differentiation and the control of liver-specific gene expression is attributed to hepatocyte nuclear factors (HNF), the role of this class of transcription factors in hepatocarcinogenesis is relatively poorly understood.
Using the experimental model of mouse one-step HCC progression in which a slow-growing differentiated tumor (sgHCC) rapidly gave rise *in vivo* to a highly invasive dedifferentiated fast-growing variant (fgHCC), we have investigated the fundamental mechanisms underlying HCC progression and the role of HNFs in this process.
The progression from sg to fgHCC variant was accompanied by a complete loss of cell polarity, a decrease in cell-cell and cell-matrix adhesion, activation of telomerase, extinction of liver-speci?c gene expression, ability to proliferate rapidly in the culture, invasion and metastasis. These alterations were coupled with a reduced expression of several liver transcription factors including HNF4, a nuclear receptor essential for hepatocyte differentiation. Studies of the collection of chemically induced mouse HCCs of independent origin and human HCC clinical samples revealed strict correlation of HNF4 expression with tumor differentiation status.
Forced expression of HNF4 in cultured fgHCC cells partially re-established epithelial morphology, hepatic gene expression, induced the decrease of proliferation rate and dramatically inhibited tumor growth *in vivo*. Thus HNF4 reexpression can promote the reversion of invasive HCC toward a less aggressive phenotype.
HNF4 promoter was found to be inactive in fgHCC, providing the strong evidence for the existing of HNF4 upstream mechanisms responsible for tumor progression. Some candidate genes were identified by microarray analysis of gene expression profiles in one-step HCC progression model. Investigation of the interplay of HNFs network with signaling pathways conducting the control of cell proliferation and morphology is now in progress.
These data indicates that deregulation of tissue-specific transcription regulation network might be a crucial step of epithelial tumors progression.
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755 POSTER

Role of interleukin-1 alpha in hepatic metastatic potential in pancreatic carcinoma cells

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To study the mechanism of gene expression during formation of hepatic metastasis in pancreatic cells, we performed differential display assay of two pancreatic cell lines with highly metastatic potential (BxPc-3 and Sw1990) and two cell lines with non-metastatic potential (Capan-2 and Mia PaCa-2).
There were 39 different shifts in expression, 24 in the highly metastatic group and 15 in the non-metastatic group. Further DNA sequencing, homology research, Northern blotting, and/or reserve transcription-PCR results indicated that interleukin-1 alpha was among those up-regulated in highly metastatic group. An interleukin-1 receptor antagonist was also found to reduce hepatic metastasis in an intrasplenic metastatic assay using nude mice. Antisense cDNA of interleukin 1 alpha into SW1990 caused loss of metastatic potential in nude mice, while interleukin-1 alpha transfection into MIA PaCa-2 generated metastatic potential in nude mice. EMSA assay also demonstrated NF kappa B activation in highly metastatic carcinoma cells. These results indicate that interleukin-1 alpha and activation of the NF kappa B play an important role in the acquisition of metastatic potential in pancreatic cells.

756 POSTER

Interleukin 1 B gene polymorphisms and gastric adenocarcinoma in Oman – Preliminary results

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Gastric cancer (GC) is the most common malignancy in Sultanate of Oman. Interleukin 1beta (IL-1B) gene polymorphisms have been associated with increased risk of GC in Caucasian, Asian and Hispanic populations. No previous studies examined its role in Arab population. We tested the association between IL-1B-31, IL-1B-3954, IL-1RN-(2018) polymorphisms and GC in Omani Arab patients.
Method: Genomic DNA was extracted from peripheral blood of 175 healthy blood donors, 75 gastric cancer patients. The DNA samples were analysed using TaqMan real-time polymerase chain reaction and 5' nuclease assay. The frequency of carriage of the pro-inflammatory alleles were IL-1B-31*C, IL-1B-3954 *T, and IL-1B-RN*C were 76%, 42.3%, and 33.4% respectively in GC patients compared to 67%, 47.8%, and38.2% respectively in the controls. There was no statistical association between carriage of the pro-inflammatory alleles and gastric cancer; IL-1B-31*C (odds ratio [OR] – 1.53, 95% confidence interval [CI]-0.79–2.97, p = 0.2), IL-1B-3954 *T (OR – 1.56, 95% CI-0.56–4.5, p = 0.4), and IL-1B-RN*C (OR – 0.8, 95% CI-0.45–1.47, p = 0.5).
Conclusion: In these preliminary results, there is no association IL-1B-31, IL-1B-3954, IL-1RN-(2018) polymorphisms and GC in Omani Arab patients.

