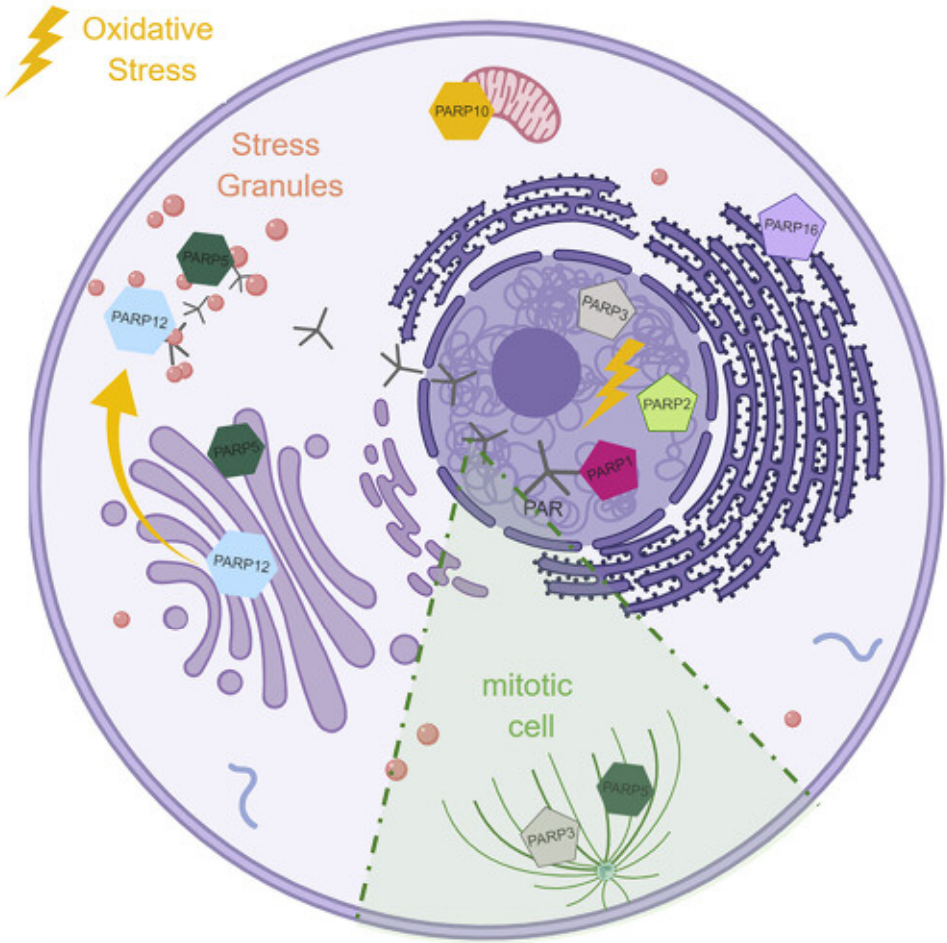
Abstracts of papers presented
at the 2020 *virtual* meeting on

THE PARP FAMILY & ADP-RIBOSYLATION

December 9–December 11, 2020



CSH Cold Spring Harbor Laboratory
MEETINGS & COURSES PROGRAM

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THE PARP FAMILY & ADP-RIBOSYLATION

December 9–December 11, 2020

Arranged by

W. Lee Kraus, *UT Southwestern Medical Center*
Andreas Ladurner, *Ludwig-Maximilians-University, Germany*
Susan Smith, *Skirball Institute NYU School of Medicine*

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Mono-ADP-ribosylation of nsP2 inhibits its proteolytic activity and thereby restricts virus replication
Sarah Krieg, Fabian Pott, Maud Verheirstraeten, Barbara Loppok, Christine Goffinet, Bernhard Lüscher, Patricia Korn.
Presenter affiliation: RWTH Aachen University, Aachen, Germany. 33

