

EDITORIAL

**NONLINEAR QUANTUM PHENOMENA AND BIOPHYSICAL ASPECTS OF
COMPLEXITY RELATED TO HEALTH AND DISEASE**L. BRIZHIK^{1,2} and A. FOLETTI^{3,4}

¹Department of Nonlinear Condensed Matter Physics, Bogolyubov Institute for Theoretical Physics, Kyiv, Ukraine; ²Wessex Institute of Technology, Ashurst, Southampton, UK; ³Department of Innovative Technologies, University of Applied Sciences of Southern Switzerland-SUPSI, Switzerland; ⁴Institute of Translational Pharmacology, CNR, Rome, Italy

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In this paper we discuss living systems as a non-linear self-interacting phenomenon, stabilized by the non-linear interaction between matter and self-created electromagnetic field. Such electromagnetic field can arise, in particular, as the radiation from electrosolitons which mediate the charge transport along macromolecules in metabolic redox processes. The non-linear nature of solitons results in an effective mechanism and leads to the synchronization of redox processes. It allows intra- and inter-cellular communication and long-range coherence in the system. One peculiar property of solitons is the resonant effect of external weak stimuli on their dynamics, which can explain the mechanism of low-intensity (non-thermal) electromagnetic therapies. We also discuss the stabilizing role of noise and spatial symmetry breaking in living organisms as open dissipative structures far from equilibrium, and health/disease states as the corresponding attractors of the system in the multi-parametric phase diagram. The essential role of electromagnetic potentials in self-regulation and self-healing processes is analyzed, based on the long-range matter-field interaction and fast information transfer, provided by the electromagnetic potentials.

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**DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF
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CENTRAL PRECOCIOUS PUBERTY: FROM PHYSIOPATHOLOGICAL MECHANISMS TO TREATMENT

V. CHIRICO¹, A. LACQUANITI^{2,3}, V. SALPIETRO¹, M. BUEMI², C. SALPIETRO¹
and T. ARRIGO¹

¹*Department of Pediatric Sciences, University of Messina, Messina, Italy;* ²*Department of Internal Medicine, University of Messina, Messina, Italy;* ³*Department of Internal Medicine, Mediterranean Institute for Transplantation and Advanced Specialized Therapies, ISMETT, University of Pittsburgh Medical Center, Palermo, Italy*

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Puberty is a complex, coordinated biological process with multiple levels of regulations. The timing of puberty varies greatly in children and it is influenced by environmental, endocrine and genetic factors. Precocious puberty (PP) is an important issue, affecting between 1 in 5.000-10.000 children. The physiopathological mechanism is still unknown. From an etiological point of view, PP may be subdivided into gonadotropin-releasing hormone (GnRH) -dependent and independent causes. GnRH-dependent PP, often called central precocious puberty (CPP), is based on hypothalamic-pituitary-gonadal axis activation associated with progressive pubertal development, accelerated growth rate and advancement of skeletal age. Conversely, peripheral precocious puberty (PPP) is related to sex steroid exposure, independently of hypothalamic-pituitary-gonadal (HPG) axis activation. Kisspeptins play a central role in the modulation of GnRH secretion with peripheral factors that influence the timing of puberty, such as adipokines and endocrine disrupting chemicals. Moreover, PP could be related to genetic disorders, involving pivotal genes of the HPG axis. The standard test used to verify HPG activity is the gonadotropin response to administered GnRH analogs. We describe the physiopathological mechanisms of PP and its clinical implications, analysing diagnostic flow-chart and new potential biomarkers that could reveal PP. An update of the current literature was also carried out regarding the recent novelty for treatment.

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EDITORIAL

**RELATIONSHIP BETWEEN SEROTONIN AND MAST CELLS:
INHIBITORY EFFECT OF ANTI-SEROTONIN**

S.K. KRITAS¹, A. SAGGINI², G. CERULLI³, A. CARAFFA⁴, P. ANTINOLFI⁴,
A. PANTALONE⁵, M. ROSATI⁶, M. TEI³, A. SPEZIALI³, R. SAGGINI⁷ and P. CONTI⁸

¹Department of Microbiology and Infectious Diseases, School of Veterinary Medicine, Aristotle University of Thessaloniki, Macedonia, Greece; ²Department of Dermatology, University of Rome Tor Vergata, Rome, Italy; ³Nicola's Foundation, Onlus, Arezzo, Italy; ⁴Orthopedic Division, University of Perugia, Perugia, Italy; ⁵Orthopedic Division, University of Chieti-Pescara, Chieti, Italy; ⁶Gynecology Clinic, Pescara Hospital, Pescara, Italy; ⁷Department of Neurosciences and Imaging, Faculty of Medicine and Surgery, G. d'Annunzio University Chieti-Pescara, Chieti, Italy; ⁸Immunology Division, Medical School, University of Chieti-Pescara, Chieti, Italy

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Serotonin (5-HT) is an important neurotransmitter that acts in both central and peripheral nervous system, and has an impact on cell proliferation, migration and apoptosis. 5HT exerts its effects via several receptors. Treatment with anti-5-HT receptors diminish the severity of contact allergy in experimental animals, an effect mediated by mast cells; while an agonist reduces the stress level and relieves pruritus in patients with atopic dermatitis. Mast cells are important for both innate and adaptive immunity and they are activated by cross-linking of FcεRI molecules, which are involved in the binding of multivalent antigens to the attached IgE molecules, resulting in a variety of responses including the immediate release of potent inflammatory mediators. Serotonin is present in murine mucosal mast cells and some authors reported that human mast cells may also contain serotonin, especially in subjects with mastocytosis. Here we report the interrelationship between mast cells, serotonin and its receptor inhibitor.