757 POSTER

Analysis of C-KIT mutations in gastrointestinal stromal tumors

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Gastrointestinal stromal tumors (GIST) is the unique model for the molecular based diagnostics, prognosis and treatment of gastrointestinal mesenchymal malignancies. GISTs typically express high levels of the KIT-receptor and carry activating C-KIT mutations, primarily of exons 11 and 9. We analysed C-KIT mutations by direct sequencing in 43 DNA samples from 36 GIST patients and 6 DNA samples from 5 leiomyomas and one leiomyosarcoma. All GISTs were CD117 positive and 65% GISTs were CD34 positive. Mutations of 11 exon were found in GISTs of stomach (68%, 17/25) and intestine (36%, 4/11). The most frequent deletions were located in the region of 551–563aa. with mutations of one of 557, 558 or 559 aminoacid. We did not found any correlation between this mutation and level of malignancy of GIST. In four GISTs with low malignancy we found insertions of different size in the region of 576–585aa of 11 exon. Point mutations of 11 exon were rare. Mutations of 9 exon (duplications of 502–503aa) were found exclusively in GISTs of intestine (45%, 5/11). Such tumors were CD34 negative, rather agressive and had poor prognosis. All DNA samples from 5 leiomyomas and one leiomyosarcoma were CD117 negative without c-KIT mutations in 11 and 9 exons. We conclude that the type and location of C-KIT mutation may be the additional parameter for predicting prognosis and effectiveness of treatment for GISTs.

758 POSTER

Decreased xanthine oxidoreductase is a predictor of poor prognosis in early stage gastric cancer

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Background: Xanthine oxidoreductase (XOR) is a key enzyme in the degradation of DNA, RNA and high energy phosphates. Alterations in XOR expression have been reported in experimental tumorigenesis. We showed previously that breast **cancer** is accompanied by a decrease in XOR expression in about half of the cases, and loss of XOR independently identifies breast cancer patients with unfavorable prognosis. The purpose of the present study was to assess the clinical relevance of XOR in gastric **cancer**.
Materials and Methods: In this study we determined the XOR levels by immunohistochemistry in tissue microarray specimens of 337 patients with gastric **cancer** and assessed the relation between XOR expression and a series of clinicopathologic variables as well as disease specific survival.
Results: XOR expression was moderately decreased in 41% and undetectable in another 14% of the tumors as compared to the corresponding normal tissue. Decreased XOR was associated with advanced stage, deep tumor penetration, diffusely spread tumor location, positive lymph node status, large tumor size, non-curative disease, cellular aneuploidy, high S-phase fraction and high cyclooxygenase-2 expression, but not with p53 expession or Borrmann classification. Downregulation of XOR was associated with unfavourable outcome, and the cumulative five year gastric specific survival in patients with strong XOR expression was 47% compared to 22% in those with moderate-to-negative expression ($P < 0.0001$). This was also true in patients with stage I-II ($P = 0.0124$) and lymph node negative ($P = 0.018$) disease as well as in patients with smaller ($\leqslant 5$ cm) tumors ($P = 0.02$).
Conclusions: Our data suggest that XOR expression in gastric cancer might be a new marker for a more aggressive gastric cancer biology, similar to that as previously reported for breast cancer.

