



Programme B: Diagnostics and Therapeutics
Research Workshop on
Mind-Body Interactions Research Workshop

Post-Workshop Report

Re: Workshop held
December 10-11, 2008
Inn at the Forks
Winnipeg, Manitoba

February 2009

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Executive Summary

AllerGen NCE Inc. (AllerGen) is one of 15 Networks of Centres of Excellence supported by the federal government to foster partnerships between university, government, industry and not-for-profit organizations that help turn Canadian research and entrepreneurial talent into economic and social benefits for Canadians.

On December 10-11, 2008, AllerGen Programme B: Diagnostics and Therapeutics Research Leader, Dr. Dean Befus and Dr. Anita Kozyrskyj, both from the University of Alberta, hosted a strategic planning workshop in Winnipeg, Manitoba. This workshop provided investigators working on projects aligned with AllerGen's Mind-Body Interactions and Allergic Disease research thrust an opportunity to report on their research progress and identify and prioritize future directions for high impact research investments aligned with potential for social and economic impact.

The workshop was attended by 24 participants, comprising researchers, research trainees, research administrators, policy makers and the Scientific Director of AllerGen NCE Inc.

Numerous strategic opportunities were identified by workshop participants in mind-body research related to health and allergic diseases. These opportunities fell into four overarching categories of research that could be developed into programmatically linked projects:

1. Biomarkers – Build on AllerGen's existing cellular and molecular mechanisms, neuroimmunology and neuroendocrine immune regulation research and CHILD Study data and sample collection, work across levels with animal and human models to identify the causes of allergic disease, and develop new diagnostics and therapeutics
2. Epigenetic analyses – Build towards the development of a national epigenetic core technologies analysis platform in Canada that facilitates the development of diagnostic tools and new therapeutic approaches to allergic disease
3. Intervention studies – Undertake research that has high potential to directly inform and/or affect public policy and/or healthcare practice and reduce the prevalence of allergic disease and/or improve the quality of life of allergic disease sufferers with strong links to mechanistic studies towards the longer-term development of new diagnostic tools and therapeutic approaches
4. Canadian Mother and Child Stress Study – Develop a significant, integrated programme of research studying the effects on allergic and related immune disease of changes in the mother-infant dyad integrating societal intervention, biologic intervention and stress research leading to policy and therapeutic outcomes.

AllerGen NCE Inc. is currently inviting integrated and networked research proposals for the period 2009-2012 with letters of intent due on March 15, 2009 and invited full proposals due on May 31, 2009.

Participants recommended that Mind-Body Interactions and Allergic Disease researchers develop research proposals for 2009-2012 that focus on short-term deliverables and impacts on user sectors. An additional recommendation was that there should be extensive planning to develop a transformational, multidisciplinary and nationally-networked Mind-Body research programme that AllerGen could support from 2012-2019.

Immediate next steps for AllerGen investigators interested in pursuing Network-supported research within the emerging AllerGen Mind-Body research team are to meet at the Mind-Body Interactions and Allergic Disease research workshop at the AllerGen Annual Conference, February 15 – 17, 2009. This event is an opportunity to further the planning of and collaborative, team approach to the development of programmatically integrated and networked Mind-Body Interactions and Allergic Disease research proposals in response to AllerGen's Request for Proposals 2009-2012.

1. Introduction

On December 10 -11, 2008 Dr. Dean Befus, AllerGen NCE Inc. (AllerGen) Research Leader, Programme B: Diagnostics and Therapeutics, Professor, Department of Medicine, University of Alberta and Dr. Anita Kozyrskyj, Research Chair, Maternal-Child Health and the Environment and Associate Professor, Department of Pediatrics, University of Alberta, hosted a Mind-Body research planning workshop in Winnipeg, Manitoba.

The meeting objectives were to:

1. Facilitate networking among AllerGen researchers and trainees engaged in Mind-Body research;
2. Facilitate information sharing about progress to date on Network-supported Mind-Body research, its relevance to decision-makers and potential follow-on research and knowledge translation activities to 2012; and
3. Undertake strategic visioning for the development of future Mind-Body research proposals that are strategically aligned with the research priorities and mandate of AllerGen in preparation for the development of submissions to a Requests for Proposals (RFP) for projects to be supported by AllerGen from 2009-2012.

Anticipated outcomes of the meeting included:

1. Update on Mind-Body Interactions and Allergic Disease Research team members' progress on currently funded AllerGen projects;
2. Identification of opportunities for research impact aligned with AllerGen's mission;
3. identification of future directions for Mind-Body research aligned with AllerGen's strategic research thrusts;
4. Potential collaborations among Mind-Body researchers and other AllerGen research teams; and
5. Identification of strategies for successful Mind-Body researcher participation in the AllerGen RFP for 2009-2012.

The workshop was attended by 25 participants, including mind-body investigators and research trainees, policy makers, research administrators and the Scientific Director of AllerGen, Dr. Judah Denburg. A copy of the agenda is provided in Appendix A. A complete participants list is provided in Appendix B.

The balance of this report summarizes the discussions and recommendations emanating from workshop.

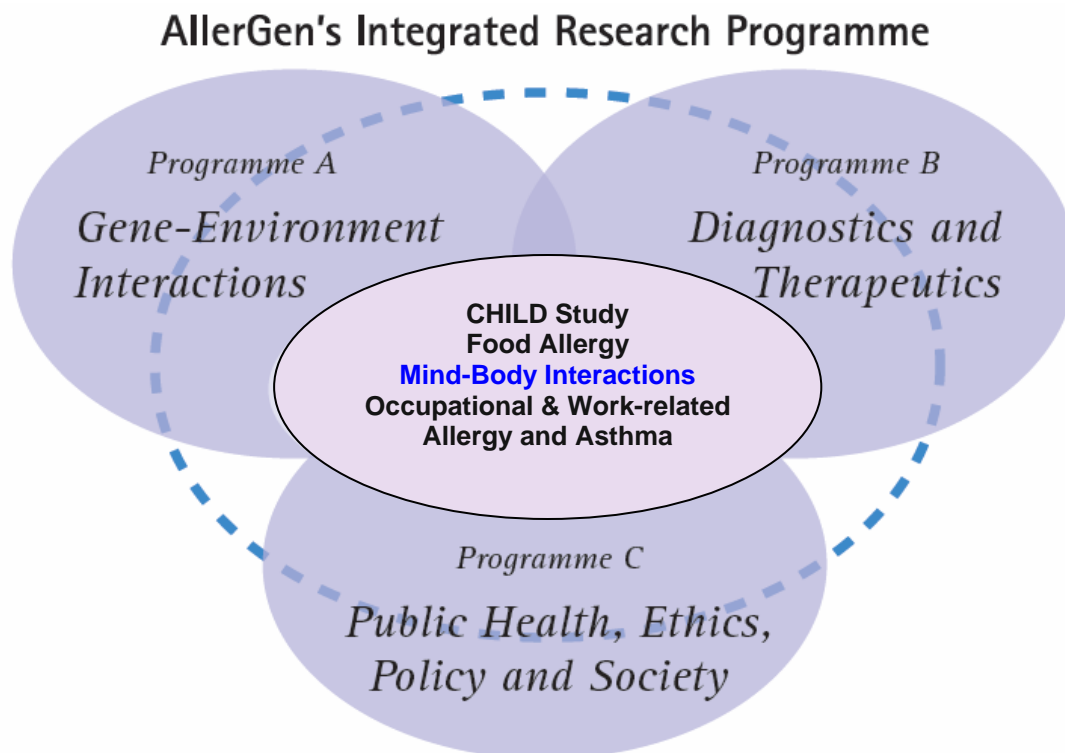
2. AllerGen Strategic Priorities and Mind–Body Research Objectives

In 2008, AllerGen underwent a mid-term review conducted by an independent international expert panel on behalf of the federal Networks of Centres of Excellence (NCE) program. This review required AllerGen to provide both a report on progress to date as well as an updated strategic plan.

AllerGen research priorities fall within three research programmes that focus network research on areas of strategic importance to the generation of new knowledge with potential for social and economic impact in the area of allergic and related immune disease. These three programmatic thrusts are:

1. **Programme A** – Gene-Environment Interactions
Strategic Focus: Genetics, environmental exposures, and gene-environment interactions in allergy and asthma
2. **Programme B** – Diagnostics and Therapeutics
Strategic Focus: Biomarkers, immune monitoring and drug development/discovery
3. **Programme C** – Public Health, Ethics, Policy and Society
Strategic Focus: Allergic disease management and surveillance

Figure 1: AllerGen's Research Programme Structure



In addition, AllerGen seeks to invest in four cross-programmatic, multidisciplinary research thrusts that have been fostered by AllerGen since 2005 and have been identified as continuing research investment priorities for 2009-2012.

These cross-programmatic research teams in priority areas are:

Established Cross-programmatic Teams

- 4. The Canadian Healthy Infant Longitudinal Development (CHILD) Study
- 5. Food Allergy and Anaphylaxis

Emerging Cross-programmatic Teams

- 6. Mind-Body Interactions and Allergic Disease
- 7. Occupational and Work-related Allergy and Asthma.

