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*EDITORIAL*

# ROLE OF MACROPHAGES IN THE PATHOGENESIS OF ATHEROSCLEROSIS AND AORTOCORONARY GRAFT DISEASE

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**Atherosclerosis and disease of graft implanted to bypass occluded coronary or peripheral arteries are similar processes. Patency of implanted grafts is of paramount importance in respect to long-term outcomes. Although few cell types participate in atherosclerotic plaque formation, macrophages play a crucial role. In this article we review the fate of monocytes that infiltrate vessel wall following endothelium damage, and then undergo transformation to macrophages (identified as CD68 positive cells) and eventually lead to severe stenosis of vessel. Opposing biological activity of two subpopulations of macrophages and their impact on plaque instability and its calcification is also presented. At the end of this paper, a possible clinical significance of pre-existing, CD68 positive cell infiltration of vessel wall, applied as aortocoronary grafts, is discussed.**

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*EDITORIAL*

# IL-33 MEDIATES ALLERGY THROUGH MAST CELL ACTIVATION: POTENTIAL INHIBITORY EFFECT OF CERTAIN CYTOKINES

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**Mast cells (MCs) are hematopoietic immune cells commonly found in adjacent to blood vessels in the lamina propria of airway mucosa. They are important in allergic reactions since the cross-linking of their surface high affinity receptor FcεRI induces activation of these cells, and provokes the synthesis, degranulation and release of inflammatory mediators including arachidonic acid-derived eicosanoids (de novo synthesized), stored enzyme mediators, and inflammatory TH1 and TH2 cytokines, and chemokines. Interleukin (IL)-33 participates in innate and adaptive immunity and inflammation and, acting on CD34+ cells, causes MC differentiation and maturation. IL-33 is generated by activated immune cells, and activates MCs which degranulate and release pro-inflammatory mediators. IL-33 is very important in mediating allergic inflammation and can be induced by IL-1 beta. It is also called "alarmin" and is an inflammatory cytokine IL-1 family member, expressed from mocytes and MCs, which binds its receptor ST2, provoking its release after cell damage. MC-derived allergic compounds in response to IL-33 is critical to innate type 2 immunity. IL-37 is expressed by immune and non-immune cells after pro-inflammatory stimulus. IL-37, an anti-inflammatory cytokine, binds IL-18Rα and suppresses pro-inflammatory IL-1 beta released by activated immune cells such as macrophages. Here, we hypothesize that pro-inflammatory IL-1 family member cytokines released by activated MCs, mediating inflammatory allergic phenomenon, can be suppressed by IL-37.**

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# BALANCE BETWEEN EPITHELIAL AND STROMAL MARKER EXPRESSION AND DISTRIBUTION IN PRIMARY CULTURE MODEL OF PORCINE ENDOMETRIUM DURING REAL-TIME CELL PROLIFERATION

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**The similarity between humans and pigs, when it comes to tissue morphology, makes *Sus scrofa* not only a good research model, but also a potential source of cells for tissue engineering. Cell samples obtained from the pig donor, could be influenced *in vitro,* in order to become a source of tissue material for xenotransplantation, reconstructive and regenerative medicine. Significant amounts of data point to especially major similarities in pig and human reproductive systems. Because of that, particular scientific focus is centered on research concerning porcine COCs, theca and granulosa cells in primary cultures. One of the aspects of the reproductive process, that is still largely undiscovered, is the interaction between preimplantation blastocyst and maternal uterine tissues. In this study, we used molecular analysis techniques, such as RT-qPCR and immunocytochemistry, to analyze the expression and distribution of cytokeratin 18 and panCytokeratins 8, 18 and 19 and vimentin in porcine luminal endometrial epithelial cells, coupled with analysis of their behavior in RTCA. The results have confirmed the presence of epithelial, as well as stromal cell markers in the cells, varying in levels at different stages of culture. They have also given insight into the modes of proliferation and differentiation of studied cells in *in vitro* culture, as well as providing additional proof for the possible mesenchymal transdifferentiation of epithelial cells.**

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# AZITHROMYCIN INFLUENCES AIRWAY REMODELING IN ASTHMA VIA THE PI3K/Akt/mTOR/HIF-1α/VEGF PATHWAY

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**Asthma is a respiratory disease that affects people of all walks of life, and is a hotspot of continuous research, with significant manpower and resources invested in its study. Airway remodeling is an important associated pathological change, and a mark of the irreversible damage produced by asthma. It involves compositional and functional changes in the cells of the airway walls, leading to reversible structural changes, and complicating treatment. Airway remodeling is mediated by different inflammatory pathways which have been targeted for treatment, with good results. However, given its complexity, systematic study of the pathogenesis of airway remodeling is still needed, and additional targeted therapies are necessary. Macrolide drugs, such as erythromycin, azithromycin, and clarithromycin, have antibacterial effects and also influence the cytokine secretion of macrophages and T-lymphocytes. They have direct effects on a variety of cytokines, inhibiting inflammation and reducing airway reactivity. In this study, we investigated the protective effect of azithromycin on airway remodeling through the phosphoinositol-3 kinase/Akt/mechanistic target of rapamycin kinase/hypoxia-inducible factor 1α (HIF-1α)/vascular endothelial growth factor (VEGF) pathway. We observed that a long course of azithromycin could significantly reduce airway reactivity and ovalbulmin-induced pathological alterations in asthmatic mice. Gene expression analysis confirmed that HIF-1α and VEGF were significantly down-regulated following a long course of azithromycin administration.**

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# ENZYME LINKED RECEPTOR PROTEIN SIGNALING PATHWAY IS ONE OF THE ONTOLOGY GROUPS THAT ARE HIGHLY UP-REGULATED IN PORCINE OOCYTES BEFORE *IN VITRO* MATURATION

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**Before being able to fully participate in the processes associated with its function as a female gamete, the oocyte needs to undergo a range of changes to achieve its mature form. These morphological, biochemical and metabolomic processes are induced by the somatic tissues surrounding the oocyte, through the expression of specific transcription and growth factors. The maturation of the oocyte is highly important for the proceedings that lead to successful fertilization, early embryonic development and implantation. Domestic pigs were used as models for our study, with the cumulus-oocyte complexes obtained from the ovaries that were recovered at slaughter. After shedding of the cumulus, oocytes were assessed with BCB test, with the viable ones chosen to undergo *in vitro* maturation. With the use of expression microarrays, we analyzed gene expression before and after IVM and detected major changes in both genes that were proven to be associated with oocyte maturation before (*FOS, VEGFA, CHRDL1, TGFBR3, FST, INSR, ID1, TXNIP, SMAD4, MAP3K1, EIF2AK3* and *KIT*) and genes not previously linked with reproduction associated processes (*MYO1E, PHIP, KLF10* and *SHOC2)*. All the genes were briefly described, with consideration of possible involvement of the newly discovered elements of the transcriptome in the process of oocyte maturation.**

