Phosphoinositide Biology: New Therapeutic Targets beyond Class I PI3K

February 11–15, 2018 | Sagebrush Inn & Suites | Taos, New Mexico | USA

Scientific Organizers:
Emilio Hirsch, Fondazione per la Ricerca Biomedica – ONLUS, Italy
Tamas Balla, NICHD, National Institutes of Health, USA
Cristina Donini, Medicines for Malaria Venture, Switzerland

Phosphoinositides have been recognized since the 1980s as important regulatory lipids supporting signal transduction from G protein-coupled receptors and receptor tyrosine kinases. The discovery of PI 3-kinases and their roles in carcinogenesis and immune regulation has created a fertile ground for translational expansion of the phosphoinositide field with a focus on cancer and inflammation. Most of these advances focused on Class I PI3Ks and PIP3-mediated signaling. However, research on other PI kinases and phosphoinositides has expanded substantially over the years. Class II and -III PI 3-kinases and less characterized 3-phosphorylated phosphoinositides are now rapidly emerging as key controllers of development, trafficking, nutrition-sensing and autophagy. Furthermore, phosphoinositides different from the 3-phosphorylated species are gaining momentum in many aspects of cell physiology and pathology. Exciting new developments include PI 4-kinases controlling vesicular trafficking and non-vesicular lipid transfer between membrane contacts, and new details are emerging on the role of inositol lipid phosphatases in trafficking, endocytosis and ciliary function. The recently recognized roles of PI 4-kinases as obligate host factors for certain RNA viruses, and their importance in parasitic organisms such as Plasmodium falciparum or Legionella pneumophila, have raised significant interest from pharmaceutical companies that now focus on inositol lipids other than the products of PI 3-kinases. By expanding our knowledge of phosphoinositides beyond class I PI3K products, this Keystone Symposia meeting represents a unique opportunity to bolster the growing interest in these under-explored avenues with a strong potential for translational impact.

Session Topics:
- Phosphoinositide Gradients and Lipid Transport at Membrane Contact Sites
- PI 4-Kinases as Possible Drug Targets
- Inositide Phosphatases in Cancer and Development
- Workshop: New and Emerging Paradigms and Possible Drug Targets
- Structural Insights into Pharmacological Targeting of Lipid Kinases
- Phosphoinositides Directing Trafficking for Degradation
- Monoinositide Phosphatases
- Beyond Class I PI 3-Kinases
- PIP Kinases as Emerging Drug Targets

Scholarship Application & Discounted Abstract Deadline: October 10, 2017
Abstract Deadline: November 8, 2017
Discounted Registration Deadline: December 12, 2017

Note: Scholarships are available for graduate students and postdoctoral fellows and are awarded based on the abstract submitted. Submitting an abstract is an excellent opportunity to gain exposure for your work. Abstracts submitted by the abstract deadline will also be considered for short talks on the program.

Meeting Hashtag: #KSphospho
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SUNDAY, FEBRUARY 11

Arrival and Registration

MONDAY, FEBRUARY 12

Welcome and Keynote Address

*__Emilio Hirsch__, Fondazione per la Ricerca Biomedica – ONLUS, Italy

*__Tamas Balla__, NICHD, National Institutes of Health, USA

__Pietro V. De Camilli__, Yale University School of Medicine, USA
Phosphoinositide Signaling in the Control of Membrane Dynamics and Interactions

Phosphoinositide Gradients and Lipid Transport at Membrane Contact Sites

*__Gerry Hammond__, University of Pittsburgh, USA

__Bruno Antonny__, Institut de Pharmacologie Moleculaire et Cellulaire, France
PI4P as an Energy Source for Cholesterol Transfer by OSBP through the Activity of two PI4-Kinases with Contrasting Membrane-Binding Properties

__Tamas Balla__, NICHD, National Institutes of Health, USA
The Role of PI4KA in Controlling Membrane Lipid Dynamics

__Jen Liou__, University of Texas Southwestern Medical Center, USA
The Role of ER-PM Junctions in Phosphoinositide Homeostasis and Ca2+ Signaling

__Raghu Padinjat__, National Centre for Biological Sciences, India
Short Talk: Tuning of Lipid Transfer Reactions at Membrane Contact Sites in Drosophila Photoreceptors

