

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Genomic Instability and DNA Repair (X1)

Scientific Organizers: Katharina Schlacher, Irene Chiolo and Ralph Scully

Sponsored by (Cell Research), Chinese Society for Cell Biology and Pfizer Inc.

Precision Genome Engineering (X2)

Scientific Organizers: Laura Sepp-Lorenzino and Matthew Porteus

March 19-23, 2023 • Fairmont Chateau Whistler • Whistler, BC, Canada

Sponsored by (Cell Research), Chinese Society for Cell Biology, DCVC Bio, Ionis Pharmaceuticals, Inc., Novo Nordisk A/S, Pfizer Inc., Synthego, Takeda Pharmaceutical Company Limited and Ultragenyx Pharmaceutical Inc.

Scholarship Deadline: December 28, 2022 / Abstract Deadline: December 28, 2022 / Discounted Registration Deadline: January 18, 2023

SUNDAY, MARCH 19

Arrival and Registration (4pm Start)

MONDAY, MARCH 20

Welcome and Keynote Session (Joint) (8am Start)

***Katharina Schlacher**, MD Anderson Cancer Center, USA

***Laura Sepp-Lorenzino**, Intellia Therapeutics, USA

Titia de Lange, Rockefeller University, USA

APOBEC3-Dependent Kataegis and TREX1-Driven Chromothripsis During Telomere Crisis

Jennifer A. Doudna, HHMI/University of California, Berkeley, USA
The CRISPR Revolution: The Power and Promise of Gene Editing

Genome Instability and Cancer (Joint) (9:50am Start)

***Katharina Schlacher**, MD Anderson Cancer Center, USA

André Nussenzweig, NCI, National Institutes of Health, USA
Genome Instability in Post-Mitotic Cells

Stephen C. West, Francis Crick Institute, UK
DNA Repair – Structures and Mechanisms

Agnel Sfeir, Memorial Sloan Kettering Cancer Center, USA
Restricting MMEJ to Mitosis: The Role of RHINO

Workshop 1: The Past and Future of DNA Repair/Replication (2:30pm Start) (X1)

***Kristina Schmidt**, University of South Florida, USA

Michelle Swift, Dana-Farber Cancer Institute, USA
Dynamics of the DYNLL1/MRE11 Complex Regulates DNA End Resection and Recruitment of the Shieldin Complex to DSBs

Yuan He, Northwestern University, USA
Structure Basis of DNA Double-Strand Break Repair by NHEJ

Sinem Usluer, Medical University of Graz, Austria
Disordered Regions Mediate the Interaction of p53 and MRE11

Justine Sitz, University of Copenhagen, Denmark
Untangling the Genome Maintenance Functions of BRCA1 during Unperturbed Cell Cycle

Brian B. Rodemoyer, University of South Florida, USA
A Novel Interaction between the Bloom's Syndrome DNA Helicase BLM and an Interphase-specific Condensin II Complex Aids in Maintaining Genome Stability

Roundtable Discussion: Genome Editing Ethics (2:30pm Start) (X2)

***Fyodor D. Urnov**, University of California, Berkeley, USA

Sekar Kathiresan, Verve Therapeutics, USA

Jennifer A. Doudna, HHMI/University of California, Berkeley, USA

Anna Kwilas, Food and Drug Administration, USA

Natalia Gomez-Ospina, Stanford University, USA

Fork Protection and Cancer Therapy (5pm Start) (X1)

***Alessandro Vindigni**, Washington University, USA

Mechanisms of Replication Fork Recovery in BRCA-deficient Tumors

***Sharon B. Cantor**, University of Massachusetts Medical School, USA
Replication Gaps Underlie BRCA Deficiency and Therapy Response

Li Lan, Massachusetts General Hospital, USA
Understanding and Targeting R-Loops and mRNA-Dependent DNA Repair in Cancer

Andrew Elia, Massachusetts General Hospital, Harvard Medical School, USA

Short Talk: Regulation of Replication Fork Remodeling by RFWD3

Priyanka Verma, Washington University, USA

Short Talk: Communication between Base Damage and Replication-fork Remodeling Dictate Responses to PARP Inhibitor Therapy in BRCA-mutant Cancer