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# EXPRESSION OF IL-17A, E, AND F AND THEIR RECEPTORS IN NON-SMALL-CELL LUNG CANCER

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**Lung cancer is the leading cause of cancer-related morbidity and mortality worldwide. Interaction of nascent or established lung tumour cells with various cytokines and infiltrating immune cells has been implicated in lung cancer pathogenesis. In this study, we systematically analysed immunoreactivity for IL-17A, IL-17E and IL-17F and their relevant receptors in the lung sections from non-small cell lung cancer (NSCLC) and normal control. Immunoreactivity for IL-17A, IL-17F, IL-17RA and IL-17RC, but not IL-17RB was significantly elevated in NSCLC compared with controls, while IL-17E was reduced. The median numbers of infiltrating lymphocytes and neutrophils and global macrophage (CD68) immunoreactivity of phagocytes were also elevated in NSCLC compared with control tissue sections. Furthermore, correlation between the expression of IL-17A and its receptors IL-17RA and IL-17RC varied according to NSCLC histopathological type. These data suggest that IL-17A, E, F and their receptors IL-17RA, RB, RC may be involved in the pathogenesis of NSCLC. Further understanding of the relationship between the IL-17/IL-17R axis and the tumour inflammatory microenvironment may reveal new therapeutic targets.**

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# CROSS-TALK BETWEEN APELIN AND VASOPRESSIN IN RESPONSE TO DIFFERENT OSMOTIC STIMULI IN TYPE 2 DIABETIC RATS

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**Apelin, a peptide hormone that has been linked to insulin resistance, obesity and glucose metabolism, coexists with arginine vasopressin (AVP) in hypothalamic magnocellular neurons that control body fluid homeostasis. The significant correlation between serum glucose and serum osmolarity in uncontrolled DM indicates the need for adequate compensation, but how apelin and AVP contribute to this is still unsettled. This study aims to investigate the interaction between apelin and AVP in osmotic regulation in type 2 diabetes mellitus (T2DM), and to explore the underlying mechanism. Forty-eight adult male albino rats were divided into six groups: control (isotonic, ip 0.9% NaCl; hypotonic, ip distilled water; hypertonic, ip 2% NaCl) groups and T2DM (isotonic, hypotonic, hypertonic) groups. Serum levels of AVP, apelin, Na, glucose, serum and urine osmolarity were measured; kidney samples were taken for Aquaporin 2 channels (AQP2) and epithelial sodium channel gamma subunit (ENaCγ) gene expression. Hypothalamic tissue sections were used for immunohistochemical staining of apelin and AVP. Both in control and diabetic groups serum apelin, showed a significant negative correlation with serum AVP ($r=-0.533$, $p\leq 0.001$). Serum apelin and AVP were inversely proportional to their hypothalamic protein expression. Serum apelin and AVP were significantly higher in diabetic rats ($P= 0.001$) yet their percentage change in response to hypo and hyper-osmotic stimuli (1.5±0.7, -0.34±0.15 and -0.38±0.13, 1.95±0.36, respectively) was less pronounced when compared to control rats (3.28±0.52, -0.59±0.12 and -0.45±0.13, 2.58±0.93, respectively). Na and ENaCγ levels significantly increased in hypertonic rats, while AQP2 gene expression significantly increased in hypotonic rats. Both apelin and AVP reacted to osmotic stimuli in T2DM but with less sensitivity than in control rats. In spite of its abnormal increased levels in diabetic rats, apelin maintained its role through counteracting AVP action.**

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# GENES INVOLVED IN REGULATION OF CELLULAR METABOLIC PROCESSES, SIGNALING AND ADHESION ARE THE MARKERS OF PORCINE BUCCAL POUCH MUCOSAL CELLS LONG-TERM PRIMARY CULTURED *IN VITRO*

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**Extraordinary abilities for continuous proliferation and differentiation, associated with constant renewal triggered by stimulation from the mastication process, together with the relative lack of aesthetic complications associated with post-surgery healing, have highlighted buccal pouch mucosa as a potential source of explants that could be used in transplantation and tissue engineering. Additionally, this tissue plays a major role in the oral drug delivery process, which brings special interest to its molecular properties in the context of new drug development. There is therefore a need to analyse the exact mechanisms of oral mucosa functioning, especially when it comes to the processes that are associated with the potential clinical applications. In this study we analysed a complete transcriptome of long-term *in vitro* cultures of porcine buccal pouch oral mucosa cells. Using a microarray approach, we focused on genes associated with cellular metabolic processes, signalling and adhesion, from 4 gene ontology groups: "Positive regulation of cellular component movement", "Positive regulation of cellular process", "Positive regulation of intracellular signal transduction" and "Single organism cell adhesion". Nineteen genes (CCL8, CXCL2, PLK2, DUSP5, PTGS2, LIF, CCL2, ATP1B1, REL, ITGB3, SCARB1, UGCG, PDPN, LYN, ETS1, FCER1G, TGFB1, RFC4, LMO2) with fold changes higher than |2| and p value <0.05 were identified, described in context and analysed. While the study needs much further validation to become applicable in a clinical environment, it yields valuable information about the transcriptomic basis of oral mucosal cell functioning *in vitro*, that might serve as a reference for further research, aiming to apply this knowledge in clinical situations.**

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*LETTER TO THE EDITOR*

# XUEBIJING ENHANCES NEUROPROTECTIVE EFFECTS OF ULINASTATIN ON TRANSIENT CEREBRAL ISCHEMIA VIA Nrf2-ARE SIGNAL PATHWAYS IN THE HIPPOCAMPUS

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**Prior studies have demonstrated that ulinastatin (UTI) plays a beneficial role in regulating cerebral ischemic injury evoked by cardiac arrest (CA). It is noteworthy to find interventions that can enhance effects of this drug and thereby increase its clinical application. Xuebijing (XBJ) is comprised of extracts from Chinese herbs and has been widely used in China as an anti-endotoxicity drug for the treatment of sepsis and ischemic disorders associated with multiple organ dysfunction syndrome. Thus, in this study we examined the effects of a combination of UTI and XBJ to improve neural injury in the process of neurological functions after transient cerebral ischemia. Our results show that CA impaired Nrf2-antioxidant response element (Nrf2-ARE) and superoxide dismutase (SOD) in the hippocampus CA1 region. This process further amplified products of oxidative stress, namely 8-isoprostaglandin F2α (8-iso PGF2α) and 8-hydroxy-2'-deoxyguanosine (8-OHdG). A lower dose of UTI failed to restore Nrf2-ARE and attenuate 8-iso PGF2α and 8-OHdG SOD following CA; however, systemic administration of XBJ amplified the effects of this dose of UTI on antioxidative signal pathway of the hippocampus. Overall, the results of this study have implications for the enhanced neuroprotective role played by a combination of XBJ and UTI in improving neural injury observed in transient cerebral ischemia; and Nrf2-ARE signal is a part of key mechanisms that are involved in neuroprotective effects of XBJ and UTI.**

