



ADVANCES IN  
MOLECULAR AND  
CELL BIOLOGY, 36

SERIES EDITOR  
E. Edward Bittar

CAVEOLAE AND LIPID RAFTS:  
ROLES IN SIGNAL  
TRANSDUCTION AND THE  
PATHOGENESIS OF  
HUMAN DISEASE

VOLUME EDITORS  
Michael P. Lisanti and Philippe G. Frank

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# Caveolae and Lipid Rafts: Roles in Signal Transduction and the Pathogenesis of Human Disease

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2005



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Elsevier Academic Press  
525 B Street, Suite 1900, San Diego, California 92101-4495, USA  
84 Theobald's Road, London WC1X 8RR, UK

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ISBN-13: 978-0-4445-1500-3  
ISBN-10: 0-444-51500-3  
ISSN: 1569-2558

PRINTED IN THE UNITED STATES OF AMERICA  
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## Preface

Caveolae are 50–100 nm plasma membrane invaginations found at the surfaces of most terminally differentiated cell types. Palade (1953) and Yamada (1955) first morphologically identified caveolae (a.k.a., plasmalemmal vesicles) about fifty years ago—in both endothelial and epithelial cells. Their organization and cellular localization indicated that these organelles might play an important role in the transport of molecules between different peripheral compartments. However, at that time, their molecular composition remained completely unknown.

In 1992, almost 40 years later, Glenney & Soppet (1992) and Rothberg *et al.* (1992) were the first to identify the most important structural protein of caveolae, namely caveolin. This protein was re-named caveolin-1 after the discovery of two other caveolin genes, caveolin-2 and caveolin-3. Subsequent studies clearly demonstrated the essential role of caveolin-1 in the formation of caveolae, as well as in the regulation of cell signaling.

The existence of caveolae was initially considered controversial (Severs, 1988); they were thought to represent an EM fixation artifact. However, several groups have now biochemically purified caveolae, using caveolin-1 as a marker protein for the organelle (Lisanti *et al.*, 1994a; Schnitzer *et al.*, 1995; Smart *et al.*, 1995; Anderson, 1998). In addition, the absence of caveolae in caveolin-1 deficient mice dramatically demonstrates their existence in a normal in vivo environment (Drab *et al.*, 2001; Razani *et al.*, 2001; Zhao *et al.*, 2002; Cao *et al.*, 2003).

Simons and collaborators were among the first to propose the concept and the existence of lipid raft domains (Simons and Ikonen, 1997); it is now well accepted that caveolae represent a subset of these lipid rafts. The specific lipid composition of caveolae (sphingolipid and cholesterol-rich) led to the idea that these microdomains may play an important role in the regulation of cellular cholesterol homeostasis (Brown and London, 1998; Liscum and Munn, 1999; Fielding and Fielding, 2001) (see Section 1 of the book).

Besides the important role of caveolae in the regulation of endocytosis (see Section 2 of the book), the enrichment of signaling molecules in caveolae suggested that these domains play a key role in the regulation and organization of various cell-signaling cascades—forming “pre-assembled signaling complexes” (Lisanti *et al.*, 1994b) (see Section 3 of the book).

Finally, more recent studies using caveolin-deficient mice have confirmed many of the “controversial hypotheses” put forth in earlier publications (Drab *et al.*, 2001; Razani *et al.*, 2001; Zhao *et al.*, 2002; Cao *et al.*, 2003). However, even if caveolin proteins are not essential for life, they still play a critical role in the pathogenesis of a number of human diseases, as highlighted in studies using caveolin-deficient mouse animal models.

These studies have shown that caveolin proteins play an important role in regulating muscular, cardiovascular, and pulmonary patho-physiology (see Section 4 of the book). Furthermore, the negative regulatory role of caveolin-1 in various signaling pathways has suggested that caveolin-1 may indeed function as a tumor suppressor gene. Clear genetic links between the caveolin proteins and human disease have now been established in patients suffering from muscular dystrophy, cardiomyopathy, and breast cancer.

Overall, this book summarizes the essential features and functions of caveolae in cells, mouse animal models, and in human disease. We thank all the excellent contributors who extensively participated in making this book possible.

Philippe G. Frank and Michael P. Lisanti

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