

# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## Cancer Epigenetics: New Mechanisms and Therapeutic Opportunities (J4)

Scientific Organizers: Cigall Kadoch and Christopher Vakoc

Sponsored by Incyte Corporation

## Gene Regulation: From Mechanisms to Disease (J3)

Scientific Organizers: Karen Adelman and Patrick Cramer

January 26-30, 2020 • Keystone Resort • Keystone, CO, USA

Sponsored by Moderna

Discounted Abstract & Scholarship Deadline: October 1, 2019 / Abstract Deadline: October 29, 2019 / Discounted Registration Deadline: November 26, 2019

### SUNDAY, JANUARY 26

#### Arrival and Registration

### MONDAY, JANUARY 27

#### Welcome and Keynote Address (Joint)

\***Karen Adelman**, Harvard Medical School, USA

**Shelley L. Berger**, University of Pennsylvania, USA  
*Epigenetic Pathways as Targets in Human Cancer*

#### Fundamentals of Gene Regulation (Joint)

\***Liling Wan**, University of Pennsylvania, USA

**Eva Nogales**, University of California, Berkeley, USA  
*Structural Insights into the Regulation of the Gene Silencer PRC2*

**Patrick Cramer**, Max Planck Institute for Biophysical Chemistry, Germany  
*Mechanisms of Chromatin Transcription*

**Danny F. Reinberg**, HHMI/New York University, USA  
*Polycomb, Inheritance and Disease*

**Dylan J. Taatjes**, University of Colorado Boulder, USA  
*Short Talk: Selective Inhibition of Human CDK7 Reveals High-Confidence Targets and Suggests a New Model for TFIIH Function in Transcription*

#### Workshop 1 (J4)

\***Yael David**, Memorial Sloan Kettering Cancer Center, USA

**Alessandro Gardini**, Wistar Institute, USA  
*A Role for Nuclear PP2A in Transcription Regulation*

**Ruhee Dere**, Baylor College of Medicine, USA  
*KDM4A Regulates Microtubule Methylation and Genomic Instability*

**Gerard L. Brien**, Smurfit Institute of Genetics, Ireland  
*Disruption of Development Enhancer and PRC2 Function by H3K27M in DIPG*

**Tharu M. Fernando**, Genentech, Inc., USA  
*Characterization and Therapeutic Implications of SMARCA4 Mutations in Cancer*

**Noa Furth**, Weizmann Institute of Science, Israel  
*The Combinatorial Epigenetic Landscape of High Grade Pediatric Gliomas in Single Molecule Resolution*

**Brian J. Abraham**, St. Jude Children's Research Hospital, USA  
*Predicting Master Transcription Factors from Pan-Cancer Expression Data*

**Elizabeth Allene Martin**, UCSF, USA  
*OGT, a Nutrient-Sensing Enzyme, Controls DNA Methylation in Mouse Embryonic Stem Cells*

#### Workshop 1: Structure and Function of Chromatin (J3)

\***Patrick Cramer**, Max Planck Institute for Biophysical Chemistry, Germany

**Ksenia Finogenova**, Max-Planck Institute of Biochemistry, Germany  
*Structural Basis of Nucleosome Binding by PRC2 and Its Inhibition by H3K36 Methylation*

**Aaron Johnson**, University of Colorado School of Medicine, USA  
*RNA Matchmaking Remodels LncRNA Structure and Promotes PRC2 Activity*

**François Robert**, Institut de Recherches Cliniques de Montreal, Canada  
*Transcribed Chromatin, Rather Than RNA Polymerase II Itself, Recruits FACT to Active Genes*

**Jitendra Thakur**, Fred Hutchinson Cancer Research Center, USA  
*Architectural RNA Is Required for Heterochromatin Organization*

**Gilad Yaakov**, Weizmann Institute of Israel, Israel  
*A Novel Histone Molecular Timer Reveals Minute-Resolution Nucleosome Turnover*

