

# Join Keystone Symposia for the 2016 conference on:

# Ubiquitin Signaling

## March 13–17, 2016

### Whistler Conference Centre | Whistler, British Columbia | Canada

Scientific Organizers:
Philip Cohen, Michael Rape and Titia K. Sixma

*Joint with the conference on **NF-κB and MAP Kinase Signaling in Inflammation***

*Many components of the ubiquitin system are involved in controlling cellular processes, and the deregulation of this system underlies many diseases. The meeting will focus on how ubiquitylation controls processes such as autophagy, neurodegenerative diseases, hypertension, the immune system and the activation of NF-κB. It will include talks on how the ubiquitin system is controlled by protein phosphorylation, the specificity and regulation of deubiquitylases and the structural analysis of E3 ligases and large protein complexes that coordinate ubiquitylation and related events. Additional sessions will feature diseases caused by abnormalities in ubiquitylation and the progress that is being made in targeting the ubiquitin system for the development of improved drugs to treat cancer and other diseases.*

*Session Topics:*

- Regulation of the Ubiquitin System by Deubiquitylases and Phosphorylation
- Role of Ubiquitylation in Control of Autophagy
- Ubiquitination-Dependent Modulation of NF-κB Signaling I & II (Joint)
- Large Machines
- Ubiquitylation and Human Disease
- Structural Analysis of E3 Ligases and DUBs
- Small Molecules and Therapeutics
- Meeting Wrap-Up: Outcomes and Future Directions

**Submitting an abstract is a great way of participating in the conference through poster presentation and possible selection for a short talk.**

***Scholarship & Discounted Abstract Deadline: Nov 11, 2015***
***Abstract Deadline: Dec 14, 2015***
***Discounted Registration Deadline: Jan 13, 2016***

For additional details, visit **www.keystonesymposia.org/16X3**.

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# KEYSTONE SYMPOSIA
on Molecular and Cellular Biology

## Ubiquitin Signaling (X3)

**Scientific Organizers: Philip Cohen, Michael Rape and Titia K. Sixma**

*Sponsored by Cell Research and Genentech, Inc.*

## NF-kappaB and MAP Kinase Signaling in Inflammation (X4)

**Scientific Organizers: Steven C. Ley, Zhijian 'James' Chen and Jenny P.Y. Ting**

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### SUNDAY, MARCH 13

**Arrival and Registration**

### MONDAY, MARCH 14

**Keynote Session (Joint)**

*__Steven C. Ley__, Francis Crick Institute, UK

*__Michael Rape__, University of California, Berkeley, USA

**Louis M. Staudt**, NCI, National Institutes of Health, USA
*Blocking NF-kappaB Activation as a Therapeutic Approach in Cancer*

**Ning Zheng**, University of Washington, USA
*Targeting Regulatory Enzymes in Ubiquitin Signaling*

**Regulation of the Ubiquitin System by Deubiquitylases and Phosphorylation (X3)**

*__Philip Cohen__, University of Dundee, UK

**Titia K. Sixma**, Netherlands Cancer Institute, Netherlands
*Controlling the Isopeptidases: Regulation of Deubiquitination Reactions*

**Mads Gyrd-Hansen**, University of Oxford, UK
*CYLD limits Lys63- and Met1-linked Ubiquitin at Receptor Complexes to Regulate Innate Immune Signaling*

**Richard J. Youle**, NINDS, National Institutes of Health, USA
*Ubiquitin Signals on Mitochondria Promote Mitophagy via Autophagy Receptors*

**NF-kappaB Signaling in Cancer (X4)**

*__Louis M. Staudt__, NCI, National Institutes of Health, USA

**Michael Karin**, University of California, San Diego, USA
*How NF-kappaB Orchestrates Inflammation*

**Daniel Krappmann**, Helmholtz Zentrum München, Germany
*CARMA1-BCL10-MALT1 Signaling in Adaptive Immunity and Lymphoma*

**Dinis P. Calado**, Francis Crick Institute, UK
*NF-kappaB Cooperating Events in Mature B Cell-Derived Malignancies*

**Workshop 1: Structural Biology and Biochemistry of Ubiquitylation (X3)**

*__Rachel Klevit__, University of Washington, USA

**Maria Sunnerhagen**, Linkoping University, Sweden
*Structure of a TRIM21 - UBE2E1 Complex Reveals the Specificity of E2, Ubiquitin and Substrate Recognition by TRIM E3 RINGs*

