



# DNA Replication and Recombination

April 2–6, 2017 | Santa Fe Community Convention Center | Santa Fe, New Mexico | USA

## Scientific Organizers:

**John F.X. Diffley**, Cancer Research UK, London Research Institute, UK

**Anja Groth**, University of Copenhagen, Denmark

**Scott Keeney**, HHMI, Memorial Sloan-Kettering Cancer Center, USA

## Joint with the meeting on **Genomic Instability and DNA Repair**

*DNA replication and recombination are common to all cells. Errors in these processes lead to many diseases in humans, including cancer, and many fundamental questions are still unresolved. Due to recent technical advances in microscopy and other techniques, these dynamic processes can now be studied in time and space in both prokaryotes and eukaryotes. Moreover, breakthroughs in the biochemical reconstitution of processes in DNA replication and recombination repair as well as single particle electron microscopy promise to reveal new mechanisms at near-atomic resolution; and new DNA sequencing technologies make it possible to study these key processes in great detail. Mechanistic similarities across the three domains of life provide new basic principles while differences identify potential targets for therapeutic intervention. The Keystone Symposia “DNA Replication and Recombination” meeting has historically been one of the premiere meetings in this field and one of the very few that brings together scientists working in replication and recombination across all life forms. Because of the close relationship between DNA replication and recombination and their importance for genome stability, this meeting will be held jointly with the Keystone Symposia meeting on “Genomic Instability and DNA Repair.” Talks at the “DNA Replication and Recombination” meeting will focus on the mechanism and regulation of these processes, with an emphasis on multiple organisms and multiple approaches. Talks in joint sessions will center on the metabolism of stalled replication forks and the importance of chromatin in replication, recombination and genome stability.*


## Session Topics:

- Replication/Repair Structure and Function
- Starting Recombination
- Interplay between Chromatin Structure and DNA Replication/Repair (Joint)
- Regulating Recombination
- Replication Fork Progression and Restart
- Replication Initiation Mechanisms
- Replication Fork Establishment and Replication Coupled Repair (Joint)
- Finishing Recombination

**Scholarship Application & Discounted Abstract Deadline: December 5, 2016**

**Abstract Deadline: January 12, 2017**

**Discounted Registration Deadline: February 2, 2017**



Note: Scholarships are available for graduate students and postdoctoral fellows and are awarded based on the abstract submitted.

*Upper image courtesy of: The Web site of the National Cancer Institute (<http://www.cancer.gov>)*

Meeting Hashtag: #KSdna

[www.keystonesymposia.org/17Z2](http://www.keystonesymposia.org/17Z2)

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# KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

## DNA Replication and Recombination (Z2)

Scientific Organizers: John F.X. Diffley, Anja Groth and Scott Keeney

Sponsored by Editas Medicine, Inc.

## Genomic Instability and DNA Repair (Z1)

Scientific Organizers: Julia Promisel Cooper, Marco F. Foiani and Geneviève Almouzni

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### SUNDAY, APRIL 2

#### Arrival and Registration

### MONDAY, APRIL 3

#### Welcome and Keynote Session (Joint)

\***Julia Promisel Cooper**, NCI, National Institutes of Health, USA

\***Scott Keeney**, HHMI/Memorial Sloan Kettering Cancer Center, USA

**Tatsuya Hirano**, RIKEN, Japan

*Condensin-Based Chromosome Organization*

**Johannes C. Walter**, Harvard Medical School, USA

*Mechanisms of Replication-Coupled Repair*

#### Replication/Repair Structure and Function (Z2)

\***John F.X. Diffley**, Francis Crick Institute, UK

**Michael E. O'Donnell**, Rockefeller University, USA

*Structure and Function of the Eukaryotic Replisome*

**Tyler H. Stanage**, University of Wisconsin-Madison, USA

*Short Talk: The Escherichia coli RarA Protein is Involved in the Switch between DNA Replication and Translesion Synthesis in vivo*

