Fennell JP, Baker AH, editors. Hypertension, Methods and Protocols. Totowa, New Jersey: Humana Press; 2005. 501 page. ISBN 1-59259-850-1; price: $135.00.

Field of Medicine: Hypertension, molecular medicine, genetics, and bioinformatics.

Format: Hardcover book.

Audience: Researchers in cardiovascular pathophysiology, especially in pathogenesis and pathophysiology of hypertension.

Purpose: To provide an extensive overview and detailed description of methods and protocols used in research of hypertension.

Content: The book is organized in seven parts and twenty nine chapters covering models of hypertension, assessment of free radicals in endothelial dysfunction, nucleic acid techniques, proteins and proteomics, gene transfer and gene therapy, stem cell research, and bioinformatics in research of hypertension. The first part describes experimental models of hypertension, consisting of chapters on congenic/consomic models of hypertension, mouse knock-out models of hypertension, production of transgenic models of hypertension, and blood pressure measurement methods in small animals. The second part deals with the methods of free radical detection in endothelial dysfunction (analysis of superoxide anion production in tissues, measurement of reactive oxygen species by chemiluminiscence, and wire myography of isolated small vessels). In the third part, methods in nucleic acid research are presented (selection of candidate genes, extraction of RNA from cells and tissues, gene polymorphism analysis, generation of antisense oligonucleotides, and others). The fourth part describes proteomic approach in the research of hypertension. The fifth part presents methods in gene therapy – the ways of gene transfer (adenoviral and non-viral gene transfer), antisense inhibition of the renin-angiotensin in hypertension, and modulation of gene expression by RNA interference. The sixth part introduces protocols for isolation, cultivation, and maintenance of embryonic stem cell lines and embryonic stem cell-derived cardiomyocytes. Chapters of the seventh part cover the field of bioinformatics.

Highlights: Detailed description of state-of-art methods in hypertension research is provided. The contributors are recognized experts in their fields. The protocols are clearly and precisely written, with troubleshooting notes, which ensure the reproducibility. Also, numerous relevant references are selected.

Limitations: Some of the chapters lack figures, such as that describing methods of blood pressure measurement in small laboratory animals. Also, in contrast to other chapters, the chapter describing gene therapy for hypertension, with emphasis on antisense inhibition of the renin-angiotensin system, does not provide a detailed description of the respective protocols, but rather a review of the effects of the renin-angiotensin inhibition by antisense oligonucleotides.

Related reading: To my knowledge, there are no other similar comprehensive texts on methods on hypertension research. Nevertheless, there are many recent titles covering various methods that can be used for hypertension research, such as Heiser's Gene Delivery to Mammalian Cells: Viral Gene Transfer Techniques (Methods in Molecular Biology) (Humana Press, 2003), Sundberg's and Ichikis Genetically Engineered Mice (Research Methods for Mutant Mice) (CRC Pres, 2005), Inocenti's Pharmacogenomics, Methods and Applications (Humana Press, 2005), and Bioinformatics and Drug Discovery by Larson RS (Humana Press, 2005), among others.

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El-Deiry WS, editor. Death receptors in cancer therapy. Totowa (NJ): Humana Press; 2005. 374 pages; ISBN 1-58829-172-3; price: US$ 165.00

Field of medicine: Oncology, pharmacology.

Format: Hard cover.

Audience: Researchers and students in immunology, cancer research, pharmacology, and oncology.

Purpose: To provide in-depth review of the latest understanding of the molecular events that regulate apoptotic cell death, presenting the molecules that provide targets for agonists or antagonistic designed to modulate death signalling for therapeutic purposes.

Content: Around ten years ago, Humana Press created a series "Cancer Drug Discovery and Development," whose current editor is Beverly A. Teicher (Genzyme Corporation, Framingham, MA). The series aims to bring up-to-date information on the latest developments in the broad field of cancer research, from genetics and animal models to the new approaches in cancer treatment.

The present volume was edited by Wafik S. El-Deiry, from the University of Pennsylvania School of Medicine, who was one of the top 50 most-cited scientists in the 1990's. Dr El-Deiry, along with 51 contributors, who all work on cell-death research, tried to give us a comprehensive and detailed overview of current progress in the field.

The first chapter, "Mammalian cell death pathways – intrinsic and extrinsic," is actually the central part of the book, introducing a reader to the problems of regulation of life and death at the level of a single cell. This chapter also reviews basic concepts of the intrinsic apoptotic pathway, ie, the one that is not triggered by the activation of the death receptors, which makes it an excellent primer on apoptosis. Therefore, I can cordially recommend it to graduate students involved in almost every field of basic and clinical biomedical research.

