TLR2: A CROSSROADS BETWEEN INFECTIONS AND AUTOIMMUNITY?

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Environment has both pathogenic and protective roles in the determination of autoimmune disease development, possibly through infectious agents. TLR2 has the capability to recognize the widest range of PAMPs, and it is important for the recognition of mycobacteria and gram-positive bacteria. Here we review recent information showing that TLR2 ligands, its signaling machinery and the effects of its engagement on T cell polarization and differentiation, all play a decisive role in experimental models of autoimmunity. Thus, we propose that engagement of TLR2 is an important crossroads between encounter with bacteria and development of self-reactive diseases.

PERI-IMPLANT DISEASES AND HOST INFLAMMATORY RESPONSE INVOLVING MAST CELLS: A REVIEW

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Mast cells (MCs) are motile granule-containing cells that originate from bone marrow pluripotential haematopoietic cells, circulate in blood and extravasate in tissues where they play an important role in inflammation, host defense and tissue repair. We herein review the English literature over the past twenty years concerning the biology and function of MCs with particular focus on their role in the inflammatory process in dental implant failure due to osseointegration absence or to peri-implantitis. Due to immunological or non-immunological stimulation, in a few minutes MCs release prestored granule-associated mediators into the extracellular environment promoting pro-/anti-inflammatory events/response. MCs can either protect the host by activating defense mechanisms and initiating tissue repair and osseointegration if their function is transient, or lead to considerable tissue damage if it is inappropriate and continuous leading to osseointegration absence or peri-implantitis. We hypothesize that administration of histamine receptor antagonists, serine protease inhibitors and MC preformed mediator release inhibitors before and after implantation could represent novel therapeutic strategies to improve the osseointegration, the functionality and longevity of implants or prevent and treat peri-implant inflammatory conditions.
A high level of cholesterol is associated with obesity, cardiovascular diseases and atherosclerosis. Immune response in atherosclerosis is mediated by chemokines which attract monocytes, leading to the innate immune response characterised by the production of cytokines. The immunoregulatory cytokines are an important bridge between innate and adductive immunity. TH1 cytokines are involved as effector T cells in inflammatory response, while TH2 cytokines can be anti-inflammatory such as IL-10 and IL-4. It is well known that statins enhance the production of TH2 cytokines whereas the secretion of TH1 cytokines is suppressed. For this purpose, we studied the significance of anti-inflammatory effect and suppression of inflammation by statins. In this paper we revisited the role of cholesterol and cytokines IL-18, IL-10, IL-12, TNF-α, interferon-γ, and chemokines in inflammatory diseases.

A NOVEL MONOCLONAL ANTIBODY AGAINST HUMAN CD80 AND ITS IMMUNE PROTECTION IN A MOUSE LUPUS-LIKE DISEASE


Blockade of the interactions between CD28/CTLA-4 and their ligands, CD80 (B7, B7.1)/CD86 (B70, B7.2), is an attractive means to induce antigen-specific peripheral tolerance in autoimmune disease and organ transplantation. In this study, we generated and characterized a monoclonal antibody (Clone 4E5) against human CD80. 4E5 could recognize both human and mouse CD80 and suppress mixed lymphocyte reaction in vitro. To investigate their potency for clinical use, we further administrated 4E5 to a mouse lupus-like disease model (C57BL/J6) induced by Pristane. 4E5 could inhibit the immune response and attenuate the severity of lupus-like disease. The data showed 4E5 function and suggested that blockade of CD80/CD28 co-stimulatory signal pathway with 4E5 is a promising strategy to decelerate the progression of lupus-like disease and other autoimmune diseases.
ATTENUATION OF EXPRESSION OF EXTRACELLULAR MATRIX GENES WITH SIRNAS TO SPARC AND CTGF IN SKIN FIBROBLASTS OF CTGF TRANSGENIC MICE

