18 Study of the localization of HPV types 16 and 18 E6/E7mRNA in the precancerous lesions and carcinoma in situ of uterine cervix by in situ hybridization. H. Kioka, N. Nagai, K. Shigemasa, Y. Katsube, A. Fujiwara. Dept. Obst. and Gynec, Hiroshima Univ. Sch. Med., Hiroshima.

The early genes E6/E7 of human papillomavirus (HPV) types 16 and 18 were considered as one of the carcinogenic factors of uterine cervix. We investigated the localization of HPV DNA and E6/E7mRNA of types 16 and 18 in the precancerous lesions and carcinoma in situ (CIS) of uterine cervix with biotinylated HPV 6/11, 16, 18 DNA probes and E6/E7 RNA probes by in situ hybridization. The results showed, 1)HPV 16 DNA was detected 16.7% in mild dysplasia, 38.2% in moderate dysplasia, 54.3% in severe dysplasia, 44.1% in CIS, so HPV 16 DNA positive rate tended to increase with the grade of lesions. 2)E6/E7mRNA was observed in the cytoplasm of the dysplastic cells or cancer cells of HPV DNA positive cases. 3)CIS were found later in 7 of 9 cases of E6/E7mRNA positive group. This suggests that detection of E6/E7mRNA may predict the prognosis of cervical lesions.

19 Structure and expression of an integrated human papillomavirus type 16 genome amplified in a cervical carcinoma cell line. H. Shirasawa, T. Nunoyama, S. Sekiya, H. Takamizawa, Dept. Obst. and Gynec., Chiba Univ. Sch. Med., Chiba.

The cervical carcinoma cell line QG-U contains only integrated monomeric human papillomavirus type 16 (HPV16) DNA that is transcriptionally active. We have cloned two *Bam*HI fragments of QG-U cell DNA that contain the integrated HPV 16 DNA sequences.

The analysis of the cloned fragments showed that integration interrupts the HPV 16 genome in open reading frames (ORFs) E2 and L2. The E6, E7, E1, E4, L1 ORFs and noncoding region (NCR) were shown to remain intact. Furthermore, abundant expression of E6/E7 ORFs and reading through to the flanking cellular sequence were indicated by Northern blot analysis. Southern blot analysis of the QG-U DNA using the flanking cellular sequences as probes indicated that the transcriptionally active viral genome was amplified with its flanking sequences. These results suggest the implication of the HPV16 genome DNA in the process of carcinogenesis and the maintenance of malignancy.

20 Association of human papillomavirus types with histological types of cervical carcinomas. H.Yoshikawa,S.Koi*,H.Yokota,E.Yamamoto,T.Matsukura**, T.Kawana* and M.Mizuno, Dept.Obst.and Gynec.,Univ. of Tokyo,Tokyo,*Dept. Obst.and Gynec.,Branch Hosp. of Tokyo Univ.,Tokyo,**Dept.Enteroviruses, National Institute of Health,Tokyo.

To determine the association between HPV types and histological types of cervical carcinomas, we have searched for HPV16DNA and HPV18DNA by Southern blot hybridization method in 158 specimens of invasive cervical carcinomas(139 squamous cell carcinomas, 13 adenosquamous carcinomas and 6 adenocarcinomas). The incidence of HPV16 was higher in squamous cell carcinomas(53/139[38.1%]) than in adenosquamous carcinomas and adenocarcinomas(3/19[15.8%]) and that of HPV18 was significantly higher in adenosquamous carcinomas and adenocarcinomas(7/19[36.8%]) than in squamous cell carcinomas(5/139[3.6%])[P 0.005]. No specimens had both HPV16DNA and HPV18DNA. These data suggest that HPV16 and HPV18 have different target cells, which generate histologically different types of carcinomas.