EDITORIAL

CAN VITAMIN A MEDIATE IMMUNITY AND INFLAMMATION?

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Vitamins are natural components of foods and are organic compounds distinct from fat, carbohydrates and proteins. Vitamin A is the generic descriptor for compounds with the qualitative biological activity of retinol. Unlike beta-carotene, vitamin A is not an antioxidant and its benefit is related to possible boosting of immune reactions. The effect of vitamin A on immune function is wide-reaching and its deficiency appears to affect immunity in several ways. Innate and adaptive immune responses are affected in some way by lack of vitamin A. Retinoids seem to act on differentiation of lymphocytes, antibody production, phagocytosis of macrophages, NK, Treg, and T helper cell activity. In addition, in humans, signs of a vitamin A deficiency also include the dysregulation of cytokine/chemokine generation and release. However, excess of vitamin A has been demonstrated to have toxic effects in most species studied. Here we summarize some important effects of vitamin A in immunity and inflammation.

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DEVELOPMENT OF TWO *SALMONELLA*-BASED ORAL VACCINES AGAINST HUMAN RESPIRATORY SYNCYTIAL VIRUS

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Human respiratory syncytial virus is the most common cause of bronchiolitis and other respiratory infections in infants and the elderly worldwide. We have developed two new oral vaccines using *Salmonella typhi* TY21a to carry and express the immunogenic epitopes of RSV fusion (F) and attachment (G) glycoproteins on its surface, separately. To evaluate the efficacy of the designed vaccines, BALB/c mice were orally immunized and then infected with RSV. Immune response analyses showed that cell-mediated, mucosal and humoral immunity in the vaccinated mice were significantly enhanced compared to the control group. Both vaccines generated a balanced Th1/Th2 immune response which is crucial for efficiency of vaccines against RSV. Furthermore, histopathological examination proved that these vaccines were safe as they did not cause any Th2-associated adverse effects in the lungs of RSV-infected mice. The findings of this research suggest that *Salmonella*-F and *Salmonella*-G vaccine candidates may have strong potential to prevent RSV infection.

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PROBING HEAD-TO-TOE DEFORMATION LAW ASSESSMENT FOR ABDOMINAL TUMOR THROUGH RESPIRATORY MOVEMENT SIMULATION AND CTVision RADIATION RESEARCH

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This paper aims to explore head-to-toe deformation law for abdominal tumor with CTVision and self-designed respiratory movement simulation mold and meanwhile verify the accuracy and correctness of the treatment. In experimental group, a self-designed respiratory movement mold was used. The image was scanned out by CT scanning based on the movement state and then sent to the planning system to compare the location variation of tumor and formulating the treatment plan accordingly, followed by verification and verified derivation values observation. A total of 21 cases of abdominal tumor were included in the case group. Their breathing movement was detected under a simulated locator and then the data was recorded. The image was scanned and sent to the planning system to compare the location variation of the tumor, the patients then underwent 3D conformal therapy (3D-CRT) and we performed verification and observed verified derivation values. Finally, the results of the case group and the experimental group were compared. The mean of the verified derivation values was smaller than respiratory motion values in experimental group (t=-10.78, P=0, P<0.05); the mean of verified derivation values of the patients was smaller than respiratory motion values in group f, g, h, i, j, l, n, o, p, q, r, s t, u in the case group (P<0.05); no remarkable difference was found between the two values in group a, b, c, k and m (P>0.05); group e was unable to undergo the statistical test since its standard deviation was 0; the mean of the verified derivation values was higher than respiratory motion values in group d (P>0.05). In conclusion, radiation therapy applied with CTVision proved to be accurate and convincing in the treatment of abdominal tumor.

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

THE INFLAMMATORY MILIEU AND THE INSULIN LIKE GROWTH FACTOR AXIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE FOLLOWING RECOMBINANT HUMAN GROWTH HORMONE TREATMENT

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It is unclear whether recombinant human growth hormone (rhGH) in inflammatory bowel disease (IBD) alters cytokine profile. The objective of this study is to evaluate changes in cytokines and systemic markers of the insulin growth factor axis following 6 months of rhGH treatment in children with IBD. In a six-month randomised control trial in children with IBD treated with rhGH at 0.067 mg/kg/day and controls (11 in each group), we measured pro-, anti-inflammatory cytokines and systemic markers of the IGF axis (total IGF-1, free IGF-1, total IGFBP-3, ALS, IGFBP-2) at baseline (T+0), and six months (T+6). Results expressed as median (range). In the rhGH group, TNFα was 3.1pg/ml (2.9, 100.6) and 3.6pg/ml (3.1, 5.3) at T+0 and T+6, respectively (p=0.85), whereas in the controls this was 3.3pg/ml (2.7, 4.0) and 3.1pg/m l (2.7, 4.7), respectively (p=0.79). In the rhGH group, IL1β was 18.0pg/ml (5.0,716.7) and 18.0pg/ml (1.7, 52.2) at T+0 and T+6 respectively(p=0.90), whereas in the controls this was 19.8pg/ml (4.1, 27.1) and 19.1pg/ml (2.4,77.3), respectively (p=0.65). None of the twenty-eight other cytokines analysed was different at T+6 in either group. Despite increase in total IGF1 in the rhGH group (p=0.03), free IGF1, IGFBP3, ALS and IGFBP2 did not change in either group at T+6. Percentage change in IGFBP3, was significantly associated with percentage change in IL2 (r=0.77, p=0.009) and IL4 (r=0.58, p=0.01). Percentage change in ALS was significantly associated with percentage change in IL2 (r=0.90, p<0.0001) and IL4 (r=0.63, p=0.04). Although changes in markers of the GH/IGF-1 axis do show an association with cytokines (IL-2, IL-4) in pediatric IBD, six months of rhGH treatment was not associated with any significant changes in levels of a range of pro and anti-inflammatory cytokine. Careful evaluation of disease process is required in future trials of rhGH in paediatric IBD.