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Transgenic mice that over-express connective tissue growth factor (CTGF) in fibroblasts under the control of an enhancer/promoter element of the Col1a2 gene (Col1a2-CTGF) recapitulate multiorgan fibrosis similar to fibrosis observed in Scleroderma (SSc). In this study we investigate the regulation of secreted protein acidic and rich in cysteine (Sparc) and Ctgf siRNAs on the expression of several extracellular matrix components in the fibroblasts derived from Col1a2-CTGF transgenic mice. Three fibroblast lines were obtained from each of wide type C57BL/6 and CTGF transgenic C57BL/6, and were transfected with Sparc siRNA or Ctgf siRNA. Real-time quantitative RT-PCR and Western blotting were used to examine the transcription and protein levels of type I collagen, CTGF and SPARC. Student’s \( t \)-tests were used to determine the significance of the results. Our results showed that Col1a2 and Ctgf increased expression at both transcriptional and translational levels in the fibroblasts from the Col1a2-CTGF transgenic mice compared with those in the fibroblasts from their normal wild-type littermate. The treatment with Sparc siRNA or Ctgf siRNA attenuated the mRNA and/or protein expression of the Col1a2, Ctgf and Sparc in these fibroblasts. Sparc and Ctgf siRNAs also showed a reciprocal inhibition at transcript levels. Therefore, our results indicated that both SPARC and CTGF appeared to be involved in the same biological pathway, and they have the potential to serve as a therapeutic target for fibrotic diseases such as SSc.
Despite their histological resemblance to colorectal adenocarcinoma, there is little information on the molecular events involved in the pathogenesis of intestinal-type sinonasal adenocarcinoma (ITACs). The aim of this paper is to evaluate the possible role of TP53 and Bcl-2 gene defects in ITAC by investigating the immunohistochemical expression of TP53 and Bcl-2 gene products in a group of ethmoidal ITACs associated with occupational exposure. A retrospective study on 15 patients with pathological diagnosis of primary ethmoidal ITAC was conducted. Representative formalin-fixed, paraffin wax-embedded block from each case was selected for immunohistochemical studies using the antibodies against p53 and Bcl-2. Clinical-pathological data were also correlated with the staining results. The results of immunohistochemical examination demonstrated that poorly differentiated cases showed a higher percentage of p53 and Bcl-2 expressing cells in comparison to well-differentiated cases. No correlation was found with other clinico-pathological parameters, including T, stage and relapses. The relationship between up-regulation of p53 and Bcl-2 and poorly differentiated ethmoidal adenocarcinoma suggests a role of these genes, in combination with additional genetic events, in the pathogenesis of ITAC.
The liver sustains the greatest damage from ethanol (EtOH) abuse. EtOH and its metabolites impair hepatocyte metabolism, causing intracellular accumulation of proteins and lipids and increasing radical oxygen species production. These processes are toxic to the mitochondrial respiratory chain and to mitochondrial DNA. We have recently shown that supplementing the diet of rodents with an essential amino acid-enriched mixture (EAAem) significantly increases mitochondrial mass and number in cardiac and skeletal muscles and improves mitochondrial function in aged animals. Thus, in this study we sought to test whether EAAem supplementation could reduce EtOH-induced liver damage. Groups of adult male Wistar rats were fed a standard diet and water ad libitum (the control group), drinking water with 20% EtOH (the EtOH group), or drinking water with 20% EtOH and EAAem supplementation (1.5 g/kg/day) (the EtOH+EAAem group) for 2 months. The blood EtOH concentration was measured, and markers for fat (Oil-Red-O), mitochondria (Grp75, Cyt-c-ox), endoplasmic reticulum (Grp78), and inflammation (Heme Oxigenase 1, iNOS, and peroxisomes) were analyzed in the liver of animals in the various experimental groups. EAAem supplementation in EtOH-drinking rats ameliorated EtOH-induced changes in liver structure by limiting steatosis, recruiting more mitochondria and peroxisomes mainly to perivenous hepatocytes, stimulating or restoring antioxidant markers, limiting the expression of inflammatory processes, and reducing ER stress. Taken together, these results suggest that EAAem supplementation may represent a promising strategy to prevent and treat EtOH-induced liver damage.
HCG HASTENS BOTH THE DEVELOPMENT OF MAMMARY CARCINOMA AND THE METASTATIZATION OF HCG/LH AND ERBB-2 RECEPTOR-POSITIVE CELLS IN MICE