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*LETTER TO THE EDITOR*

# PATIENT-REPORTED QUALITY OF LIFE AFTER ENDOSCOPIC SURGERY FOR PITUITARY LESIONS: A META-ANALYSIS

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**Patient-reported outcomes are now considered as an important part of overall outcome assessment of a surgical intervention. The objective of the current study was to evaluate the patient-reported quality of life (QoL) of the subjects of endoscopic pituitary surgery. A literature search was carried out in several electronic databases and study selection was based on pre-determined eligibility criteria. Meta-analyses of standardized mean difference (SMD) were conducted to observe significance of difference between preoperative and postoperative scores of important tools. Sixteen studies were included [931 patients; 51.16 years (95% CI 49.13, 53.19) age; 48.41 % (43.74, 53.08) males]. Generally, there was no significant differences between postoperative and preoperative health-related QoL after postoperative month 1 or after fourth postoperative month. QoL after endoscopic pituitary surgery remains unchanged predominantly but may deteriorate in regard to physical role and sinonasal outcome transiently.**

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

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*LETTER TO THE EDITOR*

# DETECTION OF SERUM PROCALCITONIN AND HYPERSENSITIVE C-REACTIVE PROTEIN IN PATIENTS WITH PNEUMONIA AND SEPSIS

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**Sepsis, a systemic inflammatory response syndrome induced by infection, has high rates of morbidity and mortality. Pneumonia is a major cause for sepsis; however, pneumonia complicated by sepsis is a difficult clinical diagnosis. To assess the clinical relevance of serum procalcitonin (PCT) and hypersensitive C-reactive protein (hs-CRP) in early diagnosis of pneumonia complicated by sepsis, 220 patients with pneumonia who were admitted to hospital from July 2015 to July 2016 were enrolled in this study. The patients were divided into non-sepsis (N=82), mild sepsis (N=97), severe sepsis (N=23), and septic shock (N=18) groups. The patients were also divided into a survival group (N=186) and a death group (N=34) according to their prognosis at 2 weeks. The PCT and hs-CRP levels and Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores of the two groups were evaluated. The PCT level and APACHE-II score showed a progressively increasing tendency in the non-sepsis, mild sepsis, severe sepsis, and septic shock group; the differences between all pairs of groups were significant (P<0.05). The hs-CRP level was significantly lower in the non-sepsis group than in the other groups (P<0.05), but differences among the other groups were not significant (P>0.05). The areas under the receiver operating characteristic curves of PCT and hs-CRP for diagnosis of pneumonia complicated by mild and severe sepsis were 0.841 and 0.817, respectively. The optimal cut-off points for pneumonia and sepsis were ≥0.5 ng/mL and ≥55 mg/L, respectively; the sensitivity and specificity were 71.42% and 82.13%, and 75.04% and 53.61%, respectively. The sensitivity and specificity of diagnosis based on PCT and hs-CRP were 89.32% and 85.68%, respectively. PCT and hs-CRP are used to assess the severity of pneumonia in combination with sepsis in new-borns, but PCT is more strongly related to the severity of sepsis than is hs-CRP. Detection of PCT in combination with hs-CRP facilitates the early diagnosis of pneumonia and sepsis in new-borns, as well as monitoring of the treatment response and prediction of the prognosis.**

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*LETTER TO THE EDITOR*

# GLP-1, A POWERFUL PHYSIOLOGICAL INCRETIN: AN UPDATE

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**Food intake, especially carbohydrates, release incretin, which is an endocrine transmitter. Among the various endocrine modulators, Glucagon-like peptide 1 (GLP-1) is more effective in stimulating the release of insulin and more powerful regulator of physiological functions. Mainly (GLP-1) receptors are expressed in lungs, α and β cells of pancreatic islets and the nervous system. Peripheral tissues, gastrointestinal tract and extra pancreatic tissues i.e., vascular smooth muscle, kidney and heart, also contain high affinity receptors for GLP-1. The aim of this systematic review was to gather the available published evidence of the functions performed by GLP-1 through the activation of its receptor in various organs. This review suggest that GLP-1 receptor signaling helps prevent beta cell apoptosis and conserve function and morphology of human islet. The effect of GLP-1 signaling in weight loss in diabetic patients was proved by previous studies. The long term use of GLP-1 receptor agonists reduces cardiovascular and renal complications in diabetic patients. Significant evidence was found in previous literature for its effect on pancreatic secretions. The secretions of many enzymes and hormones, such as trypsin, lipase and glucagon, inhibited significantly while the increase in levels of insulin and somatostatin was reported in many studies. GLP-1 has a prominent role in cardiac functioning and increases the heart rate considerably. Based on the vast impact of GLP-1 on physiological functions, many GLP-1 receptor agonists can be made that can increase the healthy life span.**

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*LETTER TO THE EDITOR*

# EFFECT OF NERVE ROOT BLOCK GUIDED BY ULTRASOUND ON CERVICOGENIC PAIN AND ITS INFLUENCE ON IMMUNE FUNCTION

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**Cervicogenic pain is a common chronic disease that needs individualized treatment according to the place of pain. This study aimed to observe the effect of ultrasound-guided nerve root block in the treatment of cervicogenic pain and its influence on immune function. A total of 30 patients (group A) with cervical discogenic pain (CDP) were treated by selective cervical nerve root block and 30 patients (group B) with CDP were treated with cervical spinal block under the X-ray C-arm guidance. The two groups of patients were examined with regard to the analgesic effect by Numerical Rating Scale (NRS), and the changes in the preoperative and postoperative range of motion in the neck (ROM). In addition, weekly pain attacks and the duration of each attack were recorded. The content of $CD3^+$, $CD4^+$ and $CD8^+$ in the peripheral blood T lymphocyte subsets in the two groups was evaluated by flow cytometry. The levels of these subsets were compared 24 h before treatment, 24 h after treatment, 3 days (d) after treatment and 7 d after treatment. At the time periods of 24 h, 3 d, and 7 d after treatment, the NRS of the two groups decreased significantly compared with before treatment ($P<0.01$). The changes of the ROM, the number of weekly pain attacks, the duration of each pain attack, and the stiffness of the head and neck were significantly lower in the two groups compared with those prior to the treatment ($P<0.05$). In group A and group B, the number of $CD3^+$, $CD4^+$ and $CD8^+$ T cells 24 h and 3 d after treatment increased significantly compared with that noted before treatment ($P<0.05$). Seven days after treatment, the levels of $CD3^+$, $CD4^+$ and $CD8^+$ T cells in the peripheral blood T lymphocytes of group A were significantly higher than those of group B ($P<0.05$). Selective cervical nerve root block under ultrasound is an effective method for the treatment of cervical discogenic pain. The effect is better than that of the X-ray C-arm-guided cervical block method. The mechanism of selective cervical nerve root block under ultrasound may be related to the regulation of the content of $CD3^+$, $CD4^+$, $CD8^+$ T cells in the peripheral blood T lymphocyte subsets and the enhancement of cellular immunity.**

