Mediators of interleukin-1 beta action Na(+)-K(+)ATPase in Caco-2 cells.

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Interleukin-1-beta has been demonstrated previously to reduce the activity and expression of the Na(+)-K(+) pump in the rat jejunum and colon. This work attempts to elucidate the signal transduction pathway underlying its effect using Caco-2 cells. IL-1beta reduced, in these cells also, the activity and expression of ATPase, in a dose and time-dependent manner. The down-regulatory effect of the cytokine on the ATPase was not evident, when p38 MAP kinase was inhibited, but appeared in presence of inhibitors of MEK and NFkappaB, although activation of NF-kappaB was demonstrated by western blot analysis. The effect of IL-1beta on the pump disappeared in the presence of indomethacin, a COX inhibitor. Exogenous PGE2 reduced the expression of the pump within 15 minutes, and this effect was still apparent when p38MAPK was inhibited. Curcumin, a JNK/AP-1 inhibitor, partially abolished the effect of IL-1beta on ATPase expression but did not interfere with the effect of PGE2. These results indicate that IL-1beta reduces the expression of ATPase independently of NFkB but, through a major pathway involving p38 and COX-2/PGE2, and another pathway involving JNK/AP1.

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