



conference

Anti-Inflammatory Drugs

Pasteur Institute

October 6 - 7, 2005

Inflammation and anti-inflammatory drugs: general presentation

R J Flower

Biochemical Pharmacology, William Harvey Research Institute, Charterhouse Square, London EC1M 6BQ

Inflammation is one of the oldest afflictions of mankind and was recognised and documented by ancient physicians of all cultures. Likewise, most early pharmacopoeias contained an abundant selection of putative anti-inflammatory substances derived from herbs, mineral or animal extracts. Whilst most of these have proved to be ineffective, some form the basis of our present battery of anti-inflammatories. In this connection one thinks particularly of the plants which we now know to contain salicylic acid, many of which were mentioned in ancient pharmacopoeias or herbals. The story of how these extracts were transmuted into the drug aspirin, and the subsequent development from this of a range of NSAIDs and more latterly, COX2 inhibitors, will form part of the substance of this lecture.

The clinical use of the other major group of anti-inflammatories, the glucocorticosteroids had a different origin. It was the clinical trial of cortisone, by Hench in 1949, which initiated the era of glucocorticoid pharmacology. Over the years...

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Evaluation of Statin in Decreasing the Early Mortality and Morbidity of Acute Coronary Syndrome A Clinical Trial in Shaheed Rajaie Cardiovascular Medical and Research Center

Dr Pascal Eschwege

Department of Urology Hôpital Bicêtre, Le Kremlin Bicêtre, France

Synthetic anti-inflammatory drugs include traditional anti-inflammatory drugs such as non steroidal anti-inflammatory drugs (NSAID) but also new compounds such as cyclooxygenase/lipoxygenase inhibitors, nitric oxide-releasing NSAIDs and others.

NSAIDS are among the most widely prescribed drugs over the world. Through their anti-inflammatory they represent a choice treatment in various inflammatory disease such as arthritis, rheumatism as well as the aches and pain of everyday life. However their use is often limited by the side effects they produce...

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Mechanisms of Action of the Biological Anti-Inflammatory Drugs

Pr Pierre Miossec

Department of Immunology and Rheumatology, Hôpital Edouard Herriot, 69437 Lyon Cedex 03

Anti-TNF- α therapy has shown clear efficacy in the treatment of Rheumatoid Arthritis (RA). A similar benefit was also observed in other forms of arthritis, in psoriasis and in Crohn's disease where clinical expression, anatomical distribution, underlying mechanisms are very different. This indicates that a large proportion of these mechanisms largely responsible for the clinical expression, are in fact non-specific.

The long list of possible targets complicates the interpretation if one wants to take into account each factor. If the discussion is limited to the so-called pro-inflammatory cytokines, this group includes in addition to TNF α and IL-1, IL-6, IL-12, IL-17, IL-18, IL-21, IL-23, to limit the list to interleukins. The easiest way to understand the positive clinical effect of a single inhibitor is to consider that cytokines interact as a team. The concept would be the same when applied to a football team or a working team. The total effect or productivity of a team is not only the sum of the individual contribution / effort of each member. It rather reflects the interaction between each team member inside the team and with the outside world. A team has to have a leader but a leader alone has limited effect compared to that of the whole team...

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Latest advances in the anti-inflammatory treatment of rheumatoid arthritis

J Morel and B Combe

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Rheumatoid arthritis (RA) is characterized by a chronic inflammation of joints leading to a progressive and irreversible joint destruction. The efficacy of anti-rheumatic drugs (DMARDs) such as methotrexate, leflunomide or salazopirine has been demonstrated, but successful treatment of RA depends on an early initiation. Basic research and the resulting better understanding of mechanisms of inflammation, allowed the identification of new targets and the design of novel biologic agents, such as TNF antagonists. Although the etiology of RA remains incompletely defined, much progress has been made recently in the comprehension of mechanisms leading to joint inflammation. In the joint (of RA patients?), the aggressive front of synovial tissue, called pannus, invades and destroys local articular structure. The pannus is characterized by a synovial hyperplasia that is mainly composed of fibroblast like synoviocytes (FLS) combined with a massive infiltration of lymphocytes and macrophages. There are many evidences that RA is an auto-immune disease due to an unidentified antigen. This includes the presence of activated T cell in the synovial (fluid?) of RA patients, auto-antibodies such as rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP) in their serum and is the association of certain HLA class II genes which code for a molecule directly involved in antigen presentation. One therapeutic strategy, therefore, consists in targeting cells B or T cells...

