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Upstream Mechanism of p53 Activation: Ref1-modulation induced by Selenium

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Tumor suppressor protein p53 inducing protective cellular responses such as cell cycle arrest and DNA repair has been identified to be activated by various stresses either genotoxic damage or non-genotoxic damage. However, the mechanism of p53 activation has not clarified yet. In this study, we investigate the signaling pathway of p53 activation by selenomethionine (SeMet), identified as one of the organic selenium compounds that prevent cancer without DNA damage. Our data show that p53 activation is induced by altering redox status of p53 protein in SeMet-treated cells. Indeed, we demonstrate the relevance of redox factor (ref1) in the mechanism of p53 activation, showing that p53-dependent response in SeMet treatment was blocked by a dominant-negative Ref1. Furthermore DNA repair was significantly activated in SeMet-treated cells on p53-dependent pathway. These evidences suggest that p53-mediated DNA repair might be modulated under redox signaling in the presence of SeMet.

Keyword : Selenium, p53, Ref1