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Editorial

EDITORIAL

Editorial of special issue on pharmacotherapeutics of digestive tumors

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It is my pleasure to present you with a Thematic Issue on "Pharmacotherapeutics of Digestive Tumors" in *Gastroenterology Report* (GR). Despite chemotherapy having been widely used in cancer treatment, the median survival for most stage IV digestive cancers is <1 year, with the exception of small-bowel and colorectal adenocarcinoma because of drug resistance. Recently, growing investigations have demonstrated that molecular-targeted therapy and the immunotherapy of immune-checkpoint inhibition such as the programmed death-1 (PD-1)/PD-1 ligand (PD-L1) antibody may be considered promising treatment options. Therefore, we continue focusing on the novel treatment strategies of digestive cancer in this Thematic Issue, which contains both review articles and original research articles.

Cetuximab, an IgG-1 monoclonal antibody (mAb) of epidermal growth factor receptor (EGFR), inhibits the phosphorylation of EGFR and its downstream molecules such as AKT, ERK, and STATs, and was used to treat the patients with metastatic colorectal cancer (mCRC). However, drug resistance limits its successful therapy. Dr Ye and colleagues summarize the underlying mechanisms of the resistance to anti-EGFR therapy.

Furthermore, Professor Wei and her colleagues focus on *BRAF* and *KRAS* mutations to illustrate the mechanisms of chemotherapeutic and anti-EGFR therapeutic resistance and then to discuss how to improve the efficacy of anticancer drugs and the strategy of prospective personalized therapy for mCRC patients with *BRAF* and *KRAS* mutations. We believe that understanding the mechanistic insights is of benefit in improving the efficacy and safe application of combination therapy.

Alteration in the composition of gastric and esophageal microbiota links to carcinogenesis, progress, and immunotherapeutic efficacy in digestive tumors. It poses a novel combination therapy of immune-checkpoint inhibition such as the PD-1/PD-L1 antibody with optimal modulation of the microbiome. Professor Pan and Zhang provide a comprehensive overview in this field.

Mitochondrial alterations are evident in all stages of tumorigenesis and targeting mitochondrial pathways has emerged as an anticancer therapeutic strategy. The Wnt-signaling pathway regulates many fundamental cellular functions such as stem-cell maintenance, mitochondrial metabolism, and dynamics. Crosstalk between mitochondria and Wnt signaling presents a feed-forward loop in which Wnt activation regulates mitochondrial functions, which, in turn, drives Wnt signaling. These suggest that the blockage of the crosstalk between mitochondria and Wnt signaling could be a novel therapeutic strategy to cure malignancies. Professor Theiss and colleagues provide an overview in this field.

The application of an anticancer-drug-sensitive test has been well documented. We summarize the key advances in the development of the approaches of anticancer-drug-sensitive tests. Recently, we developed a new method of a conditional reprogrammed cancer micro-tissue cultural drug-sensitive test system, which may be used for a precision-medicine evaluation and individualized therapeutic guidance.

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