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Latest Advances in the Anti-Inflammatory Treatment of Inflammatory Bowel Disease

Dr. Gerd Bouma

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The inflammatory bowel diseases (IBD), Crohn's disease and ulcerative colitis, are chronic inflammatory disorders of the gastrointestinal tract that are most likely due to a dysregulated mucosal immune response to the endogenous mucosal microflora. Enormous progress has recently been made in the understanding of these diseases through the study of murine models of mucosal inflammation and by the evaluation of patients for their patterns of cytokine production. It has emerged that Crohn's disease is a Th1- inflammation driven by IL-12 and IFN- γ , whereas ulcerative colitis is most probably a Th2- inflammation driven by IL-13. A second area of progress is in the identification of specific genetic abnormalities responsible for disease. The new data in this area has come both from the study of murine models of inflammation and from genome wide searches in patients. The most important finding is that some 20% of Crohn's disease is due to a recessive mutation in NOD2/CARD15, an intra-cellular sensor of peptidoglycans. The recent immunologic and genetic insights concerning IBD pathogenesis provide a roadmap for new therapeutic approaches to these diseases. Traditional treatment of IBD is based on aminosalicylates and steroids...

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Inflammation and atherosclerosis

Mustapha Rouis

*nuclear receptors, lipoproteins and atherosclerosis.- Institut Pasteur de Lille
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Atherosclerosis is the principal cause of death in developed countries. Over the years, much attention has been focused on the contributions of abnormal lipid metabolism and vascular wall injury to the atherosclerotic process. Thus, atherogenesis has been inversely related to the high density lipoprotein concentration. However, atherosclerosis is also associated with oxidation phenomena and with a cellular immune response in the arterial lesions and a humoral immune response directed towards oxidized lipoproteins, certain microbes and other antigens.

Initial injury of the arterial endothelium, in response to cardiovascular risk factors, results in endothelial dysfunction, such as increased adhesiveness (increase of E-selectin, P-selectin, ICAM-1 and VCAM-1 molecules) and permeability of the endothelium, and formation of vasoactive molecules, cytokines, chemokines and growth factors. Such inflammatory responses stimulate recruitment of monocytes to the endothelium, and migration and proliferation of smooth muscle cells to form the initial atherosclerotic lesion. Atherosclerotic lesions begin as fatty streaks underlying the endothelium of large arteries. Recruitment of monocytes, their subsequent differentiation into macrophages and their uptake of low density lipoprotein (LDL)-derived cholesterol are cellular events contributing to fatty streak formation, which is driven by oxidative modifications in components of LDL. Progressive accumulation of macrophages and their uptake of oxidized LDL lead to development of the lesions. Thus, the development of macrophages 'foam cells' that contain massive amounts of cholesterol esters is a characteristic of the atherosclerotic plaque. This phase of lesion development is influenced by interactions between monocytes/macrophages and T cells that result in a broad range of cellular and humoral responses and the acquisition of many features of a chronic inflammatory state. Inflammation plays also a major role in atherosclerotic plaque disruption and thrombosis.

Myocardial infarction results from acute coronary thrombosis caused by erosion or rupture of coronary atheroma, particularly at sites of thinning of the lesion's fibrous cap of a vulnerable atherosclerotic plaque. Plaque rupture is associated with a large lipid core, a thin fibrous cap and an excess of inflammatory cells over vascular smooth muscle cells (SMC)...

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Oxidative Stress and Inflammation: What Roles for Antioxidants as Anti-Inflammatory Drugs?

Dr Marvin Edeas

French Society of Antioxidants, Paris, France

The evidence of the presence of an imbalance between oxidants and antioxidants or oxidative stress in various diseases is now overwhelming. There is also now good evidence that oxidative stress may have a role in many of the injurious and inflammatory events which occur as part of the pathogenesis of this condition.

Oxidative stress play a fundamental role in the up regulation of genes for pro-inflammatory cytokines which are important in this condition, but also results in protective mechanisms such as the up regulation of antioxidant enzymes. The central role of the oxidative stress, the tumor necrosis factor- α (TNF- α) expression and protective effects of various antioxidants will be discussed. Activation of the transcription factor NF-Kb by oxidants is critical for the tumor necrosis factor- α (TNF- α)-induced inflammatory response...

