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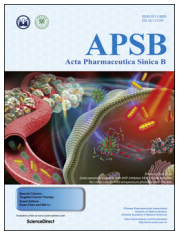

Editorial Preface for Targeted Cancer Therapy

Chemotherapy has been used for treatment of human cancer since early 1900 with purified natural products or synthetic compounds to kill rapidly growing tumor cells or to reduce their growth. However, chemotherapy is also toxic to some rapidly proliferating normal cells such as bone marrow, therefore causing undesirable side effects. With recent advances in molecular biology, genetics, and signaling transduction, many types of cancer can be traced back to mutation(s), abnormal pathway activations, or altered expressions of a molecule, a pathway, and/or a group of proteins, which can be targeted to specifically inhibit cancer cells, but not normal tissues. In 2002, Dr. Charles Sawyers used "Targeted cancer therapy" to review the development in this field for the first time[1]. In the last decade, cancer drug targets have been extended to signaling pathways, protein–protein complexes, and signaling networks in tumor cells, tumor stromal tissues, and immune systems[2,3].

In this special column, serval invited researchers with diverse expertise in targeted cancer therapy reviewed recent developments with the goal to facilitate the process from the target discovery to drug development and to clinical applications. This special column contains seven review papers and four original research papers, representing a comprehensive coverage for recent advances of targeted cancer therapy.

In the review paper section, Dr. Liu[4] summarized the current understanding of HER3 receptor biology in various types of cancers and presented strong rationales that therapeutic inactivation of HER3 and/or its downstream signaling could overcome drug resistance and improve the outcomes of cancer patients. Taxanes are first-line anticancer drugs for a number of cancers, including castration-resistant prostate cancer (CRPC). However, the prolonged use of taxanes often leads to multidrug resistance and thus limits their clinical efficacy. Dr. Chen[5] reviewed the recent development of p38 MAPK signaling integration with its specific phosphatase PTPH1 in Kras oncogenesis and their effects on human colon and breast cancer growth through their individual and common targets. Dr. Li[6] summarized recent advances in elucidating resistant mechanisms to taxanes and discussed potential therapeutic strategies for improved treatment of CRPC. The paper from Dr. Wang's group[7] summarized recent development of targeting mutated oncogenic proteins in lung cancer and discussed about the future of personalized medicine in lung cancer. The review from Drs. Zhang and Wu's group[8] highlighted recent developments and the application of CAR-T cell therapy in different hematological malignancies, and suggested potential directions for future improvement on the effectiveness of these adoptive cell therapies. Finally, Dr. Huang[9] reviewed recent developments in the mitogen-activated protein kinase (MAPK) signaling in cancer and summarized progresses made on the development of small molecule inhibitors targeting the MAPK pathway. In particular, this review highlighted the importance and advantages of developing ERK inhibitors to overcome resistance to current inhibitors that target the upstream elements in the MAPK pathway.

In the research paper section, we included several papers using diverse strategies to overcome therapeutic drug resistance. The overexpression of several ATP-binding cassette (ABC) transporters is a well-recognized multidrug resistance mechanism, and proper drug combinations can overcome these resistance. Towards this direction, Dr. Fu's laboratory[10] found olmutinib, an epidermal growth factor receptor tyrosine kinase inhibitor, can significantly increase the drug retention and therapeutic efficacy of several chemotherapeutic drugs in ABCG2-overexpressed cancer cells. This finding encourages further clinical evaluation on the combination of olmutinib with traditional chemotherapy in ABCG2-overexpressing cancer patients. Drs. So and Tipoe[11] reported that a garlic-derived compound *S*-allylmercaptocysteine (SAMC) targets the low-density lipoprotein receptor-related protein 6 (LRP6), which is frequently over-expressed in tumor tissues of human hepatocellular carcinoma (HCC). Their studies suggested that LPR6 could be a potential drug target of HCC, and that SAMC is promising therapeutic agent for treating certain HCC subtypes. Photothermal therapy (PTT) is a clinically used strategy for cancer treatments, and enhancing the heat-sensitivity of tumor cells can provide a solution to maintaining the therapeutic efficacy of PTT. Towards this goal, Dr. Qian's laboratory[12] reported that gold nanorods together with HSP inhibitor VER-15508 micelles can attenuate the heat-resistance of tumor cells and enhance the therapeutic outcome of mild-temperature photothermal therapy. Finally, Dr. Yallapu[13] reported that a polymer/paclitaxel self-assembly (PTX-SA) formulation show improvement in paclitaxel delivery to cancer cells, potentially enhancing the therapeutic efficacy of paclitaxel in breast cancer.

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We sincerely hope that this special column will serve as a platform to facilitate development of targeted cancer therapy with the ultimate goal to cure human cancer.

References

1. Sawyers C. Targeted cancer therapy. *Nature* 2004;**483**:294–7.
2. Comoglio PM, Trusolino L, Boccaccio C. Known and novel roles of the *MET* oncogene in cancer: a coherent approach to targeted therapy. *Nat Rev Cancer* 2018;**18**:341–58.
3. Vennin C, Murphy KJ, Morton JP, Cox TR, Pajic M, Timpson P. Reshaping the tumor stroma for treatment of pancreatic cancer. *Gastroenterol* 2018;**154**:820–38.
4. Lyu H, Han A, Polsdofer E, Liu S, Liu B. Understanding the biology of HER3 receptor as a therapeutic target in human cancer. *Acta Pharm Sin B* 2018;**8**:503–10.
5. Qi X-M, Wang, Mortensen M, Wertz R, Chen G. Targeting an oncogenic kinase/phosphatase signaling network for cancer therapy. *Acta Pharm Sin B* 2018;**8**:511–7.
6. Bumbaca B, Li W. Taxane resistance in castration-resistant prostate cancer: mechanisms and therapeutic strategies. *Acta Pharm Sin B* 2018;**8**:518–29.
7. Jiang W, Cai G, Hu PC, Wang Y. Personalized medicine in non-small cell lung cancer: a review from a pharmacogenomics perspective. *Acta Pharm Sin B* 2018;**8**:530–8.
8. Zhao Z, Chen Y, Francisco NM, Zhang Y, Wu M. The application of CAR-T cell therapy in hematological malignancies: advantages and challenges. *Acta Pharm Sin B* 2018;**8**:539–53.
9. Liu F, Yang X, Geng M, Huang M. Targeting ERK, an Achilles' Heel of the MAPK pathway, in cancer therapy. *Acta Pharm Sin B* 2018;**8**:554–64.
10. Zhang Z, Guo X, To KK, Chen Z, Fang X, Min Luo, et al. Olmutinib (HM61713) reversed multidrug resistance by inhibiting the activity of ATP-binding cassette subfamily G member 2 *in vitro* and *in vivo*. *Acta Pharm Sin B* 2018;**8**:565–76.
11. Xiao J, Xing F, Liu Y, Lv Y, Wang X, Ling M-T, et al. Garlic-derived compound S-allylmercaptocysteine inhibits hepatocarcinogenesis through targeting LRP6/Wnt pathway. *Acta Pharm Sin B* 2018;**8**:577–88.
12. Tang X, Tan L, Shi K, Peng J, Xiao Y, Li W, et al. Gold nanorods together with HSP inhibitor-VER-155008 micelles for colon cancer mild-temperature photothermal therapy. *Acta Pharm Sin B* 2018;**8**:589–603.
13. Chowdhury P, Nagesh PK, Khan S, Hafeez BB, Chauhan SC, Jaggi M, et al. Development of polyvinylpyrrolidone/paclitaxel self-assemblies for breast cancer. *Acta Pharm Sin B* 2018;**8**:604–16.

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