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An Inverse Linear Correlation between Uterine and Ovarian Levels of Ornithine Decarboxylase and S-Adenosylmethionine Decarboxylase in the Rat (41215)

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Abstract. The activities of the enzymes ornithine decarboxylase and *S*-adenosylmethionine decarboxylase at 9:00 AM were determined in the uterus and ovary of rats as a function of the estrous cycle. The uterine levels of both enzymes were highest at proestrus and lowest at estrus. On the other hand, the ovarian levels of both enzymes were highest at estrus and lowest at proestrus. Plotting the logarithms of each of the enzyme levels in the ovary versus the corresponding logarithm of the same enzyme observed in the uterus showed a linear correlation with a negative slope both during the estrous cycle and during proestrus alone. The changes in the activities of both enzymes in the uterus could be directly correlated with the growth of this organ observed during the estrous cycle.

The levels of ornithine decarboxylase (ODC), the rate-limiting enzyme in the biosynthesis of polyamines, are increased in tissues stimulated by various hormones (1). Polyamines have been suggested to be involved in growth through the stimulation of RNA and protein synthesis (2).

The injection of 17β-estradiol into ovariectomized (3) or immature (4) rats stimulates ODC in the uterus. Changes in polyamine contents and ODC activities in the rat uterus have been related to the estrous cycle (5). On the other hand the change of ODC activities in the ovary is associated with the release of LH from the pituitary during the estrous cycle (6). The injection of LH or HCG also stimulates ODC in the ovaries of the rats (7–9).

The preovulatory surge of gonadotropins in rats is accompanied by rapid changes in the peripheral levels of ovarian steroids. On the afternoon of proestrus the elevated estradiol concentration declines as the plasma levels of LH and FSH rise (10, 11).

Therefore it is of interest to determine the correlation of ODC and SAMDC activities between ovary and uterus during the normal estrous cycle.

Materials and Methods. *Animals and chemicals.* Intact Fischer 344/CR rats (Charles River Breeding Laboratories, Wilmington, Mass.) weighing 150 to 240 g were used in these studies. The animals were housed in hanging plastic cages and received food (NIH 07 Chow) and water *ad libitum*. The stage of estrous cycle in each animal was determined by histological examination of a vaginal smear. DL-[*carboxyl*-1-^{14}C]Ornithine monohydrochloride (sp act 45.0 mCi/mmole) and [*carboxyl*-1-^{14}C]adenosyl-L-methionine (sp act 55 mCi/mmole) were purchased from New England Nuclear Corporation (Boston, Mass.).

Tissue preparation. The rats were generally killed by decapitation at 9:00 AM. The uterus and ovaries were quickly removed, weighed, minced, and homogenized in 5 vol of ice-cold solution containing 0.25 *M* sucrose, 0.01 *M* sodium phosphate buffer, pH 7.0, 0.2 *M* pyridoxal phosphate, 0.5 m*M* dithiothretiol, and 0.1 m*M* EDTA. The samples were then centrifuged at 105,000*g* at 4°C for 60 min. The supernatants were used for enzyme assays. All procedures were run at 0 to 4°C.

Enzyme assays. ODC was assayed by our recent modification (17) of the method of Russell and Snyder (12). SAMDC was assayed by a modification (17) of the method

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of Pegg and Williams-Ashman (13). The specific activity of each enzyme was expressed as picomoles CO_2 liberated per milligram protein per 30 min.

Results. The average ODC and SAMDC levels in rat uterus and ovaries as a function of the estrous cycle are shown in Table I. Uterine ODC activity was lowest at estrus, increased markedly during diestrus II and peaked at proestrus; the ODC level at proestrus was six times that observed at estrus. The transition from proestrus to estrus was marked by a rapid decline in the uterine ODC level (Table I). On the other hand, the ODC levels in the ovary were lowest during proestrus, increased markedly from proestrus to estrus, and were followed by a gradual decline during diestrus I, and diestrus II to proestrus. SAMDC levels in the uterus and ovary tended to parallel the ODC levels in the same tissue (Table I). A significant correlation was observed between individual ODC and SAMDC activities in both the uterus and ovary ($r = 0.82, P < 0.001$; $r = 0.52, P < 0.01$, respectively). When the individual ovarian ODC activities were plotted versus the corresponding ODC levels in the uterus in a log–log plot, a significant inverse correlation was observed ($r = -0.865, P < 0.001$) (log $y = -0.93 \log x + 4.09$) (Fig. 1). Similarly, plotting the individual ovarian SAMDC levels versus their corresponding uterine

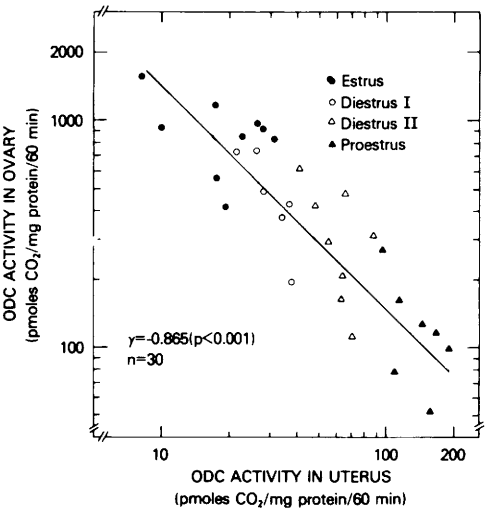

FIG. 1. Correlation between ODC activity in the uterus and in the ovary during the estrous cycle.

