Antiapoptotic effect of interleukin-2 (IL-2) in B-CLL cells with low and high affinity IL-2 receptors.

Abstract:

Although B chronic lymphocytic leukemia (B-CLL) cells express the alpha chain of the interleukin-2 (IL-2) receptor CD25, little is known about the effect of IL-2 on apoptosis in B-CLL cells. We have shown previously that stimulation of B-CLL cells with a CpG-oligonucleotide induces IL-2 high affinity receptors. In our current work, we analyzed the effect of IL-2 on apoptosis in resting B-CLL cells and in our model of activated B-CLL cells (CD25 high cells). IL-2 had modest antiapoptotic activity in resting B-CLL cells. In contrast, IL-2 was much more potent to prevent apoptosis in activated cells. Prevention of cell death was also associated with the maintenance of the mitochondrial membrane potential. While only limited regulation of apoptosis controlling proteins was observed in resting B-CLL cells, IL-2 had strong effects on MCL-1, Bcl-xl, and survivin expression and inhibited Bax cleavage in CD25 high cells. Interestingly, expression of Bcl-2 was reduced. Addition of IL-2 to activated B-CLL cells caused rapid phosphorylation of Akt, while IL-2 failed to significantly phosphorylate Akt in resting B-CLL cells. Pharmacological inhibition of Akt by LY294002 restored sensitivity of activated B-CLL cells to fludarabine. IL-2 might be an important survival factor in activated B-CLL cells and might contribute to disease progression by upregulation of several critical antiapoptotic proteins.