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COLLAGEN IMPLANTS IN EXPERIMENTAL TENDON INJURY IN RABBITS: A CLINICAL, ULTRA-STRUCTURAL AND BIOMECHANICAL INVESTIGATION

A. MOSHIRI¹, A. ORYAN², A. MEIMANDIPARIZI¹ and N. MAFFULLI^{3,4}

¹Division of Surgery and Radiology, Department of Clinical Sciences, School of Veterinary Medicine, Shiraz University, Shiraz, Iran; ²Department of Pathology, School of Veterinary Medicine, Shiraz University, Shiraz, Iran; ³Centre for Sport and Exercise Medicine, Barts and the London School of Medicine and Dentistry, University of London, Queen Mary, United Kingdom; ⁴Department of Musculoskeletal Medicine and Surgery, University of Salerno School of Medicine and Surgery, Salerno, Italy

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This study investigated the effects of hybridized micro and nano structured collagen implants on tendon healing in an experimental tendon injury in rabbits. Fifty mature male New Zealand white rabbits were randomly divided into two groups of treated and control. Two cm of the left Achilles tendon were discarded. In the treated group, a 3-dimensional (3D) collagen implant was engineered and implanted in the defect area. No implant was used in the control group. At day 120 after injury, the Achilles tendon of the animals were ultrasonographically (days 0-120 after injury) and radiographically (day 120 after injury) examined, and the animals were euthanized. The tendons were dissected and used for gross pathological, histopathological, ultra-structural and biomechanical investigations. Application of the collagen implant significantly increased the diameter of the newly regenerated tissue in the defect area compared to the control tendons. Treatment also significantly increased the echogenicity and homogeneity of the injured area, the diameter of the collagen fibrils and fibers, maturity of the tenoblasts, number of tenocytes, collagen density, alignment, ultimate and yield load, stiffness, stress and modulus of elasticity. The collagen implants were almost totally absorbed 120 days after surgery. No inflammatory reaction or tissue degeneration or necrosis was evident in the treated tendons compared to the control ones. 3D collagen implants produced a newly regenerated tendinous tissue at the defect area that was morphologically and biomechanically superior to the control group. This collagen implant was biocompatible and biodegradable with high bio-safety in rabbits.

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

SERUM GLYCOPEPTIDOLIPID CORE IgA ANTIBODY LEVELS IN PATIENTS WITH CHEST COMPUTED TOMOGRAPHY FEATURES OF *MYCOBACTERIUM AVIUM-INTRACELLULARE* COMPLEX PULMONARY DISEASE

Y. SHIMIZU^{1,4}, A. TAKISE¹, H. MORITA², Y. HOSOMI³, N. KASAHARA¹,
T. KAWATA¹, T. HORIE¹, Y. ISHII⁴ and M. YAMADA⁵

¹Department of Respiratory Medicine, ²Department of Diagnostic Radiology, ³Department of Laboratory Medicine, Maebashi Red Cross Hospital, Maebashi, Gunma Japan; ⁴Department of Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University School of Medicine, Mibu, Tochigi, Japan; ⁵Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Gunma, Japan

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Measurement of serum glycopeptidolipid core IgA antibody (GPL antibody) was recently reported to show a high sensitivity and specificity for diagnosing *Mycobacterium avium-intracellulare* complex (MAC) pulmonary disease (MAC-PD), but its clinical value has not been confirmed. This study aims to evaluate the seropositive rate in patients with suspected MAC-PD based on chest computed tomography (CT), and to examine whether GPL antibody reflects the extent of lung involvement on CT or the number of bacteria in sputum, retrospectively. Among 66 patients with suspected MAC-PD on CT, 36 patients were negative for MAC by culture and 30 were positive. Sputum grades of MAC were evaluated by fluorochrome microscopy of sputum smears. The lungs were divided into six regions to assess the extent of disease. Serum levels of GPL antibody were measured with an enzyme immunoassay (cut-off value >0.7 U/ml). The GPL antibody positive rate was 19.4% among patients who were negative for MAC by culture versus 73.3% among culture-positive patients. The serum level of GPL antibody was significantly correlated with the sputum smear grade ($r=0.43$, $p<0.05$) and was also correlated with the number of lung regions showing MAC-PD features on CT ($r=0.43$, $p<0.05$). Some MAC-PD patients may have CT features of MAC with positive level of GPL antibody, although the diagnosis cannot be confirmed by culture. GPL antibody levels reflect the pulmonary burden of MAC, as assessed from the sputum smear grade and number of involved regions on chest CT.

