

THE NOTCH MEETING 2009

27 September – 1 October

Presentations at the Notch Meeting may not be considered as published scientific papers and may not be cited or reported in the press except as personal communications (with the presenter's permission). Given these assurances we hope you will speak openly and not introduce any data or experiments that you are not prepared to discuss in full. In participating in the conference you agree neither to record presentations or posters by electronic or photographic means, nor to make printed references to The Notch Meeting presentations, posters and discussions. You will also agree to omit references to The Notch Meeting from any publication.

PROGRAM

There will be 20 minute and 10 (*) minute talks including discussions.

Please note that there may be last minute changes in both the order of the speakers and the speakers. Any such changes will be announced at the meeting.

Keynote speaker: Tom **Kirchhausen** (Harvard Medical School, USA), Thursday 1 October.

SUNDAY, September 27

- 17:00 – 19:30 Guided tour of the New Acropolis Museum (Pls notify Symvoli at: Symvoli.TheNotchMeeting@symvoli.gr if you wish to attend)
- 17:00 - 20:30 Registration (The Athens Plaza Hotel)
- 20:30 Reception (The Athens Plaza Hotel)

MONDAY, September 28

POSTER SESSION

- 09:00 - 09:10 Opening Remarks
- 09:10 - 11:00 **I. Molecular Aspects of Signaling**
Chairs: **S. Bray** / **R. Kopan**
- Gerry **Weinmaster** (UCLA School of Medicine, USA)
"Notch ligand endocytosis and force generation measured by optical tweezers"
- Alain **Israel** (Institut Pasteur, France)
"Trafficking regulates the activity of the Notch ligands"
- Sarah **Bray** (Cambridge University, UK)
"Context specificity and dynamics of the Notch response"
- Tilman **Borggreffe*** (Max-Planck-Institute, Germany)
"Notch signaling and the histone demethylase KDM5a dynamically regulate H3K4 trimethylation"
- Raphael **Kopan** (Washington University, School of Medicine, USA)
"Mapping the domains involved in paralog dominance among Notch receptors"

Achim **Gossler** (Medizinische Hochschule Hannover, Germany)
"Delta1 function in mouse fetal arteries"

11:00 - 11:30 Coffee Break

11:30 - 12:30 **I. Molecular Aspects of Signaling** (continued)
Chairs: **S. Bray / R. Kopan**

Anne C. **Hart** (MGH and Harvard Medical School, USA)
"Notch signaling in adult C. elegans neurons regulates behavior"

Cynthia **Guidos*** (The Hospital for Sick Children, Research Institute, Canada)
"Regulation of Notch Signaling Strength and Specificity by Fringe Proteins"

Kerstin **Huenniger*** (FLI Jena - Leibniz Institute for Age Research, Germany)
"Notch1 signaling is mediated by importins alpha 3, 4, and 7"

Motoo **Kitagawa*** (Chiba University Graduate School Of Medicine, Japan)
"Mastermind-1/Mastermind-2 are essential components of Notch signaling pathway"

Lizi **Wu*** (University of Florida, USA)
"Molecular insights into Notch signaling-mediated transcription from protein complex analysis"

12:30 - 13:00 **II. Structural Studies, Biochemistry**
Chair: **S. Blacklow**

Rhett **Kovall** (University of Cincinnati College of Medicine, USA)
"Structure and function of Notch pathway transcription complexes"

Robert **Haltiwanger*** (Stony Brook University, USA)
"Mapping O-Fucose and O-Glucose Modification Sites on the Extracellular Domain of Notch"

13:00 - 16:00 Lunch Break

16:00 - 17:00 **II. Structural Studies, Biochemistry**
Chair: **S. Blacklow**

Stephen **Blacklow** (University of Pennsylvania and Brigham and Women's Hospital, Harvard Medical School, USA)
"Mechanistic insights into normal and pathophysiological Notch activation"

Penny **Handford** (University of Oxford, UK)
"Molecular basis of Notch regulation by Jagged/Serrate ligands"

Doug **Barrick** (The John Hopkins University, USA)
"Sequence determinants that control Notch activation and EBNA2 misactivation"

17:00 - 17:30 Coffee Break

17:30 - 19:00 **III. Developmental Regulation, Cell Fates in Specific Systems**
Chairs: **A. Bigas / B. Ohlstein**

