



## Advances in mechanism and treatment strategy of cancer

Ye Zeng

Institute of Biomedical Engineering, West China School of Basic Medical Sciences and Forensic Medicine, Sichuan University, Chengdu 610041, China

Correspondence to: [ye@scu.edu.cn](mailto:ye@scu.edu.cn)

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Cancer is one of the most serious diseases with high incidence and high mortality rate threaten human health and quality of life. The researches on mechanisms of cancer development and metastasis, and effective and reasonable treatment strategies are of great significance. The traditional treatments for tumors such as surgery, radiotherapy, and chemotherapy have some benefits, but many drawbacks such as drug-resistance and side-effects. With the emergence of new therapeutic methods such as tumor-targeted drugs and immune drugs, the survival of cancer patients is improved, but reports on cardiac damage caused by therapeutic drugs are increasing.

The tumor-targeted therapy inhibits the process of carcinogenesis via targeting the proto-oncogenes and the cellular signaling pathways involved in the tumor growth and metastasis. It has strong specificity and remarkable efficacy. There will be more and more targeted drugs applied to the clinic. Nowadays, the biggest concern of many targeted drugs in phase II and III clinical studies is the cardiotoxicity, such as mitochondrial dysfunction, endothelial cell damage, and coronary spasm (1, 2).

The tumor-targeted drugs are mainly including antibodies and tyrosine kinase inhibitors (TKIs). Bevacizumab and trastuzumab are antibody-drugs. Bevacizumab is a vascular endothelial growth factor (VEGF) inhibitor, which is used for the treatment of colorectal cancer, non-small cell lung cancer, renal cell carcinoma, and polymorphism glioblastoma. Trastuzumab is mainly used for the treatment of proto-oncogene human epidermal growth factor receptor 2 (HER2)-positive breast cancer, which significantly improved the prognosis of metastatic breast and gastric cancers that overexpressing HER2. The TKIs such as imatinib, sorafenib, sunitinib, vade-tanib, pazopanib and crizotinib were used for various tumors. All those drugs showed cardiotoxicity (2, 3).

In this special issue, we collected basic, translational and clinical studies, meta-analysis, as well as review articles that contribute towards understanding signaling mechanisms of tumor progression and metastasis, microenvironment, vasculogenic mimics/angiogenesis, identification of biomarkers for early diagnostics, clinical therapeutic approaches, and current concepts in the

prevention and treatment of human cancer.

It has demonstrated that autophagy is involved in multiple processes in cancer development and metastasis. In the original research articles, Jiang S et al (4) revealed Icaritin induced apoptosis and inhibited autophagy in multi-drug resistant SKVCR ovarian cancer cell via activating mammalian target of rapamycin (mTOR) pathway, which suggested Icaritin may serve as a novel therapeutic approach to resolve multidrug resistance in ovarian cancer treatment by inhibiting autophagy. Yao K et al (5) investigated the effect of Bacillus Calmette Guérin (BCG) on gastric cancer cell line MGC-803 and the potential cooperation of BCG and lymphocyte in determining the final fate of cancer cells. They showed that BCG promotes lymphocyte immunocompetence to induce cell apoptosis and autophagy in MGC-803 cells, might through inducing release of IFN $\gamma$  from peripheral blood lymphocytes, which suggested that BCG has an anti-tumor effect by directly attacking gastric cancer cells and by inducing immunity. Liu Q et al (6) investigated the effect of luteolin on the sensitivity to ovarian cancer cells and demonstrated that luteolin suppresses autophagy but enhances the sensitivity to cisplatin through suppressing the expression of poly(ADP-ribose) polymerase-1 (PARP1). Hekmatshoar Y et al (7) detected the mechanism of drug resistance of imatinib and found that autophagy plays a crucial role in imatinib resistance. Thus, autophagy plays an important role in drug-resistance and sensitivity of cancer cell.

