Abstract

The present study provides evidence that activated spleen lymphocytes from Walker 256 tumor bearing rats are more susceptible than controls to tert-butyl hydroperoxide (t-BOOH)-induced necrotic cell death in vitro. The iron chelator and antioxidant deferoxamine, the intracellular Ca2+ chelator BAPTA, the L-type Ca2+ channel antagonist nifedipine or the mitochondrial permeability transition inhibitor cyclosporin A, but not the calcineurin inhibitor FK-506, render control and activated lymphocytes equally resistant to the toxic effects of t-BOOH. Incubation of activated lymphocytes in the presence of t-BOOH resulted in a cyclosporin A-sensitive decrease in mitochondrial membrane potential. These results indicate that the higher cytosolic Ca2+ level in activated lymphocytes increases their susceptibility to oxidative stress-induced cell death in a mechanism involving the participation of mitochondrial permeability transition.

Keywords

cell death, free radicals, immune response, lymphopenia, mitochondrial permeability transition, spleen lymphocyte.