**Keda Zhou**, University of Colorado Boulder, USA  
*FACT Caught in the Act of Manipulating the Nucleosome*

**Giulia Cova**, Max Planck Institute for Molecular Genetics, Germany  
*TAD-Shuffling at the FGF8 Locus Causes Split-Hand/Foot Malformation Type 3*

**Yuan He**, Northwestern University, USA  
*Cryo-Electron Microscopy Structure of a Nucleosome-Bound SWI/SNF Chromatin Remodeling Complex*

#### Enhancer Structure in Cancer (J4)

\***Asifa Akhtar**, Max Planck Institute of Immunobiology and Epigenetics, Germany

**Ashby Morrison**, Stanford University, USA  
*Epigenetic Regulation of Carcinogen Susceptibility*

**Richard A. Young**, Whitehead Institute for Biomedical Research, USA  
*Gene Dysregulation, Condensates and Drugs*

**Bin Wu**, Agios Pharmaceuticals Inc, USA  
*Molecular Mechanisms Mediating Relapse Following Ivosidenib Monotherapy in Patients with IDH1-mutant Relapsed or Refractory Acute Myeloid Leukemia*

**Liling Wan**, University of Pennsylvania, USA  
*Short Talk: Chromatin Reader Dysregulation in Cell Fate Control and Cancer*

**Lena Afeyan**, Massachusetts Institute of Technology, USA  
*Short Talk: Formation and Regulation of Estrogen Receptor-Mediated Transcriptional Condensates in Breast Cancer*

**Lukas Chavez**, University of California, San Diego, USA  
*Short Talk: Targeting of Tumors as Informed by Oncogenic 3D Genome Organization*

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### Imaging of Transcriptional Dynamics (J3)

\***Karla M. Neugebauer**, Yale University, USA

**Ibrahim Cissé**, Massachusetts Institute of Technology, USA  
*Super-Resolution Imaging of Transcription in Living Mammalian Cells*

**Danette L. Daniels**, Promega Corporation, USA  
*Kinetic Monitoring of Protein Interactions and Targeted Degradation in Live Cells*

**Jennifer F. Kugel**, University of Colorado Boulder, USA  
*Short Talk: Single-Molecule Studies Resolve Heterogeneity in the Activity of Transcribing Complexes to Reveal Steps in Transcription That Dictate the Activity of Pol II*

**Benjamin R. Sabari**, University of Texas Southwestern Medical Center, USA  
*Short Talk: Enhancer Features that Drive Formation of Transcriptional Condensates*

**Michael S. Levine**, Princeton University, USA  
*Visualizing Developmental Dynamics in Drosophila Embryos*

### Poster Session 1

#### TUESDAY, JANUARY 28

### Epigenetic Modifications of Chromatin and RNA (Joint)

\***Ali Shilatifard**, Northwestern University, USA

**Tony Kouzarides**, University of Cambridge, UK  
*Modifications of RNA: Their Function and Role in Cancer*

**Asifa Akhtar**, Max Planck Institute of Immunobiology and Epigenetics, Germany  
*Dosage Compensation of the X Chromosome: A Complex Epigenetic Assignment Involving Chromatin Regulators and lncRNAs*

**Anne Brunet**, Stanford University, USA  
*Epigenetic Regulation of Stem Cell Aging*

**Salvador Aznar Benitah**, ICREA and Institute for Research in Biomedicine, Spain  
*Epigenetic Influence of Our (Fatty) Diet on Metastatic-Initiating Cells*

**Peter Hsu**, University of Washington, USA  
*Short Talk: Structural Basis of H2B Ubiquitination-Dependent H3K4 Methylation by COMPASS*

### Human Disease Models of Chromatin Regulation (J4)

\***Paola Grandi**, Cellzome AG, a GSK Company, Germany

**Hao Zhu**, University of Texas Southwestern Medical Center, USA  
*Targeting Chromatin Remodeling Complexes for Tissue Regeneration*

**Paola Grandi**, Cellzome AG, a GSK Company, Germany  
*Click Chemistry and Preclinical Evaluation of Targeted Epigenetic Therapies*

