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Plurihormonal adenoma development in the rat pituitary following long-term administration of estrogen

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It is well known that long-term administration of estrogen provoked pituitary to induce prolactin-producing adenoma (E2-PRLoma) in Fischer rat. E2-PRLoma has been employed as an animal model of human PRL-producing pituitary tumors in a large number of studies. Currently, we found that multi-hormone producing nodules in female SD rat pituitary were induced by very long-term administration of estrogen. Herein, we report results of histopathological analyses of these lesions. Female Crl:CD rats, 7 weeks old, were purchased from Charles River Co. Animals were injected with 10 mg/kg of estradiol every other week intramuscularly for 22–36 weeks. Ten of the 11 PRLoma model rats had proliferative nodular lesions composed of large eosinophilic cells resembling gonadotrophs inside the PRLoma. These lesions were positive for PRL, TSHβ, and α subunits and were negative for GH, LHβ, ACTH, and S-100. Double immunostaining revealed that these large eosinophilic cells showed coexpression of PRL and TSHβ, PRL and α subunits, and TSHβ and α subunits. Those results clarified that long-term estrogen administration to female SD rats induced multi-hormone producing neoplastic pituitary nodules that expressed PRL, TSHβ, and α subunits. We consider that this animal model is useful for pathogenesis analyses and therapeutic agent development concerning human multi-hormone producing pituitary adenomas.

CP-26

Immunohistochemical and morphological analyses of cancer metastasis of mediastinal lymph nodes by "in vivo cryotechnique"

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[INTRODUCTION] Angiogenesis and lymphangiogenesis modulate hypoxic signaling of cancer cells and contribute to metastasis of various cancers including the lung cancer. In the present study, using Lewis Lung Carcinoma (LLC), we have examined the relationship between lymphatic vessels and the hypoxic signal molecule, hypoxia-inducible-factor-1α (HIF-1α) with "in vivo cryotechnique" (IVCT).

[MATERIALS AND METHODS] Cultured LLC cells (1×10^3) suspended in 20 μl PBS with 10 μg of Matrigel were directly injected into the lung parenchyma of adult C57BL/6 mice. Lung and mediastinal lymph nodes were directly cryofixed by IVCT, and then freeze-substituted (FS) in acetone containing 2% paraformaldehyde. Some of the tissues were routinely embedded in paraffin wax and stained with hematoxylin-eosin or immunostained for HIF-1α and LYVE-1 by the ABC-DAB method.

[RESULTS] Conventional HE-staining and immunostaining for LYVE-1 clearly showed that open lymphatic vessels were well maintained with IVCT, and LLC cells were found in lymphatic sinus and follicles of the lymph nodes. Immunoreaction products of HIF-1α were detected in nuclei of LLC cells around necrotic cell areas. Howeover, HIF-1α immunoreactivity was not found in metastatic LLC cells within mediastinal lymph nodes.

[CONCLUSION] IVCT was demonstrated to be a powerful technique to observe LLC cells invading into the lymph nodes through lymphatic vessels without technical artifacts during specimen preparation steps. A further experiment will be needed to reconfirm the hypoxic conditions of various cells in the cancer tissues.