

**JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS**

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**JOURNAL OF BIOLOGICAL REGULATORS & HOMEOSTATIC AGENTS**

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**ABSTRACTS**

**1. Interrelationship between vitamins and cytokines in immunity**

M.L. Castellani, Y.B. Shaik-Dasthagirisah1, D. Tripodi2, A. Anogeianaki3, P. Felaco4, E. Toniato1, M.A. De Lutiis4, M. Fulcheri5, S. Tetè2, R. Galzio6, V. Salini7, A. Caraffa8,

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Cytokines are important proteins that modulate immunity and inflammation. Vitamins are also involved in immunity and inflammation. They are found to restore the ability of some cells to produce certain cytokines. Vitamin deficiency appears to affect the mechanism of immune cells, though the impact of reduced cytokine response in vitamin malnutrition is not clear. Vitamin D is involved in many medical conditions, such as infections and inflammation, and mediates innate immunity. Deficiency of vitamin D increases the risk of infectious and inflammatory diseases. In addition, this vitamin modulates Treg function and IL-10 production which is important for therapeutic treatment. Vitamin A increases inflammatory response and is involved in tissue damage; moreover, vitamin A is a key modulator of TGFbeta which can suppress several cytokines. Vitamin E, an anti-ageing compound, is associated with a defect of naive T cells and may inhibit some inflammatory compounds such as prostaglandin generation. *J Biol Reg Homeost Ag 2010; 24:385-390.*

## **2. Subjective assessment of palatability, digestibility and emotions in healthy volunteers after ingestion of an iced dessert: preliminary report**

M. Garzaro, L. Raimondo, J. Nadalin, G. Pecorari and C. Giordano

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Dietary habits can be influenced by several factors such as emotional status and food palatability represented by food smell, taste, texture, appearance and temperature. The aim of this study is to assess the palatability and digestibility of a coffee-flavored iced dessert

ingested at the end of a standardized meal and its impact on emotional status in a sample of 30 healthy female volunteers. Thirty healthy female volunteers, after ENT and psychological assessment, were asked to fill in a Psycho-Emotional Questionnaire to assess their basal emotional pattern before the consumption of an iced coffee-flavored dessert after a standard meal. After the meal they filled in an Organoleptic-Sensory questionnaire, a Dynamic Digeribility questionnaire and again a Psycho-Emotional Questionnaire. In our study, most of the subjects found the tested coffee-flavoured iced dessert pleasant according to the Organoleptic-Sensorial Questionnaire (OSQ), in terms of taste, aspect, texture and smell; moreover, in 29 subjects the Dynamic Digestibility Questionnaire (DDQ) resulted in a good digestive experience. By means of the Psycho-Emotional Questionnaire (PEQ), an improvement of feelings and mood, associated with good data of digestibility and palatability was recorded. Although this observation is not statistically significant, the results seem to show a positive correlation between pleasure in eating such a product and emotional status. These data are preliminary and need further investigations on a larger population, in order to confirm this association, also in a mixed population, comparing male and female eating behaviour. *J Biol Reg Homeost Ag 2010; 24:391-395.*

### **3. Ghrelin but not obestatin regulates insulin secretion from INS1 beta cell line via UCP2-dependent mechanism**

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The mitochondrial UCP2 mediates glucose-stimulated insulin secretion by decreasing intracellular ATP/ADP ratio. Insulin secretion is a tightly regulated process. Ghrelin, as well as obestatin, were intensively studied to determine their ability to modify insulin secretion. Ghrelin is considered to be an inhibitor of insulin release from pancreatic islets, however little is known about the effects of obestatin. In our study we demonstrate the stimulating effects of both peptides on insulin secretion in INS1 cells. Furthermore, we investigate the potential role of UCP2 in mediating the effects of both peptides on insulin secretion. UCP2 mRNA expression was down-regulated by ghrelin in the presence of 26.4 mM glucose, however it was unchanged after obestatin treatment. Our results confirm that UCP2 could be involved in the stimulating effect of ghrelin on insulin release from INS1 cells. *J Biol Reg Homeost Ag 2010; 24:397-402.*