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DYNAMIC CHANGES IN DNA METHYLATION STATUS IN PERIPHERAL BLOOD MONONUCLEAR CELLS FOLLOWING AN ACUTE BOUT OF EXERCISE: POTENTIAL IMPACT OF EXERCISE-INDUCED ELEVATIONS IN INTERLEUKIN-6 CONCENTRATION

P.J. ROBSON-ANSLEY^{1,2}, A. SAINI³, C. TOMS¹, L. ANSLEY¹, I.H. WALSHE⁴,
M.A. NIMMO⁵ and J.A. CURTIN⁶

¹*Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, UK;*

²*Department of Physiological Sciences, Stellenbosch University, South Africa;* ³*Department of Physiology and Pharmacology, Karolinska Institutet, Sweden;* ⁴*School of Sport, University of Stirling, Stirling, UK;* ⁵*School of Sport, Exercise and Health, Loughborough, UK;* ⁶*The University of Manchester, Manchester Academic Health Science Centre, University Hospital of South Manchester NHS Foundation Trust, Manchester, UK*

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The aim of the present study was to examine the relationship between interleukin (IL)-6 concentrations and DNA methylation in the peripheral blood mononuclear cells (PBMCs) of trained runners after a bout of prolonged, strenuous exercise. Eight healthy trained males completed a treadmill run at 60% $v\dot{V}O_{2max}$ for 120 min followed by a 5-km time trial in a fasted condition. Whole blood samples were taken prior to, immediately before and 24 h following exercise. From these samples, PBMCs were isolated for analysis and plasma IL-6 concentrations were measured. The methylation status of DNA extracted from PBMCs was analysed using the Illumina 27k methylation beadchip platform. Global DNA methylation status was unaltered immediately and up to 24 hours following a bout of prolonged exercise in comparison to pre-exercise. Despite no change in global DNA methylation, plasma IL-6 concentrations were significantly related to the DNA methylation status of 11 genes. Our study demonstrates that the methylome is stable, while discovering a novel link between exercise-induced increases in circulating IL-6 and the DNA methylation status of 11 individual genes. Based on our preliminary findings, the mechanisms by which changes in plasma IL-6 concentrations and DNA methylation in response to exercise interact require further study.

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ASSOCIATION BETWEEN THE EXPRESSION OF LHR, FSHR AND CYP19 GENES, CELLULAR DISTRIBUTION OF ENCODED PROTEINS AND PROLIFERATION OF PORCINE GRANULOSA CELLS IN REAL-TIME

B. KEMPISTY^{1,2}, A. ZIÓŁKOWSKA¹, S. CIESIÓŁKA¹, H. PIOTROWSKA³,
P. ANTOSIK⁴, D. BUKOWSKA⁴, M. NOWICKI¹, K.P. BRÜSSOW⁵ and M. ZABEL⁶

¹Department of Histology and Embryology, Poznań University of Medical Sciences, Poznań, Poland; ²Department of Anatomy, Poznań University of Medical Sciences, Poznań, Poland;

³Department of Toxicology, Poznań University of Medical Sciences, Poznań, Poland;

⁴Department of Veterinary, Poznań University of Life Sciences, Poznań, Poland;

⁵Institute of Reproductive Biology, Leibniz Institute for Farm Animal Biology, Dummerstorf, Germany; ⁶Department of Histology and Embryology, Wrocław Medical University, Poland

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The process of granulosa cell luteinization is part of the main process determining growth, differentiation and proliferation of these cells. Although the mechanisms underlying the regulation of luteinizing hormone receptor (LHR), follicle stimulating hormone receptor (FSHR) and cytochrome P450 aromatase expression in mammalian granulosa cells is well understood, still little is known about the expression of mRNA and encoded proteins in relation to cell proliferation and luteinization *in vitro*. Porcine granulosa cells were observed *in vitro* at a 168-h period while undergoing real-time proliferation using an RTCA system. Furthermore, LHR, FSHR and CYP19 mRNA expression were detected using RQ-PCR after 168 h of *in vitro* culture (IVC) at 24-h intervals, and LHR, FSHR and P450arom were examined by confocal microscopic observation at 0 h, 24 h, 48 h, 96 h, and 168 h of IVC. We found increased expression of LHR and CYP19 mRNA at 24 h and 48 h of IVC compared to the other stages ($P < 0.01$, $P < 0.001$), whereas FSHR mRNA was higher only at 0 h ($P < 0.001$). In contrast, LHR, FSHR and P450arom protein expression was significantly higher at the end of the 168-h IVC period compared to 0 h, 24 h, 48 h and 96 h ($P < 0.001$). LHR, FSHR and P450arom were distributed in the cytoplasm of porcine GCs at each time point of IVC. When analyzing cell proliferation, differences in cell index were observed (at least $P < 0.05$) between the first (0-24 h) and the last period (144-168 h) of IVC; however, soon after 24 h of IVC a logarithmic increase in proliferation was also seen. We assume that the expression of LHR, FSHR and CYP19 mRNAs depends on the period of *in vitro* cultivation and may be linked with the luteinization process of porcine GCs. Furthermore, the patterns of mRNA and protein expression suggest a post-transcriptional regulation of LHR, FSHR and P450arom. In summary, it can be presumed that mRNA and protein expression and *in vitro* luteinization and proliferation of porcine GCs are regulated by different mechanisms, because not all of these processes are correlated.

