

# Colon Cancer Diagnosis and Therapy

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Editors

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*This book is dedicated to our families, our  
teachers, and friends*

# Preface

Colorectal cancer (CRC), a heterogenous disease, is the third most commonly diagnosed cancer. As it is highly malignant, it is the second leading cause for cancer-related mortalities. As estimated by the American Cancer Society for the year 2020, 43,340 rectal cancer cases and 104,610 colon cancer cases were diagnosed. The mortality rate estimated for CRC was 53,200 for this year. The conventional therapy is surgery followed by radiation and chemotherapy. However, recurrence after surgery and therapies is a major obstacle that results in metastatic stages. In general, the 5-year survival rate is always considered a hurdle due to lack of early diagnostic tests as well as disease recurrence following treatment. Additionally, both modifiable and non-modifiable risk factors are primary causes for the occurrence of CRC. Modifiable risk factors include being physically inactive, overweight, smoking, and consumption of alcohol, while the unmodifiable risk factors are age and inherited syndromes (HNPCC and FAP). Thus, it is essential for the researchers and clinicians to develop novel therapeutic strategies to diagnose CRC at earlier stages via biomarkers. In this volume, our authors have included novel advanced diagnostic and therapeutic strategies for CRC treatment.

The common diagnostic options for CRC detection are colonoscopy and FOBT, while novel diagnostic strategies include molecular biomarkers to improve early detection of CRC. Our authors have described varied molecular techniques for diagnosis of CRC along with recent therapeutic strategies in this volume. The conventional therapeutic regimens include chemo and radiotherapy. Despite the many advances in research, patients often develop metastasis and recurrence. This is mainly attributed to the intratumoral heterogeneity nature of CRC. Hence, studying single cancer cell resolution at molecular level to understand the heterogeneity of the tumor is very much essential for therapy and prediction of CRC. Dariya et al. have described all essential applications of single cell technology in CRC. Additionally, inactivation of mismatch repair genes responsible for microsatellite instability are detected in almost 90% of HNPCC and 15% of sporadic CRC cases. The inactivation of these mismatch repair genes is due to the hypermethylation of promoter region of these genes. The epigenetic alterations likely promote escape of apoptosis of cancer cells. Thus, targeting these genes or identifying them

as biomarkers potentiates the diagnosis of CRC in its early stages. In our volume, Gupta et al. have described role of DNA mismatch repair genes in CRC progression. Furthermore, the research studies demonstrated that in addition to tumor microenvironment, extracellular vesicles play a major role in cell-cell communication. The extracellular vesicles are cell derived vesicles that possess lipids, proteins, mRNA, and small RNA. The extracellular vesicles secreted by the cancer cells play a crucial role in promoting metastasis. Thus, impairing biogenesis and secretions of extracellular vesicles by the cancer cells would potentiate the cancer therapy. In another way, they are also considered efficient cargo that can deliver therapeutic drugs to the target cells for cancer therapy. The extracellular vesicles also function as biomarkers and are included in diagnosis and prognosis for cancer metastasis. Thus, extracellular vesicles are promising tools for diagnosis and therapy. Merlin et al. have outlined the importance of extracellular vesicles in CRC growth, metastasis, diagnosis, and therapy. Moreover, targeting glycolysis is now an attractive clinical strategy in cancer diagnosis and therapy. This is due to the predominant nature of the cancer cells that produce energy by glycolysis followed by lactic acid fermentation even in the presence of oxygen, otherwise known as “Warburg Effect.” Thus, glycolysis is important for carcinogenesis. Therefore, researchers are now focusing on targeting the inhibitors against the critical enzymes involved in glycolysis, which showed a promising anticancer effect. In this regard, Jaiswara et al. have described the emerging therapeutic approach of targeting the aerobic glycolysis in colon cancer cells. Similarly, targeting glutamine would be an effective approach to treat CRC cells, because glutamine is required as a supplement for cancer cells culturing and is utilized as fuel for various cycles like the tricarboxylic acid cycle. In this volume, our authors have outlined the applications of targeting glutamine metabolism in CRC. With advances in research, nanotechnology is now gaining global consideration due to its improved standards for diagnosis and therapy that avoid toxicity to the healthy cells. This nanotechnology includes engineering of novel organized materials capable for diagnosis and therapeutic approach. The nanoparticles included for CRC therapy were based for identification of tumor, cancer biomarkers, and drug delivery by using biologically targeted contrast agents. In this volume, Reshmitha et al. and Vijay et al. have outlined nanotechnology approach for CRC diagnosis and therapy, as well as recent advances in nanomedicine-based drug targeting.

