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Anticancer Effect and Gene Expression Regulation of Major Constituent of Green Tea, EGCG in Gynecologic Cancers

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A constituent of green tea, (-)-epigallocatechin-3-gallate (EGCG) has been known to possess antiproliferative properties. We investigated the anticancer effects of EGCG in human papillomavirus (HPV)-16 associated cervical cancer cell line, CaSki and human ovarian cancer cell line, SKOV-3, OVCAR-3 and PA-1. Also, clinical efficacy of green tea extracts (polyphenon E and EGCG) delivered in a form of ointment or capsule in patients with human papilloma virus (HPV) infected cervical lesions. EGCG showed growth inhibitory effects in CaSki and ovarian cancer cell lines in a dose-dependent fashion and cell cycle arrest. The cell cycle was arrested at the G(1) or G(1)/S phase by EGCG. When CaSki and SKOV-3 cells were tested alteration in the gene expression using 384 cDNA microarray and cell cycle macroarray assay each. EGCG differentially regulated the expression of genes and proteins (Bax, p21, Retinoblastoma, cyclin D1, CDK4, Bcl-X(L)), showing a possible gene regulatory role of EGCG. These data supports that EGCG can inhibit cervical, ovarian cancer cell growth through induction of apoptosis and cell cycle arrest as well as regulation of gene expression in vitro. Fifty-one patients with cervical lesions (chronic cervicitis, mild, moderate and severe dysplasia) were divided into four groups, as compared with 39 untreated patients as a control. Poly E ointment was applied locally to 27 patients twice a week. Overall, a 69% response rate (35/51) was noted for treatment with green tea extracts, as compared with a 10% response rate (4/39) in untreated controls ($P<0.05$). Thus, these data collected here demonstrated that green tea extracts in a form of ointment and capsule are effective for treating cervical lesions, suggesting that green tea extracts can be a potential therapy regimen for patients with HPV infected cervical lesions. Thus, EGCG likely provides an additional option for a new and potential drug approach for cervical and ovarian cancer patients.