**Karlene A. Cimprich**, Stanford University, USA

*When RNA Meets DNA: Dangerous Liaisons in the Genome*

**Alessandro Costa**, Francis Crick Institute, UK

*Cryo-EM Approaches to Understanding the Eukaryotic Replisome*

**Matthew L. Bochman**, Indiana University, USA

*Short Talk: Hrq1, The Yeast Homolog of RecQ4, Inhibits Telomerase Activity on Long Telomeres*

#### Mechanisms of DNA Repair (Z1)

\***Timothy C. Humphrey**, University of Oxford, UK

**Wei Yang**, NIDDK, National Institutes of Health, USA

*Structural Insights into Translesion DNA Polymerases*

**James E. Haber**, Brandeis University, USA

*Short Talk: Rad51-Mediated Double-Strand Break Repair and Mismatch Correction of Highly Diverged Substrates*

**Joseph J. Loparo**, Harvard Medical School, USA

*Short Talk: Single-Molecule Imaging of Non-Homologous End Joining*

**Michael D. Stone**, University of California, Santa Cruz, USA

*Mechanical Transitions in Long Duplex Telomere DNA Molecules*

**Fena Ochs**, University of Copenhagen, Denmark

*Short Talk: Dynamic Chromatin Superstructures Safeguard Integrity of Nuclear Compartments Challenged by DNA Breakage*

#### Workshop 1: Recombination and Repair (Z2)

**Tracey E. Beyer**, Biotech Research and Innovation Centre, Denmark  
*Ontogeny of Genome Rearrangements in Budding Yeast*

\***Simon N. Powell**, Memorial Sloan Kettering Cancer Center, USA  
*Replication Fork Cleavage Occurs within 100bp from Local ATM Signaling of Site-Specific DNA Replication Block in Human Cells*

**Erin Hannah Sybouts**, University of Texas Health Science Center at San Antonio, USA

*Recombination and BLM Helicase Compensate for Replication Fork Defects in the Absence of 53BP1 Protein*

**Shane McDevitt**, Temple University Lewis Katz School of Medicine, USA

*Mechanisms of RNA-Transcript Templated DNA Recombinational Repair Promoted by RAD52*

**Susanne S. C. Bantele**, Max Planck Institute of Biochemistry, Germany

*Regulation of the Conserved Chromatin Remodeler Fun30SMARCAD1 at DNA Double-Strand Breaks*

**Walter J. Chazin**, Vanderbilt University, USA

*Mechanisms for Counting and Handoff by Human DNA Primase- A Role for the 4Fe-4S Cluster?*

**Holger Puchta**, Karlsruhe Institute of Technology, Germany  
*The RTR Complex Partner RMI2 and the DNA Helicase RTEL1 Are Both Independently Involved in Preserving the Stability of 45S rDNA Repeats in Arabidopsis thaliana*

**Christian Biertuempfel**, Max Planck Institute of Biochemistry, Germany

*DNA Recognition Features of Human Holliday Junction Resolvase GEN1*

#### Workshop 1: Genome Instability and DNA Repair I (Z1)

\***James E. Haber**, Brandeis University, USA

**Elena Balkanska-Sinclair**, Duke University, USA

*The BRD4-NUT Fusion Protein from Nut-Midline Carcinoma modulates DNA Damage Signaling and Ionizing Radiation Response*

**Michael M. Cox**, University of Wisconsin-Madison, USA

*Ionizing Radiation Resistance in Experimentally Evolved Escherichia coli Populations*

**Nitika Taneja**, NCI, National Institutes of Health, USA

*SNF2 Family Protein Fft3 Suppresses Nucleosome Turnover to Promote Epigenetic Inheritance and Proper Replication*

**Ryan M. Baxley**, University of Minnesota, USA

*Progressive Genomic Instability and Telomere Erosion in Human Cells following Inactivation of a Single MCM10 Allele*

**Michael H. Hauer**, Friedrich Miescher Institute for Biomedical Research, Switzerland

*Histone Degradation in Response to DNA Damage Enhances Chromatin Dynamics and Recombination Rates*

**Mariano Labrador-San Jose**, University of Tennessee, USA  
*Components of the DNA Damage Response Pathway, ATR and ATM, Modulate Chromatin Insulator Activity through Phosphorylation of Histone H2Av at Insulator Sites*

