

Preface

The intestinal epithelium is the largest mucosal surface in the body and functions as a barrier between the host and its external environment. Cells within the mucosal surface are renewed every four to five days and this renewal is subject to stringent regulation in order to maintain homeostasis [1–3, 6, 7]. Studies indicate that colorectal cancer is the consequence of stepwise perturbations to major signaling pathways important in controlling various cellular functions [4, 5]. Eventually these alterations lead to the development of disease, often with heterogeneous phenotype and clinical outcome. In the last decades considerable effort has been made towards understanding of the mechanisms underlying development and progression of intestinal tumorigenesis. Furthermore, new discoveries in the fields of stem cells research, epigenetics, non-coding RNA and epithelial-to-mesenchymal transition have greatly improved our understanding of this disease. Recent data regarding the function of the gut microbiota in influencing both normal intestinal homeostasis on the one hand and on the other chronic inflammation, which may lead to cancer formation, open new possibilities for preventive treatment. Finally, emerging proteomics and genomics approaches aimed at developing novel cancer biomarkers may lead to earlier detection and enhance treatment options.

Colorectal cancer (CRC) is the fourth most common type of the cancer in the world with the American Cancer Society estimating that 132,700 new cases and 49,700 deaths from cancers of the colon and rectum will occur in the United States in 2015 (see <http://www.cancer.org/cancer/colonandrectumcancer/detailedguide/colorectal-cancer-key-statistics>). Noteworthy, the death rate of the colorectal cancer has declined in the past two decades and this is mainly due to introduction of early screening and improvements in the treatment of this disease.

This volume includes in-depth reviews of many recent developments in the field of intestinal tumorigenesis with an emphasis on the latest discoveries that have resulted in identification of novel mechanisms underlying cancerous transformation. We hope this volume provides readers with the information necessary in understanding important recent work on the mechanisms of intestinal tumorigenesis and comprehending the complexity of the process. It is also our desire that this volume serves to entice new researchers to participate in future studies geared towards understanding the mechanisms underlying development and progression of colorectal cancer. Finally we hope that this volume opens discussions in the scientific community and shapes the future research in this field.

In Chap. 1, Gala and Chung introduce the fundamental basis of hereditary colorectal cancer syndromes. Chapter 2, by Prasad and Jung, comprehensively reviews the role of microsatellite instability in intestinal tumorigenesis; including mechanisms, mouse models, and finally the clinical implications. In Chap. 3, Bell, Lo and Shroyer review intestinal epithelial stem cell characteristics and the mechanisms of their function in epithelial homeostasis and touch upon the important role of these intestinal stem cells in tumor development. This is followed by a discussion by Harris, Gao and Evers on the role of the PI3K signaling pathway plays in intestinal tumorigenesis. In Chap. 5, Moreira, Balaguer and Goel review the role of epigenetics in intestinal tumorigenesis as well as the potential for using epigenetic modifications as CRC biomarkers. Chapter 6 by Nishida and Calin provides an overview of the functions of microRNAs in intestinal tumorigenesis. The effects of the gut microbiome, and associated inflammation, in homeostasis and tumor development are reviewed in Chap. 7 by Posocco, Dmitrieva and Grivennikov and Chap. 8 by Dheer, Davies and Abreu, respectively. Recently, studies have revealed an important role that lipids play in regulating intestinal homeostasis and tumorigenesis. In Chap. 9 Garcia-Barros, Coant and Snider discuss the involvement of shingolipids in intestinal tumorigenesis. There are many other important factors that lie at the basis of intestinal tumorigenesis, the effects of one that affects all—aging—are thoroughly reviewed by Nautiyal, Purvis and Majumdar in Chap. 10. In Chap. 11, Cao and colleagues presents an extensive overview of the role epithelial-to-mesenchymal transitioning plays in intestinal tumorigenesis. Koyuturk and Nibbe advocate the importance for developing robust biomarkers of CRC and discusses integrative networks in Chap. 12. Finally, Grady and colleagues summarize the latest targeted therapies being developed directed towards colorectal cancer development and progression in Chap. 13.

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Mechanisms of Development & Progression

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