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Phenolic Derivatives: A Study On The Relationship Between Structure, Activity And Physicochemical Parameters

F. Borges, R. Calheiros, J.B. Sousa¹, S.M. Fiuza¹, A. Gaspar, N. Milhazes, F. Roleira, E. Tavares da Silva, J. Garrido, E. Garrido, C. Siquet, S. Reis, L.A.E. Batista de Carvalho, M.P.M. Marques

Polyphenols, bioactive substances commonly found in plants, are reducing agents supposed to be involved in the defence against oxidative damage, due to their antioxidant and radical scavenging properties. Phenolic derivatives and flavonoids were shown to display remarkable anti-inflammatory and growth-inhibition properties towards human cancer cell lines. Nevertheless, the mechanisms underlying the protective action of phenolic compounds towards these pathologies are not yet completely understood, although numerous evidences indicate that they are strongly dependent on their structural characteristics. In the last few years, this subject has become an emergent topic of research, in view of developing new and more effective phenolic agents to be used for therapeutic purposes...

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Side Effects Of Anti-Inflammatory Drugs

John L. Wallace

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The use of nonsteroidal anti-inflammatory drugs (NSAIDs) has been primarily limited by their toxicity in the gastrointestinal tract, but these agents can also produce severe side effects in the renal, hepatic and cardiovascular systems. The recent withdrawal of two selective COX-2 inhibitors has focused attention on the cardiovascular adverse effects of NSAIDs. All NSAIDs, regardless of selectivity for COX-1 versus COX-2, cause small, but clinically significant increases, in systemic blood pressure. Even these small changes can result in substantial increases in the incidence of stroke. The gastrointestinal toxicity of NSAIDs is closely linked to their ability to suppress mucosal prostaglandin synthesis. Both COX-1 and COX-2 are important sources of gastroprotective prostaglandins. Indeed, selective inhibition of one isoform does not result in significant gastric damage -- it is necessary to inhibit both isoforms for mucosal ulceration to occur. The renal toxicity of NSAIDs, like that in the GI tract, appears directly linked to the suppression of prostaglandin synthesis.

The cardiovascular toxicity of selective COX-2 inhibitors exceeds that of conventional NSAIDs. This appears to be related to the ability of these agents to suppress systemic prostacyclin synthesis while not affecting platelet thromboxane synthesis.

Nitric oxide-releasing NSAIDs have been shown to exhibit markedly less GI toxicity than conventional NSAIDs. Moreover, unlike...

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How can we evaluate the efficiency of an anti-inflammatory drug ?

Jean-Pierre Pujol

Laboratory of Connective Tissue Biochemistry, Faculty of Medicine – 14032 CAEN Cedex, France

One of the greatest unmet medical needs is the effective treatment of inflammatory and autoimmune diseases. These diseases are currently being treated with relatively old drugs such as the nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids and methotrexate, which have limited efficiency and/or inadequate safety profiles. Inflammation is one of the most important processes involved in the defence of an organism ; however, it often progresses to painful or chronically harmful diseases needing pharmacological treatment. Most immunoinflammatory diseases are characterized by an abnormal accumulation of inflammatory cells (including T lymphocytes, plasma cells, monocytes/macrophages, neutrophils and platelets) that, along with tissue endothelial cells and fibroblasts, release a complex array of arachidonic acid derivatives : prostaglandins (particularly PGE₂), thromboxanes and leukotrienes, together with cytokines, growth factors, oxygen and nitrogen radicals (reactive oxygen species, ROS) and destructive enzymes that cause local damage and sometimes proliferation and fibrosis.

The NSAIDs, or aspirin-like drugs, which have been used since the introduction of acetylsalicylic acid into medicine in 1899, are an heterogeneous group of compounds which share many pharmacological properties, particularly their inhibitory effect on the cyclooxygenase (COX) activity, which are involved in the formation of prostaglandins and thromboxanes. Until recently, there has been no firm evidence that suggested that NSAIDs could act through any other mechanism than their ability to block cyclooxygenase and, with time, this property has become a sort of dogma in our notion of NSAID mechanism...

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When inflammation leads to cancer

Alain Chariot

Laboratory of Medical Chemistry, CTCM, University of Liege, CHU, Sart-Tilman, 4000 Liege, Belgium

Chronic inflammatory diseases and cancer are characterized by many constitutively activated signalling pathways that cause the aberrant expression of cytokines, chemokines and anti-apoptotic genes. Among these signalling pathways, the ones that lead to NF- κ B activation appear to play a critical role in these diseases.