Natural Editing and Repair Mechanisms (5pm Start) (X2)

***Toni Cathomen**, University Medical Center Freiburg, Germany
Quantitative Evaluation of Chromosomal Rearrangements in Gene-Edited Human Stem Cells by CAST-Seq

Anna Kwilas, Food and Drug Administration, USA
Regulatory Approach for Gene Therapies Incorporating Human Somatic Genome Editing A CBER Perspective

Jacob E. Corn, ETH Zürich, Switzerland
Short Talk: TREX1 Restricts CRISPR-Cas9 Genome Editing in Human Cells

Chance Meers, Columbia University, USA
Short Talk: Transposon-encoded DNA Endonucleases use Guide RNAs to Selfishly Bias their Inheritance

Dahlia Rohm, Duke University, USA
Short Talk: Targeted Activation of the Imprinted PWS Locus via CRISPR/Cas9-based Epigenome Editing

Poster Session 1 (7:30pm Start)

TUESDAY, MARCH 21

Nuclear and Chromatin Dynamics in DNA Repair (8am Start) (X1)

***Irene Chiolo**, University of Southern California, USA
DNA Repair Mechanisms in Heterochromatin

Matthias Altmeyer, University of Zurich, Switzerland
Dynamics and Functions of DNA Repair Compartments

Karim Mekhail, University of Toronto, Canada
Nuclear Dynamics in DSB Repair from Yeast to Humans

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Genomic Instability and DNA Repair (X1)

Scientific Organizers: Katharina Schlacher, Irene Chiolo and Ralph Scully

Sponsored by (Cell Research), Chinese Society for Cell Biology and Pfizer Inc.

Precision Genome Engineering (X2)

Scientific Organizers: Laura Sepp-Lorenzino and Matthew Porteus

March 19-23, 2023 • Fairmont Chateau Whistler • Whistler, BC, Canada

Sponsored by (Cell Research), Chinese Society for Cell Biology, DCVC Bio, Ionis Pharmaceuticals, Inc., Novo Nordisk A/S, Pfizer Inc., Synthego, Takeda Pharmaceutical Company Limited and Ultragenyx Pharmaceutical Inc.

Scholarship Deadline: December 28, 2022 / Abstract Deadline: December 28, 2022 / Discounted Registration Deadline: January 18, 2023

Philipp Oberdoerffer, Johns Hopkins University, USA
Epigenetic Control of Base Excision Repair as a Cancer Vulnerability

Marton Tibor Kovacs, Institut Curie, France
Short Talk: DNA Damage-induced Nuclear Envelope Rupture: A New Cancer Vulnerability

Aline Marnef, CNRS, France
Short Talk: DSB-induced RNA:DNA Hybrid Accumulation Arise from Transcriptional Repression Correlates with Resection

Plant and Animal Science Gene Editing Applications and Regulatory Path (8am Start) (X2)

Yi Jin, Inari Agriculture, USA
Seeding Change through Genome Editing with Inari's SEEDesign (TM) platform

***Rodolphe Barrangou**, North Carolina State University, USA
CRISPR Applications and Implications in Ag and Forestry

Irina A. Polejaeva, Utah State University, USA
Advancing Large Animal Model Development using CRISPR/Cas 9 Editing

John D. Laurie, Agriculture and Agri-Food Canada, Canada
Improved Plant Regeneration and Cas9 Cleavage Detection for Gene Editing in Wheat

Katie Willis, Imperial College London, UK
Autosomal Editors for Efficient Genetic Biocontrol

Workshop 2: New Approaches and Technologies to Study Genome Stability (2:30pm Start) (X1)

Maga Rowicka, University of Texas Medical Branch, USA
Quantitative DSB Mapping and Computational Modeling of Mechanisms of DSB Formation

Jeroen van den Berg, Hubrecht Institute, Netherlands
Acceleration of Genome Replication Uncovered by Single-cell Nascent DNA Sequencing

Neesha Kara, Babraham Institute, UK
Genome-wide Mapping of DNA Replication and Damage in Senescence using TrAELseq