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**Mitch McVey**, Tufts University, USA

*Coordination of ATPase and Polymerase Activities of Drosophila DNA Polymerase Theta during Interstrand Crosslink and Alternative End-Joining Repair of Double-Strand Breaks*

**Hilda A. Pickett**, Children's Medical Research Institute, Australia  
*BLM and SLX4 Play Opposing Roles in Recombination-Dependent Replication at Human Telomeres*

### Starting Recombination (Z2)

\***Bernard de Massy**, Institut de Génétique Humaine, France

**Scott Keeney**, HHMI/Memorial Sloan Kettering Cancer Center, USA  
*Breaking and Chewing DNA during Meiosis*

**Florencia M. Pratto**, NIDDK, National Institutes of Health, USA  
*Linking Replication and Meiotic Recombination Initiation in Mammals*

**Kara A. Bernstein**, University of Pittsburgh School of Medicine, USA  
*Short Talk: The Function of the Shu Complex and the Rad51 Paralogs in Repair of Replication Intermediate by Promotion of Rad51 Presynaptic Filament Assembly*

**Maria Jasin**, Memorial Sloan Kettering Cancer Center, USA  
*Protecting the Genome by Homologous Recombination*

**Sofija Mijic**, Institute of Molecular Cancer Research, Switzerland  
*Short Talk: Replication Fork Reversal Triggers Fork Degradation in BRCA2-Defective Cells*

### RNA Metabolism and Genome Stability (Z1)

\***Hengyao Niu**, Indiana University Bloomington, USA

**Vihandha Wickramasinghe**, Peter MacCallum Cancer Centre, Australia  
*Effects of Altered RNA Processing on Genome Stability and the Proteome*

**Frédéric L. Chedin**, University of California, Davis, USA  
*Short Talk: R-Loop Formation is a Hallmark of Active Early Replication Origins in Mammalian Genomes*

**Julius Brennecke**, IMBA - Institut für Molekulare Biotechnologie GmbH, Austria  
*An RNA-Based Genome Immune System Safeguards Genome Stability*

**Eric A. Hunt**, New England Biolabs, USA  
*Short Talk: Prokaryotic Argonauts and their Potential as New Molecular Tools*

**Alice Meroni**, University of Milan, Italy  
*Short Talk: DNA Polymerase  $\epsilon$  Sensitizes Cells to Nucleotide Pool Deprivation in Absence of RNase H*

**Francesca Storici**, Georgia Institute of Technology, USA  
*Short Talk: Double-Strand Break Repair by Transcript RNA Is Stimulated by Rad52 and Requires Limited End Resection*

### Poster Session 1

#### TUESDAY, APRIL 4

#### Interplay between Chromatin Structure and DNA Replication/Repair (Joint)

\***Jennifer A. Cobb**, University of Calgary, Canada

\***Anja Groth**, University of Copenhagen, Denmark

**Geneviève Almouzni**, Centre National de la Recherche Scientifique, France

*Shaping Chromatin in the Nucleus, the Bricks and the Architects*

**Gary Karpen**, Lawrence Berkeley National Laboratory, University of California, Berkeley, USA

*Regulation of DNA Repair in Heterochromatin and Euchromatin*

**Francesca Mattioli**, HHMI/Colorado University Boulder, USA  
*Short Talk: DNA-Mediated Association of Two Histone-Bound CAF-1 Complexes Drives Tetrasome Assembly in the Wake of DNA Replication*

**Robert A. Martienssen**, Cold Spring Harbor Laboratory, USA  
*RNAi Promotes Heterochromatic Silencing through Replication-Coupled Release of RNA Polymerase II*

**Bernard de Massy**, Institut de Génétique Humaine, France  
*The Control of Initiation of Meiotic Recombination by PRDM9*

**Philipp Oberdoerffer**, NCI, National Institutes of Health, USA  
*Short Talk: Replication Stress Shapes a Protective Chromatin Environment Across Fragile Genomic Regions*