NF- κ B is a ubiquitously expressed family of transcription factors controlling the expression of numerous genes involved in inflammatory and immune responses. Deregulated NF- κ B is a hallmark of solid and haematological malignancies as well as inflammatory diseases. We will show how NF- κ B is activated in response to pro-inflammatory cytokines and TLR ligands and which genes are regulated by this transcription factor in normal cells. Moreover, we will highlight the molecular mechanisms underlying constitutive and deregulated NF- κ B activation and will...

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Anti-Inflammatory Drugs and Neurodegenerative Diseases

Jari Koistinaho, A.I. Virtanen

Institute for Molecular Sciences, University of Kuopio, Kuopio, Finland

Inflammation has emerged as a significant pathogenic factor in most if not all neurodegenerative diseases. While inflammatory responses such as infiltration of leukocytes and activation of microglia are beneficial to the extent that they destroy CNS pathogens and degrade irreversibly injured tissue in the central nervous system, they have the potential to exert neurotoxic functions. Currently, anti-inflammatory therapies are considered as treatments of many neurodegenerative diseases, including multiple sclerosis (MS), Parkinson's disease (PD), Alzheimer's disease (AD), Huntington's disease (HD) and amyotrophic lateral sclerosis (ALS)...

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Anti-inflammatory drugs and dermatological disease

Christopher EM Griffiths

Dermatology Centre, The University of Manchester, Manchester, UK

A major advance in the management of inflammatory disease has been the introduction of biological therapies (biologics). Biologics for therapy of inflammatory disease were pioneered in the management of arthritis and inflammatory bowel disease although trials of biologics in dermatology have been limited predominantly to psoriasis. There are two main approaches: T-cell-targeting and cytokine modulation. T-cell-targeted approaches include alefacept and efalizumab. Alefacept, an LFA-3 fusion protein and efalizumab, an anti-CD11a antibody, are effective in 25% of patients with psoriasis. They appear safe in the medium term and in the case of alefacept may induce long-term remission in some patients; efalizumab has been used continuously for more than 3 years. Cytokine modulation includes inhibition of proinflammatory cytokines such as TNF, eg infliximab, etanercept and adalimumab, or cytokine switching with a Th2 cytokine such as IL-4. The TNF-targeted biologics are effective also for psoriatic arthritis. Infliximab is particularly effective over the short-term in that >80% of patients with psoriasis are significantly improved within 10 weeks. Some biologic approaches such as those targeting adhesion molecules, eg anti-E-selectin, appear ineffective; these anti-selectin approaches may be better utilised in maintenance of psoriasis once cleared with a fast-acting therapy...

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Anti-Inflammatory Drugs and Veterinary Medicine

F. Thoulon

DVM - R&D Project Manager Research Centre, Vetoquinol SA, Magny-Vernois, 70204 Lure

Over the last 10 years, pain management has become one of the high-profile topics in companion animal medicine, making veterinary analgesics for small animals one of the fastest growing segments of the animal health market. In 1996, the total market for veterinary analgesics (excluding nutraceuticals) was about \$40 million, of which less than \$10 million were used in small animals. In 2004, small animal product sales had grown to about \$190 million, over 90% of which being NSAIDs.

However, there are still a significant population of dogs and cats with painful conditions that do not benefit from pain management: 40% of dogs diagnosed with osteoarthritis, one third of dog neuter surgeries and one half of cat neuter surgeries do not receive a specific pain management. Moreover, just like paediatric patients, veterinary patients do not always clearly express or quantify their pain, making it sometimes difficult to recognize and evaluate. Objective assessment needs specific validated tools (VAS, scoring system...), which are still lacking.

Another difficulty in the field of developing AIDs for animals is the number of different species, all of which reacting differently (pharmacokinetics, pharmacodynamics, metabolism...). Extrapolating data from one species to another can be quite hazardous, especially with regards to toxicity.

