Fibronectin (FN) is one of the earliest proteins to be laid down in the extracellular matrix and its accumulation in the areas of skeletogenesis suggests its involvement in the early stages of bone formation. FN is important for the initial cellular interaction with biomaterial. In the absence of serum, osteoblast-like MG63 cells attach well but spread poorly on either AP or AP-ND substrates. Pre-adsorption with serum or FN improves cellular interaction, an effect better pronounced on AP-ND coating. In a single protein adsorption study, FITC-labeled FN showed enhanced deposition on AP-ND layers, consistent with the significantly improved cell adhesion, spreading and focal adhesion formation (in comparison to SS and AP), particularly at low FN adsorption concentrations (1 μg/ml). Higher FN concentrations (20 μg/ml) abolished this difference, suggesting that the promoted cellular interaction of serum (where FN is low) is caused by the greater affinity for FN. Moreover, it was found that MG63 cells tend to rearrange both adsorbed and secreted FN on the AP-ND layer, suggesting a facilitated FN matrix formation.

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EVALUATING MEFV GENE MUTATIONS IN PATIENTS WITH BEHCET'S DISEASE

Ayşenur Cetişli[1], Mustafa Kulaç[1], Fadime Mutlu İçduygu[2], Asuman Özgöz[2], Kuyaş Hekımler[2] and Necat İmirzalioğlu[2]

Departments of [1]Dermatology and [2]Medical Genetics, School of Medicine, Afyon Kocatepe University, Afyonkarahisar, Turkey

Background: Behcet's disease is characterized by repetitive aphthous ulcers, genital ulcers, uveitis, skin lesions and articular, neurologic and vascular gastrointestinal involvement. Encouraging results have been reported in some MEFV gene studies for Behcet's disease. E148Q, M694I, M680I, M694V, V726A MEFV gene mutations are reported to cause some symptoms in Behcet's disease. This study investigated whether there is a relation between MEFV gene mutations and Behcet's disease. *Methods:* Forty Behcet's disease patients without FMF diagnosis and symptoms in themselves or their family and twenty healthy controls were included in the study. Following DNA isolation E148Q, M694I, M680I, M694V, V726A mutations were carried out by real time PCR. *Results:* According to MEFV mutation scanning, eight patients and one healthy control were heterozygous for M694V; two patients and one healthy control were heterozygous for M680I; two patients were heterozygous for V726A; four patients were heterozygous, one healthy control was homozygous, two healthy controls were heterozygous for E148Q. No M694I mutation was observed in either group. *Conclusion:* There was not a statistically significant difference in MEFV mutation frequencies between Behcet's disease patients and the healthy controls. Furthermore, total mutation frequency was found to be 35% and M694V showed the highest frequency compared to the other mutations.

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ANTI-ANGIOGENIC EFFECTS OF METOPROLOL AND α-LACTALBUMIN ON PRIMARY AND METASTATIC COLON CANCER CELL LINES

Sevinc Inan, H. Seda Vatansever, Derya Gozuacik and Fatma Karaca

Department of Histology and Embryology, Faculty of Medicine, Celal Bayar University, Manisa, Turkey

Background: Angiogenic factors, such as vascular endothelial growth factor (VEGF), its receptors, matrix metalloproteases (MMPs) and nitric oxide synthase (NOS), are involved in the progression of many carcinomas. The aim of this study was to investigate the anti-angiogenic effects of metoprolol succinate, a selective β1 receptor blocker, and α-lactalbumin on primary and metastatic human colon cancer cell lines by using indirect immunohistochemical methods. *Methods:* Primary (Colo-320) and metastatic (Colo-741) human colon cells were cultured in RPMI-1640 medium, containing 10% fetal bovine serum, 1% L-glutamine and 1% penicillin/streptomycin solution in a humidity incubator at 37°C, containing 5% CO_2. Cells were grown on coverslips and incubated with metoprolol and/or α-lactalbumin for 48 h. Cells were fixed and immunostained with anti-VEGF, anti-flk-1, anti-eNOS, anti-iNOS, anti-MMP-2 and anti-MMP-9 primary antibodies using the avidin-biotin-peroxidase method. Staining intensities were measured using a semi-quantitative method. ANOVA statistical tests were used to compare the measurements. *Results:* Primary and metastatic colon cancer cells had moderate/strong VEGF and iNOS immunoreactivities; moderate/mild flk-1 and eNOS immunoreactivities; mild MMP-2 and MMP-9 immunoreactivities, respectively. Decreased immunoreactivities were detected on colon cancer cells in metoprolol and α-lactalbumin treated groups ($p<0.05$). *Conclusion:* Strong/ moderate VEGF and NOS immunoreactivities on colon cancer cells may suggest an increase of cell invasion or metastasis. Due to their anti-angiogenic effects, metoprolol and α-lactalbumin may be used as additional drugs for cancer therapy.

