rectum. Among 329 patients with known family history, 132 (40.1%) had positive FH. The overall rate of abnormal immunostaining for hMLH1, hMSH2, hMSH6 and PMS2 were 4.4%, 7.2%, 3.5%and 4.9% respectively. Overall 44 patients (12.7%) had at least one abnormal MMRP staining. Abnormal MMRP were not significantly associated with histopathologic factors including T stage, N stage and grade. There was no difference in MMRP staining as a result of whether patients were male or female except PMS2 that was significantly more abnormal in male ($p = 0.083$). Abnormal staining of MMRP were seen further in colon than in rectum that was significant for hMLH1 ($p = 0.044$). Patients with family history of CRC had more abnormal staining that was significant for hMSH2 ($p = 0.061$). There was no difference in MMRP staining according to vital status.
Conclusion: Our results suggest that abnormal MMRP is associated with clinical factors such as family history of CRC but not with pathologic factors. Abnormal MMRP is more important pathway for carcinogenesis in colon than rectal cancer.

370 POSTER

Two pathways of carcinogenesis in patients with colorectal cancer less than 45 years old

M. Molaei[1], A. Motlagh[2]. [1]*Shahid Beheshti Medical University, Research Center for Gastrointestinal and Liver Disease (RCGLD), Tehran, Iran;* [2]*Shahid Beheshti Medical University, Cancer Research Center (CRC), Tehran, Iran*

Background: Colorectal cancer (CRC) arises from a complex series of molecular changes that involve at least two different pathways. These include microsatellite instability (MSI) pathway and chromosomal instability (CIN) pathway. The aim of this study was the determination of predominant pathway involved in carcinogenesis of patients with CRC less than 45 years old with and without family history (FH) of CRC.
Materials and Methods: In our study surgical pathology specimens of 108 patients with CRC less than 45 years old were immunostained for DNA mismatch repair proteins (MMRP) including hMLH1, hMSH2, hMSH6 and PMS2. Beta-catenin and P53 were also examined for CIN pathway.
Results: Totally 108 patients with median age of 40 (20−45) were evaluated. Fifty seven patients were male and 51 were female. The site of tumor in 84 patients was colon and in 14 were rectum. Among 96 patients with known family history, 33 (34.4%) had positive FH. The overall rate of abnormal immunostaining were MLH1 8.3%, MSH2 18.5%, MSH6 8.3%, PMS2 11.1%, P53 74.1% and beta catenin 35.2%. Meanwhile abnormal staining for hMSH2 and hMSH6 were significantly more seen in patients with positive family history ($p = 0.008$ and $p = 0.032$ respectively). Patients with positive FH for CRC had significantly more abnormal MMRP (54.5% vs. 20.6%, $p = 0.001$) and less positive p53 (54.5%vs. 81%, $p = 0.006$) than patients with negative FH. Patients with early T, N stage tumor had at least one more abnormal MMRP than advance T, N stage ($P = 0.050$ for T and $P = 0.030$ for N stage). Among different factors abnormal hMSH2 had significant association with lower cancer related death ($P = 0.060$). Patients with rectal cancer had more abnormal MMRP than patients with colon cancer but not significantly (35.7% vs. 29.8%, $p = 0.655$) and positive p53 staining for rectal and colon cancer were 71.4% and 72.6% respectively. Both in colon and rectal cancer patients with negative family history had more prevalent positive p53 (80.4% vs. 56.7%, $p = 0.022$ for colon and 81.8% vs. 33.3%, $p = 0.099$ for rectal cancer).
Conclusion: Our study indicates that even in CRC less than 45 years old, the main pathway for carcinogenesis in patients with negative family history is CIN, but in positive family history MSI is as effective as CIN. However main pathway in both colon and rectal cancer is CIN.

371 POSTER

Activation of signalling pathways by increased expression of HC GP-39 in brain tumors

V.M. Kavsan[1], V.V. Dmitrenko[1], K.A. Shostak[1], Y.A. Zozulya[2]. [1]*Institute of Molecular Biology and Genetics, Biosynthesis of nucleic acids, Kiev, Ukraine;* [2]*A.P. Romodanov Institute of Neurosurgery, Neurooncology, Kiev, Ukraine*

