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EDITORIAL

STRESS, INFLAMMATION AND NATURAL TREATMENTS

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Stress and inflammation have become the curses of our times and are the main pathogenetic factors in multiple diseases that are often comorbid and include allergies and asthma, eczema and psoriasis, fibromyalgia syndrome, mast cell activation syndrome, irritable bowel syndrome, myalgic encephalomyelitis/chronic fatigue syndrome and autism spectrum disorder (ASD). Unfortunately, there are no effective drugs. Cross-talk between mast cells and microglia in the hypothalamus and amygdala could explain stress-induced inflammation. We recently showed that the "alarmin" IL-33 could play a major role through its synergistic action with the neuropeptide substance P to stimulate human mast cell secretion of the pro-inflammatory molecules IL-1β, TNF and VEGF. A new formulation using pure luteolin with Ashwagandha has now been developed and could be of significant benefit to patients suffering from these diseases.

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EDITORIAL

DOES THE PURINERGIC SYSTEM AFFECT EXTRACELLULAR MATRIX FUNCTIONS IN THE CENTRAL NERVOUS SYSTEM?

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Exracellular matrix (ECM) consists of a plethora of proteins and polysaccharides, which aggregate into an organized network connected to the surface of the producing cells. It is structurally and functionally present in all components of tissues and organs and represents the substrate on which cells adhere, migrate, proliferate and differentiate, influencing their survival, shape and function. In response to acute (trauma) or chronic (degenerative) insults, brain ECM modifies its composition and function, actively contributing to "scar forming" gliosis or tissue degeneration/remodelling. Moreover, morphological changes in dendritic spines associated with extracellular matrix remodeling play key roles in rewiring synaptic circuitry pertinent to memory formation. In the present report, we collected the main acquisitions on the functional interplay between ECM alterations and the adenine-/guanine-based purine system with particular regard on how purine compounds and their respective receptors may affect and be affected by changes of the cerebral ECM.

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

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EDITORIAL

STIMULATED MAST CELLS RELEASE INFLAMMATORY CYTOKINES: POTENTIAL SUPPRESSION AND THERAPEUTICAL ASPECTS

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Mast cells (MCs) are derived from bone marrow precursors and are immune cells involved in acute and chronic inflammation. MCs are ubiquitous and play a crucial role in innate and acquired immunity. They are activated through cross-linking of their surface high affinity receptors (FcεRI), leading to immediate secretion of stored inflammatory mediators, and late production and release of pro-inflammatory cytokines/chemokines without degranulation. Therefore, MCs are important in inflammatory responses. Members of the interleukin (IL)-1 cytokine family, such as IL-1 and IL-33, and various antigens markedly increase IL-1 and tumor necrosis factor (TNF) expression and secretion from MCs. One of the latest cytokines is IL-33, an IL-1 family member acting via its ST2/IL-1R4, which has been shown to regulate MCs. IL-1 and IL-33 are cytokines found to be implicated in many inflammatory disorders including rheumatoid arthritis, atherosclerosis and psoriasis. In general, IL-1 family member cytokines play a pro-inflammatory role and increase the pathological state. IL-37 is a member of the IL-1 family with anti-inflammatory activity through inhibition of pro-inflammatory cytokines. IL-37 particularly suppresses IL-1-mediated innate inflammatory response, but also acts on the acquired immune response. IL-37 is activated by pro-inflammatory agents and cytokines, playing a protective role against inflammation. This cytokine is a natural regulator of immunity and is a therapeutic promise against inflammatory diseases. Since IL-1 is produced by and activates MCs to release IL-33 and TNF, here we hypothesize that MCs can be inhibited by IL-37 and therefore reduce their pro-inflammatory activity. However, the maturation, transport and secretion of IL-37 remain to be clarified.

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CYCLIN-DEPENDENT KINASE 7 IS A POTENTIAL THERAPEUTIC TARGET IN PAPILLARY THYROID CARCINOMA

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Given the pathological incidence of metastases or radioiodine-refractory papillary thyroid carcinoma (PTC) is increasing worldwide, patients have little alternatives when choosing effective drugs. Therefore, it is necessary to develop new therapeutic targets for PTC treatment. CDK7 is a member of the cyclin-dependent protein kinase (CDK) family, which plays an important role in various types of cancers. In this study, we found CDK7 were upregulated in PTC cell lines compared to normal thyroid cells using qRT-PCR and Western blot. Furthermore, using cell counting kit-8 (CCK-8) assay and 5-ethynyl-2-deoxyuridine (EdU) assay, we discovered cell growth ratio was positively correlated to the expression level of CDK7. Cell cycle analysis showed that the cells with higher CDK7 expression levels were prone to be in S phase. More importantly, we tested the inhibitory effects of BS-181 on CDK7 both *in vitro* and *in vivo*. Results obtained from this study indicated that BS-181 not only suppressed the cell proliferation *in vitro*, but also inhibited the tumor growth in nude mouse without changing mRNA and protein levels of CDK7. In conclusion, our study might provide a novel potential target for PTC therapy.

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17β-ESTRADIOL INHIBITS HEPATIC iNOS VIA THE ACTIVATION OF THE ESTROGEN RECEPTOR ER-α AND INHIBITION OF ERK1/2-miR-221 AXIS

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17β-Estradiol (E2) is known to negatively regulate inducible nitric oxide (NO) synthase (iNOS) expression via estrogen receptor alpha (ER-α) activation in aortic vascular smooth muscle cells. Therefore, we sought to determine whether E2 can inhibit iNOS *in vivo* in hepatic tissue via the activation of ER-α and whether extracellular signal-regulated kinases 1/2 (ERK1/2)-miR-221 axis is involved in this process. Male Wistar rats were treated with a bolus injection of E2 intraperitoneally (40 μg/kg), and 24 hours after treatment the animals were sacrificed and the livers excised. The protein levels of iNOS, p50 and p65 subunits of nuclear factor κB (NFκB), ERα, ERK1/2 and protein kinase B (Akt), as well as the association of ERα/Src in liver lysates were assessed by Western blot. The expression of hepatic miR-221 was analyzed by qRT-PCR. Results show that E2 reduced hepatic iNOS protein expression ($p < 0.01$), the protein level of ERα ($p < 0.05$), ERK1/2 ($p < 0.05$), Akt phosphorylation ($p < 0.001$) and miR-221 expression ($p<0.05$). In contrast, hepatic ERα/Src kinase association level ($p < 0.05$) increased after E2 treatment. Our results indicate that E2 inhibits hepatic iNOS via molecular mechanisms involving the activation of the ER-α and inhibition of ERK1/2-miR-221 axis.