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GASTROINTESTINAL SYMPTOMS IN IDIOPATHIC PULMONARY FIBROSIS PATIENTS TREATED WITH PIRFENIDONE AND HERBAL MEDICINE

Y. SHIMIZU^{1,2}, Y. SHIMOYAMA³, A. KAWADA³, M. KUSANO⁴, Y. HOSOMI⁵,
M. SEKIGUCHI⁵, T. KAWATA¹, T. HORIE¹, Y. ISHII², M. YAMADA³, K. DOBASHI⁶
and A. TAKISE¹

¹*Department of Respiratory Medicine, Maebashi Red Cross Hospital, Maebashi, Gunma, Japan;*

²*Department of Pulmonary Medicine and Clinical Immunology, Dokkyo Medical University School of Medicine, Mibu, Tochigi, Japan;* ³*Department of Medicine and Molecular Science, Gunma University Graduate School of Medicine, Maebashi, Gunma, Japan;* ⁴*Department of Endoscopy and Endoscopic Surgery, Gunma University Hospital Gastroenterology, Maebashi, Gunma, Japan;*

⁵*Clinical laboratory Center, Maebashi Red Cross Hospital, Maebashi, Gunma, Japan;* ⁶*Gunma University School of Health Sciences, Maebashi, Gunma, Japan*

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Pirfenidone is an antifibrotic agent for patients with pulmonary fibrosis, but this drug has adverse gastrointestinal (GI) effects. The first aim of this study was to assess GI symptoms due to pirfenidone by using a new questionnaire for reflux symptoms and dysmotility symptoms. Whether adding herbal medicine of rikkunshi-to improved GI symptoms due to pirfenidone therapy was also investigated. This was a randomized controlled trial performed on 17 IPF patients. The patients were assigned to two groups, and the study period was 8 weeks. The pirfenidone group received pirfenidone therapy for 8 weeks with add-on rikkunshi-to from 4 weeks, while the control group did not receive either of these agents. To assess the effects of RK, plasma levels of acyl-ghrelin and des-acyl-ghrelin, serum KL-6 and surfactant protein-D, and pulmonary function tests were monitored. GI symptoms were most severe during the initial 2 wks of pirfenidone therapy at a dose of 600 mg/day. Both reflux symptoms and dysmotility symptoms deteriorated. Rikkunshi-to improved GI symptoms to the level prior to pirfenidone therapy. Plasma levels of des-acyl-ghrelin and acyl-/des-acyl-ghrelin ratio changed significantly at 8 weeks compared to 2 weeks. GI adverse events due to PFD were most severe in the first 2 weeks of treatment at a dose of 600 mg/day, and both reflux and dysmotility symptoms deteriorated, but the drug was well tolerated at 1200 mg/day. Rikkunshi-to contributed to improvement of GI symptoms, but plasma ghrelin levels did not reflect the improvement of GI symptoms.

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FREQUENCY OF BACTERIA CAUSING URINARY TRACT INFECTIONS AND THEIR ANTIMICROBIAL RESISTANCE PATTERNS AMONG PEDIATRIC PATIENTS IN WESTERN IRAN FROM 2007-2009

M. YASEMI¹, H. PEYMAN¹, K. ASADOLLAHI², A. FEIZI¹, S. SOROUSH^{3,4},
A. HEMATIAN⁴, F.A. JALILIAN^{3,4}, M. EMANEINI⁵, M.Y. ALIKHANI⁶ and M. TAHERIKALANI^{3,4}

¹Student Research Committee, Ilam University of Medical Sciences Ilam, Iran; ²Department of Clinical Epidemiology, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran;

³Clinical Microbiology Research Center, Ilam University of Medical Sciences, Ilam, Iran;

⁴Department of Medical Microbiology, School of Medicine, Ilam University of Medical Sciences Ilam, Iran; ⁵Department of Microbiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran; ⁶Department of Microbiology, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

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Urinary Tract infections (UTIs) are among the most common infections in infants and neonates. The aim of the current study was to evaluate the frequency of bacteria causing UTI and their relevant drug resistance patterns among infants and neonates hospitalized in Ilam province, Western Iran during 2007-2009. A total of 220 cases of UTI were enrolled in this cross-sectional retrospective study. A standard checklist was used for demographic and clinical data to be collected from their health records. Data was then analysed using SPSS version 16.0. More than two-thirds (64.8%) of the cases were female. *E. coli* (44.5%), *Klebsiella spp.*, (18.6%), *Enterobacter spp.*, (15%) and *Staphylococcus spp.* (12.7%) were the most common microorganisms isolated from UTIs, respectively. High rates of resistance to tetracycline, ampicillin, and nalidixic acid were observed among these isolates. Similar to other studies, *E. coli* was the most common bacteria causing UTI and showed a high rate of resistance against most of the antimicrobial agents. Determining the antimicrobial sensitivity can be helpful for physicians in choosing an appropriate treatment for patients suffering from UTI, and also to reduce the complications related to serious UTI.