**Katrin E. Rittinger**, Francis Crick Institute, UK
*Structural and Functional Characterization of TRIM Family E3 Ligases*

**Catherine L. Day**, University of Otago, New Zealand
*Activation of Ubiquitin Transfer by Secondary Ubiquitin–RING Docking*

**Seth F. Harris**, Genentech, Inc., USA
*Structural Insights Into WD-Repeat 48 Activation of Ubiquitin Specific Protease 46*

**Aysegul Ozen**, Genentech, Inc., USA
*Engineering the USP7 Catalytic Domain for Activity*

**Hirotaka Takahashi**, Ehime University, Japan
*Establishment of Deubiquitinating Enzyme Protein Array Based on Wheat Cell-Free System for a Novel Biochemical Tool*

**Workshop 1 (X4)**

*__Zhijian 'James' Chen__, University of Texas Southwestern Medical Center, USA

*__Shao-Cong Sun__, University of Texas MD Anderson Cancer Center, USA

**Jian Zhang**, Ohio State University, USA
*Anti-Fungal Innate Immune Response Mediated by C-Type Lectin Receptors Dectin-1 and Dectin-2 Is Regulated by E3 Ubiquitin Ligase Cbl-b*

**Claire Tocheny**, National Institutes of Health, USA
*Inflammatory Disease and Immunodeficiency due to Mutation in IkappaBalpha*

**Marc Riemann**, Leibniz Institute on Aging - Fritz Lipmann Institute, Germany
*Classical NF-kappaB Signaling via RelA and c-Rel Controls the Development of Medullary Thymic Epithelial Cells*

**Firaz Mohideen**, Harvard Medical School, USA
*Systematic Quantitative Proteomics in Response to TNFalpha Signaling Reveals Dynamic Alterations in the Architecture of the Cellular Phospho-proteome*

**Isabel Meininger**, Helmholtz Zentrum München, Germany
*Alternative Splicing of MALT1 is Critical for Signaling and Activation of CD4+ T Cells*

**Meri Kaustio**, FIMM/University of Helsinki, Finland
*Heterozygous Mutations in NFKB1 cause Immunodeficiency and Autoinflammation*

**Mélanie Juilland**, University of Lausanne, Switzerland
*CARMA1- and MyD88-Dependent Activation of Specific AP-1 Complexes is a Hallmark of ABC Diffuse Large B-cell Lymphomas*

**Role of Ubiquitylation in Control of Autophagy (X3)**

*__Richard J. Youle__, NINDS, National Institutes of Health, USA

**James H. Hurley**, University of California, Berkeley, USA
*Mechanistic and Structural Insights into Autophagy Initiation*

**J. Wade Harper**, Harvard Medical School, USA
*Ubiquitin Signaling for Mitophagy*

**Ivan Dikic**, Goethe University Medical School, Germany
*Ubiquitin Regulation of Selective Autophagy*

**Xavier Jacq**, MISSION Therapeutics Ltd., UK
*Short Talk: Inhibitors of USP30 as a Potential Treatment of Parkinson's disease and Other Mitochondrial Dysfunctions*

### NF-kappaB Signaling in Immunity (X4)

***Manolis Pasparakis**, University of Cologne, Germany
*The Interplay between NEMO, NF-kB and RIPK1 in Cell Death and Inflammation*

**Steve D. Gerondakis**, Monash University, Australia
*Is NF-kappaB1 a Tumor Suppressor?*

**Xiaoxia Li**, Cleveland Clinic Foundation, USA
*IRAK Regulation of NF-kappaB and MAP Kinase Activation*

***Ulrich K. Siebenlist**, NIAID, National Institutes of Health, USA
*Short Talk: The B-Cell Tumor Promoter Bcl-3 Controls Inflammation-Associated Colon Tumorigenesis*

### Poster Session 1

## TUESDAY, MARCH 15

### Ubiquitination-Dependent Modulation of NF-kappaB Signaling I (Joint)

***Vishva M. Dixit**, Genentech, USA

**Zhijian 'James' Chen**, University of Texas Southwestern Medical Center, USA
*Regulation of Antiviral Innate Immunity by Ubiquitination and Phosphorylation*

