AllerGen

Gene-Environment Interactions

BACKGROUNDER

GENE-ENVIRONMENT INTERACTIONS (GxE)

ENABLING PLATFORM

Research Leaders: Drs Jeff Brook and Michael Kobor

OBJECTIVE

Gene-Environment Interactions involves well-established teams of investigators working nationally and globally to apply genetic and environmental research innovation and new knowledge on nature and nurture (epigenetics, maternal-child interactions, lifestyle and stress), with the twin goals of discovering novel therapies and diagnostics, as well as implementing novel public health interventions and policies across AllerGen's Legacy Projects.

NEED FOR RESEARCH

Much is known about allergic diseases, yet there remains considerable unexplained heterogeneity in their patho-genesis. A simple 'one size fits all' management and prevention strategy is thus unlikely to succeed.

A key challenge for this research is to determine how genetics and environmental exposures combine to produce several different allergic disease phenotypes and sub-phenotypes. Meeting this challenge will enable tailored preventive and treatment strategies and maximize the effectiveness and economy of risk reduction strategies to improve quality of life and productivity among Canadians.

The AllerGen Legacy Projects (CHILD, CIC and CanFAST) have great potential to meet this challenge. However, to better enable the Legacy Projects, there is need for a dedicated effort to explore 1) the mechanisms of GxE interactions and 2) the methods for measuring exposures and detecting biological responses.

The real-world complexity presented by multiple, interacting environmental exposures occurring over time and by genetic and phenotypic variability further necessitates the focused research and development being conducted within the GxE Platform.

The work of GxE, its feedback into the Legacy Projects and translation to partners in society at large—such as multiple levels of government, health care practitioners and educators—ultimately will enable tailored preventive and/or treatment strategies for different patients or populations, thus maximizing the effectiveness and economy of risk reduction strategies.

The GxE Platform represents a spectrum of research that is unparalleled. Its aim is to advance a solid understanding of how our genetic make-up and our environment can lead to, and exacerbate, asthma and allergic disease. The new and/or stronger evidence it provides will help us to reduce the burden placed on society by these conditions.

Gene-Environment Interactions Enabling Platform Projects

12GxE1: Better Exposure Avoidance Measures (BEAM) and New Environmental Sensor Tool

(PI: Brook)

Evidence indicates that certain chronic diseases in adults may arise, in part, as downstream health consequences of 'immune deviation' and inflammation first manifested as allergy and asthma in childhood. Identifying these reduction measures is believed to be critical to future disease prevention in Canada and globally.

Development and application of improved exposure measurement tools—the ultimate intended outcome of this project—are essential for this purpose, and will lead to new understanding of asthma and chronic disease, thereby contributing to AllerGen's patient and public health policy imperative.

12GxE2: *Rapid Environmental Effects on Genes: the Lens of Epigenetics*

(PI: Kobor)

This project aims to determine how genetics and environmental exposures combine to produce several different allergic disease phenotypes and sub-phenotypes. Although many environmental exposures have been linked to childhood asthma, research has just begun to unravel how environmental exposures contribute to the developmental origins of asthma and related atopic disorders.

Epigenetics, an emerging interdisciplinary research area, offers a mechanism by which environmental exposures can get "under the skin" to regulate the activity of genes relevant to allergic diseases and asthma. This project has the potential to guide the identification of epigenetic patterns as biomarkers for allergies and asthma in peripheral and accessible tissues, which may also have applications in diagnostics.

12GxE3 - *Allergy-Brain Connection (ABC) Research Team*

(PIs: Kozyrskyj, Letourneau)

The ABC studies examine rates and predictors of stress and depression in a population of ethnically diverse Canadian immigrant women during pregnancy and the postpartum period. They aim to determine the association between maternal stress and depression, on the one hand, and the development of allergic disease and asthma in offspring, on the other. Ensuring that vulnerable, new immigrant women are represented in these studies is a priority of the ABC program of research.

12GxE4 - *Strengthening the Case for Ongoing Reduction of Exposure to Traffic-Related Air Pollution (SCORE-TRAP)*

(PI: Carlsten)

This research team is interested in children because of their particular vulnerability to air pollution due to rapid lung growth. The research team created the Traffic, Asthma, Genetics (TAG) study, an epidemiological effort combining seven international birth cohorts, involving over 20,000 children. The aims of this study include testing specific pharmacological regimens for prevention of clinically-relevant airway effects induced by TRAP-allergen co-exposure as well as developing policy recommendations that reflect the hypothesized lowering of threshold effects due to TRAP.

The experimental approach of this study is ideal for understanding the mechanisms by which TRAP may worsen the lung's response to allergen exposures. The ubiquitous nature of the population exposure to TRAP, coupled with the current evidence of its impacts, strongly suggests that public health benefits can be realized by minimizing exposure. This could be achieved through reductions in emissions through newer vehicles and fuels, or changes in urban structure to minimize the length of time people are in or near heavy traffic.