The availability of veterinary AIDs is restricted by regulatory aspects: just like for human drugs, veterinary drugs has to be registered by specific authorities (EMEA/CVMP in Europe, FDA/CVM in the USA). The registration dossiers are based on the same requirements: quality (for both API and final product), safety (in the target species but also for the final user, i.e. the animal's owner) and efficacy. The only specific veterinary matter is the residue part (IIB) for drugs intended for use in food-producing animals, designed to assess the potential

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Natural Anti-inflammatory Drugs: Recent Developments

Thomas Simmet

Natural Anti-inflammatory Drugs: Recent Developments

Despite the advances of combinatorial chemistry natural products remain a major source of innovative therapeutic agents for numerous ailments including infectious diseases, cancer, lipid disorders, inflammation and immunomodulation. Further, they serve as lead compounds for drug development and have proven to be invaluable biochemical tools for the identification of novel biological targets.

Recently, the nuclear factor κ B (NF- κ B) has gained much attention because deregulation of NF- κ B and I κ B phosphorylation is a hallmark of chronic inflammatory diseases and cancer. Indeed, the transcription factor NF- κ B integrates multiple signals that are involved in inflammation, angiogenesis, cell migration and proliferation as well as survival. The expression of various proinflammatory genes encoding adhesion molecules and cytokines, but also of antiapoptotic genes is regulated by the transcription factor NF- κ B. Therefore, NF- κ B serves as an important molecular switch leading to chronic inflammation and the development of various cancers. In addition, recent data on colitis- and hepatitis-associated cancer in mice provide molecular evidence that the clinically well-known link between inflammation and cancer development might at least partially be based on constitutive NF- κ B activation. On this background correction of the aberrant and persistent...

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Systemic low dose antisense delivery and anti-inflammatory effect using Smarticles® vectors

Dr. Una Rauchhaus

Novosom AG, Germany

CD40, while being a well described target for the initiation and propagation of immune responses, was found to resist antisense or siRNA approaches in animals so far. We here for the first time describe the specific down regulation of CD40 protein expression in a therapeutic setting using the Smarticles® technology as a carrier system for antisense oligonucleotides (ASO).

A specific ASO directed against rat CD40 was validated first in vitro. Smarticles formulated CD40 ASO, but not free ASO was found to be preventive as well as therapeutic after local application in models of Inflammatory Bowel Disease. We observed high therapeutic activity using minute amounts of the formulated drug and found no activity in scrambled or unformulated controls.

Moreover, we for the first time were also able to systemically delivery CD40 antisense using the Smarticles® class of vectors. In models for rheumatoid arthritis, we achieved significant inhibition of inflammation and destruction with CD40 ASO formulated in Smarticles. Again, free antisense was inactive, even at high amounts.

The presentation will highlight the Smarticles® system as a general tool for the delivery of oligonucleotides, opening the door towards product development based on these classes of drugs...

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Signaling Pathways and the Future of Anti-inflammatory Drugs

Alan J. Lewis

Signal Pharmaceuticals, Celgene, San Diego, CA

The therapeutic success of biologics to modulate inflammatory cytokines such as TNF alpha, IL-1 and IL-6 has resulted in numerous attempts to discover and develop small molecules capable of replicating their successes. Signaling pathways have provided fertile ground for this approach with special attention to MAK kinase pathways such as p38 and JNK as well as targeting NFkB and additional kinase targets recently shown to play important roles in cytokine modulation. Modulation of cyclic AMP via PDE4 has also shown considerable promise. Numerous additional small molecules including corticosteroids as well as analogues of thalidomide also are capable of controlling cytokine production. It is anticipated that many of these approaches will compliment and maybe even replace the currently used anti-inflammatory agents in current clinical use...

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Anti-Inflammatory and Anti-Arthritic Activity of 2-Methoxyestradiol In A Rat Model Of Collagen-Induced Arthritis

Dr. Ernest Brahn

UCLA School of Medicine, Los Angeles, CA; 2EntreMed, Inc., Rockville, MD USA

Objectives.

2-Methoxyestradiol (2ME2) has antiproliferative, proapoptotic, and antiangiogenic activity. It is currently in oncology clinical trials as Panzem®. 2ME2 may have a role in the treatment of non-oncologic diseases, such as rheumatoid arthritis, in which angiogenesis is an integral component. Preliminary studies in the murine Arthrogen-CIA® model demonstrated that 2ME2 inhibited inflammation and disease progression. In the current study, 2ME2 was assessed in the rat collagen-induced arthritis (CIA) model of chronic autoimmune inflammatory joint disease.

Methods.

