61 Transformation of primary cultured rat embryonal fibroblast by HPV16 E7 region. J.Nishida,H.Kato,T.Imamura,T.Arima,T.Iwanaga,N.Wake,K.Fujinaga*, Dept.Obst.and Gynec.,Medical Inst.of Bioregulation,Kyushu Univ.,Oita,*Dept. of Molecular biol.Cancer Res.Inst.Sapporo Medical Col., Sapporo.

HPV16 has been detected in cervical cancer with high incidence. The consistent presence of E7 region(E7)in specimens in which HPV16 had been detected, suggested the important role of this region in cervical carcinogenesis. To define the transforming ability of E7,we performed transfection experiments on primary cultured rat embryonal fibroblast(REF),using E7 expression plasmid pMoE7 containing E7 between molony murine sarcomavirus LTR and SV40 polyA signals. Because the E7 product had the striking homology to the two out of three conserved domains of adenovirus type5 E1A(Ad5E1A),which could induce complete transformation of REF by cooperation with EJras,Ad5E1B,and Ad12E1B,respectively,E7 was transfected with same combinations. REF was immortalized by E7 alone and all three types of transfections. Though colony forming ability was shown in cells by E7+Ad5E1B and E7+EJras transfections, tumor forming ability was observed only in cells cotransfected by E7 and EJras. Imcomplete transformation induced by cooperation of E7 and Ad5E1B or Ad12E1B suggested the possibility that decreased transforming ability of E7 was derived from the non-homologous regions between Ad5E1A and E7.

62 Tumorigenic transformation of primary cells by human papillomavirus types 16 and 18. Y.Hayashi,T.Iwasaka,M.Yokoyama,K.Hara,T.Hachisuga, H.Sugimori, Dept.Obst.and Gynec.,Saga Med.Sch.,Saga.

To investigate oncogenicity of human papillomavirus (HPV) on primary Syrian hamster embryo (SHE) cells, HPV-6,11,16 and 18 DNAs were transfected into SHE cells. Tumorigenicity was studied by s.c. inoculation of cells into nude mice. The foci were formed in every dish except pBR322 transfected control. Cells were isolated from the foci and propagated. Inoculation at passage 4 yielded no tumor in any groups. Some of the cells senesced until passage 15, but others escaped from senescence and grew into immortalized cell lines. By inoculation of cells at passage 18-28, tumors were formed only in mice inoculated with HPV-16 DNA transfected cells. Moreover, by inoculation of cells at passage 43-58, tumors were also formed in mice inoculated with HPV-18 DNA transfected cells. These results indicate that HPV-16 or HPV-18 DNA alone can lead primary cells to tumorigenic phenotype by repeating cell passage.

63 A novel monoclonal antibody against squamous cell carcinoma. M. Inoue, K. Nakanishi, T. Sasagawa, G. Ueda, O. Tanizawa, The Department of Obstetrics and Gynecology, Osaka University Medical School, Osaka.

The monoclonal antibody, INS-2, was raised against rat fibroblasts transformed by open reading frames E6 and E7 of human papillomavirus (HPV) DNA. In immunoperoxidase testing of frozen sections, the INS-2 antibody was reactive with all squamous cell carcinomas of the uterine cervix and esophagus tested. In contrast, no antibody binding was detected with adenocarcinomas of various origins. Similarly, normal tissues, lymphoid cells and erythrocytes from multiple donors were negative, except that binding localized at basal cells in normal squamous epithelium was observed. Interestingly, strong staining was observed in dysplastic cells of cervical intraepithelial neoplasia and at the growing edge of squamous cell carcinomas. The antigen for the INS-2 antibody is a non-sialyl glycoprotein with Mw. 40,000 and appears to be a squamous cell-specific cell differentiation marker, although it is not related to HPV-DNA-derived protein.