

Summaries of the chapters

Summary

William M. Selig, Eric T. Whalley and James L. Ellis

Asthma

Asthma is predominantly a chronic inflammatory condition of the lower airways characterized by varying degrees of airway obstruction or hyperresponsiveness and long-term ultrastructural abnormalities which may mitigate the effectiveness of some of the currently available therapies. These structural changes (airway edema, airway epithelial sloughing, increased airway wall thickening, extracellular matrix abnormalities, and increased airway vascularity) ultimately contribute to airway remodeling and fibrosis. The dominant inflammatory cells responsible for the pathogenesis of asthma include the T cell, mast cell, eosinophil, basophil, and macrophage. Experimental evidence continues to be assimilated using various *in vivo* animal models (from mouse to primate) to explore the pathogenesis of asthma. There has been a relative explosion in areas such as genomics, bioinformatics, and molecular pharmacology to help us to better understand these various animal models and apply this understanding to the human condition.

This chapter highlights and pay particular attention to the following with respect to animal asthma models: 1) introduction of any new models or procedural changes within existing models, 2) new insights into pathogenesis or pathophysiology provided by the respective animal models of asthma, and 3) novel pharmacological approaches or new drugs tested in these models. While relatively few new therapeutics have been introduced in this area in recent years, use of some of the animal models of “asthma” discussed herein provide researchers with useful *in vivo* models to explore important components of the human asthmatic response and may foster the further development of novel, anti-inflammatory therapeutic approaches to treat this debilitating disease.

Keywords: airway hyperresponsiveness; fibrosis; remodeling; house dust mite; transgenic; SCID; mucus; bronchoalveolar lavage; chemokine; cytokine; T cell; dendritic cell; immunomodulatory; phosphodiesterase; eosinophilia; ragweed

Summary

Christopher S. Stevenson and David C. Underwood

In vivo modelling systems for chronic obstructive pulmonary disease

COPD is a smoking-related disorder that is the 4th leading cause of death worldwide for which no effective therapies exist. The disease is characterized by an accelerated rate of age-related lung function decline due to structural changes in the lung consisting of mucus hypersecretion, airway remodelling (eg., fibrosis), and emphysema. These changes are believed to result from the persistent, abnormally elevated inflammation that is a hallmark of the disease. While no single animal model replicates the degree of lung destruction observed in the human disease condition, there are models that can mimic many of the same types of pathologies using disease-relevant agents. This chapter focuses on recent advances in two classic modelling systems which use elastase or cigarette smoke to replicate the destructive pathologies associated with COPD. In addition, a short review of transgenic mouse models that resemble pathological aspects of COPD is also included. The combination of new

pharmacology and the use of genetically modified mice in these models highlight and provide new insights into the role of inflammation in molecular pathogenesis of COPD.

Keywords: COPD, cigarette smoke, elastase, emphysema, mucus, fibrosis, oxidant stress, protease, IL-1beta, IFN-gamma

Summary

Azzeddine Dakhama and Erwin W. Gelfand

Murine models of allergen-induced airway hyperresponsiveness and inflammation

Asthma is a complex syndrome shaped under the influence of genetic and environmental factors. Despite intense research, effective therapies to prevent its development or to interrupt its progression are still lacking, and for many asthmatics conventional therapy fails to prevent the progressive loss of lung function. To some extent, this failure reflects the absence of full understanding of the mechanisms underlying asthma pathogenesis. Because of these deficiencies and intrinsic differences, human asthma remains difficult to model in its entirety in laboratory animals. Nonetheless, considerable progress is being made using murine models mimicking allergic inflammation and airway hyperresponsiveness, the hallmarks of bronchial asthma. For the most part, these models allow for testing hypotheses and defining potential mechanisms that may lead to development of novel therapies.

Key words: Murine models, asthma, allergen, airway hyperresponsiveness, airway inflammation, Asthma, the human disease

Summary

Lawrence S. Chan

Skin inflammatory disorders

In this chapter, animal models of two common, chronic, inflammatory skin disorders, atopic dermatitis and psoriasis, were described and their potential utility for understanding pathophysiology of the diseases and for pre-clinical investigation of candidate drug efficacy were discussed. The basic rationales for selecting these two diseases are that these diseases represent chronic inflammatory skin conditions impacting our society in the most significant way, that the in vivo models of inflammatory skin diseases are most useful to investigate complex biological interactions in diseases of the chronic nature (rather than diseases of the acute nature), and that the included models for these diseases were developed recently (with the earliest atopic dermatitis and psoriasis models developed in 1997 and 1995, respectively) and therefore containing the most updated information. More over, these models, in comparison to prior models, are much closer to the human diseases on clinical, histological, and immunological grounds, therefore they are better models for the purpose of studying the disease mechanisms and of screening new therapeutic candidates.

Keywords: skin, inflammation, atopic dermatitis, psoriasis, cytokines, chemokines, allergens, angiogenesis, vascular endothelial growth factor, T cells, B cells, mast cells, IgE, antigen presenting cells

Summary

Pierangelo Geppetti, Serena Materazzi, Paola Nicoletti and Marcello Trevisani

In vivo models of neurogenic inflammation

The inflammatory response to injury consists of the activation of several local protective mechanisms involving different cellular systems. Among the mechanisms and systems that exert their effects rapidly, peptide transmitters (substance P, neurokinin A and calcitonin gene-related peptide) released from peripheral endings of capsaicin-sensitive primary sensory neurons (evoking neurogenic inflammation) play a major role in the response to tissue injury. Capsaicin-sensitive neurons possess small and dark cell bodies, located in dorsal root, trigeminal and vagal ganglia (C-fibres) and non myelinated or thinly myelinated fibres (A- δ type). Neurogenic inflammation may affect the vascular district where it causes vasodilatation, plasma protein extravasation and leukocyte adhesion to endothelial cells of venules. Extravascular actions mediated by neurogenic mechanisms are bronchoconstriction and bronchorelaxation, increase in seromucous glands secretion and release of mediators from the airway epithelium. Here, we reported a list of experimental approaches for the study of neurogenic inflammation both *in vitro* and *in vivo*.

Keywords: neurogenic inflammation, capsaicin-sensitive neurons, Substance P (SP), Calcitonin gene-related peptide (CGRP), plasma protein extravasation, mucus secretion, bronchoconstriction, neurogenic vasodilatation

Sreekant Murthy

Animal models of inflammatory bowel disease

H. Andreas Kalmes and Christopher F. Toombs

Preclinical models of vascular inflammation

In Vivo Models of Inflammation

Volume 2

Stevenson, C.S.; Marshall, L.A.; Morgan, D.W. (Eds.)

2006, X, 203 p. 19 illus., Hardcover

ISBN: 978-3-7643-7757-1

A product of Birkhäuser Basel