#### **4. Montelukast reduces eosinophilic inflammation by inhibiting both epithelial cell cytokine secretion (GM-CSF, IL-6, IL-8) and eosinophil survival**

J. Mullol<sup>1,2,4</sup>, F.B. Callejas<sup>1,4</sup>, E. Méndez-Arancibia<sup>1,4</sup>, M. Fuentes<sup>1,4</sup>, I. Alobid<sup>2,4</sup>, A. Martínez-Antón<sup>1,4</sup>, A. Valero<sup>3,4</sup>, C. Picado<sup>3,4</sup> and J. Roca-Ferrer<sup>1,4</sup>

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Leukotriene receptor antagonists, such as montelukast (MK), are currently used to treat rhinitis and asthma, but their anti-inflammatory role in eosinophil inflammation is not well understood. The aim of this study is to investigate the effect of MK on an in vitro model of upper-airway eosinophil inflammation by reducing pro-inflammatory cytokines from both nasal mucosa (NM) and polyp (NP) epithelial cells and reducing eosinophil survival primed by epithelial cell secretions. Epithelial cells were stimulated with fetal bovine serum (FBS) with/without MK for 24 hours, and cytokine concentrations in epithelial secretions were measured by ELISA. After incubating peripheral blood eosinophils with epithelial cell-conditioned media (ECM) with/without MK up to 3 days, eosinophil survival was assessed by Trypan blue dye exclusion. Results are expressed as mean  $\pm$  SEM of cytokine concentration (% of control) or eosinophil survival (%). Epithelial cell stimulation increased GM-CSF, IL-6, IL-8, and sICAM-1 secretion in both NM and NP. MK had a significant inhibitory effect on FBS-induced GM-CSF, IL-6, and IL-8 secretion, but not sICAM-1, in both NM and NP. MK also showed an inhibitory effect ( $p < 0.05$ ) on ECM-induced eosinophil survival from both NM (from  $10^{-5}M$  to  $10^{-7}M$ ,  $n=7$ ) and NP (at  $10^{-5}M$ ,  $n=7$ ), after 3 days of incubation. These anti-inflammatory effects on epithelial cell cytokine secretion and on eosinophil survival suggest that montelukast may contribute to the reduction of eosinophilic inflammation in upper-airway inflammatory diseases such as rhinitis and nasal polyposis. *J Biol Reg Homeost Ag 2010; 24:403-411.*

#### **5. Androgen- and insulin-related gene signature using a specific low density oligoarray androchip 2 in peripheral blood mononuclear cells in agonists, recreational athletes and sedentary subjects**

D. Minella<sup>1</sup>, M. Biancolella<sup>1,§</sup>, B. Testa<sup>1</sup>, G. Prosperini<sup>2</sup>, R. Zenobi<sup>3</sup>, G. Novelli<sup>1,4,5</sup> and M.G. Giganti<sup>3</sup>

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The early detection of genomic biomarkers (e.g. RNAs) through analysis of circulating blood cells could have a substantial impact on biomedicine, particularly in monitoring clinical trials, drug toxicity and doping in athletes. To achieve this goal, it is essential to develop methods that are sufficiently sensitive to detect biomarker alterations during normal biologic processes, pathogenic processes, and/or in response to therapeutic or other intervention. Using a low density microarray (AndroChip 2) we detected a transcriptional profiling signature of 190 genes related to androgen and insulin metabolism pathway, in peripheral blood mononuclear cell (PBMC) in subjects with different intensities of sports activities. We demonstrated that androgen and insulin gene transcriptional levels are independent to sports activity and therefore potentially suitable for drug monitoring and/or drug doping (such as anabolic androgen steroid AAS abuse) and or gene doping. *J Biol Reg Homeost Ag* 2010; 24:413-423.