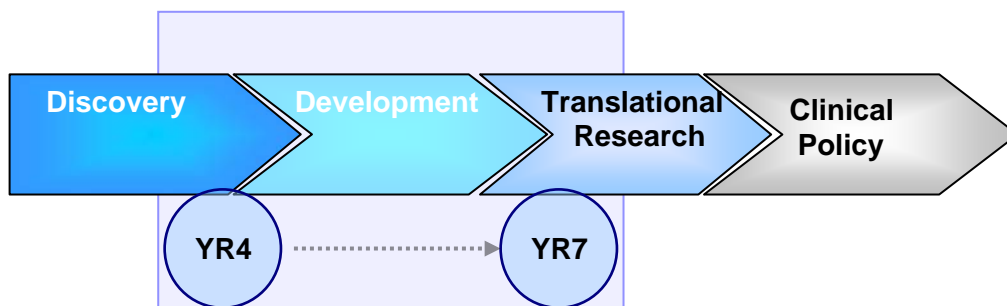
As an *Emerging Cross-programmatic Team*, Mind-Body Interactions and Allergic Disease research was approved by AllerGen’s Board of Directors and the NCE program for continued investment to 2012. AllerGen, unlike research funding agencies, is expected to support research that is on a translational continuum towards social and economic impact. Since 2007, AllerGen has been committed to fostering integrated multidisciplinary programmes of research containing programmatically linked projects undertaken by nationally networked research teams committed to advancing allergic and related immune disease knowledge and technology translation, transfer and commercialization.

2 Types of Translational Research

- “T1”: bench to bedside; interface between basic science and clinical medicine – end point is production of promising new treatments with clinical and commercial value
- “T2”: research to practice; ensuring new treatments and research knowledge reach patients or populations for whom they are intended, and are implemented correctly

AllerGen’s goal over the next three years in the area of Mind-Body Interactions and Allergic Disease research is to foster the development of multidisciplinary, nationally networked teams moving research from the discovery and development phase to translational research and intervention strategies that may be utilized nationally to decrease the impact of allergic disease.

Figure 2: Operational Priorities: Mind-Body Interactions and Allergic Disease Research to 2012



Building on and aligned with existing research investments, AllerGen’s Mind-Body Interactions and Allergic Disease research investment objectives to 2012 are:

- 1) **Mind-Body Interactions** - Investigate novel neuroimmune (mind-body) interactions in allergy and asthma, and apply relevant findings to network research. Investigate mind-body changes associated with stress, depression, psychosocial state or socio-economic status. Translate findings to inform policy development both provincially and nationally.

- 2) **Models of Allergic Disease** – Development of experimental *in vivo* and *in situ* models of stress, depression and allergic disease that can be utilized by other network research projects.
- 3) **Allergic Disease Epigenetics** – Investigate epigenetic factors in the development and expression of allergic diseases and asthma, including the analysis of epigenetic variation, and identification of relationships among environmental triggers, epigenetic changes, and socio-biological development, especially in early-life.
- 4) **Intervention Strategies** – Investigate psycho-social intervention strategies leading to new approaches to disease management. Design educational and research intervention strategies to influence research and policy development around Mind-Body research.
- 5) **Psychosocial Impacts** – Examination of the psychosocial impacts upon individuals living with allergies, asthma, and anaphylaxis in the context of individuals, families, and special or marginal communities and associated public policy implications.

In addition, the creation of multidisciplinary research and knowledge translation training opportunities, and the establishment of multi-institutional networking and cross-sectoral partnership arrangements are critical to successful realization of AllerGen's vision and mission, of which development and transmission of new knowledge to those who can generate new goods and services is the centrepiece. AllerGen encourages all research teams to generate partnership opportunities with a wide range of potential public and private sector organizations. Within the NCE model, partnerships are considered essential to addressing the complex challenges that allergic/immune diseases pose to society.

3. Mind-Body Research Progress Reports

Mind-body researchers attending the workshop were invited to present their research progress and discuss findings to date. Specifically, researchers were asked to:

- Share project information;
- Position their research in relation to the Gee and Payne-Sturges 2004 stress-exposure framework distributed in advance of the workshop¹;
- Share research user perspectives on the findings to date; and
- Identify future research strategies to leverage the network structure and focus future mind/body research on high impact/value science in collaboration with potential research users.

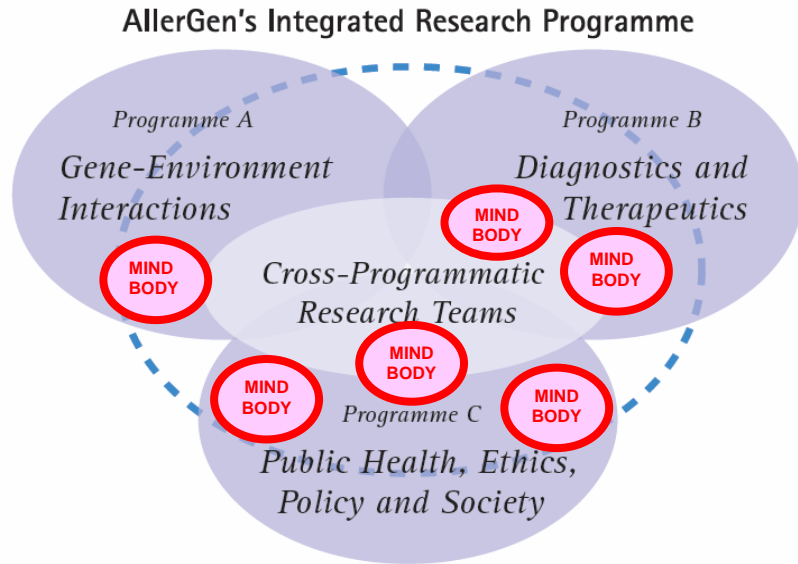
Table 1 illustrates AllerGen's investments to date in Mind-Body Interactions and Allergic Disease research.

¹ See "Environmental Health Disparities: A Framework Integrating Psychosocial and Environmental Concepts", Gilbert C. Gee, University of Michigan School of Public Health, Department of Health Behavior and Health Education, Ann Arbor, Michigan, USA and Devon C. Payne-Sturges, Office of Policy, Economics and Innovation, and Office of Children's Health Protection, U.S. Environmental Protection Agency, Washington, DC, USA in *Environmental Health Perspectives*, Vol. 112, No.17, December 2004, Pp. 1645 – 1653.

Table 1: Currently Funded AllerGen Mind-Body Research Projects
Programme A: Gene-Environment Interactions (2007-2009)
1. Postpartum distress and childhood asthma (<i>formerly - Maternal stress in early childhood and the development of asthma</i>), Anita Kozyrskyj (Alberta), Denise Daley (UBC)
2. Stress and social economic questionnaires in Mini-CHILD/CHILD (Greg Miller and Edith Chen, UBC)
2005-2007:
3. The Canadian Healthy Infant Longitudinal Development (CHILD) Study
Programme B: Diagnostics and Therapeutics
2005-2007:
4. Effects of probiotics on murine model of asthma, John Bienenstock, Paul Forsythe, McMaster, April 1, 2005 - March 31, 2006
2007-2009:
5. Perinatal stress and programming of allergic responses, Petra Arck, John Bienenstock (McMaster)
6. Neuroendocrine regulation of allergic reactions in animal models: Translation to humans, Dean Befus (Alberta), Joe Davison (Calgary), O'Byrne (McMaster)
AllerGen Mind-Body Research 2007-2009: Programme C: Public Health, Ethics, Policy and Society (2007-2009)
7. Neuroimaging and environmental suggestibility in asthma, Glenda McQueen (Calgary)
8. Stress, allostatic load and risk of allergies and asthma in children of immigrants, Claudio Soares (McMaster)
9. Stress, asthma and atopy socio-spatial investigations, Anita Kozyrskyj (Alberta)

AllerGen Mind-Body research investments to date cut across all three programmatic research thrusts, as illustrated in Figure 3.

Figure 3: Strategic Positioning of AllerGen-supported Mind-Body Interactions and Allergic Disease Research to 2008