The epidemiological and experimental findings from the past decades have determined that the dietary intake is associated with risk of CRC occurrence. This is due to the influence of diet that effects interacting mechanisms like inflammation, immune responsiveness and obesity. Thus, an alteration in the diet would therefore be a promising approach to reduce CRC incidence. In this volume, Shinde et al. and Kulshrestha et al. have outlined the dietary habits and associated risk for CRC occurrence and incidence. Additionally, in this volume are preventive effects on CRC with the use of Indian food. The Indian traditional cuisine ingredients are rich in preventive therapeutic strategies that aim to reduce the incidence and mortality rate of the patient. Moreover, the Indian herbals are highly rich in phytochemicals with varied medicinal properties including antioxidative, anticarcinogenic and anti-

mutagenic. Researchers are now widely focusing on combinational therapies for cancer treatment including phytochemicals along with chemodrugs. Phytochemicals may have the ability to sensitize the tumor cells to chemodrugs and reduce adverse effects. In this volume, Durgambica et al. have given the latest insight into therapeutic potentiality of phytochemicals against CRC. As an example, seaweeds, rich in terpenoids, polyphenols, polysaccharides, and steroids, are found to have promising pharmacological activities like cancer therapy. Pandey et al. have explored seaweeds as potential human colon cancer therapy. Similarly, Sandeep et al. also have described naturally available chemo-sensitizing and immunomodulatory agents in colon cancer.

The intestinal bacteria like *Helicobacter pylori* infects the gastro mucus epithelial layer. This results in peptic ulcers, gastritis, and eventually results cancerous diseases like CRC. Therefore, knowledge about the casual relationship and mechanism behind the risk for CRC occurrence from to *H. pylori* infection is essential. Our volume includes chapters describing the role of bacterial infection in colon carcinogenesis and the associated therapeutic approaches. Use of probiotics is now widely encouraged to exclude the pathogenic intestinal flora and reduce the carcinogenic secondary bile acids, thus preventing colon cancer. Although previous studies have shown that probiotics have an inhibitory effect on tumor development, it, however, remains unclear and proper investigation is necessary. In this volume, Anaga et al. included therapeutic approach of probiotics in colon cancer therapy.

Altogether, the present editorial book provides an in-depth understanding of novel diagnostic and therapeutic options currently available. Our authors have explored current advances included the applications for CRC diagnosis and therapy. It is our immense pleasure to present this comprehensive summary to the scientific community for the benefit of patient care.

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## About the Editors



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Postdoctoral fellowship award. He received advanced research training from the Centre of Veterinary Health Sciences, Oklahoma State University, Stillwater, USA. He uses *in vitro*, *in vivo*, and *in silico* models to explore the role of bioactive compounds against lung diseases and cancer prevention. Dr. Shukla's current research interest is to evaluate phytomedicines against lung pathologies and cancer. He has published over 25 research papers in highly reputed International journals having high impact factors and has presented more than 15 abstracts at various national and international conferences. Dr. Shukla has been working as a faculty member since 2013 in the Department of Biotechnology, Guru Ghasidas Vishwavidyalaya.



**Naveen Kumar Vishvakarma** is currently assistant professor of biotechnology at Guru Ghasidas Vishwavidyalaya. He earned his master's degree in microbiology and then did his doctoral research in tumor immunology. During his doctoral research, he worked in the area of tumor acidity-mediated immunosuppression. After completing doctoral research work, he worked as postdoctoral fellow/research associate at Banaras Hindu University, Manitoba Institute of Cell Biology (Canada), and Moffitt Cancer Center and Research institute (USA). During his work at Moffitt Cancer Center, he demonstrated the role of

acidic tumor microenvironment in selection of aggressive phenotype with metabolic alterations. In 2013, he joined HNB Garhwal University as assistant professor and later moved to his current position at Guru Ghasidas Vishwavidyalaya in 2014. His current research interest includes modulation of tumor metabolism, evaluating derivative anticancer drugs, and chemosensitization.