initially developed to measure organ blood flow, is also useful for estimating tumor blood flow in rats.

460 POSTER

Soluble P-selectin correlates with plasma vascular endothelial growth factor (P-VEGF) levels in patients with thoracic carcinoma

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Introduction: Vascular endothelial growth factor regulates tumour angiogenesis. Debate exists as to whether P-VEGF measured in patients with cancer is derived from VEGF released from tumour cells or from in-vivo platelet activation. The aim of this study is to investigate how plasma soluble P-selectin (sP-selectin), a marker of in-vivo platelet activation, relates to P-VEGF levels in patients with thoracic cancer.

Methods: Blood was obtained from 91 patients with carcinoma of the lung (n=53) or thoracic oesophagus (n=38) and 36 controls. Seventy-three of the cancer patients had localised disease and 18 had advanced disease (mediastinal involvement or systemic dissemination). The P-VEGF (pg/ml) and plasma sP-selectin (ng/ml) levels were investigated using specific ELISA kits. The platelet count (x109/l) was measured using a Sysmex SE-9500 automated haematology analyser. Data were expressed as median, with statistical analysis by Mann-Whitney U Testing. Correlation analysis was undertaken using Spearman's Rank testing.

Results: Patients with advanced thoracic carcinoma had a significantly elevated median sP-selectin level compared to controls (60.3 vs. 40.1; $p<0.0001$). Plasma VEGF was raised in patients with advanced disease compared to controls (84.5 vs. 21.2; $p<0.0001$). There was no significant difference in P-VEGF levels between those with localised disease and the controls. The median platelet count was increased in the patients with localised disease compared to controls (258 vs. 234; $p<0.05$) and between patients with advanced carcinoma and controls (395 vs. 234; $p<0.0001$). The sP-selectin levels correlated with the P-VEGF levels in all the cancer patients ($r=0.30$; $p<0.01$) but not in the control patients. The platelet count in the cancer patients correlated with the sP-selectin and the P-VEGF levels ($r=0.44$; $p<0.0001$ and $r=0.30$; $p<0.005$ respectively). The platelet count did not correlate with sP-selectin nor P-VEGF levels in the control patients.

Conclusion: There is a correlation between sP-selectin and P-VEGF in patients with thoracic cancer and both are elevated in advanced disease. Further research should be directed in establishing if this has an independent effect on the progression of cancer.

461 POSTER

Retinoic acid induced G1 arrest in hepatocarcinoma cell lines

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Purpose: Retinoids (RA) have been known to regulate growth and differentiation of epithelial cells. Treatment of various types of cancer cells with RA resulted in growth inhibition and apoptosis. RAR beta has been suggested to play an important role in the biological functions of RA. RAR beta expression is suggested to associate with the cellular sensitivity to retinoid in cancer cells. It has been shown that RA treatment caused cell cycle arrest at G1 phase through enhanced expression of cyclin dependent kinase inhibitor p21 in leukemia cells and lung cancer cell lines. Therefore, we examined whether all-trans retinoic acid (atRA) caused to arrest a cell cycle, resulting in a growth inhibition in Korean hepatoma cell lines. We investigated the expression of proteins related to a cell cycle.

Methods: Korean hepatoma cell lines (SNU354, SNU449) were purchased from Korea Cell Line Bank. Cell lines were maintained in RPMI medium containing 10% fetal bovine serum. Cells were treated with 10 μM atRA as an indicated time period. Percent growth inhibition was calculated with cell number from atRA treated cells compared to that from control cells. After atRA treatment, cells were harvested and were lysed with RIPA buffer containing protease inhibitors. Total cell lysates were resolved on 8 - 12% SDS-PAGE gel and transferred to PVDF membrane. Blots were reacted with desired antibodies. Cell cycle arrest was analyzed using FACScan after atRA treatment.

Results: Treatment of Korean hepatoma cells with atRA resulted in cell growth inhibition and the sensitivity of cells to atRA was related to induction of RAR beta expression. atRA-treated hepatoma cells showed cell cycle arrest at G1 phase starting from 3h treatment in atRA-sensitive SNU354 but it was delayed in atRA-less sensitive SNU449 cell line. Although increased expressions of both p21 and p27 proteins were observed in atRA-treated SNU354 cells, expression of p27 was not increased in SNU449 cells after atRA treatment. Since expression of p53 was not changed by atRA in both cell lines, induction of p21 and p27 could independently occur in atRA treated cells.

Conclusion: Based on our results, we concluded that retinoic acid treatment induced expression of p21 and p27 proteins, resulting in cell cycle arrest at G1 phase and inhibition of cell growth in Korean hepatoma cell lines. We suggested that expression of p27 was more likely related to the RA sensitivity of hepatoma cells.

462 POSTER

PPARgamma expression in esophageal cancer and effect of PPARgamma ligands

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Purpose: Peroxisome proliferator-activated receptor gamma(PPAR)is a nuclear receptor that has a regulatory role in differentiation of adipocyte and its expression has also been shown in several types of cancers, such as colon cancer and breast cancer, in recent years. The present study examined the expression of the PPAR in human esophageal cancer cell lines and the effect of the PPAR ligands on cell growth of these cell lines. Methods: Expression of the PPAR in five esophageal cancer cell lines were examined by Reverse transcription-polymerase chain reaction (RT-PCR) and Western blot analysis. Effect of the PPAR ligands, troglitazone and pioglitazone, on cell growth of the cell lines was investigated in vitro. Apoptotic assay and cell cycle analysis after PPAR ligand treatment were also performed. Results: PPAR expression was detected in all cell lines tested with RT-PCR and Western blot analysis. Both of PPAR ligands inhibited cell growth of esophageal cancer cell lines in dose-dependent manner. Fow cytometry demonstrated a increase fraction of Gl phase and decrease of cells in S phase after PPAR ligand treatment, and apoptotic cells after treatment were slightly increased. Conclusions: PPAR is expressed in esophageal cancer. The cell growth of esophageal cancer cells is inhibited by PPAR ligands. Our results suggest that PPAR might be a promising target of anti-cancer treatment for esop

463 POSTER

Studying of mechanisms involved in the maintenance of hepatoma differentiation status.Role of HNF4

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Purpose of the study: We have obtained a new experimental model comprising a highly differentiated slow growing transplantable mouse hepatocarcinoma (sgHCC) and its dedifferentiated fast growing variant (fgHCC) aroused from sgHCC by rapid, possibly one-step progression. The aim of this study was comparative characterization of sgHCC and fgHCC variants and analysis of possible role of liver-specific transcription factors in the maintenance of hepatoma differentiaton status.

Materials and methods: RT-PCR, Northern blot hybridization analyses and immunohistochemical staining were used to investigate the levels of liver-specific genes expression and synthesis and localization of ECM components. Transient transfection analyses with luciferase reporter vectors were used to estimate the transcriptional activity of Hepatocyte Nuclear Factor 4 (HNF4) promoter.

Results: We have found that fgHCC differs from sgHCC by lose of cell polarity and striking decrease in cell-cell and cell-ECM adhesion. It is also characterized by complete loss or strong downregulation of the expression of HNF4, which is known to be an essential regulator of liver differentiation and can induce epithelial morphogenesis in dedifferentiated hepatomas. fgHCC variant failed to express wide number of liver-specific genes.

The expression of exogenous HNF4 in cultured fgHCC led to restoration of number of liver-specific functions. In some of HNF4 transfected clones we had observed partial transition to epithelial phenotype. In transient