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	TTER TO THE EDITOR		
Acute or chronic infl	ammation role in gastro	ointestinal oncology	
Inflammation and gas	strointestinal cancers		
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Abstract

The following letter to the editor highlights the review titled "Inflammatory bowel disease-related colorectal cancer: Past, present and future perspectives" in *World J Gastrointest Oncol* 2022 March 15; 14(3): 547-567. It is necessary to explore the role of inflammation in promoting tumorigenesis and development of gastrointestinal cancers.

Key Words: Inflammatory; gastrointestinal cancers; development

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Core Tip: Gastrointestinal cancers are systematic tumors with the largest number of patients in the world. Most patients are prone to migration, invasion or other malignant phenotypes. The treatment strategies mainly include surgical resection, radiotherapy and chemotherapy in clinic. However, the survival rate of cases still cannot be significantly improved. Recently, the relationship between inflammation and gastrointestinal tumors has been gradually clarified, and chronic inflammation plays an important role in the occurrence and deterioration of tumors. The main purpose of this letter is to illustrate the key role of inflammation in tumor progression and potential therapeutic directions.

TO THE EDITOR

We read with interest review by Snehali Majumder *et al.* ^[1], which is titled "Inflammatory bowel disease-related colorectal cancer: Past, present and future perspectives". The tumor pathogenesis is much complex and not yet clear. Recently, inflammation induced and promoted tumor occurrence and deterioration, and the presence of high levels of inflammatory factors in many tumor patients has gradually become clear. Gastrointestinal system is one of the most prone to inflammation. Patients with chronic inflammation are more likely to develop cancer

than those without inflammation, about liver cancer, pancreatic cancer, stomach cancer and colon cancer. Studies have demonstrated that hepatitis b virus (HBV) patients were more likely to get cancer of the liver, prognosis and survival time is far less than the patients with HBV [2]. Patients with pancreatitis had a 4.8-times significantly higher risk to develop cancer than those without pancreatitis [3]. Helicobacter pylori (HP) is one of the important risk factors for gastric cancer patients, and HP will induce the occurrence of chronic gastritis [4]. In addition, patients with colitis have an increased mortality of colon cancer by 15% [1]. Therefore, if the potential biomarkers can be identified by early intervention of the synthesis, secretion and release of inflammatory factors, it may have great clinical significance for gastrointestinal tumors and improve the overall understanding of gastrointestinal tumors.

The interleukin family is the most common biomarker of inflammation. IL-1β, IL-6 and IL-10 are involved in the development and progression of gastrointestinal tumors. On the other hand, external stimuli, such as excessive oxidative stress, promote the secretion and release of the IL family, while the IL family itself has a certain feedback activation effect, thus exacerbating the inflammatory response ^[5]. In colitis-cancer, IL-6 and other factors promote epidermal cell damage, and prolong inflammatory damage will lead to abnormal proliferation of epidermal cells, which, if not controlled, will eventually lead to gene epigenetic modification mutation and ultimately induce tumgenesis ^[6,7]. TNF, another classic inflammatory factor, can promote the activation of neutrophils or macrophages to aggravate tissue damage by regulating MCP-1 and other mRNA expressions ^[8]. Moreover, TNF accelerates the inflammatory process and thus lead to the occurrence of tumors ^[9]. In addition, the role of CCL family in gastrointestinal tumors is gradually becoming clear. CCLs infiltrated tissues by recruiting macrophages and releasing ILs family or TNF, further leading to local inflammatory infiltration of tissues, gene mutation and ultimately tumorigenesis ^[10].

Interestingly, some papers showed that chronic inflammatory responses promoted tumorigenesis and development, while acute inflammation is currently considered to inhibit tumor progression (Figure 1) [11]. The new clinical research paper indicated that

colonic cancer patients who developed a cancer recurrence, with higher IL-6 and TNF, which belong chronic inflammatory factors. However, acute inflammatory factors IL-10 and IFN-γ were lower expression compared with those who did not recurrence ^[7]. IL-12 is an acute inflammatory factor, which could inhibit tumor progression in gastrointestinal tumors, and its high expression leads to a longer survival time ^[12]. Additionally, interferon family is also a potential therapeutic biomarker, like IFN-γ, which could inhibit the occurrence and progression of gastrointestinal tumor by regulating cellular immunity, controlling cell cycle or promoting cell apoptosis^[13, 14]. Moreover, interferon family has been approved by FDA for the treatment of tumors ^[15].

In conclusion, inflammation is involved in the entire gastrointestinal tumor process. The worse inflammation is mainly chronic inflammation, which can be induced by many reasons, such as unhealthy high-fat diet, excessive use of antibiotics, imbalance of intestinal flora and so on [16]. Snehali Majumder *et al* systematically summarized the role of inflammatory factors in colon cancer [1]. However, they failed to study and consider the role of acute inflammation in colon cancer. Therefore, inflammatory factors should be considered as important triggers to optimize current diagnosis and treatment strategies for early tumor diagnosis.

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