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CHLAMYDOPHILA PNEUMONIA AND INCREASED *TLR4* GENE EXPRESSION IN LEUKOCYTES ARE ASSOCIATED WITH ACUTE MYOCARDIAL INFARCTION

L.G. LIMA-NETO^{1,2}, R.D.C. HIRATA¹, A.D. LUCHESSI¹, V.N. SILBIGER¹,
D. CAVICHIOLI¹, E.S. DOS SANTOS³, A.G.M. SOUSA³, S.R.S. SPROVIERI⁴,
E.B. DE SOUSA-JUNIOR⁴, F.C.P. DOS SANTOS⁵, S. COLOMBO⁵
and M.H. HIRATA¹

¹*School of Pharmaceutical Sciences, University of Sao Paulo, Sao Paulo, Brazil;*

²*Laboratory of Immunology, CEUMA University, Sao Luis, Brazil;* ³*Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil;* ⁴*School of Medical Sciences, Santa Casa of Sao Paulo, Sao Paulo, Brazil;* ⁵*Institute Adolfo Lutz, Sao Paulo, Brazil*

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We investigated the relationship of the positivity for *Chlamydomphila pneumoniae* (*Cpn*) and *Mycoplasma pneumonia* (*Mpn*), inflammatory and metabolic markers, and mRNA expression and polymorphisms of the *TLR2*, *TLR4*, *IL-6* and *TNFA* genes with acute myocardial infarction (AMI). Two hundred and eighteen individuals (98 AMI and 120 non-AMI) were selected at two Clinical Centers. Blood samples were drawn to extract DNA and RNA and to measure laboratory variables including anti-*Cpn* IgM and IgG. *Cpn* and *Mpn* genomic DNA as well as *TLR2*, *TLR4*, *IL-6* and *TNFA* mRNA expression were evaluated by quantitative real-time PCR (qPCR). Gene polymorphisms were detected by PCR-HRM. AMI patients had higher positivity for *Cpn*-DNA (17.3%) than non-AMI group (6.7%, $p=0.018$). In addition, *Cpn*-DNA positivity was an independent predictor of risk for AMI (OR: 2.56, CI: 1.08 - 6.04, $p=0.031$). Positivity for anti-*Cpn* IgG and *Mpn*-DNA was similar between AMI and non-AMI ($p>0.05$). *TLR4* mRNA expression was higher in AMI than non-AMI individuals ($p=0.005$). *CD14* -260C>T, *TNFA* -308A>G, *TLR2* c.2258G>A, *TLR4* c.896A>G and *TLR4* c.1196C>T variants were not associated with increased risk for AMI ($p>0.05$). In the AMI group, individuals carrying *CD14* -260CC genotype had higher hsCRP levels than CT/TT carriers ($p=0.041$). These results are suggestive that *Cpn*-DNA positivity and increased *TLR4* mRNA expression in blood leukocytes may be associated with AMI and could be useful markers to evaluate the severity and progression of the atherosclerotic disease in AMI patients.

ALLERGY-RELATED CHANGES IN LEVELS OF CD8⁺CD25⁺FOXP3^{bright} TREG CELLS AND FOXP3 mRNA EXPRESSION IN PERIPHERAL BLOOD: THE ROLE OF IL-10 OR TGF- β

M. EUSEBIO¹, P. KUNA², L. KRASZULA¹, M. KUPCZYK²
and M. PIETRUCZUK¹

¹*Department of Laboratory Diagnostics, Medical University of Lodz, Poland;* ²*Department of Internal Medicine, Medical University of Lodz, Poland*

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There is an increasing body of evidence that alterations of regulatory T (T_{reg}) cell numbers and functions lead to immune disorders. Accordingly, understanding the regulatory mechanisms that maintain peripheral regulatory T (T_{reg}) cell homeostasis is key to the development of effective targeted biologic therapies. We previously demonstrated the effects of IL-10 or TGF- β on distinct CD8⁺CD28⁻ T cell subsets *in vitro*. Allergy-related changes of CD8⁺CD25⁺FoxP3^{bright} T_{reg} cells and FoxP3 mRNA expression in peripheral blood were assessed by means of multicolor flow cytometry and real-time polymerase chain reaction (RT-PCR). Co-stimulation of CD8⁺CD25⁺ T cells with anti-CD3/CD28 in the presence of either IL-10 or TGF- β increased the frequency of CD8⁺CD25⁺FoxP3^{bright} T_{reg} cells in patients with asthma and controls. Likewise, CD8⁺CD25⁺ T cell activation with anti-CD3/CD28 and TGF- β increased FoxP3 mRNA expression in all groups. Anti-CD3/CD28 and IL-10 appeared to regulate FoxP3 mRNA expression in a phenotype-dependent manner. Specifically, co-stimulation by anti-CD3/CD28 and IL-10 markedly increased FoxP3 mRNA expression in the severe asthma group whereas it had opposite effects on this value in other groups. Taken altogether, these data suggest that IL-10 and TGF- β may modulate FoxP3 expressions at the protein and mRNA levels in respect to their need for peripheral tolerance.

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

ASSESSMENT OF BIOPHYSICAL THERAPY IN THE MANAGEMENT OF PAIN IN CURRENT MEDICAL PRACTICE COMPARED WITH IBUPROFEN AND PLACEBO: A PILOT STUDY

A. FOLETTI^{1,2}, P. BARON^{2,3}, E. SCLAUZERO^{2,3}, G. BUCCI^{2,3}, A. RINAUDO^{2,3}
and R. ROCCO^{2,3}

¹*Institute of Translational Pharmacology, CNR, Rome, Italy;* ²*Clinical Biophysics International Research Group, Lugano, Switzerland;* ³*General Practitioner, Regione Friuli Venezia Giulia, Italy*

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Pain management is a daily part of current medical practice. The aim of this pilot study was to assess the efficacy of a biophysical procedure (Med Select 729) compared to a usual pain killer drug (Ibuprofen), and to placebo in order to disclose some effective procedures to be employed especially in elderly people with multiple comorbidities, in patients with allergy to chemical drugs or previous side effects, in non-responders to usual medications, and in chronic diseases to reduce overload. A total of 66 patients were divided in 3 groups. After one week of biophysical therapy they showed similar effect to ibuprofen and after one month the statistical significance was achieved with $p < 0.02$ in comparison to placebo. We conclude that biophysical therapy was shown to be an effective and safe procedure for the management of pain in current medical practice.

