCI journals (Citations 5000+, H-index 37). He was awarded as the 2nd Prize of Natural Science: Macao Science and Technology Awards twice and CNPHARS Annual Young Pharmacologists in 2016

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