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SELENITE SUPPRESSES HYDROGEN PEROXIDE-INDUCED CELL APOPTOSIS THROUGH INHIBITION OF ASK1 AND ACTIVATION OF PI3-K/AKT PATHWAYS

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The relationship between selenium and signal molecules is not well elucidated yet. It was found that physiological concentration of selenite, less than 3 μM, reduced ASK1 activity and induced of PI3-Kinase/Akt pathways in HT1080 cells. Duration of these signal molecules by selenite was much longer than that by growth factors and other stresses. The longer duration time of these signal molecules may be important to maintain normal functions against stresses. Selenite increased cell proliferation through upregulation of Bcl-2 expression, mitochondrial membrane potential, ATP generation and glucose uptake mediated by PI3-Kinase pathway. High concentration of H_2O_2 increased an apoptotic signal molecule, ASK1, which resulted in Bcl-2 downregulation, membrane potential disruption, decreasing ATP and glucose uptake, and activation of caspases. However, an antiapoptotic signal molecule, Akt, was also activated by H_2O_2 but duration of its activation was much shorter. Selenite blocked apoptosis induced by H_2O_2, which was related to blocking ASK1 and further stimulating PI3-Kinase/Akt activities. Selenite blocked mitochondrial membrane potential disruption by 400 μM H_2O_2. Selenite also blocked caspase-9 and -3 activities and apoptosis induced by 500 μM H_2O_2 even after mitochondrial membrane disruption. These observations demonstrate that selenite increase cell proliferation and maintaining cell survival by activating the antiapoptotic signal and blocking the apoptotic signal.