**Liis Uuskula-Reimand**, SickKids Research Institute, Canada  
*Short Talk: Enhancer Function and Topoisomerase II beta in Hepatocellular Carcinoma*

**Nicholas C. Gomez**, Rockefeller University, USA  
*Short Talk: Stem Cell Reprogramming during Oncogenesis*

**Raphaël Rodriguez**, Institut Curie, France  
*Short Talk: CD44 Regulates Epigenetic Plasticity by Mediating Iron Endocytosis*

### Coupling of Transcription and RNA Processing (J3)

\***Alexander Stark**, Research Institute of Molecular Pathology - IMP, Austria

**Yongsheng Shi**, University of California, Irvine, USA  
*Probing 3' End Formation of Coding and Non Coding RNAs*

**Karla M. Neugebauer**, Yale University, USA  
*Dynamics of Co-Transcriptional Splicing*

**Daisy Castillo-Guzman**, University of California, Davis, USA  
*Short Talk: Uncovering Novel Roles for Splicing Factor SF3B1 in Transcription Dynamics and R-Loop Metabolism*

**Megan Insko**, Boston Children's Hospital, USA  
*Short Talk: CDK13 Mutations Drive Melanoma via Accumulation of Prematurely Terminated Transcripts*

**Torben Heick Jensen**, Aarhus Universitet, Denmark  
*Transcription Termination and Links to RNA Processing/Decay Pathways*

### Poster Session 2

#### WEDNESDAY, JANUARY 29

### Synthetic Lethal Vulnerabilities in Cancer (J4)

\***Adrian P. Bracken**, Trinity College Dublin, Ireland

**Ali Shilatifard**, Northwestern University, USA  
*Principles of Epigenetics and Chromatin in Development and Human Disease*

**Scott A. Armstrong**, Dana-Farber Cancer Institute, USA  
*Targeting Chromatin Complexes in Leukemia*

**Christopher Vakoc**, Cold Spring Harbor Laboratory, USA  
*Squamous Trans-Differentiation in Pancreatic Cancer*

**Tannishtha Reya**, University of California, San Diego, USA  
*Stem Cell Signals in Cancer Heterogeneity and Therapy Resistance*

**Jeff Magee**, Washington University, USA  
*Short Talk: KMT2C/MLL3 Deletions Convey a Selective Advantage to Multiply-Divided HSCs by Blunting Cytokine- and Stress-Induced Lineage Commitment*

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**Jiangbin Ye**, Stanford University, USA

*Short Talk: Deciphering Warburg Effect: The Connection between Metabolism, Epigenetics and Tumor Differentiation*

### Communication between Promoters and Enhancers (J3)

\***Torben Heick Jensen**, Aarhus Universitet, Denmark

**Geeta J. Narlikar**, University of California, San Francisco, USA  
*Can Phase-Separation Explain the Biological Properties of Heterochromatin?*

**Steven L. McKnight**, University of Texas Southwestern Medical Center, USA

*Low Complexity Sequences in Gene Regulation*

**Jesse M. Engreitz**, Harvard University and Broad Institute, USA  
*Short Talk: Genome-Wide Maps of Enhancer-Gene Connections Link Immune Disease Risk Variants to Target Genes*

**R. Babak Faryabi**, University of Pennsylvania, USA  
*Short Talk: Notch-Instructed 3D Cancer Genomes*

**Tom Owen-Hughes**, University of Dundee, Scotland  
*Short Talk: Selective Enhancer Decommissioning Following Acute Depletion of the ARID1A Subunit of Mammalian SWI/SNF Complexes*

**Alexander Stark**, Research Institute of Molecular Pathology - IMP, Austria  
*Decoding Regulation: Global Screens to Uncover How Sequence Dictates Gene Activity*

**Karen Adelman**, Harvard Medical School, USA  
*Interactions Between Coding and Non-Coding RNA loci*

### Developmental Epigenetics and Transcription (J4)

\***Alessandro Gardini**, Wistar Institute, USA

**Adrian P. Bracken**, Trinity College Dublin, Ireland  
*PRC2 Complexes in Development and Disease*

**Marcus Buschbeck**, Josep Carreras Leukaemia Research Institute, Spain  
*Histone Variants Regulate 3D Chromatin Architecture and the Inflammatory Response of Cancer Cells*