Inhibition of cell proliferation and induction of cell apoptosis are still important treatment strategies for various cancers. He X et al (8) developed a recombinant adenovirus containing an apoptotic gene Fas-associated protein with death domain (FADD) to suppress the growth of colorectal cancer, which might provide novel toll for selectively target colorectal cancer. Xia X and Zhou X (9) found knockdown of Sirtuin 1 significantly inhibited cell proliferation and promoted cell apoptosis of paclitaxel-resistant cervical cancer cells, suggesting that Sirtuin 1 serves as a potential therapeutic target in paclitaxel-resistant cervical cancer. Miao X et al (10) reported that miR-140-5p was low expressed in retinoblastoma, and it could negatively regulate the proliferation possibly via directly targeting transcriptional acti-

vities of cell migration-inducing protein (CEMIP), and cell adhesion molecule 3 (CADM3). The regulation and mechanism of apoptosis are remained unclear.

Metastasis is the most deadly and least understood aspect of cancer (11). The serum visfatin was significantly associated with the histology and metastasis in hepatocellular carcinoma (12). Liang N et al (12) reported that visfatin induced HCC cell migration via upregulation of miR-21, which provides a novel basis for the diagnosis of HCC. Zhang X et al (13) demonstrated that  $5 \times 10^6$  cells/mL and  $1 \times 10^5$  cells/mL are the optimal cell concentrations for the subcutaneous and experimental metastatic lung cancer mice models, respectively.

Traditional Chinese Medicines exhibited efficacy to tumorigenesis. Ke B et al (14) investigated the role of flavored Guilu Erxian decoction in the treatment of cisplatin-induced side-effects in bone marrow mesenchymal stem cells and demonstrated that flavored Guilu Erxian decoction could abrogate the side-effects of cisplatin via the activation of phosphoinositide 3-kinase (PI3K)-AKT-mTOR pathway. Li Z et al (15) demonstrated the interaction of PI3K and amplified in breast cancer 1 (AIB1) is involved in estrogen treated breast cancer cells. Lu J et al (16) reviewed the anti-depression role of *Xiaoyao San* and the anti-tumor effect of its active ingredients.

Jiang D et al (17) analyzed a cohort of 363 lung cancer patients along with 363 age- and gender-matched healthy subjects. They revealed low total bilirubin level [OR (95%CI), 1.12 (1.02-1.23)], aspartate transaminase [OR (95%CI), 1.12 (1.02-1.23)], and alanine transaminase [OR (95%CI), 1.12 (1.02-1.23)] were risk factors in lung cancer.

Peng Z et al (18) confirmed that serum miR-141 was overexpressed in colorectal cancer patients and suggested miR-141 in miR-200 family is a high-risk diagnostic marker for the early diagnosis of colorectal cancer. In other meta-analyses, Liu T et al (19) demonstrated that microRNA-17 might be a novel potential biomarker in the diagnosis of colorectal cancer. Yan G et al (20) demonstrated that Th17 cells and Th17-related cytokines may be involved in the pathogenic mechanisms of colorectal cancer.

In the case-report, Ma J et al (21) reported a misdiagnosis case of aggressive angiomyxoma and suggested that pathological and immunohistochemical examination are important for avoiding misdiagnosis.

Although these investigations contribute towards understanding the mechanisms in tumorigenesis, drug-resistance and side-effects, and identifying biomarkers for early diagnostics and treatment of cancer. Based on the observations, new therapeutic approaches for clinical and rehabilitative purposes might be developed in the future. In addition, we must pay attention to the cardiac injury caused by targeted drugs. To prevent cardiotoxicity of tumor-targeted drugs and immune drugs, we must first understand their roles in endothelial dysfunction, mechanism in cardiotoxicity, find relevant predictive biomarkers, and develop strategies to limit the cardiovascular toxicity during cancer treatment.

### Conflict of interest

The author reports no conflicts of interest.

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