Thomas **Gridley** (The Jackson Laboratory, USA)
"Notch Signaling During Cardiovascular and Oocyte Development in Mice"

Angeliki **Louvi** (Yale University School of Medicine, USA)
"Functions of mammalian NOTCH3"

Anna **Bigas** (IDIBELL, Spain)

Julian **Lewis** (London Research Institute-Cancer Research UK)
"Choosing a final fate in the gut stem-cell system: the role of Delta-Notch signaling"

TUESDAY, September 29

POSTER SESSION

09:00 - 11:00

III. Developmental Regulation, Cell Fates in Specific Systems

(continued)

Chairs: **A. Bigas / B. Ohlstein**

Nick **Gaiano** (The Johns Hopkins University, School of Medicine, USA)
"Activity-dependent Notch signaling in neurons requires Arc/Arg3.1"

Olivier **Pourquié** (Howard Hughes & Stowers Institute for Medical Research, USA)

Christos **Delidakis** (Institute of Molecular Biology & Biotechnology FoRTH & University of Crete, Greece)
"Characterization of functional motifs of the Delta intracellular domain"

Ajay **Chitnis** (Unit on Vertebrate Neural Development, Laboratory of Molecular Genetics, NICHD, Bethesda)

Benjamin **Ohlstein** (Carnegie Institution, USA)
"A Transient Niche Regulates the Specification of Drosophila Intestinal Stem Cells"

David Sprinzak*(Caltech, USA)
"Cis Interactions between Notch and Delta Generate Mutually Exclusive Signaling States"

11:00 - 11:30

Coffee Break

11:30 – 12:00

III. Developmental Regulation, Cell Fates in Specific Systems

(continued)

Chairs: **A. Bigas / B. Ohlstein**

Edward **Giniger*** (NINDS, NIH, USA)
"Notch is essential for axon guidance between successive segments of the Drosophila CNS"

Ben Z. **Stanger*** (University of Pennsylvania, USA)
"Notch regulates liver development through a novel tubulogenesis mechanism"

Franz **Oswald*** (University of Ulm, Germany)
"RITA, a novel modulator of Notch signalling, regulates neurogenesis via nuclear export of RBP-J"

12:00 – 13:30

IV. Notch Immunology

Chairs: **I. Bernstein / I. Screpanti**

Iannis **Aifantis** (NYU School of Medicine, USA)
"Regulation of hematopoietic stem cell differentiation and transformation by the g-secretase complex"

Irwin **Bernstein** (Fred Hutchinson Cancer Research, USA)
"Notch2 Enhances Generation of Hematopoietic Stem and Progenitor Cells during Marrow Regeneration"

Justin **Roderick*** (University of Massachusetts Amherst, USA)
"Notch1 facilitates immune-mediated bone marrow failure in a mouse model"

Koji **Yasutomo*** (The University of Tokushima, Japan)
"Notch controls effector and memory responses of CD4+ T cells"

Rui **Benedito*** (Max-Planck Institute for Molecular Biomedicine, Germany)
"The Notch ligands Dll4 and Jagged1 have opposing effects on angiogenesis"

13:30 - 16:00 Lunch Break

16:00 - 16:50 **IV. Notch Immunology** (continued)
Chairs: **I. Bernstein / I. Screpanti**

Isabella **Screpanti** (University "La Sapienza", Italy)

Barbara **Osborne** (University of Massachusetts-Amherst, USA)
"Notch1 regulates NF-kB activation in T cells via cytosolic interactions with PKC"

Michelle A. **Kelliher*** (UMass Medical School, USA)
"Targeting the Leukemia Initiating Cells in a Mouse T-ALL Model"

16:50 – 17:20 Coffee Break

17:20 – 19:20 **V. Notch Signal Integration: Crosstalk, Genetic Circuitries**
Chairs: **S. Artavanis-Tsakonas / U. Lendahl**

Nick **Baker** (Albert Einstein College of Medicine, USA)
"Patterning Neurogenesis: A Dynamical Model of Ommatidial Crystal Formation"

Lluís **Espinosa*** (IMIM-Hospital del Mar, Spain)
"Hes1: a missing link in the crosstalk between Notch and NFkB."