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ASSOCIATION BETWEEN PROGESTERONE AND ESTRADIOL-17BETA TREATMENT AND PROTEIN EXPRESSION OF PGR AND PGRMC1 IN PORCINE LUMINAL EPITHELIAL CELLS: A REAL-TIME CELL PROLIFERATION APPROACH

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The correct functionality (sensitivity and receptivity) of endometrial tissue is regulated by paracrine and endocrine pathways that activate several mediators or metabolic pathways and gene cascades. This study aimed to investigate the influence of E2 and P4 on progesterone receptor (PGR) and progesterone receptor membrane component 1 (PGRMC1) protein expression in porcine luminal epithelial cells and their influence on the proliferation of these cells in real-time. Surface uterine luminal epithelial cells were removed using sterile surgical blades from uterine horns of ten crossbred anestrus gilts. Following treatment with collagenase I, cells were separated and transferred into 48-well E-Plates for use in a real-time cell analyzer (RTCA). The luminal epithelial cells were cultured *in vitro* (IVC) in standard DMEM cell culture medium and incubated with E2 (10 pg/ml, 40 pg/ml, 500 pg/ml) and P4 (10 ng/ml, 40 ng/ml, 500 ng/ml). The cell proliferation index was analyzed after 0-240 h, 0-120 h, 120-240 h. After using the RTCA analysis we found increased proliferation of luminal epithelial cells after treatment of low doses of P4 (10 and 40 ng/ml), (P<0.001). Higher doses of P4 led to decrease of proliferation (P<0.001). Conversely, higher doses of E2 (500 pg/ml) increased the proliferation index as compared to low doses (10 pg/ml) and control (P<0.001). Confocal microscopic observations revealed that higher concentrations of E2 upregulate the expression of both PGR and PGRMC1. Additionally, P4 used in lower concentrations stimulated the expression of these receptors, too. Our study presents a new influence of E2 and P4 on the expression of PGR and PGRMC1 and on the real-time proliferation of porcine luminal epithelial cells. The relationship between PGR or PGRMC1 expression and the proliferation of luminal epithelial cells may be influenced (up- or down regulated) by E2 or P4 in a steroid type- and dose-dependent manner.

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BIOMARKERS FOR THE EVALUATION OF IMMUNOLOGICAL PROPERTIES DURING THE SHIKOKU WALKING PILGRIMAGE

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It is important to determine the immunological properties for the maintenance of health. We chose the Shikoku Walking Pilgrimage to assess the proper biomarkers for the evaluation of immunological properties. We examined whether the Shikoku Walking Pilgrimage could have a positive effect on the mental and physical health of walking participants by using several biomarkers proposed by our laboratory. Twelve non-randomized healthy male volunteers including 3 twice attendees walked the Shikoku Walking Pilgrimage distance of 58.9 km over 3 days. Plasma, serum, urine, and saliva were collected from the volunteers during the pilgrimage and at 1 week before and after it. Immunological biomarkers, including lipid metabolism, oxidative stress, immune function, and catecholamines, were measured. Additionally, mood state scores, alertness, autonomic nervous system activity, and body motion levels during sleep were assessed. A significant decrease was observed in the subjective tension-anxiety levels and in the concentrations of serum low-density lipoprotein cholesterol, plasma hydroxyoctadecadienoic acid (HODE), and urine adrenaline during the pilgrimage as compared to the values of these parameters before the participants embarked on the pilgrimage. The serum levels of brain-derived neurotrophic factor (BDNF) were significantly increased 1 week after the pilgrimage relative to those assessed previously. No significant differences in subjective fatigue and the flicker perception threshold were observed. These results suggest that the Shikoku Walking Pilgrimage can exert a positive effect on mental and physical health as particularly shown in the reduction of tension-anxiety and oxidative stress without the accompaniment of fatigue. HODE correlated significantly with typical immunological marker natural killer cell activity and immunoglobulin G. This suggests that there are promising biomarkers such as HODE, NK activity, BDNF, LDL-c, and IgG for assessing the immunological properties.

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EFFECT OF TRIMETAZIDINE ON SERUM INTERLEUKIN-6 AND C-REACTIVE PROTEIN CONCENTRATIONS IN PATIENTS WITH STABLE CORONARY ARTERY DISEASE

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Trimetazidine is widely used in the treatment of stable coronary artery disease (CAD) and its cytoprotective effect has been confirmed in animal studies and in many clinical trials. Given the inflammatory milieu of CAD and trimetazidine effect on the inflow of neutrophilis to the ischemic area, it is interesting to consider whether trimetazidine actions could be also explained through the inhibition of inflammatory mediators, including cytokines. The aim of this study was to (i) examine the influence of treadmill exercise test (TET) on serum C-reactive protein (CRP) and interleukin-6 (IL-6), and (ii) the influence of three-month trimetazidine therapy on serum CRP and IL-6 concentrations. One hundred and fifty-six patients with stable CAD were included. TET was performed (according to the standard Bruce protocol) twice for all subjects – at baseline and after the three-month trimetazidine treatment. Serum IL-6 and CRP concentrations were determined prior to and after performing each TET. Exercise led to the increase of CRP (2.35 *vs* 2.81 mg/L, p<0.05) and IL-6 concentrations (1.64 *vs* 1.92 pg/ml, p=0.0318) in patients without trimetazidine. Three-month treatment resulted in the increase in the TET duration (378.0s *vs* 410.9s, p<0.05) and decrease in serum CRP concentration, both before (2.35 *vs* 1.51 mg/L, p<0.05) and after TET (2.81 *vs* 1.69 mg/L, p<0.05). There was no significant increase of CRP after the second TET (1.51 *vs* 1.69 mg/l, p=NS). Three-month trimetazidine treatment increased IL-6 concentrations (1.64 *vs* 2.23 pg/mL, p<0.05). TET was not associated with further changes in IL-6 concentrations (2.23 *vs* 2.18 pg/mL, p=NS). Serum IL-6 and CRP concentrations increase during exercise in patients without trimetazidine. Three-month trimetazidine prolonged the duration of TET. Moreover, it resulted in the reduction of CRP concentration The increase of IL-6 concentration after three-month trimetazidine treatment and the lack of changes of its concentration after TET is associated with yet another mechanism of trimetazidine.

