About the Editors

Universitat Autònoma de Barcelona

Rafael Rosell

Rafael Rosell is Head of Medical Oncology, Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona; President and Founder, Pangaea Biotech, SL, USP Dexeus, Barcelona; Head of Medical Oncology, Dr Rosell Oncology Institute, USP Dexeus, Barcelona; Founder and President of the Spanish Lung Cancer Group. He is also Professor at the Autonomous University of Barcelona. He is involved in application of translational genetic research to the clinical setting and has implemented large-scale screening for EGFR mutations in lung cancer patients in Spain to select patients for treatment with EGFR inhibitors instead of chemotherapy.

Jia Wei

Jia Wei is currently working at the Comprehensive Cancer Center, Affiliated Drum Tower Hospital to Medical School of Nanjing University & Clinical Cancer Institute of Nanjing University, Nanjing, China. She received more than 1 year training in customized therapy based on molecular biology under the supervision of Rafael Rosell at the Pangaea Biotech SL laboratory, USP Dexeus University Institute, Barcelona. She has extensive experience in translational research in lung cancer and gastric cancer.

Santiago Ramon y Cajal

Santiago Ramon y Cajal trained as a pathologist at the Jimenez Díaz Foundation and the University of Yale. From 1990 to 2003, he worked at the Puerta de Hierro Clinic in Madrid, and since 2003 has served as Chairman/Director of Medical Pathology Service at Vall d'Hebron Hospital in Barcelona, Spain. He is also Professor of Medicine at the Autonomous University of Barcelona. He received the National Award for best young researcher in 1997, and is an Academic Member of the National Academy of Medicine of Spain. The basis of his clinical and basic research focuses on identification of new oncogenic factors and new approaches in gene and molecular therapy.

Miquel Taron

Miquel Taron is a molecular biologist and Head of the Molecular Biology Laboratory, Catalan Institute of Oncology, Hospital Germans Trias i Pujol, Badalona, and Director of Pangaea Biotech SL Molecular Biology Laboratory in Barcelona. He has over 19 years experience in molecular biology with broad experience in the analysis of molecular markers for translational research in cancer patients, and has been key in setting up molecular analysis studies as part of the Spanish Lung Cancer Group.

Foreword

Integrating molecular knowledge in clinical decision-making for personalized cancer management

A user-friendly handbook for physicians, biologists and patients

Rafael Rosell, Jia Wei, Santiago Ramon y Cajal and Miquel Taron

The main goals of this book are to offer a straightforward guide to the wealth of information on cancer genetics currently available in basic scientific journals, and to illustrate the multiple opportunities for application of this knowledge to daily clinical practice. A growing number of cancer mutations are considered ‘driver mutations’, involved in the development or progression of a tumor, many with significant diagnostic, prognostic and therapeutic implications [1]. The model of *KIT* mutations in gastrointestinal stromal tumors (GIST) and the exquisite response to imatinib is one of the first examples of the effect of targeted therapies in cancer treatment. The discovery of the presence of *EGFR* mutations in a subset of lung cancers has been one of the major breakthroughs in selecting patients for adequate treatment [2]. Other alterations, which it is becoming mandatory to screen for prior to determining correct treatment, are *ALK* translocations in lung cancer [3] and, more recently, *ROS1* rearrangements [4]. *BRAF* mutations have become particularly relevant in the treatment of melanomas, with the development of novel BRAF-specific inhibitors [5]. Today, we are in the position to identify somatic mutations that can provide real-time information

permitting us to take informed clinical decisions. It is highly recommendable to perform such mutational analyses using profiling technologies in Clinical Laboratory Improvement Amendments (CLIA) facilities [1]. As the repertoire of selective therapeutic compounds continues to grow, testing in tumor tissue samples – often including small specimens from biopsies in formalin fixation and paraffin embedding – has become essential for laboratory analyses, such as multiplex clinical assay [6] or second- or third-generation deep sequencing [1].

Importantly, all cancers, with or without driver mutations and including those with *KRAS* mutations, make use of critical growth and survival pathways, including the canonical phosphatidylinositol 3-kinase (PI3K)-AKT and mitogen-activated or extracellular signal-regulated protein kinase kinase (MEK)–extracellular signal-regulated kinase (ERK) signaling [7]. Through the different chapters in this book, beginning with GIST and moving through melanoma, ovarian cancer, triple-negative breast cancer, gastric cancer, mesothelioma and lung adenocarcinoma, the reader can appreciate the clinical relevance of these signaling pathways and some of the downstream components that can be analyzed for use as predictive markers in clinical practice. At the same time, visualization of these signaling pathways in the figures can facilitate understanding of the mechanisms of acquired resistance to novel targeted therapies that are becoming ever more clear [8,9]. Throughout the chapters, the reader will also find an explanation of the function of the DNA repair signaling pathway, with multiple components that make complexes with *BRCA1* and will be able to comprehend their potential prognostic and predictive role.

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