CHEMOKINE SYSTEM: NEW INFLAMMATORY MARKERS ON THE HORIZON

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Chemokines and their receptors direct cell migration in homeostatic and inflamed conditions, thus they are major players in key events of immune-mediated disorders. Indeed, much evidence indicates a non-redundant role of the chemokine system in several human diseases, ranging from classical immune-mediated pathologies, such as autoimmune and allergic diseases and transplant rejection, to neoplastic and vascular diseases. Increasing emerging evidence suggests the possible role of chemokines as biomarkers for monitoring disease activity, predicting relapses, monitoring surgical and pharmacological therapy and for providing prognostic indications. Several methods are now available for the detection and measurement of chemokines and their receptors in body fluids and tissues. The advantage of these assays is that they may be used in clinical laboratory and are directly applicable for biomedical diagnosis, representing a powerful tool which could dramatically improve screening, diagnosis and monitoring of diseases in the very near future.
INTER-RELATIONSHIP BETWEEN CHEMOKINES AND MAST CELLS

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The inflammatory response is mediated by immunological and chemotactic factors, proteins of the complement system, histamine, serotonin, arachidonic acid products and cytokines. All these compounds, including cytokines/chemokines, are major contributors to the symptoms of inflammation. Cytokines/chemokines, commonly referred to as “biological response modifiers”, are relatively new compounds for possible use in stimulation of the immune response, and display a number of overlapping abilities to stimulate cells of various lineages and differentiation stages; nonetheless, most of these compounds are potent inflammatory mediators. Mast cell mediators are either contained within secretory granules or can be synthesized de novo and can be released upon activation by either a massive degranulation, or by a selective release of specific molecules. These cells accumulate in the stroma of a variety of inflamed and transformed tissues in response to locally produced chemotactic factors for immune-cells, such as RANTES and MCP-1. Here we describe some connections between mast cells and chemokines.
Apart from controlling appetite and, by extension, energy homeostasis, the neuropeptide, Orexin A, seems to be directly or indirectly involved in many other normal functions, e.g., circadian timing system, regulation of liquid homeostasis, and control of water uptake by the organism, alternation of the sleep-waking and alertness cycle, possible reactions of experimental animals under conditions of high stress, pathophysiology of sleeping disorders—for example, narcolepsy, control of blood pressure and heartbeat, release and circulation of hormones, and, finally, activation of the hypothalamus-pituitary-adrenal axis (1-3).

The involvement of Orexin A in the aforementioned functions of the organism is possibly due to the extremely large dispersion of the neuraxes of the orexigenic neurons, which are located both in the central and the peripheral nervous system (3-5).

The brain-gut axis

Orexin A and its corresponding receptor are also present in the enteric nervous system, suggesting

THE EFFECT OF PORCINE OREXIN A ON GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE PLASMA CONCENTRATIONS IN PIGS

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The orexigenic system was discovered in 1998. It consists of two neuropeptides, Orexin A and Orexin B. Researchers have focused more on Orexin A, since its intracerebroventricular injection into the lateral ventricle of the rat’s brain causes an increase in the consumption of food. Besides, it seems that, apart from appetite, Orexin A regulates many other physiological functions with unknown regulatory and metabolic mechanisms. Orexin A is produced by a small group of neurons located in and around the lateral hypothalamic area. It has been known for decades that the latter is involved in regulating feeding in mammals. An intravenous injection of Orexin A causes changes in insulin and glucagon plasma concentrations in rats. In this study, we investigated the possible effects of the central administration of porcine Orexin A on glucose-dependent insulinotropic polypeptide plasma concentrations in pigs, and examined whether these changes are related to the possible effect of the neuropeptide on the enteroinsular axis.
ROLE OF SULPHATED POLYSACCHARIDES FROM SARGASSUM WIGHTII IN THE CONTROL OF DIET-INDUCED HYPERLIPIDEMIA AND ASSOCIATED INFLAMMATORY COMPLICATIONS IN RATS