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METHYL MERCAPTAN AND HYDROGEN SULFIDE PRODUCTS STIMULATE PROINFLAMMATORY CYTOKINES IN PATIENTS WITH NECROTIC PULP TISSUE AND ENDODONTICALLY TREATED TEETH

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Bacterial infections of the residual dentin or infected pulp tissue are responsible for most cases of endodontic treatment failures. Persisting microorganisms in necrotic pulp tissue produce sulphur components such as methyl mercaptan and hydrogen sulfide as well as thioether derivatives. Although there is emerging evidence that these sulphur compounds stimulate immune cells and induce the inflammatory cascade, the immunological mechanisms of local and systemic inflammation have not been described. In this retrospective study we evaluated the *ex-vivo* immune response of peripheral blood mononuclear cells to sulphur compounds in 53 patients with clinical or radiologic endodontic treatment failure, 20 patients with clinical discomfort or radiological findings without previous endodontic treatment and a control group of 31 patients who had received successful endodontic treatment at least five years previously. Patients with endodontic abnormalities showed significantly higher *ex-vivo* sulphur compound-stimulated interferon-gamma (IFN-γ) and interleukin-10 (IL-10) levels as compared to the control group. The association between *ex-vivo*-stimulated cytokines and endodontically derived sulphur compounds was further substantiated by the fact that the number of IFN-γ and/or IL-10-positive patients decreased significantly 3-8 months after re-treatment of the root canal or tooth extraction. Furthermore, serum tumor necrosis factor-alpha (TNF-α) levels were higher in patients than in controls, and at the same time, the TNFA -308 G/A polymorphism was associated with endodontic treatment failure in our study population. We conclude that a cellular immune response to sulphur compounds contributes to the inflammatory process observed in relation to endodontic treatment failures.

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SILENCING OF STAT4 GENE INHIBITS CELL PROLIFERATION AND INVASION OF COLORECTAL CANCER CELLS

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Signal transducers and activators of transcription (STAT) play critical roles in development, proliferation, and immune defense. However the consequences of STAT hyperactivity can predispose to diseases, including colorectal cancer. In the present study, we aimed to evaluate the function of STAT4 in human colorectal cancer (CRC). The expression of STAT4 was examined by immunohistochemical assay using a tissue microarray procedure. A loss-of-function experiment was carried out to investigate the effects of lentivirus-mediated STAT4 shRNA (Lv-shSTAT4) on cell proliferation and invasive potential indicated by MTT and Transwell assays in CRC cell lines (SW480 and Caco2). As a consequence, it was found that the expression of STAT4 protein was significantly increased in CRC tissues compared with that in adjacent non-cancerous tissues (ANCT) (71.1% *vs* 44.4%, *P*=0.015), and was related with the Duke's staging and depth of invasion in CRC patients (*P*=0.022; *P*=0.001). Silencing of STAT4 gene suppressed cell proliferation and invasion of CRC cells. Taken together, these findings demonstrate that increased expression of STAT4 is positively correlated with the depth of invasion in CRC patients, and inhibition of STAT4 expression represses the growth and invasion of CRC cells, suggesting that STAT4 may be a promising therapeutic target for the treatment of CRC.

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EFFICACY OF A FOOD SUPPLEMENT IN PATIENTS WITH HASHIMOTO THYROIDITIS

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Thyroid inflammation has been commonly seen in recent decades, due to a series of factors and is considered as the most frequent thyroid illness. It is characterized by some distinctive traits, which include morphological and hormonal modifications, often in association with an elevated anti-thyroid autoantibody title. The aim of the therapy is to improve symptoms as fast as possible, treating inflammation and subsequent hypothyroidism, when present. Therefore, we evaluated the efficacy of a Food Supplement (FS) containing enzymes which is commonly used in various inflammatory processes and is able to modulate immune reactions during inflammation in a very rapid and efficacious way. An open, controlled study was then designed and 45 patients with Hashimoto thyroiditis were enrolled and divided into 3 groups (FS alone; thyroid hormones alone; FS plus thyroid hormones). Blood, morphological and subjective parameters were considered. The results obtained indicate that the FS used in our study is efficacious and safe when used alone and/or in combination with thyroid hormones in the treatment of autoimmune thyroiditis, as documented by the improvement of the majority of the parameters considered. The efficacy was considered faster than thyroid hormones alone as far as subjective symptomatology is considered. In conclusion, the use of the food supplement evaluated herein during inflammation may be considered an additional tool in clinicians' hands, when facing patients with autoimmune thyroiditis, especially in presence of subjective symptomatology, in order to rapidly alleviate it.

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A CYTOTOXIC ANALYSIS OF A SARDINIAN PLANT EXTRACT CREAM ON HUMAN ORAL PRIMARY CELL CULTURES: AN *IN VITRO* STUDY

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Wound healing agents support the natural healing process, reduce trauma and likelihood of secondary infections and hasten wound closure. The aim of this work was to evaluate the effect of different concentration of a new Sardinian plant cream (RD7) on two human primary cultures: Periodontal Ligament Stem Cells (hPDLSCs) and Gingival Fibroblasts (hGFs) derived from oral tissues in terms of morphological changes, cell proliferation and wound healing properties. RD7, is an interactive dressing containing phytocomplex derived from Sardinian endemic or not, medicinal plant extracts, with an important anti-radical, anti-inflammatory and antiseptic activity finalized to rapidly promote tissue regeneration and the formation of granulation tissue. hPDLSCs and hGFs were seeded at different concentrations (0.5, 1, 2.5 and 5 mg/ml) of RD7. The cell proliferation and viability was evaluated using colorimetric assays (MTT assay) and trypan blue exclusion test. Meanwhile, the morphological cell changes were evaluated by means of optic (OM) and scanning electronic microscopes (SEM). The induction of the migratory properties was evaluated by means of wound healing assay. *In vitro* results, using hPDLSCs and hGFs, showed a decrease of cell growth starting at 24 h of incubation, at high concentrations (2.5 mg/ml and 5 mg/ml). This cell growth reduction was associated to evident morphological changes, whilst, at low concentrations (0.5 and 1 mg/ml) a typical unchanged morphology of both hPDLSCs and hGFs was shown. Wound healing assay showed a complete wound full closure occurring after 24 h of treatment in samples treated with low concentration of RD7. The results of the present work indicate that low concentrations of RD7 have no cytotoxicity effect, stimulate cell proliferation and contribute to induce the migratory properties in hPDLSCs and hGFs, therefore it could be considered a new product for use in clinical practice.