I find it odd that the book was not divided into sections, because it is quite obvious that the topics of certain chapters are quite related. For example, six chapters deal with the basic biology of the death-inducing members of tumour necrosis family (TNF) receptors. Chapter 3, "Structures of TNF receptors and their interactions with ligands," introduces the currently known "death receptors" – TNF receptor 1 (TNFR1), fibroblast-associated cell surface antigen (Fas), death receptor (DR)3, DR4, DR5, DR6, ectodysplasin A receptor (EDAR), and $p75^{NGFR}$. Those receptors are known for their unique ability to trigger the assembly of protein complexes that lead to the initiation of apoptotic cascade upon stimulation by a ligand. Proteins that bind to the death receptors and link them with the downstream parts of the cellular apoptotic machinery are called the adaptor proteins and are discussed in chapter 5, whereas the next chapter focuses on the group of enzymes called the caspases (cystein *aspases*), which are the central executioners of apoptosis. As the engagement of death receptors could lead to cell death, it is not a surprise that their expression, on either gene or protein level, is tightly regulated. The basic mechanisms of regulation are dealt with in chapter 9, while further insight into roles of p53 and nuclear factor κB (NFκB) in the regulation of death receptor-induced apoptosis is provided by chapters 12 and 14, respectively.

Signalling through the death receptors could kill not only normal, but also a malignant cell. As a matter of fact, the induction of apoptosis

in malignant cells is one of the effector mechanisms of conventional cancer treatments. Unfortunately, the tumor cells have developed various mechanisms to block the activation of cell suicide mechanisms. For example, the increased resistance to apoptosis could be based on the inactivation of the p53 pathway (chapter 2, "Resistance to apoptosis in cancer therapy"), silencing of pro-apoptotic genes through methylation (chapter 13), or mutations of death receptors (chapter 8). Fortunately, there are ways to circumvent the problem of decreased sensitivity of cancer cell to apoptosis. For instance, synthetic retinoids can induce apoptosis of human cancer cells through several mechanisms, one of which is induction of death receptor expression (chapter 11). Another approach, discussed in chapter 18 is to modulate the activity of death receptor signalling inhibitors. The authors point to cellular FLICE-like inhibitory protein (c-FLIP), a physiological inhibitor of caspase-8, as a promising target for such interventions. Moreover, it is possible to combine chemotherapy with death receptor ligands to achieve enhanced antitumor activity (chapter 21).

The TNF-related apoptosis-inducing ligand (TRAIL) is a member of a TNF family of ligands, with unique selectivity for triggering apoptosis in tumour cells. Interestingly, TRAIL seems not to be active against normal mammalian cells and does not exhibit cytotoxicity in mice or non-human primates. In the other words, TRAIL seems like a good candidate for a "magic bullet" and it should not be a surprise that four chapters of the book are dedicated to TRAIL: "Death signalling and therapeutic applications of TRAIL" (chapter 7), "Regulation of TRAIL receptor expression in human melanoma" (chapter 10), "TRAIL in cancer therapy" (chapter 15), "Regulation of TRAIL-induced apoptosis by transcriptional factors" (chapter 17), and "Expression and regulation of death receptors in multiple myeloma and prostate carcinoma" (chapter 16).

In addition to TRAIL, another member of TNF family of ligands that could be potential pharmacological agent is Fas ligand. Although Fas ligand can effectively induce apoptosis in various cell types, including malignant cells, its use is limited by serious side effects. Therefore, considerable effort is put into development of Fas ligand delivery directly into tumour. Various aspects of Fas ligand/Fas signalling, as well as some promising experiments with adenoviral delivery of Fas ligand could be found in chapter 19. A quite similar issue, ie, targeted expression of genes encoding TNF-α, Fas ligand, and TRAIL is further discussed in chapter 20.

Highlights: As previously mentioned, the first chapter should be compulsory reading for graduate student in biomedical disciplines. Useful features include summaries, given with most chapters and diagrams depicting signalling pathways.

Limitations: There is some redundancy in the book, but most readers probably will not mind it. An index is provided, but I did not find it helpful. The order of the chapters is quite bizarre, and the editor should have done much better job. Finally, although many schemes and diagrams are included, I could not help noticing that they look a bit crude and primitive. Or am I just too much of a *Nature* fan?

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Bachárová L, Kyselovič J, Slezák J, editors. Experimental hypertension and ischemic heart disease. Bratislava (Slovakia): VEDA, Publishing House of the Slovak Academy of Sciences; 2005. 236 pages; ISBN 80-224-0856-5

Field of medicine: experimental cardiology and cardiovascular pharmacology, physiology, pathophysiology, biochemistry, and biophysics.

Format: Hardcover book.

Audience: Researchers in the various fields of experimental cardiovascular sciences, especially cardiovascular pharmacology, physiology, and pathophysiology.

Purpose: The book is a compilation of selected articles covering topics from the basic cardiovascular research. The authors introduced their own work and contributions in respective fields. The book is a source of information on experimental models, and can be useful for the researchers because it presents both well-established and recently introduced techniques. It is encouraging for the researchers in the experimental cardiovascular science and demonstrates rapid increase in knowledge and development of experimental methodologies.

