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TOPORS modulates H2AX discriminating genotoxic stresses

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H2AX plays an important role in chromatin reorganization implicated in DNA repair and apoptosis under various DNA damaging conditions. In this study, the interaction between TOPORS and H2AX was verified in vitro and in vivo using mammalian cell extracts exposed to diverse DNA damaging stresses such as ionizing radiation, doxorubicin, camptothecin, and hydrogen peroxide. In vitro assays for ubiquitination revealed that TOPORS functions as a novel E3 ligase for H2AX ubiquitination. TOPORS was found to be dissociated from H2AX proteins when cells were exposed to oxidative stress, but not replication-inducing DNA damaging stress. The protein stability of H2AX was decreased when TOPORS was ectopically expressed in cells, and oxidative stresses such as hydrogen peroxide and ionizing radiation induced recovery of the H2AX protein level. Therefore, these biochemical data suggest that TOPORS plays a key role in the turnover of H2AX protein, discriminating the type of DNA damaging stress. [This work was supported by Grant No. 2010T100100303 from the MKE, Republic of Korea.]

Key words : H2AX, camptothecin, doxorubicin, ionizing radiation, hydrogen peroxide.

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