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Breast cancer is more frequent in human nulliparae, whereas its incidence is reduced by early full-term pregnancy. Rodent studies suggest that chorionic gonadotropin secretion during pregnancy affords protection by inducing breast structure differentiation. Opposite effects, however, have been observed in cancer prone transgenic mice overexpressing the β subunit of chorionic gonadotropin or pituitary luteinic hormone (LH). Here we assessed the effect of administration of human chorionic gonadotropin (hCG) for 21 days (corresponding to the duration of a mouse pregnancy) in virgin female mice transgenic for the activated rat (r-) ERBB-2 oncogene (BALB-neuT). In these mice, the onset of atypical mammary duct hyperplasia and its progression towards multiple mammary carcinomas is accelerated by hCG. hCG enhances the in vitro proliferation and in vivo metastatization of tumor cells from a BALB-neuT mammary tumor expressing the hCG/LH as well as the ERBB-2 receptors. These findings suggest that hCG favours the growth and progression of hCG/LH and ERBB-2 receptor-positive breast tumors.
This study explores the inducing-apoptotic activity of the ethanol extract of *Duchesnea indica* Focke on treatment of herpes simplex encephalitis. Cell models were employed and divided into 4 groups: normal group, virus group, *Duchesnea indica* group and dexamethasone group. Cytopathic effect examination was employed to detect apoptosis of PC-12 and BV-2 cells. ELISA was used to measure TNF-α and IL-1β, and Greiss method to measure NO secretion. Flow cytometry assay for caspase-3 expressions was performed. As a result, the ethanol extract of *Duchesnea indica* could protect the neuron cell model from impairment by virus. In the cell model of microglia stimulated by herpes simplex virus (HSV), with the ethanol extract intervention, TNF-α, IL-1β and NO levels were significantly decreased and cell death of BV-2 cells were markedly increased. The expression level of caspase-3 was notably elevated after the extract intervention. In conclusion, the ethanol extract of *Duchesnea indica* can reduce HSV-induced inflammatory injury on neuron due to the induction of microglia apoptosis.
GENE EXPRESSION PROFILE OF HUMAN COLON CANCER CELLS TREATED WITH CROSS-REACTING MATERIAL 197, A DIPHTHERIA TOXIN NON-TOXIC MUTANT

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Cross-Reacting Material 197 (CRM197) is a diphtheria toxin non-toxic mutant that has shown anti-tumor activity in mice and humans. It is still unclear whether this anti-tumorigenic effect depends on its strong inflammatory-immunological property, its ability to inhibit heparin-binding epidermal growth factor (HB-EGF), or even its possible weak toxicity. CRM197 is utilized as a specific inhibitor of HB-EGF that competes for the epidermal growth factor receptor (EGFR), overexpressed in colorectal cancer and implicated in its progression. In this study we evaluate the effects of CRM197 on HT-29 human colon cancer cell line behaviour and, for CRM197 recognized ability to inhibit HB-EGF, its possible influence on EGFR activation. In particular, while HT-29 does not show any reduction of viability after CRM197 treatment (MTT modified assay), or changes in cell cycle distribution (flow cytometry), in EGFR localization, phospho-EGFR detected signals (immunohistochemistry) or in morphology (scanning electron microscopy, SEM) they show a change in the gene expression profile by microarray analysis (cDNA microarray SS-H19k8). The overexpression of genes like protein phosphatase 2, catalytic subunit, alpha isozyme (PPP2CA), guanine nucleotide-binding protein G subunit alpha-1 (GNAI1) and butyrophilin, subfamily 2, member A1 (BTN2A1) has been confirmed with real-time-qPCR. This is the first study where the CRM197 treatment on HT-29 shows a possible scarce implication of endogenous HB-EGF on EGFR expression and cancer cell development. At the same time, our results show the alteration of a specific and selected number of genes.
DETECTION OF RESPIRATORY VIRUSES IN THE 2009 WINTER SEASON IN ROME: 2009 INFLUENZA A (H1N1) COMPLICATIONS IN CHILDREN AND CONCOMITANT TYPE 1 DIABETES ONSET

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We investigated clinical characteristics and complications, particularly type 1 diabetes onset, in children hospitalized for 2009 pandemic influenza A (H1N1) virus and compared number of consultations, rate of hospitalization and virus identification in children hospitalized for acute respiratory symptoms (ARS) during the winter season 2009-2010 and 2004-2005. Patients were tested for 2009 H1N1 virus and 14 respiratory viruses on pharyngeal brush/nasal aspirates, using a RT-PCR or nested PCR assays. Consultations and hospitalizations were extracted from operative system GIPSE. The total number of consultations increased by 12%, consultation rate for ARS by 13% and number of hospitalizations by 56% from 2004-2005 to 2009-2010. In 2004-2005, Influenza A virus was identified in only 7% of hospitalized children, while in 2009-2010 the 2009 H1N1 virus was identified in 21%. Three children attending the hospital for ARS and 2009 H1N1 infection had ketoacidosis as the onset manifestation of type 1 diabetes. By comparing the number of new diabetes diagnoses among the two winter seasons, we found a higher number of new diagnoses in October 2009-January 2010 than in the same period in 2004-2005 (19 vs 10). Six children (13%), all presenting with pre-existing diseases, were admitted to the pediatric intensive care unit. No children died. The outbreak of this novel virus has increased pediatric consultation rates and hospitalizations compared with previous winters without causing deaths. The children at highest risk for severe infection are those with comorbidities. The 2009 H1N1 virus seems in some way involved in the pathogenesis of type 1 diabetes.
A NEW ANTI-INFECTIVE STRATEGY TO REDUCE ADHESION-MEDIATED VIRULENCE IN *STAPHYLOCOCCUS AUREUS* AFFECTING SURFACE PROTEINS

