the migration potential. Additionnaly, the paxillin, a central protein of focal adhesion contact points, is highly downregulated when E2F2 is inhibited.
Conclusions: This study showed that inhibition of E2F2 gene expression leads to morphological rearrangements and the proliferation and migration potentials are reduced. These effects could result from a reduced expression of integrins and paxillin which are structural compounds of focal adhesion contributing to cell adhesion and motility. These results will be comforted in *in vivo* xenograft experiments to ascertain the good prognostic value of E2F2 deletion and strengthen the hypothesis that E2F2 expression deregulation could play a key role in human colon tumour initiation/progression but not dissemination.

6025 POSTER

Association Between ESR1 and ESR2 Polymorphisms and Risk of Colorectal Cancer in Chinese Han Population

H.L. Wu[1], X.L. Yuan[1], H.H. Xiong[1], G.Y. Hu[1], J. Cai[1], H. Xu[2], J. Hu[2], J.G. Chen[3], X.P. Chen[2]. *[1]Wuhan Tongji Hospital, Oncology Department, Wuhan, China; [2]Wuhan Tongji Hospital, Surgery Department, Wuhan, China; [3]Wuhan 8th Hospital, Surgery Department, Wuhan, China*

Background: Epidemiologic and biologic evidence suggests that estrogen may play an important role in pathological progress of colorectal cancer (CRC) and lung cancer. As the action of estrogens is regulated by the estrogen receptor (ESR), the objective of this study is to investigate whether variants *ESR1* and *ESR2* genes confer genetic risk to CRC and lung cancer, and different genetic effect between males and females in the Chinese Han population.
Material and Methods: Two SNPs rs2234693, rs9340799 in *ESR1* and two SNPs rs1256049, rs4986938 in *ESR2* were genotyped. For CRC, two independent studies including 331 cases and 378 cases with a shared common controls with 747 subjects were enrolled. For the lung cancer, 609 patients and 700 controls were selected for analysis.
Results: The minor allele T of *ESR2* rs1256049 was associated with increased CRC risk (adjusted $P = 0.025$, $OR = 1.21$). More specifically, when cases were divided into two groups by gender, variation in the *ESR2* rs4986938 was associated with an increased risk of CRC in men (adjusted $P = 0.005$, $OR = 1.57$), but it did not contribute to the disease susceptibility in women. Lacking of association was observed between lung cancer and *ESRs*.
Conclusions: This study shows that *ESR2* rs4986938 polymorphisms may be linked with increased CRC susceptibility and furthermore, this association is gender specific. This study also indicates that *ESR2* rs1256049 confers a significant risk of CRC. Our findings further suggest a possible role of *ESR2* variants on CRC.

6026 POSTER

MDGA1 Expression and Promoter Methylation Analysis in Colorectal Cancer

C. De Juan Chocano[1], J. Head[1], J. Espada[2], A. Morán[1], T. Fernández-Marcelo[1], I. Pascua[1], A. Sánchez-Pernaute[3], A. Torres[3], M. Benito[1], P. Iniesta[1]. *[1]Faculty of Pharmacy Complutense University, Biochemistry and Molecular Biology, Madrid, Spain; [2]CSIC-UAM, Biomedical Research Institute "Alberto Sols", Madrid, Spain; [3]San Carlos Hospital, Surgery Service, Madrid, Spain*

Background: Human *MDGA*1 gene encodes a Glycosylphosphatidylinositol (GPI) anchored protein containing a MAM domain (Meprin, A5 protein, receptor-protein tyrosine phosphatase m). This gene was isolated in our laboratory and genomic organization as well as gene expression patterns in normal human tissues and tumours has been reported. MDGA1 protein is a 955 aminoacids glycoprotein (37 kDa) attached to the cell membrane by a GPI anchor and localized in lipid rafts. We have also reported that MDGA1 expression increases cell motility and cell-cell adhesion and reduces adhesion to extracellular matrix proteins in MDCK cells.
In the present study we have analysed *MDGA*1 expression level and promoter methylation status of the gene in colorectal cancer. Patients and methods: Forty-three primary colorectal tumours were obtained from patients who underwent surgery at San Carlos Hospital in Madrid (Spain). As control samples, a pool of eight-ten normal tissues from colon was used. *MDGA*1 expression was analysed in all these samples by real time quantitative PCR using the TaqMan® gene expression system. For *MDGA*1 methylation analysis genomic DNA was treated with sodium bisulfite by using BisulFlash® DNA modification kit. The methylation status of *MDGA*1 was then determined by Methylation-Specific Polymerase chain reaction (MSP). Results: Our results shown a significant down regulation of *MDGA*1 gene expression, as compared to normal tissues, in 25 of the 43 colorectal tumours analysed (58%). We next analyzed the methylation status of *MDGA*1 promoter in tumour tissues to establish a potential relationship with gene expression.
Conclusion: Expression of *MDGA*1 is downregulated in human colorectal tumours. To our knowledge, no study of *MDGA*1 promoter methylation and gene expression has been reported so far.

