

An investigation of genome-wide transcriptional and methylation profiles in Chinese immigrants to elucidate molecular mechanisms of allergy and asthma

Prevalence patterns for asthma and allergy have consistently been found to be significantly higher in Western countries, including Australia, than in developing countries, such as China, and to be higher in urban than in farming/rural areas [1-3]. These different prevalences cannot be explained by genetic dissimilarity between ancestral populations or rapid genetic changes. Environmental factors inherited in the Western environment/lifestyles through their influences on epigenetic regulation and gene expression, have been proposed to be responsible for this disproportionate prevalence of allergic conditions. Investigating these factors using fresh approaches, such as those proposed in this application, will potentially provide the key to understanding why asthma and allergy are more common in Western countries. This should in turn lead to effective intervention strategies. Chinese immigrants living in an 'experimental environment', the Western environment in Australia, and using their time in years of living in Australia as a dose variable, represents a unique opportunity to examine this study's main hypothesis, that the Western environmental influences have altered epigenetic, and transcriptional (gene expression) profiles in humans and this is the mechanism by which allergy and asthma have increased in countries like Australia.

AIMS

1. To compare genome-wide methylation in newly arrived Chinese immigrants (< 6months) with Chinese immigrants who have lived in Australia (the Western environment) for more than 3 years;
2. To compare genome-wide gene expression in newly arrived Chinese immigrants with Chinese immigrants who have lived in Australia for more than 3 years;
3. To focus on the differences in methylation and transcriptional profiles of asthma candidate genes [4] between the two groups of Chinese immigrants, thereby elucidating the molecular mechanisms of allergy and asthma.

This proposal takes advantage of 'a natural experimental environment' (Western environment) in which Chinese immigrants are living and employs novel high-throughput molecular techniques to investigate the influence of the Western environment on genome-wide methylation and gene expression. This study has the potential to identify genome-wide methylation and gene expression signatures for asthma and allergy. This study also has the potential to identify novel pathogenetic pathways for asthma and allergy by systematically analysing the huge volume of methylation and gene expression data. Ascertaining the role of these underlying mechanisms for asthma and allergy may identify a source of novel and more effective treatments.

Ege, M.J., et al., Exposure to environmental microorganisms and childhood asthma. *N Engl J Med*, 2011. 364(8): p. 701-9.

2. Lai, C.K., et al., Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax*, 2009. 64(6): p. 476-83.

3. Ait-Khaled, N., et al., Global map of the prevalence of symptoms of rhinoconjunctivitis in children: The International Study of Asthma and Allergies in Childhood (ISAAC) Phase Three. *Allergy*, 2009. 64(1): p. 123-48.
4. Vercelli, D., Discovering susceptibility genes for asthma and allergy. *Nat Rev Immunol*, 2008. 8(3): p. 169-82.