Calcium Signaling

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COLD SPRING HARBOR LABORATORY PRESS
Cold Spring Harbor, New York • www.cshlpress.com

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Articles online at www.cshperspectives.org

Printed in the United States of America

Executive Editor	Richard Sever
Managing Editor	Maria Smit
Project Manager	Barbara Acosta
Permissions Administrator	Carol Brown
Cover Designer	Denise Weiss
Publisher	John Inglis

Front cover artwork: The image depicts the complex regulation of adenylyl cyclase (AC) by Ca^{2+}. Ca^{2+} and cyclic AMP are key intracellular messengers with many bidirectional links to control each other's activity. In particular, Ca^{2+} controls the production of cyclic AMP in a variety of ways. Such regulation can be direct or via an intermediary Ca^{2+}-sensitive enzyme. Some ACs specifically respond to Ca^{2+} derived from store-operated Ca^{2+} channels (SOCCs). Ca^{2+} can also regulate AC by binding to calmodulin (CaM), and the Ca^{2+}/CaM complex can then affect AC activity. Ca^{2+}-bound CaM can also activate Ca^{2+}/CaM-activated kinase and calcineurin, both of which may regulate AC. Indirectly, Gβγ subunits from Gαq-linked receptors can also regulate AC activity. In addition, Gαq can activate phospholipase C, which converts phosphatidylinositol 4,5-bisphosphate (PIP_2) to diacylglycerol and inositol trisphosphate ($InsP_3$). DAG activates protein kinase C (PKC), which can also modulate the activity of AC. $InsP_3$ binds to, and activates, its receptors ($InsP_3R$) on the endoplasmic reticulum (ER), thereby releasing Ca^{2+} from the ER stores into the cytoplasm. This emptying of the ER Ca^{2+} stores triggers extracellular Ca^{2+} entry via SOCC. Further details can be found in the article by Halls and Cooper.

Library of Congress Cataloging-in-Publication Data

Calcium signaling / edited by Martin D. Bootman . . . [et al.].
p. cm.
Includes index.
ISBN 978-0-87969-903-1 (hardcover : alk. paper)
1. Calcium--Physiological effect. 2. Cellular signal transduction.
I. Bootman, Martin D.
QP535.C2C266319 2011
612.3'924--dc23
2011024271

10 9 8 7 6 5 4 3 2 1

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Preface

TWENTY YEARS AGO, IT WAS JUST ABOUT POSSIBLE TO READ and digest most of the papers on calcium signaling that appeared in such disparate areas as muscle function, neurobiology, and development. Scanning lists of publications contained in the *Current Contents* booklet would reveal that only very few pieces of a colossal jigsaw puzzle had been unearthed, but with each publication additional pieces were added, giving some clarity to the overall picture. The situation is rather different now. Libraries are virtual, and publications can be immediately searched and accessed. However, the growth of the calcium signaling literature over the past decades has been such that it is now impossible to read extensively as a generalist. Indeed, a simple search for "calcium signaling" returns more than 35,000 hits in PubMed. One thus feels genuinely sorry for students and postdocs who join this fast-moving area. They must read so much just to catch up. The published literature is no less daunting for established scientists trying to explore the wider relevance of the biology they focus on.

That is where this volume comes in: It provides a detailed expert snapshot of the calcium signaling field as it stands right now and gives some insight into the history of the discoveries too. The chapters illustrate the considerable breadth of calcium signaling mechanisms used by cells. Further, they describe the impact of calcium signals on a diverse range of cellular processes. Reading through them provides insight into both the generic nature of calcium signaling and also its unique tissue- and function-specific characteristics in some settings. The grand challenges are to understand how cellular calcium signaling proteomes determine the physiology of cells and how subtle changes in those proteomes lead to disease. This volume goes some way to explaining both issues in many different situations. It can be loosely grouped into chapters dealing with calcium signal generation/modulation and chapters exploring downstream consequences of calcium signals. However, the considerable overlap between these themes emphasizes the fact that cellular calcium signaling proteomes are plastic and can both determine and be determined by the specific characteristics of calcium signals.

We would like to express our sincere thanks to Richard Sever at Cold Spring Harbor Laboratory Press, who provided the motivation to compile this volume. Grateful thanks also go to Joan Ebert and Barbara Acosta at Cold Spring Harbor Laboratory Press, who tracked the progress of all the manuscripts and gave timely reminders of things that needed to be done. Finally, we must thank all the authors, who have taken time out of their busy schedules to write such excellent chapters.

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April 15, 2011