759 POSTER

Relative risk according to the DNMT3B C → T promotor polymorphism in gastric cancer

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Background: As the recent research about methylation is gone, the methylation of CpGisland was reported to important pathway of tumorigenesis as another epigenetic modification. This methylation process is mediated by DNA-methyltransferase (DNMTs) and DNMT1, DNMT3B was confirmed as active subtypes. It was reported that the activity of DNMT3B increased in bladder, colorectal, renal and pancreas cancer. DNMT3B genc increases activity of promotor about 30% in cases of C → T promotor polymorphism in vitro. Exact pathway of promotor polymorphism is undefined, but Tvariant increases translation of DNMT3B and derives hypermethylation of tumor suppressor gene and cause functional inactivity in human. In this study we recognize about correlation between the rate of C → T promotor polymorphism of DNMT3B gene and susceptibility in gastric cancer.
Materials and methods: 176 patients who was diagnosed of gastric cancer was case group and control group was 70 patients woho was identitied H.pylori infection in gastrofiberoscopic examination. All patient group and control groups picked 10cc blood sample and extracted DNA and performed PCR, we extracted 380 bp target DNA and performed restriction reaction rsing Avrll enzyme (New England Biolab, Inc). In case there is T variant, we could confirm two bands that have 207 bp and 173 bp. We analysed data using SPSS statistically.
Results: In case there is T variant, it is 150 cases (85.2%) – CT (71.6%), TT (13.6%), CT+TT (85.2%) in cancer group and is significantly higher in the cancer group than the control group (42 cases (60.0%) – CT (42.9%), TT (17.1%), CT+TT (60.0%) ($p < 0.05$). In multivariant analysis, relative risk in CT (heterozygote type) was high 4.523 times than cc (wild type), and it was high 2.154 times in TT (homozygote type), and increased 3.846 time in case is CT+TT (T variant) ($p < 0.05$). However, If there was T variant, we can assume that the relative risk of gastric cancer increases 3.846 times. But, there was no significance correlation with stage, differentiation and Lauren's classification by T variant. The infection rate of H. pylori was 34.6%, the rate of gastric cancer is higher in H. pylori positive groups (87.1%) than negative groups (63.4%). In case of T variant, H. pylori infection rate was increased about 1.19 times, but there was no statistical significance.
Conclusions: In these results, we can conclude that T variant of CNMT3B promotor gene shows about 1.42 times higher than normal and the relative risk increase 3.846 times if there is the T variant of DNMT3B promotor gene in gastric cancer. However, there is no relation between T variant and pathologic status and H.pylori infection rate.

760 POSTER

Duplex RT-PCR improves accuracy in detecting lymph node micrometastasis in early gastric cancer

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Background: We previously reported that MUC2 is a useful marker in the detection of lymph node micrometastasis (LMM) in gastric cancer *(J surg oncol. 2004; 88: 63–70)*. However, MUC2 is rarely expressed in early poorly-differentiated adenocarcinoma. To improve accuracy in detection of LMM in gastric cancer, we paid attention to a novel gene, *TFF1*, which is preferentially expressed in diffuse-type gastric cancer cells. We have examined its potential as a novel marker for the detection of lymph node micrometastasis in gastric cancer, and investigated a novel method for LMM detection in gastric cancer.
Material and methods: We selected 33 histologically node negative (pN0) early gastric cancer patients who underwent curative surgery in our surgery department between July 2002 and June 2004. This study group consisted of 22 mucosal cancer and 11 submucosal cancer patients. Each lymph node was dissected into two pieces. One piece was formalin fixed and paraffin embedded for histological examination. The other was used for duplex (MUC2 and TFF1) reverse transcriptase-polymerase chain reaction (RT-PCR) assay.
Results: MUC2 and TFF1 were expressed in 22 of 33 (66.7%) and 30 of 33 (90.9%) of the gastric carcinoma specimens. MUC2 and TFF1 were expressed in 5 of 13 (38.5%) and 13 of 13 (100%) undifferentiated carcinoma specimens. The positive rate of TFF1 was significantly higher than that of MUC2 in the undifferentiated carcinoma specimens ($P = 0.002$). All carcinoma specimens were positive for MUC2 and/or TFF1. MUC2 was expressed in 15 of 310 lymph nodes (4.8%) from 6 patients (18.2%). TFF1 was expressed in 9 of 310 lymph nodes (2.9%) from 6 patients (18.2%). The detection rate of LMMs was raised until 6.8% (21 lymph nodes) and 33% (11 patients) by using duplex RT-PCR assay. We were able to detect LMMs in 7 of 22 patients (31.8%), especially in mucosal cancer. In the 7 cases, 3 cases were MUC2 positive/TFF1 negative and the other 4 cases were MUC2 negative/TFF1 positive. Duplex assay revealed no false positive results in the control specimens.
Conclusions: Duplex RT-PCR assay provides higher accuracy than either MUC2 or TFF1 alone to detect LMM in early gastric cancer.

