P-IS-6 Change of human papillomavirus type 16 DNA level in women with cytological abnormality

Department of Perinatal and Maternal Medicine, National Defense Medical College[1],Department of Obstetrics and Gynecology, National Defense Medical College[2],Department of Biomedical Laboratory Sciences, Graduate School of Health Sciences, Tokyo Medical and Dental University[3]
Hidenori Sasa[1], Kanoko Imai[2], Noriko Makimura[2], Toshio Tanaka[3], Kenichi Furuya[2]

[Objective] To assess the change of DNA level of human papillomavirus (HPV) type 16 in women with cervical intraepithelial neoplasia (CIN). [Methods] Cervical specimens were obtained during past four years from 394 women in the first trimester of pregnancy with normal cytology, 174 women with abnormal cytology (CIN), and 28 patients with invasive cervical cancer with the informed consent. The polymerase chain reaction (PCR) was used to detect HPV DNA with a pair of consensus primers for L1 region. Typing of HPV DNA was performed by the restriction fragment length polymorphism with restriction enzymes. We used a real-time PCR assay for quantification of HPV16 DNA and compared the HPV DNA level among the specimens of same women. [Results] The prevalence of HPV DNA was 14.7% in the pregnant women with normal cytology, 78.7% in women with abnormal cytology, and 64.3% in patients with invasive cervical cancer. HPV type 16 was by far the most prevalent HPV type among all groups. The DNA level of HPV type 16 was similar among the grade of cytological abnormalities. The DNA level of HPV type 16 did not change significantly during four years in the thirty cases with abnormal cytology. [Conclusion] Our data suggest that HPV-positive women with cytological abnormality need follow-up because of their high-risk HPV types and its unchangeable virus DNA level during several years.

P-IS-7 Novel interaction between HPV E6 and BARD1 (BRCA1-associated ring domain 1) and its biologic roles

Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Catholic University Medical College, Seoul, Republic of Korea
Jeong-Hoon Bae, Eun-Kyoung Yim, Chan-Joo Kim, Seong-Eun Namkoong, Jong-Sup Park

Human papillomavirus (HPV) is associated with the majority of cervical cancers and encode a transforming protein E6, which interacts with the tumor suppressor p53. We looked for p53-independent HPV 16 E6 interacting proteins using yeast two-hybrid screening and identified BARD1 (BRCA1-associated ring domain 1). Here we showed that BARD1 was not degraded by E6 and it formed a physical complex with E6. Moreover, the mutations of metal motif in zinc finger region decreased ability of E6 to interact with BARD1. Transient co-expression of BARD1 increased the p53-mediated activation of p21WAF1 promoter despite the presence of E6. We showed that the existence of BARD1 gene as a p53 tumor co-suppressor inactivated HPV E6 expression and it acted as a NF-κB regulator in cervical carcinoma cells. These findings suggest that BARD1 play an important role in the biological activities as a tumor suppressor and in cervical carcinogenesis through transcriptional regulation of p53 and NF-κB.

P-IS-8 Antiproliferative and antiviral effects by etoposide in HPV-associated cervical cancer cells

Department of Medical Bioscience[1],Division of Gynecologic Oncology, Department of Obstetrics and Gynecology, Catholic University Medical College, Seoul, Republic of Korea[2]
Yong-Seok Lee[2], Eun-Kyoung Yim[1], Chan-Joo Kim[2], Sung-Eun Namkoong[2], Jong-Sup Park[1,2]

Etoposide, podophyllotoxin derivatives, which has exhibited pronounced biological activity as strong antiviral agents and as antiproliferative agents for human malignancies including lymphomas, germinal tumors, and lung cancer. We tried to analyze the antiproliferative activity as well as the antiviral effects of etoposide in cervical cancer cells.
In the HPV-associated cervical cancer cells, etoposide showed antiproliferative activity through the membrane death receptor-mediated apoptotic pathway involving activation of caspase-8 with an Apo-1/CD95 (Fas) -dependent fashion as well as antiviral activity through the down-regulation of HPV E6 and E7 viral oncogenes, resulting in activation for p53 and Rb tumor suppressor genes.
Key words : etoposide, apoptosis, cervical cancer cell, E6, E7