__Jana Humpolickova__†, Institute of Organic Chemistry and Biochemistry, Czech Republic
Short Talk: Biophysical Determinants of Liposome-Reconstituted Lipid Transport by ORP5/ORP8

PI 4-Kinases as Possible Drug Targets

*__Antonella De Matteis__, Telethon Institute of Genetics and Medicine, Italy

__Nihal Altan-Bonnet__, NHLBI, National Institutes of Health, USA
Lipid Blueprints for Viral Replication and Transmission

__Kasturi Haldar__, University of Notre Dame, USA
Targeting a Mechanism of Artemisinin Resistance in Plasmodium falciparum Malaria

__Cristina Donini__, Medicines for Malaria Venture, Switzerland
MMV048, a Plasmodium PI4K Inhibitor as Potential Malarial Treatment

__Radim Nencka__†, IOCB Prague, Czech Republic
Short Talk: Phosphatidylinositol 4-Kinase IIIβ Inhibitors as Potential Therapeutics

Poster Session 1

TUESDAY, FEBRUARY 13

Inositide Phosphatases in Cancer and Development

*__Amy Kiger__, University of California, San Diego, USA

__John D. York__, Vanderbilt University, USA
Coordinated and Independent Biological Functions of Inositide Phosphatase Activities in Synaptojanins

__Jeremy F. Reiter__, University of California, San Francisco, USA
Cilia Have a Distinct Composition of Phosphoinositides and Other Lipids Critical for Signaling

__Christina Anne Mitchell__, Monash University, Australia
Identification of Novel Roles for Inositol Polyphosphate 5-Phosphatases

__Antonella De Matteis__, Telethon Institute of Genetics and Medicine, Italy
The Phosphoinositides and the Golgi Complex

__Gerry Hammond__, University of Pittsburgh, USA
Short Talk: SAC1 Degrades its Lipid Substrate PtdIns4P in the Endoplasmic Reticulum to Maintain a Steep Chemical Gradient with Donor Membranes

__Leonardo Salmena__, University of Toronto, Canada
Short Talk: INPP4B-Associated Leukemic Stem Cell Self-Renewal as a New Target in AML therapy

Workshop: New and Emerging Paradigms and Possible Drug Targets

*__Cristina Donini__, Medicines for Malaria Venture, Switzerland

__Evzen Boura__†, Institute of Organic Chemistry and Biochemistry, Czech Republic
Hijacking of PI4KB by Picornaviruses – Structural Insights and the Role of ACBD3

__Igor Cestari__†, Center for Infectious Disease Research, USA
Phosphatidylinositol Regulation of Antigenic Variation and Telomere Silencing in Trypanosomes

__Brooke M. Emerling__, Sanford Burnham Prebys Medical Discovery Institute, USA
Phosphatidylinositol-5-Phosphate 4-Kinases in the Control of Cellular Lipid Metabolism and Autophagy

__Michael P. Sheetz__, Mechanobiology Institute, National University of Singapore, Singapore
DNA Damage Causes Rapid Accumulation of Phosphoinositides for ATR Signaling

__Carmen Sivakumaren__, Harvard University, USA
Targeting the PIP4K2 Lipid Kinase Family in Cancer using Novel Covalent Inhibitors

__Yoko Yoshikawa__, Kobe University Graduate School of Medicine, Japan
Development of Anti-Cancer and Anti-Inflammatory Drugs Targeting Phospholipase Cε

Structural Insights into Pharmacological Targeting of Lipid Kinases

*__Evzen Boura__, Institute of Organic Chemistry and Biochemistry, Czech Republic

__John E. Burke__, University of Victoria, Canada
Structural Basis of Regulation and Inhibition of Phosphatidylinositol 4-Kinase III Beta (PI4KIIIB)

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Ujjini H. Manjunatha, Novartis Institute for Tropical Diseases, USA
Cryptosporidium Lipid Kinase Is a Promising Molecular Target to Treat Cryptosporidiosis

Roger L. Williams, Medical Research Council, UK
Structural Mechanisms of Regulation of the PI3K Superfamily

Chunmei Chang, University of California, Berkeley, USA
Short Talk: Rubicon Inhibits the PI3KC3 Complex II by Blocking a Membrane Docking Site

