I S－5 Effects of EGF on chemosensitivity of cervical squamous carcinoma cells (CaSki) to cisplatin (DDP) and actinomycin-D (ACT-D)

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[Objectives] To address chemosensitivity of CaSki cells to DDP and ACT-D modulated by EGF.
[Methods] Cultured CaSki cells were treated with EGF (100 ng/ml) and DDP or ACT-D simultaneously for 3 hours (short exposure) or 24 horus (continuous exposure), then after 72 h in the short exposure experiments or immediately in the continuous exposure experiments, proliferative potential of cultured cells was evaluated using colorimetric (MTT) assay. After treatment, cells were subjected to DNA fragmentation and immunoblot analyses.
[Results] 1) DDP and ACT-D induced apoptosis in CaSki cells. 2) Apoptosis in CaSki cells was accompanied by an increased expression of a novel protein--apoptosis specific protein (ASP). 3) After 72 h following 3 h exposure, EGF enhanced DDP-induced cell death, while had no significant effect on ACT-D-induced cell death. 4) After 24 h exposure, EGF enhanced ACT-D induced apoptosis, while had no significant effect on DDP-induced apoptosis.
[Conclusions] 1) EGF enhanced the sensitivity of CaSki cells to DDP and ACT-D. 2) For the enhancement of sensitivity of CaSki cells to DDP, short exposure for 3 h may be apropriate; while for the augmentation of sensitivity of CaSki cells to ACT-D, continuous exposure for 24 h may be necessary. 3) The mechanisms for EGF to sensitize Caski cell to DDP and ACT-D seem to be different.

I S－6

Underexpression of $p21^{waf1/cip1}$ and p27 in cervical carcinoma

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Modern molecular biological studies prove that the mechanisms for controlling tumor growth might involve direct regulation of the cell cycle which is controlled by a series of catalytic protein kinase complexes consisting of cyclins and cyclin-dependent kinases(CDKs). Recent studies have discovered a number of specific proteins which inhibit the activity of the CDK-cyclin complexes, thereby providing an additional level of regulation and further complexity to cell cycle control. Among these cell cycle inhibitors, $p21^{waf1/cip1}$ and p27 have been thoroughly studied. However, the role of $p21^{waf1/cip1}$ and p27 in the tumorigenesis of the uterine cervix has been poorly defined.

We used immunohistochemical techniques to study the expression of these cell cycle inhibitors in formalin-fixed, paraffin-embedded cervical tissue to explore the relationship between cyclin/CDK inhibitors and cervical carcinoma. Cervical tissues were analyzed from 46 patients with invasive cervical cancer, 30 cases with cervical intraepithelial neoplasia(CIN) and 22 control cases who underwent hysterectomy due to benign gynecologic disease at Yonsei University College of Medicine.

All CDK inhibitors were strongly expressed in the reverse cell hyperplasia and kiolocytes, whereas they revealed significantly decreased expression in neoplastic tissues($p<0.05$). Normal endocervical cells revealed focal and weak expression of all CDK inhibitors.

These results were consistent with the concept that underexpression of CDK inhibitors may play an important role in neoplastic transformation in cervical carcinoma.