**Pascal Meier**, Institute of Cancer Research, UK
*Tipping the Response to TNF in Favor of Death*

**Domagoj Vucic**, Genentech, Inc., USA
*Short Talk: Ubiquitin Ligase Activity of XIAP Regulates NOD2 Mediated Inflammatory Signaling*

**Michaela U. Gack**, University of Chicago, USA
*Regulation of Antiviral Signaling by TRIM E3 Ligases*

**David Komander**, Walter and Eliza Hall Institute of Medical Research, Australia
*Regulating Linear Ubiquitin Chains with OTULIN*

### Poster Session 2

### Workshop 2: Physiology of Ubiquitin-Dependent Signaling (X3)

***Michael Rape**, University of California, Berkeley, USA

**Pieter J. Eichhorn**, National University Singapore, Singapore
*USP15 Regulates SMURF2 Kinetics through C-Lobe Mediated Deubiquitination*

**Tohru Ishitani**, Medical Institute of Bioregulation, Kyushu University, Japan
*Ubiquitin-Mediated NF-kappaB Degradation Directs Dorsal-Ventral Patterning in Vertebrate Early Embryo*

**Brooke L. Latour**, Radboudumc, Netherlands
*De novo Loss of Function Mutations in the Deubiquitinating Enzyme USP9X cause a Female Specific Syndrome Characterized by Developmental Delay and Distinct Congenital Malformations*

**Eli Arama**, Weizmann Institute of Science, Israel
*Spatial Regulation of a CRL3 Complex by a Krebs Cycle Component Restricts Caspase Activation to the Vicinity of the Mitochondria during a Non-apoptotic Cellular Process in Drosophila*

**Steven H. Spoel**, University of Edinburgh, UK
*Transcriptional Activation by E3 and E4 Ubiquitin Ligases*

**Alexandra Greer**, Genentech, Inc., USA
*Ubiquilin1 is Uniquely Required for Cell Cycle Entry and Proliferation Downstream of B-cell Receptor Signaling*

**Satpal Virdee**, University of Dundee, UK
*Engineered E2~Ub Conjugates as Probes of E3 ligase Transthiolation Activity*

### Large Machines (X3)

***Brenda A. Schulman**, Max Planck Institute of Biochemistry, Germany

**Andreas Martin**, University of California, Berkeley, USA
*26S Proteasome Assembly and Conformational Changes Control Substrate Deubiquitination by Rpn11*

**Nicolas H. Thomä**, Friedrich Miescher Institute for Biomedical Research, Switzerland
*Regulation of Cullin-RING-ligase activity by CSN*

**Raymond J. Deshaies**, Amgen, Inc., USA
*Regulation of CRL Assembly: The Adaptive Exchange Hypothesis*

**Jessica A. Gasser**, Broad Institute of MIT and Harvard, USA
*Short Talk: Genome-Wide CRISPR-Cas9 Screen Reveals Genes Required for the Effect of Lenalidomide on the CRL4-CRBN Ubiquitin Ligase*

### Transcriptional Regulation in Inflammation (X4)

***Michael Karin**, University of California, San Diego, USA

**Alexander Hoffmann**, University of California, Los Angeles, USA
*Dynamic Control of NFkB*

**Irina A. Udalova**, University of Oxford, UK
*IRF5 Orchestrated Regulation of Inflammatory Programme in Macrophages*

**Neal Silverman**, University of Massachusetts Medical School, USA
*Short Talk: Regulation of Drosophila Innate Immune NF-kappaB Signaling by Amyloidal Proteins*

**Stephen T. Smale**, University of California, Los Angeles, USA
*Global Analysis of Transcriptional Cascades Induced by Inflammatory Stimuli*

## WEDNESDAY, MARCH 16

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### Ubiquitylation and Human Disease (X3)

*__Ingrid E. Wertz__, Genentech, Inc., USA

**Michael Rape**, University of California, Berkeley, USA
*Ubiquitin-Dependent Regulation of Craniofacial Development*

**Dario Alessi**, University of Dundee, UK
*Control of Blood Pressure*

**Noam Zelcer**, Academic Medical Center, University of Amsterdam, Netherlands
*Short Talk: USP2 Regulates the LDLR Pathway through Deubiquitylation of the E3-ubiquitin Ligase IDOL*