## **6. Neuropeptide expression in the airways of COPD patients and smokers with normal lung function**

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Neurogenic mechanisms seem to play a role in the pathogenesis of chronic obstructive pulmonary disease (COPD), as suggested by a number of *in vitro* data. However, few studies have investigated the presence of neuropeptides in the airways of patients with COPD, and they have yielded conflicting results. The aim of this study is to compare the expression of the neuropeptide substance P (SP), vasoactive intestinal peptide (VIP), and neuropeptide Y (NPY) in the airways of smokers with and without COPD. Surgical lung samples were obtained from 15 smokers with COPD and 16 smokers with normal lung function, who underwent lobectomy for a solitary lung carcinoma. Airway expression and distribution of SP, VIP, and NPY were identified by immunohistochemistry and analyzed by a

computerized image analysis system. Compared to smokers with normal lung function, COPD patients exhibited an increased immunoreactivity for SP and VIP, paralleled by a decreased NPY expression in the epithelium and glands, and a decreased expression of all these three neuropeptides in the smooth muscle layer. Therefore, in the present study we have documented a different expression and distribution of the neuropeptides SP, VIP, and NPY in the airways of smokers with and without COPD. These findings suggest a possible involvement of such neuropeptides in the pathogenesis of some changes occurring in COPD. *J Biol Reg Homeost Ag* 2010; 24:425-432.

## **7. Hypothalamus-hypophysis-thyroid axis function in healthy aging**

G. Mazzoccoli, V. Pazienza<sup>1</sup>, A. Piepoli<sup>1</sup>, L.A. Muscarella<sup>1</sup>, M. Inglese, A. De Cata, F. Giuliani<sup>2</sup> and R. Tarquini<sup>3</sup>

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There is an increased frequency of dysthyroidism in elderly people. We investigated whether there are differences among healthy young-middle-aged and elderly people in the 24-hour secretory profiles of TRH, TSH and free thyroxine. The study was carried out on fifteen healthy young-middle-aged subjects (range 36-55 years, mean age $\pm$ s.e. 44.1 $\pm$ 1.7) and fifteen healthy elderly subjects (range 67-79 years, mean age $\pm$ s.e. 68.5 $\pm$ 1.2). TRH, TSH and free thyroxine serum levels were measured in blood samples collected every four hours for 24 hours. The area under the curve (AUC), the mean of 06:00h–10:00h–14:00h and the mean of 18:00h–22:00h–02:00h hormone serum levels and the presence of circadian rhythmicity were evaluated. A normal circadian rhythmicity was recognizable for TRH and TSH in young–middle-aged subjects and for TSH in elderly subjects. Elderly subjects presented lower TSH levels, whereas there was no statistically significant difference in TRH and free thyroxine serum levels between young–middle-aged and elderly subjects. Aging is associated with an altered TSH secretion. *J Biol Reg Homeost Ag* 2010; 24:433-439.

## **8. Resveratrol inhibits isoprostane production in young and aged rat brain**

A. Chiavaroli, L. Brunetti, G. Orlando, L. Recinella, C. Ferrante, S. Leone, P. Di Michele, C. Di Nisio and M. Vacca

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Resveratrol (3,5,4'-trihydroxystilbene), a viniferin polyphenolic compound, has been shown to have neuroprotective effects and we tested its possible antioxidant activity in young and aged rat brain, evaluating, in vitro, synaptosomal 8-iso-prostaglandin F<sub>2</sub>α (8-iso-PGF<sub>2</sub>α) production as a marker of oxidative stress. We found that in young rat brain synaptosomes resveratrol perfusion had no effect on basal 8-iso-PGF<sub>2</sub>α production, but quenched to basal levels the increased 8-iso-PGF<sub>2</sub>α production induced by hydrogen peroxide. On the other hand, in aged rats, resveratrol was able to decrease 8-iso-PGF<sub>2</sub>α production both basally and after hydrogen peroxide-induced oxidative stimulus. In conclusion, our findings show that the antioxidant effects of resveratrol in rat brain could play a neuroprotective role in aging, when the increased burden of oxidative stress is faced by defective antioxidant mechanisms. *J Biol Reg Homeost Ag 2010; 24:441-446.*