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*Staphylococcus aureus* is a flexible microbial pathogen frequently isolated from community-acquired and nosocomial infections. The use of indwelling medical devices is associated with a significant risk of infection by this bacterium which possesses a variety of virulence factors, including many toxins, and the ability to invade eukaryotic cells or to form biofilm on biotic and abiotic surfaces. The present study evaluates the anti-infective properties of serratiopeptidase, a secreted protein of *Serratia marcescens*, in impairing virulence-related staphylococcal properties, such as attachment to inert surfaces and adhesion/invasion on eukaryotic cells. SPEP seems to exert its action by modulating specific proteins. Proteomic studies performed on surface proteins extracted from SPEP-treated *S. aureus* cultures revealed that a number of proteins are affected by the treatment. Among these we found the adhesin/autolysin Atl, FnBP-A, SecA1, Sbi, EF-Tu, EF-G, and alpha-enolase. EF-Tu, EF-G and alpha-enolase are known to perform a variety of functions, depending on their cytoplasmic or surface localization. All these factors can facilitate bacterial colonization, persistence and invasion of host tissues. Our results suggest that SPEP could be developed as a potential “anti-infective agent” capable to hinder the entry of *S. aureus* into human tissues, and also impair the ability of this pathogen to form biofilm on prostheses, catheters and medical devices.

AN ITALIAN STUDY ON HEALTH-RELATED QUALITY OF LIFE AND FATIGUE IN PATIENTS WITH CHRONIC FATIGUE SYNDROME AND PATIENTS WITH CHRONIC HCV VIRUS INFECTION: SIMILARITIES AND DIFFERENCES

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Severe fatigue and a significantly reduced health-related quality of life (HRQoL) have been described in patients with chronic fatigue syndrome (CFS) in comparison with patients affected by chronic hepatitis C (CHC) and other chronic medical conditions. We examined 39 CFS and 49 CHC patients to explore whether fatigue and a poor HRQoL represent a greater medical and social problem in CFS than in CHC. The severity of fatigue and the HRQoL were assessed using the Fatigue Impact Scale (FIS) and the Health Status Questionnaire Short Form-36 (SF-36), respectively. The statistical analysis showed both a higher score of fatigue and a lower HRQoL in CFS patients compared to CHC patients. Furthermore, in CHC patients the FIS evaluation showed a significantly reduced score of the psychosocial domain in comparison with the other domains. Multivariate linear regression analysis revealed female gender as the most important positive variable in chronic hepatitis C patients for total score of FIS. In conclusion, CFS was associated with severe and disabling fatigue and an impaired HRQOL. In particular, both fatigue and all aspects of HRQOL perceived by CFS patients were significantly impaired compared to CHC patients. Consequently, management of fatigue should be considered a priority in order to improve HRQOL in CFS patients. In CHC patients the impact of fatigue on HRQoL was less significant than in CFS patients, even though the FIS evaluation showed a significant impairment of the psychosocial domain.
Solid tumors such as head and neck squamous cell carcinoma (HNSCC) display an intense interaction between tumoral factors and the immune system. Functional modulation of tumor-infiltrating and peripheral blood immune cells plays an important role during tumor progression. In this pilot study we compared biological functions of polymorphonuclear granulocytes (PMN) from the peripheral blood of HNSCC patients and healthy subjects. PMN were simultaneously isolated from the peripheral blood of HNSCC patients and healthy donors for functional analysis (apoptosis, production of reactive oxygen species (ROS), cytokine release and immunophenotyping). PMN from HNSCC patients showed a significantly lower inducible production of ROS ($P = 0.02$) and reduced spontaneous apoptosis ($P = 0.008$) compared with PMN from healthy donors. Under standard culture conditions, there was no significant difference regarding the release of inflammatory cytokines between PMN from HNSCC patients and PMN from healthy donors. Confirming previous observations, serum concentrations of PMN-related cytokines were significantly higher in the peripheral blood of HNSCC patients than in that of controls. Importantly, immunophenotyping revealed an increased number of immature PMN in PMN fractions isolated from HNSCC patients. Peripheral blood PMN from HNSCC patients and healthy donors show distinct functional differences. The presence of increased numbers of immature stages of PMN in HNSCC patients may partly contribute to the changes observed. After recruitment to and infiltration of the tumor, PMN may be further modulated in the local tumor microenvironment. This pilot study justifies functional analyses of myeloid cells in larger cohorts of patients with HNSCC.
Most autoinflammatory disorders typically come out in the pediatric population, although a limited number of patients may experience disease onset during adulthood. To date, a late disease onset has been described only in familial Mediterranean fever, caused by mutations in the \textit{MEFV} gene, and in tumor necrosis factor receptor-associated periodic syndrome, caused by mutations in the \textit{TNFRSF1A} gene. The relative rarity and lack of information on adult-onset autoinflammatory diseases make it likely that mutations will be found in an even smaller percentage of cases. With the aim of improving the genetic diagnosis in adults with suspected autoinflammatory disorders, we recently identified a set of variables related to the probability of detecting gene mutations in \textit{MEFV} and \textit{TNFRSF1A} and, in addition, we have also proposed a diagnostic score for identifying those patients at high risk of carrying mutations in these genes. In the present study we evaluated the preliminary score sensitivity and specificity on a wider number of patients in order to validate the goodness of fit of the model. Two hundred and nineteen consecutive patients with a clinical history of periodic fever attacks were screened for mutations in...
COMBINATION TREATMENT OF FLAG WITH NON-PEGYLATED LIPOSOMAL DOXORUBICIN (MYOCET™) IN ELDERLY PATIENTS WITH ACUTE MYELOID LEUKEMIA: A SINGLE CENTER EXPERIENCE

