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ACTIVATION OF THE BRADYKININ SYSTEM BY ANGIOTENSIN-CONVERTING ENZYME INHIBITORS

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The Bradykinin (BK) system has a very significant role in the regulation of blood pressure (BP). Hence, reduced activity of BK receptors mediated via decreased circulating endogenous kinin might explain the cause of high BP. This system also governs the activation of the angiotensin system at various axes in control of the physiological BP. The BK receptor antagonists can block the hypotensive action of angiotensin-converting enzyme inhibitors (ACEIs) in hypertensive and normotensive animals. The hypotensive action of BK is highly increased with ACEIs or kininase II inhibitor treatment. The development of specific BK agonists may provide a new direction to explore the experimental approach for examining the role of BK in hypertension. Eur. J. Inflamm. 2010;8:55-61.

IL-34 A NEWLY DISCOVERED CYTOKINE

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In this study we describe some biological effects of IL-34, a newly discovered cytokine. We show that IL-34 stimulates monocyte cell viability and directly modulates the number and function of monocytes and regulates myeloid cell growth and differentiation. Moreover, since IL-34 in mice is involved in osteoporosis, an antagonist of this cytokine could be beneficial for the treatment of this disease. *Eur. J. Inflamm.* 2010;8:63-66.

COMPARISON OF THE BONE TURN-OVER MARKERS IN PATIENTS WITH MULTIPLE SCLEROSIS AND HEALTHY CONTROL SUBJECTS

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One of the major concerns for patients with multiple sclerosis (MS) is developing osteoporosis, especially when corticosteroid treatment is used. The aim of the present study is to compare the bone turn-over markers in patients with multiple sclerosis and healthy control subjects. A total of 176 subjects were enrolled in this case-control. Ninety-one MS patients with mean age of 35.26 ± 8.76 yrs were randomly selected from the Committee on Multiple Sclerosis Registry. The control group was composed of 85 healthy subjects who were recruited from the Iranian Multicenter Osteoporosis Study (IMOS). Fasting serum levels of parathyroid hormone (PTH), 25 (OH) D3, osteocalcin and cross laps were measured in two groups. Hip and spine BMD were measured using DXA. Our findings showed significant differences in hip BMD and its T-score and Z-score values between MS patients and the control group. Osteoporosis prevalence at hip area of the MS patients was almost 5 times higher than the control group [OR=4.66, (95% CI 0.97 to 22.27), RR=4.29, (95% CI 0.95 to19.32), p value=0.03]. No significant difference was found in BMD L2-L4, BMD T-score and BMD Z-score of lumbar area between two groups. The PTH and cross laps serum concentrations in MS patients were significantly higher than the control group. We did not find significant difference in serum osteocalcin level between the two groups. We concluded that in our study the serum levels of bone resorption markers in MS patients were significantly higher than the healthy control group. This may explain, at least in part, the elevated susceptibility of MS patients for developing osteoporosis. *Eur. J. Inflamm.* 2010;8:67-73.

PREPARATION AND CYTOTOXICITY EFFECT OF ANTI-HEPATOCELLULAR CARCINOMA SCFV IMMUNOLIPOSOME ON HEPATOCARCINOMA CELL IN VITRO

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The use of PE38 for cancer therapy has attracted considerable attention for a long time. However, the extensive use of PE38 is prohibited by its severe side effects. Even though immunotoxin PE38 has been researched for cancer therapy, it has displayed low antitumor activity. The aim of this study is to compare the killing efficacy on Hepatocellular carcinoma (HCC) SMMC-7721 cell of immunoliposome PE38, immunotoxin PE38 and liposome PE38. In this study, the stericly stabilized liposomal PE38 was prepared using soybean phosphatidylcholine, cholesterol, and Cholesterol-PEG-COOH. The humanized anti-hepatoma disulfide-stabilized Fv (hdsFv25) was coupled to stericly stabilized liposomes using the N-hydroxysuccinimide ester method. The immunoliposome PE38 was prepared in our lab using the above-mentioned single-chain antibody. The hdsFv25-immunoliposomes were immunoactive as determined by ELISA assay. Immunoliposome PE38 can kill SMMC-7721 cells in vitro with higher efficiency than non-targeted liposomes. These results indicate that immunoliposome PE38 may be potential in the treatment of hepatocarcinoma. Eur. J. Inflamm. 2010;8:75-82.