761 POSTER

Gastric cancer susceptibility in the P53 codon 72 polymorphism

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Background: The P53 codon 72 polymorphism results in either arginine or proline, there are many studies to clear the relationship between P53 codon 72 genotypes and specific cancer risk and susceptibility. Recently, the P53 codon 72 polymorphism has been extensively studied to determine the risk factors responsible for carcinogenesis. The purpose of this study was to investigate the association of the genotype distribution of the P53 codon 72 polymorphism and gasric cancer susceptibility via in comparison of gastric cancer group and normal control genotypes. We also studied the relation between the distribution of P53 codon 72 genotypes and the state of P53 immunohistochemical staining, infectivity of Helicobacter pylori and the clinicopathologic findings in gastric cancer patients.
Materials and methods: In our study, the samples consisted of 145 gastric cancer patients and 77 normal controls. The analysis was performed by polymerase chain reaction (PCR), restriction fragment length polymorphism (RFLP) method using DNA extracted from gastric cancer patients blood and normal controls blood.
Results: The frequency of three genotypes arg/arg, arg/pro and pro/pro in gastric cancer patients was 41.1%, 38.6% and 20.0%. In controls, it was 36.3%, 53.2% and 10.3%. There was no statistical significance ($p = 0.312$, 0.665). There was no correlation between the frequency of the three genotypes and the state of P53 immunohistochemical staining infectivity of H. pylori. The pro/pro homozygote was more frequent in lymph node metastasis (25.6% vs 7.3%, $p = 0.026$).
Conclusions: The P53 codon 72 polymorphism does not contribute to gastric cancer susceptibility. The P53 codon 72 polymorphism is not associated with the state of P53 immunohistochemical staining and the infectivity of H. pylori but pro/pro genotype is associated with the lymph node metastasis in gastric cancer patients.

762 POSTER

Value of elevated Ki67 index (>10%) and p53 protein expression as prognostic factors in GIST

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Background: Gastrointestinal stromal tumors are the most common mesenchymal tumors and express CD117. But the prediction of the malignant potential of GISTs is still difficult. The aim of this study is to evaluate the prognostic accuracy of elevated Ki67 index and p53 overexpression in combination with classical prognostic factors(tumor size and mitotic index.
Material and Methods: A retrospective study was conducted of 84 patients who had re-evaluated to confirm diagnosis based on immunohistochemical analysis with CD117 expression, between Jan 1991 and Dec 2001. Cases were classified and very low, low, intermediate and high risk group according to 2001 NIH consensus symposium. Elevated Ki67 index was assign to the lesion that displayed 10% or more of immunoreactive cells. And p53 expression is assign to the area with 5% or more of eosinophilic nucleus.
Results: The elevated Ki67 was noted in 37 (44.0%) out of 84 cases. High risk patients showed elevated Ki67 index frequently ($P < 0.0001$) and there was significant difference between elevated Ki67 and survival rate ($P = 0.0417$). The p53 expression was noted in 32 (38.1%) out of 84 cases. p53 expression was significantly higher in high risk patients ($P = 0.0081$). But, there was no significant difference between p53 expression and survival rate. As a result of multivariable analysis, tumor size ($P = 0.0059$), mitotic rate ($P = 0.0016$) and elevated Ki67 index ($P = 0.0384$) were proved as significant independent prognostic factors.