Robin Sebastian, NIH/NCI/CCR, USA
Chromatin Topology Restricts DNA Replication at Double-strand Breaks

Xia Ding, Pfizer, Inc., USA
Cohesin Instability at Replication Forks Leads to Accumulation of Toxic G-quadruplex Structures and Confers PARPi Sensitivity

Anoek Friskes, Netherlands Cancer Institute, Netherlands
Dynamic, Higher-order Filament Formation to Facilitate DNA Repair

***Kyungjae Myung**, Institute for Basic Science, South Korea
Precision Targeting Tumor Cells using Cancer specific InDel-mutations with CRISPR

Peter Ly, University of Texas Southwestern Medical Center, USA
Mitotic Clustering of Pulverized Chromosomes from Micronuclei

Inflammation and Genomic Instability (5pm Start) (X1)

Karl-Peter Hopfner, Ludwig-Maximilians-University Munich, Germany
Structures of MRE11 and cGAS

Katharina Schlacher, MD Anderson Cancer Center, USA
Mitochondrial and Nuclear BRCA/FANC DNA Replication Stability in Disease and Cancer

***Roger Greenberg**, University of Pennsylvania, USA
Genome Instability and Inflammation

***Julia Sidorova**, University of Washington, USA
Short Talk: Innate Immunity Mediator STING Modulates Nascent DNA Metabolism at Stalled Forks in Human Cells

Julia Li, University of California San Diego, USA
Short Talk: Hidden in our Own Genome: A Previously Missing Link between Epstein Barr Virus and Cancer

Delivery of Gene Editors: Potency, Biodistribution, Safety (5pm Start) (X2)

***Christian Dombrowski**, Intellia Therapeutics, USA

Daniel J. Siegwart, University of Texas Southwestern Medical Center, USA
Multiplexed SORT LNPs for Enhancing CRISPR/Cas Gene Editing Cancer Therapy through Modulating Tumor Mechanical Properties

Charles Gersbach, Duke University, USA
Intended and Unintended Consequences of in vivo Editing

Jennifer R. Hamilton, University of California, Berkeley, USA
Short Talk: Cell Type-programmable CRISPR-Cas9 Delivery for Human T Cell Engineering

Lauren Goetsch, Mekonos, Inc, USA
Short Talk: Utilizing Surface-Functionalized Nanoneedles for Physical Cargo Delivery into Cells

Poster Session 2 (7:30pm Start)

WEDNESDAY, MARCH 22

Genome Editing and DNA Repair (Joint) (8am Start)

***Matthew Porteus**, Stanford University School of Medicine, USA

Maria Jasin, Memorial Sloan Kettering Cancer Center, USA
Genome Modification by Natural and Artificial DNA Breaks

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Genomic Instability and DNA Repair (X1)

Scientific Organizers: Katharina Schlacher, Irene Chiolo and Ralph Scully

Sponsored by (Cell Research), Chinese Society for Cell Biology and Pfizer Inc.

Precision Genome Engineering (X2)

Scientific Organizers: Laura Sepp-Lorenzino and Matthew Porteus

March 19-23, 2023 • Fairmont Chateau Whistler • Whistler, BC, Canada

Sponsored by (Cell Research), Chinese Society for Cell Biology, DCVC Bio, Ionis Pharmaceuticals, Inc., Novo Nordisk A/S, Pfizer Inc., Synthego, Takeda Pharmaceutical Company Limited and Ultragenyx Pharmaceutical Inc.

Scholarship Deadline: December 28, 2022 / Abstract Deadline: December 28, 2022 / Discounted Registration Deadline: January 18, 2023

***Tanya T. Paull**, University of Texas at Austin, USA
Regulation of DNA Double-Strand Break Repair and Oxidative Stress Signaling

Daniel Durocher, Lunenfeld-Tanenbaum Research Institute, Canada
Genome Kintsugi

David Pellman, Dana-Farber Cancer Institute, USA
Mechanisms Driving Rapid Genome Evolution

Petr Cejka, Institute for Research in Biomedicine, Switzerland
Short Talk: Mechanism of DNA End Sensing by the MRE11 Complex: Implications for CRISPR Based Genome Editing and Telomeres

