

PREFACE

Hepatocellular carcinoma (HCC) has become a major global health problem and is responsible for a steadily increasing number of cancer-related deaths. It is the most common form of liver cancer, with large disparities in incidence due to the geographical variation in the prevalence of risk factors. The high incidence rates of HCC in Africa and Asia are mainly attributed to the dietary exposure to aflatoxin B1 and chronic hepatitis B virus (HBV) infection. Western countries report fewer cases, with chronic hepatitis C virus (HCV) infection, alcohol abuse, metabolic syndrome, and non-alcoholic fatty liver disease as dominant causes. Although the risk factors for HCC development are well known and great advances have been made through HBV vaccinations, direct-acting antivirals for HCV treatment, and aflatoxin eradication programs, the overall incidence and mortality rates of HCC are still rising.

To tackle the burden of HCC, it is essential to understand the principle molecular and cellular processes as well as fundamental clinical challenges. This book aims to provide an overview on several important disease aspects. Chapter 1 reviews recent studies assessing the potential cellular origins of HCC. Chapter 2 describes the newly discovered regulatory roles of the tumor microenvironment on tumor growth and progression, with particular focus on extracellular matrix factors. Important starting points in the long pipeline from drug discovery to clinical translation of potential treatments are appropriate and well-designed models of disease that enable a thorough understanding of context-specific mechanisms. The authors of Chapter 3 and Chapter 4 have therefore outlined the most commonly used *in vitro* systems and animal models of chronic liver disease and HCC in great detail. Non-alcoholic fatty liver disease and non-alcoholic steatohepatitis have been growing in prevalence worldwide at alarming rates. Hence, Chapter 5 provides an overview of metabolic reprogramming and dysregulation of lipid metabolism as a newly recognized hallmark of HCC. The last three chapters focus on clinical aspects of HCC management and treatment. Chapter 6 details the currently accepted standards and challenges for the surgical management of HCC, while Chapter 7 provides an overview of the recent developments in the field of tyrosine kinase inhibitors, including survival benefits and adverse events. Finally, Chapter 8 discusses multidrug resistance to chemotherapy and potential approaches to overcome this remaining clinical obstacle.

Unmet clinical needs are most effectively addressed through close collaborations between basic researchers and clinicians, thus effectively capitalizing on each other's strengths and expertise. I therefore aimed to make this book of interest to both scientists and clinicians and provide useful insights and stimulation for constructive discussions. This project would not have been possible without the hard work and commitment of all authors. I sincerely thank everyone for their valuable contributions.

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