

Zukowska Z, Feuerstein GZ, editors. The NPY family of peptides in immune disorders, inflammation, angiogenesis and cancer. (Progress in inflammation research, Parnham MJ series editor). Basel, Switzerland: Birkhauser Verlag; 2006. 258 pages; ISBN-10: 3-7643-7159-5; price: US \$169.00.

Field of medicine: Peptide research, inflammation research.

Format: Hard-cover book with 258 pages, including 9 tables and 37 figures (7 in color).

Purpose: To present a comprehensive state-of-the-art review of the field and to discuss the frontiers of neuropeptide Y (NPY) research and related drug development.

Contents: The book has 17 articles divided into four chapters. Current research indicates that the immune system and inflammatory reactions are governed and regulated by powerful neuronal mediators derived from the central and peripheral nervous systems. The NPY family of peptides is one of these mediators. These peptides belong to a diverse group of neuropeptides that act via multiple receptors, Y1-Y5, which are widespread not only in neurons but also in a variety of non-neural and immune cells. Evolutionary ancient and structurally conserved, these peptides have been known as important regulators of many essential systems, such as blood pressure and cardiac function, food consumption and energy homeostasis. NPY was originally described as an ancillary, sympathetic co-transmitter that modulates the release and action

of the primary neurotransmitter, norepinephrine. This peptide and its family members, have recently emerged as strong regulators of biological functions such as energy and metabolism, neural and endocrine modulation, immune surveillance and inflammatory reactions, tissue growth, regeneration and remodeling, and integrated responses to stress.

These diverse functions may serve a multitude of survival and adaptive behaviors, such as hibernation, defense and aggression (integrated neuroendocrine, cardiovascular, and skeletomuscular responses), reproduction, and foraging resources. The authors present key elements of recent scientific explorations to support the notion that peptides from the NPY family act not only as neurotransmitters and neuroendocrine modulators but also as immune and inflammatory modulators, cytokines, and growth factors.

In this book, experts in the field analyze recent evidence supporting the role of NPY family of peptides in regulation of the immune/inflammatory system with special reference to its medical and therapeutic implications. In a short introduction chapter, Zukowska and Feuerstein describe NPY

family of proteins and their wide physiological roles from neurotransmitters to immune modulators, cytokines and growth factors. The chapter "Biology of the NPY family of the peptides, their receptors and processing enzymes" starts with Larhammar and Salaneck's article on the evolution of the NPY, peptide YY (PYY), and pancreatic polypeptide (PP), and their receptors. Here we can learn how these genes evolved and how their functions changed. The authors also address functional implications of redundancies inherent in this family of peptides and present some remarkable examples of NPY evolutionary role. The second article in this chapter focuses on the molecular pharmacology of the NPY family of peptides' receptor systems and provides basic information necessary for understanding the diversity of receptor functions, signaling, and regulation, and their spatial distribution in the central and peripheral nervous system and gut. The comprehensive review of NPY/PYY/PP receptor biology is supplemented by a thorough discussion of present and future therapeutic perspectives. The remaining two articles in this chapter contain more discrete elaborations on NPY/PYY peptide processing and metabolism, illustrating the richness of functional diversification in this family of peptides. Unlike in the case of classical neurotransmitters, such as acetylcholine, which is enzymatically inactivated proteolytic cleavage of the NPY peptide family, both the precursors and the mature peptides, NPY1-36 and PYY 1-36, yield fragments that exercise novel biological functions. How this feature of the system offers possibilities of new therapeutics by manipulation of specific peptidases is discussed here. The next chapter, "The NPY family of peptides in immune disorders and inflammation," comprises four articles. First three articles describe the role of the NPY family of proteins in immunological system, more specifically in inflammatory reactions, immunological surveillance, and in stress responses. In particular, the role of NPY and its receptors in neurogenic inflammation and stress-

dependent immune diseases is reviewed, and innovative opportunities to treat host-defense pathological reactions via selective NPY receptor and enzyme processing drugs are discussed. The last section extends this topic to pain research. This article describes actions of NPY Y1 and Y2 receptors in acute pain and following inflammation and neuropathic pain models.