SAMDC levels on a log–log plot showed a significant inverse correlation in the enzyme levels of the two tissues ($r = -0.56, P < 0.05$) (log $y = -0.3 \log x + 2.36$) (Fig. 2). Plotting the individual enzyme levels in the uterus versus the reciprocal of the corresponding enzyme level in the ovary of the same animal also led to significant linearity ($r = 0.791$ and 0.453 for ODC and SAMDC, respectively). The changes in uterine weight during the four periods of the estrous cycle in the rat paralleled the changes observed in ODC activity. A significant correlation was

TABLE I. ODC AND SAMDC ACTIVITIES IN THE UTERUS AND OVARY OF THE RAT DURING THE NORMAL ESTROUS CYCLE

Stage of cycle		Wet weight[a] (mg %)	ODC[b]	SAMDC[b]
Uterus				
Proestrus	(7)[c]	341.1 ± 45.7[d]	69.6 ± 6.1	135.5 ± 16.3
Estrus	(9)	212.5 ± 14.2	10.5 ± 1.4	57.4 ± 7.9
Diestrus I	(6)	187.6 ± 15.6	15.8 ± 1.3	100.5 ± 13.2
Diestrus II	(8)	256.2 ± 22.2	31.4 ± 2.6	97.5 ± 6.4
Ovary				
Proestrus	(7)	15.9 ± 1.0	64.5 ± 13.3	50.9 ± 3.4
Estrus	(9)	15.1 ± 0.9	452.7 ± 56.4	76.8 ± 6.2
Diestrus I	(6)	16.1 ± 1.3	248.0 ± 43.3	54.6 ± 4.6
Diestrus II	(8)	18.2 ± 0.9	162.4 ± 30.1	59.0 ± 4.7

[a] Relative organ weights (organ weight/100 g body wt).
[b] pmoles CO_2 formed/mg protein/30 min.
[c] Number of rats per group.
[d] Mean ± SE.

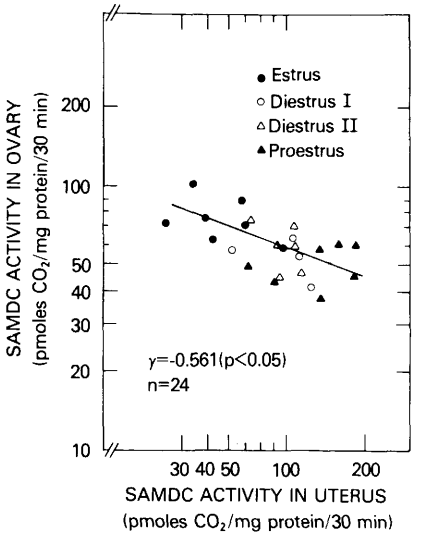

FIG. 2. Correlation between SAMDC activity in the uterus and in the ovary during the estrous cycle.

observed between the individual uterine ODC or SAMDC levels and the wet weight of the uterus throughout the estrous cycle ($r = 0.70, P < 0.001; r = 0.52, P < 0.02$, respectively). No correlation could be observed between the weights of the ovaries and the levels of ODC or SAMDC (Table I).

Discussion. The present studies have shown significant inverse linear correlations between the 9:00 AM levels of ODC and SAMDC in the uterus and their corresponding levels in the ovaries of rats. The uterine levels of both enzymes were highest at proestrus and lowest at estrus. The high uterine activity of ODC at proestrus is in agreement with other biochemical observations (4, 5); uterine wet weight, polyamine levels, and polysome contents are also at their maximum during proestrus and at a minimum at estrus during the estrous cycles. The present report indicates a significant correlation between the uterine levels of ODC and SAMDC during the estrous cycle. However, Russell and Taylor observed that following the administration of estrogen to female rats, the adaptive response of uterine SAMDC was quite large while that of ODC was relatively small (15). The differences between the two sets of observations are difficult to reconcile. The changes in the activities of ODC and SAMDC in the uterus could be directly correlated with growth during estrus. However, the changes in the enzyme activities in the ovaries could not be correlated with ovarian growth during the estrous cycle. ODC activity in the ovary is markedly increased during the relatively large growth of this organ seen during pregnancy (16).

SAMDC in the ovary was not altered by the injection of LH or HCG (7). However, ovarian ODC activity was increased 4 hr after the injection of LH and HCG. Ovarian ODC levels appear to reflect the plasma levels of LH (6, 10, 11). The peak of both ovarian ODC and plasma LH in rats is observed at proestrus; the peak of ODC activity appeared 3 to 4 hr following the peak of LH (6, 10, 11). It is known that on the afternoon of proestrus the elevated plasma levels of estradiol decline as the surge of LH occurs (10, 11, 14). The present results are consistent with earlier findings that the uterine contents of ODC and polyamines are a function of plasma estradiol levels (5). Therefore, the inverse correlation of the ODC activity in the uterus and ovary during the estrous cycle appears to result from the preovulatory surge of LH which induces ODC in the ovary and from the corresponding drop in plasma estradiol, the hormone regulating ODC in the uterus. This finding indicates a harmonized regulation of ODC and SAMDC activities in the uterus and ovary during the normal estrous cycle.

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