Spyros **Artavanis-Tsakonas** (Harvard Medical School, USA)

Urban **Lendahl** (Karolinska Institute, Sweden)

Keith **Brennan*** (University of Manchester, UK)
"Crosstalk between Dishevelled and the Notch signalling pathway"

Marek **Mlodzik*** (Mount Sinai School of Medicine, USA)
"Mechanistic Interactions between Notch-signaling and the Frizzled/PCP core pathway"

Lakshmi R. **Perumalsamy*** (National Centre for biological sciences- TIFR, India)
"Notch signaling impinges on mitochondrial remodeling proteins for the regulation of cell survival"

David **Ish Horowicz** (London Research Institute, CR-UK)
"Regulation of Wnt and Notch activity during somitogenesis by integrin signaling"

WEDNESDAY, September 30

POSTER SESSION

09:00 - 11:00 **VI. Notch Disease Models and Oncogenesis**
Chairs: **M. Milan / S. Krishna**

Freddy **Radtke** (Ecole Polytechnique Federation de Lausanne, EPFL/ISREC Switzerland)
"Notch signalling in haematopoietic and skin tumors"

Ryoichiro **Kageyama** (Institute for Virus Research, Kyoto University, Japan)
"The role of Hes1 oscillations in regulation of stem/progenitor cells"

Warren **Pear** (University of Pennsylvania, USA)

Sudhir **Krishna** (National Centre for Biological Sciences –TIFR-, India)
“Tumorigenic properties and Notch signaling profile of a CD66 sub-set of cells from both primary human invasive cervical cancers and CaSki cells”

Marco **Milán** (IRB Barcelona, Spain)
“A role of receptor Notch in ligand cis-inhibition in Drosophila”

11:00 - 11:30

Coffee Break

11:30 - 13:40

VI. Notch Disease Models and Oncogenesis (continued)
Chairs: **M. Milán / S. Krishna**

Maria **Dominguez-Castellano** (Instituto de Neurociencias de Alicante, CSIC-UMH, Spain)
“Notch and NFkappaB signalling pathway in tumour metastasis in Drosophila.”

A. P. **Weng*** (BC Cancer Agency, Canada)
“Acute T-cell leukemias remain dependent on Notch signaling despite PTEN and INK4A/ARF loss”

Ralf H. **Adams*** (Max-Planck-Institute for Molecular Biomedicine, Germany)
“The Notch ligands Dll4 and Jagged1 have opposing effects on angiogenesis”

Masanori **Aikawa*** (Brigham and Women's Hosp, Harvard Medical School, USA)
“Notch signaling promotes macrophage activation and atherosclerosis”

Andreas **Fischer*** (Vascular Biology, Medical Faculty Mannheim, Germany)
“The cerebral cavernous malformation protein CCM1 inhibits angiogenesis by activation of Notch”

Thierry **Pedrazzini*** (University of Lausanne Medical School, Switzerland)
“Essential role of the Notch pathway in the adult heart during the adaptive response to stress”

Stefano **Indraccolo*** (Istituto Oncologico Veneto – IRCCS, Italy)
“Cellular interactions in tumor dormancy: Notch3 regulation of MKP-1 promotes tumor cell survival”

Sean **Egan*** (The Hospital for Sick Children, Toronto, Canada)
“Lfng regulates mammary stem/progenitor cells and suppresses tumor formation”

Pallavi **Kshetrapal*** (Harvard Medical School, USA)
“Notch mediated regulation of cell proliferation in development and disease”

Olivier **Meurette*** (The University of Manchester, UK)
“Notch-activated autocrine signalling in human breast cancer”

Marco **Mazzone*** (Harvard Medical School, USA)
“Dose-dependent regulation of matrix adhesion by Notch that controls outgrowth of 3D structures”

Karisa **Schreck*** (*Johns Hopkins School of Medicine, USA*)
“Combinatorial Targeting of Notch and Hedgehog Signaling in Malignant Brain Tumors”

13:40 - 16:00

Lunch Break

16:00 - 17:30

**VII. Notch Disease Targets and Therapeutic Approaches:
Translational Biology / Drug Development**

Chair: **L. Miele**

Jon **Aster** (Brigham and Woman's Hospital-Harvard Medical School, USA)
"Novel Notch Pathway Inhibitors and Enhancers"

Adolfo **Ferrando** (Columbia University, Medical Center, USA)
"The Ubiquitin Protease DUB3 Regulates NOTCH1 Stability And Function"