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BORTEZOMIB-INDUCED PERIPHERAL NEUROTOXICITY IN HUMAN MULTIPLE MYELOMA-BEARING MICE

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The proteasome inhibitor bortezomib is an antineoplastic drug mainly used for the treatment of multiple myeloma (MM). Despite its effectiveness, bortezomib clinical use is often limited by the onset of peripheral neuropathy (BiPN). To better understand the mechanisms of BiPN several rat and mice models have been proposed, but no studies in MM-bearing animals allowing to test the antitumor activity of the selected schedules and the role of MM by itself in peripheral nervous system damage have been reported to date. Here, we carried out a study using immunodeficient C.B-17/Prkdcscid (SCID) mice injected with RPMI8266 human MM cells and treated with bortezomib 1 mg/kg once a week for five weeks. Animals were assessed with neurophysiological, behavioral and pathological methods and tumor volume measurement was performed along the study. At the end of the study BiPN was evident in bortezomib-treated animals, and this neurotoxic effect was evident using a schedule able to effectively prevent tumor growth. However, neurophysiological and pathological evidence of MM-induced peripheral nervous system damage was also reported. This model based on MM-bearing animals is more reliable in the reproduction of the clinical setting and it is, therefore, more suitable than the previously reported models of BiPN to study its pathogenesis. Moreover, it represents an optimal model to test the efficacy of neuroprotective agents and at the same time their non-interference with bortezomib antineoplastic activity.

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TRANSCRIPTIONAL ACTIVITY OF NEUTROPHILS EXPOSED TO HIGH DOSES OF COLCHICINE: SHORT COMMUNICATION

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Colchicine is an antimitotic drug which binds to tubulin and at high doses results in cytoskeleton disruption. Colchicine is believed to be an anti-inflammatory agent, though its modulatory effects on the level and transcriptional activity of genes is still a matter of debate. There is growing evidence that alterations in the cytoskeleton exert specific effects on the expression of various genes. This study was undertaken to analyze whether disrupting the microtubule cytoskeleton by colchicine modulates transcriptional levels of MEFV, NF-κB p65, NLRP3, HMGB1, and caspase-3 in neutrophils from patients with familial Mediterranean fever (FMF) and healthy subjects. In the present study, colchicine caused increased expression of NLRP3 (p=0.007) and MEFV (p=0.03), but had no effect on caspase-3, NF-κB p65 and HMGB1 genes in healthy neutrophils. FMF neutrophils were less responsive to the drug treatment. This study supports the hypothesis that, being an anti-inflammatory agent, colchicine at relatively high concentrations might lead to the activation of pro-inflammatory signalling pathways in neutrophils.

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LETTER TO THE EDITOR

CLINICAL RESEARCH ON NEUROBLASTOMA BASED ON SERUM LACTATE DEHYDROGENASE

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In recent years, more and more scholars tend to study neuroblastoma (NB) since it possesses increasing morbidity, but lack of effective treatment. This paper aims to investigate variation and clinical significance of the neuron-specific enolase (NSE) and lactic dehydrogenase (LDH) level in serum of children with NB before and after Auto Peripheral Blood Stem Cell Transplantation (APBSCT). A total of 90 children with NB from various hospitals were included in this research, and we analyzed the relationship between levels of NSE and LDH and the change of disease by comparing the two levels before and after APBSCT treatment. The results indicated that the positive rate of NSE in serum was high before treatment, and the levels of NSE and LDH were remarkably higher than those when the treatment was valid; after comprehensive treatment of chemotherapy, excision and radiotherapy, there was a significant difference of NSE and LDH levels in serum between children with complete remission (CR) and those with partial remission (PR); however, no significant differences of NSE and LDH levels were found among children in progressive stage compared to before treatment. It is believed that NSE and LDH levels are associated to the recurrence and treatment effect of NB, proving that both can reflect tumor load, therefore they can be taken as the auxiliary indicators for monitoring curative effects of NB treatment.

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LETTER TO THE EDITOR

OBSERVATION OF THE CLINICAL EFFECTS OF IONTOPHORESIS OF A CHINESE DRUG IN THE TREATMENT OF DEGENERATIVE OSTEOARTHROPATHY

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Degenerative osteoarthropathy, a kind of arthrosis induced by various factors, mainly affects articular cartilage and causes syndesmophyte formation. Its morbidity increases year by year, tending to occur more among young people than previously. This paper mainly discusses the clinical effects of iontophoresis of the Chinese drug in treating degenerative osteoarthropathy. A total of 296 cases of degenerative osteoarthropathy were randomly divided into two groups (of both genders): the iontophoresis group: the joint was treated with iontophoresis of the Chinese drug and a medium frequency electrotherapy instrument; the frequency electrotherapy group: the joint was treated only by medium frequency electrotherapy. The two groups were both treated for 30min once a day, for a total of 4 weeks. The results of the study showed that, the total effective rate in the medium frequency electrotherapy group was 74.3%, the iontophoresis group was 93.2%, indicating the curative effect of iontophoresis of the Chinese medicine. The above finding indicates that, iontophoresis has a good clinical effect in the treatment of osteoarthropathy and deserves to be promoted and applied.

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LETTER TO THE EDITOR

THE EXPRESSION OF P53, MGMT AND EGFR IN BRAIN GLIOMA AND CLINICAL SIGNIFICANCE

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In order to discuss the expression of P53, MGMT (O^6-methylguanine-DNA methyltransferase) and EGFR (epidermal growth factor receptor) in brain glioma and their clinical significance, this paper collected clinical features of 40 patients. We observed the expression of P53, MGMT and EGFR in samples using immuohistochemistry assay and analyzed their interaction, as well as their relationship to brain glioma. It was found that among 40 cases of brain glioma samples, cases with positive P53 expression accounted for 47.5%, and its expression in high-grade brain glioma was higher than in low-grade brain glioma ($P<0.05$); cases with positive MGMT expression accounted for 37.5%, and its expression in high-grade glioma and low-grade brain glioma had no statistical significance ($P>0.05$); cases with positive EGFR expression accounted for 55%, and its expression in high-grade brain glioma was higher than in low-grade brain glioma ($P<0.05$); the expression of P53, MGMT and EGFT were not correlated to age, gender or size of tumor; P53 expression was negatively correlated to MGMT expression ($P<0.05$) but positively correlated to EGFR expression ($P< 0.05$) demonstration that P53, EGFR and MGMT play important roles in the occurrence and development of brain glioma.