The third chapter, "The NPY family of peptides and angiogenesis," deals with the current information on the potential role of the NPY system in angiogenesis and regulation of vascular growth. This new area of NPY research offers great potential in ischemic re-vascularization, stem cell biology, and organ remodeling and regeneration. Its therapeutic implications span from the treatment of ischemic diseases, wound healing and retinopathy to atherosclerosis and hypertension.

The fourth chapter, "The NPY family of peptides as growth factors in neurodegenerative diseases and tumor biology," extends NPY topic on potent growth factor activities of the NPY family members in nerve regeneration and plasticity, and in tumors. Remarkable progress has been made in these fields and new therapeutics have emerged for the treatment of certain malignant tumors as well as neurodegenerative diseases.

Finally, the "Summary" by Zukowska and Feuerstein completes the book with future directions and therapeutic perspectives for NPY/PYY-based anti-inflammatory and tumor suppressor drugs.

Related reading: This book focuses on the novel role of NPY peptides in inflammation, immune disorders, angiogenesis, and proliferate diseases, which grew out of more "traditional" fields of research such as neuroscience, cardiovascular, and endocrine biology. The latter are covered in the EXS series volume, which addresses the NPY family of peptides in the cardiovascular, metabolic and central nervous system diseases. Readers can find additional information contained in the second volume edited by Zofia Zukows-

ka and Giora Z. Feuerstein: *NPY Family of Peptides in Neurobiology, Cardiovascular and Metabolic Disorders: from Genes to Therapeutics*. Additional information and in-depth analysis of particularly neuroendocrine, molecular, and pharmacologic aspects of NPY research can also

be found in previous texts such as *Neuropeptide Y and Related Peptides*, edited by M.C. Michel, and many excellent recently published reviews on NPY.

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Kaufmann SHE, Lambert PH. *The Grand Challenge for the Future. Vaccines for Poverty-Related Diseases from Bench to Field*. Basel, Switzerland: Birkhäuser Verlag; 2005. 285 pages; ISBN 978-3-7643-7175-3; price: US \$129.00

Field of medicine: Public health, immunology, microbiology, epidemiology.

Format: Hardcover book.

Audience: Public-health workers, epidemiologists, immunologists, students.

Purpose: To provide an extensive overview and detailed information of vaccines for poverty-related diseases (HIV/AIDS, tuberculosis, malaria).

Content: The main goal of this book is to review various aspects related to vaccinology. The book has seven parts: Background, Private Hand (two essays), Public-private Partnerships, Bench (three essays), Regulatory Issues, Clinical Trials (four essays), and Vaccination Programmes.

Infectious diseases remain a substantial peril to human well-being and economies despite the availability of modern drugs. Numerous measures of infectious diseases prevention are used but most experts working in the field agree that vaccination is the most efficient form of prevention. Vaccination has resulted in the eradication of smallpox, the imminent eradication of polio, and a dramatic reduction in many other infectious diseases.

In the first chapter, the authors describe the economic aspects of vaccines and vaccinations and offer a global perspective on the future. The intensified fight against poverty-related diseases has been accompanied by greater mobilization of public and private funds for research projects, including vaccine-oriented development. The role of economic evaluation in vaccine program design is likely to increase in the future. In many developing countries, economic obstacles still limit the use of existing vaccines and no rapid solution can be expected without international aid and significant financing plans. Greater recognition of the social value of prophylactic vaccination will be essential in order to let humankind benefit from the considerable scientific and economic efforts that underpin the development of new vaccines against poverty-related diseases.

The second chapter includes two essays. The first essay "How and why vaccines are made" attempts to give a perspective on the process of vaccine development: why a target is chosen, how the vaccine is licensed, and the factors involved in the modern production of a biological vaccine

for the use in humans. Three major problems for the future of vaccine production are safety, cost, and adequacy of supply. The second essay "How can the industrial world help to implement new vaccine against poverty-related diseases?" describes the intensified fight against poverty-related diseases, accompanied by an even greater mobilization of public and private funds for research projects, including vaccine development. Therefore, a global approach is required, including coordinated efforts of industry, public sector, and the developed and developing countries. Global health should be made a national priority in the developed countries, while development of new vaccines should be supported according to their public health values.