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LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS: ROLE OF HIGH RESOLUTION COMPUTED TOMOGRAPHY AND ITS RELATIONSHIP WITH OTHER PULMONARY AND CLINICO-SEROLOGICAL FEATURES

M. COLACI¹, M. SEBASTIANI¹, A. MANFREDI¹, D. GIUGGIOLI¹, G. CASSONE¹,
C.U. MANZINI¹, C. GHIZZONI¹, S. CERRI² and C. FERRI¹

¹*Rheumatology Unit, Department of Medical and Surgical Science for Adults and Children, University of Modena and Reggio Emilia, Modena;* ²*Center for Rare Lung Diseases, University of Modena and Reggio Emilia, Modena, Italy*

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The first two authors contributed equally to the manuscript

The study investigated the characteristic of interstitial lung disease in a large series of systemic sclerosis (SSc) patients by means of HRCT and the correlations between functional lung parameters, serological features and the extent of lung involvement evaluated by high-resolution computed tomography (HRCT). One hundred and seven SSc patients, consecutively investigated by means of HRCT, standard chest X-ray, and pulmonary function tests, were retrospectively evaluated. Chest radiogram and HRCT scores were strongly associated (Pearson's $r=0.82$, $p<.0001$); moreover, the first significantly correlated with spirometric parameters, even if weakly. Anti-Sc170 and anti-centromere antibodies were associated with higher ($p=0.01$) and lower HRCT score ($p=0.0002$), respectively. The extension of interstitial lung involvement in SSc evaluated with HRCT is directly proportional to functional lung parameters. HRCT, spirometry and DLco should be considered essential in the core-set of non-invasive diagnostic tools for the first-line assessment of scleroderma lung involvement.

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PHARMACOLOGICAL GSK-3 β INHIBITION IMPROVES OSTEOBLAST DIFFERENTIATION ON TITANIUM SURFACES

S. LUMETTI¹, S. FERRILLO², S. MAZZOTTA², G.M. MACALUSO¹,
M. BONANINI¹, G. PASSERI² and C. GALLI¹

¹*Department of Biomedical, Biotechnological, and Translational Sciences, University of Parma, Italy;* ²*Department of Clinical and Experimental Medicine, University of Parma, Italy*

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Rough titanium surfaces enhance the activation of Wnt canonical signaling, a pathway required for osteoblast differentiation. The present study investigated the effects of GSK3b-inhibitor (2'Z,3'E)-6-Bromoindirubin-3'-oxime (BIO) on osteoblastic differentiation on titanium surfaces with different topography and wettability. C2C12 cells were plated on pickled, acid-etched/sand-blasted (SLA), modified hydrophilic SLA titanium discs (modSLA) and stimulated with increasing doses of BIO. Activation of Wnt canonical signaling was measured with a reporter system. Gene expression was measured in the same cell system by Real Time PCR. Osteoblastic MC3T3 cells were then plated on discs with or without BIO and the expression of osteoblast specific genes was assessed by Real Time PCR. One mM BIO activated Wnt canonical signaling in C2C12 cells on all surfaces, and the highest effect was on rough surfaces. BIO markedly increased the expression of Osteoprotegerin and Osteocalcin in MC3T3 cells on rough surfaces at the concentration of 100 nM, and on all surfaces at the concentration of 1 mM. BIO enhances Wnt signaling activation and the expression of osteoblastic genes on rough surfaces and could be a viable approach to improve cell response to implant surfaces.

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CO₂ PNEUMOPERITONEUM INDUCES *IN VITRO* HYPOXIC RESPONSE CULMINATING IN APOPTOSIS OF HUMAN NEUROBLASTOMA CELLS

M. CURRÒ¹, A.S. MONTALTO², P. IMPELLIZZERI², E. MONTALTO²,
R. RISITANO¹, T. RUSSO², P. PERRONE², V. CHIRICO², T. ARRIGO²,
C. SALPIETRO², C. ROMEO² and R. IENTILE¹

¹*Department of Biomedical Sciences and Morphological and Functional Imaging, University of Messina, Italy;* ²*Department of Pediatric, Gynecological, Microbiological and Biomedical Sciences, University of Messina, Italy*

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The first two authors contributed equally to this study

The ablative role of minimally invasive surgery (MIS) in neuroblastoma (NB) is still controversial due to the possible CO₂ pneumoperitoneum side-effects on tumor aggressiveness. It is known that CO₂ produces hypoxic condition with changes in tumor microenvironment influencing cell functions. Here we investigated whether CO₂ exposure affects the transcription factor HIF-1 α and the apoptotic signalling pathway in SH-SY5Y NB cells. SH-SY5Y cells were exposed to a pressure of 15 mmHg CO₂ (100%) for 4 h (T₀) and then moved to normal condition for 24 h (T₂₄). In control and CO₂-exposed cells, we analyzed the mRNA levels and DNA binding activity of HIF-1 α . We also evaluated the proliferative activity and cell viability as well as caspase-9/3 cleavage and nuclear fragmentation. A significant increase in HIF-1 α activation was observed in SH-SY5Y cells exposed to CO₂ compared to control cells. CO₂ treatment also decreased the proliferation rate and the percentage of viable cells. In addition, the expression and cleavage of caspase-9 and -3 were significantly increased in NB cells exposed to CO₂. These data correlated with apoptotic feature observed in CO₂-treated NB cells. Our findings show that CO₂-induced hypoxic condition exerts cytotoxic effects on NB cells by eliciting mitochondrial apoptotic pathway and thereby improving the understanding of the possible clinical impact of CO₂ pneumoperitoneum on NB behavior.

