IL-1β reduces the activity and protein expression of Na⁺-K⁺-ATPase in rat kidney cells. The aim of the present study was to elucidate the signalling pathway involved, using the LLC-PK₁ cell line. In these cells IL-1β caused a time and concentration-dependent decrease in the protein expression of the Na⁺-K⁺-ATPase. Inhibition of extracellular signal-regulated kinase (ERK), nuclear factor-κB (NF-κB) and cyclooxygenase (COX), but not p38 mitogen-activated kinase (MAPK), abolished the effect of the cytokine on the pump. The activation of NF-κB by IL-1β was maximal at 20 min and declined thereafter. Inhibition of the transcription factor by pyrrolidinediethylthiocarbamate (PDTC) downregulated the ATPase. The effects of IL-1β on the pump and NF-κB were prevented by the COX inhibitor indomethacin. Exogenous PGE₂ reduced protein expression of the ATPase within 15 min, even in presence of an ERK inhibitor. It is concluded that IL-1β stimulates the mitogen and extracellular signal regulated protein kinase kinase/extracellular signal regulated protein kinase (MEK/ERK) pathway. This activates NF-κB, thus leading to increased COX-2 expression and PGE₂ release. PGE₂ in turn inhibits NF-κB and reduces the protein expression of Na⁺-K⁺-ATPase.

Keywords IL1-β - MEK - NF-κB - PGE₂ - Na⁺-K⁺-ATPase - LLC-PK₁