

Poster presentation

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## Inhibition of agonist-stimulated aldosterone production from adrenal zona glomerulosa cells by ANP is mediated by GC-A

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Atrial natriuretic peptide (ANP) is a potent inhibitor of agonist-induced aldosterone synthesis in zona glomerulosa (ZG) cells of the adrenal gland. Cellular ANP effects are mediated by two receptors: GC-A, a membrane guanylyl cyclase, and GC-C that lacks guanylyl cyclase activity. To identify which one of these two receptors is involved in inhibitory pathway of aldosterone production we developed a new model of isolation and primary culture of mouse ZG cells. Aldosterone concentration in the blood was not different in wild type and GC-A knockout mice. ANP (10 nM) significantly inhibited basal, forskolin, and Angiotensin II-stimulated aldosterone production from wild type mice, while in GC-A knockout mice ANP had no inhibitory effect on aldosterone production. Inhibition of forskolin or ACTH stimulated aldosterone production by ANP was connected with increased concentration of cGMP, stimulation of cGMP-stimulated phosphodiesterase (PDE2), and decrease of intracellular cAMP content. IBMX and the PDE2-selective inhibitor MEP-1 completely prevented ANP inhibitory effect on cAMP-stimulated aldosterone production. In contrast, ANP-dependent inhibition of Ang II-stimulated aldosterone production was not connected with PDE2 or PKG activity indicating that other cGMP-dependent mediator(s)/mechanism(s) are involved in regulation of Ang II-stimulated aldosterone production from ZG cells by cGMP.

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