Experimental Pathology/Biomarkers

P10

TGF-β1 but not VEGF expression is regulated at the protein level in endometrial cancer

G. Soufla[1], F. Porichis[1], S. Sifakis[2], S. Baritaki[1], D.A. Spandidos[1]. [1]*University of Crete, Faculty of Medicine, Laboratory of Virology, Heraklion, Greece;* [2]*University Hospital of Heraklion, Department of Obstetrics and Gynecology, Heraklion, Greece*

Vascular endothelial growth factor (VEGF) is the major stimulus for endothelial cell proliferation in endometrial carcinomas and is, therefore, associated with high angiogenesis. The role of transforming growth factor-β1 (TGF-β1) in angiogenesis and cancer development is complex, and involves aspects of tumor suppression at the initial steps of oncogenesis as well as tumor promotion as tumors evolve. In the present study we evaluated the mRNA expression pattern of VEGF and TGF-β1 by Real-Time PCR in tissue samples of 20 patients with endometrial cancer, 4 patients with complex atypical endometrial hyperplasia (AEH) and adjacent normal tissues of all patients. Western blot analysis was performed to evaluate VEGF and TGF-β1 protein levels. Transcript levels of VEGF were found to be significantly elevated in 25% of AEH cases and in 35% of endometrial cancer cases. VEGF mRNA underexpression was observed in 25% and 5% of AEH and cancer cases respectively. VEGF protein levels correlated with mRNA levels in most cases. TGF-β1 transcript levels did not differ between pathological and adjacent normal tissues, except for one case of AEH (25%) and one case of endometrial cancer (5%) where downregulation was observed. Interestingly, TGF-β1 protein levels were substantially lower in tumor samples compared to controls in 50% of AEH and 43% of cancer cases respectively. TGF-β1 protein expression was not detected in 50% of AEH and 29% of cancer tissues while it was detectable in the adjacent normal tissues. 21% of endometrial cancer tissue-pairs were found not to express TGF-β1 protein at all. Overexpression of TGF-β1 protein in the malignant compared to the adjacent normal tissue was observed in one case of advanced endometrial cancer, supporting the hypothesis of TGF-β1's tumorigenic role as tumors evolve. Post-transcriptional mechanisms seem to control TGF-β1 expression in endometrial cancer according to our findings.

P11

Evaluation of VEGF and TGFB1 mRNA expression profiles as markers of malignant transformation in cytological cervical specimens

S. Baritaki[1], S. Sifakis[2], G. Soufla[1], D.A. Spandidos[1]. [1]*University of Crete, Medical School, Virology, Heraklion, Greece;* [2]*University Hospital of Heraklion, Obstetrics and Gynecology, Heraklion, Greece*

Tumor angiogenesis has been described in almost all human cancer types comprising malignancies of the female genital tract. Based on previous findings (Soufla G, et al., Cancer letters 221: 105-11, 2005) indicating the correlation between VEGF, TGFB1 and TGFBR1 mRNA expression levels in cervical tissues with the malignant transformation of the uterine cervix,we investigated whether similar expression profiles of the above genes could also be detected in cytological cervical specimens obtained during a PAP test examination. Furthermore, we examined whether the altered mRNA patterns of the above angiogenic markers could reflect an early prognostic significance for the clinical progression of the disease. Transcript levels were assessed by real-time PCR analysis in 20 cytological cervical samples with cervical intraepithelial neoplasia (CIN) and cervical cancer, compared to that of normal cervical specimens (n=20)and correlated with the clinical stage of the disease. Our findings were in accordance with the findings obtained by using cervical tissues. A highly significant increase of VEGF mRNA expression was found upon cervical neoplastic transformation (P=0.008). Low-grade squamous intraepithelial lesions as well as high-grade lesions and CA samples exhibited higher VEGF mRNA levels compared to normal specimen group (P=0.038, 0.036, 0.03, respectively), however no significant increase in mRNA expression was observed with increased severity of the lesion. In contrast, TGFB1 transcript levels were found significantly elevated only in CIN specimen group compared to the normal (P=0.008), whereas the CA samples didn't reveal considerable differences in terms of TGFB1 expression compared to normal and CIN groups. This lack of association could be attributed to the overexpression of Ying Yang 1, a negative regulator of TGFB1 transcription during tumor progression; however the significance of this inhibition should further be investigated. Summarizing, disruption of expression patterns of the factors included in the study, in the CIN and CA specimen groups compared to controls, suggests a transcriptional dysregulation during cervical cancer development, which can easily and untimely be detected in cytological cervical material obtained during a routine PAP test examination. However, additional studies are needed to elucidate the potential use of mRNA expression profiles of the above angiogenetic factors as progression indicators in cervical carcinogenesis.

P12

Angiotensin converting enzyme inhibitors decrease the incidence of pancreatic cancer: a study of half a million US veterans

V. Khurana[1], G. Caldito[2], J.S. Barkin[3]. [1]*Overton Brooks VA Medical Center, Gastroenterology, Shreveport, LA, United States of America;* [2]*Louisiana State University HSC, Biometry, Shreveport, LA, United States of America;* [3]*Mt. Sinai Medical Center / University of Miami, Gastroenterology, Miami Beach, FL, United States of America*

AIM: To investigate the effect of Angiotensin Converting Enzyme (ACE) Inhibitors use in reducing the incidence of pancreatic cancer in the US veteran population. BACKGROUND: ACE Inhibitors are commonly used antihypertensive and nephroprotective agents. Vascular Endothelial Growth Factor (VEGF) is believed to play a major role in angiogenesis in human tumors. Blocking the VEGF inhibits angiogenesis and suppresses tumor growth. ACE inhibitors cause suppression of VEGF in experimental models, leading to their anticancer effect. ACE Inhibitors have been noted to suppress tumor growth by inhibiting tumor angiogenesis in several animal and experimental models. METHOD: US Veterans Health Administration