#### Regulating Recombination (Z2)

\***Xiaolan Zhao**, Memorial Sloan Kettering Cancer Center, USA

**Lorraine S. Symington**, Columbia University, USA  
*DNA End Resection and Repair Pathway Choice*

**Jennifer A. Cobb**, University of Calgary, Canada  
*Nej1 Regulates Repair Pathway Choice by Inhibiting Dna2-Sgs1 Mediated Resection*

**Aurele Piazza**, University of California, Davis, USA  
*Short Talk: Multi-Invasions Are Recombination Byproducts that Induce Chromosomal Rearrangements*

**Eric C. Greene**, Columbia University, USA  
*Single-Molecule Studies of Recombination Pathways*

**Sneha Saxena**, Indian Institute of Science, India  
*Short Talk: RAD51 Paralog XRCC2 Suppresses Pathological Replication Fork Progression*

#### Cell Cycle Regulation of DNA Damage Response (Z1)

\***Frédéric L. Chedin**, University of California, Davis, USA

**Tanya T. Paull**, University of Texas at Austin, USA  
*Double-Strand Break Repair Factors and R-Loop-Mediated Genomic Instability*



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**David Cortez**, Vanderbilt University School of Medicine, USA  
*Regulation of Replication Fork Stability by Single-Stranded DNA Binding Proteins*

**Kyle M. Miller**, USA  
*Chromatin Regulation of the DNA Damage Response*

**Michael P. Sheetz**, Mechanobiology Institute, National University of Singapore, Singapore

*Short Talk: DNA Damage Causes Rapid Accumulation of Phosphoinositides to Recruit ATR but not ATM*

**Linda J. Kenney**, National University of Singapore, Singapore  
*Short Talk: Salmonella Typhimurium forms Biofilms on Solid Tumors*

### Poster Session 2

### WEDNESDAY, APRIL 5

#### Replication Fork Progression and Restart (Z2)

\***Anne D. Donaldson**, University of Aberdeen, UK

**Kenneth J. Marians**, Memorial Sloan Kettering Cancer Center, USA  
*Imaging Individual Replisomes Reveals Independence and Decoupling of Polymerases During Replication*

**Anja Groth**, University of Copenhagen, Denmark  
*Chromatin Replication and Epigenome Maintenance*

**Alberto Ciccia**, Columbia University, USA  
*Short Talk: Restoration of Fork Stability in BRCA1- and BRCA2-Deficient Cells*

**Xiaolan Zhao**, Memorial Sloan Kettering Cancer Center, USA  
*Smc5/6-Mediated Control of Recombinational Repair is Critical for Genome Duplication*

**Advaita Madireddy**, Albert Einstein College of Medicine, USA  
*Short Talk: FANCD2 Facilitates DNA Replication through Common Fragile Sites*

**Joseph L. Stodola**, Washington University School of Medicine, USA  
*Short Talk: Kinetic Analysis of Lagging Strand Replication and Okazaki Fragment Maturation*

**Joseph Yeeles**, MRC Laboratory of Molecular Biology, UK  
*Short Talk: How the Eukaryotic Replisome Responds to DNA Damage in the Leading- and Lagging-Strand Templates*

#### Nuclear Dynamics and Genome Stability (Z1)

\***Arnab Ray Chaudhuri**, National Institutes of Health, USA

**Marco F. Foiani**, Istituto FIRC di Oncologia Molecolare, Italy  
*An Integrated ATR, ATM and mTOR-Mechanical Network Controlling Nuclear Plasticity and Cell Migration*

**Angela Taddei**, Institut Curie, France  
*Nuclear Organization and Chromatin Status Modulate Homologous Recombination Efficiency and Outcome*

**Irene Chiolo**, University of Southern California, USA  
*Short Talk: Highways for Repair: Nuclear Myosins and Actin Filaments Relocalize Heterochromatic DNA Breaks to the Nuclear Periphery*

**Martin W. Hetzer**, The Salk Institute, USA  
*How the Nuclear Membrane Controls Genome Function*

**Emmanuelle Fabre**, Hopital St Louis, France  
*Short Talk: DNA Damage Increases Chromatin Stiffening in Budding Yeast*