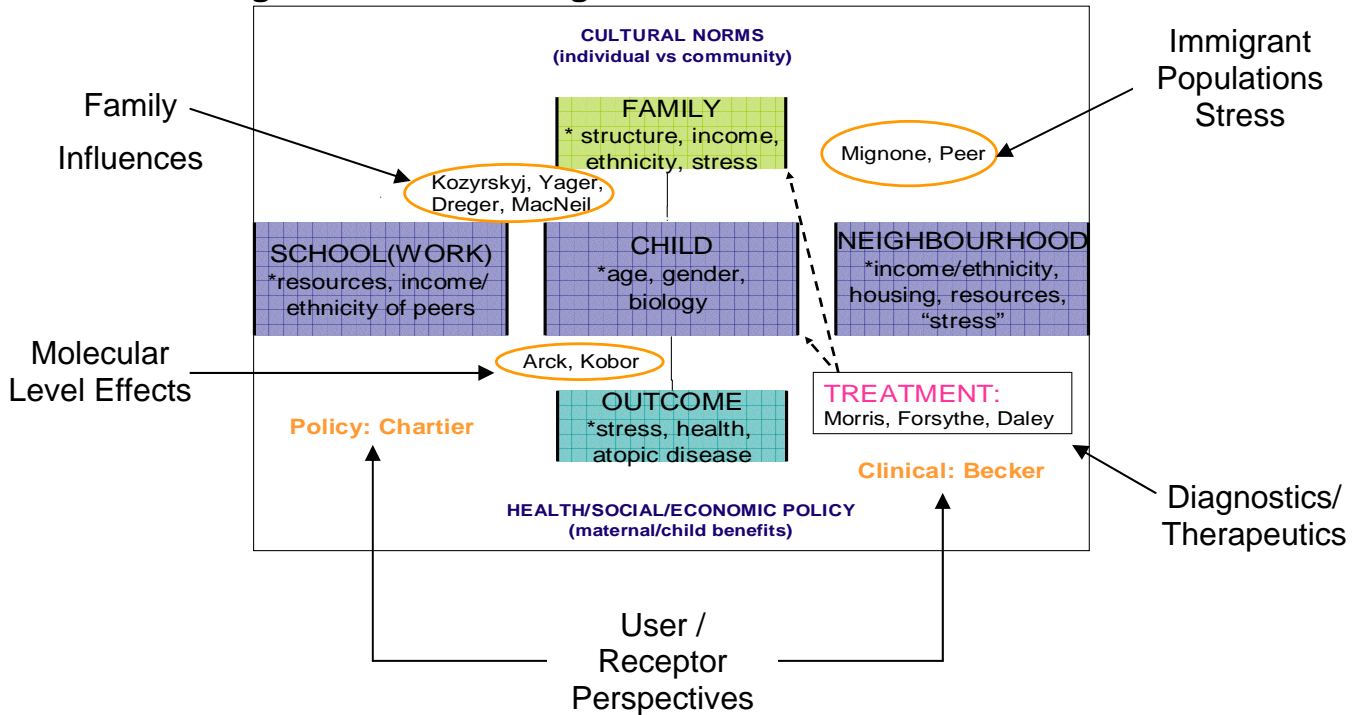


3.1 Maternal Distress, Child Stress Response and Atopic Disease: From Population-based Observations to Mechanistic Studies

Chair, Dr. Anita Kozyrskyj, Research Chair, Maternal-Child Health & the Environment, Department of Pediatrics, University of Alberta

Dr. Anita Kozyrskyj prefaced the first nine research presentations with a brief overview of the social ecological model of stress and disease, which was used to organize the related research presentations (see Figure 4).

Figure 4: Social Ecological Model of Stress and Disease



In addition to using the social ecological model of stress and disease as a common organizing framework around which the research presentations were organized, policy makers and clinicians who were representative of the communities within which Network research results would be taken up and applied, provided researchers with commentary and feedback in relation to the relevance and applicability of their research results.

The use of an organizing conceptual framework and the provision of “user sector” feedback facilitated dialogue across project teams as well as between researchers and potential research users. It also enhanced research team insight into user sector information needs and the process by which research results can be most effectively translated into policy, programs, and healthcare provision.

A summary of the key points in each presentation of currently funded research is provided below.

3.1.1 Community-level Determinants of Maternal Distress

Dr. Javier Mignone, Assistant Professor, Human Ecology, Department of Family Social Sciences, University of Manitoba
and

Heather Henley, Masters of Natural Resources Management Candidate, Natural Resources Institute, Faculty of Graduate Studies, University of Manitoba, and Research Assistant, Department of Family Social Sciences, Faculty of Human Ecology, University of Manitoba

What?

This project involves constructing and measuring the development of neighbourhood-level factors of stress. The focus is “cell to society” and “society to cell,” in order that the investigators understand how society gets under the skin and what properties of communities (households, families, neighbourhoods, cities and regions) have an impact on health/stress. The project involves a comprehensive literature review and data availability assessment. It is important that each of the levels of neighbourhood are very well specified and defined so that the completed research has sufficient explanatory power.

The project is networked across sites and disciplines, involving Anita Kozyrskyj (Alberta), Javier Mignone (Manitoba), Heather Henley (Manitoba), Susan Elliott (McMaster) and Allan Becker (Manitoba).

So What?

This research is important because it will empirically identify the community-level factors including the interactions between the physical and social environment necessary to understand potential pathways between community characteristics and maternal distress. Research results will contribute to multi-level understanding of increased asthma risk and has the potential to guide the development of preventive programs and policies.

What Next?

Next steps for this project include defining constructs, developing measures including psychometrics and eco-metrics, empirically testing the causal framework using hierarchical models and ultimately developing intervention strategies that improve asthma prevention and management.

3.1.2 Perinatal stress in immigrant mothers

Miki Peer, PhD Student & AllerGen Trainee, McMaster University
for Dr. Claudio Soares, Department of Psychiatry & Behavioural Neurosciences, McMaster University

What?

This project is testing the hypothesis that in a select population of pregnant immigrant women, those with **high levels of perceived stress** will be **more likely to give birth to infants with an atopic profile** compared to infants of immigrant women with low levels of perceived stress.

This is a prospective study of 60 immigrant women (Chinese or Arabic speaking [Latin community to be introduced shortly]) and their infants, followed from early pregnancy until one year postpartum, who are recruited through immigrant resource centres, community centres, and/or community advertising in Hamilton and the surrounding area. Three subjects are currently enrolled.

Researchers are collecting data about the subjects':

- Psychiatric history
- Health history and home environment
- Depressive symptoms
- Post-traumatic stress disorder symptoms
- Perceived stress
- Stressful life events
- Perceived social support
- Umbilical Cord blood IgE
- Skin Prick Test – In mothers and their infants (at one year)
- Salivary Cortisol (awakening response & diurnal profile) – in mothers and their infants.

Investigators involved in this project include Dr. Claudio N. Soares (McMaster), Ms. Miki Peer (PhD candidate McMaster), Dr. Susan Wasserman (McMaster). Other collaborators include Dr. John Bienenstock (McMaster), Dr. Judah Denburg (McMaster), and several community-based researchers (CBRs) from St. Joseph's Immigrant Women's Centre. Community partners involved in this project include St. Joseph's Immigrant Women's Centre, North Hamilton Community Health Centre and the Hamilton Community Foundation.

So What?

This research is important because Canada has the highest *per capita* immigration rate in the world and Hamilton has the third highest proportion of immigrants in any city in Canada (behind Toronto and Vancouver).

Health research literature consistently shows that pregnant immigrant women report more stress and depression than Canadian-born women. However, the effects of perinatal stress on the development of allergies in the infant and/or their susceptibility to allergic disease have not been extensively studied.

This study explores the association between stressor characteristics during pregnancy and the development of allergies in exposed children in a specific cultural group (immigrants from two ethnicities) and is directly aligned with the *Stress-Exposure Disease Framework* in that the framework suggests that '*racial variation in stressors may account for differences in vulnerability to health risks.*' The stress measures developed for this study include elements from both community processes and individual mechanisms, as emphasized in the framework.

What Next?

The study questionnaire has been validated in translation and is ready for use. Subject recruitment began in fall 2008.

Study results will be disseminated to partnering agencies to help design and implement new programs or strategies to mitigate the impact of stress on pregnant immigrant women, improving their health and quality of life.

The team plans to expand its investigation to non-immigrant populations by partnering with other AllerGen researchers investigating the effects of perinatal stress on susceptibility to allergic disease development. In addition, investigators are currently pursuing further funding for exploratory analyses of cord blood (i.e., for other early life markers of allergic disease, aside from IgE).

This team is also interested in partnering with the CHILD Study and the Vancouver stress cohort to expand the use of their questionnaire.

3.1.3 Maternal distress & child asthma: A Population Study

Anita Kozyrskyj, Research Chair, Maternal-Child Health & the Environment, Associate Professor, Department of Pediatrics, University of Alberta

What?

This project aims to determine the role of maternal distress in the development of childhood asthma in a large population-based cohort, including children predisposed and not predisposed to asthma and to determine whether or not association with childhood asthma is dependent on the duration of maternal distress. This research was conducted using the Data Repository of longitudinal prescription and health care records for the 1995 cohort, collected by Manitoba Health and accessed at the Manitoba Centre for Health Policy.

This study examined the history of 14,000 children from the 1995 Manitoba SAGE birth cohort to determine the likelihood of asthma at age 7 years among children exposed and not exposed to maternal distress during their first year of life and beyond.

Maternal distress is defined for the purposes of this study as one or more health care contacts (hospitalization or physician) or prescription drugs for depression or anxiety for three durations:

- One year only (postpartum only)
- One and 2-5 years (short-term)
- Recurrent exposure over 1-7 years of the child's life.

Asthma at age seven was defined as at least two physician visits or one hospitalization for asthma, or two asthma prescription drugs (validated definition).

This project is supported by programmer analysts, Shamima Huq and Matthew Dahl, and the SAGE study team. Research collaborators on this project include Xiao-Mei Mai, Patrick McGrath, Kent HayGlass, Allan Becker, Brian MacNeil (all from Manitoba).

So What?

This research is important because early life exposure to maternal distress has been shown to be an independent risk factor for the development of asthma in children. Children of mothers with recurrent distress were 1.25 times more likely to develop asthma (OR=1.25, 95% CI:1.01–1.55). Continued exposure to maternal distress in early life is associated with an increased risk of childhood asthma. Distress alters mother-infant interactions and increases susceptibility to lower

respiratory infections in infants, causes the release of pro-inflammatory cytokines in infants and alters intestinal permeability and/or microflora in infant animal models.

