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## SUMMARY & MISSION STATEMENT

We employ cell cycle resolved single cell and cell population analyses to dissect how maintenance of genome stability is coordinated with cell cycle progression, chromatin dynamics and transcription, and how deregulation of genome integrity maintenance in cancer cells creates vulnerabilities that can be exploited therapeutically.

## OVERVIEW

The research focus of the group is on genome instability in mammalian cells and its impact on cancer and ageing. Sophisticated molecular mechanisms have evolved to prevent the excessive accumulation of DNA damage and thereby guard cells against genome instability. These mechanisms are often undermined in human cancers, allowing cancer cells to accumulate mutations at significantly increased rates. While such defects in genome maintenance mechanisms can contribute to and even drive cancer development, they can also provide a therapeutic opportunity if we can identify and understand the cancer-specific vulnerabilities they entail. Our research interest is to understand how mammalian cells deal with genotoxic stress assaults and how they coordinate genome maintenance mechanisms with other vital nuclear functions. To this end we combine state-of-the-art molecular biology and biochemistry with powerful advanced cell imaging technologies, in particular employing single cell chromatin perturbations, high resolution live cell imaging, automated quantitative microscopy and software-assisted image analysis. By targeted ablation of specific gene functions and high content analyses of DNA damage and repair markers we aim at identifying concealed regulators of the cellular response network to genotoxic stress and at understanding their role for genome maintenance.

## SELECTED CANCER RELATED PUBLICATIONS

Replication-Coupled Dilution of H4K20me2 Guides 53BP1 to Pre-replicative Chromatin. Pellegrino S, Michelena J, Teloni F, Imhof R, Altmeyer M. **Cell Rep.** 2017 May 30;19(9):1819-1831.

Cell Cycle Resolved Measurements of Poly(ADP-Ribose) Formation and DNA Damage Signaling by Quantitative Image-Based Cytometry. Michelena J, Altmeyer M. **Methods Mol Biol.** 2017;1608:57-68.

Inherited DNA lesions determine G1 duration in the next cell cycle. Lezaja A, Altmeyer M. **Cell Cycle**. 2018;17(1):24-32.

Liquid demixing of intrinsically disordered proteins is seeded by poly(ADP-ribose). Altmeyer M, Neelsen KJ, Teloni F, Pozdnyakova I, Pellegrino S, Grøfte M, Rask MB, Streicher W, Jungmichel S, Nielsen ML, Lukas J. **Nat Commun.** 2015 Aug 19;6:8088.

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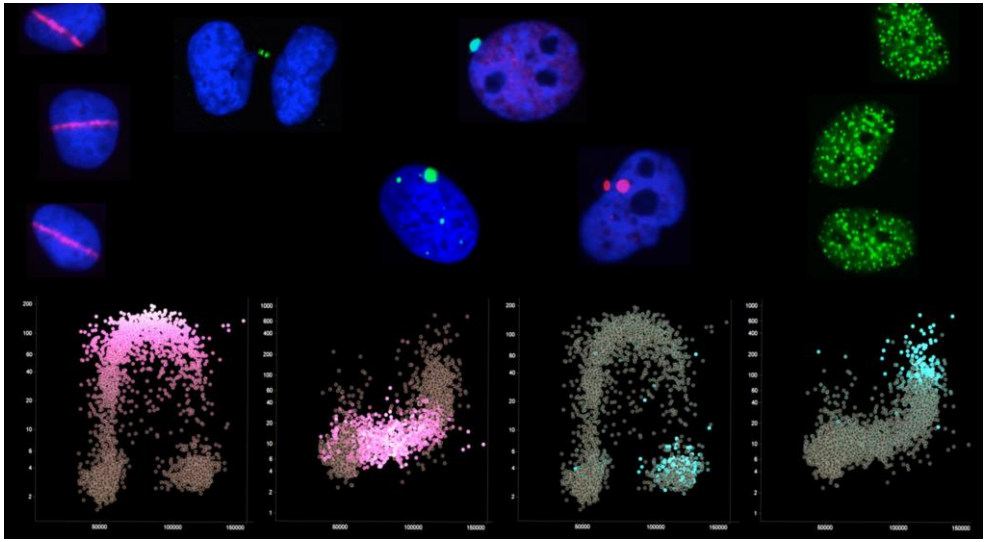
TRIP12 and UBR5 suppress spreading of chromatin ubiquitylation at damaged chromosomes. Gudjonsson T, Altmeyer M, Savic V, Toledo L, Dinant C, Grøfte M, Bartkova J, Poulsen M, Oka Y, Bekker-Jensen S, Mailand N, Neumann B, Heriche JK, Shearer R, Saunders D, Bartek J, Lukas J, Lukas C. **Cell**. 2012 Aug 17;150(4):697-709.



**Cellular responses to genotoxic stress are being analysed by our group in multiple dimensions at both the single cell and cell population level using quantitative image-based cytometry (QIBC).**