

Genomic Instability and DNA Repair

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

Scientific Organizers:

Julia Promisel Cooper, National Cancer Institute, National Institutes of Health, USA

Marco F. Foiani, Istituto FIRC di Oncologia Molecolare, Italy

Geneviève Almouzni, Centre National de la Recherche Scientifique, France

Joint with the meeting on *DNA Replication and Recombination*

Genome stability is the foundation upon which all cellular and organismal processes depend. This conference will grapple with the intricate array of biochemical reactions orchestrated by the cell to replicate, repair and segregate chromosomes accurately despite constant threats from spontaneous and environmentally-induced damage. Defects in these reactions lead to genomic instability, a confirmed driver of cancer and degenerative diseases. Fascinating and therapeutically crucial questions remain about the mechanisms underlying chromosome stability, and cross-disciplinary approaches are required to address them. How do epigenetic chromatin marks influence repair of underlying DNA sequences, and how can we predict the effects of chemotherapeutic agents that alter such marks? To what extent is the nucleus organized into subdomains with distinct functions; how are these subdomains altered when cells move or differentiate? How are the myriad helicases, nucleases and polymerases coordinated to safeguard genome stability, why are these molecules often mutated in human disease, and how can we ameliorate the effects of such mutations? What is the array of strategies available to cancer cells as they achieve unlimited proliferation? This conference has a history of bringing together investigators from diverse subfields who otherwise rarely meet. Cutting-edge concepts in translational, genomic, cellular, molecular, RNA and structural biology will be dissected to take the conversation to unprecedented levels of depth and breadth. The concurrent conference on “DNA Replication and Recombination” will provide additional opportunities for cross-talk. Both conferences are committed to nurturing interactions among longtime experts in the field with students, postdocs and investigators new to the field.


Session Topics:

- Mechanisms of DNA Repair
- RNA Metabolism and Genome Stability
- Interplay between Chromatin Structure and DNA Replication/Repair (Joint)
- Cell Cycle Regulation of DNA Damage Response
- Nuclear Dynamics and Genome Stability
- DNA Repair and Human Diseases
- Replication Fork Establishment and Replication Coupled Repair (Joint)
- Telomeres and Centromeres

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: Tom Ellenberger, Washington University School of Medicine in St. Louis, and Dave Gohara, Saint Louis University School of Medicine

Meeting Hashtag: #KSgenomic

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KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Genomic Instability and DNA Repair (Z1)

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

Sponsored by AstraZeneca, Bayer HealthCare Pharmaceuticals, Editas Medicine, Inc., EMD Serono Research and Development Institute, Inc., Journal of Molecular Cell Biology (JMCB) and TESARO, Inc.

DNA Replication and Recombination (Z2)

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

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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

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

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

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

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

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?

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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

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 Argonautes and their Potential as New Molecular Tools

Alice Meroni, University of Milan, Italy
Short Talk: DNA Polymerase ϵ 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

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

Florecia 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

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

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

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 γ 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

Regulating Recombination (Z2)

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

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

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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

Poster Session 2

WEDNESDAY, APRIL 5

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

Replication Fork Progression and Restart (Z2)

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

Kenneth J. Mariani, 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

Poster Session 3

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

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

Replication Initiation Mechanisms (Z2)

***Kenneth J. Mariani**, 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

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Dominik Boos, University of Duisburg-Essen, Germany

Short Talk: MTBP Is an Essential Replication Initiation Factor with Vertebrate-Specific and Sld7-Like Features

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: 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

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

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

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

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

Meeting Wrap-Up: Outcomes and Future Directions (Organizers) (Z2)

FRIDAY, APRIL 7
Departure

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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

Telomeres and Centromeres (Z1)

***Maria Teresa**

Teixeira, CNRS –

UMR 8226, France

Titia de Lange,

Rockefeller

University, USA

How Shelterin

Solves the

Telomere

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*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 Kinetochore
Assembly and
Nuclear Envelope
Breakdown*

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 Paralogs*