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The incidence of acute myeloid leukemia (AML) increases with age, but results of intensive chemotherapy in elderly patients are disappointing. Non-pegylated liposomal formulations of doxorubicin (Myocet™) have been developed with the aim of reducing systemic and cardiac toxicity especially in the elderly. We evaluated the efficacy and toxicity profiles of fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG) regimen given in association with Myocet™ in 35 patients with AML, median age 69 years (range 61-83 years). Nineteen (54.3%) had newly-diagnosed AML, twelve (34.3%) patients had secondary AML (ten with Myelodisplastic Syndrome, two with Primary Myelofibrosis) and 4 (11.4%) patients had had a late relapse (> 12 months) of AML. Complete remission (CR) and partial remission (PR) were obtained in twenty-two (63%) and 3 (8.5%) patients, respectively. Seven (20%) patients showed a resistant disease. There were 3 early deaths (8.5%). Six patients (17%) experienced severe cardiovascular toxicity. The median overall survival (OS) was 12 months (range 1-52 months) with a median disease-free survival (DFS) of 20 months (range 1-48 months). One-year and two-year DFS were 78.9% and 26.7%, respectively. This study demonstrates that in elderly patients with AML, FLAG-Myocet™ combination shows promising efficacy response with acceptable toxicity, enabling most patients to receive further treatments, including transplantation procedures.

METALLOSIS FOLLOWING KNEE ARTHROPLASTY: A HISTOLOGICAL AND IMMUNOHISTOCHEMICAL STUDY

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Metallosis represents a rare and severe complication of knee replacement surgery. It is caused by the infiltration and accumulation of metallic debris into the peri-prosthetic structures, deriving from friction between metallic prosthetic components. In knee arthroplasty, this event generally occurs as a result of polyethylene wear of the tibial or metal-back patellar component. The real incidence of metallosis is still unknown, although it seems to be more frequent in hip than in knee arthroplasty. The metallic debris induces a massive release of cytokines from inflammatory cells, making a revision necessary whenever osteolysis and loosening of the prosthesis occur. We report four patients who underwent revision of their knee arthroplasty because of severe metallosis. In one of these patients, polyethylene wear had determined friction between the metal-back patellar component and the anterior portion of the femoral component. In the remaining three cases, metallosis was caused by friction between the femoral and tibial prosthetic metal surfaces, resulting from full-thickness wear of the tibial polyethylene. T lymphocytes were activated by metal particles present in periprosthetic membranes. In all patients, one-stage revision was necessary, with rapid pain disappearance and a complete functional recovery of the knee joint.
LONG-TERM N-ACETYLCYSTEINE THERAPY IN SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE: A RETROSPECTIVE STUDY