Background: The aim of this research is determination and characterization of potential molecular markers for human brain tumors and their possible interaction with main signal pathways in eukaryotic cells. Such knowledge is necessary not only for understanding the tumorigenesis, but also the mechanisms of normal brain functioning.
Materials and Methods: Diffrentially expressed genes were determined by Serial Analysis of Gene Expression (SAGE); gene expression have been analysed by Northern hybridization.
Results: The comparison of 9 glioblastoma and 5 human adult normal brain SAGE-libraries revealed 129 genes with >5-fold differences, 44 of them met the criteria for genes overexpressed in tumors. The majority of these genes are related only to a few functional groups: genes encoding proteins involved in angiogenesis, immune response, extracellular matrix, drug-resistance, and several genes are related to the mitogen-activated protein kinase cascades: CD74, EGFR, CTGF, IGFBP5, IGFBP7, and IGFII. We found unusual processing of IGF-2 primary transcript in meningiomas and ependimomas, anomaly expression of IGF-II may contribute towards tumorigenesis. Increasing of IGF-I gene expression was not found in glioblastomas. It is possible to suppose that glial tumor development is activated by some other way. C hitinase 3-like 1 gene encoding human cartilage glycoprotein-39 (HC gp-39 or YKL-40) was among the most upregulated genes and as was shown recently, it initiates cellular responses very similar to those elicited by IGF-1: activates both extracellular signal-regulated kinase (ERK) – and protein kinase B (AKT)-mediated signalling cascades, which are associated with the control of mitogenesis. Both proteins act synergistically with respect to their growth-stimulating activity; both suppress the cytokine-induced secretion of MMPs.
Conclusions: Since deregulation of the IGF system and HC-gp39 is a frequent pattern in tumors, IGFs/IGFBPs/HC-gp39 should be included in the panel of tumors markers used for histopathological diagnosis and serological surveillance procedures in various malignancies. Novel antisense and iRNA strategies targeting components of IGF-axis and HC-gp39 may offer additional options for treatment of malignant gliomas.

372 POSTER

Role of hepatocyte growth factor/c-met signaling in regulating urokinase plasminogen activator on invasiveness in human hepatocellular carcinoma: a potential therapeutic target

L. Kyung Hee[1], K.I.M. Min Kyoung[1], C.H.O.I. Eun Young[1], J.A.N.G. Byung Ik[2], L. Heon Ju[2], K. Tae Nyeun[2], K. Hong Gin[3], Y. Sung Soo[3], K. Jung Hye[4], K. Jae-Ryong[4]. [1]*Yeungnam University hospital, Hematology-Oncology, Daegu, Korea;* [2]*Yeungnam University hospital, Gastro-Enterology, Daegu, Korea;* [3]*Yeungnam University hospital, General Surgery, Daegu, Korea;* [4]*Yeungnam University hospital, Biochemistry and Molecular Biology, Daegu, Korea*

Background: Hepatocyte growth factor (HGF), its transmembrane tyrosine kinase receptor (c-Met) and urokinase type plasminogen activator (uPA) is a key protein in the plasminogen activation system, which plays a proteolytically important role in the invasion and metastasis of various types of cancers. However, the mechanisms by which HGF/c-Met signaling mediates cancer progression and metastasis are unclear.
Methods: this study was designed to investigate the roles of HGF/c-Met in tumor progression and metastasis in HepG2 and Hep3B hepatoma cell lines.
Results: Treatment with HGF increased c-Met phosphorylation in a dose-dependent manner. Activity of c-Met phosphorylation was peak at 1 to 3 minutes later after HGF treatment and then declined. HGF enhanced the protein level and the activity of uPA in HepG2 and Hep3B cells and also uPAR protein level increased in a HGF dose dependent manner. HGF increase cell invasion through matrigel. A monoclonal antibody against human uPA receptor, mAb 3936, inhibited HGF-mediated tumor cell invasion in a dose dependent manner. Down-regulation of uPA using uPA-shRNA induced a decrease in in vitro cell invasion in HepG2 cells.
Conclusions: These results suggest that HepG2 and Hep3B cells express functional c-Met, which may provide a target for a therapeutic basis to interfere with metastases of cancer cells by inhibiting uPA system-mediated proteolysis.

373 POSTER

Role of manganese superoxide dismutase on growth and invasive properties of human estrogen-independent breast cancer cells

Z. Kattan, V. Minig, M. Dauça, P. Becuwe. *Laboratory of cell biology, University of Nancy 1, Cell biology, Vandoeuvre lès Nancy, France*

Background: Manganese superoxide dismutase (MnSOD) is known to play a role in cancer. MnSOD exerts a tumor suppressive effect in estrogen-dependent human breast cancer cells. In the present study we investigated the in vitro role of MnSOD in the growth of some aggressive and highly metastatic estrogen-independent breast cancer cells, i.e. MDA-MB231 and SKBR3 cells.
Experimental procedures: This in vitro study used estrogen-dependent and estrogen-independent breast cancer cell lines. Antisense RNA strategy was used to inhibit MnSOD expression and to study consequence on breast cancer cell growth and invasiveness.
Results: We show that estrogen-independent cells expressed a significantly higher basal MnSOD level compared to estrogen-dependent human breast cancer cell lines (MCF-7 and T47D). For MDA-MB231 cells, the high MnSOD level was accompanied by an overproduction of