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Dynamic alteration in H3 serine10 phosphorylation is G1-phase specific during ionization radiation induced DNA damage response in human cells

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Histone mark, H3Serine10 phosphorylation plays a dual role in a cell by maintaining relaxed chromatin for active transcription in interphase and condensed chromatin state in mitosis. However, its cell cycle specific behaviour and regulation during DNA damage response is largely unexplored. In the present study, we demonstrate for the first time that H3Serine10 phosphorylation decreases specifically from irradiated G1-enriched cells irrespective of the damaging agent or the origin of cell line. Interestingly, the loss occurs predominantly from H3.3 variant which is a transcription activation mark like H3Serine10 phosphorylation itself, suggesting that the alteration might be implicated in transcription repression. Further, G1-cell cycle phase specific reversible loss of H3Serine10 phosphorylation in response to IR-induced DNA damage is mediated by opposing activities of phosphatase, MKP1 and kinase, MSK1 of the MAP kinase pathway. Furthermore, blocking of H3Serine10 dephosphorylation by MKP1 inhibition impairs DNA repair process and results in poor survival of cells. Collectively, our data proposes a pathway regulating G1 cell cycle phase specific reversible reduction of H3S10P on IR induced DNA damage and also raises the possibility of combinatorial modulation of H3S10P with specific inhibitors to target the cancer cells in G1-phase of cell cycle.

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