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Glutathione depletion-induced chromosomal DNA fragmentation associated with apoptosis and necrosis.

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Abstract

Chromosomal DNA and mitochondrial dysfunctions play a role on mammalian cell death induced by oxidative stress. The major biochemical dysfunction of chromosome is the presence of an ordered cleavage of the DNA backbone, which is separated and visualized as an electrophoretic pattern of fragments. Oxidative stress provides chromatin dysfunction such as single strand and double strand DNA fragmentation leading to cell death. More than 1 Mb of giant DNA, 200-800 kb or 50-300 kb high molecular weight (HMW) DNA and internucleosomal DNA fragments are produced during apoptosis or necrosis induced by oxidative stress such as glutathione (GSH) depletion in several types of mammalian cells. Reactive oxygen species (ROS)-mediated DNA fragmentation is enhanced by polyunsaturated fatty acids including arachidonic acid or their hydroperoxides, leading to necrosis. Mitochondrial dysfunction on decrease of trans membrane potential, accumulation of ROS, membrane permeability transition and release of apoptotic factors during apoptosis or necrosis has been implicated. This review refers to the correlation of chromosomal DNA fragmentation and apoptosis or necrosis induced by GSH depletion, and the possible mechanisms of oxidative stress-induced cell death.

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