

Advances in Experimental Medicine and Biology 991

Daniel G.S. Capelluto *Editor*

# Lipid-mediated Protein Signaling

 Springer

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# Advances in Experimental Medicine and Biology

Volume 991

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Editor

# Lipid-mediated Protein Signaling

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## Preface

The intention of this volume is to provide readers with an update on the role of lipids as signaling molecules and how they direct protein signaling to downstream effectors. To understand the specific mechanisms underlying these processes, we recruited renowned scientists who have contributed relevant work in the various areas of lipid signaling research. The objectives of this volume are to summarize recent developments in our understanding of how lipids provide specificity for signaling and to review the role of compartmentalization in lipid-mediated signaling pathways.

The initial chapters of this volume are dedicated to sphingolipid-mediated signaling pathways. The first chapter by Jiang and colleagues addresses in great detail sphingomyelin-triggered signaling, its role in lipid rafts, regulation of the sphingomyelin synthase 1 and 2, and their relationship with physiological conditions such as insulin-mediated responses. A chapter by Yahi et al. addresses the structural basis for gangliosides and cholesterol recognition by alpha-synuclein and the driving forces for the insertion of this protein into the plasma membrane. The chapter by Capelluto et al. reviews the controversial role of membrane sulfatides in cell signaling with an emphasis on their role in platelet aggregation.

Next, a set of five chapters centers on phosphoinositide-mediated signaling. Zimmermann et al. focuses on the mechanisms by which PDZ domains bind phosphoinositides and the structural basis for specificity, regulation, and significance of lipid recognition. The chapter by Overduin and colleagues deals with phosphatidylinositol 4-phosphate (PtdIns(4)P)-mediated signaling in the Golgi apparatus, with particular emphasis on the functional and structural basis of Golgi-associated PtdIns(4)P-binding proteins. Ross and colleagues review the cellular function of phosphatidylinositol (4,5)-bisphosphate (PtdIns(4,5)P<sub>2</sub>), using the PtdIns(4,5)P<sub>2</sub>-binding tumor suppressor Phosphatase and Tensin homolog deleted on chromosome 10 (PTEN) as a model to understand how the lipid controls the membrane binding properties of the protein and introducing neutron reflectivity as a new tool to study the orientation and shape of phospholipid mediated membrane-bound proteins. The chapter by Degterev et al. summarizes the cellular role of phosphatidylinositol 3,4,5-trisphosphate (PtdIns(3,4,5)P<sub>3</sub>) particularly on what refers to pleckstrin-homology domain functions, implications of this phosphoinositide in health and disease, and a thorough review of current drugs employed for targeting intracellular PtdIns(3,4,5)P<sub>3</sub> levels. Gillaspay highlights the function of

phosphoinositides, the effect of their derivatives, inositol 1,4,5-trisphosphate and inositol hexakisphosphate, and their impact on plant growth and development.

The final three chapters are devoted to the emerging role of non-phosphoinositide phospholipids and their derivatives in signaling. Wang and colleagues give the readers an overview of phosphatidic acid (PA)-mediated signaling, including most recent studies on PA-interacting proteins, effect of PA in membrane structure, and in PA-mediated signaling processes with an emphasis in studies carried out in plants. Grinstein et al. examine phosphatidylserine-mediated cell signaling including current methods of phospholipid visualization in live cells. Changes in the level and relocalization of phosphatidylserine in the cell membrane are discussed as well as its extracellular role under conditions such as hemostasis and apoptosis. The closing chapter by Greenberg et al. describes mitochondrial cardiolipin-mediated signaling, including the relationship of cardiolipin with longevity defects, apoptosis, and cardiolipin-defective remodeling.

The editor thanks and acknowledges the contributors for providing their review chapters in a timely fashion and the Springer SBM staff for their cooperation during the editing process.

