

[課程－2]

審査の結果の要旨

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This project divided into 2 different studies, each of which has beneficial contribution in research field.

1- As for endometriosis study

Endometriosis mouse model was established by I.P. injection of minced uterine fragments into peritoneal cavity of homologous BALB/c recipient mice while PBS injected for control mice. In this study, the pregnancy protocol consisted of 2 parts where mating onset differed. The early study, the mating started day 1 while in the late study, mating started at day 42. The finding in the early study, endometriosis mice took significantly longer time to conceive than control mice. In addition, the labor onset of endometriosis group delivered significantly earlier than control mice. As for the conceptus analysis, in the early study, weight and count were comparable between groups. As for the late study, pups body weight was significantly lower in endometriosis group, but PW and BW/PW were not different between the groups. Although litter size was comparable between the groups, the number of resorbed pups were higher in endometriosis group. This model demonstrated infertility, preterm labor, and fetal growth restriction, which is consistent with previously reported clinical studies of pregnant women with endometriosis. This endometriosis mouse model may be suitable for studies that investigate the mechanism by which endometriosis

adversely affects perinatal outcome.

2- As for adenomyosis study

Adenomyosis was started to be seen within a week after the establishment. There was no complication that was detected at any time of sacrifice throughout the whole study up to postoperative 2 months. The established lesion resembled typical human adenomyosis lesion that contains both gland and stroma within muscular compartment that change in structure and size over time. The entire volume increased significantly as they aged. In addition, when the volume of gland and that of stroma were analyzed independently, both were significantly larger in comparison to lesion in the early group. Further, when analyzing cell proliferation by Ki67 expression, endometrial epithelia of the lesion was highly proliferative in the early group while the stroma part was highly proliferative in the late group. As for the vascular density, the later group showed higher vascular density compared to the early group. Also, the fibrosis surrounding the adenomyosis lesion significantly increased as mice aged. This adenomyosis model was proven to be conceive, suggesting that the model can be applied for a pregnancy outcome analysis. In addition, study showed that lesions persisted after their deliveries. The current study established a novel adenomyosis mouse model that can be analyzed quantitatively in terms of their number and volume. Correctively, this model can be applied to evaluate the pathogenesis of adenomyosis, to test the efficacy of its therapeutic agents, and the effect of the lesion on pregnancy and vice versa.

It is expected that these models will be used in the future to elucidate the effects of endometriosis and adenomyosis on adverse fertility and perinatal outcome and to establish the therapeutic approach to prevent and treat them.

よって本論文は博士（医学）の学位請求論文として合格と認められる。