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JOURNAL ARTICLE

# Interleukin-1beta regulates nitric oxide production and gamma-glutamyl transpeptidase activity in sertoli cells

S. B. Meroni, A. M. Suburo and S. B. Cigorraga
Centro de Investigaciones Endocrinologicas (CEDIE) Hospital de Ninos "R Gutierrez," Buenos Aires, Argentina.

Several cytokines have been involved in the regulation of Sertoli cell function. Further investigations are required to elucidate the role of interleukin-1beta (IL1beta) in Sertoli cell physiology. Twenty-day-old rat Sertoli cell cultures were used to investigate a possible role of IL1beta in the regulation of gamma-glutamyl transpeptidase (gammaGTP) and to elucidate the signaling pathway utilized by this cytokine. GammaGTP is a membrane-bound enzyme that has been involved in amino acid transport across the plasma membrane and in protection from oxidative stress through its importance in the regulation of glutathione levels. Previous studies suggested that IL1beta stimulates NO biosynthesis in other cell types. Therefore, we investigated whether IL1beta modified the level of nitrite, a stable metabolite of NO, in Sertoli cells. Dose-response curves to IL1beta for gammaGTP activity and nitrite production were observed. The increments observed in gammaGTP activity and nitrite production were partially and completely blocked by simultaneous treatment with the NO synthase inhibitor aminoguanidine. Treatment of Sertoli cell cultures with the NO donors sodium nitroprusside and S-nitroso-N-acetylpenicillamine resulted in an increase in gammaGTP activity. The presence of neural, endothelial, and inducible isoforms of NO synthase (NOS) was investigated by a immunohistochemical technique using specific antibodies. The 2 constitutive isoforms were present under basal conditions, and the inducible protein appeared in IL1beta-treated cultures. Finally, translocation of NF-kappaB p65 subunit to the nucleus in IL1beta-treated cultures was observed. These findings suggest that the action of IL1beta on Sertoli cell gammaGTP activity is partially mediated via activation of NF-kappaB and increments in iNOS and cellular production of NO.



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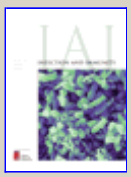



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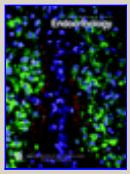

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