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The 5-HT3 receptor is a pentameric ligand-gated cation channel located in the central and peripheral nervous system and on extraneuronal locations like lymphocytes, monocytes and fetal tissue. Serotonin receptor gene expressions and their alterations in RA diseases have not been reported. The aim of this study is to show whether the serotonin receptor gene expresses on peripheral blood lymphocytes and also to characterise the lymphocyte serotonin receptor expression profiles in patients suffering from rheumatoid arthritis (RA). In the present study, using RT-PCR technique, the research team investigated 5-HT3A receptor gene expression in peripheral blood lymphocyte cells (PBMC) of forty healthy individuals compared to forty RA patients. The PBMC was separated from whole blood by Ficoll-hypaque. Total cellular RNA was extracted and then cDNA was synthesized. The research team analyzed quantitatively gene expression profile by Real time-PCR using primer pairs specific for 5-HT3A receptor and for β-actin as internal control. Each PCR product of 5-HT3A receptor was confirmed by DNA sequencer ABI 3700 capillary system (Applied Biosystem, USA). The results showed that the 5-HT3A receptor gene is detected on the lymphocytes of both normal control and RA patients. There was a significant difference between 5-HT3A receptor expression profile in RA and that of healthy individuals. Moreover, no SNP-based change on sequenced fragments was observed. In conclusion, the present study indicated that not only human lymphocytes in normal individuals and patients express 5HT3A receptor, but the expression pattern of 5HT3A receptor gene is different between normal controls and RA patients. Moreover, after sequencing no changes in either controls or patients were observed. The above-mentioned changes can contribute to new information related to the pathogenesis...
Inverse relationship between circulatory levels of glucocorticoids and melatonin has been reported for most of the vertebrates including human beings. We report the importance of glucocorticoid along with melatonin in avian immune regulation in an Indian tropical bird, *Perdicula asiatica* with *in vivo* and *in vitro* approach. Dexamethasone (30µg/bird/day) treatment of the male birds suppressed the immune activity as judged by the spleen activity (mass, anatomy), circulating total leukocyte, and lymphocyte count, blastogenic response, increased % apoptosis and cytokine (IL-2) production by splenocytes. Melatonin (25µg/100g B.wt./day) treatment increased the above-mentioned immune parameters whereas melatonin together with dexamethasone restored the suppressed immune parameters by dexamethasone to control level. *In vitro* melatonin (2.5 pM) supplementation to splenocyte cultures restored the dexamethasone (2 µM) suppressed splenocyte proliferation, % apoptosis and IL-2 production. Therefore, melatonin antagonized the suppressive effect of synthetic glucocorticoid on all immune parameters studied *in vivo* as well as *in vitro*. Furthermore, exogenous administration of dexamethasone and melatonin treatment altered the circulatory level of corticosterone and melatonin in an inverse manner. It is therefore, suggested that a hormonal trade-off between glucocorticoid and melatonin exists under *in vivo* and *in vitro* conditions, being involved in maintenance of the immune function of *P. asiatica* probably by involving cytokines i.e. IL-2 mediated pathway. *Eur. J. Inflamm.* 2010;8:89-97.
observed after treatment with troglitazone or aspirin. These results show for the first time that human adipocytes, and not preadipocytes, can produce SAA in response to inflammatory cytokines and that this process can be modulated. *Eur. J. Inflamm.* 2010;8:99-105.

SAFETY IN CONSTRUCTION YARDS: PERCEPTION OF OCCUPATIONAL RISK BY ITALIAN BUILDING WORKERS

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The purpose of this study is to analyse the perception of occupational risk by building workers in an area of Central Italy. Three hundred male building workers compiled questionnaires including 7 different types of dangers: falling from height, cuts and wounds to body and eyes, manual handling of loads, noise, vibrations and dust inhalation. The workers quantified, on a scale of one to five, the potential injury and frequency of occurrence of each risk, as well as providing information on the possibility of checking/avoiding the risk. Furthermore, attendance of the workers at previous specific courses on accident prevention and the effectiveness of these was evaluated. A possible correlation between the perception of job risk and having had previous injuries was also assessed. The results showed that about 35% of workers do not consider their job hazardous; moreover, the risk perception is higher regarding dangers producing immediate injury, as opposed to those producing occupational illnesses. Moreover, there is no direct relationship between considering the job dangerous for health and having attended training courses, while the relationship between risk perception and past injuries is more marked. In conclusion, accident prevention training is essential for building workers; however, it is even more important to improve the quality of workers’ information in order to increase their awareness of danger. *Eur. J. Inflamm.* 2010;8:107-115.

STRESS CHARACTERISTICS IN DIFFERENT WORK CONDITIONS: IS IT POSSIBLE TO IDENTIFY SPECIFICITY OF RISK FACTORS BY THE QUESTIONNAIRE METHOD?

