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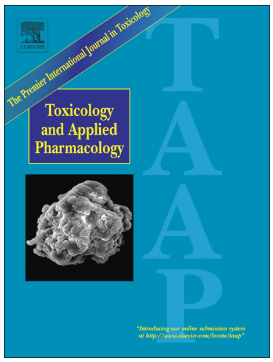

Solubility changes of promyelocytic leukemia (PML) and SUMO monomers and dynamics of PML nuclear body proteins in arsenite-treated cells

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Abstract

Promyelocytic leukemia (PML) and a suite of other proteins form nuclear bodies (NBs) where SUMOylation of PML and tumor suppression events occur in response to arsenite (As^{3+}) treatment. Soluble PML is rapidly modified to the insoluble form in response to As^{3+}, yet the relationship between the solubility change and nuclear localization of PML and PML-nuclear body (PML-NB) proteins remained elusive. We have investigated differences in the solubility change of well-known PML-NB proteins such as death-associated protein 6 (DAXX), SUMO, and PML in genetically engineered HEK293, and Jurkat and HL60 cells. The solubility of PML and SUMO2/3 monomers in RIPA solution decreased in 2 h in response to As^{3+}. Live image analysis of GFP-PML revealed that extranuclear PML was insoluble in RIPA irrespective of the As^{3+}-treatment and PML in PML-NBs, which was soluble in the untreated cells, was converted to insoluble forms by As^{3+}. The solubility of DAXX was not changed by As^{3+}, even though PML and DAXX co-localized completely in the subcellular compartments. Murine double mutant 2 (MDM2), which is known to interacts with intranuclear PML, did not affect the As^{3+}-induced solubility change of PML. These results indicate that As^{3+} selectively reorganizes PML and SUMO2/3 monomers into insoluble forms in PML-NBs, and then PML SUMOylation proceeds.

Keywords : PML; Arsenic; Solubility; SUMOylation; DAXX; MDM2