**Yael David**, Memorial Sloan Kettering Cancer Center, USA  
*Revealing Cancer-Associated Epigenetic Events using Novel Chemical Tools*

**Siddhant U. Jain**, University of Wisconsin-Madison, USA  
*Short Talk: Inhibition of PRC2 Activity by EZHIP and H3 K27M in High-Grade Pediatric Gliomas*

### Defining Regulation in Single-Cell Cells (J3)

\***Emma Farley**, University of California, San Diego, USA  
*Regulatory Principles Governing Enhancer Function in Development and Disease*

**Nikolaus Rajewsky**, Max Delbrück Center for Molecular Medicine, Germany

*Insights into Principles of Gene Regulation by Single Cell Sequencing in Space and Time*

**Rickard Sandberg**, Karolinska Institutet, Sweden  
*Decoding Transcriptional Regulation and Kinetics Using Single-Cell Transcriptomics*

**William J. Greenleaf**, Stanford University, USA  
*A Single Cell Framework for Multi-Omic Analysis of Disease Identifies Malignant Regulatory Signatures*

**Sarah Hainer**, University of Pittsburgh, USA  
*Short Talk: Profiling of Pluripotency Factors in Single Cells and Early Embryos*

### Poster Session 3

#### THURSDAY, JANUARY 30

### Chromatin Regulatory Modulation: Novel Small Molecule-Based Approaches (J4)

\***Jane A. Skok**, New York University School of Medicine, USA

**Eric R. Olson**, Syros Pharmaceuticals, USA  
*Therapeutic Applications of Altering Tumor Cell Gene Expression*

**Rab K. Prinjha**, GlaxoSmithKline, UK  
*Epigenetic Inhibition in Cancer: Emerging Strategies and Approaches*

**Jane A. Skok**, New York University School of Medicine, USA  
*CTCF and its Impact on Gene Regulation and Interplay with CTCF Function*

**Daniel De Carvalho**, University Health Network, Canada  
*Epigenetic Regulation of Retroelements as an Emerging Therapeutic Opportunity in Cancer*

**Allyson M. Freedy**, Harvard University, USA  
*Short Talk: CRISPR-suppressor Scanning Reveals a Nonenzymatic Role of LSD1 in AML*

**Jacob G. Kirkland**, Stanford University, USA  
*Short Talk: Chromatin Regulators Mediate Anthracycline Sensitivity in Breast Cancer*

### Gene Control in Development (J3)

\***Michael S. Levine**, Princeton University, USA

**Emma Farley**, University of California, San Diego, USA  
*Regulatory Principles Governing Enhancer Function in Development and Disease*

**François Fuks**, Université Libre de Bruxelles, Belgium  
*Transcriptome-Wide Distribution and Function of RNA Modifications*

**Robert A. Martienssen**, Cold Spring Harbor Laboratory, USA  
*Small Non-Coding RNA in Replication and Quiescence*

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**Laura A. Banaszynski**, University of Texas Southwestern Medical Center, USA

*Short Talk: Mechanisms of Enhancer Activation Using the Histone Variant H3.3*

**Wenqing Cai**, Boston Children's Hospital, USA

*Short Talk: Enhancer-Dependence of Cell-Type-Specific Gene Expression Increases with Developmental Age*

**Raja Jothi**, NIEHS, National Institutes of Health, USA

*Short Talk: Bivalent Chromatin Does Not Poise Genes for Rapid Activation*

**Kathrin Plath**, University of California, Los Angeles, USA

*A New Mode of Xist Action*

### Workshop 2 (J4)

\***Chao Lu**, Columbia University, USA

**Srinivas Vinod Saladi**, Harvard Medical School, USA  
*Revealing Oncogenic Role of ACTL6A, Subunit of SWI/SNF Chromatin Remodeling Complex in Squamous Cancers*

