YW3-11 Chemokine expression in renal cell carcinoma

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The presence and potential role of chemokines in clinical tumors remains poorly understood. Chemokines are a large family of chemoattractant cytokines with several members also able to regulate angiogenesis. We hypothesized that chemokines may play an important role in regulating tumor growth in renal cell carcinoma (RCC). To begin to test this hypothesis, chemokine gene expression and its influence on the prognosis, cellular infiltration, and angiogenesis in RCC were examined. Intratumor expression of chemokine was examined using real-time PCR. The expression of IP-10, MIG, MIP-1 β , and RANTES was significantly increased in tumor compared to normal kidney tissues. Stage 1 to 3 tumors expressing high levels of IP-10, MIG, MIP-1 β and RANTES did not recur after curative surgery. The intratumor expression level of IP-10, MIG, RANTES and MIP-1 β showed a positive correlation with the degree of CD8⁺ cell infiltrating in the tumor, and an inverse correlation to microvessel density. A flow cytometry study for chemokine receptor expression (CXCR3 and CCR5) on tumor infiltrating lymphocytes (TIL) showed the specific recruitment of lymphocytes into tumors via chemokine-receptor interaction. These results suggest that the antitumorigenic effect of IP-10, MIG, RANTES and MIP-1 β may result from the recruitment of lymphocyte infiltration and/or inhibition of angiogenesis in RCC.

YW3-12 The single nucleotide polymorphisms in renal cell carcinoma

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Each individual has many single nucleotide polymorphisms (SNPs) that together create a unique DNA pattern for that person. The development of detailed SNP maps of the human genome coupled with high-throughput genotyping technologies may allow us to unravel complex genetic traits, such as cancer. SNPs are also expected as useful genetic markers for their association with disease susceptibility. We evaluated SNPs of TNF- α and hMSH3.

SNPs of TNF- α in renal cell carcinoma (RCC)

It has been reported that the TNF- α allele may have a correlation with some carcinoma, such as ovarian cancer, colorectal cancer, lymphoma, and many types of leukemia. We tested three different polymorphic loci (-238, -308, and 488) of TNF- α to investigate whether there are any genotype changes or mutations that are associated with the onset and metastasis of renal cell carcinoma. The relative risk of incidence for RCC was 6.5-fold higher in people with the GA genotype at the locus -238 ($P < 0.001$) and 2.9-fold higher in people with the GA genotype at the locus 488 ($0.01 < P < 0.025$) when comparing to normal tissue from RCC patients with healthy control.

SNPs of MSH3 in RCC

Recent study from our laboratory has shown that hMSH3, a DNA mismatch repair gene, is down-regulated in RCC. We hypothesize that the SNPs of hMSH3 gene are involved in pathogenesis of RCC. The relative risk of incidence for RCC was 4.1-fold higher in people with the GG genotype at the locus 1045 compared to wild-type.

YW3-13 The function and role of novel protein Niban in multistep renal carcinogenesis.

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Introduction ; Carcinogenesis consists of multiple steps and carcinoma development is associated with multiple genetic and epigenetic alterations. We previously isolated a novel gene *Niban*, which is expressed in renal carcinogenesis. Interestingly, the expression of Niban was observed even in early preneoplastic lesions. Niban contains an N-terminal conserved domain of dnaJ, suggesting that Niban functions as a stress protein in carcinogenesis. In this study, we analyzed the expression of Niban under various stress conditions. **Methods** ; We investigated the expression of Niban in NIH3T3 cells under various stress conditions, including heat shock, oxidative stress, hypertonic stress, administration of endotoxin and serum depletion. We also investigated the expression of Niban in the presence of activators or inhibitors of MAPK. **Results** ; The expression of Niban was upregulated by the addition of various stress. Interestingly, this upregulation was also observed by administration of anisomycin, which is MAPK activator, and was suppressed by the inhibition of JNK. **Conclusions** ; Under the stress of carcinogenesis, the expression of Niban was induced, and might protect the initiated cells from cell death. This induction might be regulated by JNK. Future study of its function may provide new insights into multi-step renal carcinogenesis.

YW3-14 RENAL CELL CARCINOMA CELL LINE-DERIVED GANGLIOSIDES INDUCE DEGRADATION OF BCL-2 AND APOPTOSIS IN T LYMPHOCYTES ; PREVENTION BY A GANGLIOSIDES SYNTHESIS INHIBITOR.

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INTRODUCTION AND OBJECTIVES : It has been reported that gangliosides shed by renal cell carcinoma (RCC) may induce apoptosis in T cells. Here, we examined whether a RCC cell line (SK-RC-45) would inhibit expression of Bcl-2 protein and induce apoptosis in activated peripheral blood T cells. In addition, effects of a gangliosides synthesis inhibitor (PPPP) on blocking degradation of Bcl-2 in T cells induced by SK-RC-45 were examined.

METHODS : Activated T cells from healthy volunteers were co-incubated with monolayers of SK-RC-45 cells pre-incubated with PPPP. Following co-culture, T cells were isolated and subjected to TUNEL assay as well as western blot analysis. In addition, gangliosides of SK-RC-45 cells incubated with PPPP were harvested and subjected to HPTLC analysis. **RESULTS** : SK-RC-45 cells induced apoptosis in activated T cells. However, in the presence of PPPP, the induction of DNA breaks as well as the degradation of Bcl-2 were prevented in both T cells. Furthermore, reduction of the cellular ganglioside content of SK-RC-45 cells by PPPP were observed in HPTLC.

CONCLUSIONS : The fact that SK-RC-45-induced degradation of Bcl-2 as well as cytochrome-c release was prevented by PPPP suggested that these phenomena are ganglioside dependent.