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RELATIONSHIP BETWEEN PON1 GENE Q192R POLYMORPHISM AND OXIDATIVE STRESS OF REPERFUSION

Olcay Isbir[1], Ozlem Timirci Kahraman[2], Uzay Gormus[3], A. Burak Dalan[4] and H. Arzu Ergen[2]

[1]Department of Anesthesiology and Reanimation, Faculty of Medicine, Acibadem University, Istanbul, Turkey;
[2]Department of Molecular Medicine, Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey;
[3]Department of Biochemistry, Faculty of Medicine, Istanbul Bilim University, Istanbul, Turkey;
[4]Yeditepe University Hospital, Istanbul, Turkey

Background: The HDL-associated enzyme paraoxonase 1 (PON1) plays a preventive role against oxidative stress. The purpose of this study was to investigate a possible association of the PON1 Q192R polymorphism with the risk of developing oxidative stress after reperfusion. *Patients and Methods:* Knee replacement surgery is an ischemia/reperfusion model by usage of tourniquet applied on the knee area to restrict the blood flow during the operation. The study constituted of 51 patients undergoing elective arthroscopic knee surgery and 50 healthy individuals. PON 1 gene Q192R polymorphism was performed by polymerase chain reaction and restriction fragment length polymorphism. Statistical analyses were performed using SPSS for Windows version 11.0. *Results:* Distribution of genotypes of the PON1 Q192R polymorphism was approximately: 80.4% (QQ), 15.7% (QR) and 3.9% (RR) in the patient group and 30% (QQ), 4% (QR) and 66% (RR) in the healthy controls. The frequency of the QQ genotype was higher in patients compared to controls ($p<0.05$, $\chi^2=0.507$, OR=9.567 95% CI: 3,818-23,970). *Conclusion:* Our data suggest that the PON1 192 wild-type (QQ) genotype may be associated with the risk of oxidative stress after reperfusion in Turkish population.

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KRAS IMMUNOHISTOCHEMICAL ANALYSIS IN *HELICOBACTER PYLORI*-ASSOCIATED CHRONIC GASTRITIS AND GASTRIC CANCER

Hairuszah Ithnin[1], Razana Mohd Ali[1], Nurulhafizah Samsudin[1] and Arni Talib[2]

[1]Department of Pathology, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Malaysia;
[2]Department of Pathology, Kuala Lumpur Hospital, Malaysia

Background: KRAS is a proto-oncogene and its protein upregulation is believed to play a role in promoting cancer. In this study, we investigated KRAS expression in gastric cancer and *Helicobacter pylori*-associated chronic gastritis (HPCG), a known precursor for gastric cancer. We aimed at determining a possible protein marker for early development of gastric cancer. *Methods:* The expression of KRAS in 62 cases of HPCG and 31 cases of gastric cancer was investigated immunohistochemically on archived formalin-fixed, paraffin-embedded specimens. Slides were scored using four-step scoring system (0, 1+, 2+, and 3+) and were analyzed with Wilcoxon Signed-rank test and Mann Whitney *U*-test, SPSS version 17.0. We considered $p<0.05$ to be significant. *Results:* The expression of KRAS in gastric cancer was found to be significantly higher than in HPCG ($p=0.02$). We found 20 (68%) of 31 gastric cancer cases with moderate to strong KRAS expression and 15 (24%) of the 62 HPCG cases had moderate immunoreactivity. In both conditions, the KRAS expression was significantly higher than in its adjacent normal areas ($p=0.00$). *Conclusion:* Overexpression of KRAS was significantly higher in gastric cancer compared to HPCG. Further studies are necessary to ascertain the role of KRAS in the development of HPCG to gastric cancer.

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DIFFERENTIAL EXPRESSION AND REGULATION OF CALCIUM ION TRANSPORT-RELATED GENES, TRPV6, PMCA1, NCKX3 AND CABP-28K, IN HUMAN PLACENTAL BEWO CELLS

Eui-Bae Jeung, Hyun Yang and Kyung-Chul Choi

Laboratory of Vet Biochemistry and Molecular Biology, College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk, Republic of Korea

Background: Preeclampsia is a pregnancy-specific disease characterized by the *de novo* development of concurrent hypertension, proteinuria and oxidative stress in the placenta. During last trimester of gestation, the Ca^{2+} transport from mother to fetus increases in response to the accelerated demand for Ca^{2+} caused by bone mineralization in the fetus. The calcium transporters TRPV5 and 6 are cytosolic diffusion of Ca^{2+} bound to calcium binding proteins (CaBP-9k/-28k) and basolateral extrusion of Ca^{2+} through plasma membrane Ca^{2+}-ATPase 1(PMCA1) and to a lesser extent by $Na^+/K^+/Ca^{2+}$ exchanger (NCKX3). *Methods:* Cell membrane and cytosolic calcium transporters, *i.e.*, TRPV6, PMCA1, NCKX3 and CaBP-28k, were investigated by RT-PCR and Western blot analysis at induced oxidative stress in human placental BeWo cells. *Results:* In hypoxia, the expression of TRPV6 mRNA and protein level was not altered; however NCKX3 and CaBP-28k were induced by hypoxia in BeWo cells compared with a control (normoxia). In addition, the expression of PMCA1 mRNA and protein was decreased at hypoxic BeWo cells. *Conclusion:* These results indicate that calcium transporters, TRPV6, PMCA1, NCKX3 and CaBP-28k, are distinctly expressed by induced oxidative stress, suggesting that alterations of these calcium transporters may be a determinant factor affecting calcium transfer by hypoxic stress in BeWo cell model.