Content: Dr. Bachárová and her coeditors have edited a useful but limited monograph on selected areas of experimental cardiology. The book is a product of work of twenty authors, many of them distinguished scientists and researchers, and is composed of fifteen chapters. Each chapter consists of a short introduction, followed by titled paragraphs that deal with specific aspects of the topic; the most important messages are summarized in short conclusions: the chapter ends with a list of references. The material is presented comprehensively and concisely. The chapters are supplemented with illustrations, summary tables, and diagrams.

The first chapter describes research in the structural determinants of the state-dependent inhibition of the L-type Ca^{2+} channel containing $Ca_v1.2$ by dihydropyridines, ie, the identification of the location of dihydropyridines interaction site on the channels. It also offers some novel approaches to the investigation of $Ca_v1.2$ and other high voltage activated calcium channels, a promising target for cardiovascular research and therapy.

The second chapter deals with functional visualization of cardiovascular system and new possibilities for getting information about both structural and functional characteristics of the heart and blood vessels. The reader will be introduced to DECARTO (Dipolar Electro-Cardio Topography) mathematical model and optical coherence tomography. DECARTO shows the ventricular activation by time series of maps, called decartograms, in 2D and 3D projections and visualize a subtle changes in QRS complex. Optical coherence tomography is a useful tool for evaluation of the atherosclerotic lesions in blood vessels.

The next four chapters bring new information on the morphological and pathophysiologic changes related to nitric oxide homeostasis and deficiency in experimental models. The authors describe how inhibition of nitric oxide synthetase leads to myocardial fibrosis and remodeling of the arterial wall, and explain details regarding the expression and cellular control of nitric oxide synthetase activity in the rat cardiomyocytes and the role of reactive oxygen species, lipopolysacharides, and cytokines in the ischemic preconditioning of the heart. The role of nitric oxide in modulation of structural changes of the cardiac and vascular structures induced by hypertension as well as the multiple effects of nitric oxide

and its deficiency in vascular system are also covered.

The following chapters deal with a re-evaluation of the classical electrocardiographic voltage criteria for estimation of left ventricular mass, pharmacologic prevention of cardiac remodeling by calcium channel blockers and β-blockers, mechanisms of antihypertensive effects of antioxidant substances, role of protein kinases in regulation of cellular processes in ischemic myocardium, adaptive mechanisms against ischemia involving mitochondrial KATP channels, and long-term effects of exogenous donors of nitric oxide on arterial wall and hypertension.

The chapter on endogenous protective mechanisms in the heart of patients with diabetes mellitus provides an insight into the processes involving subcellular structures and metabolism of myocyte. The author provides his own results obtained from the rat models with acute streptozotocin-induced diabetes.

The fourteenth chapter presents morphological alterations which can be seen in capillaries in the heart of a diabetic patient and finally end as a diabetic cardiomyopathy. Pathohistological subcellular alterations of myocardial capillaries and structural markers of angiogenesis in the heart are illustrated.

The last chapter focuses on connexin-43 and cell-to-cell gap junction changes due to several endocrinologic disorders or advanced age. The authors present their hypothesis that such changes, associated with structural remodeling of the heart and/or calcium overload, predispose to generation of re-entrant circuits and increased susceptibility to both atrial and ventricular fibrillation.

Highlights: The selected chapters included in this book will enable the readers to recognize the importance and the potential of experimental models and investigations in cardiovascular medicine. Those with specific interest in some areas of experimental cardiovascular sciences will be able to benefit from this book. This book confirms the common need for further research in the experimental cardiology and emphasize the need for further integrated approach of many topics. Almost all chapters include good quality photographs and/or schematic illustrations of mechanisms and processes.

Limitations: The book is written for experts in basic research. Like other similar monographs, this book presents the current developments in several fields of cardiovascular science, makes this knowledge available, and serves for referencing.

The title of the book is not informative enough for the content. However, I agree that it could be difficult to make a concise and more accurate title, and at the same time to cover the chapters of such wide and heterogeneous fields. While "experimental hypertension" part of the title could be accepted and justified, experimental ischemic heart disease is too wide a topic. On the other hand, some chapters falls a bit outside of the title, for example the one on functional visualization of cardiovascular system and the last chapter on atrial and ventricular fibrillation.

I would have preferred if the authors had been more thorough in their presentation of the unresolved issues, which would have helped to set the stage for the topic in some chapters. Although it is not in the primary scope of the book, a more of critical assessment of the current status and future prospects for the specific topics would have been welcome. As a clinician, I would have liked more links provided to clinically relevant issues and diseases. Finally, the editors could have been more successful in entwining the discussions by different authors in their chapters to avoid overlap, such as that in discussions related to nitric oxide, reactive oxygen species, and hypertension.

Related reading: Chapters end with a list of related readings, providing an insight into the sources of additional information and the basis for more in-depth study on the topic.

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