Methods in Enzymology

Volume 190

RETINOIDS

Part B

Cell Differentiation and Clinical Applications

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Retinoids

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Cell Differentiation and Clinical Applications

EDITED BY

Lester Packer

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Preface

Spectacular progress and unprecedented interest in the field of retinoids prompted us to consider this topic for two volumes in the *Methods in Enzymology* series: Volume 189, Retinoids, Part A: Molecular and Metabolic Aspects and Volume 190, Retinoids, Part B: Cell Differentiation and Clinical Applications.

From a historical perspective we know that studies in the 1930s showed that vitamin A (retinol) and retinal had a role in the visual process. It was also recognized that some link between vitamin A and cancer incidence existed. Several decades ago it was discovered that retinoic acid had a dramatic effect on the chemically induced DMBA mouse skin carcinogenesis model in which enormous reductions in the tumor burden were observed. This led to the realization that retinoids had important effects on cell differentiation. This resulted almost immediately in the synthesis and evaluation of new retinoids. Indeed, the effects of retinoids on cell differentiation appear to be more universal and of greater importance than their light-dependent role in vision and microbial energy transduction.

Progress has been rapid, and the importance of accurate methodology for this field is imperative to its further development. The importance of methodology applies to the use of retinoids in basic research in molecular, cellular, and developmental biology, and in clinical medicine. In medicine, applications have been mainly to cancer and in dermatology to the treatment of skin diseases and skin aging. As new retinoids are being tested in biological models and in clinical medicine, interest in the nutrition and pharmacology of retinoids has arisen. Moreover, the beneficial effects of retinoids in pharmacological treatment have led to a recognition of the "double-edged sword" of toxicity (teratogenicity).

In Section I of this volume, Cell Differentiation, the effects of retinoids in various cell differentiation systems are covered. Many new systems in which retinoids exhibit their effects have been employed. Both normal diploid cells and cell lines *in vitro* have been used, and the methods and systems employed are presented. In addition, tissue and organ culture are important areas for retinoid methodology. The effects of retinoids as morphogens and teratology agents are also included. In Sections II, Nutrition, Tissue and Immune Status, and Antioxidant Action, and III, Pharmacokinetics, Pharmacology, and Toxicology, nutritional and pharmacological methods are presented. Retinoids in the treatment of skin disease and in cancer chemotherapy are probably the most important areas in which methodological developments have occurred. New methodology has also

revealed the antioxidant activity of retinoids, and since any antioxidant may also be a pro-oxidant such considerations may be important for clinical pharmacology and therapeutics.

Volume 189 covers structure and analysis, receptors, transport, and binding proteins, and enzymology and metabolism.

I am very grateful to the Advisory Board—Frank Chytil, DeWitt Goodman, Maria A. Livrea, Leonard Milstone, Concetta Nicotra, James A. Olson, and Stanley S. Shapiro—for their unique input, advice, counsel, and encouragement in the planning and organization of this volume. In most instances, I met with every member of the board on one or more occasions to discuss the topics and to identify the most important contributors. Indeed, we found almost universal acceptance, and virtually no one turned down our invitation to contribute to this volume. In fact it was somewhat autocatalytic in that many contributors, realizing the timeliness and significance of having all of the methods dealing with retinoids included, made suggestions for additional contributions which were evaluated by the board. In a few instances we may have been somewhat overzealous, and more than one article on a method has been included. We do apologize for this slight redundancy for the sake of completeness.

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