

Mechanisms of poly(ADP-ribosyl)ation and its role in genotoxic stress response

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Motivation and Aim: PARP1 catalyzes the posttranslational protein modification with poly(ADP-ribose) (PAR) of variable chain length and branching frequency. Poly(ADP-ribosyl)ation (PARylation) is involved in diverse cellular functions, such as DNA repair, transcription, and regulation of cell death, and contributes to various pathophysiological conditions. Importantly, PARP inhibitors are being employed and further developed in clinical cancer therapy. The overall aim of our research interests is to unravel the biochemical and cellular functions of PARP1-mediated PARylation during genotoxic stress response.

Methods and Algorithms: We employ a broad spectrum of state-of the art bioanalytic, biochemical, molecular biological, bio-imaging, and genetic techniques, including quantitative isotope dilution mass spectrometry, gene expression and proteomics analyses, high-end microscopy and automated image analysis, and genetic engineering via CRISPR/Cas9.

Results: This talk will give a brief overview of our latest published results dealing with biochemical and cellular mechanisms of PARylation, including its role in the regulation of the tumor suppressor protein p53 [1–3]. In addition the relevance of PARylation in patho-physiological mechanisms in *in vivo* mouse models will be highlighted [4, 5]. Furthermore, unpublished results will be presented.

Conclusion: PARylation represents a complex and versatile post-translational modification with key roles in genotoxic stress response on a cellular level and significant contributions to patho-physiological states on the organismic level. Thereby pharmacological interventions hold a high potential in terms of cancer treatment and other pathophysiological conditions.

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