6027 POSTER

RON is Associated With Colorectal Cancer Progression via the Inhibition of Apoptosis and Cell Cycle Arrest Through the Modulation of Akt, MAPK and β-catenin Pathways

W. Bae[1], Y. Joo[2], K. Kim[3], I. Chung[1], S. Lim[4], J. Hwang[1], H. Shim[1], S. Cho[1]. *[1]Chonnam National University Hwasun Hospital, Hematology-Oncology, Hwasun Jeonnam, Korea; [2]Chonnam National University Hwasun Hospital, Gastroenterology, Hwasun Jeonnam, Korea; [3]Chonnam National University Medical School, Pharmacology, Gwangju, Korea; [4]Chonnam National University Hwasun Hospital, Center for Biomedical Human Resource, Hwasun Jeonnam, Korea*

Background and Aims: Recepteur d'Origine nantais (RON) is associated with the induction of oncogenic properties including malignant transformation, migration and proliferation. Moreover, overexpression of RON has been observed in various human epithelial cancers. The aims of current study were to evaluate whether RON affects tumour cell behaviors and oncogenic signaling pathways in human colorectal cancers, and to examine the relationship of its expression with various clinicopathological parameters and patient survival.
Methods: To study the biological role of RON on tumour cell behavior and oncogenic signaling pathways in human colorectal cancer, we used small interfering RNAs (siRNA) to knockdown endogenous RON gene expression in human colorectal cancer cell lines, SW480 and DLD1. To study the role of RON in human colorectal cancer progression, we have used an immunohistochemical technique to localize RON protein in paraffin-embedded tissue blocks obtained from 161 colorectal cancer patients.
Results: Knockdown of RON by siRNA diminished invasion of human colorectal cancer cells. The proportion of apoptotic cells induced by transfection of RON siRNA was greater than that induced by transfection of the scramble siRNA. Knockdown of RON resulted in an arrest in the G0/G1 phase of the cell cycle. Knockdown of RON activated cleaved caspase-3, cleaved PARP and down-regulated the expression of survivin and XIAP leading to induction of apoptosis. Knockdown of RON decreased Akt and MAPK signaling proteins. Knockdown of RON blocks β-catenin activation and down-regulated c-myc and cyclin D1 gene expression. RON expression was significantly associated with lymphovascular invasion, lymph node, distant metastasis, tumour stage and poor survival.
Conclusions: These results indicate that RON is associated with human colorectal cancer progression via the inhibition of cell cycle arrest and apoptosis through the modulation of Akt, MAPK and β-catenin signaling pathways.

6028 POSTER

Mechanical Activation of Myc and Twist Oncogenes in Mouse Colon Pre-Tumoral Tissues

M.E. Fernandez Sanchez[1], S. Barbier[1], J. Whitehead[1], S. Robine[2], E. Farge[1]. *[1]Institut Curie, UMR168, Paris Cedex 05, France; [2]Institut Curie, UMR144, Paris Cedex 05, France*

Our understanding of multi-cellular tissue morphogenesis and homeostasis is being challenged by increasing evidence demonstrating the involvement of a mechano-sensitive interplay between shape-related strains and state of expression of the genome in tissues. Even though such mechanical cues have been demonstrated to be critically involved in key steps of early embryonic development *in vivo*, as well as during organogenesis, the associated primary mechano-transduction sensors and the underlying molecular mechanisms remain unknown. We show here first experimental evidence of a role of the multi-cellular tissue pressure, potentially associated to external pressure (associated to intestinal transit) or to internal pressure (associated to tumour growth), in the expression of tumour progression genes, with direct mechanical manipulation and perturbation of the tissue mimicking environmental pressure. Genetically predisposed pre-tumoral APC1638N+/− mice colon explants (Adenomatous Polyposis Coli protein, mice carrying one mutant allele APC1638N) were subjected to a mechanical deformation in a tissue compression device (1.2 mm depth for control and 0.3 mm depth for compressed). This mechanical deformation causes the Src-family kinase dependent phosphorylation of the site Y654 of interaction of the beta-catenin with E-cadherins, leading to the release of a pool of beta-catenin into the cytoplasm, which is not fully degraded due to the defect of APC expression in the APC+/− colon tissues. We observe also the nuclear translocation of beta-catenin, with activation of Twist and c-Myc target oncogenes expression. Finally, we