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Systemic sclerosis (SSc) is associated with interstitial lung diseases. The primary endpoints of this study were changes between baseline and month 24 in single-breath carbon monoxide diffusing capacity (DLco). The secondary endpoints were: vital capacity (VC), forced expired volume in 1 sec (FEV1), total lung capacity (TLC), scores of high resolution computed tomography (HRCT) of the chest, number of adverse effects. In this study, we retrospectively investigated data from SSc patients who had undergone therapy with high-dose intravenous N-acetylcysteine (NAC) at a dosage of 15 mg/Kg/h for 5 consecutive hours every 14 days. After NAC therapy median values of DLco (69.5% vs 77.7%), VC (99% vs 101.3%) and TLC (93% vs 98.3%) significantly increased. We did not observed any significant changes from baseline in FEV1 value and HRTC score. The improvement in lung function was more evident in SSc patients without radiological signs of pulmonary fibrosis than in patients with pulmonary fibrosis. In SSc patients with mild-moderate pulmonary fibrosis intravenous NAC administration slows the rate of deterioration of DLco, VC and TLC. In conclusion, this retrospective study demonstrates that long-term therapy with intravenous NAC ameliorates pulmonary function tests in SSc patients.
The present study aims to assess the protective role of the antioxidant enzyme catalase (CAT) with relation to hydrogen peroxide (H$_2$O$_2$) degradation in oxygen plus water on electrophysiological and fluorescence changes induced by in vitro ischemia and on brain damage produced by transient in vivo ischemia. Neuroprotective effects of CAT were determined by means of electrophysiological recordings and confocal fluorescence microscopy in the hippocampal slice preparation. Ischemia was simulated in vitro by oxygen/glucose deprivation (OGD). In vivo ischemia was produced by transient middle cerebral artery occlusion (MCAo). A protection of the rat CA1 field excitatory postsynaptic potential (fEPSP) loss caused by a prolonged OGD (40 min) was observed after exogenous CAT (500 U/mL) bath-applied before a combined exposure to OGD and H$_2$O$_2$ (3 mM). Of note, neither H$_2$O$_2$ nor exogenous CAT alone had a protective action when OGD lasted for 40 min. The CAT-induced neuroprotection was confirmed in a transgenic mouse model over-expressing human CAT [Tg(CAT)]. In the presence of H$_2$O$_2$, the hippocampus of Tg(CAT) showed an increased resistance against OGD compared to that of wild-type (WT) animals. Moreover, CAT treatment reduced for about 50 min fEPSP depression evoked by repeated applications of H$_2$O$_2$ in normoxia. A lower sensitivity to H$_2$O$_2$-induced depression of fEPSPs was also indicated by the rightward shift of concentration-response curve in Tg(CAT) compared to WT mice. Noteworthy, Tg(CAT) mice had a reduced infarct size after MCAo. Our data suggest new strategies to reduce neuronal damage produced by transient brain ischemia through the manipulation of CAT enzyme.
TRANSCRIPTIONAL PROFILE OF DENERVATED *VASTUS LATERALIS* MUSCLE DERIVED FROM A PATIENT 8 MONTHS AFTER SPINAL CORD INJURY: A CASE REPORT

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A lack of motor neurons abolishes both neurotrophic factor secretion and contractile activity in muscle, which impairs mass, contractile properties, and fibre-type characteristics of the muscle. However, the molecular pathways that can be stimulated or repressed in the scenario of spinal cord injury remain unknown. We investigated for the first time the transcriptional profile of a young male patient 8 months after spinal cord injury. Adaptive metabolic changes of complete denervated skeletal muscle were revealed. In particular, the main molecular pathways involved include metabolic and proteolitic pathways, mitochondrial and synaptic function, calcium homeostasis, sarcomere and anchorage structures. Our data depict the molecular signalling still present in complete denervated skeletal muscle fibres a few months after spinal cord injury. These data could be of interest also to design a specific therapeutic approach aimed at the electrical-stimulation of severe atrophied skeletal muscle.
Chronic Rhinosinusitis with or without Nasal Polyps (CRSwNP and CRSsNP) may be characterized by different cytokine profiles. Generally, Th2 cytokines and eosinophilic infiltration have been reported to be more specific of CRSwNP compared to CRSsNP, where neutrophils seem to play a major role. The epithelial cell-derived thymic stromal lymphopoietin (TSLP) has been recently identified as a key factor in Th2-inflammatory response. The aim of this study is to investigate the expression of TSLP Receptor (TSLP R) in surgical specimens obtained from patients affected by CRSwNP (n=10) and CRSsNP (n = 5) by immunohistochemical techniques (immunostaining score, IS). TSLP R expression was significantly higher in the inflammatory infiltrate and in the epithelial cells of CRSwNP, CRSsNP patients compared to the control group (IS 4.5±0.68, 4.4±1.44 and 0.43±0.3 respectively, p=0.0024 for inflammatory infiltrate and IS 5.8±0.92, 7.8±2.06 and 0.86±0.55 respectively, p=0.0018 for epithelial cells). No significant difference was observed in IS of inflammatory infiltrate and epithelial cells in CRSwNP compared to CRSsNP. Very low IS for TSLP R was found in connective tissue of all the samples, with no difference among the groups. TSLP receptor is highly expressed in CRS compared to controls and independently from the polyps suggesting an early common inflammatory pathway in the two CRS phenotypes.
URINARY EXCRETION OF 5-HYDROXY-3-INDOLEACETIC ACID IN DYSTIMIC/DEPRESSED, ADULT OBESE WOMEN: WHAT CORRELATIONS TO HEPATIC STEATOSIS?

