I S—13 cDNA cloning of placental protein 5 (PP5), a serine proteinase inhibitor, and its mRNA expression in human ovarian cancer cell lines

Dept. of Ob/Gyn and Kihara Inst. for Biological Res.*, Yokohama City Univ. School of Medicine. Etsuko Miyagi, Fumiki Hirahara, Tsuneo Nakazawa, Kaori Udagawa, Itsuo Gorai, Hiroshi Minaguchi and Kaoru Miyazaki*

Some kinds of serine proteinases have been revealed to contribute to the process of cancer invasion and metastasis. To understand the regulatory mechanism of the serine proteinases, we have recently surveyed their inhibitors secreted by various human cancer cell lines. In the present study, a 29-kDa trypsin inhibitor was purified from culture medium of human glioblastoma cell line T98G. Analysis of its partial amino acid sequences and cloned cDNA indicated that the inhibitor was identical to placental protein 5 (PP5), a placenta-derived glycoprotein with serine proteinase inhibitor activity. The deduced amino acid sequences of PP5 demonstrated that it belonged to the Kunitz-type serine proteinase inhibitor family, and was identical to a recently reported inhibitor of the blood coagulation system, tissue factor pathway inhibitor-2 (TFPI-2). Extremely high amounts of PP5 transcript were detected in the full-term placenta. 4 out of 5 ovarian carcinoma cell lines also contained significant amounts of PP5 transcript. The results indicate that PP5 may be involved in (1) organogenesis of the placenta; (2) extracellular matrix degradation by ovarian cancers in the process of their progression; (3) cancer-induced coagulopathay.

I S—14 Genetic progression model in ovarian cancer with comparative genomic hybridization (CGH).

1. UCSF, 2. Kyoundo Hosp., 3. Yale U. H. Iwabuchi[1], H. Sakunaga[2], M. Sakamoto[2], T. Sugishita [2], Y. Tenjin [2], T.Yang-Feng [3], D. Pinkel [1], J.W.Gray [1]

We have performed comparative genomic hybridization (CGH) using DNA obtained from 49 common epithelial ovarian tumors (benign 11, low grade16, high grade 22) with goal of developing a model for genetic progression in common epithelial ovarian cancer. Five general features are apparent from these studies: 1) $3q^+$, $6p^+$, $8p^-$, $8q^+$, $11p^-$, $11q^+$, $16q^-$, $17p^-$, $17q^-$, $22q^-$, and Xp^- are found to be gene dosage abnormalities associated with histological grade (Test for linear trend in proportion, $p<0.01$). 2) $6p^+$, $8p^-$, $11p^-$ and $11p^+$ are recognized as high grade specific gene dosage abnormalities. 3) Many of the genetic abnormalities are correlated. Specially, strong correlations (Fischer, $p<0.01$) were observed for 22 aberration pairs. 4) Tumors with one or more of those abnormalities usually carry more abnormalities per tumor (>15/tumor) than tumors that do not (<7/tumor). 5) $16q^-$ showed a significant correlation with survival ratio (Kaplan-Meier, $p<0.01$). Taken together, these observations suggest a pararell pathway model for genetic progression in which $17p^-$. $17q^-$ and $3q^+$ are independent inital genetic events, $8q^+$, $16q^-$, $22q^-$ and Xp^- are intermediate events and $6p^+$, $8p^-$, $11p^-$, and $11q^+$ are late events. This work was supported by Imagenetics.