Elevation of apoptotic potential by anoxia hyperoxia shift in NIH3T3 cells.

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Abstract

Apoptosis has been hypothesized to be mediated through the induction of free radicals via oxidative pathway. In this study, we demonstrated the induction of cellular apoptosis by anoxia-hyperoxia shift, but not by anoxia or hyperoxia alone in NIH3T3 cells. The decrement of ROS by anoxia thus appears to be an essential early event leading to apoptosis. G1 arrest was detected in anoxia-treated cells, and postanoxic oxygen recovery could reverse this effect, and induce apoptosis. On analysis of the binding activity of AP-1, we found biphasic induction of binding ability in cells undergoing anoxia-hyperoxia shift. In the early stage of anoxia, a transitional increase of AP-1 binding activity was detected, which was reduced to the minimal levels after 24 h of anoxia. During the period of postanoxic hyperoxia treatment, the binding activity of AP-1 was reinduced and increased remarkably with time up to 24 h. These results were in accordance with the expressions of c-jun and c-fos proteins. Enhancement of poly(ADP-ribosyl)ation activities, especially ADP-ribosylation of histone H1 was detected in post-anoxic hyperoxia-treated cells, and cleavage of PARP and activation of caspase 3 were also observed in post-anoxic hyperoxia (recovery) treated cells, but not in anoxia-treated cells. We propose that the differential induction of c-jun/c-fos (AP-1) gene expressions and sequential activation of PARP activity are essential in anoxia/hyperoxia-induced apoptosis.