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The cathepsin B inhibitor, z-FA-FMK inhibits Jurkat T cell proliferation through oxidative stress

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The cathepsin B inhibitor, benzyloxycarbonyl-phenylalanine-alanine fluoromethyl ketone (z-FA-FMK) was found to readily inhibit Jurkat T cell proliferation at non-toxic concentrations. We showed that z-FA-FMK treatment leads to a decrease in intracellular glutathione (GSH) with a concomitant increase in reactive oxygen species (ROS) levels in Jurkat T cells. The inhibition of Jurkat T cell proliferation induced by z-FA-FMK were abolished by the presence of low molecular weight thiol-containing antioxidants such as GSH, N-acetylcysteine (NAC), L-cysteine but not with D-cysteine, which cannot be metabolized to GSH. These results suggest that the depletion of intracellular GSH is the underlying cause of z-FA-FMK-induced inhibition of cell proliferation in Jurkat T cells. Similarly, L-buthionine-sulfoximine (BSO) which blocks GSH biosynthesis also inhibits Jurkat T cell proliferation. In the presence of BSO, NAC has no effect on the inhibition of cell proliferation mediated by z-FA-FMK. Taken together, these results demonstrated that the inhibition of Jurkat T cell proliferation induced by z-FA-FMK is due to oxidative stress via the depletion of GSH.

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