Syngeneic rats (n=66) were immunized on day 0 with native type II collagen and randomized to one of six protocols: prevention arms (initiated on day 0 with either 30mg/kg or 100mg/kg); treatment arms (beginning on the day 10, arthritis onset, with 10mg/kg, 30mg/kg, or 100mg/kg); or vehicle arm. All doses were given daily by gavage. Hindlimbs were scored each day for clinical arthritis severity using a standardized method based on the degree of joint inflammation. High resolution digital radiographs of hindlimbs were obtained at the conclusion of the study (day 28) as were serum IgG antibodies to the relevant antigen, native type II collagen.

Results...

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Inhibition of acute and chronic lung inflammation by a novel PDE 4 inhibitor

Isabelle Couillin, Caroline Mary, Isabelle Maillet, Bernhard Ryffel, Philippe Bernard

CNRS, IEM2815, and Green Pharma, SA, Orleans, France

Chronic obstructive pulmonary disease (CPOD) and allergic asthma are major causes of chronic illness and mortality and there is a major medical need to have more efficacious therapies. GP0203, is a novel specific PDE IV inhibitor, which inhibits the production of TNF by LPS stimulated human monocytes in culture in the nM range. We tested the in vivo inhibitory effects of intranasally administered GP0203 in acute and chronic inflammatory models in mice. First, GP0203 inhibited acute LPS-induced airway resistance and neutrophil recruitment into the lung at 10 µg per mouse. Second, GP0203 reduced acute and chronic inflammation induced by bleomycin which models chronic obstructive pulmonary disease (COPD). Third, GP0203 attenuated bronchial hyperreactivity and eosinophil recruitment in a model of antigen induced allergic asthma. The preliminary data suggest that GP0203 is highly effective in three different inflammatory models in vivo and may have a therapeutic potential in COPD and allergic asthma...

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**Evaluation of Statin in Decreasing the Early Mortality and
Morbidity of Acute Coronary Syndrome
A Clinical Trial in Shaheed Rajaie Cardiovascular Medical and Research
Center**

**Shahmohammadi Mousavi A.MD, Peighambari MM. MD, Madani M. MD, Zafaranloo N.
MD**

*Shaheed Rajaie Cardiovascular Medical and Research Center, Tehran, Iran & Iran University of Medical
Science, Tehran, Iran*

Lipid lowering therapy with statin reduces the risk of cardiovascular events in acute coronary syndrome (ACS). Preclinical and clinical evidence also indicates that, in addition to their lipid lowering effects, statin may reduce inflammation, improve endothelial function and increase plaque stability.

Methods:

We enrolled 220 patients who had been hospitalized for an acute coronary syndrome (Unstable angina, Non STE MI) within the preceding 30 days and compared 20 mg of Simvastatin daily (B group) with patients haven't received that (A group). The primary end point was; a composite of deaths, myocardial infarction, documented unstable angina requiring rehospitalization, revascularization (Performed at least 30 days after randomization) and stroke. Follow up lasted one month....

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Modulation Of Human Lymphocyte Functions In Vitro By A Prostanoid Ep2 Receptor Agonist

J.G. Zhang, R. L. G. Sheldrick, M. Ali, R. A. Borman and K. L. Clark

Pharmagene Laboratories Ltd, Royston, SG8 5HD, UK

Prostaglandin E2 (PGE2) exerts its functions in multiple target tissues via the stimulation of four subtypes (EP1-4) of receptor. The engagement of PGE2 with its receptors can result in pro-inflammatory as well as anti-inflammatory responses, depending on the type of receptors present in target tissues. Experimental evidence from animal models and a limited number of human subjects has indicated an anti-inflammatory role of EP2 receptor activation, but more data are needed in support of its utility in anti-inflammatory therapeutics in man. Therefore, we examined the effects of PGE2 and the EP2 receptor selective agonist, butaprost, on the proliferation of and cytokine production by human peripheral blood lymphocytes stimulated by anti-CD3 antibody...

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Conference Registration

Paris Anti-Inflammatory Drugs - 6,7 october 2005

To register, please fill in this form and return it by regular mail to the Paris Anti-Inflammatory Drugs 2005 secretariat :
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anti-inflammatory2005@wanadoo.fr - <http://www.isanh.com>

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Cancellation policy :

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Cancellations of registration received one month before the conference date will be refunded minus 350 Euros administrative charges.

For cancellations received after this date, no refund can be made. All refunds are settled after the conference.