Blacksburg, VA, USA

Daniel G.S. Capelluto



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## Abbreviations

5PTase	Inositol polyphosphate 5-phosphatase
ABA	Abscissic acid
ABI1	Abscissic Acid Insensitive 1
ABC	ATP-binding cassette
ALCAT1	Acyl-CoA:lysoCL acyltransferase 1
AP-1	Adaptor protein 1
aPKC	Atypical protein kinase C
Arf	ADP-ribosylation factor
ASA	Arylsulfatase A
At	<i>Arabidopsis thaliana</i>
BAI1	Brain specific angiogenesis inhibitor 1
BAR	Bin/amphiphysin/Rvs
BTHS	Barth syndrome
BTK	Bruton's tyrosine kinase
Cav	Caveolin
CCV	Clathrin-coated vesicle
CD1	Cluster of differentiation 1
CDK	Cyclin-dependent kinase
CDP-DAG	Cytidine diphosphate-diacylglycerol
Cer	Ceramide
CERT	Ceramide transport protein
CGT	UDP-galactose: ceramide galactosyltransferase
CL	Cardiolipin
COI1	Coronatine Insensitive 1
COP II	Coat protein complex II
CP	Capping protein
Crd1	Cardiolipin synthase
CST	3'-Phosphoadenosine-5'-phosphosulfate:cerebroside sulfotransferase
CTR1	Constitutive Triple Response 1
CTX-A3	Taiwanese Cobra cardiotoxin A3
Cyt c	Cytochrome c
Dab2	Disabled-2
DAG	Diacylglycerol
DHA	Docosahexaenoic acid
DHR	Disc-large Homology Region
DRM	Detergent resistant membrane

---

E	Endosome
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
eIF3	Eukaryotic initiation factor 3
ENTH	Epsin amino-terminal homology
EpsinR	Epsin-related protein
ER	Endoplasmic reticulum
ERK	Extracellular signal-regulated kinase
FAPP	Four-phosphate adaptor protein
FERM	Four point one/Ezrin/Radixin/Moesin
FoxO	Forkhead-box Class O
FYVE	Fab1/YotB/Vac1/EEA1
G-3-P	Glycerol-3-phosphate
G6P	Glucose 6 phosphate
GAPC	Glyceraldehyde-3-phosphate dehydrogenase
GCS	Glucosylceramide synthase
GEF	Guanine nucleotide-exchange factor
GEP4	PGP phosphatase
GFP	Green fluorescence protein
GGA	Golgi-localized gamma ear-containing, ARF-binding protein
GLTP	Glycolipid transfer protein
GOLPH3	Golgi phosphoprotein 3
GPCR	G protein-coupled receptor
GPI	Glycosyl phosphatidylinositol
GPL	Glycerophospholipid
GRASP	Golgi reassembly and stacking protein
GUK	Guanylate-like kinase
HDL	High-density lipoprotein
HEK	Human embryonic kidney
HOG	High osmolarity glycerol
IGF-I	Insulin-like growth factor I
IL-1	Interleukin-1
IMP	<i>myo</i> -inositol monophosphatase
IMPL	IMP-like
Ins(1,4,5)P <sub>3</sub>	Inositol 1,4,5-trisphosphate
InsP	Inositol phosphate
InsP <sub>6</sub>	Inositol hexakisphosphate
IPC	Inositol phosphoceramide
IPK	Inositol kinase
IPMK	Inositol phosphate multikinase
IR	Insulin receptor
IRS	Insulin receptor substrate
JA-ILE	Jasmonic acid-isoleucine
JA	Jasmonic acid
JAZ	Jasmonate ZIM-domain
KIND	Kinase non-catalytic C-lobe
L <sub>4</sub> -CL	Tetralinoleoyl-CL
LE	Late endosome