Third chapter includes only one essay – "New approaches towards development, production and use of developing-country market vaccines in developing countries." This chapter mainly describes the economic aspects of introduction of new vaccines in developing countries. Antigenic diversity, naturally occurring mutations and microbial selection under immunological pressure influence the global epidemiology of microbial pathogens targeted by novel vaccination strategies. The principal obstacle to new vaccines introduction to developing countries has been their cost. The public health impact of conjugate vaccines has also been described. Introduction of new conjugate vaccines into the developing countries could drastically reduce mortality caused by enteric bacteria, such as *S. typhi*, *S. paratyphi*, *Shigellae*, *E. coli*, and *V. cholerae O1 and O139*. It has recently been estimated that there are over 350 vaccine candidates currently under development against nearly 100 infectious diseases. Until a few years ago, a vaccine has been developed mostly on the basis of its technical feasibility within a decent time frame, which had remarkable consequences.

In the chapter four, the first essay describes how novel vaccination strategies for poverty related diseases must, at a global and comprehen-

sive level, deal with the specific issues related to both the target micro-organism and target population. Given the poor infrastructure and incomplete health-care system in many developing countries, vaccines are often the only pharmaceutical products that can make a substantial impact on public health. The second essay describes the requirement for vaccine adjuvants, as well as the side effects of widely used human adjuvants. The third essay describes vaccination in the context of immunological immaturity.

The fifth chapter reports about regulatory issues in the development of new vaccines with a special emphasis on safety aspects. One of the major differences between vaccines and other pharmaceuticals is the fact that they are given to healthy people, and predominantly to children. As a consequence, safety is the major focus in the assessment of vaccines.

In the sixth chapter, entitled Clinical Trials, the first essay discusses the link between ethical issues and clinical trials in the developing countries. The second essay deals with vaccine safety and adverse events. To provide independent scientific assessments of vaccine safety issues, World Health Organization established a Global Advisory Committee on Vaccine Safety in 1999. The third essay in Chapter 6 describes the importance of the discovery of a new vaccine candidate and the demonstration of its safety, immunogenicity, and protectivity in animal models, which is the first step toward introduction of the vaccine into public health practice. The longest phase, and arguably the most uncertain, laborious, and expensive one in vaccine development includes clinical testing in humans. This clinical testing must minimally demonstrate acceptable safety and suitable protection in the population that will ultimately be targeted for the vaccine in public health practice. The fourth essay in the chapter 6 describes practical aspects of phase 3 vaccine trials in the developing countries. Factors including epidemiological variations by geographic region (circulating serotypes, carriage, co-infections), differences

in cost-benefit ratios, characteristics of preferred formulations because of production and cold chain capacity may result in the development of vaccines that, although suitable for industrialized countries, might not be the most appropriate for developing countries. Additional challenges reside in the pressing need for rapid assessment of clinical efficacy. Vaccine trials represent a long, complex, and expensive endeavor.

The last chapter, Vaccination Programmes, reviews some of the important issues which must be considered before the introduction of new vaccines into the National immunization programs. Some examples are added to illustrate characteristic issues for particular vaccines.

Highlights: The book contains all essential information on different aspects of vaccination. It shows how, within a few decades, vaccinology has emerged as a unique discipline through the

increasing confrontation of the scientists in vaccine research with the intricate network of obstacles to be overcome.

It gives an excellent overview of industrial manufacturing, financial, public health, and social difficulties and effects of vaccination. Issues range from immunology to epidemiology, from genetics to ecology, from economics to industrial engineering, from social sciences to primary health care. This book also gives an excellent overview of the economic aspects of vaccines and vaccinations and offers a global perspective on its future. It provides an important link between vaccine development and application under the particular conditions in developing countries.

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