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JOURNAL ARTICLE

Effects of luteinizing hormone, follicle-stimulating hormone, and epidermal growth factor on expression and kinase activity of cyclin-dependent kinase 5 in Leydig TM3 and Sertoli TM4 cell lines

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We examined the effects of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and epidermal growth factor (EGF) on the expression and kinase activity of cyclin-dependent kinase 5 (Cdk5) in Leydig TM3 and Sertoli TM4 cell lines. Hormonal regulation of the expression and activity of Cdk5 by using normal and hypophysectomized rat testes was also investigated to elucidate its role. Cdk5 levels and kinase activity were significantly elevated in TM3 cells that were grown in the presence of 7.5% serum, EGF, or LH and were associated with an increase in testosterone production compared with controls. These increases were accompanied by an increase in proliferation of TM3 cells after treatment with serum or EGF but not with LH suggest that Cdk5 may be involved in cellular differentiation that is induced with LH treatment. In contrast, the presence of neither serum, EGF, nor FSH had a significant effect on Cdk5 activity levels in the Sertoli TM4 cell line, and there was no correlation with proliferative activity or transferrin levels. A significant decrease in Cdk5 expression and activity were noted in rat testis after hypophysectomy compared with normal rat testis and is associated with a simultaneous decrease in testosterone and transferrin levels. Immunohistochemical analysis revealed that Cdk5 was strongly expressed in the nuclei and cytoplasm of Leydig cells, Sertoli cells, spermatogonia, and peritubular cells of normal adult rat testis. After hypophysectomy, the pattern of Cdk5 staining differed markedly from that in normal rat testis and a profound reduction in staining of Cdk5 was observed in each tubule. Our results suggest that LH and EGF influence and modulate Cdk5 expression and activity in Leydig TM3 cells and may, conceivably, be involved in signal transduction cascades that are initiated by hormones or growth factors. Cdk5 in Sertoli TM4 cells is likely to possess some constitutive functions that are not affected by the cells' proliferation state. Moreover, Cdk5 is probably involved in the constitutive and hormonally stimulated activities of the rat testis, in addition to its involvement in cell proliferation.

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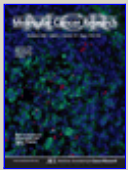
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