PARP-1 modulates HIF-1α selective recruitment to chromatin during hypoxia
Juan Manuel Martí, Ángel García-Diaz, Daniel Delgado, Javier Oliver Pozo, Ester M. Hammond, Françoise Dantzer.
Presenter affiliation: Institute of Parasitology and Biomedicine López-Neyra, Granada, Spain. 34

TCDD-inducible poly-ADP-ribose polymerase (TIPARP/PARP7) regulates AHR biology and dioxin toxicity in rat
Alexandra S. Long, David Hutin, Puck N. Norell, Kim S. Sugamori, Peng Shao, Denis M. Grant, Jason Matthews.
Presenter affiliation: University of Toronto, Toronto, Canada. 35

Poly(ADP-ribose) modulates the liquid-liquid phase separation and cytotoxicity of C9orf72 dipeptide repeat proteins
Ke Zhang, Lin Guo, Valina L. Dawson, Ted M. Dawson, Thomas E. Lloyd, Jeffrey D. Rothstein.
Presenter affiliation: Mayo Clinic, Florida, Jacksonville, Florida. 36

FRIDAY, December 11—10:00 AM US EST

SESSION 5 STRUCTURE AND MECHANISMS: DNA REPAIR AND GENOME STABILITY

Chairpersons: **Francoise Dantzer,** CNRS-BSC-UMR7242, Illkirch, France
Michael Nielsen, NNF Center for Protein Research, Copenhagen, Denmark

PARP inhibitor effects on PARP-1 allostery and retention on DNA breaks
John M. Pascal, Levani Zandarashvili, Marie-France Langelier, Uday Kiran Velagapudi, Mark A. Hancock, Jamin D. Steffen, Ramya Billur, Zain M. Hannan, Andrew J. Wicks, Dragomir B. Krastev, Stephen J. Pettitt, Christopher J. Lord, Tanaji T. Talele, Ben E. Black.
Presenter affiliation: Université de Montréal, Montréal, Canada. 37

PARP-1 MODULATES HIF-1α SELECTIVE RECRUITMENT TO CHROMATIN DURING HYPOXIA

Juan Manuel Martí[1], Ángel García-Diaz[1], Daniel Delgado[1], Javier Oliver Pozo[1], Ester M Hammond[2], Françoise Dantzer[3]

[1]Institute of Parasitology and Biomedicine López-Neyra, Cellular biology and immunology, Granada, Spain, [2]University of Oxford, Oxford Institute for Radiation Oncolog, Oxford, United Kingdom, [3]University of Strasbourg, Research Institute of the Strasbourg Biotechnology School, Strasbourg, France

Cell's adaptation to hypoxia is mainly controlled by the hypoxia inducible transcription factor HIF-1α and its over-expression is associated with tumor bad prognosis. PARP-1 is known primarily for having an important role in DNA repair and the inhibition of PARP activity is recognized for the treatment of cancers with specific defects in homologous recombination repair.
In this study we uncover a new pathway demonstrating that in response to a hypoxic challenge poly(ADP-ribose) (PAR) is synthesized, HIF-1α is post-transcriptionally modified (PTM) and stabilized by PARylation at specific K/R residues located at its C-terminus. Using an unbiased ChIP-seq approach we demonstrate that PARP-1 dictates hypoxia-dependent HIF-recruitment to chromatin in a range of HIF-regulated genes, while analysis of HIF-binding motifs (RCGTG) reveals that the absence of PARP-1 restrains the flexibility in the use of hyipoxia responsive elements in gene promoters. PARP-1 absence also limits HIF-1α location specifically near the TSS region of its target genes. Consequently, the cells are poorly adapted to hypoxia, showing a reduced fitness during hypoxic induction. Together, these results provide a conceptual advancement in the fine-tuning of the hypoxic response by the identification of a backup strategy to maintain HIF-1α activation and dissect a key mechanism acting in the initiation of the hypoxic response that might be targeted in the tumor context with the use of PARP inhibitors.