

PREFACE

Gastrointestinal cancers are a leading cause of death among patients worldwide. The polygenic and heterogeneous nature of gastrointestinal cancers are characterized by alterations in multiple molecular pathways throughout their development, posing a big challenge for patient risk stratification and treatment options. Gastrointestinal cancers are common, and treatments are more effective when the cancers are detected at an early stage, which, unfortunately, is a challenge. About 10% of the gastrointestinal cancers are attributed to various genetic risk factors whereas the remaining 90% are sporadic, which further complicates timely diagnosis and subsequent development of management strategies, necessitating the need for a better understanding of the origin, and the development of better treatment strategies for gastrointestinal cancer. This book, contributed by an international team of clinicians and basic scientists, provides select, clinically significant aspects of gastrointestinal cancer.

The first three chapters focus on colorectal cancer, the most predominant of gastrointestinal cancers. *Chapter 1* provides an overview of colorectal cancer with emphasis on epidemiology, etiology, pathogenesis, clinical manifestations, diagnosis, treatment, prognosis, and prevention strategies. Identifying modifiable risk factors to reduce the incidence and morbidity of colorectal cancer is beneficial on an individual and public health level. There is a great emphasis on the role of lifestyle and diet as risk factors for colorectal cancer. As the diet we consume is processed by the gastrointestinal system, the putative role of the diet in colorectal cancer cannot be underestimated. *Chapter 2* summarizes our understanding of the role of lifestyle and diet on colorectal cancer incidence and survival and argues that lifestyle modification is essential for prevention and treatment of colorectal cancer for improved patient outcomes. Metastasis is the major cause of cancer-related deaths. The process of metastasis is multifactorial, and one such mechanism is epithelial-mesenchymal transition. It is a morphogenetic event in which cancer cells lose their epithelial characteristics and gain mesenchymal features with an increased migratory and invasive potential. *Chapter 3* discusses the fundamentals of epithelial-mesenchymal transition, how it leads to cancer progression, metastasis, resistance to radiotherapy and chemotherapy, and how various components of the epithelial mesenchymal transition can be used as potential markers or therapeutic targets for metastasis inhibition, along with the obstacles in the development of drugs targeting epithelial mesenchymal transition.

Gastrointestinal stromal tumors are mesenchymal tumors, thought to arise from the interstitial cells of Cajal. Gastrointestinal stromal tumors are mostly formed in the stomach and the small intestine. These tumors do not have specific endoscopic or radiological features. The treatment for confirmed gastrointestinal stromal tumors is surgery if the lesion is resectable with no metastases, or therapy with tyrosine kinase inhibitors if the lesion is unresectable, metastatic, or recurrent. *Chapter 4* discusses the clinicopathological features of gastrointestinal stromal tumors and describes the standard minimally invasive management techniques. Macrophages have a differential role in tumor biology: the M1 macrophages are anti-tumoral, and the

M2 macrophages are pro-tumoral. A subpopulation of these macrophages is described as tumor-associated macrophages and several studies have described the importance of extracellular vesicles derived from tumor-associated macrophages in the advancement and progression of gastrointestinal cancers. *Chapter 5* highlights the role of macrophage-derived extracellular vesicles in gastric, hepatic, pancreatic, and colorectal tumors. It discusses the importance of molecules and cell signaling pathways involved in this context and emphasizes the relevant role of these extracellular vesicles in tumor development. Gastrointestinal tumors are highly heterogeneous, characterized by alterations in multiple molecular pathways. Harnessing these molecular pathways can help the development of innovative therapeutic strategies. To this end, *Chapter 6* describes the prognostic and predictive potential of a multigene signature in gastrointestinal cancer. A validated panel of prognostic gene signature and score system that robustly and reliably predicts overall survival in gastric cancer patients, and how this signature can identify gastric cancer patients who may benefit from adjuvant FOLFOX chemotherapy are explored.

Pancreatic ductal adenocarcinoma has one of the worst survival rates among adult cancers, with only 11% in the United States surviving five years after diagnosis. The majority of patients are diagnosed with late-stage disease, since early-stage pancreatic ductal adenocarcinoma is typically either asymptomatic or presents with non-specific symptoms. By providing physicians with actionable information early enough for the cancer to be removed surgically, the overall 5-year pancreatic ductal adenocarcinoma survival rate could increase from 11% to over 50%. In *Chapter 7*, the authors describe the development and clinical implementation of a proteomic, multi-biomarker blood test for the early detection of pancreatic ductal adenocarcinoma. *Chapter 8* examines the incidence and mortality rate of stomach cancer worldwide, with emphasis on figures in Brazil. Data on new cases and deaths due to stomach cancer for 2020 and projections for 2040 are evaluated. Although both incidence and mortality rates currently exhibit a downward trend in most countries, including Brazil, the number of new cases and deaths each year is not negligible, indicating the need for continued actions to reduce exposure to stomach cancer risk factors and the expansion of early diagnoses with timely treatment. Esophageal cancer is currently the eighth most common cancer, and the sixth leading cause of death from cancer in the world due to its highly aggressive nature. The advent of minimally invasive surgical techniques has reduced morbidity and mortality of esophagectomy without compromising the oncological outcomes. *Chapter 9* provides a comprehensive account of McKeown mini-invasive esophagectomy technique.

I thank the authors for their dedication and intellectual contribution in bringing this book to fruition. I am confident the book will be a valuable resource to clinicians and basic scientists alike.

Jose Andres Morgado-Diaz, PHD
Cellular and Molecular Oncobiology Program, Cellular Dynamic
and Structure Group, Instituto Nacional de Câncer – INCA
Rio de Janeiro, Brazil
September 2022

DOI: <https://doi.org/10.36255/exon-publications-gastrointestinal-cancers.preface>