PPARγ and estrogen receptor (ER) in breast cancer cells. The present study was carried out to evaluate the transcriptional activity of PPARγ isoforms, PPARγ1 and PPARγ2, and ERα in human breast cancer cell lines treated with ligands for PPARγ and ERα, 15deoxy-prostaglandin J_2 (15d-PGJ_2) and 17β-estradiol (E2) respectively, by quantitative Real-Time PCR using homologous internal standards. ER-positive (MCF-7) and ER-negative (MDA-MB-231) breast cancer cells were treated with EC_{50} doses of 15d-PGJ_2 and 10 nM E2 alone or in combination for up to 48 hrs. The ERα, PPARγ1 and PPARγ2 mRNA expression levels were significantly up regulated ($p < 0.05$) in MCF-7 cells treated with 15d-PGJ_2 or E2 alone. The combined treatment of 15d-PGJ_2 and E2 however, significantly down regulated the ERα mRNA expression, showed no significant difference in PPARγ1 mRNA expression and up regulated the PPARγ2 mRNA expression level in MCF-7 cells. The PPARγ1 mRNA expression was significantly up regulated in MDA-MB-231 cells treated with 15d-PGJ_2 alone and in combination with E2. In contrast, no significant difference in the PPARγ1 mRNA expression level was observed in E2 treated cells. The mRNA expression of PPARγ2 was significantly down regulated in MDA-MB-231 cells treated with 15d-PGJ_2 but not with E2 treatment. Interestingly, a significant up regulation of PPARγ2 mRNA expression was observed in these cells when treated with the combination of 15d-PGJ_2 and E2. The differential expression of PPARγ1, PPARγ2 and ERα in ER-positive and ER-negative breast cancer cells suggests a complex regulation of these transcription factors in breast carcinogenesis, the mechanism of which remains to be elucidated.

576 Poster

Inactivation of the FHIT gene in clear cell renal carcinomas

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FHIT is a tumour suppressor gene which is frequently inactivated in different types of cancer. Yet little is known about the mechanism of FHIT inactivation in clear cell renal carcinomas. Since genetic alterations were not frequently observed in DNA corresponding to the FHIT gene in renal tumours, to elucidate the mechanism of FHIT gene silencing we examined 22 paired samples of clear cell renal carcinoma and non-malignant renal tissue for the methylation of the FHIT 5'CpG island by methylation-specific PCR. Hypermethylation of the FHIT 5'CpG island was detected in 54.5% of clear cell renal carcinomas. Bisulfite sequencing of the FHIT 5'CpG island confirmed the results obtained by methylation-specific PCR for selected samples. We showed that expression of the FHIT gene is inversely correlated with hypermethylation of the FHIT 5'CpG island in the selected samples. Our results suggest that hypermethylation of the FHIT 5'CpG island may be responsible for inactivation of the FHIT gene in clear cell renal carcinomas.

577 Poster

Profile of methylaion of tumour related genes in breast cancer in Tunisian women

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Background: It is becoming increasingly recognized that aberrant hypermethylation of gene promoter regions is an important mechanism inducing transcriptional silencing of tumor suppressor genes in various human cancer including breast carcinomas. There are several reports on methylation profiles of breast cancer patients from Western population. However, to our knowledge there is no study in Arabian populations till date. It is important to note that Tunisia belong to low incidence zone of breast carcinoma with standardized incidence of 19.6 per 100 000 women. The present study was undertaken to evaluate the DNA methylation profile of tumor-related genes in Tunisian breast carcinomas.

Methods: One hundred and nine invasive ductal carcinomas diagnosed at the Department of Pathology at Farhat-Hached Hospital of Sousse (Tunisia) were investigated for the methylation status of a panel of fifteen known tumor-suppressor and -related genes by methylation-specific polymerase chain reaction. Both specific methylated and unmethylated primers were used for PCR and the products were visualized with agarose gel electrophoresis.