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ROLE AND INFLUENCE OF P75 NTR RECEPTOR ON ANTIOXIDATIVE DAMAGE OF RETINAL PIGMENT EPITHELIAL CELLS

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The study aimed to investigate the role and mechanism of the p75 NTR receptor in the oxidative damage of retinal pigment epithelial cells (RPE). RPE cells transfected with the p75 NTR receptor were used as the experimental group, and the untransfected RPE cells as the control group. BrdU (5-Bromo-2-deoxyUridine) was used to detect cell proliferation activity; PI/Annexin V-FITC (fluorescein isothiocyanate, FITC) double staining was used to detect the apoptosis rate of the cells. The expression of reactive oxygen species (ROS) in cells was observed by laser microscope, and the expression of ROS, mitochondrial markers, and C expression of cytochrome in cells was detected by flow cytometry. Western blot was used to detect the Fas protein, pyrolysis Caspase-3, and expression level of the vascular endothelial growth factor 165 (VEGF165) protein. The results showed that the proliferation activity of RPE cells in the experimental group decreased gradually with the increase of transfection time, and the apoptosis rate of RPE cells in the experimental group increased gradually with the increase of transfection time, and the apoptosis rate of RPE cells at each time point was significantly higher than that of the control group. The fluorescence intensity of ROS in the experimental group was significantly stronger than that in the control group ($P<0.01$). The fluorescence intensity of cytochrome C in the RPE cells in the experimental group was significantly higher than that in the control group, while the number of positive mitochondria markers in the experimental group was less than that of the control group and the fluorescence intensity was weakened. The expression of Fas protein, Caspase-3 and VEGF165 protein in the experimental group was significantly higher than that in the control group ($P<0.01$). In conclusion, p75 NTR receptor may be a cause of oxidative damage in RPE cells.

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APOPTOSIS OF HEPATOCARCINOMA CELLS $HepG_2$ INDUCED BY *HUAIER* EXTRACT THROUGH REGULATION OF HBx and CEACAM1 GENE EXPRESSION

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Huaier **can effectively inhibit the growth of tumor cells by enhancing the immune system. However, the mechanism of its function is still not clear. The current study aimed to explore the possible mechanism of *Huaier* in inhibiting human hepatocarcinoma cells by observing its effect on proliferation and invasion in hepatocarcinoma cells, $HepG_2$ and $HepG_2$-X, which stably express the HBx gene, and by comparing the levels of mRNA transcription and protein expression of HBx and CEACAM1 in $HepG_2$ cells and $HepG_2$-X cells when treated with different concentrations of *Huaier*. $HepG_2$ cells and $HepG_2$-X cells were treated with 0, 1.5, 3.0, and 6.0 g/L-1 *Huaier* extract *in vitro*. MTT assay was used to measure the inhibition of cell proliferation. The transwell cell model coated with Matrigel glue was used to detect the invasion of $HepG_2$ and $HepG_2$-X cells *in vitro*. Flowcytometry was used to observe changes in cell cycle. Real-time PCR and Western blot were used to detect HBx and CEREAM1 mRNA transcription and protein expression separately. *Huaier* extract can inhibit $HepG_2$ and $HepG_2$-X cell proliferation in a time- and dose-dependent manner. The A value of $HepG_2$-X cells in each group was higher than that of $HepG_2$ cells. Compared with the control group, the invasion ability of $HepG_2$ and $HepG_2$-X cells decreased significantly after treatment with *Huaier* extract, in a dose-dependent manner. The cell cycle of $HepG_2$ and $HepG_2$-X was arrested at S phase. The distribution of G0/G1 phase decreased gradually with the increase of the concentration of *Huaier* extract, and the proportion of G0/G1 phase distribution declined. After treating with *Huaier* extract, mRNA transcription and protein expression of HBx in $HepG_2$ and HepG2-X declined, while those of CEACAM1 increased, reflecting a dose-dependent manner ($P<0.05$). Therefore, we concluded that the inhibitory effect of *Huaier* extract on hepatocarcinoma cell proliferation might function through down regulation of HBx gene expression and upregulation of CEACAM1 gene expression.**

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SOX2 GENE EXPRESSION AND ITS ROLE IN TRIPLE NEGATIVE BREAST CANCER TISSUES

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The aim of this work was to study the expression of SOX2 gene in triple negative breast cancer and its role. One hundred and twenty specimens of paraffin-embedded triple negative breast cancer (TNBC) tissues were collected from Harbin Medical University Cancer Hospital, Heilongjiang, China between January 2014 and March 2018. The expression of SOX2 was detected using immunohistochemistry, and the relationship between the expression of SOX2 and clinical features was analyzed. Breast cancer cell lines (normal group, SOX2 interference group, SOX2 overexpression group) were cultured *in vitro* to detect the proliferation and cloning ability of the cell lines. The expression of SOX2 was related to lymph node metastasis and stage of breast cancer ($P < 0.05$), but was not related to age, menopause or tumor size ($P > 0.05$); the expression of SOX2 in the overexpression group was significantly greater than that in the normal group after 72 hours, and no significant difference between the overexpression group and the interference group was observed. The number of clone cells with a diameter of 0.5 mm in the interference group was lower compared to the normal group, and that of the overexpression group was higher, but not significant. SOX2 is associated with the high invasiveness of breast cancer and can be used as a therapeutic target to inhibit the metastasis of cancer cells. SOX2 can promote the proliferation of breast cancer cells and affect the size of clone cells in its involvement in clone.

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LONGITUDINAL STUDY ON THE EFFECT OF ORAL HYGIENE MEASURES ON THE SALIVARY COUNT OF MICROBIAL SPECIES WITH CARIOGENIC POTENTIAL

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The effect of oral hygiene education measures and professional tooth cleaning on the salivary levels of microbial species with high cariogenic potential (i.e. *Streptococcus mutans*, *Lactobacillus* spp. and *Candida albicans*) was evaluated at different time points. At time 0, high salivary carriage rates were recorded in the study group (n=30). Fifty percent of the subjects harbored all three species in their saliva, 27% harbored 2 species, and 23% only one species. At 3 months after oral hygiene measures, a statistically significant reduction was observed in salivary count of *S. mutans* and *Lactobacillus* spp. The percentage of subjects harboring all three species was also highly reduced, along with an overall improvement of clinical and risk factors parameters. At 8 months after oral hygiene measures, *S. mutans* and *Lactobacillus* spp. load was still statistically lower than that recorded at time 0, although an increment in bacterial load and a partial worsening of clinical and risk factors parameters were observed. *S. mutans* count in saliva inversely correlated with salivary pH, while it positively correlated with *C. albicans* salivary levels. The results obtained suggest that strengthening of the motivation and administration of oral hygiene instructions and professional tooth cleaning every 6-8 months, might be necessary to control salivary levels of cariogenic species.