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*LETTER TO THE EDITOR*

# PIG3 SUPPRESSES GASTRIC CANCER PROLIFERATION BY REGULATING p53-MEDIATED APOPTOSIS

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**Gastric cancer (GC), the third leading cause of cancer mortality and the fifth most common cancer in the world, still is an important health problem worldwide. P53-inducible gene 3 (PIG3) was initially isolated in an investigation to identify the genes that were induced by p53 in human colorectal cancer cells. PIG3 can also regulate the stability of p53 through suppressing the process of the MDM2-mediated ubiquitination of p53. The aim of this study is to explore the expression level of PIG3 in human GC and further investigate the function and mechanism of PIG3 in human GC. Five cell lines and 30 matched GC tissue samples and adjacent tissue samples were used for this study, and MTT assay, colony formation assay, flow cytometry analysis and Western blot were carried out. Expression of PIG3 was found to be frequently reduced in GC. Restoration of the expression of PIG3 inhibited cell proliferation, induced cell apoptosis and further activated P53 signaling in BGC823 cells. In conclusion, we demonstrated that expression of PIG3 is frequently reduced in GC tissue, and PIG3 suppressed human GC growth through p53-mediated apoptosis. PIG3 may act as a potential diagnostic marker and a potential therapeutic target of GC.**

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*LETTER TO THE EDITOR*

# PHYLOGENY AND COMPARATIVE MODELING OF PHYTOCHELATIN SYNTHASE FROM CHLORELLA SP. AS AN EFFICIENT BIOAGENT FOR DETOXIFICATION OF HEAVY METALS

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**Phytochelatins (PCs) found extensively in algae and plants are important for detoxification of heavy metals from soil and wastewater, and their synthesis is mediated by an enzyme phytochelatin synthase (PCS). In this study, a phylogram was generated to study evolutionary relationships of PCS from various organisms. It was revealed that PCS from green algae and plants are orthologs as both have evolved from a common ancestor. PCS from cyanobacteria appeared in two different clades showing that they have followed different lineages during evolution. Structural modeling was also carried out by building a 3D model of PCS from *Chlorella variabilis* using software Modeller v9.16. The predicted structure will be helpful for protein engineering strategies and to understand its interactions with other proteins. The biological biosorption capacity of *Chlorella vulgaris* (a green alga) was determined to remove Cd, Cu and Pb from industrial effluents. The biosorption of three heavy metals from industrial waste water was investigated under various conditions like pH, biomass concentration, contact time and temperature. Bio-removal of heavy metals was carried out by exposing culture of *C. vulgaris* to water samples of different heavy metal concentrations. The decrease in Cd, Cu and Pb quantities after 1 to 7 days of incubation period were 83%, 84% and 82.5%, respectively. In view of this, *Chlorella* spp. could be used on a large scale to detoxify heavy metals and clean up contaminated environments.**

0393-974X (2018)

Vol. 32, no. 5, 1199-1204 (2018)

*LETTER TO THE EDITOR*

# HIGH SENSITIVITY C-REACTIVE PROTEIN AS A CARDIOVASCULAR RISK MARKER IN INDEPENDENT COMMUNITY-LIVING ELDERLY PERSONS

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**An alarming fact is that increasing numbers of cardiovascular disease (CVD) events occur more often among elderly individuals without previous occurrence of CVD. There are numerous modifiable risk factors such as dyslipidemia,-and inflammatory markers, as well as cardiovascular events risk charts, in the identification and prevention of cardiovascular morbidity and mortality among elderly population. Thus, the aim of this study was to analyze some CVD risk factors as well as international CVD risk charts in independent community-living elderly persons in relation to their hs-CRP concentration in serum. Of 516 elderly Caucasians, 50 were non-smoking, with no positive history of chronic or acute diseases. The patients' clinical, biochemical and CVD risk charts were recorded. The CRP values were categorized according to the known cut-off points for stratification of cardiovascular risk: low risk patients with hs-CRP of <1 mg/L (low hs-CRP), moderate risk with hs-CRP of 1-3 mg/L (moderate hs-CRP) and high risk with hs-CRP of >3 mg/L (high hs-CRP). The groups did not differ in terms of age, anthropometric measures, fasting glucose, creatinine and uric acid concentration or analyzed CVD risk scales. The relationship between hs-CRP levels and both lipid profile and arterial blood pressure are linearly dependent ($p<0.02$). The negative correlation for the hs-CRP and fasting glucose and DIA were found in low hs-CRP ($r= -0.619$; $p<0.05$ and $r= -0.580$; $p<0.05$ respectively) and for the hs-CRP and uric acid ($r=-0.850$; $p<0.05$) in the moderate hs-CRP risk group. Thus, this study should greatly simplify decision-making for clinicians around the world.**

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*LETTER TO THE EDITOR*

# CHANGES IN ELECTROLYTES AND URIC ACID EXCRETION DURING AND AFTER A 100 KM RUN

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**Physical activity leads to changes in water and electrolyte homeostasis and to enhanced purine metabolism. The typical abnormalities observed after exercise are hyperkaliemia, hyper- or hyponatremia and hyperuricemia. The possible explanations of hyperuricemia are: increased metabolism and decreased elimination of uric acid. Changes in uric acid excretion are commonly observed in disturbances of sodium and water homeostasis. The aim of this study was to evaluate changes in electrolytes and uric acid excretion during a very long period of exercise. Twenty subjects with a mean age of 40.75±7.15 years took part in a 100 km run. The route of the run was based on the university stadium track. All subjects were experienced amateur runners, with a mean time of regular running of 6.11±7.19 years. Blood was collected before the start, after every 25 km and 12 hours after the run. The levels of electrolytes, creatinine, uric acid, cortisol, aldosterone, creatine kinase, C-reactive protein and interleukin-6 were measured. Creatinine clearance, urinary potassium-to-sodium ratio, fractional excretion of electrolytes and uric acid were calculated. Seventeen runners completed the study. Significant increases in sodium (from 141.65±1.90 to 144.29±3.65mmol/l), potassium (from 4.53±0.34 to 5.03±0.42mmol/l), creatinine (from 0.88±0.11 to 1.10±0.20mg/dl) and uric acid (from 5.15±0.87 to 5.94±1.50 mg/dl) were observed after 100 km ($p < 0.05$). Other significant changes during the study were noted in fractional excretions of sodium (from 0.86±0.29 to 0.33±0.13%) and potassium (from 6.66±2.79 to 18.90±10.01%), probably reflecting the decrease in renal blood flow (RBF) and increase in renal tubule reabsorption. The fractional excretion of uric acid slightly increased but without statistical significance from 5.34±1.51 to 6.09±2.34%. The results of our study showed that during very long but not very intensive exercise there is no change in uric acid excretion, although at the same time profound changes in electrolyte excretion are found. Both hyperuricemia and hyperuricosuria may be harmful, therefore it seems logical that the best way to avoid those abnormalities is to maintain fractional uric acid excretion.**