### **9. Carotenoids and asymptomatic carotid atherosclerosis**

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High plasma concentrations of lycopene and β-carotene have been associated with reduced prevalence of cardiovascular disease. The aim of this study is to compare plasma concentrations of these carotenoids in subjects with or without ultrasonic evidence of asymptomatic carotid atherosclerosis. One hundred and sixty-five subjects underwent physical examination and ultrasonic measurement of common carotid artery intima-media thickness. Analysis of variance and logistic regression methods were used to determine whether differences existed between participants with or without ultrasonic evidence of asymptomatic carotid atherosclerosis. Of the 165 participants, 80 exhibited evidence of carotid atherosclerosis (carotid intima-media thickness > 0.8 mm), while 85 did not (carotid intima-media thickness ≤ 0.8 mm), while 85 did not (carotid intima-media thickness < 0.8 mm). Participants with ultrasonic evidence of carotid atherosclerosis exhibited significantly greater body mass index, significantly higher serum concentrations of total cholesterol, LDL-associated cholesterol and triglycerides, and significantly higher plasma concentrations of uric acid, C-reactive protein and fibrinogen. In contrast, participants with ultrasonic evidence of carotid atherosclerosis exhibited significantly lower plasma concentrations of lycopene and β-carotene. These results suggest that lycopene and β-carotene may play important roles in delaying the development of the early asymptomatic



stage of carotid atherosclerosis. Encouraging adequate intakes of antioxidant carotenoids may provide an important public health service. *J Biol Reg Homeost Ag* 2010; 24:447-452.

## **10. Treatment of lesions of the rotator cuff**

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The impingement syndrome and tendinopathy of the rotator cuff are the most common causes (complaints) of pain and disability of the shoulder. The aim of this study is to evaluate the efficacy of a specific rehabilitative protocol, integrated with the administration of a nutritional supplement, in the conservative rehabilitative treatment as well as in post-surgery, of patients with lesions of the rotator cuff. Two groups with syndrome of the rotator cuff were formed to follow different therapeutic courses, in relation to the choice of each subject to undergo the conservative treatment (Arm A) or the surgical one (Arm B). In Arm A the study included the association of therapy with ESWT (shock waves) with the proprioceptive Multi Joint System, for rehabilitating joint movement and muscle strength of the shoulder, and a specific nutritional supplement to reduce the pain and conserve the cartilage tissue. Between February 2009 and June 2009, we enrolled 30 subjects (randomized into three homogenous groups A1, A2, A3), average age  $45 \pm 10$  years, with rotator cuff syndrome with calcification of the shoulder, diagnosed through clinical examination and investigative instruments (X-ray, echography or NMR). In Arm B, from September 2009 to January 2010, we enrolled 50 patients (randomized into two groups, B1 and B2), 24 male (average age 58.4: min 28 and max 78) and 26 females (average age 59.5: min 30 and max 80), who had undergone rotator cuff operations and acromionplasty for non-massive lesions without important gleno-humeral instability, with either open or arthroscopic procedures. The analysis of the results of Arm A highlights that in terms of reducing pain the main benefits were found in Group A1 where the supplement was given. From the analysis of the data of Arm B, in both groups an improvement of the first 4 items evaluated was evident. In Group B1, 84% of the patients declared to be satisfied and improved and 16% were dissatisfied; in Group B2, where the nutritional supplement was given, 92% were satisfied and 8% were dissatisfied. In conclusion, we retain that in cases of rotator cuff syndrome, an integrated rehabilitative approach, whether conservative or post-surgical, directed at taking total control of the patient, must observe particular attention to the optimization of the articular tissular metabolic balance in order to favour better functional recovery. *J Biol Reg Homeost Ag* 2010; 24:453-459.

## **11. Deliberate self-harm in substance-dependent patients and relationship with alexithymia and personality disorders: A case-control study**

M.C. Verrocchio, C. Conti and M. Fulcheri.