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IMPACT OF TREATMENTS ON FECAL MICROBIOTA AND FECAL METABOLOME IN SYMPTOMATIC UNCOMPLICATED DIVERTICULAR DISEASE OF THE COLON: A PILOT STUDY

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Symptomatic uncomplicated diverticular disease (SUDD) affects 50% of people having diverticulosis. We performed a pilot study assessing the effect of current treatments on fecal microbiota and metabolome in SUDD. Thirteen consecutive females with SUDD were treated with a 2-week therapeutic trial of 30 g/day fiber supplementation (3 patients), 1.6 g/day of mesalazine (3 patients), 900 billion/day of probiotic mixture VivoMixx® (3 patients), or 800 mg/day of rifaximin (4 patients). Stool samples were collected at entry (T0), at the end of the 2-week therapeutic course (T1), and 30 (T2) and 60 days (T3) after the end of the therapeutic course. Real-time PCR quantified targeted microorganisms. Fecal metabolome patterns were studied by high-resolution proton NMR spectroscopy. At cumulative analysis, symptoms significantly decreased at each time point during follow-up ($p<0.0001$), and only left-lower quadrant pain increased again at T3. The overall bacterial quantity was not altered by the treatments. The amount of *Akkermansia muciniphila* species was significantly reduced at T1 ($p=0.017$) and at T2 ($p=0.026$), while at T3 the reduction was not significant in comparison to enrollment ($p=0.090$). Fecal molecular profile showed significant changes at T1 and T2, while at T3 it became similar to that of T0. Differences were found for 18 of the quantified molecules (tryptophan, phenylalanine, tyrosine, 4-hydroxyphenylacetate, urocanate, X-6.363, X-5.779, uridylate, galactose, X-4.197, threonine, sarcosine, methionine, 2-oxoisocaproate, 5-aminolevulinate, alanine, leucine, valerate). Metabolome and microbiota changed in patients with SUDD under treatment, confirming a possible role of dysbiosis/dysmetabolome in the pathology.

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ONE-YEAR FOLLOW-UP SHOWING EFFECTS OF SINGLE INTRA-ARTICULAR INJECTION OF HYALURONIC ACID (1,500-2,000 kDa) IN SYMPTOMATIC KNEE OSTEOARTHRITIS

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Clinical evidence on knee osteoarthritis suggests that intra-articular administration of hyaluronic acid may be useful in the management of patients with persistent pain. This study assesses the duration of effectiveness of a single intra-articular hyaluronic acid injection in a large population of patients with knee osteoarthritis. This retrospective post-marketing cohort study collected data from the ANTIAGE Registry (http://www.antiagefbf.it/registro), selecting patients of age ≥ 40 years, with symptomatic knee osteoarthritis (Kellgren-Lawrence grade I-III) of ≥ 12 months duration, and ≥ 12 months of follow-up. Patients had received a single intra-articular injection of high molecular weight hyaluronic acid (1,500-2,000 kDa) at baseline. WOMAC Osteoarthritis Index total scores measured using the LK 3.1 scale and 10 cm VAS pain scores were evaluated before IA Injection and at 6, 9, 10, 11 and 12 months. Blood cell counts, uricemia, erythrocyte sedimentation rates and levels of C-reactive protein were measured at baseline and 12 months. Time from initial treatment to second injection up to 12 months was recorded to assess event-free survival. Included patients (n = 187) were 53.5% female and had a mean (±SD) age at baseline of 62 (±16.6) years and mean (±SD) body mass index of 26.2 (±2.5) kg/m². Mean (±SD) WOMAC index total score and VAS pain scores were 60.9 (±7.1) and 5.9 cm (±1.8), respectively. There were statistically significant reductions compared to baseline in mean WOMAC index total score and VAS pain score at all time points ($p < 0.01$ at 6 and 9 months; $p < 0.05$ at 10, 11 and 12 months for both parameters). These results support the clinical effectiveness and safety of hyaluronic acid for up to 12 months for pain relief and function improvement in patients with knee osteoarthritis, confirming previous data on intra-articular administration of hyaluronic acid as chronic therapy in the management of knee osteoarthritis.

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LETTER TO THE EDITOR

MOLECULAR MECHANISM OF ACTION OF VALPROATE ACID ALONE OR IN COMBINATION WITH CHLORPROMAZINE IN THE EPIGENETIC REGULATION OF SCHIZOPHRENIA

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This study aimed to assess the molecular mechanism of the histone deacetylase inhibitor (HDACI) valproate acid (VPA) alone or in combination with the antipsychotic drug chlorpromazine in the epigenetic regulation of schizophrenia. A total of 60 perinatal CD-SD rats were divided in a control group (16 animals) and a schizophrenia model group (44 animals). For the schizophrenia model group the rats received phencyclidine (PCP) 10 mg/kg/day by intradermal injection on days 7, 9, and 11 after birth. The model was confirmed by the Morris water test in 40 rats. The control and model rats were divided into 7 groups. The Real Time PCR assay was used to detect the mRNA expression changes of GABA system gene [GABBR1 (GABA B receptor 1)], GAD1 (glutamic acid decarboxylase1), GAD2 (glutamic acid decarboxylase2), Lipase metabolic key enzyme LPL (lipoprotein lipase) gene, glutamate neurotransmitter gene GRIA2 (AMPA subtype glutamate receptors 2), inward rectifier potassium channel members KCNJ4 (potassium voltage-gated channel subfamily J member 4) and neuropeptide signal gene TAC1 (tachykinin precursor 1,TAC1) in four brain regions: the prefrontal cortex (PC), the amygdala (AM), the caudate-putamen (CPU) and the hippocampus (HIP). The platform arrival time of PMV and PMVC groups was significantly reduced compared to the PM group, the reduction being more significant in the PMV group. In the four brain regions of the epigenetic animal model of schizophrenia, the expression of GABBR1, GAD1, and GAD2 genes increased significantly. Following administration of HDACI VPA, the mRNA expression of this gene in the four brain regions decreased or approached normal levels. GABBR1 GAD1 and GAD2 are likely to be the target genes affected by the HDACI VPA.

