

The time of development during which these changes occur is one of cell diversification, including differential decreases in the mitotic rates of different cell types. The relation between the histone changes and these events may be clearer when we know whether specific late histone forms are confined to specific cell types or specific regions of the genome (or both). The persistence of the early histone forms after the synthesis ceases raises the question of where these forms reside in subsequently synthesized chromatin. The answer to this question would reveal much about the assembly of chromatin during DNA replication.

There are few clues to the mechanisms of these developmental modulations in histone synthesis. Although messenger RNA (mRNA) that codes for histones begins to be synthesized within a few cell divisions after fertilization (18), actinomycin D prevents neither histone synthesis nor morphogenesis until the blastula stage (5, 19). In the presence of actinomycin, therefore, histone synthesis represents translation of a store of histone mRNA in the unfertilized egg (19, 20). Since at least two of the switches in histone synthesis (X-off and H2A_β-on) occur well before the stage at which development becomes sensitive to actinomycin, these particular switches either are under translational control or do not occur in the presence of actinomycin and are not needed to reach a morphologically normal blastula stage. In contrast, the synthesis of the γ and δ forms of H2A and H2B does not begin until a stage when mRNA synthesis is required for further development. Whether the synthesis of these forms depends on new transcription remains to be determined.

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- The histone nomenclature used is that adopted at the Ciba Foundation symposium on structure and function of chromatin, 1975, in which H1 = f1, H2A = f2a, H2B = f2b, H3 = f3, and H4 = f2a1.
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Prostaglandins in Rabbit Blastocysts

Abstract. *Rabbit blastocysts recovered at 144 hours post coitum contained the prostaglandins F and E-A. We suggest that one or more of these prostaglandins act as mediators in blastocyst steroidogenesis. (In another study we have demonstrated steroidogenesis in rabbit blastocysts.)*

There is strong evidence that steroid hormones are synthesized by morulae and blastocysts of rats (1), mice (2), hamsters (3), and rabbits (4, 5). Various approaches could be used to obtain more information about steroidogenesis in preimplantation embryos. Since it has been suggested by a number of authors (6) that prostaglandins (PG's) act as mediators in steroidogenesis, the present study was made to determine whether rabbit blastocysts contain PG's.

Sexually mature female New Zealand rabbits (Langshore Rabbitry, Augusta, Mich.) were mated and immediately thereafter injected intravenously with 50 international units (I.U.) of human chorionic gonadotropin (hCG) to ensure induction of ovulation. At 144 hours post coitum, the rabbits were killed and their uteri excised and flushed with 5 ml of saline (0.9 percent NaCl) in order to recover blastocysts. The

saline contained indomethacin (10 μ g/ml) to inhibit possible PG synthesis while handling blastocysts. The blastocysts were washed three times in saline-indomethacin and were then homogenized in saline-indomethacin, extracted with a mixture of ethyl acetate, isopropanol, and 0.1N HCl (3:3:1) according to Orczyk and Behrman (7), and radioimmunoassayed without chromatographing the extracts. For the assay of PGF an antibody previously described (8) was used. A second antibody used reacts equally with PGE and PGA, but does not cross-react with PGF; thus the PG measured in this assay is referred to as PGE-A.

In addition to blastocysts, uterine flushings from rabbits that were 144 hours pregnant or 144 hours pseudopregnant (injected with 50 I.U. of hCG to induce ovulation) were similarly extracted and assayed.

Table 1. Prostaglandins (PG's) F and E-A in groups of rabbit blastocysts recovered at 144 hours post coitum.

Sample No.	Rabbit No.	PG's per sample (ng)		Blastocysts per sample (No.)
		F	E-A	
1	1, 1a	8.6	7.3	15
2	2	8.6	8.7	10
3	3	9.7	7.0	11
4	4	7.3	3.8	7
5	5	5.8	6.7	5
6	6	1.3	2.7	8

Table 2. Prostaglandins (PG's) F and E-A in uterine flushings of pregnant (P) and pseudopregnant (PSP) rabbits at 144 hours after an ovulation-inducing injection.

Rabbit No.	PG's from both uteri (ng)	
	F	E-A
4 (P)	10.8	5.6
5 (P)	7.0	5.9
6 (P)	2.6	2.6
7 (PSP)	3.9	3.8
8 (PSP)	4.9	7.0

Saline-indomethacin blanks, extracted and assayed concurrently with the samples, were below the limits of sensitivity of the assays (80 pg for PGF and 100 pg for PGE-A).

The amounts of PGF and PGE-A in groups of 144-hour blastocysts are shown in Table 1. When expressed as PG per blastocyst, the amount was highest in sample No. 5 (1.16 ng of PGF per blastocyst) and lowest in sample No. 6 (0.16 ng of PGF per blastocyst). This rather wide variability could have been caused by differences in blastocyst volume which ranged from 4 to 32 mm³.

