Regulation of Na, K-ATPase gene expression by steroid hormones

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Summary

To determine whether gluco- and mineralocorticoids have specific actions on Na, K-ATPase gene expression in vascular tissue, we used Northern blot analysis to compare the effects of dexamethasone (DEX) and aldosterone (ALDO) on Na, K-ATPase α1- and β1-subunit mRNA expression in cultured vascular smooth muscle cells from rat aortae. DEX at 10^{-6} M increased α1-mRNA level 2.5-fold at 24 h and β1-mRNA level 9.9-fold at 12 h. ALDO at 10^{-6} M increased α1-mRNA level 2.7-fold at 48 h and β1-mRNA level 10.9-fold at 6h. The half-maximal stimulation of both α1- and β1-mRNA levels occurred at a concetration of $5\text{-}7\times10^{-9}$ M DEX, whereas it occurred at a concentration of $2\text{-}3\times10^{-9}$ M ALDO. The glucocorticoid receptor antagonist RU38486 inhibited both DEX- and ALDO-mediated induction of β1-mRNA. The mineralocorticoid receptor antagonist spironolactone inhibited ALDO-mediated induction of β1-mRNA, whereas it had no effect on DEX-mediated induction of β1-mRNA. Removal of Na from the extracellular medium caused no effect on DEX-mediated induction of β1-mRNA, whereas it inhibited ALDO-mediated induction of β1-mRNA. Addition of a specific inhibitor of the Na/H exchange, ethylisopropylamiloride, had no effect on DEX-mediated induction of β1-mRNA, whereas it resulted in a significant inhibition of ALDO-mediated induction of β1-mRNA. We conclude that 1)both DEX and ALDO induce Na, K-ATPase α1- and β1-mRNA expression in a time- and dose-dependent manner; 2) DEX-mediated induction of β1-mRNA occurs only through glucocorticoid receptors, whereas ALDO-mediated induction of β1-mRNA occurs through both gluco- and mineralocorticoid receptors; and 3)DEX-mediated induction of β1-mRNA occurs through Na-independent mechanisms, whereas ALDO-mediated induction of β1-mRNA, at least in part, occurs through Na-dependent mechanisms, including stimulation of the Na/H exchange.