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LETTER TO THE EDITOR

TANSHINONE IIA PROTECTS AGAINST CARDIAC FIBROSIS THROUGH INHIBITION OF β-TUBULIN EXPRESSION

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Cardiac fibrosis is a significant global health problem that occurs after pathological stimuli to the cardiovascular system. Previous researchers have shown the protective role of *Salvia miltiorrhiza* Bunge (Danshen) as well as its extracted compound Tanshinone IIA (Tan IIA) against cardiac fibrosis. However no previous work has shown the effects of Tanshinone IIA on cardiac cytoskeleton or the possible relations with its role on cardiac fibrosis. The present study confirms that Tan IIA inhibits the proliferation of mouse cardiac fibroblasts in cultures by MTT assay. It was also observed that Tan IIA decreases β-tubulin expression, especially in the perinuclear area of fibroblasts. Furthermore, we presented by Western blot that TanII A attenuates VEGF expression through HIF-1α and Keap1-Nrf2 pathways, which could be the underlying mechanisms of the Tan IIA's role on cardiac fibrosis. This work demonstrated, for the first time, that the protective role of TanII A against cardiac fibrosis through inhibition of cardiac β-tubulin involves regulation on the antioxidant pathways.

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LETTER TO THE EDITOR

BRASSINOSTEROID BIOSYNTHESIS, STRESS RESISTANCE IN PLANTS, AND APPLICATION OF BRASSINOSTEROIDS IN PLANT BIOTECHNOLOGY

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Brassinosteroids (BRs) are newly discovered plant hormones that protect the plants from biotic and abiotic stress. Plants produce these hormones at all times, however, the quantity and location of their production vary. It has been demonstrated that BRs help the plants to regulate their response to stress conditions and make them more resistant to pest attack, extreme hot or cold environment, water scarcity, and salinity, among other types of stress. Manipulation of genes involved in the synthesis of BRs in different plants is a feasible strategy for genetic improvement of crop production and stress tolerance.

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LETTER TO THE EDITOR

CORRELATION BETWEEN RHEUMATOID ARTHRITIS AND IMMUNOLOGICAL CHANGES IN A RHEUMATOID ARTHRITIS RAT MODEL

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Rheumatoid arthritis is an autoimmune disease characterized by the synovitis of joints and the modulation of chronic inflammation determined by increased levels of inflammatory cytokines. This study aimed to investigate the characteristics of the immunological profile of the cells of the synovial membrane and the expression of IL-10 and IL-17 in a rheumatoid arthritis rat model in order to provide a target-directed treatment for immunological control. Eighty female Wistar rats were randomly divided into a rheumatic arthritis model group (model group) and a control group, 40 animals per group. After the successful rheumatoid arthritis rat model was obtained, 10 animals were sacrificed from each group every week starting from the third week till the sixth week and the expression levels of CD3, CD21, and CD68 in the synovial region along with the blood level of IL-10 and IL-17 were assessed. At the four stages after modeling, the expression of CD3 in the model group increased compared with the control group ($P<0.05$). The expression of CD21 was different between the model group and the control group, but the difference did not reach statistical significance ($P>0.05$). The expression of CD68 determined at weeks 4 and 5 after modeling was increased compared to the control group ($P<0.05$). At 6 week after modeling, IL-10 levels in the model group were higher than those in the control group ($P<0.05$). At weeks 4 and 5 after modeling, the level of IL-17 in the model group increased compared to the control group ($P<0.05$). The level of IL-17 increased with the increase of synovial inflammation in the rheumatoid arthritis-induced rats, and the level of IL-10 increased as the inflammation subsided, which shows that both cytokines are related to the occurrence and development of rheumatoid arthritis and its inflammation.

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LETTER TO THE EDITOR

miR-200b PROMOTES CELL PROLIFERATION AND INVASION IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA THROUGH NOTCH1

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MicroRNA-200b (miR-200b) functions as an oncogenic regulator in human lung cancer. However, the effect of miRNA-200b on the development and progression of T-Cell acute lymphoblastic leukemia (T-ALL) remains largely unknown. In this study, we evaluated the impact of miR-200b in T-ALL cell proliferation, survival and invasion using gain and loss of function approaches. Human Jurkat cells, a widely used *in-vitro* T-ALL cell model, were transfected with miR-200b mimic or miR-200b inhibitor. miR-200b mimics substantially inhibited Jurkat cell proliferation and invasion while significantly stimulating cell apoptosis compared to the control miRNA-treated cells. In contrast, Jurkat cells treated with anti-miR200 demonstrated induction of cell growth and invasion but repression of cell apoptosis. Such effect was accompanied by the corresponding alteration in NOTCH1 expression, suggesting that NOTCH1 might be the target gene for miR-200b function in Jurkat cells. In summary, our findings demonstrate that miR-200b may serve as a potential therapeutic target for T-ALL by negatively regulating the NOTCH1 signaling pathway.

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LETTER TO THE EDITOR

DIFFERENTIAL EXPRESSION OF CYP2J2 GENE AND PROTEIN IN *CAMELUS DROMEDARIUS*

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CYP2J2 is a member of the cytochrome P450 superfamily. It had been described in different mammalian species; however, no studies have described this gene in *Camelus dromedarius*. CYP2J2 is an epoxygenase enzyme which oxidizes various fatty acids, mainly arachidonic acid, via NADPH-dependent epoxidation to generate epoxyeicosatrienoic acids (EETs). It is a multi-functional enzyme that plays crucial roles in inflammation, cancer, drug metabolism, and embryo development. It controls the water re-absorption in the kidney and maintains the blood pressure and glucose homeostasis. This study is considered the first report investigating the differential expression profiles of the CYP2J2 mRNA and protein in the liver, heart, and kidney of *Camelus dromedarius*. A total of 30 samples were used to determine the expression of both CYP2J2 mRNA and protein using qRT-PCR and western blotting methods, respectively. The mRNA level of *CYP2J2* was significantly elevated in the liver compared to that in the heart and kidney. The tissue distribution of the CYP2J2 protein was coherent to its transcript level in the kidney, but not in the liver and heart samples. The difference between the CYP2J2 mRNA and protein distributions in the three studied organs may be attributed to the mechanism by which the CYP2J2 might be involved in the adaptability of the camel to the arid environment.

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LETTER TO THE EDITOR

CARBON MONOXIDE MODULATES MELATONIN SYNTHESIS IN PORCINE PINEAL CELLS *IN VITRO*: A PRELIMINARY STUDY

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Two main isoforms of heme oxygenase (HO-1 and HO-2), the main enzyme of heme metabolism, were identified in the pineal gland. This suggests possible interactions between the melatonin synthesis pathway and the HO system. The aim of this study was to investigate the participation of carbon monoxide (CO), an HO by-product, on the melatonin synthesis pathway. Tests were carried using primary cell cultures of porcine pineal glands. The tricarbonyldichlororuthenium (II) dimer (CORM-2) compound was used as a CO donor at concentrations of 1 and 3 μM, as low concentrations of CORM-2 affect the regulation of the melatonin synthesis pathway in pineal cells *in vitro*. In addition, the presence of Sn-protoporphyrin-IX, an HO inhibitor, changed the melatonin response of pineal cells. These results suggest the existence of an intermediate mechanism in the pineal gland, which is associated with HO activity, that is involved in the modulation of melatonin synthesis.