Raymond Blind, Vanderbilt University School of Medicine, USA
Short Talk: Intrinsic Kinase Auto-Regulation Mediated by Disordered Domains: Crystallographic and Enzyme Kinetic Analyses of the Human Inositol Polyphosphate Multikinase (IPMK)

Poster Session 2

WEDNESDAY, FEBRUARY 14

Phosphoinositides Directing Trafficking for Degradation

*__Volker Haucke__, Leibniz Institut für Molekulare Pharmakologie, Germany

Lois S. Weisman, University of Michigan, USA
Multiple Mechanisms Dynamically Regulate the Signaling Lipid PI(3,5)P2

Haoxing Xu, University of Michigan, USA
Lipid Regulation of Lysosomal Ion Channels

Mariella Vicinanza, Cambridge Institute for Medical Research, UK
PI(5)P Regulates Autophagy

Ankita Jaykumar, University of Texas Southwestern Medical Center, USA
Identifying Novel Functions of WNK1 Pathway in Autophagy

Benoit Bilanges, University College London, UK
Short Talk: Vps34 PI 3-Kinase Inactivation Enhances Insulin Sensitivity through Reprogramming of Mitochondrial Metabolism

Golam Saffi, Ryerson University, Canada
Short Talk: Lysosome Enlargement during PIKfyve Inhibition Occurs through Lysosome Coalescence Instead of Increased Biosynthesis

Monoinositide Phosphatases

*__Lois S. Weisman__, University of Michigan, USA

Volker Haucke, Leibniz Institut für Molekulare Pharmakologie, Germany
Phosphoinositide Conversion Directs Vesicular Trafficking

Jocelyn Laporte, Institute of Genetics and Molecular and Cellular Biology, France
Myotubularin Phosphoinositides Phosphatases Implication and Targeting in Neuromuscular Diseases

Amy Kiger, University of California, San Diego, USA
Coordination of Class II PI3-Kinase and Mtm PI3-Phosphatase Functions

Elizabeth A. Allen, University of Massachusetts Medical School, USA
Short Talk: Discovery of a Myotubularin-Related Phosphatase in Autophagy

Andrew T. Hale, Vanderbilt University School of Medicine, USA
Short Talk: Coordinated Inositide Lipid-Phosphatase Activities of Synaptojanin Modulate Actin Cytoskeleton Organization

Poster Session 3

THURSDAY, FEBRUARY 15

Keynote Address

*__Emilio Hirsch__, Fondazione per la Ricerca Biomedica – ONLUS, Italy

Pier Paolo Pandolfi, Beth Israel Deaconess Medical Center, Harvard Medical School, USA
Novel Modes of PI3K Signaling Regulation and Deregulation in Disease Pathogenesis

Beyond Class I PI 3-Kinases

*__Lewis C. Cantley__, Weill Cornell Medicine, USA

Emilio Hirsch, Fondazione per la Ricerca Biomedica – ONLUS, Italy
Class II PI3K Signaling in Cancer

James Dowling, Hospital for Sick Children, Canada
3-Phosphoinositide Metabolism in Muscle Development, Muscle Disease and as a Therapeutic Target

Jonathan M. Backer, Albert Einstein College of Medicine, USA
PIK3CB Signaling in Breast Cancer

York Posor, University College London, UK
Short Talk: PI3K-C2α in dsRNA Sensing and Inflammation

Antonija Jurak Begonja, University of Rijeka, Croatia
Short Talk: PI3P Modulates Megakaryocyte Maturation and Platelet Production through Late Endosomes/Lysosomes

PIP Kinases as Emerging Drug Targets

*__Pier Paolo Pandolfi__, Beth Israel Deaconess Medical Center, Harvard Medical School, USA

Lewis C. Cantley, Weill Cornell Medicine, USA
Type 2 Phosphatidylinositol-5-Phosphate 4-Kinases in Cancer

Richard A. Anderson, University of Wisconsin Medical School, USA
Agonist-Stimulated PI3,4,5P3 Generation by Scaffolded Phosphoinositide Kinases

Atsuo T. Sasaki, University of Cincinnati, USA
PI5P4Kbeta Is an Intracellular GTP Sensor for Metabolism and Tumorigenesis

Meeting Wrap-Up: Outcomes and Future Directions (Organizers)

*__Tamas Balla__, NICHD, National Institutes of Health, USA

FRIDAY, FEBRUARY 16

Departure