364 Studies on ras oncogene activation in endometrial cancer. I.Fujimoto, Y.Shimizu, K.Yokosuka, K.Yamauchi, K.Hasumi, K.Masubuchi, Dept. Gynec., Cancer Institute Hospital Tokyo.

Point mutation (P.M.) of ras oncogenes has been noticed to be closely related to colon, lung and pancreas carcinoma. As to endometrial carcinoma, few reports have been noticed. Method: DNA was extracted in an ordinary technique from cancer tissues. Detection of P.M. of K-ras codon 12 was performed through the procedure of PCR and synthesized oligonucleotide hybridization. Result: The incidence of P.M. of K-ras codon 12 was 30% (7/23). Positive P.M. cases were all in stage I. We analysed the clinicopathologic behavior of endometrial carcinoma, divided into positive and negative P.M. groups. Poor prognostic groups (deep myometrial invasion, lymphnode metastasis) were found in 57% in the positive group, in contrast 31% of negative group in the positive group.

365 *Ras* gene activation in neoplasms of the human female reproductive tract. T. Enomoto, Lab. of Comparative Carcinogenesis, NCI-FCRDC, Frederick MD 21702,

We previously reported that activation of K-*ras* plays a significant role in the etiology of endometrial adenocarcinoma (Cancer Res. 50: 6139-6145, 1990). To further investigate the role of *ras* activation in the development of endometrial adenocarcinoma, we surveyed cystic, adenomatous, and atypical hyperplasia and additional cases of endometrial and cervical carcinoma for the presence of point mutations by dot blot analysis with mutation specific oligonucleotide probes and by direct sequencing. Frequency of *ras* gene mutations were significantly higher in endometrial adenocarcinoma of uterine corpus (11/29 (38%), 10 K-*ras*, 1 N-*ras*) than in squamous cell carcinoma of the uterine cervix (1/23 (4%), p=0.0041, 1 K-*ras*). *Ras* gene mutations were lower but not significantly in atypical hyperplasias (2/16 (13%), 2 K-*ras*) than in grade 1 endometrial carcinomas (4/13, (30%)). Neither 6 adenomatous hyperplasias or 12 cystic hyperplasias contained *ras* mutations. It is more likely that *ras* mutations occur as a later event rather than as an initiating event in the etiology of endometrial carcinoma. In ovary, K-*ras* mutations occurred significantly more frequently in mucinous adenocarcinomas (6/8, 75%) than in all non-mucinous types of epithelial tumors combined. These findings may imply the existence of an oncogenic pathway in mucinous adenocarcinomas that is also common to such morphologically similar tumors as pancreatic and colorectal carcinomas in which mucin secretion is common and frequent K-*ras* activation is also observed.

366 Detection of K-ras mutation and immunohistochemical investigation in endometrial adenocarcinomas and cervical adenocarcinomas. K.Itoh, K.Ohtomo, H.Makino, Y.Ide, A.Endoh, K.Shikano, N.Ozawa, S.Satoh, H.Sasano*, A.Yajima, Dept. Obst. and Gynec. Tohoku Univ. Sch. Med., Miyagi. *Dept. Pathol.

Samples of human endometrial adenocarcinomas and cervical adenocarcinomas were screened for the presense of single site DNA mutation at codon 12 of K-ras gene using oligonucleotide hybridization of DNA amplified by the polymerise chain reaction (PCR), and were analyzed for c-myc, erb-B2, and EGFR overexpression with immunohistochemistry.

Mutation of K-ras gene was found in three of 21 endometrial adenocarcinomas (14%) and two of 7 cervical adenocarcinomas (29%).

In immunohistochemical study, overexpression of c-myc and EGFR were found in almost all adenocarcinomas, although overexpression of erb-B2 was found in nine of 30 adenocarcinomas (30%).

No correlation between mutation of K-ras gene and overexpression of c-myc, erb-B2, and EGFR was found in these adenocarcinomas.