This association is observed for maternal distress which is recurrent from birth, but not if it is limited to the postpartum period only.

This research policy has implications for postnatal screening and intervention programs for maternal distress.

What Next?

Next steps for this project include testing these associations in other Canadian populations using the same and different measures of maternal distress, e.g.,

- SAASSI: NLSCY – with Letourneau;
- CHILD Study subjects;

as well as studying mechanisms by assessing child stress response through the SAASSI project.

3.1.4 The CHILD Study: Examining the role of psychosocial factors in the development and progression of asthma/allergies

Sarah Yager, Project Coordinator, University of British Columbia

What?

This project focuses primarily on answering the question “how does stress get under the skin?” Secondary questions include:

- What is the role of stress on the onset of asthma?
- What is the differential toxicity of stress, SES, etc. on asthma outcomes?
- How does stress synergize with genes and the environment?

The CHILD Study psychosocial platform undertakes questionnaires prenatally at 18 wks GA, 34 wks GA, and then yearly postnatally.

Measures taken include:

- Chronic and acute stress
- Maternal depression
- Socioeconomic status
- Social support.

Primary hypotheses are four-fold:

1. Prenatal maternal stress will affect Th2 responses to allergens, with downstream implications.
2. Life stress will heighten vulnerability to asthma and allergies.
3. "Social" and "physical" environments will synergize to influence vulnerability to asthma/allergies.
4. Low social class will boost risk for disease, partly through social and partly through physical environs.

The CHILD Study pilot phase is complete, with over 50 mothers recruited, 20 interviews completed, 11 deliveries, and 10 cord blood samples collected.

So What?

This research is important because it will assist in understanding the:

- Connection between epigenetic marks to GR & B2AR in CB
- Expression of GR, B2AR genes and others that drive inflammation – such as IL4, IL5, IL13
- Th1, Th2 immune responses in CB
- Interactions of stress with pollution and indoor allergens, etc.

What Next?

Next steps for this project include seeking greater sample diversity (the majority of subjects are upper middle class in terms of total family income and level of education). The team seeks to expand its recruitment area as of January 2009, with the aim of attracting participants from a diversity of social and economic status.

3.1.5 Lower Cortisol Levels in Asthmatic Children Exposed to Recurrent Maternal Distress from Birth

Lisa Dreger, PhD Candidate, Department of Psychology, University of Manitoba

What?

This project examines the association between maternal distress and the stress response system (plasma cortisol levels) in children with and without asthma, focusing on vulnerability at the level of the individual including the effects of individual stressors, individual stress and related health effects.

The hypothesis for this study is that exposure to recurrent maternal distress will be associated with heightened cortisol levels following an acute stressor in children without asthma and with blunted cortisol levels in children with asthma.

This project cross-cuts AllerGen Programs A: Gene-Environment Interactions and C: Public Health, Ethics, Policy and Society.

The research team includes Anita Kozyrskyj (Alberta), Kent HayGlass (Manitoba), Allan Becker (Manitoba) and Brian McNeil (Manitoba).

Research partners include the Manitoba Institute for Child Health and the Manitoba Centre for Health Policy.

So What?

This research is important because findings suggest that exposure to maternal distress restricted to the first year of life predicted elevated cortisol levels in children, regardless of asthma status (> 40% increase). This suggests that exposure to recurrent maternal distress seems to be associated with different stress response functioning in children both with and without asthma.

Research results also suggest that children without asthma exposed to maternal distress beyond the postnatal period experienced a 25.9% *increase* in cortisol while children with asthma exposed to maternal distress beyond the postnatal period experienced a 5.2% *decrease* in cortisol.

This research has policy implications for the development and support of postnatal screening programs for maternal distress that impact child health.

What Next?

Next steps for this project include additional research into the pathways of maternal distress including testing additional markers of child stress responses and including early life measures of child stress. This research can be usefully linked to ongoing studies of birth weight and cortisol/DHEA: SAASSI (McNeil) as well as studies of community level determinants of maternal and child stress.

3.1.6 The Association between Birth Weight, Overweight, Asthma and Stress Markers in Children Aged 7-10 years

Brian MacNeil, Associate Professor and Chair, MSc Rehabilitation Program Committee, Department of Physical Therapy, University of Manitoba

What?

This project focuses on answering the question “What are the relationships between birth weight, current weight, stress biomarkers and asthma?” Research examines the degree to which the early life environment is predisposing individuals to asthma in later life.

Subjects are drawn from the case control sample of SAGE study, using Manitoba Health records looking for low birth weights (<2500g) and maternal distress defined by healthcare visits and prescriptions. Low birth weight is used as a surrogate measure of stress in the environment. Clinical evaluation of children at 7-10 yrs was undertaken. Cortisol and dehydroepiandrosterone (DHEA) assayed from plasma samples is taken from the SAGE case-control sample at age 7-10 after exposure to a cumulative acute stressor of skin pinprick testing, methacholine challenge and venipuncture.

A multiple linear regression model was used to assess low birth weight, overweight, and asthma as predictors of cortisol, DHEA and cortisol/DHEA ratios which were adjusted for age, gender, maternal distress.

Research collaborators include Anita Kozyrskyj (Alberta), Allan Becker (Manitoba), Pat McGrath (Dalhousie), Kent HayGlass (Manitoba) and trainees Lisa Dreger, Xiao-Mei Mai, Darcy Heron and Lauren Yallop.

So What?

This research is important because it will help us understand the role of environment in determining risk of allergic disease and identify significant environmental factors such as maternal stress as a source of individual child stress.

The target audience for the results of this research would be health policy makers and could lead to the development of publicly funded programs to identify and address early life factors that may predispose children to disease throughout their lifecycle and the development of a program of pregnancy screening for maternal distress.

Results may also feed into the Consensus Statement being developed by the Institute of Health Economics, Alberta (Healthy Mothers – Healthy Babies) about how to prevent low birth weights.

What Next?

Next steps for this project include incorporating additional measures of early life stress to include stress markers prior to age 7 such as atopic dermatitis and skin infections as well as repeating clinical assessments of the children at ages 10-11 and again at 12-13 years of age. Finally, it would

be useful to assess the effects of community stressors, including the effects of residential segregation in order to understand the community level determinants of maternal and child stress.

In the longer term, it would be valuable to track stress markers at or near birth to capture very early stage DHEA and fetal adrenal gland activity data and to study pathways of maternal distress by testing longitudinal markers of the child's stress response, starting from early life by measuring postnatal skin infections/atopic dermatitis and cortisol/DHEA in school age and pre-adolescence (i.e., SAASI project (Darcy Heron)).

3.1.7 Animal models of perinatal stress

Petra Arck, Brain Body Institute, McMaster University

What?

This project focuses on an emerging area of research referred to as fetal programming. It evaluates the impact of environmental insults *in utero* on the incidence of disease in later life. The aim is to identify if and how prenatal exposure to stress (including psychosocial and environmental concepts) increases susceptibility to allergic diseases in later life.

Research involves the development of a mouse model and recruitment of a birth cohort.

The research team includes McMaster/Brain-Body Institute: Arck lab (Chris Bruenahl), P. Forsythe, J. Bienenstock, M. Inman, S. Elliot, C. Soares, M. Peer, M. Steiner, M. Sears, and J. Denburg (all from McMaster). The addition of S. Elliot (McMaster) is planned and pending. Collaborators at the Charité in Berlin include M. Pincus, U. Wahn and T. Keil.

So What?

This research is important because it aims to understand and develop strategies to address primary prevention of allergies, and Canadians (and other nations) may benefit from the identification of individuals at risk. This research is fundamentally interdisciplinary and would be difficult to undertake without a multidisciplinary, networked approach and structure. Research results can contribute to the development of guidelines towards primary prevention of allergic diseases during pregnancy.

What Next?

Next steps for this project include

- Development of concepts for primary prevention of allergic diseases by therapeutic approaches in mice
- Establishment of a pregnancy cohort (recruitment between gestation week 8-18)
- Development of guidelines based on risk factor algorithms during early pregnancy
- Approach the CHILD Study team with a proposal to look at the very early pregnancy phase if possible, given the CHILD Study schedule (CHILD Study does not recruit subjects until the 12th week of pregnancy)
- It was suggested by participants that this project could lead to linkages with the research projects of MacNeil, Arck and Kozyrskyj in order to study atopic eczema as a clinical marker of allergy and link this to stress biomarkers
- Participants also suggested that this study could be linked to the Soares/Peers study.

3.1.8 Epigenetics of Perinatal Stress – Epigenetic Variations in Humans

Michael Kobor, Centre for Molecular Medicine and Therapeutics, University of British Columbia

What?

The goal of this research is to advance the understanding of genomic embedding of experiences through epigenetic mechanisms. The main finding of this research will be the characterization of human epigenetic variation and its predictors.

While the human genome does not change, Kobor noted that throughout life, many different epigenomes develop from the more than 200 cell types in the human body.

This study focuses on stress-associated epigenetic programming, examining social-economic-status, subjective stress perception and inflammatory markers. Kobor is using the Illumina Golden Gate™ System to undertake high-throughput measurement of specific DNA methylation sites, including CpG islands.

Research collaborators include Edith Chen and Greg Miller (UBC Psychology), Hunter Fraser (Rosetta Inpharmatics, Stanford University) and a number of outstanding technical staff including Alexandra Fok, Sarah Neumann.