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The aim of this study is to identify, by a brief ad hoc questionnaire, specific dimensions of perceived occupational stress that could be relevant in two different work conditions of female workers: visual display unit (VDU) operators, for whom the risk of work-related stress is already known in literature, and kindergarten teachers, for whom very few studies have examined this risk. A questionnaire, prepared specifically for workers, was filled in by 70 all-female kindergarten teachers and 70 all-female VDU operators. The two groups were matched for age and length of service. The questionnaire was examined by factor analysis
Kindergarten teachers show significantly higher values of the questionnaire total score than VDU operators, indicating a higher level of perceived stress related to their occupation. In particular, the factor scores concerning perceived load of work responsibilities, the first of the three factors accounting for the structure of the questionnaire (1. perceived load of work-responsibility; 2. independence and autonomy in performing work-duties; 3. negative features of work interfering with psycho-physical wellbeing) are significant between groups. Compared to VDU operators, kindergarten teachers perceive a more stressful condition of responsibility in taking independent decisions and autonomously managing their work. When appropriate comparisons are performed between groups of workers operating under different occupational conditions, it is possible to identify, using an ad hoc questionnaire, different sources of occupational stress which are effective in the work environment of different categories of female workers. *Eur. J. Inflamm.* 2010;8:117-123.

**RITUXIMAB RESCUE THERAPY FOR REFRACTORY EARLY ACUTE REJECTION AFTER LIVER TRANSPLANTATION**


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Rejection of a liver transplant is a rare but serious event which can be life threatening. T-cells were supposed to be the major, if not the only key player in allograft rejection. However, during recent years B-cell function has regained attention. A chimeric monoclonal antibody against CD20 protein (rituximab) successfully reversed a multi-drug resistant rejection in a liver transplant recipient. Following an uncomplicated postoperative course, the patient showed biopsy-confirmed acute rejection on postoperative day 28. Despite treatment with steroids, increased tacrolimus doses and anti-thymocyte globulin (ATG) the rejection could not be resolved. Repeated biopsies confirmed ongoing acute cellular rejection; however, a humoral component of rejection could not be fully excluded and rituximab treatment was initiated. Liver function showed a subsequent melioration accompanied by convalescence of the patient. No adverse side effects associated to rituximab administration were observed. Promising results with rituximab were reported for heart and kidney transplant recipients suffering from humoral rejection. To our knowledge this is the first report of a successful rescue therapy of a multi-drug-resistant liver allograft rejection with rituximab. The addition of rituximab might be a valuable option to overcome severe, multi-drug-resistant rejection, although humoral nature of rejection is not proven by histology. *Eur. J. Inflamm.* 2010;8:125-129.

**INTERDISCIPLINARY FACTORS OF NEUROPATHOLOGY IN SCHIZOPHRENIA**

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In the etymology of schizophrenia, the genetic component seems to play an essential role. Studies have shown more than 130 genes of susceptibility for schizophrenia: the majority of these studies, however, has yet to be confirmed- they are searching for more definition on
the relevant functions of the genetic variation of schizophrenia. Recent studies suggest that a cluster of candidate genes in the interconnected network pathways are implicated in transmission of the glutamate the plasticity of the synapses, in oxidative stress, myelination and the profitability of oligodendrocytes. Previous neuropathological studies on schizophrenia did not identify specific neurodegenerative characteristics of this disease. Scientific evidence suggests that the physiopathology of schizophrenia involves alterations of the intracellular transmission pathway, those which are associated with reduced cerebral volume in some structures of white and gray matter. In particular, in schizophrenia, a reduction of medium cerebral volume has been observed, as has a reduction of the cortical regional volumes with reference to the frontal, temporal, and parietal areas of the brain - this is all in addition to a reduction of the prefrontal cortex, hippocampus, amygdala, thalamus, and the cerebellum. The cytoarchitectonic alterations in schizophrenia may be an expression of the pathology’s processing, as are axonal damage and loss, reduction of myelination, and loss of neuropil. These all contribute to the reduction of the volume of the cerebral parenchima, and the corresponding augmentation of the cerebral spinal fluid. The inheritance of schizophrenia may appear high/elevated, but not a certain eventuality. In analysis of subtype specifics. However, this statistics remains significant in all studies. The role of the environmental factors in the development of schizophrenia is highlighted by studies which have been conducted on monozygotic patients affected by schizophrenia. While their genetic code is 100% similar, that is to say, entirely identical, one of the pair can be diagnosed as schizophrenic, while the other of the monozygotic pair has the 50% of the possibility not to contract schizophrenia. It is well known that genetic and environmental factors influence multiple aspects of human behavior, they can increase the susceptibility towards a mental disturbance. The reciprocal effects of these factors are placed in two distinct and diverse categories: gene environment interaction, which expresses the terminal genetic variations of susceptibility to environmental risk, and environmental gene correlations, where the genetic variability can increase or reduce the likelihood of the exposure to environmental determinant risk, includes early stressful events of life. *Eur. J. Inflamm.* 2010;8:131-136.