

## I S—23

**Establishment of HPV18 URR-E6/E7 gene expressing transgenic mice for in vivo experiment of cervical cancer**

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**Objectives :** Papillamavirus(HPV) is associated with the development of malignant squamous neoplasms of the cervix, vulva, penis, and anus and also induce formation of benign squamous epidermal tumors(warts). The transcriptional initiation site of the HPV E6 and E7 genes lies immediately upstream of the E6 ORF in the URR (Upstream Regulatory Region) of the viral genome. HPV research has been hampered by the mucosotropic nature of HPV viruses which produce few virions in vivo. And the lack of an proper animal model has also prevented HPV research, related with oncogenesis. To analyze the transcriptional activities of the URR, and function of E6 and E7 gene, we have produced transgenic mice expressing HPV-18 E6 and E7 genes.

**Methods :** Prototype HPV-18 URR/E6/E7 was obtained by PCR and linked to SV40 poly-A sequence. Such transgene, ~20kb fragment, was then microinjected into one cell (C57/BL6 X SJL)F2 embryos. F2 embryo was then transferred into pseudo-pregnant ICR recipients. Analysis of the gene expression of the transgenic mice is currently in progress.

**Results :** We have produced 4 transgenic mice and analysis of the gene expression of the transgenic mice is currently in progress.

**Conclusion :** The transgenic mouse model system is likely to be a useful system for investigating HPV-18 E6/E7 gene functions in vivo and the neoplastic progression of the genital epithelium.

## I S—24

**High-risk HPV DNA as primary screening in old women**

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**Objective:** To evaluate clinical role of HPV test in elder women (age over 50 years old), we analyzed the presence of high-risk human papillomavirus (HPV) in cervical swab obtained from elderly women according to the grade of cervical cytology, and evaluated its clinical value.

**Methods:** The study was based on 81 elderly women with abnormal smears referred for colposcopy from Feb. 1997 to Sept. 1998. We used the HPV profile to test all patients for high-risk HPVs. Oncogenic-associated HPVs typing (type 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68) was measured by Hybrid capture method. Cytological examination by Papanicolaou smear based on the Bethesda system and cervical biopsy was done under colposcopy.

**Results:** The cytological results were high-grade squamous intraepithelial lesion (HSIL) in 10, low-grade squamous intraepithelial lesion (LSIL) in 32, atypical squamous cells of undetermined significance (ASCUS) in 26, and normal in 13. High-risk HPVs were positive in 20% of HSIL, 75% of LSIL and 38% of ASCUS of cervix. The detection rate of cervical dysplasia assayed by HPV-DNA testing (+/-) combined with Pap smear was 80%, 8% (12/15,2/24) for ASCUS group, 96%, 38%(23/24,3/8) for LSIL, and 50%, 50%(1/2,4/8) for HSIL. Statistically, a clinical significant detection rate was observed in ASCUS and LSIL ( $P < 0.05$ ). Comparing with colposcopic diagnosis and final histopathologic findings, the sensitivity of cervical cytology for noninvasive precursor (cervical intraepithelial neoplasia) or cancer in elderly women were 69% in swabs, 62% in Hybrid capture, and 80% in Hybrid capture combined with a Papanicolaou smear.

**Conclusion:** In elder women, HPV-DNA testing with Hybrid capture may be an effective tool in improving cervical screening program for ASCUS and LSIL group.