
Preface

Chemotherapy is used to treat many types of cancer. A large number of drug classes are in use, including the vinca alkaloids, taxanes, antibiotics, anthracyclines, DNA alkylators, other DNA damaging agents, hormones, and interferons. More potent analogs of existing drugs and novel agents directed at new targets are continuously being developed. Over the last few years, agents that affect COX-2, PPAR γ , and various signal transduction pathways have received much attention. To identify which agents are effective for which types of tumors, it is important to develop accurate in vitro and preclinical in vivo screening systems that can identify the cytotoxic and/or cytostatic potential of an agent on established tumor cell lines or cells isolated from individual fresh cancer biopsy specimens removed from cancer patients. Chemosensitivity testing allows the selection of drugs that appear sensitive in the laboratory, thus offering patients a better chance of response.

One of the main problems associated with chemotherapy has been that patient tumors with the same histology do not necessarily respond identically to the same agent or dose schedule of multiple agents. Identifying the presence of resistance mechanisms and other determinants for drug sensitivity in order to classify tumors into response categories has been an ongoing research effort. Advances in our understanding of the genetic and protein fingerprints of primary tumors and their metastases has opened a door to the possibility of customizing therapy to individuals. There is accumulating evidence suggesting that laboratory screening of samples from a patient's tumor may help select the appropriate treatment(s) to administer, thereby avoiding ineffective drugs, and sparing patients the side effects normally associated with these agents.

The aim of these two volumes on *Chemosensitivity* of the *Methods in Molecular Medicine* series, is to comprehensively present protocols that can be used to (a) assess chemosensitivity in vitro and in vivo, and (b) assess parameters that modulate chemosensitivity in individual tumors. Volume I presents an overview in Chapter 1 and then covers *In Vitro Measures of Chemosensitivity*, includes clonogenic, colorimetric, fluorometric, and histochemical approaches. Volume II, Part I, *Measurements of DNA Damage, Cell Death, and Regulators of Cytotoxicity*, includes methods to detect chromosome loss and breakage, changes in cell cycle, expression of members of the bcl-2 family of proteins, expression of caspases and PARP cleavage, metabolic factors influencing sensitivity, measurements of drug retention, expression of drug resistance proteins, and measurements of ceramide and sphingolipids associated with drug sensitivity. Volume

II, Part II, *Genomics, Proteomics, and Chemosensitivity*, addresses DNA microarrays for gene profiling, genetic manipulation to identify genes regulating chemosensitivity, proteomics using 2D-PAGE and mass spectrometry, and bioinformatics approaches. The last part, *In Vivo Animal Modeling of Chemosensitivity*, covers protocols to establish clinically meaningful metastatic and orthotropic models of solid and liquid tumors, statistical approaches to analyze preclinical data, and animal imaging approaches that can be used to assess chemosensitivity such as GFP-tagged genes, SPECT using ^{99m}Tc -annexin, PET imaging with ^{18}F FDG, and magnetic resonance imaging.

Each chapter is written by someone experienced with the methodology and contains a detailed introductory section with references of how the technique has been used in the past, a list of materials and equipment needed to perform the assay, and a step-by-step set of instructions for each method. At the end of each chapter a “Notes” section is included with useful information, helpful hints, and problems and pitfalls to be aware of, in order to make the assay run smoothly and allow for easy interpretation of data.

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