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Hypercholesterolemia and associated cardiovascular complications continue to occur in a great number of people. However, certain coastal populations have lower incidence of cardiovascular and other diseases, which may be attributed to regular intake of seaweeds in their diet. Seaweeds contain sulphated polysaccharides (SPS) which demonstrate a wide spectrum of biomedical properties and are phytochemical analogues of mammalian heparin sulphate. This knowledge served as the major impetus for exploring the therapeutic potential of SPS from the brown algae Sargassum wightii and SPS from Fucus vesiculosus in experimental rats against diet-induced hyperlipidemia and associated inflammatory complications. Adult male Wistar rats were divided into six groups with six rats in each. The control group (group I) was left untreated while group II rats were fed with a high cholesterol diet (CCT diet – normal rat chow with 4% cholesterol, 1% cholic acid and 0.5% thiouracil) for 14 days. Rats in groups III and IV received SPS from S. wightii (SW group) and SPS from F. vesiculosus (FV group) (5mg/kg b.wt/day, subcutaneously) during the last 7 days, respectively. Rats in groups V and VI were fed with a high cholesterol diet for 14 days and in addition were given SPS from S. wightii (CCT + SW group) and SPS from F. vesiculosus (CCT + FV group) at the weight of 5mg/kg b.wt/day, subcutaneously during the last 7 days, respectively. The adverse effects of hypercholesterolemia were evident from increased levels of serum lipid status and inflammatory complications manifested by augmented levels of plasma tumour necrosis factor-alpha (TNF-alpha), C-reactive protein (CRP), fibrinogen, inducible nitric oxide synthase (iNOS), nitric oxide (NO), cyclooxygenase (COX-2) and lysosomal enzymes. Treatment with algal SPS considerably restored the above abnormalities. SPS from S. wightii and SPS from F. vesiculosus were almost equally effective in mitigating hypercholesterolemia and related inflammatory complications.
ELISPOT AND ELISA ASSESSMENT OF INTERFERON-GAMMA AFTER SUBLINGUAL IMMUNOTHERAPY

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Allergic rhinitis (AR) is characterized by a Th2 polarized immune response, and specific immunotherapy modifies this arrangement, restoring a physiologic Th1 profile. Sublingual immunotherapy (SLIT) is widely prescribed. The aim of the study is to evaluate two different methods for assessing IFN-γ, namely ELISPOT and ELISA, before and after a pre-seasonal SLIT course as marker for Th1 response. Thirty-eight AR patients with pollen allergy assumed pre-seasonal SLIT for 3 months. Patients’ blood samples for assessing IFN-γ serum levels were collected before initiating SLIT (baseline – T0), after 3 months pre-seasonal SLIT course (T1), and three months after completion of SLIT (T2). IFN-γ-specific producing cells, after allergen stimulation, were assessed by cytokine ELISPOT at the same time points. IFN-γ-specific producing cells significantly increased after SLIT both at T1 and T2 (p=0.0002). On the contrary, ELISA assessment did not reveal an increase in IFN-γ serum levels at any time point. In conclusion, these results demonstrate that ELISA assessment of serum IFN-γ is not suitable for identifying an early response.
The observation of the ciliated cell dynamics by phase-contrast microscope has allowed a profound study of some parameters of the cellular components. The aim of this preliminary study is to assess the surviving time of ciliary cells using the phase-contrast microscope. Nasal cytology was carried out on 50 healthy volunteers. The ciliary beat time was assessed by a video-camera connected with a PC. The time of ciliary beat persistence was extraordinarily long (mean 210 minutes, with range 74 -1260). The ciliary activity remained valid as rhythm, synchronism and metachronality. In conclusion, this preliminary study demonstrated that cilia has an energetic autonomy of great importance, able to allow a valid functional activity also in the case of partial sufferance of the cellular unit.
LETTER TO THE EDITOR

USEFULNESS OF IFN-GAMMA RELEASE ASSAYS IN CLINICAL MANAGEMENT OF DIFFICULT TB CASES: EVIDENCE FROM CLINICAL PRACTICE

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Performance of T-SPOT.TB™ (TS-TB) and QuantiFERON TB Gold-In tube (QFT-IT) assays was evaluated for detection of M. tuberculosis (Mtb) infection in patients with suspected extra-pulmonary or smear-negative pulmonary tuberculosis (TB) in a low prevalence country. Twenty-one out of 35 patients were affected by active TB. Mtb culture isolation was achieved in 76% of cases. Tuberculin skin testing (TST), TS-TB, and QFT-IT yielded a positive result in 67%, 95% and 81% of cases, respectively. Agreement of interferon-γ release assays and TST was 70% (κ=0.18 for TS-TB; κ=0.46 for QFT-IT). Increased sensitivity of blood assays (>80%) improved diagnostic evaluation of difficult TB cases.
Inflammatory chronic diseases involving joints together with other organs are usually treated with a systemic approach. In a few cases, where arthritis is not responsive to traditional treatments, an intra-articular (I.A.) therapy could be useful. Furthermore, patients not eligible for systemic therapy with anti-TNF or other DMARDs, as well as patients with an initial arthritis with the involvement of a single joint, such as the knee or hip joint, could use the I.A. injection therapy. In this article we report our experience with five patients affected by rheumatic inflammatory diseases, not responding to traditional systemic DMARDs-based therapies or not eligible for systemic use of biological response modifiers who underwent ultrasound-guided I.A. injection of Infliximab. Three of 5 patients showed a positive and long-lasting response to treatment with local Infliximab. Safety profile was good according to literature data. Moreover, in this article we review the literature on this therapeutic approach. This is the first report of I.A. use of Infliximab in the hip joint.