So What?

Epigenetics unites and integrates disciplines. It refers to persistent and heritable alterations in genome information that do NOT involve changes in DNA sequence. Two important windows for external programming effects on the epigenome are *in utero* and *early life*. Epigenetics has great promise as a biomarker correlating with allergic disease.

What Next?

There are a number of synergies developing from AllerGen-supported epigenetics research. This includes collaborations with the CIFAR Experience-based Brain and Biological Development (EDBBD) Program. BC-based Human Early Learning Partnership (HELP), psychosocial researchers in AllerGen (Chen, Millar (UBC)), and UBC iCapture researchers (P. Paré, J. Hogg and D. Knight).

3.1.9 A Policy Maker's Perspective on the Value of and Opportunities for Future Research Applications

Mariette Chartier, Research Scientist, Healthy Child Manitoba Office and Community Health Science, University of Manitoba

Chartier noted that policy makers are interested in AllerGen's policy relevant findings. It is important, however, to keep in mind that policy makers are a "mixed-bag." They are not all the same, but in general they are looking for clear directions, documents that are readily comprehensible and conclusions that are translated into lay language and identify options for action. Academics need to "sell" their research results. It can be very challenging to identify the policy implications of your research results, so it helps to develop collaborations with policy makers early on to help identify this.

In some cases, research in promising areas is just beginning and little is known so it can be important and in the public interest for researchers to be both circumspect and judicious in responding to requests for policy advice when knowledge in certain areas is still emerging.

For example, Manitoba policy makers would be interested in opportunities available to AllerGen researchers to address questions relevant to the Healthy Child Manitoba program. Chartier noted that research does have an influence on policy when the evidence is strong, the timing is right and people are ready to hear it.

Researchers often ask “How do I get my research information to where it is needed and where it can make a difference in decision-making?” Chartier recommended that researchers invest in knowledge synthesis, systematic reviews and systematic analyses because these types of knowledge are “very well received” by policy makers.

Chartier notes that the role of policy makers is to act, and they cannot wait until researchers do all the research possible on a given issue. Policy makers must act, often in the context of a great deal of uncertainty. As a result, if researchers add too many caveats to their reporting of research results, it reduces its value and usefulness to policy makers. It is helpful when researchers report on what is working.

Chartier believes that society has, by and large, bought into the biological and medical models of health and that if researchers can demonstrate that “this is true in mice,” then the public can understand that this is also likely true in people.

Researchers have had a significant impact on policy makers. Clyde Hertzman, for example, has had an important influence on policy related to the early childhood environment. In addition, analysis of epidemiological data and provincial-level data is very important to policy makers. Research focusing on mothers and young children is believed to be very important and the results of public sector investments in early life programming is now showing that it pays dividends to society in terms of the quality of life of children as they mature.

Chartier noted that the fact that stress is an important factor for mothers is new and important and that this type of research creates an opportunity to inform policy makers interested in child health. In Manitoba, a maternal-child health task force is in place to study maternal birth weights. In addition, public health nurses work with new mothers using a list of 39 risk factors to screen for maternal distress.

With respect to community level research, it will be important that researchers are in a position to specify which factors are most important with respect to community and neighbourhood characteristics and optimal health because policy makers will be looking for evidence about what to do.

With respect to epigenetics research, public servants are trying to figure out what is the best way to ensure the health of our population, so conclusions need to link what is known about outcomes with policy options and actions.

3.2 Maternal Distress, Child Stress Response and Atopic Disease: Molecular Pathways and Therapeutic Innovations

Chair, Dr. Dean Befus, University of Alberta

Dr. Dean Befus, Chair introduced the next three research presentations, which focused on AllerGen’s Mind-Body research arising from the study of molecular pathways and therapeutic innovations.

3.2.1 Neuroendocrine regulation of allergic reactions in animal models: Translation to humans

Katherine Morris, PhD, Postdoctoral Fellow, Department of Medicine, University of Alberta and

Dean Befus, PhD, Professor, Department of Medicine, University of Alberta

What?

Salivary gland function and gene expression may be altered in allergic individuals. It is known that inflammation of the labial salivary glands occurs in 74% of asthma patients (but not COPD). It is hypothesized that salivary gland dysfunction may contribute to asthma, particularly in stressed individuals. If the ganglion that feeds the salivary gland is removed, inflammation is reduced, confirming the anti-inflammatory and anti-shock properties of certain peptides.

In this project, AllerGen investigators collected salivary gland samples from control and asthmatic patients, evaluated inflammation in glands by histology, performed microarray analyses to globally visualize gene expression differences and correlated the histology with microarray results towards identifying new pathways and new targets for asthma therapy.

In addition, stress can worsen allergic diseases including asthma *via* the HPA axis and autonomic nervous system, which modulates the secretion of anti-inflammatory mediators. This pathway may be dysregulated in stress-related allergic disease and is, therefore, a target for therapy.

This collaboration involves Investigators and trainees from U of A (Dean Befus), U of C (Ron Mathison and Joe Davison), McMaster University (Paul O'Byrne), and UBC (Mark Wilkinson) as well as industry partners - AIM Therapeutics and Imulan.

So What?

This research has the potential to identify some of the biological links between stress and poor asthma outcomes in humans. Therapeutic interventions targeted at these pathways may be useful in individuals where stress is unavoidable.

This team has identified endogenous anti-inflammatory peptides regulated by the autonomic nervous system (stress). Derivatives of these natural peptides show therapeutic promise in pre-clinical models. Research into this pathway will help uncover how stress leads to asthma exacerbations.

New therapies for allergic inflammation in stressed individuals will be of social and economic benefit to Canadians by increasing productivity and improved health.

What Next?

The team plans to continue its studies on mechanisms with new collaborative strategies by engaging the UBC biomarkers group to develop new understandings of drug action, taking advantage of "Omics" platforms and *in vivo* studies to test candidate peptides from humans and novel therapeutics in partnership with AIM Therapeutics. Finally, the team plans to undertake translational studies on human asthma biopsy samples (in collaboration with McMaster) and follow-up on these findings. Workshop participants also suggested that patients with Shogrin's Syndrome (a salivary dysfunction) should be studied, and that epithelial cell types should be mapped.

Outcomes of this research will be the development of robust screening assays to test new peptides (therapeutics or human equivalents); the extension of mechanistic knowledge; and the salivary transcriptome will be investigated in human subjects.

3.2.2 Treatment with Probiotics

Paul Forsythe, PhD, Assistant Professor, Department of Medicine, McMaster University and The Brain-Body Institute, St. Joseph's Healthcare
and

John Bienenstock, PhD, Professor, Department of Medicine, McMaster University and The Brain-Body Institute, St. Joseph's Healthcare

What?

The hypothesis being tested in this research project is that by modulating gut microbiota, one can influence the immune response.

The goal of this research is to determine the effect of treatment with commensal bacteria (probiotics) on stress responses and allergic disease in animal models.

To date, the team has confirmed that oral treatment with certain commensal bacteria can induce a regulatory immune response; modulate activity of the peripheral nervous system and alter components of the central nervous system that are associated with attenuation of allergic airway responses; changes in HPA response; and reduced anxiety like behavior.

Research is being conducted by a large, multi-disciplinary team with members drawn from the Brain-Body Institute, McMaster University (10 individuals, 9 disciplines); The Firestone Institute for Respiratory Health (3 individuals); Alimentary Pharmacobiotic centre (UCC, Ireland) (4 individuals) and an industrial partner (Alimentary Health Ltd. (Ireland)).

So What?

Aligned with the stress framework, this project has shown that probiotic therapy may decrease the detrimental effects of stress on an individual's health outcome; alter stress perception and represent environmental enrichment through improved microbial balance.

This research has the potential to make a social and economic impact by aiding in the design of new therapies for allergic disease that correct or prevent the immune imbalance underlying the disorder rather than only controlling symptoms. It also shows potential for use as an early life intervention that confers long-term protection against the development of allergic disease and other stress-associated disorders.

What Next?

Short term 1-2 yrs:

- Determine the impact of early-life probiotic treatment on development of immune and stress responses
- Determine if probiotic treatment can attenuate the detrimental effects of stress on allergic disease.

Longer term 2 – 3 years:

- Identify bacteria strains and develop treatment strategies that will maximize potential clinical benefits.

These additional steps will ultimately culminate in a clinical trial of selected commensal bacteria and determine their applicability as an allergic airway inflammation disease therapeutic.

3.2.3 Relationship between MTHFR and Maternal Stress and Risk for Childhood Asthma

Denise Daley, University of British Columbia
and
Anita Kozyrskyj, University of Alberta

What?

Single Nucleotide Polymorphisms (rs1801131 and rs1801133) within the Methylene tetrahydrofolate reductase (MTHFR) gene result in lower serum folate levels and higher total homocysteine levels. Folate is important in DNA repair and homocysteine plays an important role in cognitive function.

The objective of this research project is to identify and define the relationship between childhood asthma, exposure to maternal stress and MTHFR genotypes. While there is no known association with childhood asthma or maternal stress, there is evidence to support interaction effects.

Single Nucleotide Polymorphisms (rs1801131 and rs1801133) have been associated with susceptibility to many complex diseases including asthma, atopy, cancer, depression, anxiety, major mood disorders, and cognitive impairment.