Each of the two uteri of pregnant and pseudopregnant rabbits was flushed with 5 ml of saline-indomethacin. The amount of PG's in these flushings is shown in Table 2.

Prostaglandins have been demonstrated in practically all tissues that have been investigated. The present results demonstrate, for the first time, PG's in a pre-implantation embryo—the rabbit blastocyst. Because the blastocyst has the capacity to synthesize a wide range of compounds, we suggest that it synthesizes the PG's it contains. However, since synthesis has not been proved yet, we have to consider that the PG's may be transferred from the uterine lumen into the blastocyst. A gonadotropin similar to hCG or luteinizing hormone has been demonstrated in rabbit blastocysts (9). It was suggested that this gonadotropin stimulates steroidogenesis in the blastocyst (4). We now propose that one or more of the PG's found act as mediators in blastocyst steroidogenesis.

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Neuroplasticity in the Sparing or Deterioration of Function after Early Olfactory Tract Lesions

Abstract. *Mating behavior in male hamsters depends on the sense of smell. Thus, complete transection of the lateral olfactory tract in adults eliminates mating. If the cut is made early in life, however, mating is spared. Partial section of the tract in adults does not affect mating, but similar cuts in the neonate lead to impaired mating performance later in life. Observed postsurgical rearrangements in the connections of axons in the lateral olfactory tract may explain both the sparing and the deterioration of function.*

Infants often show a remarkable degree of functional sparing after brain lesions that are devastating when they occur in adults (1). Neuroanatomical plasticity has been proposed as one possible way of accounting for such sparing (2), but strong evidence for this has only recently been found in mammals. Using a behavioral marker for visual function, Schneider and Jhaveri (3) described how axonal rearrangement after early lesions can have either adaptive or pathological consequences depending on the nature of the new connections formed. The present experiments extend this principle to the aftereffects of transection of central olfactory fibers, a neural system that likewise offers simple behavioral markers for the presence of functioning anatomical connections.

The axons from the olfactory bulb run caudally on the surface of the olfactory cortex, where most of them are collected into a compact bundle, the lateral olfactory tract (LOT) (4, 5). In the adult male hamster, bilateral transection of the LOT eliminates mating (6), a behavior that is dependent on the sense of smell (7, 8). Partial LOT section in adulthood, however, does not cause this deficit (6). The present experiments show that after complete LOT section in the neonate, mating capacity later in life is spared. After partial LOT section in the neonate, however, mating capacity later in life is impaired. Both behavioral sparing and behavioral deterioration apparently depend on the postoperative rearrangement of cut and neighboring uncut axons in the olfactory tract.

The experiments were performed in two stages. First, the LOT was cut unilaterally and the normal development of mating behavior was confirmed. Then, the contralateral olfactory bulb was removed so that any residual functional contribution of the previously cut side would be uncovered. This procedure was followed because even some normal, unoperated hamster pups fail to mate when they reach sexual maturity. It was thus necessary to confirm that all the experimental animals were capable of mating before they were subjected to a bilateral lesion of the olfactory system.

In 27 male golden hamster pups 3 days of age, and in 14 adults 6 weeks of age, the

LOT bundle was exposed unilaterally and transected either completely or partially (9). The hamsters were then allowed to grow to sexual maturity, and they were given extensive sexual experience beginning 5 to 15 weeks after surgery. In these mating tests a sexually receptive female was placed in the male's home cage (8), and the vigor of the male's sexual behavior was rated on a four-point scale (legend, Fig. 1A). Each test was ended after 5 minutes or after the first ejaculation, and successive tests were separated by at least 2 days. All of the animals mated vigorously (legend, Fig. 1A), an expected result since previous studies showed that neither unilateral LOT section nor unilateral bulbectomy performed in adulthood affects mating (6-8).

Next, the functional contribution of the previously cut LOT was assessed by removing the olfactory bulb on the intact side (main and accessory parts) and then giving an additional series of up to 17 mating tests over the next 2 to 28 weeks (10).

After this period of behavioral analysis, the distribution of olfactory bulb efferents that survived the original LOT cut or became rearranged because of it (or both) was traced by using either silver-staining or autoradiographic techniques (11). The anatomical analyses were done with knowledge of the animal's age at the time of the first operation but without knowledge of either its behavioral performance or the completeness of the LOT cut.

In the eight hamsters that underwent complete LOT section (first operation) at 6 weeks of age, subsequent contralateral bulbectomy essentially eliminated mating behavior (Fig. 1A). This is consistent with the earlier demonstration of severe deficits in mating behavior following bilateral LOT cuts in adulthood. In animals tested as long as 6 months after the bulb lesion no recovery was evident, nor did mating appear when the duration of tests was extended from 5 to 30 minutes.

In contrast, all but two of the hamsters that underwent complete LOT section at 3 days of age continued to mate after the contralateral bulbectomy. And while postoperative mating performance was not consistently vigorous from test to test as it had been previously (Fig. 1A), the loss was