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*LETTER TO THE EDITOR*

# TUMOR POTENTIAL IN RAT WOUNDS AFTER SHORT- AND LONG-TERM ADMINISTRATION OF PLATELET-RICH PLASMA: AN UPDATE

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**Comment on: Omar NN, et al. Tumor potential in rat wounds after short- and long-term administration of platelet-rich plasma. J Biol Regul Homeost Agents. 2017 Oct-Dec;31(4):889-899. Platelet-Rich Plasma (PRP) is a promising concentrate. But are there any disadvantages or contraindications regarding its application? Is the use of PRP indicated in wounds of patients undergoing resection for cancer. The presence of growth factors could promote tumor proliferation and recurrence. It is of the utmost importance to recognize any possible contraindication before we call it safe. The role of PRP in tumorigenicity deserves further experimental investigation and large-scale prospective randomized clinical trials.**

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*LETTER TO THE EDITOR*

# ARTEMISININ AMELIORATES THE SYMPTOMS OF EXPERIMENTAL AUTOIMMUNE MYASTHENIA GRAVIS BY REGULATING THE BALANCE OF Th1 CELLS, Th17 CELLS AND TREG CELLS

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**Myasthenia gravis (MG) is an autoimmune disease characterized by fatigue and muscle weakness. Artemisinin and its derivatives were reported to be experimentally used to treat autoimmune diseases, such as systemic lupus erythematosus (SLE) and experimental allergic encephalomyelitis (EAE). Here, we tested the effects of artemisinin on experimental autoimmune myasthenia gravis (EAMG). Our data confirmed that artemisinin markedly ameliorated the symptoms of EAMG rats. There was a decreased level of tumor necrosis factor-α (TNF-α) and IL-17+ cells in mononuclear cells (MNCs), and an increased level of transforming growth factor-β1 (TGF-β1) and Treg cells in MNCs. These findings indicate that artemisinin may be a new choice for MG treatment.**

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*LETTER TO THE EDITOR*

# EFFECTS OF DIFFERENT DEGREES OF DEPRESSION ON INFLAMMATORY RESPONSE AND IMMUNE FUNCTION IN PATIENTS WITH OVARIAN CANCER

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**The aim of this study was to explore the effect of depression of different degrees on inflammatory response and immune function in patients with ovarian cancer. One hundred and eight cases of ovarian cancer according to the Federation Internationale of Gynecologie and Obstetrigue (FIGO) stage II~III who visited the Gynecology Department of Affiliated HongQi Hospital of MuDanJiang Medical University between September 2015 and May 2017 were enrolled in the study. After being hospitalized, they were divided into two groups according to their Beck Depression Inventory (BDI) scores. The total score of BDI is 63, with 0~4 for the normal group (25 cases), 5~13 for the mild depression group (24 cases), 14~20 for the moderate depression group (28 cases), and 21~63 for the severe depression group (31 cases). The immune function, inflammatory reaction, tumor markers [CA125, human epididymis protein-4 (HE4), insulin-like growth factor-I (IGF-I)], platelet technology and D-dimer index were compared between the four groups. The results showed that there were different levels of depression in patients with ovarian cancer in II~III stage, and the degree of depression could stimulate the level of serum-6, and TNF -α in serum increased. The proportion of $CD3^+$, $CD4^+$ and NK cells in patients with severe depression decreased, and their immunity also decreased. Depression increased the levels of CA125, HE4 and IGF-I in serum and ascites of ovarian cancer patients, and increased the risk of tumor progression and recurrence. Hypercoagulability existed in patients with ovarian cancer, and tumor associated depression could increase platelet count in plasma and increase D-dimer level. To sum up, depression can affect the level of micro inflammation in patients with ovarian cancer. In particular, depression can reduce cellular immune responses, affect the progression free survival of ovarian cancer patients, and reduce their overall survival rate.**

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*LETTER TO THE EDITOR*

# RELATIONSHIP BETWEEN SLEEP DISORDERS AND LYMPHOCYTE SUBSETS AND CYTOKINES IN PATIENTS WITH LUNG CANCER

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**This study aimed to investigate the relationship between sleep disorders and lymphocyte subsets and cytokines in patients with lung cancer undergoing radiotherapy, and to establish a theoretical foundation for predicting sleep disorders and preventing interventions in radiotherapy in lung cancer patients. Ninety-two patients with lung cancer requiring radiotherapy were selected as the study subjects. The patients' demographic data and disease-related conditions were investigated. Their quality of sleep was measured before radiotherapy, after two and four weeks of radiotherapy, and at the end of radiotherapy. According to the Pittsburgh Sleep Quality Index Number Table (PSQI), patients with PSQI score> 7 points were put into a sleep disorder group, and patients with PSQI score 0-7 were put into a normal sleep group. Lymphocyte subsets were enumerated and cytokine levels (IL-6, IL-1β) were measured during these four periods. The difference in sleep disorders at four weeks between patients with or without synchronous chemotherapy was statistically significant (P<0.05). The levels of lymphocyte subsets in the sleep disorder group and the control sleep group showed no difference in the index of lymphocyte subsets before radiotherapy. In the sleep disorder group, $CD4^+$ cells were lower after two weeks of radiotherapy (P<0.05). After four weeks of radiotherapy, $CD3^+$, $CD4^+$, and $CD16^+56^+$ subsets were lower (P<0.05). At the end of radiotherapy, there was no difference in each index. There was no significant difference in IL-6 levels between the two groups before radiotherapy, after two weeks, or after four weeks (P>0.05). At the end of radiotherapy, IL-6 levels in the sleep disorder group were higher than those in the control sleep group (P<0.05). There was no significant difference in IL-1β between the two groups (P>0.05). In conclusion, monitoring of T-lymphocyte subsets and IL-6 levels in patients is enhanced during radiotherapy. Clinically effective programs of radiotherapy for lung cancer improve the body's immune status.**

0393-974X (2018)

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# TREATMENT MECHANISM OF TOLEROGENIC DENDRITIC CELLS ON RHEUMATOID ARTHRITIS

