MAMMALIAN PROGESTERONE RECEPTORS: BIOSYNTHESIS, STRUCTURE

AND NUCLEAR BINDING

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Because estrogen and progesterone receptors may be involved in the endocrine sensitivity of certain breast and endometrial carcinomas (1,2), considerable interest has been generated in the study of steroid receptors in hormonally sensitive tumors. In this chapter, we will review some recent progress on three aspects of receptor biology as applied to mammalian progesterone receptors: regulation of receptor biosynthesis, structure of the receptor and nuclear binding of the steroid-receptor complex.

REGULATION OF PROGESTERONE RECEPTOR SYNTHESIS BY ESTROGEN

In vivo studies have demonstrated that the progesterone-binding capacity of uterus (3,4) and vagina (4) is stimulated by estrogen. Although it has been recognized for some time that prior estrogen action is necessary for progestational responses, the mechanism is not well understood. Estrogen-mediated stimulation of progesterone receptor formation offers one possible explanation.

Studies with the guinea pig (5), rat and mouse (6) and hamster (7) indicated that the concentrations of uterine progesterone-binding components varied during the reproductive cycle. During the 4-day hamster estrous cycle, cellular concentrations of receptor increased during diestrus and reached a peak at proestrus, corresponding to the increase in serum estradiol levels (7). Formation of the 6-7S progesterone binding component occurred during the follicular phase of the cycle. The uterine progesterone receptor concentration
decreased slowly following ovariectomy at proestrus, and was rapidly restored by estrogen treatment. These results supported the idea that estrogen action during the cycle promoted formation of the progesterone receptor.

In the hamster, progesterone treatment given early on the day of proestrus caused a rapid premature depletion of receptor from the cytosol fraction (7,8). Cellular concentrations of receptor dropped markedly between proestrus and estrus, corresponding to the time of preovulatory progesterone secretion (7). Thus, variations in progesterone receptor levels during the female cycle may be attributed to the cyclic pattern of estrogen and progestin secretion.