Gregory Davis, Sangamo Therapeutics, USA
Short Talk: Epigenetic Editing and Gene Regulation Using Designed Zinc Finger Proteins

Panel Discussion: Addressing COVID-19-Related Challenges for Women in Science (2:30pm Start) (X1)

Tanya T. Paull, University of Texas at Austin, USA

***Irene Chiolo**, University of Southern California, USA

***Katharina Schlacher**, MD Anderson Cancer Center, USA

Xiaolan Zhao, Memorial Sloan Kettering Cancer Center, USA

Helle D. Ulrich, Institute of Molecular Biology, Germany

Titia de Lange, Rockefeller University, USA

Workshop (2:30pm Start) (X2)

***Matthew Porteus**, Stanford University School of Medicine, USA

***Laura Sepp-Lorenzino**, Intellia Therapeutics, USA

Romina Marone, University of Basel, DBM, Switzerland
Function-preserving Single Amino Acid Substitutions Shield Hematopoietic Stem and Progenitor Cells from CD117 Targeted Immunotherapy in vivo

Gabriele Casirati, Dana Farber Cancer Institute, USA
Multiplex Epitope-Engineered HSPCs to Enable multi-target CAR-T Cell Immunotherapy for Acute Myeloid Leukemia

Samuele Ferrari, Vita-Salute San Raffaele University, Italy
Uncovering Upsides and Pitfalls of Base and Prime Editing in Hematopoietic Stem Cells

Ayal Hendel, Bar Ilan, Israel
Multiplex HDR for Correction Simulation of SCID by CRISPR Genome Editing in Healthy Donor Human HSPCs

Sean McCutcheon, Duke University, USA
CRISPR-based Epigenome Editing Screens Identify Transcriptional and Epigenetic Regulators of Human CD8 T Cell Function

Replication Coupled Repair (5pm Start) (X1)

***Helle D. Ulrich**, Institute of Molecular Biology, Germany
When the Fork Meets the Cytoskeleton - Functions of Myosin VI in DNA Repair and Replication Stress

Xiaolan Zhao, Memorial Sloan Kettering Cancer Center, USA
Integrative Analysis Reveals Unique Structural and Functional Features of the Smc5/6 Complex

***Ralph Scully**, Beth Israel Deaconess Medical Center, USA
Stalled Fork Repair in Health and Disease

Shyam K. Sharan, National Cancer Institute, USA
Short Talk: DNA Mismatch Repair Independent Role of MLH1 in Suppressing Genomic Instability in BRCA2-Deficient Cells

Anna Malkova, University of Iowa, USA
Short Talk: Unraveling Mutagenic Potential of Break-induced Replication

Editing Technology Development (5pm Start) (X2)

***Gregory Davis**, Sangamo Therapeutics, USA

Alex Marson, University of California, San Francisco, USA
A Functional CRISPR Dissection of Gene Networks Controlling Human Regulatory T Cell Identity

Cecilia Cotta-Ramusino, Tessera Therapeutics, USA
Gene Writing: A New Genome Engineering Technology

Avencia Sanchez-Mejias, Integra Therapeutics, Spain
Short Talk: Characterization and Deployment in vivo of FiCAT Genome Writer

Steve E. Glenn, Integrated DNA Technologies, USA
Short Talk: Engineering an Improved Protein-Based HDR Enhancer

Y. Bill Kim, Pairwise, USA
Short Talk: A Novel Mechanistic Framework for Precise Sequence Replacement Using Reverse Transcriptase and Diverse CRISPR-Cas Systems

Poster Session 3 (7:30pm Start)

THURSDAY, MARCH 23

RNA Functions in Genome Stability (8am Start) (X1)

***Karlene A. Cimprich**, Stanford University, USA
A Novel Function for the DNA Replication Fork Remodeler HLTF in Genome Maintenance

Fabrizio d'Adda di Fagnana, IFOM ETS – The AIRC Institute of Molecular Oncology, Italy
RNA Synthesis at DNA Lesions

***Francesca Storici**, Georgia Institute of Technology, USA
RNA-Directed DNA Double-Strand Break Repair in Yeast and Human Cells

Eric J. Brown, Perelman School of Medicine, University of Pennsylvania, USA
Impact of DNA Repeat Transcription on ATR Inhibitor-driven Genomic Breaks

Clara Bonnet, Institut Curie, France
Short Talk: An RNA-protein Interaction at DNA Replication Forks

KEYSTONE SYMPOSIA

on Molecular and Cellular Biology

Genomic Instability and DNA Repair (X1)

Scientific Organizers: Katharina Schlacher, Irene Chiolo and Ralph Scully

Sponsored by (Cell Research), Chinese Society for Cell Biology and Pfizer Inc.