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**This study aims to explore the possible mechanism of treatment of collagen-induced rheumatoid arthritis (RA) by tolerogenic dendritic cells (tDCs). Different methods were used to induce and cultivate tDCs, and suitable conditions for tDC cultivation were explored. The experimental RA induced by collagen in mouse was treated by the obtained tDCs, and the possible mechanism was explored. The serum concentration of TNF-α, IFN-β, IL-4 and anti-type II collagen antibody were detected by ELISA. The anti-type II collagen antibody of mice without treatment was higher than that without disease onset, while the Blank-DC group, VIP-DC group and Bay-D had no statistically significant differences (*P*>0.05). Compared to the group without disease onset, the TNF-α level of those without treatment was significantly higher, while INF-γ, IL-1β and IL-4 concentration showed no significant difference (*P*>0.05). Compared to the untreated group, the TNF-α and IL-1β concentration after VIP-DC treatment were significantly decreased, while IL-4 was increased (*P*<0.05). In summary, VIP-DC and Bay-DC alleviate joint inflammation, synovitis and bone erosion by reducing the production of anti-type II collagen antibody, inhibiting proinflammatory factors and increasing inflammation inhibitors**

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*LETTER TO THE EDITOR*

# VITAMIN D RECEPTOR GENE POLYMORPHISMS AND PROSTATE CANCER

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**Prostate cancer (PC) is the most common cancer among men worldwide and its pathogenesis is complex. The development of PC depends on family and environmental factors. Vitamin D can** be **associated with both of these factors. Its reduced serum concentration has been reported in a number of tumors. However, in the case of PC, the study results are conflicting. Polymorphism of VDR gene may also be involved in the development of this cancer. The aim of the study was to compare the frequency of selected polymorphisms in patients with PC and in men without this disease. Seventy-two Caucasian males aged 35-75 years with histologically proven PC (T1/T2) were enrolled in the study group. Seventy-two random age-matched Caucasian out-patient subjects formed the control group. VDR (*FokI, BsmI and TaqI*) gene polymorphism (rs2228570, rs1544410, rs731236) was determined by TaqMan® SNP Genotyping. The Hardy-Weinberg Equilibrium (HWE) - p> 0.05 was in all studied polymorphisms. Deviations from the HWE were not found. There were no differences between the study group and the control group. No difference was found when the groups were compared in terms of age or the Gleason score.**

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*LETTER TO THE EDITOR*

# DECREASED SERUM LEVELS OF INTERLEUKIN-35 AMONG MULTIPLE SCLEROSIS PATIENTS MAY BE RELATED TO DISEASE PROGRESSION

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**The regulatory role of interleukin (IL) -35 in the immunopathogenesis of multiple sclerosis (MS) is suggested in very few studies. We aimed to measure serum levels of IL-35 among clinically isolated syndrome (CIS) and relapsing-remitting MS (RRMS) patients and evaluate the associations between this cytokine and the disease clinical course. This cross-sectional study was conducted during 2017 in a referral university clinic. Forty patients and 40 healthy controls were included in the study. The level of IL-35 in the serum of all subjects was determined by ELISA. Serum level of IL-35 was reduced (p = 0.003) in RRMS in comparison with healthy controls. Moreover, the mean serum level of IL-35 among new cases (diagnosed within the 6 months prior to the study) decreased compared to healthy controls but it was not statistically significant (P=0.059). The mean serum level of IL-35 was significantly higher in new cases compared with other cases (p=0.048). Overall, we found decreased serum level of IL-35 among RRMS patients compared to the healthy controls. Our finding provides a view of the possible role of IL-35 in MS pathogenesis and the potential therapeutic targets.**

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*LETTER TO THE EDITOR*

# ASSOCIATION BETWEEN 5,10-METHYLENETETRAHYDROFOLATE, GENE POLYMORPHISM AND CONGENITAL HEART DISEASE

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**This article is to investigate the association between C677T polymorphism of 5, 10-methylenetetrahydrofolate (MTHFR) gene and congenital heart defects (CHD). Two hundred thirty-five nuclear families (father, mother and child) with CHD were enrolled in the study (experimental group), and two hundred thirty-five healthy nuclear families were selected as a control group. Under the case-control study, the C677T polymorphism of MTHFR gene was detected with polymerase chain reaction-restriction fragment length polymorphism and DNA sequencing. The distribution of genotype frequency in the CHD group and control group were analyzed. SPSS 13.0 software was used to analyze the data. The distribution of genotype frequency at C677T polymorphism site was significantly different between the CHD group (including ventricular septal defect, atrial septal defect, tetralogy of fallot, double outlet right ventricle, patent ductus arteriosus) (child and mother) and healthy control group (child and mother). There were no differences between CHD group-fathers and healthy control group-fathers. Analyses of the MTHFR genotypes of CHD nuclear family data with transmitted disequilibrium test (TDT) and haplotype-based haplotype relative risk statistical method both revealed significant indications that the parents transmitted more T allele of MTHFR to their CHD children. TT genotype of MTHFR gene is associated with CHD, and a mother or a child with T allele has a much higher risk of CHD.**

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Vol. 32, no. 5, 1261-1265 (2018)

*LETTER TO THE EDITOR*

# INFLUENCE OF CIRCADIAN RHYTHM ON EXHALED BREATH PROFILING BY ELECTRONIC NOSE

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**Electronic noses (e-noses) are a cheap and easy method for exhaled Volatile Organic Compound (VOC)-analysis which has shown its potential in several diseases. Before obtaining a full validation of these instruments in clinical settings, a number of methodological issues still have to be established. We aimed to investigate a potential influence of circadian variation on VOC-profile analyzed by an e-nose in healthy subjects. We enrolled 22 adults free of any known diseases. A sequence of exhaled breath samplings were performed on all participants at predetermined hours (7am, 12pm, 17pm, 23pm) and analyzed by an e-nose (Cyranose 320). According to Principal Component Analysis, significant circadian variations of the exhaled VOC-profile were shown for Principal Component (PC) 1 and 3. In detail, PC1 and PC3 values were significantly higher in the morning compared to the afternoon and evening (for all parameters $p<0.05$). Successive Linear Discriminant analysis confirmed the findings above. The daily variations in VOCs-profile, with the peak in the morning, could be relevant for future clinical applications, especially in the choice of optimal time for sampling patients.**

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*LETTER TO THE EDITOR*

# INTERNAL NASAL DILATATOR (NAS-AIR®) IN PATIENTS WHO SNORE

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**Snoring is a very common human habit, and for this reason it is considered more a social nuisance that a disease symptom. The nasal valve area has the minimal cross-sectional area of the upper airways. A problem at this level may easily induce impaired breathing and consequently snoring, therefore nasal dilation might significantly improve this complaint. Nas-Air® is a new internal nasal dilator which was tested on 41 outpatients who snore. Snoring duration, assessed by smartphone, visual analogue scale for the perception of sleep quality were measured before and during Nas-Air® use. A significant reduction of snoring time and an improvement of sleep quality were achieved during Nas-Air® wearing. In conclusion, the present study demonstrates that Nas-Air® is an internal nasal dilator able to reduce snoring time and improve sleep quality.**

