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Mechanisms of Drug Resistance in Cancer Therapy

Springer

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Preface

The remarkable advances in precision medicine and the development of targeted cancer treatments have generated significant optimism based on the assumption that a better knowledge of genetic or molecular features sustaining cancer growth could determine long-term control of many types of cancer and potentially cure the majority of patients. After several years of basic and translational research, the oncology community has tempered this optimism by the recognition that in only a minority of patients cure can be achieved by innovative strategies such as targeted therapies, immunotherapy and cytotoxic agents. In the vast majority of cancer patients, cancer wins the battle, and the reason for this failure is drug resistance. Ultimately, advanced cancer patients die because some or all of their tumour cells exhibit or develop resistance to available therapeutic strategies. The challenge of drug resistance therefore represents an important barrier that hinders the ultimate goal of cure or at least long-term control of cancer.

As a corollary of this, response rates in the setting of tumour progression/relapse are dismal. Despite the considerable importance of drug resistance to cancer therapies, our understanding of their biological mechanisms – and plausible therapeutic avenues to intercept them – remains highly incomplete.

Knowledge of specific resistance mechanisms can inform novel therapeutic approaches to counter this phenomenon, and improvement of our understanding of key driver genes could guide new therapeutics approaches capable of eliciting meaningful tumour responses in patients with advanced malignancies.

As previously reported with chemotherapy, it is reasonable to suppose that a combination of multiple targeted therapies and immunotherapy strategies as well as planned sequence of treatments will be necessary to effectively prevent and/or treat drug-resistant cancers. The potential number of therapeutic combinations is immense; thus, new preclinical paradigms are needed to prioritize high-yield combinations and define the genetic or molecular contexts in which they would most likely be efficacious. To improve outcome of patients a strict collaboration between academia and industry will be needed so that the appropriate resources and innovation may be brought to bear on this challenge. The goal to achieve durable control of many cancer subtypes will likely require dedicated, multidisciplinary teams of preclinical and clinical experts that work together guided by rigorous translational and analytical science.

With the increasing armamentarium of anticancer agents and the advent of powerful high-throughput screening techniques, there are now unprecedented opportunities to understand and overcome drug resistance through the clinical assessment of rational therapeutic drug combinations and the use of predictive and prognostic biomarkers to enable patient stratification and tailor treatments.

The main aim of this book is to offer to the readers an updated overview on the possible reasons of failure of new and promising therapeutic opportunities.

The first part of the book covers the basic mechanisms of such hot topics. The other chapters cover specific pathways of resistance that from the knowledge of basic mechanisms translate this information in clinical routine or in translational clinical research.

Readers will discover diverse perspectives of the contributing authors (such as basic scientists, clinical pharmacologists and clinicians) and extensive discussions of issues including pharmacodynamic and pharmacokinetic mechanisms of resistance, alterations in the drug target, activation of prosurvival pathways, ineffective induction of cell death and plasticity of microenvironment.

This book will be of interest to scholars and researchers, biologists, pharmacologists, medical oncologists, haematologists and immunologists.

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Contents