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JOURNAL ARTICLE

Initial predominance of the oxidative activity of type I 11beta-hydroxysteroid dehydrogenase in primary rat Leydig cells and transfected cell lines

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Glucocorticoids suppress testosterone production in Leydig cells. The level of glucocorticoid action is set within the Leydig cell by the number of glucocorticoid receptors and by the activity of 11beta-hydroxysteroid dehydrogenase (11betaHSD). This enzyme acts either as an oxidase inactivating glucocorticoid or as a reductase amplifying its action. It is currently unknown whether extracellular conditions might cause 11betaHSD oxidative and reductive activities in Leydig cells to change inversely or independently. The aim of the present study was to determine whether extracellular conditions set in vitro by various culture time and media components, such as glucose and pyruvate, affect the relative rates of 11betaHSD oxidation and reduction. Primary rat Leydig cells and cell lines (COS1 and CHOP cells) transfected with 11betaHSD-I complementary DNA (cDNA), were incubated with 25 nmol/L (physiologic range) or 500 nmol/L (stress range) concentrations of radiolabeled substrates, corticosterone or 11-hydrocorticosterone, for 0 to 24 hours. Oxidative activity predominated over reductive activity under initial conditions when product formation increased linearly with time. For example, in Dulbecco's modified Eagle medium/F12 medium (containing 5.5 mmol/L glucose), the peak ratio of oxidation to reduction (with 1 denoting equivalence of oxidative and reductive activities) was 5.5 in rat Leydig cells, 19.7 in COS1 cells, and 20.8 in CHOP cells. Glucose stimulated reductive activity but did not change the predominant direction of 11betaHSD catalysis at earlier times. In COS1 cells transfected with 11betaHSD-I cDNA, oxidative activity rapidly increased during the first 2 hours of the incubation, then gradually decreased while reductive activity increased steadily. The relative ratio of oxidation to reduction rapidly declined to less than 0.5 at 6 hours, and thus the favored direction of catalysis changed from oxidation to reduction. However, in transfected CHOP cells, 11betaHSD oxidative activity rapidly increased during the first 2 hours and continued to increase for 24 hours. The ratio of oxidative to reductive activity rapidly declined but kept above 1 in CHOP cells for 24 hours, and the favored direction of catalysis remained predominantly oxidative. These results revealed that 11betaHSD-I is a predominant oxidase initially in Leydig cells and 2 cell lines, and that the oxidative activity is gradually lost over time. The data suggest that type I 11betaHSD is a predominant oxidase in Leydig cells in vivo.

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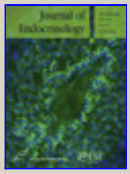

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C Chandras, T E Harris, A L. Bernal, D R E Abayasekara, and A E Michael
PTGER1 and PTGER2 receptors mediate regulation of progesterone synthesis and type 1 11{beta}-hydroxysteroid dehydrogenase activity by prostaglandin E2 in human granulosa lutein cells
J. Endocrinol., September 1, 2007; 194(3): 595 - 602.
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V. Sharp, L. M Thurston, R. C Fowkes, and A. E Michael
11{beta}-Hydroxysteroid dehydrogenase enzymes in the testis and male reproductive tract of the boar (Sus scrofa domestica) indicate local roles for glucocorticoids in male reproductive physiology
Reproduction, September 1, 2007; 134(3): 473 - 482.
[Abstract] [Full Text] [PDF]

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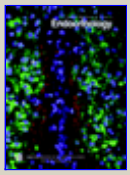
N. Sunak, D. F Green, L. R Abeydeera, L. M Thurston, and A. E Michael
Implication of cortisol and 11{beta}-hydroxysteroid dehydrogenase enzymes in the development of porcine (Sus scrofa domestica) ovarian follicles and cysts
Reproduction, June 1, 2007; 133(6): 1149 - 1158.
[Abstract] [Full Text] [PDF]



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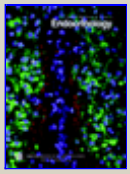
K. C. Jonas, C. Chandras, D. R. E. Abayasekara, and A. E. Michael
Role for Prostaglandins in the Regulation of Type 1 11{beta}-Hydroxysteroid Dehydrogenase in Human Granulosa-Lutein Cells
Endocrinology, December 1, 2006; 147(12): 5865 - 5872.
[Abstract] [Full Text] [PDF]



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R.-S. Ge, Q. Dong, E.-m. Niu, C. M. Sottas, D. O. Hardy, J. F. Catterall, S. A. Latif, D. J. Morris, and M. P. Hardy
11{beta}-Hydroxysteroid Dehydrogenase 2 in Rat Leydig Cells: Its Role in Blunting Glucocorticoid Action at Physiological Levels of Substrate
Endocrinology, June 1, 2005; 146(6): 2657 - 2664.
[Abstract] [Full Text] [PDF]

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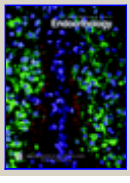
J. R. Seckl, N. M. Morton, K. E. Chapman, and B. R. Walker
Glucocorticoids and 11beta-Hydroxysteroid Dehydrogenase in Adipose Tissue
Recent Prog. Horm. Res., January 1, 2004; 59(1): 359 - 393.
[Abstract] [Full Text]



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G.-M. Wang, R.-S. Ge, S. A. Latif, D. J. Morris, and M. P. Hardy
Expression of 11{beta}-Hydroxylase in Rat Leydig Cells
Endocrinology, February 1, 2002; 143(2): 621 - 626.
[Abstract] [Full Text] [PDF]