Focus on gastrointestinal and liver cancers

ARTICLE INFO

Keywords:
Gastric cancer
Liver cancer
Colorectal cancer
Esophageal cancer

ABSTRACT

Digestive cancers, such as colorectal cancer, gastric cancer and liver cancer, remain major threats to human health in coming decades and their epidemiology is under dynamic changes. Recent advances in genotyping and sequencing technologies together with other molecular and cellular biology techniques have led to a clearer delineation of the pathogenic mechanisms underlying genetic and environmental factors that contribute to digestive cancers. Such expansion of knowledge continues to fuel the development of novel biomarkers and therapeutics. In this special issue of Seminars in Cancer Biology, hot topics in basic and translational research of digestive cancers will be reviewed.

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1. Changing epidemiology of major digestive cancers

Digestive cancers, including colorectal cancer (CRC), gastric cancer (GC), and liver cancer, are major threats to human health. According to Global Cancer Statistics, these three major digestive cancers are estimated to account for 23.5% and 27.0% of total non-cutaneous cancer incidence and death, respectively, in 2008 [1]. The epidemiology of digestive cancers is under dynamic changes owing to the changing prevalence and distribution of etiological factors. CRC incidence in many developing countries, including Asian countries, has increased 2- to 4-fold over the last two decades and has now reached a rate comparable to that of developed countries, with Westernization of diet playing a key role in this trend [2]. Obesity, an increasingly prevalent global health issue, is also expected to become an important risk factor of CRC [3]. Hepatocellular carcinoma (HCC) incidence rates in Asian countries are more than four times as high as rates in North America. However, HCC incidence in Asian countries is decreasing as a result of reduced consumption of aflatoxin B1-contaminated food and infant hepatitis B virus (HBV) immunization whereas HCC incidence in many Western countries is now on the rise owing to increased chronic HCV infection [4]. The increasing prevalence of obesity, non-alcoholic fatty liver diseases (NASH) and metabolic syndrome is also expected to have impacts on HCC incidence [5]. In this issue, Yu et al. and Tian et al. will discuss the epidemiology and molecular mechanisms of NASH-associated HCC [6,7]. The worldwide incidence and mortality rates of GC are decreasing, probably caused by increased availability of fresh fruits and vegetables and decreased consumption of salted and preserved foods, reduction in chronic Helicobacter pylori infection, and increased screening activities in some high-risk countries [8]. Nevertheless, GC remains the fourth most common cancer and the second leading cause of cancer death in the world [1]. Herein, Shiotani et al. will examine evidence regarding the efficacy of H. pylori eradication on lowering GC incidence and provide us with specific recommendations on GC prevention [9].

2. From genome to microenvironment and microbiota

Deciphering genetic information in the genome is key to understanding the biological basis of tumorigenesis. The advent of genome-wide association studies and next-generation sequencing technologies has provided investigators with powerful platforms for the identification of disease susceptibility genes and somatic genetic alterations that underlie carcinogenesis. With increasing studies utilizing these advanced technologies to study human cancers, Wong et al. will provide a comprehensive review on cancer susceptibility genes and somatic genetic alterations in CRC and discuss the impacts of novel sequencing technologies on future CRC genetic studies [10]. Aside from cancer genomic studies, recent discoveries in microRNA research have reshaped our understanding of the role of these small non-coding RNAs in digestive cancers. Pertaining to clinical practice, the use of microRNAs as diagnostic and prognostic biomarkers in digestive cancers have been promulgated [11,12]. To this end, Sakai et al. will analyze the most recent studies on microRNAs in esophageal cancer in relation to their biological and clinical significance [13]. Besides genetic and epigenetic alterations, dynamic interactions between cancer cells and their microenvironment play a key role in modulating malignant phenotypes, such as metastasis and angiogenesis. In this respect, Catalano et al. will discuss the influences of hypoxia and oxidative stress on CRC stem cells [14] whereas Tang et al. will address the regulation of cancer phenotypes by stress hormones through the cell surface β-adrenoceptors [15]. Microbial dysbiosis as a microenvironmental factor is also recently recognized to play a causative role in CRC [16,17]. Liu et al. will provide us an excellent review on the recent progress on how gut microbiota regulates intestinal
homeostasis and the pathogenesis of inflammatory bowel disease and CRC [18].

3. The way beyond

Understanding the basic molecular mechanisms of cancers has led to the development of novel targeted therapies, such as cetuximab (an anti-epidermal growth factor receptor monoclonal antibody) and bevacizumab (an anti-vascular endothelial growth factor-A monoclonal antibody). Hereof, Yu and Liu will focus on the anticancer mechanisms of a new class of molecular therapeutics known as BH3 mimetics and delineate how autophagy, a growingly investigated cellular process, regulates cancer cells’ response to these drugs [19]. With more insights into the molecular pathogenesis of digestive cancers, it is anticipated that a growing number of molecular therapeutics will be added to the armamentarium to fight against digestive cancer in humans in the near future. Apart from clinical advancement, the expansion of knowledge in biomedical sciences has also led to the development of other disciplines. In this regard, Locarnini et al. will propose a model for the origin and evolution of HBV in the context of the developmental history of human beings [20].

Conflicts of interest statement

The authors declare that there are no conflicts of interest.

References


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