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LETTER TO THE EDITOR

CLINICAL RESEARCH OF PERSIMMON LEAF EXTRACT AND GINKGO BILOBA EXTRACT IN THE TREATMENT OF VERTEBROBASILAR INSUFFICIENCY

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This paper aims to compare the curative effects of persimmon leaf extract and ginkgo biloba extract in the treatment of headache and dizziness caused by vertebrobasilar insufficiency. Sixty patients were observed, who underwent therapy with persimmon leaf extract and ginkgo biloba extract based on the treatment of nimodipine and aspirin. After 30 days, 30 patients treated with persimmon leaf extract and 30 patients with ginkgo biloba extract were examined for changes in hemodynamic indexes and symptoms, such as headache and dizziness. The results showed statistically significant differences of 88.3% for the persimmon leaf extract and 73.1% for the ginkgo biloba extract, P<0.05. Compared to the group of ginkgo biloba extract, the group of persimmon leaf extract had more apparent improvement in the whole blood viscosity, plasma viscosity, fibrinogen, hematokrit, and platelet adhesion rate, and the difference was statistically significant (P<0.05 or P<0.01). Based on these analyses, it can be concluded that persimmon leaf extract is better than ginkgo biloba extract in many aspects, such as cerebral circulation improvement, cerebral vascular expansion, hypercoagulable state lowering and vertebrobasilar insufficiency-induced headache and dizziness relief.

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LETTER TO THE EDITOR

CHANGES OF SERUM VASCULAR ENDOTHELIAL GROWTH FACTOR OF PATIENTS WITH RECTAL CANCER BEFORE AND AFTER NEOADJUVANT CHEMOTHERAPY AND TUMOR PROGRESS

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In the rapid development of armamentarium, neoadjuvant chemotherapy has become an important part of a multi-instrument comprehensive treatment of malignant tumor, which presents promising application prospects. This paper researches changes of Vascular Endothelial Growth Factor (VEGF) and Vascular Endothelial Growth Factor-2 (VEGF-2) in serum of patients with rectal cancer before and after neoadjuvant chemotherapy and discusses how tumor progression rules relate to curative effect and prognosis. Enzyme linked immunosorbent serologic assay (ELISA) was applied for the detection of VEGF expression and VEGF-2 expression of 45 patients with rectal cancer (treatment group) before and after neoadjuvant chemotherapy, which was compared to the expressions of 45 healthy people (control group). After 8 weeks of continuous neoadjuvant chemotherapy, the results did not present obvious differences of VEGF and VEGF-2 expression in patients with different curative effects between pre-chemotherapy and post-chemotherapy. However, VEGF and VEGF-2 expression of patients with CR+PR and NC significantly decreased. This proved the excellent curative effect of neoadjuvant chemotherapy, with which the expressions of VEGF and VEGF-2 of rectal cancer patients decreased. The above experiment provides new ideas for the application of neoadjuvant chemotherapy in treating rectal cancer.

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LETTER TO THE EDITOR

EFFECT OF INTEGRIN COMBINED LAMININ ON PERIPHERAL BLOOD VESSEL OF CEREBRAL INFARCTION AND ENDOGENOUS NERVE REGENERATION

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The third Chinese nationwide survey on causes of death states that cerebrovascular disease, accounting for 22.45% of total deaths, ranks as the first cause of death among rural and urban residents. It has become a serious public health problem since it has the highest disability and fatality rate among single diseases. Cerebral infarction is the most common cerebrovascular disease. In order to enhance the treatment response of cerebral infarction, this paper established male Sprague Dawley (SD) rat reperfusion model with 2 h of cerebral artery embolism by suture method. Neurological function deficit was scored according to rat improvement 24 h after model establishment, and 50 rats with scores between 10 and 13 were included in an ultimate experiment and were randomly divided into 5 groups: undisturbed control group, vascular endothelial growth factor (VEGF) up-regulated vessel group, endostatin down-regulated vessel group, ventricle injected Cxc Chemokin Receptor 4 (CXCR4) antibody group, ventricle injected α6β1 antagonist (GoH3 antibody) group, respectively. The experiment was initiated after grouping and measurement of the relative data. The obtained results showed that the behavioral recovery of the VEGF group was more obvious compared with the control group, and the differences were statistically significant. The research was carried out using decreased modified neurological severity scores (mNSS), and the time a rat took to remove a pasted object. However, the behavioral recovery in the endostatin group, anti-CXCR4 group and GoH3 group was slow, and the difference was statistically significant, which showed as slowly decreased mNSS scoring and inconspicuous improved time of a rat removing a sticker. Compared with the control group, the number of peripheral BrdU+/ vWF+ cells of rat cerebral infarction in the VEGF group increased, and the peripheral VEGF expression quantity of cerebral infarction increased, thus the difference was statistically significant. However, cells in the endostatin group, anti-CXCR4 group, and GoH3 group were fewer and VEGF expression was reduced, and the difference was statistically significant. All these findings suggest that the promotion of angiogenesis after cerebral infarction can better provide the vascular niche for the proliferation, migration and differentiation of neural stem/progenitor cells (NSPCs), thereby further promoting endogenous nerve regeneration. NSPCs can always closely connect with vessels through the interaction of integrin α6β1 and laminin; furthermore, under the support provided by the vascular niche and the chemotaxis of stromal cellderived factor (SDF-1), NSPCs can migrate from the subventricular zone (SVZ) to the periphery of infarction.