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SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE EVALUATION: COMPARISON BETWEEN SEMIQUANTITATIVE AND QUANTITATIVE COMPUTED TOMOGRAPHY ASSESSMENTS

A. ARIANI¹, F. LUMETTI¹, M. SILVA², D. SANTILLI¹, F. MOZZANI¹,
G. LUCCHINI¹, G. DELSANTE¹ and N. SVERZELLATI²

¹*Department of Medicine, Internal Medicine and Rheumatology Unit, Azienda Ospedaliero-Universitaria di Parma, Parma, Italy;* ²*Department of Clinical Sciences, Section of Radiology, University of Parma, Parma, Italy*

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The pulmonary fibrosis extent in systemic sclerosis (SSc) has a prognostic value. Chest Computed Tomography (CT) is the gold standard to detect an interstitial lung disease (ILD). Semi-quantitative scores and quantitative methods can estimate the ILD. The first ones have a considerable inter-intra-observer variability, while quantitative scores, based on distribution of lung attenuation parameters (also called CT indexes), can be obtained through expensive and not so user-friendly software. The aim of this work is to investigate whether a DICOM-viewer open-source software (OsiriX) can obtain CT indexes correlating with semi-quantitative scores. Sixty-three chest CTs of ILD-SSc patients were assessed with two semi-quantitative methods (visual extent and limited/extensive ILD grading) and then blindly processed with OsiriX to obtain the distribution parameters of lung attenuation (kurtosis, skewness and mean). Semiquantitative assessment and CT indexes were compared through the Spearman rank test and Mann-Whitney test. All CT indexes showed a statistically significant correlation of moderate degree with the visual extent semi-quantitative assessment (p-value < 0.05). Skewness was the lung attenuation distribution parameter with the strongest correlation (r = -0.378, p-value = 0.0023). Moreover, CT indexes of patients with an extensive and limited disease were statistically different (p < 0.01). CT indexes correlating with a radiological semi-quantitative ILD assessment can be obtained through OsiriX. CT indexes can be considered very helpful to discriminate patients with extensive and limited ILD.

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EXPRESSION OF TIR8 RECEPTOR IN CHICKEN TISSUES

L. TURIN, G. MANAROLLA and F. RIVA

Department of Veterinary Science and Public Health (DIVET), University of Milan, Italy

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The orphan receptor TIR8, also known as SIGIRR, belongs to the TLR/IL-1R (TIR) superfamily and plays an important role in the immune response. The signalling pathways of the receptors belonging to the TIR family are tightly regulated at multiple levels and through different mechanisms. TIR8 negatively modulates innate immunity and inflammatory responses in the areas where it is primarily expressed (gastrointestinal tract, kidney and lung). TIR8 has been well characterized in mouse, humans and in other Mammalian species, but it is still poorly known in chicken. Given the importance of gastrointestinal diseases in chicken, the aim of our study was to investigate the distribution of TIR8 in a wide panel of non-pathologic tissues and organs. TIR8 expression was analyzed in chicken samples at both levels of transcript mRNA and translated protein. The pattern of expression of TIR8 (ubiquitous) was similar to Mammals for some tissues (high levels in kidney and gastrointestinal tract), but it resulted unique for other tissues. High expression was detected in liver, pancreas and female reproductive tract. Interestingly, the receptor was highly expressed also in heterophils, the most common granulocytes of birds. Few isoforms of chicken TIR8 were detected by Western blot, suggesting the occurrence of different post-translational processing in different organs. Immunohistochemistry revealed TIR8 immunolabelling in chicken intestine and thymus. These results demonstrate that the receptor, although evolutionarily conserved, show species-specific peculiarities.

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OSTEOPONTIN, OSTEOCALCIN AND OB-CADHERIN EXPRESSION IN SYNTHETIC NANOHYDROXYAPATITE vs BOVINE HYDROXYAPATITE CULTURED OSTEOLASTIC-LIKE CELLS

A. SANTARELLI^{1,2}, M. MASCITTI¹, G. ORSINI¹, L. MEMÈ¹, R. ROCCHETTI³,
P. TIRIDUZZI¹, F. SAMPALMIERI¹, A. PUTIGNANO¹, M. PROCACCINI¹,
L. LO MUZIO⁴ and F. BAMBINI^{1,2}

¹Department of Clinical, Specialistic and Stomatological Sciences, Marche Polytechnic University, Ancona, Italy; ²Odontostomatologic Clinic, National Institute of Care and Research on Ageing, Ancona, Italy; ³Department of Pathologic Anatomy and Histopathology, Marche Polytechnic University, Ancona, Italy; ⁴Department of Clinical and Experimental Medicine, Foggia University, Foggia, Italy