Maternal depression, stress, and cognitive impairment are risk factors for the development of asthma and allergic disease.

The research team includes Anita Kozyrskyj (Alberta), Denise Daley and Julie Park (both UBC).

So What?

When mothers are stressed, stress is translated to the child. Researchers found no evidence for primary genetic association with asthma or maternal distress, but the presence of maternal distress alters MTHFR risk estimates and the direction of effects (i.e., interactions).

In equilibrium, genotype has no effect, and the T allele of rs1801133 (OR=0.87) and the C allele of rs1801131 (OR=0.53) are protective. However, in a stressful environment these same alleles increase the risk for asthma (rs1801133, OR=1.64, $P=0.00272$ and rs1801131, OR=2.25, $P=0.00001$) when compared to the referent group (same allele, no maternal distress) and may result in asthma.

Researchers conclude that:

- Maternal distress increases the risk for childhood asthma in children genetically predisposed to lower serum folate and higher total homocysteine
- There is no effect of the MTHFR genotype on risk of developing asthma in the absence of maternal stress and the system is in balance
- In a stressful environment, there may be need for increased serum folate and lower total homocysteine to maintain balance.

What Next?

- Replication in other studies (ALSPAC)
- Look at other measures of stress, such as cortisol levels
- Determine the importance of timing of the exposure (pre-pregnancy, pregnancy, postpartum, or chronic)
- Design and implement intervention studies that target prenatal nutrition and provision of better support for pregnant women and mothers, reducing the morbidity and mortality of childhood asthma.

In addition, investigators have obtained Canadian Institutes of Health Research (CIHR) support to undertake a companion study to help understand women's knowledge of the risks of post-partum depression and childhood asthma, and their perception of the links between these conditions. This project will address the influence of genetic knowledge on concepts of normalcy and responsibility with respect to postpartum distress and causes of asthma, as well as identify the best ways to communicate genetic risk, so that women can realistically assess their child's risk. The project will involve a web-based survey of women in the SAGE and MOMS (intervention) studies and a knowledge translation component.

Workshop participants suggested that folate levels in this population should be measured as well, as there is concern in some quarters that folate rich supplements may in fact cause asthma.

3.2.4 A Clinician's Perspective on the Value of and Opportunities for Future Research Applications

Dr. Allan Becker, MD, University of Manitoba

Each presentation related to research on molecular pathways and therapeutic innovations has demonstrated its potential impact on policy. With respect to probiotics, Nestlé has supplemented baby food with pre and probiotics, yet gut microbiota has been studied in only a limited way to date and there is little data to support this approach at this time. Even so, a number of clinicians have adopted probiotic therapies in combination with anti-biotic therapy, again without strong data. At the community level, some pediatricians are routinely prescribing live bacteria when they make an antibiotic prescription. In addition, people are starting to buy live bacteria food products i.e., yogurt.

AllerGen faces a challenge in terms of how it positions itself in relation to probiotic research, because in Canada and in the US (FDA), governments do not feel that the basic questions about the impact of probiotics can be answered satisfactorily at this point, and thus they do not consider probiotics to be "generally safe." Further discussion may be required to confirm how AllerGen positions itself in terms of its future investments in this area.

With respect to further research on genetics and maternal stress, it may be important to consider that while all women are recommended to take folic acid during pregnancy to prevent spinal bifida in their babies, what is not known is whether some women should not take this supplement. It is important to know this. Should AllerGen be highlighting this research for others to pursue?

Finally, Drs. Befus and Morris's project may have significant intellectual property implications. Within AllerGen, it appears that the animal models that are being developed lend themselves to some common approaches and sharing of systems, and that some additional collaboration could be realized.

3.3 Maternal Distress, Child Stress Response and Atopic Disease: New Research Directions

Chair, Dr. Allan Becker, University of Manitoba

Dr. Allan Becker, Chair introduced the next two research presentations, which focused on new directions for AllerGen's mind-body research programme.

3.3.1 Maternal Mental Health Treatment Options

Nicole Letourneau, Canadian Research Institute for Social Policy, University of New Brunswick

What?

Children with unsafe environments are at risk in terms of their health and development.

The focus of this research is to determine the effect of home-based peer support for mothers with post-partum depression (PPD) on:

- Maternal-infant interaction
- Infant mental development
- Maternal symptoms of depression
- Maternal and infant cortisol levels.

This team is particularly interested in which specific maternal care behaviours affect particular biomarkers and how children experience parental stress.

This multidisciplinary team includes N. Letourneau, PhD, RN and Canada Research Chair in Healthy Child Development (UNB), M. Stewart, PhD (Alberta), K. Hegadoren, PhD, RN, Professor and Canada Research Chair in Stress-related Disorders in Women (Alberta), C-L. Dennis, PhD RN, PhD RN, Associate Professor and Canada Research Chair in Perinatal Community Health, Lawrence S Bloomberg Faculty of Nursing (U of T), and J. D. Willms, PhD, Professor and Director of the Canadian Research Institute for Social Policy at UNB and Canada Research Chair in Human Development (UNB).

Over 360 home visits have been undertaken by the teams, located in Alberta (22) and New Brunswick (44) and sixty mothers have been recruited in the context of the *Mothers Offering Mentorship and Support (MOMS) Study*. This study is an RCT to evaluate the effect of home-based peer support on maternal-infant interaction, infant health outcomes, and postpartum depression.

The MOMs study provides:

- One-on-one support for mothers with PPD
- Support provided by mothers who have recovered from PPD
- 2 to 12 weeks of home visits, and
- Referrals to appropriate resources.

Research revealed that parenting behaviours was the most predictive variable in predicting child behaviours.

So What?

Depression following childbirth affects up to 13% of new mothers. PPD has serious implications for women's health, family functioning and children's health and development.

High cortisol predicts reduced cognition, memory attention, self-control and behavioural problems in children. In addition, poor parenting can be a source of stress. Social support may promote optimal parenting, reduce infant stress and maximize childrens' developmental potential.

Preliminary project results revealed that the intervention group experienced increased sensitivity to infant cues, increased overall caregiver interaction scores and increased baby bedtime cortisol.

The control group showed increased responses to infant distress and increased socio-emotional growth fostering activities.

What Next?

The next steps in relation to this project involve data analysis paying particular attention to cortisol connections, conducting a follow-up study of the relationship between mother-child interactions and infant stress hormone levels, establishing a Community Advisory Committee, and preparing peer-reviewed publications, fact sheets, and policy briefs.

The final results of this research project will affect PPD screening and support policies.

3.3.2 Maternal Health Policy

Mariette Chartier, Research Scientist, Healthy Child Manitoba Office and Community Health Science, University of Manitoba

What?

This project examined the real-world effectiveness of the *Families First* home visiting program for at-risk families in Manitoba. During home visits, if the client was experiencing more than three risk factors, then an intervention from the *Families First* program was triggered. The program was associated with increased maternal psychological well-being, positive parenting, social support and neighbourhood cohesion. Other factors such as maternal depression scores were not influenced.

The research revealed that home visiting programs can improve maternal psychological well-being and some of the determinants of well-being, however, additional mental health services may be needed to alleviate maternal depression.

So What?

To date, research on home visiting programs have received mixed results and few Canadian studies exist. Decreasing maternal stress and empowering families may decrease susceptibility to developing health problems in mothers and children. Prevention programs represent a small part of our health care budgets and are difficult to evaluate. These results provide evidence for beneficial effects of home visiting programs as well as ideas for improvements in program content.

What Next?

This information will continue to be shared with program staff across the province of Manitoba. We would like to link program data to a broader range of maternal and child health outcomes and also to examine if there is a cumulative beneficial effect of additional programs. This is a future research proposal that could start as early as next spring if funding is in place.

3.3.3 A Perspective on Research Opportunities in Response to Emerging Societal Needs

Dr. John Bienenstock, McMaster University

We know that stress has an effect on various aspects of function. Stress also has a major effect on certain types of “bugs” and can turn on virulent genes in situations of acute stress. The gut microbiome is something that researchers should be addressing. The “external environments that are internal to us” are widespread. There are at least 200 species of bacteria in the human stomach. “Inter-kingdom signaling” is a new term that has arisen for research that suggests that hosts and “bugs” exchange information.

There is new research suggesting that what is in your intestines determines whether or not you are obese. Research is also underway to study the acquisition of flora and the timing of your acquisition of that flora and how that affects you in later life.

It is known that allergies increase in children born by caesarian section. We know that there is an early life intervention window for animals but we don't know if there is such a window for humans.

The question for us is how early is early intervention in order to achieve the results we seek as expressed in our research outcomes.

As technology advances, we will be able to identify the individual "bugs" in the gut. For the CHILD Study, it is critical to ensure that fecal samples are collected and stored in a way that retains their integrity for future research.

With respect to metabolomics, we have not heard much about that today. However, there is a recent study by Jeremy Nicholson about autism which shows that there are urine metabolites in autistic children related to sulfur and bacterial metabolites.

Learning about resilience may be an important future direction for AllerGen researchers.

3.4 The Canadian Healthy Infant Longitudinal Development (CHILD) Study

Dr. P.J. Subbarao, Deputy Director of the CHILD Study provided workshop participants with an overview of the CHILD Study, focusing on those aspects of the Study that could provide future Mind-Body Interaction research opportunities.

