

Application Forum

Discovery of novel therapies for asthma requires suitable and relevant disease models

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INTRODUCTION

There is a major unmet need in the treatment of asthma which is growing in incidence and prevalence in industrialized countries. The prevalence of asthma has doubled in the western world over the previous 20 years due to increased exposure to indoor allergens or workplace sensitizers, more pollution and overuse of beta-2 agonists. These facts highlight the need for novel therapies, which in turn requires suitable disease models.

PASSIVE CUTANEOUS ANAPHYLAXIS MODEL

The rapid passive cutaneous anaphylaxis (PCA) model is a useful initial model for test items believed to work upon mast cells. In 24 h it can reveal whether the therapy is able to prevent the degranulation of mast cells—a major factor in the induction of an asthmatic response. It can be run on a range of species such as mice or rats.

OVA-INDUCED ASTHMA MODEL

The murine OVA-induced asthma model employed by MD Biosciences results in the characteristic features of asthma, such as eosinophilic airway inflammation, airway hyper-reactivity, elevated antigen specific IgE, goblet cell hyperplasia and airway remodeling. All of these aspects are well conserved between animal models and the human situation. In contrast in recent years there has been much discussion as to whether methods of studying lung function in pre-clinical models of allergic lung inflammation are worthwhile. Some researchers maintain that the physiological differences in rodent lung function versus human lungs mean that lung function studies in rodents are meaningless. Despite this the most consistent diagnostic feature of asthma is airway hyper-reactivity (AHR) in response to chemicals such as Methacholine. For this reason, many researchers feel that in order for an asthma therapeutic to be efficacious it must be shown to affect AHR.

Following sensitization and challenge with OVA there is a significant increase in the number of inflammatory cells

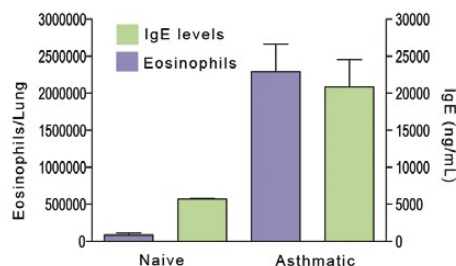


Figure 1. Eosinophils in BAL and serum IgE levels from naive and asthmatic mice.

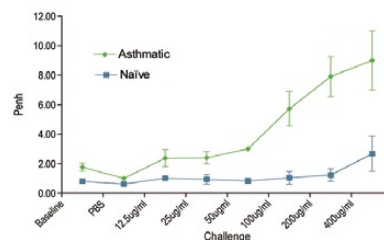


Figure 2. Increased airway hyper-reactivity in naive and asthmatic mice following administration of increasing concentrations of NECA.

found within the bronchoalveolar lavage fluid. Eosinophils predominate the granulocyte response with an increase in T lymphocytes also evident 24 h after the final challenge. The asthma induction process also results in significantly more anti-OVA IgE (Mouse OVA-IgE ELISA, Cat# OVE-IGE96, MD Biosciences, Inc.) in the serum of mice (Figure 1). Lung hyper-reactivity can be studied following aerosol challenge with a range of chemicals such as the mast cell activator NECA (Figure 2). Increasing concentrations of NECA cause increases in the lung hyper-reactivity with the lungs of asthma-induced mice responding to a greater extent than those of naive mice.

FOR FURTHER INFORMATION OR TO DOWNLOAD A WHITEPAPER:

- Passive Cutaneous Anaphylaxis Model
- OVA-induced Asthma Model
- Mouse OVA-IgE ELISA, Catalog # OVA-IGE96

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