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The synthesis of serotonin at CNS level is influenced by diet. Moreover, insulin resistance is associated with lower serotonin levels. Visceral obesity, strictly linked to hepatic steatosis is specifically associated with mild to severe somatic affective-depressive symptom clusters. Previous data support the view that depression involves serotonergic systems, reflecting low levels of urinary 5- hydroxy-3-indoleacetic acid (5-HIAA). The 24-h urinary excretion of 5-HIAA was evaluated in 76 dystimic/depressed, obese/overweight females, divided into two groups, i.e., on a hyper-caloric diet, associated with a life style characterized by leisure time sedentary behavior (LTSB, 35 women), or on a normo-caloric diet, assisted by program-based strategies aimed at promoting physical activity participation (PAP, 41 women). Beck Depression Inventory (BDI) was carried out to score the severity of dystimia/depression. Anthropometric measures, metabolic indices, severity of hepatic steatosis at sonography and HOMA were studied. Urinary levels of 5-HIAA in controls and PAP groups were comparable with a great overlap, while in the LTSB group the urinary excretion of 5-HIAA was significantly reduced in respect to that of the PAP group and obviously compared to that of the control group, 3.4±1.4 mg/L versus 6.2±2.7 mg/L and 6.4±2.6 mg/L, respectively, ANOVA test, P= 0.001. Among metabolic indices, cholesterol, HDL-cholesterol, triglycerides and uric acid were not able to predict urinary concentrations of 5-HIAA, which were not associated with hepatic steatosis; vice versa, ferritin levels, and mainly HOMA values, were independent predictors of the urinary excretion of 5-HIAA ($\beta$=0.235 and 0.45, respectively). Dystimia/depression severity was negatively predicted by urinary 5-HIAA levels in the sense that the highest BDI values were forecast by the lowest values of urinary 5-HIAA ($\beta$= -0.72). The importance of measuring the 24-h urinary excretion of 5-HIAA in follow-ups could rely on a method simultaneously mirroring the well-being status, the adherence to physical activity, which leads to improved insulin sensitivity, and the eating habits acquired by dystimic/depressed overweight/obese patients. In contrast, the significance of the urinary 5-HIAA is reduced in evaluating the severity of hepatic steatosis, likely because it is a structured process.
ANALYSIS OF EXPRESSION PROFILE OF GENE ENCODING PROTEINS OF SIGNAL CASCADES ACTIVATED BY INSULIN-LIKE GROWTH FACTORS IN COLORECTAL CANCER

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The aim of the study is to analyse gene typing with the use of the microarray technique (HG-U133A, Affymetrix), differentiating colorectal cancer tissues from tissues assessed histopathologically as healthy ones among a panel of 93 mRNA of gene encoding proteins involved in the activation of cellular signal transduction pathways by insulin-like growth factors. The study was conducted on a group of 8 colorectal cancer patients. Frozen tumor and healthy specimens from the patients were used in molecular tests. Transcript IGF2 differentiated cancer from healthy tissue. Among the genes participating in the cascade of signal transfer in cells activated by IGF, GRB10, PIK3R3, PIK3R1, and IRS1 were qualified as differentiating transcripts. IRS1 indicated over-expression in tumour. Transcript SMAD2 showed a significant changed in tumour samples (increased expression).

REDUCED SEBUM PRODUCTION IN TURNER SYNDROME: A STUDY OF TWENTY-TWO PATIENTS

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Turner’s syndrome (TS) is a genetic disorder caused by numeric and/or structural abnormalities of the X chromosome. In a previous study it was observed that acne is less frequent in TS than in the general population. Since the onset of acne in pre-pubertal or pubertal age is related to sebum production, this study evaluates sebum secretion in TS patients, comparing the results with those of a control group of age-matched healthy female subjects. A total of 22 patients affected by TS (mean age 26.56±7.89 years) and a control group of 23 age-matched healthy females were studied. Sebum production was measured using a Sebumeter SM810. Mean sebum secretion in TS subjects was significantly lower than in the control group (81.35±66.44 UA vs 147.09±33.62 UA, p<0.001) and this significant difference was found in every facial zone. The reduction of sebum secretion may explain, using a simple and non-invasive method, the absence or the low incidence of acne in TS patients.
ANTIBACTERIAL ACTIVITY OF METHYL AMINOLEVULINATE PHOTODYNAMIC THERAPY IN THE TREATMENT OF A CUTANEOUS ULCER