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LETTER TO THE EDITOR

INFLUENCE OF SERUM HMGB1 LEVEL ON THE INCIDENCE OF RESPIRATORY DISTRESS SYNDROME IN NEONATES

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The aim of this study was to analyse the correlation between high mobility group protein B1 (HMGB1) and neonatal respiratory distress syndrome (NDS), and to provide a theoretical basis for its diagnosis and prognosis. Sixty cases of neonates with respiratory distress syndrome were selected and designated as a survival group (36 cases) and a death group (24 cases) according to their prognosis. Sixty healthy neonates were also selected and designated as the control group. Peripheral venous blood and related clinical data of the neonates were collected 12-24 h after birth. Enzyme-linked immunosorbent assay (ELISA) was used to detect the level of HMGB1 in the sera of the two groups. SPSS 17 software was used for statistical analysis of the experimental data. The test results showed that the serum HMGB1 levels of those in the study group were significantly higher than those of the control group, and the difference was statistically significant (P<0.05); the serum HMGB1 levels of those in the death group was significantly higher than those in the survival group, and the difference was statistically significant (P<0.05). Serum HMGB1 level predicts the area under curve (AUC) value of NRDS as 0.872. A serum HMGB1 level of 625.2198pg/mL represents the best boundary value for predicting NRDS. The serum HMGB1 level predicts the AUC of death from NRDS children as 0.912, and a level of 786.7643pg/mL represents the best boundary value for predicting patient death. In conclusion, the level of HMGB1 in the sera of newborns can better predict the occurrence and death of NRDS, and can therefore be considered as a marker for its diagnosis, evaluation and prognosis.

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LETTER TO THE EDITOR

EFFECT OF PROPRANOLOL ON PROLIFERATION AND APOPTOSIS OF HEMANGIOMA ENDOTHELIAL CELLS IN INFANTS AND YOUNG CHILDREN

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The aim of this study was to investigate the effects of propranolol on the proliferation and apoptosis of hemangioma endothelial cells in infants and young children, and to explore the molecular mechanism of hemangioma treatment. Infant HemEC was cultured *in vitro*. HemEC cells were treated with different concentrations of propranolol (0umol/L, 25umol/L, 50umol/L, 75umol/L, 100umol/L, 125umol/L). After 24, 48 and 72 hours, the viability of the cells was examined by MTT {3-(4, 5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide} method. The apoptosis rate of the cells was measured by flow cytometry using Annexin V. The propranolol concentration was 25umol/L. After 24 h and 48 h, HemEC could slightly proliferate (P<0.05). With the concentration of ≥100umol/L, the survival time of HemEC decreased when the action time was longer than 24 h. Within a certain range, the drug efficacy was positively correlated with drug concentration and action time (P<0.05). When propranolol concentration was ≥100umol/L, it could cause HemEC apoptosis. With the increase of drug concentration and the prolongation of intervention time, the apoptosis rate increased (P<0.05). In conclusion, the inhibition of hemangiomas by propranolol may be related to the inhibition of HemEC proliferation and its promotion of apoptosis.

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LETTER TO THE EDITOR

SUPPLEMENTATION WITH L-ARGININE AFFECTS ITS METABOLIZING PATHWAYS IN RAT LIVER SUBJECTED TO BILE DUCT LIGATION

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Liver cholestasis is known to accompany several major liver disorders and is adequately mimicked in rats by ligation of the bile duct (BDL). L-arginine is a semi-essential amino acid which is involved in several important metabolic pathways that are significantly affected during cholestasis. This study was conducted in order to contribute to the understanding of the enrolment of L-arginine supplementation in cholestatic liver function. This was carried out by estimation of serum and liver tissue arginase activity, along with liver tissue citrulline, nitric oxide (NO) and polyamine concentrations. Rats subjected to BDL were treated for nine days with L-arginine (150 mg/kg) or remained without any treatment. Animals from two control groups were either subjected to medial laparotomy (sham/opened group) or were without any surgical treatment and received only L-arginine. Application of L-arginine prevented a significant increase in plasma bile acid and bilirubin concentrations, as well as enzyme biochemical markers that were increased after BDL. It is worth mentioning that L-arginine was able to cause a decrease in arginase activity and liver tissue NO concentrations that were found to be significantly altered during cholestasis. On the other hand, the changes occurring in the concentration of liver polyamines (putrescine, spermidine and spermine) and the activity of polyamine metabolizing enzymes were not notably affected by the administered L-arginine. The results of the present study revealed that exogenous L-arginine was able to ameliorate or prevent changes occurring in its metabolism in liver during cholestasis.

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LETTER TO THE EDITOR

CONTINUOUS NURSING INTERVENTION ON RECOVERY OF DIABETIC PATIENTS

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The aim of this study was to probe the influence of continuous nursing intervention on recovery of diabetic patients. From October 2016 to June 2017, 80 diabetic patients who received treatment in our hospital were selected and randomly divided into an intervention group and a control group. The intervention group received continuous nursing care including indirect follow-up, health education and home visit. The self-care ability and blood sugar of the two groups were compared three months later. The score of self-care ability in the intervention group was 89.64±1.64 and that in control group was 72.68±2.47, and a significant difference was observed (P < 0.001). The fasting blood glucose level in the intervention group was 6.62±0.86 MMOL/L, and the 2-hour post-meal blood glucose level was 8.47±1.32 MMOL/L, which were both lower than those in the control group. Continuous nursing can help monitor the recovery of patients after discharge. It is helpful to improve the self-care ability of patients, control blood sugar level, and promote recovery. It is worth wide promotion.

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LETTER TO THE EDITOR

CONTRIBUTIONS OF VSX1 GENE TO KERATOCONUS

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Keratoconus (KC) is a complex, genetically heterogeneous, multifactorial degenerative corneal disorder, with incidence of approximately 1 per 2000 of the population. KC follows an autosomal recessive or dominant pattern of inheritance and is, apparently, associated with genes which interact with environmental, genetic and/or other factors. The present report focuses on the VSX1 gene, for which there is general agreement that it is involved in KC and other corneal pathologies, and critically details the evidence for its involvement in KC.