**Heran Darwin**, New York University School of Medicine, USA
*Proteasomal Regulation of Mycobacterium tuberculosis Pathogenesis*

**Jeffery S. Cox**, University of California, Berkeley, USA
*Discrimination of Pathogens from Non-Pathogens by Innate Immune Cells*

### NLR Signaling to NF-kappaB and IRF (X4)

*__Rudi Beyaert__, Ghent University - VIB, Belgium

**Jenny P.Y. Ting**, University of North Carolina at Chapel Hill, USA
*NLRs as Regulators of NFkappaB and MAPK Signaling*

**Feng Shao**, National Institute of Biological Sciences, China
*Pyroptosis in Anti-Bacterial Immunity: Sensing and Execution*

**Benedict Seddon**, University College London, UK
*Short Talk: TNF Activation of NF-kappaB is Essential for Development of Single Positive Thymocytes*

**Thirumala-Devi Kanneganti**, St. Jude Children's Research Hospital, USA
*Regulators of Inflammatory Responses*

**Vishva M. Dixit**, Genentech, USA
*RIPK3: Role of the Kinase Activity in Necroptosis*

### Workshop 3: The Interplay between Ubiquitylation and Phosphorylation in Cell Regulation (X3)

*__David Komander__, Walter and Eliza Hall Institute of Medical Research, Australia

**Maria Isabel Acosta Lopez**, University of Nice Sophia Antipolis, France
*New Regulatory Mechanism and Cellular Function of the Tumor Suppressor HACE1*

**Niall Dillon**, Medical Research Council, UK
*Phosphorylation of the E2 Ubiquitin Conjugating Enzyme UBE2D3 Regulates Polycomb-Mediated Gene Priming in Pluripotent ES Cells*

**Jeffrey R. Johnson**, University of California, San Francisco, USA
*Ubiquitin Remnant Profiling Identifies a Novel Substrate of HIV-Mediated Ubiquitination and Degradation*

**R. Jeremy Nichols**, Parkinson's Institute, USA
*The LRRK2 Phosphorylation-Ubiquitination Cycle*

**Camillo Palmieri**, Università Magna Grecia of Catanzaro, Italy
*Regulation of IBtk-alpha Activity by mTOR-Mediated Phosphorylation*

**Nicolas Bidère**, INSERM, France
*The Paracaspase MALT1 Cleaves the LUBAC Subunit HOIL1 during Antigen Receptor Signaling*

### Workshop 2 (X4)

*__Steve D. Gerondakis__, Monash University, Australia

*__Jenny P.Y. Ting__, University of North Carolina at Chapel Hill, USA

**Simon Rousseau**, McGill University, Canada
*Differential Contributions of theTPL2-MKK1/MKK2-ERK1/ERK2 and NFkB Pathways to Oncogenic Transformation in Lymphoid Neoplasms*

**Nadine Mikuda**, Max-Delbrück-Center for Molecular Medicine, MDC, Germany
*The IkappaB Kinase Complex is a Universal Regulator of mRNA Stability in Response to Stress*

**Marina Kolesnichenko**, Max Delbrueck Center for Molecular Medicine, Germany
*Senescence Associated NFkappaB Inflammatory Response is Driven by an mRNA Destabilization Mechanism*

**Benjamin E. Gewurz**, Brigham and Women's Hospital, Harvard Medical School, USA
*The NF-kB Genomic Landscape in CD40-Stimulated Primary Human B-cells*

**Anetta Svitorka Härtlova**, Newcastle University, UK
*Scavenger Receptor MSR-JNK Pathway Control Phenotypic Switch of Alternatively Activated Macrophages*

**Ricardo Antonia**, University of North Carolina, USA
*IKK Promotes AMPK Activity by Phosphorylating Threonine 172 in Response to IL-1beta*

**Ruaidhri Carmody**, University of Glasgow, UK
*Control of MAP Kinase and NF-kappaB Pathways by the Nuclear IkappaB-like factor Bcl-3*

### Structural Analysis of E3 Ligases and DUBs (X3)

*__Titia K. Sixma__, Netherlands Cancer Institute, Netherlands

**Rachel Klevit**, University of Washington, USA
*Mechanistic Strategies of RING-Between-RING (RBR) E3 Ligases*

**Bernhard Clemens Lechtenberg**, Sanford Burnham Prebys Medical Discovery Institute, USA
*Short Talk: Structure of the HOIP-RBR/E2~ubiquitin Transfer Complex Reveals a Universal Mechanism for RBR E3 Ubiquitin Ligases*