0393-974X (2018)

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*LETTER TO THE EDITOR*

# UPDATES IN REGENERATIVE MEDICINE APPLIED TO DENTAL SCIENCES

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**Mesenchymal stem cells (MSCs) are found in high concentrations in several tissues, such as umbilical cord, adipose tissue and dental tissue. Dental stem cells reside in many areas of the oral cavity. Thanks to their abilities, dental stem cells could be used to treat diseases and to understand the basic mechanisms of developmental pathologies. There are currently numerous ongoing clinical trials evaluating a broad spectrum of conditions and situations using different stem cell populations. However, stem cell studies are raising profound ethical questions that weigh on the world of scientific research. Stem cells are always a hot topic in the scientific community. Their use is related also to their banking, as cell manipulation is also often related to medical and ethical issues. Many biomedical studies aim to treat diseases that were previously considered incurable with MSCs. All this has created the need to quickly and safely storage stem cells, usually in a stem cell biobank (SCB). Regenerative medicine is the most important approach for achieving complete tissue regeneration using stem cells isolated from adult tissues, embryonic stem cells, but also through the application of induced pluripotent stem cells (iPSC). iPSCs are non-pluripotent cells that are engineered to acquire the ability to differentiate into all different types of cells. In conclusion, the daily use of stem cells in regenerative procedures is still far from being safe and predictable, especially because of the biomedical component, often requiring experienced biologists and complex technologies for cell manipulation and cell banking.**

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*LETTER TO THE EDITOR*

# REMODELING THE NECK AND THE LOWER JAW WITH DEHOXYCHOLATE INJECTIONS

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**Nonsurgical cosmetic facial procedures have gained popularity in recent decades. These procedures are commonly referred to as facial rejuvenation, and only a few are performed in the neck region. Herein, the authors describe their experience with off-label use of deoxycholic acid (DC) injections on 18 patients for remodeling of the neck and lower jaw. The injection protocol was personalized for each patient, and lidocaine was always premixed with the DC. After the initial injection visit, at least 3 months passed before further injections were considered. All documented side effects, including swelling and dysesthesia, resolved spontaneously. All patients received follow-up for at least 3 months, and only 2 patients required a second session of injections. By personalizing the injection protocol for each patient, good outcomes were achieved, including aesthetic enhancement of the shape and contour of the jaw and neck. Although the study is limited by the relatively small sample size, the results are promising and warrant additional investigations.**

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Vol. 32, no. 5, 1285-1290 (2018)

*LETTER TO THE EDITOR*

# ANATOMICAL VARIATIONS OF THE MEDIAN NERVE AND OF THE VASCULAR-NERVOUS STRUCTURES AT THE WRIST

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**Three cases of anatomical variation of the median nerve at the wrist found during our surgical activity led us to take the opportunity to expose anatomical variations by reviewing already published reviews. Consequently, on the basis of anatomical studies, clinical reports and imaging, as a result of careful examination of the published literature, it has been observed that the interventions in such anatomical area must take into account these variations. In particular, the most performed procedure is the lysis of the transverse carpal ligament (TCL), which is not free from complications. In our opinion it is therefore necessary, in order to avoid the complications of the nervous, vascular and tendinous sections, to use some specific technical procedures.**

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*LETTER TO THE EDITOR*

# 3D SOFTWARE SCANNING, PROCESSING AND ARCHIVING PALATAL RUGAE: "IDENTITY BASE" TECHNOLOGY

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**The palatal rugae, which are anatomically described as folds or wrinkles of the palate, are located on the anterior third of the palate on each side of the palatal raphe and behind the incisive papilla, The use of palatal rugae for personal identification was suggested several years ago, and attracted interest from different researchers which created different classifications, still used in scientific literature. The "identity base" (IB) system has as its object a complex information system and a personal identification protocol by means of three-dimensional palatal scans in digital format. The usefulness of this system is based on the management needs of big data. For example, in the field of forensic odontology, IB can be useful in the identification of a living or cadaver subject; and can estimate the age of a human subject. Moreover, IB stores its associated biometric data. The IB system demonstrated to overcome the issues shown by other similar systems of digital image storage. Furthermore, its high accuracy in the identification process makes IB a reliable tool for institutions in the management of immigrants, as well as in the archiving of people under restrictive measures. Finally, IB is also a system for sharing and processing clinical images, useful in dental prosthetics to reduce the number of steps from the first visit to dental prosthesis. The next generation of big-data archiving will speak the same language as IB: the route has been already set out.**

0393-974X (2018)

Vol. 32, no. 5, 1295-1301 (2018)

*LETTER TO THE EDITOR*

# AUGMENTATION OF THE ATROPHIC MAXILLARY SINUS FLOOR: GRAFT STIFFNESS, IMPLANT SHAPE AND LENGTH

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**This study investigates the characteristics of load transmission to bone of alternative treatments for posterior maxilla edentulism with relatively limited available bone volume. Implant shape (conical and cylindrical), augmentation technique and the effect of bone-graft stiffness were taken into consideration. The finite element models of the atrophic sinus implanted with short implant were compared to two grafted-sinus models implanted with longer implants, engaged bicortically. Bone-graft stiffness was varied to describe different stages of graft-maturation (from short-term to long-term). Stress and load distributions due to axial and bending loads were compared on the bony structures. In the short-term, axial force is supported almost equally by the cortical layers and the trabecular core, while a bending load is mainly supported by the crestal cortical layer and secondarily by the cortical floor, the bone-graft supported a negligible load. Bicortical engagement produces higher load transfer to the cortical floor under axial load. In the long-term, as the stiffness of the bone-graft increases, the load is transferred progressively towards the grafted region, progressively unloading other structures, particularly the internal cortical layer.**

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*LETTER TO THE EDITOR*

# INTRA-ARTICULAR HYALURONIC ACID INJECTIONS FOR HIP OSTEOARTHRITIS

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**Although viscosupplementation has been used in the past few years both for knee and hip osteoarthritis (OA), the number of intra-articular injections and the interval between doses still remains an undetermined subject. The aim of this open retrospective study was to evaluate the clinical and functional outcome in patients with mild-moderate hip OA treated with a course of 1, 2 or 3 Hyaluronic Acid (HA) intra-articular injections. Ninety-six patients were included: 19 patients received only one injection, 24 received two injections, and 44 received three injections. Age, sex, VAS for pain and WOMAC score before each intra-articular injection, number of intra-articular injections, reasons for interrupting the treatment, adverse events, time between HA injections, and number of patients who had a total hip replacement were retrieved from the medical records of each patient. VAS and WOMAC scores were obtained from all patients also at a mean follow-up of 7 months after the last hip injection. All patients who received 1, 2 or 3 hip injections improved in VAS and WOMAC score. Three intra-articular injections provided a better outcome in terms of pain reduction compared to 1 or 2 injections. Intrarticular injections for mild-moderate hip OA were demonstrated to be effective in reducing pain and improving function. A full course of three injections provided the best result in pain control.**