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LETTER TO THE EDITOR

EXPRESSION OF PLEIOTROPHIN IN SMALL CELL LUNG CANCER

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Pleiotrophin (PTN) is a kind of heparin binding growth factor closely related to tumor progression. This study aimed to discuss the significance of the expression of PTN in benign and malignant lung cancer tissues, especially small cell lung cancer. Lung cancer samples were collected for study and lung tissue samples with benign lesions were taken as controls. The expression of PTN was detected using tissue chip combined with the immunohistochemical method, and the differences of small cell lung cancer with non-small cell lung cancer and benign lesion tissue were compared. It was found that PTN expression was mainly located in the cytoplasm and membrane of cells; PTN expression in the lung cancer group was higher than that in the control group ($p<0.01$), and PTN expression in the small cell cancer group was higher than that in the squamous carcinoma group and glandular cancer group ($p<0.05$). In addition, PTN expression quantity in patients with lung cancer were in close correlation with TNM staging, pathological type and tumor differentiation degree ($p<0.05$). PTN was found to express abnormally high in lung cancer, especially small cell lung cancer tissue. PTN is most likely to be a new tumor marker for diagnosis and prognosis of lung cancer.

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LETTER TO THE EDITOR

βig-h3 CORRELATES WITH RELATED FACTORS OF PERITONEAL METASTASIS OF GASTRIC CANCER

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βig-h3 is an extracellular matrix protein induced by transforming growth factor-β1 (TGF-β1) and involved in adhesion between cell and cell, cell and matrix. It has been proved that βig-h3 is highly expressed in human lung cancer and colorectal cancer cells, and thus it is considered to have the same effect on gastric cancer cells. This research applied histochemical staining and RT-PCR to detect the content of βig-h3 in peritoneal mesothelial cells and the content of carcino embryonic antigen (CEA) mRNA in abdominal dropsy or peritoneal washing liquid, in order to explore the relationship between the factors of peritoneal metastasis of gastric cancer and βig-h3. It was found that the positive ratio of βig-h3 in the gastric cancer group was higher than that in the benign disease group, and the positive rate of immunohistochemistry was closely related to the relative factors of peritoneal metastasis such as tumor infiltration depth, serosal types, macroscopic peritoneal metastasis, CEA mRNA, results of pleural lavage cytology (PLC) examination, etc. Research found that βig-h3 expressed distinctly in gastric cancer peritoneal metastasis, therefore, it is useful for monitoring biological behavior of gastric cancer.

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LETTER TO THE EDITOR

META-ANALYSIS ON POSTOPERATIVE COMPLICATIONS OF WRISTBAND ACUPOINT PRESSURE THERAPY

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Through searching database such as MEDLINE, CNKI, etc., this paper assesses the effect of wristband acupoint pressure, acting on the neiguan acupoint, to relieve postoperative complications of adults (mainly nausea and vomiting) using nine randomized controlled trials (RCT) and RevMan5.0. In the experimental group, acupoint pressure wristband effectively reduced the incidence rate of postoperative vomiting by acting on the neiguan point, compared to the placebo control group (RR=0.50, 95%CI: 0.37~0.66, P<0.01). As to the incidence rate of postoperative nausea, there was no statistical significance between the experimental group and the placebo control group (RR=0.85, 95%CI: 0.72~1.00, P>0.05). It was revealed that the application of acupoint pressure wristband on neiguan point in postoperative care could effectively relieve postoperative vomiting; while postoperative vomiting was not relieved distinctly. Therefore, researchers are required to carry out more reliable RCT test for further study and discussion, and nurses can bring in acupoint pressure wristband for researches on its effectiveness and adaptability.

0393-974X (2015)

LETTER TO THE EDITOR

RESEARCH ON THE INFLUENCE OF α-GalCer ACTIVATING EXPERIMENTAL AUTOIMMUNE MYASTHENIA GRAVIS MICE NKT CELLS AT DIFFERENT TIMES ON MYASTHENIA GRAVIS

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This study aims to observe the effect of natural killer T (NKT) cell activation on experimental autoimmune myasthenia gravis (EAMG) model by injecting mice with α-GalCer in enterocoelia at different times, thus to provide a new therapy for EAMG. EAMG animal model of C57BL/6 mice was established and the mice were injected with α-GalCer irritant in enterocoelia. Vα14 NKT cells were then activated through the transfer of CD1d. This paper discusses the effect of NKT cell activation on EAMG at different times by observing the variation of weight, clinical performance and relevant immunity indexes of mice. In C57BL/6 mice, the EAMG incidence rate of the Vehicle Group was 90%, the average onset duration was 37±6 days; The incidence rate of α-GalCer prevention group was 30%, the average onset duration was 51±9 days. The forward immunization of α-GalCer activates NKT and protects C57BL/6 mice from the occurrence of EAMG, which provides basis for prevention and treatment of EAMG and other autoimmune diseases.

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LETTER TO THE EDITOR

ANALYSIS OF IMMUNITY INDEX AND IMMUNOPATHOGENESIS PATTERN OF LUPUS NEPHRITIS PATIENTS

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Joint detection of anti-dsDNA antibodies, anti-U1RNP, anti-SM antibodies, anti-SSA antibodies, anti-ribosomal P protein antibodies, anti-nucleosome antivodies (Anua), anti-histone antibodies (AHA) and antinuclear antibodies brings to the early diagnosis of systemic lupus erythematosus (SLE) and speculation of renal lesion degree of lupus nephritis patients in order to choose a specific therapeutic schedule. This paper analyzed the abnormal immunology features and connections of each pathological pattern of LN renal biopsy and probed into the essence in order to provide basis for diagnosis, treatment, pathological pattern speculation and forward assessment of LN. We chose 97 cases, treated them with renal biopsy and pathological pattern classification, analyzed pathological pattern distribution, different pathological patterns and the correlation of immunity index with anti-dsDNAantibodies, anti-U1RNP, anti-Sm antibodies, anti-SSA antibodies, anti-ribosomal P protein antibodies, Anua, AHA and ANA of the first renal biopsy were taken as the experiment index. The results showed that the morbidity of the male was distinctly lower than the female and the age of onset was much lower (P<0.05); pattern I, pattern II, pattern III, pattern IV, pattern V, and pattern VI accounted for 1.0%, 3.1%, 12.4%, 47.4%,16.5%, 15.5%, 4.1%, 0%, respectively; among all the LN patients, there were respectively 59, 43, 28, 52, 51, 48, 36 and 93 cases in which anti-dsDNA antibody, anti-U1RNP antibody, anti-Sm antibody, anti-SSA antibody, anti-ribosomal P protein antibodies, Anua, AHA and ANA had increased and the positive rate was 60.8%, 44.3%, 28.9%, 53.6%, 52.6%, 49.5%, 37.1% and 95.9%, respectively. In conclusion, pattern IV is the most common of all pathological patterns of LN. Among the immunity index, anti-U1RNP antibodies and anti-SSA antibodies are positively correlated with anti-dsDNA antibodies; Anua is positively correlated with anti-dsDNA antibodies and AHA; anti-dsDNA antibodies, anti U1RNP antibodies, anti-Sm antibodies, anti SSA antibodies, AHA, anti-ribosomal P protein antibodies and ANA have no obvious correlation with LN renal lesions degree; Anua level of serum is positively correlated with LN renal lesions degree.

