16 Allelic losses and mutations of the p53 gene in human ovarian carcinoma and endometrial carcinoma. A.Okamoto, S.Yokoyama*, Y.Terashima*, Y.Sameshima, M.Terada, J.Yokota, National Cancer Center Research Institute, Tokyo, *Dep.Obst.and Gynec., Jikei Univ.Sch.Med., Tokyo.

The p53 gene on chromosome 17p is considered to be a tumor suppressor gene and frequent alterations of the p53 gene have been found in a wide variety of human cancers. We found frequent allelic loss on chromosome 17p (44%) in 24 endometrial carcinomas by restriction fragment length polymorphism (RFLP) analysis. In ovarian carcinoma, frequent allelic loss on chromosome 17 has been reoported. Therefore, we examined for allelic losses and mutations of the p53 gene in 31 ovarian carcinomas and 24 endometrial carcinomas by an RFLP analysis and by a polymerase chain reaction-single strand conformation polymorphism (PCR-SSCP) analysis. Allelic loss of the p53 gene itsself was detected in 16 of 20 informative ovarian carcinomas (80%) and 3 of 11 informative endometrial carcinomas (13%). At least eight of 9 ovarian carcinomas with mutation and one of 3 endometrial carcinomas with mutation were determined to have lost the other allelic p53 gene. These alterations of the p53 gene were detected even in stage I, indicating that p53 alterations play an important role in the development of ovarian carcinoma and endometrial carcinoma.

17 Suppression of tumorigenic phenotypes of cervical cancer cell by introduction of wild type p53 gene. J.Nishida, H.Kato, T.Honda, T.Arima, M.Nishida, S.Miyamoto, T.Sasazuki*, N.Wake, Dept.Obst. and Gynec., *Dept.Genetics, Med. Inst. Bioregulation, Kyushu Univ., Oita and Fukuoka*.

Alterations in endogenous p53 gene expression and effects of human wild type p53 gene introduced exogenously were investigated in 3 kinds of cervical cancer cell lines (SiHa, Hela, ME180), harboring HPV E6 and E7 region. Overexpression of normal sized p53 mRNA was shown in parent SiHa and ME180. Tumor formation in nude mice was suppressed remarkably in these transfectants. However, any alterations in DNA size and expression of endogenous p53 could not be noticed in Hela. Transfection of wild type p53 could suppress colony formation in soft agar cultures though any suppressive effect could not be observed for tumor formation in Hela. In vitro growth characteristics of all transfectants in 3 cell lines were compatible with those of each parent cell. These suggested that tumor cell phenotypes suppressed by the wild type p53 were not identical, being compatible with diversed effects of p53 mutations in cervical cell carcinogenesis.

18 Suppression of endometrial cancer cell phenotypes by the introduction of wild type p53. H.Kato, J.Nishida, T.Honda, T.Sasazuki*, N.Wake, Dept.Obst. and Gynec., *Dept.Genetics, Med.Inst.Bioregulation, Kyushu Univ., Oita and Fukuoka*.

In order to explore the role of normal p53 function in human endometrial carcinogenesis, alterations of tumorigenic phenotypes were evaluated in 4 endometrial cancer cell lines (Ishikawa, Hec-1, HWCA, HOOUA) transfected by the wild type p53 expression vector (pkhp53). One (Hec-1) out of the four parent lines expressed abnormal sized RNA due to the rearrangement of p53 locus and two lines (HWCA, HOOUA) had over expression of RNA. Growth rates of the transformants were reduced significantly in these 3 lines, compared with control mock transfectants. Senescence of cells was remarkable in all of the Hec-1 derived transformants. Any abnormalities in Southern or Northern blotting could not be noticed in the Ishikawa line. Although the *in vitro* growth characteristics of the Ishikawa derived - transformants were compatible with those of the parent line, colony formation in soft agar cultures and tumor forming ability in nude mice were suppressed. These suggested that the disruption of normal p53 function was essential for the multistep processes in endometrial carcinogenesis.