**Neil T. Umbreit**, Dana-Farber Cancer Institute, USA  
*Short Talk: Chromosome Bridge Resolution Requires Mechanical Forces from Actin-Based Contractility*

**Peter Ly**, University of California, San Diego, USA  
*Short Talk: Mitotic Errors Promote Chromosome Shattering and DNA Break Repair by Non-Homologous End Joining*

### Poster Session 3

#### Replication Initiation Mechanisms (Z2)

\***Kenneth J. Marians**, Memorial Sloan Kettering Cancer Center, USA

**Stephen P. Bell**, Massachusetts Institute of Technology, USA  
*Mechanism and Timing of Mcm2-7 Ring Closure During Origin Licensing*

**Stephen D. Bell**, Indiana University, USA  
*DNA Replication in the Archaea*

**Heath Murray**, Newcastle University, UK  
*Short Talk: A New Bacterial Replication Origin Element Specifies Single-Strand Initiator Binding*

**Anne D. Donaldson**, University of Aberdeen, UK  
*The Conserved Role of Rif1 as a Substrate-Targeting Subunit of Protein Phosphatase 1*

**Dominik Boos**, University of Duisburg-Essen, Germany  
*Short Talk: MTBP Is an Essential Replication Initiation Factor with Vertebrate-Specific and Sld7-Like Features*

#### DNA Repair and Human Diseases (Z1)

\***Hilda A. Pickett**, Children's Medical Research Institute, Australia

**Agnel Sfeir**, New York University School of Medicine, USA  
*Single-Molecule Analysis of mtDNA Replication Uncovers the Basis of the Common Deletion*

**Cecilia Cotta-Ramusino**, Editas Medicine, USA  
*Short Talk: Characterization of the Interplay between DNA Repair and CRISPR/Cas9-Induced DNA Lesions at an Endogenous Locus*

**Simon J. Boulton**, London Research Institute, Clare Hall Laboratories, UK  
*Mechanistic Insights into Telomere Dysfunction Disorders*

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**Madalena Tarsounas**, University of Oxford, UK

*Short Talk: MUS81 Nuclease Activity Is Essential for Replication Stress Tolerance and Chromosome Segregation in BRCA2-Deficient Cells*

**Janet Partridge**, St Jude Children's Research Hospital, USA

*Short Talk: Histone H3G34R Mutation Causes Replicative Stress, Defective Homologous Recombination and Genomic Instability in Fission Yeast*

### THURSDAY, APRIL 6

#### Replication Fork Establishment and Replication-Coupled Repair (Joint)

\***Jeannine Gerhardt**, Weill Cornell Medicine, USA

\***Karlene A. Cimprich**, Stanford University, USA

**James M. Berger**, Johns Hopkins University School of Medicine, USA  
*Physical Mechanisms for Initiating DNA Replication in Cells*

**Agata Smogorzewska**, Rockefeller University, USA  
*Stress Response at the Replication Fork*

**Eric J. Brown**, Perelman School of Medicine, University of Pennsylvania, USA

*Short Talk: Characterizing Replisome Ubiquitination upon Fork Stalling*

**André Nussenzweig**, NCI, National Institutes of Health, USA  
*DNA Breaks and End-Resection Measured Genome-Wide by End Sequencing (END-seq)*

**Helle D. Ulrich**, Institute of Molecular Biology, Germany  
*Coordination of DNA Damage Bypass with Genome Replication and Checkpoint Signaling*

**Stephane Koundrioukoff**, Institute Gustave Roussy, France  
*Short Talk: DNA Replication Compensation: A Two Steps Mechanism*

#### Workshop 2: Replication (Z2)

\***Linda B. Bloom**, University of Florida, USA  
*Active Sliding Clamp Opening in Three Steps*

**Christopher Sansam**, Oklahoma Medical Research Foundation, USA  
*DNA Replication Timing during Development Anticipates Transcriptional Programs and Parallels Enhancer Activation*

**Boris Pfander**, Max Planck Institute of Biochemistry, Germany  
*Robust Replication Control by Temporal Gaps between Licensing and Firing Phases*

