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ROLE OF ARACHIDONIC ACID METABOLISM IN MOUSE  
LEYDIG CELL TESTOSTERONE PRODUCTION

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## ABSTRACT

Like many other endocrine glands, the suspected functional significance of the arachidonic acid metabolism in the Leydig cells has been searched. It has been shown that prostaglandin F<sub>2α</sub>, a cyclo-oxygenase metabolite of arachidonic acid suppresses plasma testosterone in the male rats and its inhibitory action on Leydig cell response to gonadotropin stimulation is demonstrated in vitro. The modulating role of the endogenous prostaglandin on Leydig cell response to gonadotropic stimulation has been repeatedly supported by experiments using cyclo-oxygenase inhibitors which are shown to potentiate the steroidogenic response to gonadotropic stimulation both in vivo and in vitro. The existence and involvement of lipoxygenase metabolite(s), product(s) of the other known metabolic pathway of cellular arachidonic acid metabolism is demonstrated in this study.

Mouse Leydig cells were isolated and purified by Ficoll density gradient centrifugation. The calibrated Leydig cell suspensions, in a balanced salt solution were incubated in a constant shaking water bath under the atmosphere of 95%O<sub>2</sub>/5%CO<sub>2</sub> with gonadotropin, in the presence or absence of arachidonic acid (AA) and/or a known lipoxygenase inhibitor, nordihydroguaiaretic (NDGA). Mice were treated with indomethacin were also used in this study. Arachidonic acid (dose up to 20 μM) caused a mini-

imum but significant elevation of basal testosterone production in the medium. Addition of NDGA ( 12.5 to 50  $\mu\text{m}$  ) into the medium caused more increase in testosterone production over the stimulatory effect of AA and indomethacin, this effect of NDGA is not dose dependent. The additive effect of NDGA on the basal steroidogenic action of AA and indomethacin is attributable to the nonspecific cyclo-oxygenase inhibitory activity of the NDGA.

In the hCG-stimulated response, AA dose dependently increased the steroidogenic response to hCG ( 10 mIU ) stimulation and the production of testosterone was further increased in mouse treated with indomethacin. NDGA in the contrary dose dependently suppressed testosterone production in mouse Leydig cells from both the controls and mice treated with indomethacin. The maximum suppressive dose of NDGA could be dose dependently overcome by AA. Suggesting that the lipoygenase in the Leydig cells may be the site of action of NDGA. We therefore conclude that the metabolites of arachidonic acid, both from cyclo-oxygenase and lipoygenase pathway may be functioning as intracellular regulators of gonadotropic hormone in the Leydig cells.

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