Kam et al. Allergy, Asthma & Clinical Immunology 2010, 6(Suppl 3):P3
http://www.aacijournal.com/content/6/S3/P3

ALLERGY, ASTHMA & CLINICAL IMMUNOLOGY

POSTER PRESENTATION Open Access

Functional genomics of the peripheral blood response to allergen inhalation challenge

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From AllerGen NCE Inc.'s Fifth Annual Research Conference: Innovation from Cell to Society
Québec City, QC, Canada. 7-9 February 2010

Objective/purpose

In asthmatic individuals, airway narrowing represents the early phase of the asthmatic response to allergen inhalation challenge, occurring within thirty minutes [1]. In 50-60% of allergic asthmatic adults, the early response is followed by the late phase asthmatic response, usually starting between 3-4 hours after allergen inhalation challenge [2], and characterized mainly by cellular inflammation of the airway [3]. The pathways leading to the late response are not completely understood. Understanding these pathways is important for evaluating allergic diseases such as asthma. In contrast to the more transient isolated early response, development of the late response is associated with the hallmark inflammatory features of chronic allergic disease.

Methods

Nine adult subjects participating in ethically approved allergen challenge studies were recruited following informed consent. Inclusion criteria included non-smokers with stable, mild to moderate atopic asthma, free of other lung diseases. Subjects developing either an isolated early asthmatic response (≥20% drop in FEV1 within 2 hours) or the dual asthmatic response (early response + ≥15% drop in FEV1 between 3-7 hours) were studied. Peripheral blood was drawn just prior to inhalation challenge and 2-3 hours post-challenge. Gene expression analysis was performed using Affymetrix GeneChip® microarrays.

Findings

1783 genes were differentially expressed between pre- and post-inhalation challenge ($p \leq 0.01$). 364 genes remained significant at an FDR of 10%. Within this set, the *DNAJC1* gene (p = 7.2e-5) has been previously identified in a GWAS (genome-wide association study) as associated with asthma. Gene ontology showed perturbed activity in immune system process, mast cell secretory granules and immunoglobulin biosynthesis.

Deliverables

The peripheral blood transcriptome was perturbed between pre-allergen inhalation challenge and 2-3 hours post-challenge, with a focus on immunological functions. *DNAJC1* was identified to be a gene for possible further investigation. Additional recruitment of subjects is underway to identify more specific biological pathways that may be relevant to the onset of the late asthmatic response.

Relevance

This research will act as an initial step in identifying genes and pathways that may be involved in the more clinically severe late asthmatic response that follows the early response in more than half of the asthmatic population. The discovery of these biological pathways will allow for a better understanding of why some individuals develop a dual response instead of an isolated early response. It will also indicate potential therapeutic targets that can be utilized to minimize the late asthmatic response, leading to better treatments for people with asthma and other allergies.

Acknowledgements
We would like to thank the research participants for their involvement in this project. This research is made possible by financial support from AllerGen NCE.

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Published: 26 November 2010

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doi:10.1186/1710-1492-6-S3-P3
Cite this article as: Kam *et al.*: Functional genomics of the peripheral blood response to allergen inhalation challenge. *Allergy, Asthma & Clinical Immunology* 2010 **6**(Suppl 3):P3.