The objectives of the CHILD Study include:

- To determine whether stressful life experiences temporally precede biological and behavioural changes, and
- To determine whether these changes contribute to the development and progression of wheezing, allergy and asthma.

Dr. Subbarao noted that the CHILD Study looks at many different types of exposures, including stress, during the first years of the life of 5,000 children from conception to age five. Data are being collected about a range of variables including parental stress, socio-economic status and cultural determinants.

4. Other Canadian Networking and Research Partnership Opportunities

4.1 The Human Early Learning Partnership (HELP)

HELP is an interdisciplinary research network of faculty, researchers and graduate students from British Columbia's six major universities. Led by Dr. Clyde Hertzman, HELP facilitates the creation and application of new knowledge by working directly with government and communities. HELP works in partnership with, and receives funding from, the BC Ministries of Children and Family Development (MCFD), Education and Healthy Living and Sport.

HELP aims to make a unique international research contribution to understanding the biological, psychological and societal factors influencing children's health and development.

In pursuit of this mission, HELP will:

- Highlight the importance of the early years on health and development
- Utilize a longitudinal, life-course perspective
- Facilitate cell-to-society research collaborations and discourse
- Foster inter-disciplinary, inter-institutional, inter-cultural and inter-sectoral partnerships, and
- Facilitate knowledge exchange capable of transforming lives and communities.

AllerGen epigenetics research, undertaken by M. Kobor, is poised to forge new links and collaborations with the HELP initiative.

4.2 The Canadian Institute for Advanced Research (CIFAR)

The Canadian Institute for Advanced Research (CIFAR) supports the Experience-based Brain and Biological Development (EDBBD) Program, the focus of which has relevance to AllerGen's Mind-Body Interactions research thrust. (See <http://www2.cifar.ca/research/experience-based-brain-and-biological-development-program/> for more information about the EDBBD program).

AllerGen research leaders have been exploring opportunities to link and where possible leverage AllerGen and CIFAR research investments in mind-body interactions. Dr. Moshe Szyf, McGill University, is a member of the EDBBD research team and is providing CIFAR-AllerGen liaison between the two organizations. A one-day workshop involving the CIFAR team [(R. Barr (UBC), T. Boyce (UBC), Hertzman (UBC), M. Werker () and Kobor)] and AllerGen [(J. Denburg (McMaster), P. Paré (UBC), S. Turvey (UBC) and Kobor (UBC))] was held between the two organizations in November 2008. In addition, discussions are ongoing between the leadership of AllerGen and the EDBBD Program, and AllerGen investigators are encouraged to consider networking opportunities with CIFAR investigators working on related initiatives. A 2009-10 joint AllerGen – CIFAR mind-body researchers' workshop has been proposed for late 2009 or early 2010.

4.3 International Networking and Research Partnering Opportunities

Since 2007, AllerGen researchers have developed linkages with a range of international partner organizations which may enable Network researchers to advance future Mind-Body research in a globally networked context. These partnerships include:

- St. John's Institute of Population Health and Clinical Research (IPHCR), where AllerGen and Bangalore researchers are studying the impacts of psychological stress on respiratory disease development

- GA²LEN, a European research network, with which AllerGen researchers have developed a collaborative birth cohort data collection and data analysis process
- Karolinska Institute, with which AllerGen researchers have discussed a range of collaborative opportunities including birth cohort data collection and analysis and mind-body research collaborations.

There are significant opportunities for internationally networked mind-body research teams in AllerGen's future, particularly if the NCE program renews funding for Canadian-international networking and collaboration provided through the International Partnerships Initiative program which terminates on March 31, 2009.

5. Taking AllerGen's Mind-Body Research Thrust to the Next Level, 2009-2012 and Beyond: *How can we make the most of programmatic, networked Mind-Body Research?*

Workshop participants identified the following approaches for AllerGen investment in mind-body research:

1. Invest in Quick Wins:

- a. Build on biomarker research investments in the CHILD Study and molecular mechanisms of neuroendocrine immune regulation research
- b. Leverage existing research, e.g.,
 - Develop quasi-experimental designs for "Quick Wins" in relation to Manitoba's "Family First" program
 - Leverage CanGoFar to link probiotics and food allergy research
 - Leverage existing research to test a probiotic or molecule that AllerGen has already invested in (while noting that this type of project could be delayed due to FDA issues)
 - Leverage the AllerGen Clinical Investigator Collaborative (CIC) to test questions and models
 - Extend biomarkers research re: susceptibility (existing immune and inflammatory monitoring)
 - Leverage the SAGE Cohort which is launching its third phase of recruitment
 - Extend study of the gene cluster MTHFR and stress
 - Extend research and development related to the probiotics knowledge base
 - Extend research and development related to neuroendocrine immune regulation pathways
 - Leverage/develop population epigenetics research opportunities (unique Canadian expertise)
 - Leverage Mini-CHILD and CHILD Study subjects and samples
 - Undertake partnered research in collaboration with the Child Health Genomics (Rossant)/Genome Canada research team

2. Invest in Common Models

- a. Encourage study across levels with animal and human models
- b. Obtain a CFI core facility for epigenetic analysis in order to build core technologies as a national resource
- c. Develop a plan for multi-level data collection

3. Invest in research leading to early life intervention programs with strong potential for public policy impact

- a. Note the importance of ensuring the linkage of intervention studies across programs in the shorter term that furthers our understanding of mechanistic changes to help develop diagnostics in the longer term as well as to provide evidence to support the implementation of interventions that can prevent asthma from developing
- b. Keep in mind that research can effect public policy without understanding mechanisms

4. Invest in a major integrated study

- a. AllerGen researchers should identify a unifying theme for future investments in Mind-Body Interactions and Allergic Disease research that would be multidisciplinary, multi-level and cut across AllerGen's three major programmatic research thrusts – gene-environment interactions; diagnostics and therapeutics; and public health, ethics, policy and society.

5.1 Potential Research Collaborations, 2009-2012

Workshop participants identified the following unifying themes as opportunities for future AllerGen investment in Mind-Body Interactions and Allergic Disease research:

1. **Biomarkers Theme** – Undertake research to identify who is susceptible to allergic disease, leading to diagnostic and therapeutic innovations
 - Build on AllerGen's existing cellular and molecular mechanisms, neuroimmunology and neuroendocrine immune regulation research and CHILD Study data and sample collection, working across levels with animal and human models to identify the causes of allergic disease and develop new diagnostics and therapeutics
2. **Epigenetics Theme** – Build towards the development of a national epigenetic core technologies analysis platform in Canada that facilitates the development of diagnostic tools and new therapeutic approaches to allergic disease
3. **Interventions Theme** – Undertake research that has high potential to directly inform and/or affect public policy and/or healthcare practice and reduce the prevalence of allergic disease and/or improve the quality of life of allergic disease sufferers with strong links to mechanistic studies towards the longer-term development of new diagnostic tools and therapeutic approaches
4. **Major Integrated Study: E.g., The Canadian Mother-Child Stress Study** – Develop a study of the health effects/benefits of changing the mother-infant dyad on the prevalence and severity of allergic and related immune diseases

This approach envisions a significant, integrated programme of research that aims to understand the effects of stress on the development of and management of allergic and related immune disease focusing on the mother-infant dyad and leads to the development of societal and biologic interventions that reduce the prevalence and severity of allergic and related immune diseases and form the basis of new policy and therapeutic outcomes.

Workshop participants suggested that the following research platforms would be integral to the success of a large-scale, team research proposal of this nature:

- Phenotyping platform (behaviour and social constructs)
- Immune monitoring platform
- Eco-metrics and epigenetics platform
- Patient populations and data
- Common questionnaire tools (many of which exist)
- A bioinformatics data integrator
- Microbiotics platform

- Cognitive development platform
- Endocrine platform (to measure the endocrine response).

Workshop participants agreed that the development of a major integrated Mind-Body Interactions and Allergic Disease study would be a sizable undertaking, and would require a leader to oversee and coordinate the development of such a proposal. While this is conceptually a “tall order,” it could be scaled into doable component parts.

To bring this to fruition, AllerGen would be asked to facilitate and support the process of developing such a program of research. The exciting aspects of this approach would be the opportunity to unite the social and biological perspectives together in a single networked team. While some component parts may be “quick wins,” the overall magnitude of such a proposal is daunting.

Time is essential in order for the team to form and develop a detailed research program. The risk is that there may be a gap in terms of what will be funded in the Mind-Body thrust in the upcoming AllerGen Request for Proposals, 2009-2012.

It would be preferable to give the Mind-Body group more time – at least one year to develop a large program of research as well as to develop ways to enhance the resource base and not to fund such a proposal until all the necessary pieces are in place.

In the interim, the Mind-Body research thrust could focus on intervention studies with potential for impact on policy and practice that could be considered “quick wins” in terms of knowledge translation and transfer.

5.2 Strategies for Successful Mind-Body Researcher Participation in the AllerGen Request for Proposals, 2009-2012

Workshop participants noted that, in order to take Mind-Body research to the “next level” in Canada in the area of allergic and related immune diseases, AllerGen Mind-Body researchers must, from 2009 to 2012, work collaboratively and as a team to develop a seven-year research program plan while simultaneously undertaking research of which a significant portion is intervention-oriented.

