Proc 3rd Symp Kor Soc Dev Biol, Feb 6, 1998, pp. 10-12.

Distribution and Its Putative Significance of 20α-Hydroxysteroid Dehydrogenase (20α-HSD) Aactivity in The Rat Ovary and Placenta

Hwan Hoo Seong
National Livestock Research Institute, RDA, Suweon 441-350

Introduction

20α-Hydroxysteroid dehydrogenase (20α-HSD) is an enzyme that catabolizes progesterone to 20α-dihydroprogesterone (20α-OHP), which is recognized to be a biologically inactive steroid. This enzyme is provotal in the ovarian function in the rodent, and its physiological function and regulation are well documented. The enzyme is reported to be present in other steroid-producing tissues such as the testis and adrenal gland. Since progesterone is a precursor of biologically active steroid hormones such as androgen, estrogen and corticoids, the enzyme may be involved in regulating their secretion. The placenta produces various kinds of steroids such as progestins, androgens and estrogens. 20α-HSD activity has been reported in the human placenta at term, and the enzyme may function to reduce the levels of peripheral progesterone at term. we have found recently that the enzyme is expressed in placental tissue continuously from early to late pregnancy in the rat.

In this reported, we describe the molecular nature of rat 20α-HSD and discuss its distribution and physiological roles in the ovary and placenta.

Molecular characteristics of 20α-HSD in the rat.

20α-HSD plays a critical role in the maintenance of the unique estrous cycle of rodents. The importance of 20α-HSD in reproduction has prompted interest in the mechanism of regulation of the enzyme activity. Partial purification of rat ovarian 20α-HSD was reported by Mori and Wiest (1979), who detected a single enzyme. In this study, for purification of the enzymes from rat ovarian cytosol, three steps of chromatography were employed.

Column chromatography of the cytosol fraction on DEAE-Toyopearl anion exchange column, revealed two pearks of 20α-HSD activity at different ionic strengths, suggesting that there are two distinct enzyme molecules with different electrical charges. These fractions were designated HSD-1 and HSD-2, respectively. The purified HSD-1 and HSD-2 were analyzed by SDS polyacrylamide gel electrophoresis under reducing conditions and their molecular weights were both estimated to be 33kd. Thus,

homogeneous HSD-1 and HSD-2 were obtained by these purification steps, and used for further analysis and antibody production.

Distribution and activities of two 20α-HSD dehydrogenase isozymes in rat ovaries

The expression of activity of each isozyme was investigated in ovaries that contained a single generation of corpora lutea during pseudopregnancy. The total activity of cytosolic 20α-HSD was lower in the ovaries of these pseudopregnant rats than in ovaries containing multiple generations of corpora lutea. In normal pseudopregnancy, HSD-1 activity was low on day 5 and 9 and increased markedly on day 15, whereas HSD-2 was lower than HSD-1 and did not vary throughout pseudopregnancy. However, on days 5 and 9 of continuos-light pseudopregnancy, low activity of HSD-1 only was detected; by day 15, HSD-1 activity had increased sixfold and HSD-2 activity could be detected.

Histochemically, the activity that could be demonstrated biochemically in the proestrous rat ovaries were largely found in corpora lutea. Interestingly, a few large follicles showed strong 20α-HSD activity in the thecal cells, however, undetected in the granulosa cells. These results support the hypothesis that 20α-HSD in the thecal cell of follicle may play an important role in the follicle maturation and the regulation of ovarian function by metabolizing at to the inactive steroid.

Expression of 20α-HSD activity in rat placenta during normal pregnancy

There is a reciprocal relationship between progesterone and 20α-dihydroprogesterone during pregnancy. The activity of 20α-HSD in the ovary was on day 2 and then it decreased to a minimum value between days 10 and 18. On day 20, the activity began to increase, and a burst increase was observed on day 21. Cytosolic 20α-HSD activity was measured in the placental tissue during normal pregnancy. After removal of the embryo, remaining tissues were used as placenta on days 8, 9, 10 and 11. After day 12 of pregnancy, the enzyme activities were measured separately in the yolk sac and the remaining tissues(decidual cells and trophoblasts). Placental activity increased rapidly on day 21. Interestingly, the enzyme activity increased on days 8, 9 and 10, and then decreased to undetectable levels on day 11. The activity in the yolk sac was undetectable on day 12, then it increased on day 14 and the level was maintained until day 21, in the ramaining tissue of the placenta, the enzyme was barely detectable until day 20, and then increased rapidly on day 21. Thus the expression of 20α-HSD in the placenta may contribute to adjustment of the local envirnment of the feto-placental unit during pregnancy, because serum progesterone was maintained at a high level during this period. 20α-HSD seems to be a factor for the survival or differentiation of cells by adjusting the local steroidal environment.

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