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LETTER TO THE EDITOR

THE p75 NEUROTROPHIN RECEPTOR IN CELLS OF ORAL MUCOSAL EPITHELIUM

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The p75 neurotrophin receptor ($p75^{NTR}$) can play different roles in cells. This protein can on the one hand act in the regulation of cell growth and survival, while being an apoptosis inducing factor in different contexts. $p75^{NTR}$ regulates cell cycle not only in nerve cells but also in epithelial oral mucosal cells. In the former, neurotrophin–$p75^{NTR}$ signaling affects cell growth and survival. Recent studies showed that $p75^{NTR}$ is expressed in basal cells of oral mucosal epithelium and can be used as one of the markers of epithelial stem/progenitor cells. This role of $p75^{NTR}$ can be utilised in aspects such as tissue engineering and gene therapy. One of the examples of clinical use of cultivated oral mucosal cells is ocular surface reconstruction. $p75^{NTR}$ can be a significant marker of stem cells in studies of epithelial tissues, especially when the cells will exhibit other specific markers, such as CK13, CK14 and PCNA.

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LETTER TO THE EDITOR

CORRELATION BETWEEN SPARC, TGFβ1, ENDOGLIN AND ANGIOGENESIS MECHANISM IN LUNG CANCER

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To study the relationship between Secreted protein, acidic and rich in cysteine (SPARC), Transforming growth factorβ1 (TGFβ1), Endoglin and angiogenesis in lung cancer, 40 cases of lung cancer specimens and 40 adjacent normal lung tissues specimens were collected and 10 cases from each were selected for preparation of tissue chip. CD34 (endothelial cell marker), Endoglin human α-Smooth muscle actin, and (α-SMA) markers were performed by immunohistochemical staining, and the immuno-phenotype and the relationship between different morphologies of the microvascular wall components were evaluated. The expression of SPARC mRNA and protein, TGFβ1 mRNA and protein and Endoglin in the remaining 30 cases of lung cancer were detected by immunohistochemistry and in-situ hybridization. The result shows that the positive rates of SPARC, TGFβ1 and Endoglin in lung cancer tissues were significantly higher than those in adjacent normal lung tissues ($P < 0.05$). The expression of SPARC and TGFβ1 was negatively correlated with lung cancer. When the positive expression of SPARC increased, the micro-vessel density (MVD) marked by Endoglin decreased gradually; while the positive expression of TGFβ1 increased, MVD increased gradually, and SPARC, TGFβ1 and MVD were correlated ($P<0.05$). High SPARC mRNA expression in lung cancer tissues could inhibit the progression of lung cancer, while high TGFβ1 mRNA expression can promote the progression of lung cancer and participate in the metastasis of lung cancer. To sum up, the angiogenesis of lung cancer may be related to the interaction of SPARC, TGFβ1 and Endoglin.

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LETTER TO THE EDITOR

COMPARATIVE ASSESSMENT OF ATHEROSCLEROSIS OF RABBIT FEMORAL ARTERY BY DUPLEX ULTRASOUND SCANNING, OPTICAL COHERENCE TOMOGRAPHY AND FRACTIONAL FLOW RESERVE

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Duplex Ultrasound Scanning (DUS), Frequency-domain optical coherence tomography (FD-OCT) and fractional flow reserve (FFR) remarkably shape our understanding of the significance of coronary stenosis. The present study aimed to compare the assessment results of the atherosclerotic lesions in rabbit superficial femoral artery by DUS with that of FD-OCT and FFR. A total of 20 atherosclerotic lesions were analyzed. Morphological assessments were prospectively compared through DUS, FD-OCT and quantitative superficial femoral angiography (QFA). In addition, the correlation between DUS-derived lesion parameters and FFR was determined. The results show that, compared with FD-OCT and QFA, DUS detected larger reference diameter and higher percent stenosis. However, the minimal lumen diameter (MLD) and distance from profunda femoris to MLD were equivalent measured by the three imaging modalities. There was a poor correlation between FFR and DUS-derived percent diameter stenosis (R^2=0.198, P=0.049). In conclusion, hemodynamic significance of lesions assessed by FFR was only related with percent diameter stenosis measured by DUS.

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LETTER TO THE EDITOR

CORRELATION OF HYPERTENSION AND F2RL3 GENE METHYLATION WITH PROGNOSIS OF CORONARY HEART DISEASE

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The aim of this work was to investigate the correlation between methylation of F2RL3 gene and coronary heart disease (CHD) with or without hypertension, secondary cardiovascular events and mortality. Sixty patients with CHD who underwent a cardiovascular rehabilitation program were recruited. Group A included 30 patients with hypertension and CHD, and group B included 30 patients with non-hypertensive CHD, followed-up for more than 8 years. F2RL3 gene methylation was characterized by Sequenom matrix assisted laser desorption ionization time flight mass spectrometry. The correlation between methylation of the F2RL3 gene, hypertension and secondary cardiovascular events and all-cause mortality was analyzed by multivariate Cox, regression models that estimated confounders to control risk ratios. The results showed that during the follow-up, 3 patients in Group A developed non-fatal stroke, 2 patients died of cardiovascular disease, 1 patient died of other causes, and 4 patients in Group B developed non-fatal myocardial infarction. After adjusting for known prognostic factors, Cox model analysis showed that methylation of F2RL3 gene was closely related to hypertension and mortality. After F2RL3 included in the regression model, the correlation between hypertension and all prognostic outcomes increased. In conclusion, the methylation of F2RL3 can affect the prognosis of different types of acute coronary syndrome and is closely related to mortality.

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LETTER TO THE EDITOR

EFFICACY OF COMMERCIAL VACCINES AGAINST THE PREVALENT STRAINS OF NEWCASTLE DISEASE AND AVIAN INFLUENZA (H9N2) INFECTIONS IN BROILERS IN PAKISTAN

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The efficacy of the two commonly used commercial vaccines for Newcastle disease (ND) and low path avian influenza (LPAI) H9N2 were evaluated against field virus in broiler chicks. One hundred one-day-old commercial broiler chicks were divided into four groups (A to D) with an equal number of birds per group. Group A and B were vaccinated against H9N2 and NDV, respectively, at day 7 of age while group C served as positive infected control for H9N2 and group D for NDV. Serum samples from birds in all groups were tested for presence of antibodies against H9N2 and NDV at day 21 of age. Subsequently, on day 28 of age, groups A and C were challenged with the field strain of H9N2 virus, and Group B and D with NDV. Birds were monitored for a period of 2 weeks for development of any clinical signs and mortality. The geometric mean titer were high in groups A (4.90) and B (7.3), and low in the unvaccinated groups C (0.7) and D (1.1). The highest and lowest value of H9N2 antibody titer detected through ELISA were 1.498 and 0.502, respectively. The S/P ratios greater than 0.5 were considered positive. The highest and lowest value for NDV antibody titer detected through ELISA were 783 and 882, respectively. Serum samples with titer greater than 396 were considered positive and indicated vaccination or other exposure to NDV. On histological examination severe congestion, necrosis, degeneration, hemorrhages and leukocyte infiltration were observed in intestine, lungs, trachea and bursa of Fabricius of the non-vaccinated group post-infection. Mild tissues changes were observed in the vaccinated group. It can be concluded from the findings that the commonly used commercial vaccines may provide effective protection against the circulating H9N2 and ND virus in broiler birds by producing protective antibody titer.

