Brown RD, Ho PJ, editors. Multiple Myeloma: Methods and Protocols (Methods in Molecular Medicine, Walker JM, series editor, Volume 113). Totowa (NJ): Humana Press; 2005. 320 pages; ISBN 1-58829-392-2; price: US$125.00

Field of medicine: Hematology, oncology.
Format: Hardcover book.
Audience: Hematologists, oncologists, and other clinicians requiring novel insights into the pathogenesis and diagnostics of multiple myeloma, as well as biomedical researchers in the field of hematology and immunology.
Purpose: To present extensive body of knowledge on different aspects of multiple myeloma, including immunodiagnostics, molecular diagnostics, cytogenetics, and experimental models. The book not only describes conventional diagnostic procedures but also addresses the available mouse models for studying the disease and novel diagnostic, prognostic, and therapeutic approaches in the management of multiple myeloma.
Content: The book is divided into 23 chapters, including schematic diagrams, figures, color plates, and tables, as well as an index of important terms at the end. Typically, each chapter consists of short *Introduction*, followed by *Materials*, *methods*, *notes* and *References* sections. Within the *Materials* section, each chapter provides a detailed description of sample sources, required solutions and reagents, as well as necessary equipment. *Methods* describe all applied procedures in a step-by-step manner, with all necessary details sufficient for the implementation of a specific technique. Protocols are followed by *notes* on troubleshooting that would enable us to avoid potential pitfalls.

The first, introductory, chapter brings an overview of the disease and stresses important challenges for the future investigation. The second chapter describes the principles of malignant plasma cell immunophenotyping by flow-cytometry, useful for research purposes and in clinical practice. The authors explained sample preparation from several sources, staining procedures for the combination of antibodies, acquisition and analysis of data, and interpretation of the results. The table summarizing most relevant molecules for the characterization of plasma cells is particularly useful. The next chapter describes the procedures that determine the proliferative rate of malignant plasma cells, an important parameter of the disease biology useful for diagnosis and prognosis of multiple myeloma. The next few chapters are dedicated to available methods to determine chromosomal aberrations in myeloma cells, including conventional cytogenetics by G-banding, multicolor spectral karyotyping for the characterization of complex structural chromosome aberrations and detection of chromosome 13 deletions by fluorescent *in situ* hybridization. Comparative genomic hy-

bridization for the analysis of changes in DNA copy number, as a novel cytogenetic technique for the identification of genomic imbalances without the need to perform conventional cytogenetic analysis, is also described. It is important to introduce novel cytogenetic procedures for diagnostic, prognostic, and therapeutic purposes in multiple myeloma, since the success rate for the detection of clonally abnormal karyotypes by conventional cytogenetic analysis in short-term cultures of myeloma samples is limited due to low mitotic rate of plasma cells. The following chapters provide an introduction to other techniques useful for the detection of B-cell clonality by Southern blot analysis or polymerase chain reaction (PCR) and DNA sequencing of IgH rearrangements. Expansion of tumor clone yields a dominant clonal variable (V) gene sequence that can serve as a signature motif in myeloma cells and target for immunotherapy by DNA fusion vaccines. The implementation of real-time PCR for the detection of immunoglobulin rearrangements, as a very sensitive and quantitative technique able to evaluate minimal residual disease, is described within the eleventh chapter. The next two chapters also deal with myeloma cells at the level of nucleic acid, describing the analysis of incomplete immunoglobulin (DJH) rearrangements by PCR and identification of malignant plasma cells by mRNA *in situ* hybridization. The fourteenth and fifteenth chapters describe two mouse models available to study pathogenesis of multiple myeloma *in vivo* – the severe combined immune deficient human (SCID-hu) myeloma model and the 5T2MM murine model. Mouse models not only help in elucidating biological processes involved in multiple myeloma but also in testing the potentially new therapeutic targets. The next chapter provides a standard telomeric repeat amplification protocol for telomerase activity assay and a Southern blot terminal restriction fragment protocol for telomerase activity assay. This is of great interest for potential diagnostic, prognostic, and therapeutic application in the management of human cancers, since there is a low level or absence of telomerase activity in most non-neoplastic tissues and somatic cells and its presence in most malignant tumors. The seventeenth and eighteenth chapters deal with the antitumor immunity elicited by experimental vaccination using fusion hybrids between myeloma cell lines and dendritic cells and genetically modified myeloma cells expressing CD40 ligand. The described vaccines were able to induce tumor-specific cytotoxic T-lymphocyte response *in vitro* and protective immunity against tumor *in vivo*. The chapter 19 describes *in vitro* osteoclast-forming assay to determine myeloma cell-derived osteoclast-activating factors. By measuring the formation and activity of osteoclasts, assay serves to assess the intensity of bone resorption in a patient with multiple myeloma, which accounts for much of the morbidity associated with the disease. The next chapter introduces us to several methods for detection of clonality in expanded T-lymphocyte populations in patients with multiple myeloma as the indicator of chronic antigenic stimulation in patients with multiple myeloma and smoldering myeloma. The following two chapters describe additional procedures helpful in the diagnosis of multiple myeloma at the level of tumor DNA – detection of mismatch repair defects in malignant plasma cells by PCR and microsatellite analysis and assessment of the methylation status of CpG sites (cytosines located 5' to guanosines) by methylation-specific PCR. The book ends with the chapter describing basic information regarding DNA microarray analysis and data interpretation as a powerful tool for detection of genetic and expressional variations in the individual patient and their relation to pathology, etiology, and diagnostics in multiple myeloma.

Highlights: The book covers clinical as well as experimental aspects of multiple myeloma and provides an important set of information for

clinicians and researchers, in different fields of biomedicine, including hematology, oncology, molecular diagnostic, clinical immunology, osteoimmunology, molecular-biology, genetics, and bioinformatics. Such integrative and interdisciplinary approach is crucial for more successful achievements in the disease treatment.

Limitations: It is surprising that some important laboratory procedures relevant to multiple myeloma, such as testing the mechanisms of actions of novel drugs on myeloma cell lines in vitro or determination of cytokine expression in patients with multiple myeloma are not covered. It would be valuable to add those topics to the second edition.

Related reading: Many other books from the Methods in Molecular Medicine Series would be equally powerful and high-quality source of data for the clinicians and researchers in different fields of biomedicine. Among many others, some recently published volumes related to hematology and oncology include Lymphoma, Developmental Hematopoiesis, and Chemosensitivity (Vol. 1 and 2).

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