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CENP-B dynamics at centromeres is regulated by a SUMOylation/ ubiquitination and proteasomal-dependent degradation mechanism involving RNF4/SNURF

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Centromeric protein B (CENP-B) is a major constituent of the centromere. It is a DNA binding protein that recognizes a specific 17-nt sequence present in the centromeric alphoid satellite repeats. CENP-B importance for centromere stability has only been revealed recently. In addition to its DNA binding properties, CENP-B interacts with the histone H3 variant CENP-A and CENP-C. These interactions confer a mechanical strength to the kinetochore that enables accurate sister chromatids segregation to avoid aneuploidy. Therefore, understanding the mechanisms that regulate CENP-B stability at the centromere is a major unresolved issue for the comprehension of centromere function. In this study, we show by an in vitro approach that CENP-B is a substrate for SUMO post-translational modifications on a specific lysine residue. We show that the mutation of this K modifies the CENP-B dynamic at centromeres and its stability through a SUMOylation/ubiquitination and proteasomal-dependent degradation mechanism involving the SUMO-Targeted Ubiquitin Ligase RNF4/SNURF. Hence, our study demonstrates that the SUMOylation of CENP-B is a major post-translational modification involved in centromere dynamics.

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Changes in polyphosphoinositides content in nuclear fraction of rat liver and thymus cells after the action of cisplatin

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In recent years the evidence was accumulated that phosphoinositide signaling pathways components and various enzymes necessary for polyphosphoinositides synthesis and degradation have been identified in the nuclear interior. The existence of a nuclear phosphatidylinositol metabolism is widely recognized. Nuclear phosphoinositides have been shown to play key roles in a wide range of nuclear events, including cell proliferation and differentiation, DNA repair, mRNA splicing and also in chromatin structure and transcription.

The levels of nuclear polyphosphoinositides are changed in response to various stimuli, suggesting that they may serve for regulating specific nuclear functions. These levels may vary also in response to variuos antitumor agents, such as cisplatin (cis-diaminedichloroplatinum). Its effectiveness seems to be due to unique properties of cisplatin, to forms multiple different DNA-platinum adducts. Although the cisplatin kills cancer cells by damaging DNA and inhibiting DNA synthesis, this antitumor agent in vivo action affects manifold metabolic pathways in nuclei including the lipid metabolism. From this point of view studying changes in polyphosphoinositides content in nuclei in rat liver and thymus cells after the action of cisplatin appears to be of definite interest.

The results of our investigations revealed the significant alterations in absolute quantity of total polyphosphoinositides as well as in content of individual phosphoinositides of rat liver and thymus cells nuclear fraction after the in vivo action of cisplatin. These alterations may play an important role in mechanisms of antitumour effect realization.

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