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LETTER TO THE EDITOR

ELECTROSPUN PROBIOTICS: AN ALTERNATIVE FOR ENCAPSULATION

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Electrospinning has emerged as a potential method to fabricate nonwoven nanofibers. It has application in different fields of biomedicine as it has potential to carry antimicrobial and bioactive agents. The present investigation was conducted to optimize the process conditions and determine the viability of probiotics after being electrospun in fibers. Poly(vinyl alcohol) (PVA) was utilized as electrospun material because it possesses generally recognized as safe (GRAS) status and in dry form it acts as a high oxygen barrier and has high water solubility. This characteristic allows the easy recovery of the bacteria from electrospun fibers. The viability tests, carried out at three different temperatures (room temperature, 4°C and -20°C) showed *Bifidobacterium animalis* subsp. Lactis Bb12 (probiotic 1) and combination of *Streptococcus thermophilus* (TH-4®), *Lactobacillus paracasei* 431® and Bb-12 (probiotic 2) within the electrospun PVOH fibers remained viable after 1 week at room temperature and refrigeration temperature. The nanofibers containing probiotics prepared with 9% poly venyl alcohol showed homogenous, uniform, bead-free and smooth texture. Probiotic 1 demonstrated growth as 1.85×10^8, 1.57×10^8 and 1.71×10^8 before, 0 hour and after 1 week of encapsulation. While probiotic 2 exhibited a growth of 2.1×10^8 before electrospinning, 1.3×10^8 at 0 hour and 1.97×10^8 after one week of electrospinning. There was no change in CFU/mL count and remained 10^8 CFU/mL. The encapsulation efficiency was 84.07% and 85.73% at 0 and one week, respectively, for Probiotic 1, while probitic 2 showed 90.09% and 93.59 % encapsulation efficiency before and after one week, respectively. Considering the prolonged viability of nanofibers containing probiotics noted at room temperature, this technology can be implemented for prolonged viability of probiotics.

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LETTER TO THE EDITOR

SHORT-TERM EFFECTS OF A DIETARY SUPPLEMENT ON LOWER URINARY TRACT SYMPTOMS

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Benign prostatic hyperplasia (BPH) is one of the most common conditions affecting men over 40 years of age, typically manifesting itself with lower urinary tract symptoms (LUTS). Recently, research interest has focused in discovering a viable nutraceutical alternative to the drugs that are currently the first line of treatment for BPH. The aim of this study was to investigate the efficacy and safety of a dietary supplement containing curcumin, beta-sitosterol and oligomeric proanthocyanidins in a group of BPH/LUTS patients. One-hundred men with LUTS caused by BPH were enrolled in this study and agreed to take one tablet a day of the test dietary supplement for three months. Several parameters, such as International Prostate Symptom Score (IPSS), degree of urinary obstruction and average urinary flow were evaluated at different time points. Significant improvement in LUTS was seen after one month of treatment and a significant decrease in mean IPSS index was evident after three months of treatment. Moreover, a comparison of the mean urinary flow and of the number of subjects with bladder obstruction at three months versus one month of treatment shows a significant improvement. The study results suggest that the dietary supplement is effective for almost all the symptoms investigated, including the reduction of IPSS score and the increase of urinary flow. Moreover, the dietary supplement proved to be safe and well tolerated by the great majority of the enrolled subjects.

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LETTER TO THE EDITOR

PEDICLED PALATAL FLAP FOR SURGICAL REPAIR OF ORO-NASAL FISTULA

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Oronasal fistula can occur secondary to various pathologies, but cleft surgery is the most common. The authors propose a pedicled palatal flap technique for surgical repair of small oronasal fistula (0.5-0.8 cm), derived from their experience in the treatment of 7 patients between March 2003 and December 2007. In one case, the fistula was induced by prolonged snorting of cocaine. In the other cases, the fistulas developed after excision of a benign tumor of the palate. For the cocaine-induced fistula, failure of the repair attempt was apparent within 7 days of surgery. In all other cases, complete fistula closure was obtained, and no complications occurred.

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LETTER TO THE EDITOR

PERCUTANEOUS HEADLESS SCREWS AND WIDE-AWAKE ANESTHESIA TO FIX METACARPAL AND PHALANGEAL FRACTURES: OUTCOMES OF THE FIRST 56 CASES

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Phalangeal (P) and metacarpal (MC) fractures are very common injuries, with potentially disabling, residual impairment, deformities or stiffness. Conservative treatment represents the strategy of choice in most cases, but in unstable fractures and/or high-demanding patients, surgical fixation could be required. Ideally, the best treatment choice will be the intramedullary fixation systems, if possible without the implant protruding from the skin. Intramedullary headless screw fixation could be the reliable option to achieve a primary fixation, allowing an early active movement, with regard to the fractures site. The Authors analyzed the results achieved after 56 extra-articular unstable fractures (31 phalangeal fracture and 25 metacarpal fracture) treated with intramedullary headless compression screws. After surgery, patients underwent early mobilization without splinting. The results of the study suggest that this technique could be a reliable therapeutic option in order to obtain early mobilization and quick return to work after a phalangeal or metacarpal fracture, especially for high-demanding patients.

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LETTER TO THE EDITOR

ASSESSMENT OF NUTRITIONAL STATUS AND THERAPY IN EMERGENCY MEDICINE SETTINGS

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Hospital malnutrition is becoming a clinical concern. Our aim was to determine the prevalence of hospital malnutrition through Nutritional Risk Screening 2002 (NRS) and to evaluate nutritional risk through a prospective study. Nutritional status was assessed collecting anthropometric parameters together with the data relating to the diseases in the medical records of patients admitted to the Department of Emergency Medicine of the "Sant'Eugenio" Hospital. One hundred and sixty patients were retrospectively enrolled during a 3-month observational period. The risk of malnutrition was detected in 52% of patients (of whom 38% at risk and 62% at serious risk). The NRS score was positively correlated with patient age, days between hospital admission and nutritional assessment, disease severity, length of hospital stay and catabolism ($p<0.05$); Basal Energy Expenditure (BEE) and mean arm circumference (MUAC) were negatively correlated with positive outcome ($p<0.05$). No correlations were found in the NRS score, gender, height, weight, Body Mass Index (BMI) and Total Energetic Expenditure (TEE) (p=n.s). A high prevalence of the risk of malnutrition may be detected in the emergency medicine setting, particularly in the geriatric population. The NRS score is not strictly related to BMI, but rather is an excellent tool for disease prognosis, as well as nutritional screening.

