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JOURNAL ARTICLE

Testosterone decreases 3beta-hydroxysteroid dehydrogenase-isomerase messenger ribonucleic acid in cultured mouse Leydig cells by a strain-specific mechanism

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We previously reported a strain-related difference in basal 3beta-hydroxysteroid dehydrogenase-isomerase (3betaHSD) activity in response to testosterone in cultured Leydig cells. The data suggested that the response to testosterone was androgen receptor mediated and that testosterone was acting via a trans-acting factor distal to the androgen receptor to regulate Leydig cell basal 3betaHSD activity.

This study was designed to determine whether the previous reported strain-related difference in basal 3betaHSD activity in response to testosterone was due to a difference at the 3betaHSD protein and/or at the mRNA level. In C57BL/6J Leydig cells, 2.0 microM testosterone significantly decreased basal 3betaHSD immunoreactive mass by day 6 in culture. Treatment with 2.0 microM testosterone and 2.0 microM hydroxyflutamide, an androgen receptor antagonist, negated the inhibitory effect of testosterone on C57BL/6J 3betaHSD immunoreactive mass. Treatment with 2.0 microM testosterone also significantly decreased 3betaHSD mRNA content in C57BL/6J Leydig cells, which was detectable on day 3 in culture. In contrast to Leydig cells from C57BL/6J mice, Leydig cells from C3H/HeJ mice were not susceptible to the inhibitory effect of testosterone on 3betaHSD. Treatment with 2.0 microM testosterone had no detectable effect on C3H/HeJ 3betaHSD immunoreactive mass or mRNA content at any time point in culture. These data indicate that the testosterone-induced loss of basal 3betaHSD activity in C57BL/6J Leydig cells can be accounted for by the loss of 3betaHSD immunoreactive mass, which is preceded by the loss of 3betaHSD mRNA, and that the strain-related difference in the regulation of 3betaHSD is present at all three levels. Thus, the putative trans-acting factor involved in the mechanism whereby testosterone decreases basal 3betaHSD is likely to regulate the amount of 3betaHSD mRNA.

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