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LETTER TO THE EDITOR

THE COMPARISON BETWEEN VITAMIN D CONCENTRATION IN UPPER SILESIA PATIENTS WITH PROSTATE CANCER AND WITH BENIGN PROSTATIC HYPERPLASIA

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A number of studies have shown that vitamin D has a protective effect against the development of cancer, which may also be related to prostate cancer. Low serum vitamin D concentration has also been demonstrated in benign prostate hyperplasia. We compared serum vitamin D concentration in two groups of Polish men with prostate cancer and benign prostate hyperplasia. Each group comprised 30 patients. The concentration was determined by ELISA. To assess the difference between the study population, non-parametric Mann Whitney U test was used. The results revealed that patients with prostate cancer are deficient in vitamin D (median =25.3, quartiles q1 - q3: 13.4 -33.4). The concentration of vitamin D in the group of patients with prostate cancer was lower than in the group of benign prostatic hyperplasia with vitamin D deficiency (median =34.8, quartiles q1 - q3: 17.9 – 44.3). Vitamin D concentration in Polish men with prostate cancer is lower compared to patients with benign prostatic hyperplasia.

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JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS Vol. 29, no. 1, 213-219 (2015)

LETTER TO THE EDITOR

EFFECT OF PROLONGED DUAL ANTI-PLATELET THERAPY ON REDUCING MYOCARDIAL INFARCTION RATE AFTER PERCUTANEOUS CORONARY INTERVENTION

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This paper aimed to review the interferential effect of prolonged dual anti-platelet therapy after Percutaneous Coronary Intervention (PCI), and the influence on reducing the myocardial infarction rate. A computer search was carried out in the relevant libraries and databases, regarding all the short-term (≤ 6 months) and long-term (> 6 months) dual anti-platelet therapies, and the curative and observational studies on the effects and safety of interventional therapy. RevMan5.1 software was used to meta-analyze the standard research. A total of 8 papers were finally selected. In the randomized controlled research, meta-analysis showed that the myocardial infarction rate of a long-term dual anti-platelet treatment group was lower than the short-term treatment group [OR=0.74, 95%CI (0.56, 0.98), P<0.0001]. The meta-analysis of observational research showed that the myocardial infarction rate of the long-term treatment group was lower than the short-term treatment group [OR=0.7, 95%CI (0.45, 1.08), P=0.11]; the incidence rate of late stent thrombosis in the long-term treatment group was lower than in the short-term treatment group [OR=0.40, 95%CI (0.15, 1.07), P=0.07]. It can be concluded that in the long-term group (>6 months) dual anti-platelet therapy after PCI can reduce the incidence rate of myocardial infarction or death. In addition, long-term treatment can reduce the occurrence tendency of late stent thrombosis. Furthermore, in the long-term treatment group, serious bleeding events did not increase.

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LETTER TO THE EDITOR

RELATIONSHIP BETWEEN ADIPOQ GENE POLYMORPHISM AND LIPID LEVELS AND DIABETES

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Metabolic syndrome (MS), a series of physiological and metabolic disorders caused by insulin resistance, combines clinical syndrome of abdominal obesity, diabetes or impaired glucose regulation, dyslipidemia, hypertension and other metabolic diseases. Several studies have found that multiple single nucleotide polymorphism (SNP) exists in adiponectin gene (ADIPOQ) and some unusual mutations might be related to hypoadiponectinemia and MS. This study aims to explore the relationship between ADIPOQ gene polymorphism and lipid levels and diabetes. A total of 1,049 confirmed MS cases were selected for research. From the perspective of potential functional SNPs of ADIPOQ gene, tag SNPs, combined with environmental factors, we studied the relationship between ADIPOQ gene polymorphism and phenotype (serum adiponectin level) and further analyzed the correlation of ADIPOQ gene polymorphism and metabolic syndrome components so as to clear the relationship between ADIPOQ gene polymorphism and lipid levels and diabetes and at the same time provide a scientific basis for preventing primarily MS etiology and screening high-risk groups.

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LETTER TO THE EDITOR

CYTOGENETIC GENOTOXIC INVESTIGATION IN PERIPHERAL BLOOD LYMPHOCYTES OF SUBJECTS WITH DENTAL COMPOSITE RESTORATIVE FILLING MATERIALS

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Dental composite resins are biomaterials commonly used to aesthetically restore the structure and function of teeth impaired by caries, erosion, or fracture. Residual monomers released from resin restorations as a result of incomplete polymerization processes interact with living oral tissues. The objective of this study was to evaluate the genotoxicity of a common dental composite material (Enamel Plus-HFO), in subjects with average 13 filled teeth with the same material, compared to a control group (subjects having neither amalgam nor composite resin fillings). Genotoxicity assessment of composite materials was carried out in vitro in human peripheral blood leukocytes using sister-chromatid exchange (SCE) and chromosomal aberrations (CA) cytogenetic tests. The results of correlation and multiple regression analyses confirmed the absence of a relationship between SCE/cell, high frequency of SCE (HFC) or CA frequencies and exposure to dental composite materials. These results indicate that composite resins used for dental restorations differ extensively *in vivo* in their cytotoxic and genotoxic potential and in their ability to affect chromosomal integrity, cell-cycle progression, DNA replication and repair.

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LETTER TO THE EDITOR

ATRIAL NATRIURETIC PEPTIDE EXPRESSION IN HUMAN ARTICULAR CARTILAGE

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This immunohistochemical study aims to investigate the Atrial natriuretic peptide (ANP)-presence and localization in human articular cartilage. Fragments of articular cartilage covering the femoral head were removed from patients submitted to surgical operation after femoral neck fracture without joint disease. The samples were immunostained with anti-ANP antibody. The results demonstrate that ANP is present in chondrocytes in all the three zones of the articular cartilage. Superficial chondrocytes show strong ANP-immunopositivty. The presence of ANP in the articular cartilage suggests that ANP may play a role in cartilage metabolism by regulating transport of molecules through the different zones of the articular cartilage and in maintenance of its homeostasis; probably ANP could be also involved in the regulation of the balance between synovial fluid and the other body fluids.