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The aim of this study is to evaluate differences in the prevalence of deliberate self-harm (DSH), alexithymia, and clinical personality patterns and syndromes between treatment-seeking substance-dependents and a comparison group, and to investigate the relationship of DSH with alexithymia, and personality disorders. One hundred and fifty-four subjects participated in the study (77 substance-dependent inpatients and 77 comparison group). DSM-IV diagnoses of substance dependence were made by the clinicians of the Addiction Services following assessment that included clinical observation. Participants were evaluated by the Deliberate Self Harm Inventory, Toronto Alexithymia Scale, and Millon Clinical Multiaxial Inventory. An Identifying Information Form was used to collect demographic information (e.g. age, educational history, marital status, and employment status). Only to the clinical sample information was added on: types of substance used, age at first substance use, age at regular substance use, and previous treatment attempts. Significant group differences were found for all measures (DSH, TAS-20, MCMI-III). Among substance-dependent patients there was a significant difference between groups with and without DSH in terms of previous treatment attempts, Hypomania and Borderline personality disorder. DSH were significantly correlated with difficulty in identifying feelings in all cases in both the comparison group and in the personality disorders group, and with difficulty describing feelings in the personality disorders group. Personality disorder and drug dependency were predictors for DSH. This study suggests that treatment of substance-dependents should involve screening for deliberate self-harm behavior, difficulty identifying and describing feelings, and personality disorders. Probably, when these problems are detected, specific psychological intervention should be integrated to usual treatment for substance-dependent patients. *J Biol Reg Homeost Ag* 2010; 24:461-469.

## 12. Modulation of NF- $\kappa$ B signalling pathways by parasites

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NF- $\kappa$ B is implicated in lymphocyte development, maturation, proliferation and survival. This inducible transcription factor is widely expressed by virtually all cell types. In mammals, the genes *rela*, *relb*, *crel*, *nfkB1*, and *nfkB2* encode the five NF- $\kappa$ B protein family members RelA (p65), RelB, c-Rel, p50, and p52, respectively, which form homo- and heterodimeric DNA-binding complexes capable of regulating target gene transcription of specific biological responses differentially. NF- $\kappa$ B regulates the expression of a wide variety of genes that play critical roles in innate and adaptive immune responses, is strongly linked to the inhibition of apoptosis, and contributes to tumor growth, metastasis, and chemoresistance. Parasites have targeted several parts of the NF- $\kappa$ B pathway, allowing them to interfere with the

transcription of immune response genes. The biology of different parasites is critical in influencing the patterns and kinetics of NF-kB activity and thereby the development of subsequent immune responses. *J Biol Reg Homeost Ag* 2010; 24:471-479.

### **13. An infant with diaphragmatic eventration and respiratory distress**

A.M. Zicari, G. Tancredi, A. Rugiano, D. Zappalà, F. Midulla, L. Indinnimeo, G. De Castro, C. Celani and M. Duse

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The authors report a rare case of partial diaphragmatic eventration in a 4-month-old infant with recurrent wheezing and low serum IgA values. Because of persistent respiratory symptoms after therapy with inhaled short-acting beta2 agonists and inhaled nebulized corticosteroids, surgery was undertaken to correct the defect. Despite surgery, the clinical symptoms did not improve. Consequently, gastroesophageal reflux was considered and the diagnosis was confirmed with pH-metry, after which the infant was started on a protonic pump inhibitor therapy (PPI), achieving clinical improvement. Our experience suggests that in infants with congenital diaphragmatic eventration who present with respiratory distress gastro-oesophageal reflux should be suspected, and PPI therapy should be started before planning surgery. *J Biol Reg Homeost Ag* 2010; 24:481-484.

### **14. Interrelationship between psychology and cytokines**

C.M. Conti and M. Fulcheri

*Clinical Psychology, Psychology Faculty, University of Chieti-Pescara, Italy*

Leukocytes and other types of cells produce proteins or glycoproteins, termed cytokines, that serve as chemical communicators from one cell to another. Neuromediators are able to modulate functions of immune cells and other cells and the relationship between the central nervous system (CNS) and the endocrine system have been known for many years. Communication between nerves and immune and inflammatory cells plays a major role in the modulation of several dysfunctions including ion transport, mucosal permeability and cytokine production. Cytokines are involved in both injury and repair, and the conditions underlying these distinct outcomes are under intense investigation and debate. Evidence from medical studies implicates the immune system in a number of psychiatric disorders with known or suspected developmental origins, including schizophrenia, anxiety/depression, and cognitive dysfunction. *J Biol Reg Homeost Ag* 2010; 24:485-490.