Tim **Demuth** (Merck & Co., Inc., USA)
"Advances in clinical development of gamma secretase inhibitors"

Lucio **Miele** (University of Mississippi Medical Center, USA)
"Learning from crosstalk to develop rational Notch-targeting combinations for cancer treatment"

Andreas **Androutsellis-Theotokis*** (National Institutes of Health, USA)
"Targeting adult neural stem cells by Notch and Tie2 ligands rescues injured neurons"

17:30 - 18:00

Coffee Break

18:00 - 19:00

**VII. Notch Disease Targets and Therapeutic Approaches:
Translational Biology / Drug Development (continued)**

Chair: **L. Miele**

Antonio Carlos **Ferreira*** (IPATIMUP - Institute of Molecular Pathology and Immunology of the University of Porto, Portugal)
"Notch inhibition overturns the apoptosis resistance conferred by E-cadherin deficiency"

Ji **Liang-li*** (University of Oxford, UK)
"Notch ligand DLL4 mediates tumor resistance to anti-VEGF therapy in vivo"

Chris **Siebel*** (Genentech, Inc., USA)

Irene **Noguera-Troise*** (Regeneron Pharmaceuticals, USA)
"Development of human blocking antibodies to Dll4 in VelocImmune™ mice for anti-angiogenesis therapy"

Ronan **O'Hagan*** (AVEO Pharmaceuticals, Inc)
"Predicting Notch Inhibitor Sensitive Cancers by Biomarker Discovery"

THURSDAY, October 1

POSTER SESSION

09:00 - 11:00

VIII. Notch Trafficking: A day devoted to the cellular trafficking of Notch receptor and its ligands

Chairs: **M. Fortini / T. Klein / K. Matsuno**

Mark **Fortini** (Thomas Jefferson University, USA)

Thomas **Klein** (Institute for Genetics, Germany)
"The role of Lgd in Notch trafficking"

Kenji **Matsuno** (Tokyo University of Science, Japan)

Martin **Baron** (Faculty of Life Sciences, University of Manchester, UK)
"Deltex and endocytic Notch signal activation"

Hugo **Bellen** (Baylor College of Medicine, HHMI, TMC, USA)
"Novel Drosophila players that regulate Notch signaling"

Gavin **Chapman*** (The Victor Chang Cardiac Research Institute, Australia)
"Notch1 and Dll3 colocalise in the late endocytic compartment during somitogenesis"

Divya K. **Shah*** (Sunnybrook Research Institute, Canada)
"Differential Requirement for Delta-Like-1 and Delta-Like-4 Endocytosis in T Cell Development"

11:00 - 11:30 Coffee Break

11:30 - 13:30 **VIII. Notch Trafficking: A day devoted to the cellular trafficking of Notch receptor and its ligands** (continued)
Chairs: **M. Fortini / T. Klein / K. Matsuno**

Hamed **Jafar-Nejad** (University of Texas Health Science Center at Houston)
"Regulation of Notch signaling by the glycosyltransferase Rumi"

Tom **Kirchhausen** (Harvard Medical School, USA)

Roland **Le Borgne** (Université de Rennes 1, France)
"Drosophila AP-1 clathrin adaptor complex regulates Notch binary cell fate decision"

François **Schweisguth** (Institut Pasteur, France)

Pamela **Stanley** (Albert Einstein College of Medicine, USA)
"O-Fucose Glycan Regulation of Notch Signaling in T Cell Development"

13:30 - 15:30 Lunch Break

15:30 - 17:00 **VIII. Notch Trafficking: A day devoted to the cellular trafficking of Notch receptor and its ligands** (continued)
Chairs: **M. Fortini / T. Klein / K. Matsuno**

Marcos **González-Gaitán** (University of Geneva, Switzerland)

Marc **Muskavitch** (Boston College, USA)

Alexey **Veraksa** (University of Massachusetts Boston, USA)
"Signaling functions of the Drosophila beta-arrestin Kurtz: it's not "all about Notch"

Young Yun **Kong** (Seoul National University, South Korea)
"The importance of Mind bomb-1 in Notch signaling that regulates mammalian development"

Hideyuki **Takeuchi*** (Stony Brook University, USA)
"Novel specificity of a glycosyltransferase, Rumi, required for Notch signaling"

17:00 Closing Remarks