**Hasan Yardimci**, Francis Crick Institute, UK  
*Super-Resolution Fluorescence Imaging of DNA Replication Intermediates*

**Jon Baxter**, University of Sussex, UK  
*Transcription Promotes Replication Fork Rotation and Double-Stranded DNA Intertwining via a Cohesin-Dependent Pathway*

**Ivan Psakhye**, IFOM, FIRC Institute of Molecular Oncology, Italy  
*DDK-Mediated Regulation of the deSUMOylating Enzyme Ulp2 Facilitates DNA Replication Initiation*

#### Workshop 2: Genome Instability and DNA Repair II (Z1)

\***Michael P. Sheetz**, Mechanobiology Institute, National University of Singapore, Singapore  
**Katharina Schlacher**, MD Anderson Cancer Center, USA  
*Epigenetics-Enabled MRE11 Replication Restart by p53 Promotes Replication Pathway Homeostasis to Suppress Opportunistic Transcription Reprogramming*

**Kristijan Ramadan**, University of Oxford, UK  
*SPRTN Is a Novel Mammalian Protease with the Central Role in DNA Replication-Coupled DNA-Protein Crosslink Repair*

**Jason Sheltzer**, Cold Spring Harbor Laboratory, USA  
*Single-Chromosome Aneuploidy Commonly Functions as a Tumor Suppressor but Can Drive Genome Evolution*

**Manuel Stucki**, University of Zurich, Switzerland  
*TOPBP1 Cooperate with TCOF1/Treacle in the Nucleolar Response to DNA Double-Strand Breaks*

**Maria Teresa Teixeira**, CNRS – UMR 8226, France  
*Telomere Replication in the Absence of Telomerase: Failure, Repair and Adaptation*

**Johannes van den Boom**, University of Duisburg-Essen, Germany  
*The AAA-ATPase VCP/p97 Extracts Sterically Trapped Ku70/80 Rings from DNA in Double-Strand Break Repair*

**Catherine H. Freudenreich**, Tufts University, USA  
*Cytosine Deamination Mediates R-Loop Dependent CAG Repeat Fragility and Instability*

**Muwen Kong**, University of Pittsburgh, USA  
*Auto-PARYlation Switches PARP1 Search Mechanism from Three-Dimensional Diffusion to Anomalous One-Dimensional Sliding*

#### Finishing Recombination (Z2)

\***Maria Jasin**, Memorial Sloan Kettering Cancer Center, USA

**Stephen C. Kowalczykowski**, University of California, Davis, USA  
*Molecular Functions and Single Molecule Studies of BRCA1, BRCA2, and RAD51 Paralog*

**Petr Cejka**, University of Zurich, Switzerland  
*Processing of DNA Double-Strand Breaks for Repair by Homologous Recombination*

\***Maria Teresa Teixeira**, CNRS – UMR 8226, France

**Titia de Lange**, Rockefeller University, USA  
*How Shelterin Solves the Telomere End-Protection Problem*

**Kerry S. Bloom**, University of North Carolina at Chapel Hill, USA  
*The Molecular Basis for the Centromere Spring*

**Nausica Arnoult**, The Salk Institute for Biological Studies, USA  
*Short Talk: Regulation of DNA Repair Pathway Choice in S/G2 by the NHEJ Inhibitor CYREN*

**Julia Promisel Cooper**, NCI, National Institutes of Health, USA  
*Telomeric Control of Kinetochores Assembly and Nuclear Envelope Breakdown*

**Meeting Wrap-Up: Outcomes**

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**Ralph Scully**, Beth Israel Deaconess Medical Center, USA

*Short Talk: Microhomology-Mediated Tandem Duplications form at Tus/Ter-Stalled Replication Forks in BRCA1 Mutant Cells*

**Stephen C. West**, Francis Crick Institute, UK  
*Unresolved Recombination Intermediates as a Source of DNA Breaks and Chromosome Aberration*

**Telomeres and Centromeres (Z1)**

**and Future Directions (Organizers) (Z2)**

**Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z1)**

**FRIDAY, APRIL 7**

**Departure**