GO-03

SERPINB3 in the Chicken Model of Ovarian Cancer: A Novel Biomarker for Predicting Platinum Resistance and Survival in Patients with Epithelial Ovarian Cancer

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목적: We investigated the functional role of SERPINB3 gene in human epithelial ovarian cancer (EOC) using chickens, the most relevant animal model.

방법: In 136 chickens, EOC was found in 10 (7.4%). We compared the expression and localization of SERPINB3 mRNA and protein between normal and cancerous ovaries of chickens using reverse transcription polymerase chain reaction, in situ hybridization and immunohistochemistry, and SERPINB3 activation was detected in chicken and human ovarian cancer cell lines (OVCAR-3, SKOV-3 and PA-1) using immunofluorescence microscopy. Thereafter, we examined the prognostic value of SERPINB3 expression in patients with EOC by multivariate linear logistic regression and Cox' proportional hazard analyses.

결과: SERPINB3 mRNA was induced in cancerous, but not normal ovaries of chickens (p<0.01), and it was abundant only in the glandular epithelium of cancerous ovaries of chickens. SERPINB3 protein was localized predominantly to the nucleus of glandular epithelium in cancerous ovaries of chickens, and it was abundant in the nucleus of both chicken and human ovarian cancer cell lines. In 109 human patients with EOC, 15 (13.8%), 66 (60.6%) and 28 (25.7%) patients showed weak, moderate and strong expression of SERPINB3 protein, respectively. Strong expression of SERPINB3 protein was a prognostic factor for platinum resistance (adjusted OR, 5.94; 95% CI, 1.21-29.15), and for poor progression-free survival (PFS; adjusted HR, 2.07; 95% CI, 1.03-4.41).

결론: SERPINB3 may play an important role in ovarian carcinogenesis and be a novel biomarker for predicting platinum resistance and a poor prognosis for survival in patients with EOC.

GO-04

Tumor suppressive effect of BRD7 in EOC (epithelial ovarian carcinoma)

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목적: Objective: There have been recently reported evidences that reveal the tumor suppressive effect of BRD7 (bromodeoamin containing protein 7) in many cancers. These reports showed the down-regulation of BRD7 in cancer tissues relative to the matched normal ones and also the tumor suppressive mechanism of it. The purpose of present study is to evaluate the tumor suppressive roles of BRD7 in serous ovarian tumor cell.

방법: Method: We estimated the expression level of BRD7 mRNA in serous epithelial ovarian cancer tissues through real time PCR (semi-qRT-PCR) with specific primer sets specific to the sequence of human BRD7. After estimation of the expression level, we performed the in vitro experiment using human ovarian cancer cell lines with plasmid DNA vector parenting full length of human BRD7 to inquire into the tumor suppressive effect and downstream of BRD7.Moreover, BRD7 regulated the fractional location of β-catenin and downstream of its signaling pathway.

결과: Results: We identified the reduced expression of BRD7 in serous ovarian tumor tissues relative to the normal ovarian epithelium and furthermore analyzed distinctive expression pattern of it between type 1 and 2 serous ovarian tumor tissues. Transfection of BRD7 plasmid vector reduced cell viabilities, migration, invasion and inversely increased apoptosis of ovarian cancer cells.

결론: Conclusion: These results indicate the down-regulation of BRD7 in serous ovarian tumor. Over-expression using BRD7 plasmid vector showed tumor suppressor effect of it on the cell viability, migration, invasion and apoptosis. Specifically, metastatic abilities were the most effective aspects of BRD7 as a tumor suppressor gene. Furthermore, we identified over-expression of BRD7 changed the locus of β-catenin and activities of its signaling activity. Therefore, BRD7 could be used a new genetic marker of ovarian cancer to be exploited in therapeutic strategies with its tumor suppressive marker.