

Letter to the Editor

Hormonal Induction of Uterine Sarcomas in GR Mice not Dependent on Mammary Tumor Virus Genes or Uterine Trauma*

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HORMONE-DEPENDENT uterine sarcomas in GR mice have been described in a previous paper [1]. The tumors arose in castrated female mice treated with progesterone and estrone. However, factors other than hormones might have been responsible for the induction of the tumors. When the mice were castrated the proximal end of the uterine horns was excised, and since the tumors were always located at this end of the uterus, the trauma to the uterine tissue might have been a tumor-promoting factor. Furthermore, GR mice carry the mammary tumor virus, MTV-P [2], and it cannot be excluded that this virus is involved in tumor induction not only in the mammary gland, but also in other tissues, such as the uterus.

A congenic GR line without the Mtv-2 gene, which is probably the provirus for MTV-P, has been developed at the Netherlands Cancer Institute [3]. In the present study, mice of this strain were exposed to treatment with progesterone + estrone and to uterine trauma in order to clarify the factor(s) responsible for uterine sarcoma induction in GR mice.

A total of 199 female mice of the GR/Mtv-2⁻ strain were included in the study. All the animals were castrated. They were then divided into six groups. Group I was treated with progesterone + estrone. Progesterone was given s.c. as pellets, 10 mg per week. Estrone was added to the drinking water at a concentration of 0.5 µg/ml. Group II

was treated with progesterone alone; group III with estrone alone; and group IV was untreated. Groups V and VI were treated with progesterone + estrone and estrone, respectively, and animals of both groups had the proximal end of the uterine horns removed at castration. Thirty-three animals died during the observation period, 17 with mammary tumors, 15 in groups I and V and two in group II. The remaining 166 animals were terminated after 30 weeks of observation. The presence of tumors was recorded.

As seen in Table 1, only mice treated with progesterone + estrone developed uterine sarcomas. Whether uterine resection was performed or not did not influence the incidence of uterine sarcomas. In mice treated either with progesterone alone or estrone alone or were untreated, no uterine sarcomas arose in a total of 96 animals during the observation period. One adenoacanthoma of the uterus was observed in group V and three lymphomas were found, one in the thymus in group III and two in the spleen in group IV.

The present study demonstrates that uterine sarcomas induced in GR mice as shown previously [1] can also be induced in GR/Mtv-2⁻ mice, indicating that Mtv-genes are not required for the induction of the tumors. Furthermore, we have shown that neither progesterone nor estrone alone was sufficient for the tumor induction. This is in contrast to results obtained in DV-LP mice [4] showing that not only gestagens + estrogens but also gestagens alone induced uterine sarcomas. In CBA mice estrogens decreased the number of sarcomas induced in immature mice by chemical

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Table 1. Induction of uterine sarcomas in GR/Mtv-2⁻ mice

Hormonal treatment*	No. of animals with tumor	
	Ovariectomized mice	Ovariectomized mice with an excision of the uterus
Progesterone + estrone	5/43 (I)	4/27 (V)
Progesterone	0/22 (II)	-
Estrone	0/50 (III)	0/10 (VI)
None	0/14 (IV)	-

*Progesterone: 10 mg s.c. in pellets weekly; estrone: 0.5 µg/ml drinking water.

carcinogens while progesterone promoted sarcoma induction in mature mice [5]. Trauma to the uterus by resecting the proximal ends of the uterine horn had no effect on sarcoma induction in the present study.

In conclusion, progesterone + estrone induces

uterine sarcomas in GR mice. Neither Mtv nor trauma to the uterus is involved in the tumor induction.

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