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LETTER TO THE EDITOR

COMPARISON OF SALIVARY ANTIOXIDANT ENZYME ACTIVITY BETWEEN EX-SMOKERS AND SUBJECTS WHO HAD NEVER SMOKED

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Smoke contains oxidants such as oxygen-free radicals which are probably the major cause of damage to biomolecules. A decrease of salivary antioxidant enzymes was detected in habitual smokers. However, the effects of cigarette smoke on salivary antioxidant enzymes may persist after withdrawal from smoking. The objective of this study was to assess salivary superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activity in ex-smokers in comparison with that of subjects who had never smoked. The test group included 25 ex-smokers (13 males and 12 females; mean age: 48±8 years) who had given up smoking for at least one year but for no more than 2 years, and a control group consisting of 25 subjects (14 males and 11 females; mean age: 50±12 years) who had never smoked. Salivary samples were collected and SOD and GSH-Px activity was measured. Student's *t*-test was used to evaluate differences between groups and significant differences were observed for $p < 0.05$. A significant decrease ($p< 0.05$) of GSH-Px (14.5±2) was observed in the test group compared to the control group (30±4). However, SOD was very similar in the two groups: 0.9±0.3 in the test group and 0.8±0.3 in the controls and no significant difference was detected ($p> 0.05$). Detoxification of hydrogen peroxide by the GSH-Px was altered even after withdrawal from smoking, while the production of hydrogen peroxide, that is mediated by SOD, was not modified.

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LETTER TO THE EDITOR

WESTERN BLOT EXPRESSION OF 5-LIPOXYGENASE IN THE BRAIN FROM STRIPED DOLPHINS (*STENELLA COERULEOALBA*) AND BOTTLENOSE DOLPHINS (*TURSIOPS TRUNCATUS*) WITH OR WITHOUT ENCEPHALITIS/ MENINGO-ENCEPHALITIS OF INFECTIOUS NATURE

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***Dolphin Morbillivirus* (DMV), *Toxoplasma gondii* and *Brucella ceti* are pathogens of major concern for wild cetaceans. Although a more or less severe encephalitis/meningo-encephalitis may occur in striped dolphins (*Stenella coeruleoalba*) and bottlenose dolphins (*Tursiops truncatus*) infected by the aforementioned agents, almost no information is available on the neuropathogenesis of brain lesions, including the neuronal and non-neuronal cells targeted during infection, along with the mechanisms underlying neurodegeneration. We analyzed 5-lipoxygenase (5-LOX) expression in the brain of 11 striped dolphins and 5 bottlenose dolphins, affected or not by encephalitic lesions of various degrees associated with DMV, *T. gondii* and *B. ceti*. All the 8 striped dolphins with encephalitis showed a more consistent 5-LOX expression than that observed in the 3 striped dolphins showing no morphologic evidence of brain lesions, with the most prominent band intensity being detected in a *B. ceti*-infected animal. Similar results were not obtained in *T. gondii*-infected vs *T. gondii*-uninfected bottlenose dolphins. Overall, the higher 5-LOX expression found in the brain of the 8 striped dolphins with infectious neuroinflammation is of interest, given that 5-LOX is a putative marker for neurodegeneration in human patients and in experimental animal models. Therefore, further investigation on this challenging issue is also needed in stranded cetaceans affected by central neuropathies.**

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LETTER TO THE EDITOR

SYSTEMIC EFFECTS OF LOCALLY INJECTED PLATELET RICH PLASMA IN A RAT MODEL: AN ANALYSIS ON MUSCLE AND BLOODSTREAM

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Abundant evidence suggests that growth factors, contained in platelets alpha granules, may play a key role in the early stages of the muscle healing process with particular regard to the inflammatory phase. Although the contents of the platelet-rich plasma preparations have been extensively studied, the biological mechanisms involved as well as the systemic effects and the related potential doping implications of this approach are still largely unknown. The aim of the present study was to investigate whether local platelet-rich plasma administration may modify the levels of specific cytokines and growth factors both in treated muscle and bloodstream in rats. An additional aim was to investigate more deeply whether the local platelet-rich plasma administration may exert systemic effects by analyzing contralateral lesioned but untreated muscles. The results showed that platelet-rich plasma treatment induced a modification of certain cytokines and growth factor levels in muscle but not in the bloodstream, suggesting that local platelet-rich plasma treatment influenced directly or, more plausibly, indirectly the synthesis or recruitment of cytokines and growth factors at the site of injury. Moreover, the observed modifications of cytokine and growth factor levels in contralateral injured but not treated muscles, strongly suggested a systemic effect of locally injected platelet-rich plasma.

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LETTER TO THE EDITOR

THE HEME OXYGENASE/BILIVERDIN REDUCTASE SYSTEM IN SKIN CANCERS

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The heme oxygenase/biliverdin reductase (HO/BVR) pathway enhances cell stress response by degrading excess heme or producing antioxidant and cytoprotective molecules. Recently, members of the HO/BVR system have been proposed as biomarkers for the early diagnosis of free radical-related diseases. In this study, the presence of both the inducible and constitutive HO isoforms (HO-1 and HO-2, respectively) and BVR was evaluated by immunohistochemistry in human skin cancer samples. Moderate/strong immunoreactivities against HO-1, HO-2 and BVR were detected in 100% of the nodular malignant melanoma samples, whereas in basal cell carcinoma specimens these figures were 62%, 88% and 60%, respectively, with a faint/moderate degree of expression. Faint/moderate HO-1, HO-2 and BVR immunoreactivities were detected in 33%, 66% and 100% of melanocytic nevi samples, respectively. In conclusion, HO-1 and HO-2 and BVR were expressed in the cytosols of skin cancer cells, whereas perilesional normal epidermis showed only faint staining, thus leading to the hypothesis that the HO/BVR system is activated in skin cancers.

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