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

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*LETTER TO THE EDITOR*

# "GUIDELINES FOR THE PREVENTION AND CONTROL OF LEGIONNAIRE'S DISEASE IN ITALY": GUIDELINES OR GUIDANCE?

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**The creation of guidelines is a methodologically complex activity that requires technical expertise, resources and time. Methods of guideline production must meet at least these three criteria: multidisciplinarity, systematic review, and ranked recommendations. In May 2015, the new "Guidelines for the prevention and control of Legionnaire's disease" were published on the website of the Italian Ministry of Health in order to "gather, update and integrate in a single document all the previous national recommendations published". The critical review of the document has led us to conclude that this document does not comply with these three criteria, and we emphasize that guidelines should make decision-making easier, considering the various scientific approaches to a health problem and choosing the one considered most effective. Therefore, the persons responsible for the development of guidelines should strive to widely adopt and use current standards for the development of guidelines as a means to improve patient care and health outcomes.**

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*LETTER TO THE EDITOR*

# MEDITERRANEAN DIET AND PHYSICAL ACTIVITY IMPROVE POSTURE, FAT MASS AND SALIVARY pH

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**Many researchers have revealed that diet and physical activity influence metabolic function and posture in various stages of life. This paper aims to combine them and demonstrate how they could promote a healthy lifestyle. For this purpose, 14 healthy subjects followed a three-month protocol combining physical activity with dietary advice. At the end of the protocol, the results of the study underlined a significant reduction in fat mass, an improvement in salivary pH, and a realignment and rebalancing of body segments.**

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*LETTER TO THE EDITOR*

# MICROBIOLOGICAL RESULTS OF IMPROVEMENT IN PERIODONTAL CONDITION BY ADMINISTRATION OF ORAL PROBIOTICS

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All Authors contributed equally to this study

**Oral bacteria that degrade sulphur-containing amino acids (cysteine, cystine, and methionine) produce volatile sulphur compounds (VSCs = hydrogen sulphide, methyl mercaptan, and dimethyl sulphide) highly correlated with halitosis. When these bacteria are given the right environment, i.e. periodontal disease, cariogenic biofilm or food source they can grow in number very quickly and will start to convert proteins to VSC that, together with volatile fatty acids are largely responsible for oral malodor. Recently, the prevention of dental caries and periodontal diseases using various probiotics has been attempted. The purpose of this study was to investigate the effects of probiotics based on *in vitro* analysis, such as antibacterial activity, and to evaluate the neutralizing effect of probiotics on halitosis, the levels of VSCs were measured by gas chromatography.**

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*LETTER TO THE EDITOR*

# CLINICAL RESULTS OF IMPROVEMENT IN PERIODONTAL CONDITION BY ADMINISTRATION OF ORAL PROBIOTICS

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**Dental plaque-related diseases (cavities, gingivitis, periodontitis and halitosis) have been traditionally controlled by mechanical non-specific removal of plaque. However, many novel treatment approaches aim to inhibit the growth of pathogenic bacteria or to remove their toxins. Probiotics are viable microorganisms which, when administered in adequate amounts, provide a health benefit to the host. Recently, probiotics have been applied as new tools for the improvement of dental health. They have been used to substitute existing antibiotic treatments due to increased resistant bacteria. Probiotics not only have antibacterial activity, but they also have inhibitory effects on the reappearance of oral pathogenic bacteria. The aim of this study was to assess the clinical effect of the administration of probiotics agents in the treatment of mild to moderate periodontitis.**

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*LETTER TO THE EDITOR*

# SUPERFICIAL INFILTRATION TO TREAT WHITE HYPOMINERALIZED DEFECTS OF ENAMEL: CLINICAL TRIAL WITH 12-MONTH FOLLOW-UP

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**Hypomineralization represents one of the most common defects in tooth crowns. Thanks to a wide understanding of aesthetics, patients request a treatment to resolve these defects. Different techniques are available, such as crowns/veneers, traditional restorative treatments, microabrasion, whitening, remineralizing agents and infiltration technique. The objective of this trial is to assess the effectiveness of superficial infiltration with Icon (DMG, Hamburg, Germany) on the attenuation of crown hypomineralized lesions of various etiological origins with a 12-month follow-up. Seventeen patients with white defects of enamel in the aesthetic sector were selected. The infiltration procedure was carried out following the manufacturer's instructions. Intraoral photographs were taken before and directly after treatment in order to document the immediate change in colour. Check-ups were performed 1 and 12 months later. All the defects which were treated showed a degree of attenuation. The teeth affected by molar incisor hypomineralization (MIH) showed partial attenuation in 8 cases, and only in one case the defect disappeared. Regarding the post-trauma cases, 6 were partially attenuated and 2 disappeared. The post orthodontic defects disappeared in 6 cases and were attenuated in 5. All incipient caries defects were completely hidden. Four out of 6 cases of fluorosis disappeared. Diagnosis plays a key role in guiding the dental clinical selection of treatment. While it has always been possible to achieve a high level of attenuation in cases of fluorosis and lesions of caries origin, cases of MIH should probably be treated using more invasive techniques. Post-trauma lesions should be infiltrated with caution, and only after having informed the patient of the possible ineffective outcome.**

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*LETTER TO THE EDITOR*

# USE OF A SHORT-TERM WHOLE BLOOD INTRACELLULAR STAINING ASSAY TO STUDY THE T-CELL RESPONSE IN RESPIRATORY SYNCYTIAL VIRUS-INFECTED PEDIATRIC PATIENTS

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**The aim of the present study was the development of a reliable method to evaluate the pattern of the ongoing T-cell response in young infants affected by respiratory infection. To this purpose, we enrolled 44 infants hospitalized with a diagnosis of respiratory syncytial virus bronchiolitis. After a short-term stimulation of whole blood samples, intracellular IFN-γ and IL-4 cytokines were measured in $CD4^+$ and $CD8^+$ T-cell subsets by flow cytometry. A stringent staining and gating strategy was used in order to maximize the reduction of background noise and to exclude false positives. The frequencies of cytokine-producing T-cell subsets, albeit low, were easily quantifiable. Cytokine responses were higher in infants sampled > 7 days from the onset of symptoms. The use of a rigorous strategy for cell staining and gating, coupled with a short-term stimulation of whole blood and a careful evaluation of time elapsed from the onset of symptoms constitutes a convincing approach for future clinical studies.**

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