**Brenda A. Schulman**, Max Planck Institute of Biochemistry, Germany
*Cullin-RING E3 Ligation Mechanisms*

**Christopher D. Lima**, Memorial Sloan Kettering Cancer Center, USA
*E3 Ligases: Activities and Specificity*

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### MAP Kinase Signaling in Inflammation (X4)

*__Xiaoxia Li__, Cleveland Clinic Foundation, USA

__Steven C. Ley__, Francis Crick Institute, UK
*Regulation of Inflammation by TPL-2 MAP 3-kinase*

__Ana Cuenda__, Spanish National Biotechnology Centre, Spain
*Regulation of Inflammation by p38gamma/delta*

__Mathieu JM Bertrand__, VIB / Ghent University, Belgium
*Short Talk: NF-kB-Independent Role of IKKa/IKKb in Preventing RIPK1 Kinase-Dependent Apoptotic and Necroptotic Cell Death during TNF Signaling*

__Roger J. Davis__, HHMI/University of Massachusetts Medical School, USA
*Role of JNK in Metabolic Stress Signaling*

### Poster Session 3

## THURSDAY, MARCH 17

### Small Molecules and Therapeutics (X3)

*__Raymond J. Deshaies__, Amgen, Inc., USA

__Zhihao Zhuang__, University of Delaware, USA
*Targeting Deubiquitinase in DNA Damage Response for Anticancer Therapy*

__Alessio Ciulli__, University of Dundee, College of Life Sciences, UK
*Short Talk: Small Molecules for the VHL Cul2 E3 Ligase: VHL-HIF Inhibitors and Proteolysis Targeting Chimeras (PROTACs)*

__Georg Petzold__, Friedrich Miescher Institute for Biomedical Research, Switzerland
*Short Talk: Structural Basis of Lenalidomide-induced CK1alpha Degradation by the CRL4-CRBN Ubiquitin Ligase*

__Ingrid E. Wertz__, Genentech, Inc., USA
*Phosphorylation and Linear Ubiquitin Direct A20 Inhibition of Inflammation*

__Frank Sicheri__, Lunenfeld-Tanenbaum Research Institute, Canada
*The Structural basis for Poly-Ubiquitin Chain Cleavage and Regulation: Lessons Learned from BRCC36*

### Therapeutic Targeting of Inflammation (X4)

*__Daniel Krappmann__, Helmholtz Zentrum München, Germany

__Stefan Knapp__, University of Oxford, UK
*Targeting Bromodomains in Inflammation*

__Vanessa C. Taylor__, Rigel Inc., USA
*R191, A Small Molecule IRAK1/4 Kinase Inhibitor for the Treatment of Autoimmune and Inflammatory Diseases*

__Eric P. Hanson__, National Institutes of Health, USA
*Short Talk: Recruitment of A20 by the C-Terminal Domain of NEMO Suppresses NF-kappaB Activation and Autoinflammatory Disease*

__Vikram R. Rao__, Pfizer, USA
*The Role of IRAK4 in NFkB and MAPK Signaling: Implications for Drug Development*

### Ubiquitin-Dependent Modulation of NF-kappaB Signaling II (Joint)

*__Ivan Dikic__, Goethe University Medical School, Germany

__Shao-Cong Sun__, University of Texas MD Anderson Cancer Center, USA
*Epigenetic Regulation of NF-kB Function and Inflammation by Ubiquitination*

__Shigeki Miyamoto__, University of Wisconsin, Madison, USA
*Investigation of NF-kappaB Signaling Induced by Genotoxic Agents and Potentially Novel Activators*

__Rudi Beyaert__, Ghent University - VIB, Belgium
*The Dual Faces of Paracaspase MALT1 in Inflammation and Immunity*

__Philip Cohen__, University of Dundee, UK
*Re-Writing the Interleukin-1 Signaling Network*

### Meeting Wrap-Up: Outcomes and Future Directions (Joint)

__Philip Cohen__, University of Dundee, UK

## FRIDAY, MARCH 18

### Departure