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LETTER TO THE EDITOR

ADDITIVE MANUFACTURING AND BIOMIMETIC MATERIALS IN ORAL AND MAXILLOFACIAL SURGERY: A TOPICAL OVERVIEW

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Additive manufacturing (AM) is the term used for different and complex techniques to manufacture products with complex morphology, often referred to as "custom-made". The product is made without needing to melt the material into pre-formed molds, nor to remove it from an initial mass, as happens in subtractive processes. The additive methodology gives the AM enormous potential in the widest fields of application, from aerospace to biomedical, from dental to maxillofacial. This wide range of AM technologies can be applied to different types of polymeric materials such as plastics, resins and biopolymers that are processed to obtain optimal scaffolds. The most common synthetic and biocompatible polymeric materials for the production of biocompatible scaffolds are: polylactic acid (PLA), polycaprolactone acid (PLC) and polylactic-co-glycolic acid (PLGA); such materials interact effectively with cell behavior and tissue development. These materials are degradable in the physiological environment and the degradation products do not have harmful effects. In conclusion, new biomaterials are increasingly being studied as possible therapeutic remedies. Advances in tissue engineering are leading to the development of new scaffolds useful for bone regeneration and therefore potentially valid for applications in maxillofacial surgery.

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LETTER TO THE EDITOR

EFFECT OF SELF-ADJUSTING FILE AND WAVEONE RECIPROCATING FILE ON THE FILLING ABILITY OF OVAL-SHAPED CANALS WITH THERMOPLASTICIZED GUTTA-PERCHA

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The aim of the study was to compare the effect of Self-Adjusting Files (SAF) and WaveOne Primary file with syringe and needle irrigation on the filling ability of oval-shaped root canals obturated with thermoplasticized gutta-percha. Twenty-four single root teeth with single oval-shaped root canals were distributed into two experimental homogeneous groups. One group was instrumented and cleansed using the SAF system while in the other group the WaveOne system with syringe and needle irrigation was used. After instrumentation, the roots were filled by Thermafil Obturators and TopSeal sealer. Specimens were transversally sectioned at 2-, 5- and 7-mm levels from the apex and observed under light microscope. The percentage of gutta-percha filled area (PGFA), the percentage of sealer filled area (PSFA) and the percentage of voids area (PVA) were measured for each section, moreover the percentage of completely filled sections was evaluated. At all levels, no significant differences in terms of PGFA, PSFA, PVA and percentage of completely filled canals between groups were obtained ($P > 0.05$). On the contrary, when the data were pooled, the mean PGFA in the SAF group was 95.8%, whereas it was 93.2% in the WaveOne group ($P < 0.05$). The percentage of sections completely filled was 77.8% in the SAF group, and 52.8% in the WaveOne group ($P < 0.05$). Overall, the use of the SAF system in oval canals allows to obtain a significantly greater complete filling than the use of the WaveOne system.

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LETTER TO THE EDITOR

A NOVEL TECHNIQUE TO PREVENT SINUS MEMBRANE COLLAPSE DURING MAXILLARY SINUS FLOOR AUGMENTATION WITHOUT BONE GRAFT: TECHNICAL NOTE

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Different surgical techniques have been developed to reconstruct the posterior maxilla without bone graft. A barrier membrane usually placed internal to the sinus, without stabilizer or bone window, pushed inside the sinus cavity as the "roof" of the sinus cavity to preserve the space and help bone regeneration has been used with success. In the present technical report, the heterologous cortical lamina is used for the mechanical support of sinus membranes. The membrane is placed through two lines of 2-3 mm, mesial and distal, created at the top of the antrostomy. The half heterologous membrane is positioned on these lines and pushed to the nose wall of the sinus, and the other half is folded to cover the window. In this way the bone lamina is stable. Cone Beam Computed Tomography was used to evaluate the efficacy of bone lamina to preserve the space in sinus lifting which contributes positively to wound healing and is effective in bone formation without biomaterials.

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LETTER TO THE EDITOR

EFFICACY OF A COMBINED SEA SALT-BASED ORAL RINSE WITH XYLITOL AGAINST DENTAL PLAQUE, GINGIVITIS, AND SALIVARY *STREPTOCOCCUS MUTANS* LOAD

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Dental plaque is a biofilm which forms on the non-shedding surfaces of the oral cavity. If left untreated, the succession of dental plaque development can lead to serious complications, such as caries, gingivitis, and periodontitis. The control of dental plaque on tooth surfaces is vital for the prevention of dental plaque related diseases. In this context, antimicrobial agents may serve as a valuable complement to mechanical plaque removal. Therefore the present study was aimed to evaluate the action of a combined rinsing solution containing different antimicrobials (sea salt, xylitol and lysozyme) used individually, for the reduction of a salivary specific bacteria *(S. mutans)* colonizing oral environment.

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LETTER TO THE EDITOR

SERUM 25-HYDROXY VITAMIN D LEVELS IN ESSENTIAL HYPERTENSION

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Vitamin D may have prognostic value in hypertension patients and, in addition to conventional biomarkers, could be a valuable tool for disease management. The aim of this study was to assess the association of vitamin D status in patients with essential hypertension and to evaluate its prognostic utility. Forty-eight consecutive patients (40 Caucasian and 8 Asian) aged between 30 and 80 years (mean 61.5, range 34-84 years), were enrolled in the study. The main exclusion criteria were age < 18 years, kidney failure, onco-hematologic disease, hypo-hyperparathyroidism, osteoporosis, treatment with bisphosphonate or 25(OH) vitamin D supplementation. Of the 48 patients included in the study, hyperlipidemia was described in 28, diabetes type 2 in 8, and ischemic heart disease in 14. Serum electrolytes, calcium, sodium, and potassium concentrations were within normal range. Low 25(OH) vitamin D levels inversely correlated with essential hypertension values ($p < 0.001$) were considered extremely significant. The determination of 25(OH) vitamin D levels in patients with essential hypertension could improve the research for possible underlying conditions, which should be managed meticulously according to current guidelines.

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LETTER TO THE EDITOR

SPIDER ZYGOMA: A NEW IMPLANT REHABILITATION TECHNIQUE FOR ATROPHIC MAXILLA

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Atrophic maxilla is a challenge in dental implant surgery, and new strategies are needed. We present a new minimally-invasive approach, called "Spider Zygoma", consisting of implant-supported prosthesis with the addition of customized maxillofacial plates and screws on surface of zygomatic bone. A 3D-model of the edentulous upper jaw was used as preoperative model. Two customized bone plates were created and used as guide for placement of implants and zygomatic screws. Although this is only a pilot study, this new surgical technique seems to be safe and accurate, confirmed by the maintenance of good aesthetic and functional results after 5-year follow-up.

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