**Riyad N.H. Seervai**, Baylor College of Medicine, USA  
*The Histone Methyltransferase SETD2 Is a Tumor Suppressor with Actin Lysine Methyltransferase Activity*

**Michelle M. Mitchener**, Princeton University, USA  
*Biochemical and Cellular Libraries Reveal Cancer-Associated Histone Mutations that Perturb Nucleosome Structure*

**Adam D. Durbin**, Dana-Farber Cancer Institute, USA  
*EP300 Controls the Oncogenic Enhancer Landscape of High-Risk Neuroblastoma*

**Chao Lu**, Columbia University, USA  
*Combinatorial Targeting of Chromatin and Metabolism for Cancer Therapy*

**Bethany A. Buck-Koehntop**, University of Utah, USA  
*Investigating the Methyl-CpG Binding Protein ZBTB38 in Mediating Epigenetic-Based Transcription in Cancer*

**Jarod Waybright**, University of North Carolina at Chapel Hill, USA  
*Reader's Block: Development of Chemical Tools Targeting the Methyl-Lysine Reader MPP8*

### Workshop 2: Dynamic Gene Regulation (J3)

\***Jennifer F. Kugel**, University of Colorado Boulder, USA

**Alon Goren**, University of California, San Diego, USA  
*The Histone Deacetylase SIRT6 Restrains Transcription Elongation via Promoter-Proximal Pausing*

**Gabriella E. Martyn**, University of New South Wales, Australia  
*Revealing the Mechanism Behind Naturally Occurring Mutations which Elevate Fetal Hemoglobin*

**Kirstin Meyer**, University of California, San Francisco, USA  
*Optogenetic Dissection of YAP Transcriptional Regulation*

**Linda Z. Penn**, Princess Margaret Cancer Centre, Canada  
*Discovering the MYC Proteome Reveals Novel Mechanisms of Oncogenesis*

**Xavier J. Rambout**, University of Rochester Medical Center, USA  
*Transcriptional Coactivator PGC-1 $\alpha$  Contains a Novel CBP80-Binding Motif That Orchestrates Efficient Target-Gene Expression*

**Haoze Vincent Yu**, University of Southern California, USA  
*Feed-Forward Pioneer Factor Activity Underlies Mammalian Mechanoreceptor Cell Differentiation*

### Chromatin Structure and Function in Cancer (J4)

\***Cigall Kadoch**, Dana-Farber Cancer Institute, Harvard Medical School, USA  
*Mammalian SWI/SNF Complexes in Cancer*

**Luciano Di Croce**, CRG - Center for Genomic Regulation, Spain  
*Molecular Mechanisms Governing Cell Identity, Differentiation and Cancer Processes*

**Jikui Song**, University of California, Riverside, USA  
*Structural Studies in DNA Methylation and Links to Human Cancer*

**Agata E. Lemiesz**, Rockefeller University, USA  
*Short Talk: Novel H2B "Oncohistones" Impact Cellular Differentiation and Signaling*

**Nazar Mashtalir**, Dana-Farber Cancer Institute, USA  
*Short Talk: Mechanism of Cancer-Specific SWI/SNF Complex Targeting by the SS18-SSX Fusion Oncogene*

### Higher Order Interactions in Transcription Regulation (J3)

\***Anne Brunet**, Stanford University, USA

**Eileen E.M. Furlong**, European Molecular Biology Laboratory, Germany  
*Enhancer Promoter Communication During Embryonic Development*

**Shasha Chong**, University of California, Berkeley, USA  
*Dynamic and Selective Low-Complexity Domain Interactions Control Gene Transcription: A Single-Molecule Study*

**Valerio Orlando**, King Abdullah University of Science and Technology, Saudi Arabia  
*Short Talk: L1 RNA Knockdown Averts Heterochromatin Loss and Premature Ageing Phenotypes*

**Clodagh C. O'Shea**, The Salk Institute for Biological Studies, USA  
*Talk Title to be Announced*

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (J4)

### Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (J3)

**FRIDAY, JANUARY 31**

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Departure