Results: Of the 109 cases 23 (21%) showed methylation at 1 to 3 genes, 36 (33%) were methylated at 4 to 6 genes, and 50 (46%) were methylated in more than 6 genes. No cases were methylated at all fifteen genes and all cases showed at least one gene methylated. Hypermethylation frequencies were 78% for RASSF1A, 66% for SHP1, 61% for HIN1 and BRCA1, 47% for P16 and ER, 42% for CDH1 and APC, 40% for BLU, 35% for DAPK, 34% for RARβ2, 27% for GSTP1, 17% for TIMP3, 14% for CCND2, and 8% for hMLH1.

Conclusion: This study shows high frequencies of methylation of tumor-suppressor and -related genes in Tunisian women in comparison with Western women. These observations suggested that gene hypermethylation may be affected by ethnicity. Besides ethnicity, these epigenetic variations may also be attributed to differences in the risk factors such as life style and dietary habits. Thus, our study underscores the limitation of extrapolation of the Western data to other populations. Our findings, reported here will hopefully provide a stimulus for additional studies comparing populations with different ethnicity and risk factors.

578 Poster

Do PIKE, PIK3CA and PTEN genes in Phosphoinositide-3-kinase/Akt signaling pathway play a crucial role in progression of high-grade gliomas?

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Background: High-grade gliomas are the most common primary brain tumors and associated with poor survival. Phosphoinositide 3-kinase/AKT signaling pathway is important in the development of malignant gliomas. The PIK3CA gene, encodes the p110alpha catalytic subunit of PI3K, is activated in various cancers. PIKE (CENTG1), encodes a protein that binds to phosphorylated Akt and increases its activity, is frequently amplified in glioblastomas. phosphatase and tensin homology deleted on chromosome 10 (PTEN) is an important regulator of the PI3K/Akt pathway via its ability to antagonize PI3K. PTEN function is lost in high-grade glioma due to loss of heterozygosity or mutations and loss of this gene function associated with activated AKT levels. In this study we aimed to identify the roles of the genes which were components of the PI3K/Akt signaling pathway and correlation between their expression profiles in malignant disease progression.

Materials and methods: Human brain tumor samples were obtained from patients who underwent primary therapeutic subtotal or total tumor resection performed under surgical operation. All cases signed a written informed constant statement approved by local ethics committee. Explant cell cultures were performed from brain tumor tissues of 18 (6 female, 12 male; average age 49.72±14.83) cases. Malignant lesions have been described in the medical history of cases: anaplastic oligoastrocytoma WHO grade III (7 cases), GBM WHO Grade IV (7 cases) and brain metastasis from lung cancer (4 cases). Total RNA was isolated from tumor cells. RNA of the tumor samples were reverse-transcribed with oligo dT primers and quantified by real-time reverse transcription polymerase chain reaction (RT-PCR) performed with the LightCycler instrument. U87MG glioblastoma cell line was used as positive control.

Results: The mean relative ratios of PIK3CA, PIKE and PTEN genes were found; 162.46, 13.67 and 3733.61, respectively. There was no significant association between tumor grades/age and gene expressions. The correlation between PIKE and PTEN gene expressions was found significant especially in anaplastic oligoastrocytoma ($p<0.0001$). Similar correlation was found between PIK3CA and PIKE genes in cases with brain metastasis from lung cancer ($p=0.037$).

Conclusion: Due to these expression correlations, PI3K/Akt signaling pathway genes could be used as pivotal biomarkers and build smart and effective drug combinations of molecular targeted treatments of malignant gliomas.

579 Poster

Cyclooxygenase-2 dependent regulation of E-cadherin through the transcription repressors Snail and ZEB1 is limited to conventional gastric cancers cell lines

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Background: Approximately 10% of patients present with gastric cancer before the age of 45, so-called early onset gastric cancer (EOGC), and it is postulated that genetic factors may play a more important role than in conventional gastric cancer (presenting > 45 years old). EOGCs have been shown to have a different molecular pathway than conventional gastric cancers and we have shown previously that they have a strikingly low expression of COX-2 compared to conventional gastric cancer, where it is often overexpressed.

Aims: COX-2 regulation of E-Cadherin has been shown to occur in lung cancer and given that E-Cadherin is critical in gastric carcinogenesis, we examine the relationship between these two molecules in this study. In