Precision Genome Engineering (X2)

Scientific Organizers: Laura Sepp-Lorenzino and Matthew Porteus

March 19-23, 2023 • Fairmont Chateau Whistler • Whistler, BC, Canada

Sponsored by (Cell Research), Chinese Society for Cell Biology, DCVC Bio, Ionis Pharmaceuticals, Inc., Novo Nordisk A/S, Pfizer Inc., Synthego, Takeda Pharmaceutical Company Limited and Ultragenyx Pharmaceutical Inc.

Scholarship Deadline: December 28, 2022 / Abstract Deadline: December 28, 2022 / Discounted Registration Deadline: January 18, 2023

Platon Selemenakis, University of Texas, USA
Short Talk: 53BP1 and BRCA2 Synergy in Genome Stability

Ex vivo Gene Edited Cell Therapies (8am Start) (X2)

***Pietro Genovese**, Dana-Farber Cancer Institute, USA
Fyodor D. Urnov, University of California, Berkeley, USA
From N=1 to N=all: a Platform Approach to CRISPR-Cas Therapies for Disorders of Hematopoiesis

Natalia Gomez-Ospina, Stanford University, USA
Engineering the Blood to Treat the Brain Genome Editing

Simon N. Chu, University of California, San Francisco, USA
Developing a Genome Editing Strategy to Deliver Alpha-globin Transgene to Alpha Thalassemia Major Hematopoietic Stem Cells

Dave Vereide, Umoja Biopharma, USA
Short Talk: Arming Induced Pluripotent Stem Cells with a Synthetic Receptor Enables Massive Production of Cytotoxic Innate Lymphocytes for "off-the-shelf" Cancer Immunotherapies

Matthew Porteus, Stanford University School of Medicine, USA
Sickle Cell Disease Clinical Program

Career Roundtable (Joint) (3pm Start)

Tanya T. Paull, University of Texas at Austin, USA
Cecilia Cotta-Ramusino, Tessera Therapeutics, USA
Karl-Peter Hopfner, Ludwig-Maximilians-University Munich, Germany
Anna Kwilas, Food and Drug Administration, USA

Genomic Instability and Cancer II (5pm Start) (X1)

***Susan M. Rosenberg**, Baylor College of Medicine, USA
The DNA Damageome and Cancer

Filippo Rosselli, Gustave Roussy, France
From DNA Repair to Translation: When the Maintenance of Genetic Stability Turns to the Maintenance of Proteostasis

George Galea, European Molecular Biology Laboratory, Germany
Short Talk: The Golgi Complex is a Regulatory Hub for DNA Repair

Junjie Chen, University of Texas MD Anderson Cancer Center, USA
Short Talk: Targeting DNA Damage Responsive Pathways in Cancer Therapy

In vivo Gene Editing Drug Development (5pm Start) (X2)

***Laura Sepp-Lorenzino**, Intellia Therapeutics, USA
Clinical Results for In Vivo Knockout and Insertion CRISPR/Cas9 Programs

Sekar Kathiresan, Verve Therapeutics, USA
Clinical Programs of Base Editors for Cardiovascular Disease

Christiano Alves, Massachusetts General Hospital, USA
A Permanent Genetic Treatment for Spinal Muscular Atrophy using Base Editors

Meeting Wrap-Up: Outcomes and Future Directions (Organizers)
(6:45pm Start) (X1)

Meeting Wrap-Up: Outcomes and Future Directions (Organizers)
(6:45pm Start) (X2)

FRIDAY, MARCH 24

Departure