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Calcium phosphate ceramics have been applied in bone replacement for several decades due to their excellent biocompatibility, bioactivity, osteoconductivity and mechanical strength. Several studies have demonstrated that porous hydroxyapatite (HA) is an excellent scaffold for osteogenic proliferation and differentiation of the osteoprogenitor cells. However, different methods of synthesis and production of HA ceramic-based materials may have considerable effect on the physical and biological properties. In the present work, two hydroxyapatite-based materials, a natural hydroxyapatite ceramic of bovine origin and a synthetic nano-cristalline hydroxyapatite were tested *in vitro* with MG63 cell line. The results displayed that both the materials demonstrated a good biocompatibility. The immunocytochemical stain revealed a different positivity of the osteogenic markers between the cultures with the biomaterials, and the control culture. Western blot data confirmed the immunocytochemical stain. Both the materials tested in the present study demonstrated a good biocompatibility with the osteoblastic cells allowing, at the same time, the osteogenic differentiation, and they may be useful in clinical use.

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LETTER TO THE EDITOR

INFLUENCE OF CHRONIC CHROMIUM EXPOSITION ON THE PROCESSES OF LIPID PEROXIDATION INFLAMMATION AND PLATELET ACTIVATION IN RATS

D. MITROV¹, N. HADZI-PETRUSHEV², V. STOJKOVSKI¹, E. GJORGIEVSKA³,
H. GAGOV⁴ and M. MLADENOV²

¹Faculty of Veterinary Medicine, "Sts, Cyril and Methodius" University, Skopje, Macedonia;
²Faculty of Natural Sciences and Mathematics, Institute of Biology, "Sts, Cyril and Methodius" University, Skopje, Macedonia; ³Faculty of Dental Medicine, "Sts, Cyril and Methodius" University, Skopje, Macedonia; ⁴Faculty of Biology, Sofia University "St. Kliment Ohridski", Sofia, Bulgaria

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The aim of this study was to investigate the effect of chronic treatment with chromium hexavalent (Cr VI) on the platelet activation, inflammation and lipid peroxidation in rats. Thirty male Wistar rats weighing 251 ± 18 g were randomly assigned to one control and one Cr-exposed group. 8-iso-prostaglandin F_{2a} (8-iso-PGF_{2a}), interleukin 1 β (IL-1 β), tumor necrosis factor α (TNF- α) and creatinine (Crt), were measured in plasma, while 11-dehydro thromboxane B₂ (11-dehydro-TXB₂) in plasma and urine. Plasma levels of IL-1 β , TNF- α , 8-iso-PGF_{2a} and Crt were significantly increased in the Cr (VI)-treated in comparison to the control group. Also, in the urine of Cr (VI)-treated rats, 11-dehydro-TXB₂ was significantly increased in comparison to control rats. From the obtained data it is evident that chronic treatment with Cr (VI), accelerates arachidonic acid peroxidation in rats, which peroxidation further probably induces enhanced 11-dehydro-TXB₂ excretion rate.

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LETTER TO THE EDITOR

INHALED HYALURONIC ACID AS ANCILLARY TREATMENT IN CHILDREN WITH BACTERIAL ACUTE RHINOPHARYNGITIS

A. VARRICCHIO, M. CAPASSO, F. AVVISATI, A.M. VARRICCHIO, A. DE LUCIA,
F.P. BRUNESE and G. CIPRANDI

Associazione Italiana Vie Aeree Superiori (AIVAS) - Study Group on respiratory infections, Italy

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Acute rhinopharyngitis (ARP) is the most common upper respiratory infection in children and represents a social problem for both the pharmaco-economic impact and a burden for the family. Topical antibiotic therapy is usually effective in bacterial ARP, but ancillary treatment might improve its efficacy. Hyaluronic acid (HA) is a promising molecule that has been recently proposed in upper respiratory disorders. Therefore, the purpose of this study was to evaluate the effects of ancillary HA treatment in children with bacterial ARP. Globally, 51 children (27 males, mean age 5.9 ± 2.1 years) with bacterial ARP were enrolled in the study. At baseline, children were randomly assigned to the treatment with: 125 mg of thiamphenicol diluted in 4 mL of saline isotonic solution twice daily (group A) or with 125 mg of thiamphenicol plus 4 ml of sodium hyaluronate 0.2% plus xylitol 5% (Aluneb, Sakura Italia) twice daily (group B) administered by the nasal device Rinowash (Airliquide Medical System, Italy) and connected to an aerosol nebulizer with pneumatic compressor (1.5 bar per 5 L/min) Nebula (Airliquide Medical System, Italy), for 10 days. sVAS, nasopharyngeal spotting, neutrophils and bacteria were assessed at baseline and after the treatment. Both treatments induced significant reduction of symptom perception, spotting, neutrophil and bacteria count. However, thiamphenicol plus HA was able to significantly induce a greater effect on sVAS ($p=0.006$), neutrophil count ($p=0.01$), and bacteria count ($p=0.0003$) than thiamphenicol alone. In conclusion, this study provides the first evidence that intranasal HA, as ancillary treatment, may be able to improve topical antibiotic efficacy in children with bacterial ARP.

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