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William S. Spielman and Narayanan Parameswaran

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Printed in the USA.

Springer Science+Business Media, LLC, 233 Spring Street, New York, New York 10013, USA
<http://www.springer.com>

Please address all inquiries to the publishers:
Landes Bioscience, 1806 Rio Grande, Austin, Texas 78701, USA
Phone: 512/ 637 6050; FAX: 512/ 637 6079
<http://www.landesbioscience.com>

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RAMPs, edited by William S. Spielman and Narayanan Parameswaran. Landes Bioscience / Springer Science+Business Media, LLC dual imprint / Springer series: Advances in Experimental Medicine and Biology.

ISBN: 978-1-4614-2363-8

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Library of Congress Cataloging-in-Publication Data

RAMPs / edited by William S. Spielman, Narayanan Parameswaran.
p. ; cm. -- (Advances in experimental medicine and biology ; 744)

Includes bibliographical references and index.

ISBN 978-1-4614-2363-8

I. Spielman, William S., 1947- II. Parameswaran, Narayanan, 1970- III. Series: Advances in experimental medicine and biology ; 744. 0065-2598

[DNLM: 1. Receptor Activity-Modifying Proteins. W1 AD559 v.744 2012 / QU 55.7]

LC classification not assigned

572'.65--dc23

2011046154

PREFACE

G-protein coupled receptors (GPCRs) comprise one of the largest families of receptors studied by receptor biologists across the globe. It is also the largest family of receptors that is targeted by the pharmaceutical industry for treating various disease conditions. In this respect, questioning how GPCRs function is one of the most critical questions not only in the endeavor of drug development but also in understanding the basic physiological processes. Among the many GPCRs discovered, the calcitonin family of receptors comprise of members that regulate a number of physiological processes and are involved in many pathological conditions. Therefore, understanding how these receptors function is a critical question in the field. When Foord and his colleagues discovered that a single transmembrane protein called Receptor Activity Modifying Proteins (RAMPs) could modulate the surface expression of GPCRs of the calcitonin family, it widely opened the field of receptor life cycle. Hundreds of studies have confirmed the importance of RAMPs in the life cycle of this receptor family. This volume is intended to be a source of these basic studies that range from biochemistry to molecular biology to receptor pharmacology and physiology. The authors who have contributed to the chapters in the book are well known in the RAMPs field. This book is intended to be a source of information for scientists at different stages of their career including graduate students, post-doctoral fellows and senior scientists who are new to the RAMPs field. The chapters are also organized in a way that makes it easy to navigate through the book.

The first chapter provides a general introduction to RAMPs including its discovery. The second chapter (by Poyner and colleagues) and the third chapter (by Bomberger and colleagues) are intended to provide in depth discussion on how the different RAMP isoforms can regulate various aspects of receptor signaling especially stimulated with calcitonin gene related peptide (CGRP) and adrenomedullin. In addition, in the third chapter, Bomberger et al discuss the differences in RAMP2 and -3 with regard to their role in receptor trafficking.

Initial discovery of RAMPs suggested that they regulate GPCRs of the Class II family. Subsequent research by Dr. Henley's group demonstrated a role for RAMPs in the surface expression of Class III GPCRs. Dr. Henley and his colleagues in Chapter 4 discuss this novel feature of RAMPs.

A crucial aspect to the advancement of the RAMP field has been the generation of RAMP transgenic/knockout mice. These RAMP transgenic/knockout mice have greatly facilitated our understanding of the physiological role of these proteins. Dr. Caron's group, which pioneered many of these experiments, discusses the studies in Chapter 5. From a therapeutic point of view, it is important to consider whether RAMPs are potential drug targets. Sexton and colleagues discuss in Chapter 6, the usefulness of RAMPs as drug targets.

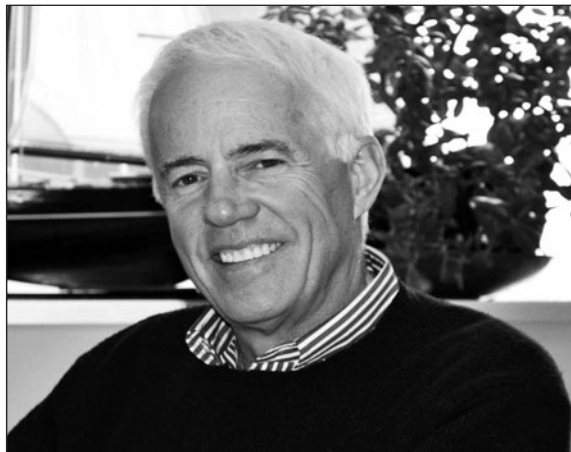
Subsequent to the discovery of RAMPs, scientists working on other receptors realized there could be proteins similar to RAMPs regulating their receptor of interest. In one particular case, Dr. Matsunami's group discovered RAMP-like proteins that regulate odorant receptors. Dr. Matsunami and his colleague discuss, in Chapter 7, this novel role of RAMP-like proteins in the regulation of odorant receptors.

RAMP expression is modulated in various diseases and Dr. Wang and his group discuss this in Chapter 8. Finally, in Chapter 9, we discuss some of the recent high impact studies that will help provide a perspective on the role of RAMPs in diseases such as cancer, hypertension and asthma.

We thank all the authors for their insightful and comprehensive contributions to this work. We also thank the publisher for their patience and suggestions in bringing *RAMPs* together in a timely manner. Editing this volume has been a rewarding experience for us, especially in terms of learning further about the functions of these single transmembrane proteins. Receptor biology is a rapidly expanding field and with the advances in cell and molecular biology and in vivo techniques, it is very likely that the field of RAMPs will explode further and many unanswered questions will be answered with in the next few years. We hope this book will serve as a useful resource for those scientists interested in not only the field of RAMPs but also in the general field of GPCR biology.

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