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We describe a 79-year-old female with a chronic venous ulceration infected by *Staphylococcus aureus* and *Enterococcus faecalis* and not responsive to conventional treatments. The patient was treated with Methyl-Aminolaevulinate Photodynamic Therapy (MAL-PDT). After four weeks the cutaneous swabs become negative and we observed a significant clinical improvement. Therefore we suppose that MAL-PDT could represent a valid therapeutic option in the treatment of infected chronic ulcers.

CLINICAL AND SEROLOGICAL FEATURES OF PATIENTS WITH SUSPECTED LYME BORRELIOSIS

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Serology is currently the method of choice for the laboratory diagnosis of Lyme borreliosis, but it must be interpreted with caution. A total of 954 patients with suspected Lyme borreliosis were evaluated on the basis of clinical and serological data. The seroprevalence of *Borrelia burgdorferi* antibodies was 4.4% (42 of the 954 serum samples). The most frequent clinical manifestation was erythema migrans which occurred in 50% of the seropositive patients, followed by neuroborreliosis (16.6%) and arthritis (11.9%). Carditis was rare. Our findings suggest that for the diagnosis of Lyme borreliosis, serologic tests need to be combined with clinical signs and symptoms.
ORAL DESENSITISATION WITH FOOD IS FOOD-SPECIFIC AND PROTEIN-SPECIFIC

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The avoidance of food(s) is the main therapeutic approach to food allergy. Nevertheless, orally- or sublingually-administered food allergens have gained attention and a number of food-allergic children can tolerate gradually increasing amounts of cow’s milk and hen’s egg. Our purpose is to show that oral desensitisation with food is an allergen-specific therapeutic approach and for this, we describe 4 illustrative children with IgE-mediated food allergy. The first was allergic to cow’s milk and hen’s egg, the second to cow’s milk, hen’s egg and fish. Both underwent oral desensitisation to both cow’s milk and hen’s egg. The third child was allergic to cow’s milk, hen’s egg and fish and underwent oral desensitisation with cow’s milk. The last child was allergic to raw but not to cooked/boiled hen’s egg and underwent oral desensitisation with hen’s egg. The first 2 children reached the clinical tolerance to cow’s milk after the cow’s milk oral desensitisation, but reached the hen’s egg tolerance only after the hen’s egg oral desensitisation. Moreover, the second child did not tolerate fish after being desensitised to both cow’s milk and hen’s egg. The third child tolerated cow’s milk, but not hen’s egg and fish, at the end of the cow’s milk oral desensitisation. The fourth child could tolerate the previously not tolerated raw hen’s egg after the oral desensitisation with raw hen’s egg. In conclusion, we indicate that oral desensitisation with food is allergen specific. The induction of the clinical tolerance to one food is not followed by the tolerance to the other food(s) that the patient is allergic to. To obtain a double or multiple food tolerance, separate desensitisation protocols, one for each food, have to be carried out. Oral desensitisation with food discriminates between raw and cooked proteins.

NARES PATIENTS HAVE MORE RESPIRATORY INFECTIONS THAN ALLERGIC SUBJECTS

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Respiratory infections (RI) represent a frequent challenge for physicians. Allergic patients could present higher susceptibility to contract RI than non-allergic subjects. Non-allergic rhinitis with eosinophils (NARES) has been little investigated. This preliminary study was performed to evaluate the number and duration of RI and their sequelae in NARES and allergic patients, and non-allergic healthy subjects. Forty healthy non-allergic subjects (22 males, mean age 29 years), 40 patients with allergic rhinitis (AR) (19 males, mean age 35), and 40 NARES patients (18 males, mean age 34) were evaluated. The considered parameters were: nasal eosinophils, total number, duration in days of RI, and RI severity. NARES patients had more eosinophils than AR patients and normal controls (p<0.01); RI duration was longer in NARES patients than in AR ones (p<0.05) and controls (p=0.01); RI were more severe in NARES patients than in AR ones (p<0.05) and controls (p<0.01); pneumonia and asthma were more frequent in both NARES and AR patients than controls (p<0.05 and p<0.01). In conclusion, this preliminary study shows that NARES may induce more severe respiratory infections than allergic rhinitis.