---

<i>Lpa.</i>	Low phytic acid
LPP	Lipid phosphate phosphatase
LPS	Lipopolysaccharide
LTP	Lipid transfer protein
MAPK	Mitogen-activated protein kinase
MD	Molecular dynamics
MDCK	Madin-Darby Canine Kidney
MIK	<i>myo</i> -inositol kinase
MIPS	<i>myo</i> -inositol phosphate synthase
MLCL	Monolysocardiolipin
MLCKLAT1	MLCL acyltransferase-1
MLD	Metachromatic leukodystrophy
MtCK	Mitochondrial creatine kinase
mTORC	Mammalian target of rapamycin complex
MyD88	Myeloid differentiation primary response gene 88
MYO18A	Myosin-XVIII A
N	Nitrogen
NBD	7-Nitro-2-1,3-benzoxadiazol-4-yl
NCS-1	Neuronal calcium sensor-1
NeuAc	Neuraminic acid
NFkB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NMR	Nuclear Magnetic Resonance
NO	Nitric oxide
NPC	Non-specific PLC
NR	Neutron reflectometry
OBD	Oxysterol-binding domain
OGT	O-linked $\beta$ -N-acetylglucosamine transferase
ORP	OSBP-related-protein
OSBP	Oxysterol-binding protein
PA	Phosphatidic acid
Par	Partition-defective
PC	Phosphatidylcholine
PDGF	Platelet-derived growth factor
PDK1	Phosphoinositide-dependent kinase-1
PDZ	PSD-95/Discs large/ZO-1
PDZBM	PDZ binding motif
PE	Phosphatidylethanolamine
PG	Phosphatidylglycerol
PGP	Phosphatidylglycerolphosphate
Pgs1	Phosphatidylglycerolphosphate synthase
PH	Pleckstrin homology
PI	Phosphoinositide
PI3K	Phosphoinositide 3 kinase
PI4K	Phosphoinositide 4 kinase
PICK1	Protein interacting with c kinase 1
PIP5K	Phosphatidylinositol 4-phosphate 5 kinase
PK	Protein kinase

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PLA	Phospholipase A
PLC	Phospholipase C
PLD	Phospholipase D
PLS-3	Phospholipid scramblase-3
PM	Plasma membrane
PP	Diphospho
PP1C $\gamma$	Protein phosphatase 1C $\gamma$
PP2C $\epsilon$	Protein phosphatase 2 C- $\epsilon$
PPP	Triphospho
PS	Phosphatidylserine
PSD	PS decarboxylase
PSS1	PS synthase 1
PtdCho	Phosphatidylcholine
PtdEth	Phosphatidylethanolamine
PtdIns	Phosphatidylinositol
PtdIns(3)P	Phosphatidylinositol 3-phosphate
PtdIns(4)P	Phosphatidylinositol 4-phosphate
PtdIns(5)P	Phosphatidylinositol 5-phosphate
PtdIns(3,4)P <sub>2</sub>	Phosphatidylinositol 3,4-bisphosphate
PtdIns(3,5)P <sub>2</sub>	Phosphatidylinositol 3,5-bisphosphate
PtdIns(4,5)P <sub>2</sub>	Phosphatidylinositol 4,5-bisphosphate
PtdIns(3,4,5)P <sub>3</sub>	Phosphatidylinositol 3,4,5-trisphosphate
PtdSer	Phosphatidylserine
PTEN	Phosphatase and tensin homolog deleted on chromosome 10
PTP-Bas	Protein Tyrosine Phosphatase Basophile
PX	Phox-homology
Pyd	Polychaetoid
r CAS	Ca <sup>2+</sup> -sensing receptor
RCT	Reverse cholesterol transport
ROS	Reactive oxygen species
RTK	Receptor tyrosine kinase
SAC-1	Suppressor of actin mutations 1-like protein
SBD	Sphingolipid-binding domain
SBM	Sulfatide-binding motif
SH3	Src Homology 3
SHIP	SH2 domain containing inositol 5-phosphatase
SK	Sphingosine kinase
SLD	Scattering length density
SM	Sphingomyelin
SMase	Sphingomyelinase
SMS	Sphingomyelin synthase
SNCA	Synuclein, alpha, non A4 component of amyloid precursor
SnRK1.1	Sucrose non-fermenting-like kinase 1.1
SnRK2	Sucrose non-fermenting-1-related protein kinase 2
SPHK	Phytosphingosine kinase
SPR	Surface plasmon resonance

---

SPT	Serine palmitoyltransferase
START	Steroidogenic acute regulatory protein-related lipid transfer
stBLM	Sparsely-tethered bilayer lipid membrane
Taz1	Transacylase tafazzin
tBID	Truncated Bid
TGN	<i>trans</i> -Golgi Network
TIM	T cell immunoglobulin mucin
TIR1	Transport Inhibitor Response 1
TLR	Toll-like receptor
TNF $\alpha$	Tumor necrosis factor $\alpha$
TSC	Tuberous sclerosis complex
VHS	Vps27/Hrs/Stam
vWF	von Willebrand factor
ZO	Zonula occludens