They recommended that AllerGen Mind-Body Interactions and Allergic Disease researchers develop high impact, interventional/translational research proposals for 2009-2012, of which the majority have short-term deliverables and user sector impacts (e.g., policy, clinical), while simultaneously planning a transformational, multidisciplinary and nationally-networked research program to 2019.

To be successful, participants indicated that mind-body researchers must be in a position to identify a “champion” who would be willing to lead the Mind-Body Interactions and Allergic Disease cross-programmatic research team through the next three-year planning process and into a seven year multidisciplinary programme of research to 2019, as well as to pull together a team grant for the 2012 competition.

6. Next Steps and Milestones

Table 1: Key Action Items	Milestone
1. Workshop report issued	February 11, 2009
2. Expressions of Interest (optional) circulated	February 12, 2009
3. AllerGen Annual Conference, <i>Innovation from Cell to Society</i> ^A , Ottawa, Ontario <ul style="list-style-type: none"> • Mind-Body Research Team Proposal Development break-out groups on February 16 and 17th, 2009 • Opportunities for networking and workshops focused on the identification of new research and partnership opportunities 2009-2012 aligned with AllerGen's strategic goals and priorities 	February 15 – 17, 2009
4. Letters of Intent due	March 15, 2009
5. Letters of Intent reviewed	April 1-2, 2009
6. RMC issues feedback to all applicants and invites a sub-set of applicants to submit Full Proposals for funding 2009-2012. <ul style="list-style-type: none"> • This feedback may include suggestions for consolidation of individual submissions into teams and networked research projects 	By April 20, 2009
7. Full Proposals due at the AllerGen Administrative Centre	May 31, 2009
8. Arm's-length external review of the scientific excellence, capacity building, strength of networking, partnerships, social-economic impacts and budgets of submitted Full Proposals by AllerGen's International Scientific Excellence Advisory Committee (ISEAC), in conjunction with non-Investigator RMC members.	By June 30, 2009
9. Programme Leaders review and submit to AllerGen for international peer review	July 15, 2009
10. Funding instalment payments commence	By August 1, 2009
11. Mind-Body researcher progress report and strategic planning workshop	Winter 2009-10
12. Mind-Body quarterly planning team meetings/teleconferences to develop a research programme 2012 - 2019	March 2010 to March 2011

7. Concluding Remarks

Two years ago, in February 2007, AllerGen hosted a mind-body workshop in Hamilton, Ontario that brought together Network investigators interested in the development of AllerGen's mind-body research agenda with four guest presenters – Drs. Rosalind Wright, Firdaus Dhabhar, Moshe Szyf and Glenda MacQueen. These researchers shared their expertise and understanding of the way in which mind-body interactions research was developing and how AllerGen researchers might contribute to it and to meaningful social and economic impacts for Canadians. The full report of the February 2007 Mind-Body research workshop is available on the AllerGen website at http://www.allergen-nce.ca/Research/Workshop_Reports.html *Programme B: Diagnostics and Therapeutics, Mind-Body Interactions, 14 February 2007, Hamilton, Ontario.*

Since that initial workshop, AllerGen Mind-Body Interactions researchers have made great strides, as evidenced in the progress detailed in this report. Nationally networked, multidisciplinary teams, linked to research partners in the user sector are forming. Translational research opportunities are arising from AllerGen's initial research investments, which in many cases have been leveraged and are strategically attracting additional funds from a range of sources.

As Network research supported from 2007-2009 nears completion, AllerGen has issued a new call for nationally networked, multidisciplinary research proposals for 2009-2012 focusing on programmatically linked projects. Mind-Body Interactions and Allergic Disease research has evolved into one of AllerGen's seven strategic research priority areas with projects cutting across all three of the Network's programmatic research thrusts – gene-environment interactions; diagnostics and therapeutics; and public health, ethics, policy and society.

NCE research programs distinguish themselves from those supported by the CIHR by virtue of their interdependent, networked research teams working across disciplines and institutions, and in partnership with potential end users of the research results. Ideally, NCE researchers work in virtual teams on complex problems that would not and could not be addressed by individual researchers working alone. These research teams are funded to be transformational agents of innovation that develop, protect, translate and apply knowledge for economic and/or social benefit to Canada.

Over the next three years, AllerGen's Mind-Body Interactions and Allergic Disease researchers have an opportunity to position themselves individually and collectively to identify and execute studies, including intervention studies, with short-term outcomes that can be very helpful from a public policy perspective. In addition, Network investigators have an opportunity to develop a programmatically integrated and networked research agenda that aligns with AllerGen's mission to undertake research in a goal-oriented context where the translation of research results facilitates the achievement of social and economic impacts benefiting Canadians and improving the quality of life for people suffering from allergic and related immune disease.

We encourage you to review this report and use it to build upon current Network research, the relationships and the spirit of collaboration and partnership that pervaded this workshop to assemble successful, innovative and high impact multidisciplinary research and research planning proposals focusing on Mind-Body Interactions and Allergic Disease for the 2009-2012 period.

Working together to 2012, we can realize our ultimate aim of launching a major, high impact Mind-Body Interactions and Allergic Disease research programme as a mature, cross-cutting research team in AllerGen's second and final phase of NCE funding, 2012- 2019.

Dean Befus
AllerGen Research Leader

Programme B: Diagnostics and Therapeutics
and
Professor and Astra-Zeneca Canada Inc., Chair in Asthma Research
Division of Pulmonary Medicine
Department of Medicine, Faculty of Medicine & Dentistry
University of Alberta

Anita Kozyrskyj
AllerGen Principal Investigator, Mind-Body Interactions and Allergic Disease
and
Research Chair, Maternal Child Health and the Environment
Associate Professor, Department of Pediatrics, Faculty of Medicine & Dentistry
University of Alberta

24 February 2009

Appendix A: Workshop Agenda

Welcome Reception & Dinner December 10, 2008

6:00 – 8:45 p.m.

Inn at the Forks, River Salon, 2nd Floor
75 Forks Market Road, Winnipeg, Manitoba



Workshop December 11, 2008

7:30 am – 4:30 pm

Manitoba Children's Museum
Kinsmen Building
45 Forks Market Road
Winnipeg, Manitoba



Contact: Lynelle Watt, Programme B Co-Coordinator
University of Alberta (780) 492-1909 (on-site cell phone: 780-990-6211)

Wednesday December 10, 2008

Inn at the Forks, River Salon, 2nd Floor, 75 Forks Market Road

Welcome Reception, Dinner and Discussion

6:00 – 8:45 p.m.

Join us for a reception at 6:00, followed by dinner and an informal workshop launch/introductory session

Thursday, December 11, 2008

Manitoba Children's Museum, Kinsmen Building, 45 Forks Market Road

Mind/Body Workshop

7:30 - 8:00	Buffet Breakfast	
8:00 - 8:20	Welcome and Introductions <ul style="list-style-type: none"> • Workshop Objectives • AllerGen strategic priorities to 2012 • AllerGen Research opportunities update 	Dean Befus Anita Kozyrskyj Judah Denburg/ Diana Royce PJ Subbarao
<i>Invited Presentations:</i> Maternal Distress, Child Stress Response and Atopic Disease: From Population-based Observations to Mechanistic Studies		Chair: Anita Kozyrskyj
8:20 - 8:40	Javier Mignone Heather Henley	Community determinants of maternal distress
8:40 – 9:00	Miki Peer for Claudio Soares	Perinatal stress in immigrant mothers
9:00 - 9:20	Anita Kozyrskyj Sarah Yager	Maternal distress & child asthma

9:20 - 9:40	Brian MacNeil Lisa Dreger Darcy Heron	Maternal distress, child stress response & child asthma
9:40 – 10:00	Petra Arck	Animal models of perinatal stress
10:00 - 10:20	Michael Kobor	Epigenetics of perinatal stress
10:20 – 10:30	RESPONDENT: Policy maker perspective on value and opportunities for future research applications in this area (M. Chartier)	
10:30 – 10:40	General Questions and Discussion	
10:40 – 11:00	Break	
<i>Invited Presentations:</i> Maternal Distress, Child Stress Response and Atopic Disease: Molecular Pathways and Therapeutic Innovations		Chair: Dean Befus
11:00 - 11:20	Katherine Morris Dean Befus	Sympathetic regulation of inflammation
11:20 – 11:40	John Bienenstock Paul Forsythe	Treatment with probiotics
11:40 – 12:00	Denise Daley Anita Kozyrskyj	Genetics of postpartum distress; societal impact
12:00 – 12:10	RESPONDENT: Clinician perspective on the value of and opportunities for future research applications (A. Becker)	
12:10 - 12:20	General Questions and Discussion	
12:20 – 1:00	Lunch	
<i>Invited Presentations:</i> Maternal Distress, Child Stress Response and Atopic Disease: New Research Directions		Chair: Allan Becker
1:00 – 1:20	Nicole Letourneau	Maternal mental health treatment options
1:20 – 1:40	Mariette Chartier	Maternal health policy
1:40 - 1:50	RESPONDENT: Researcher perspective re: research opportunities in response to emerging societal needs (J. Bienenstock)	
1:50 – 2:05	General Questions and Discussion	
2:05 – 3:00	Break-out Groups: Taking AllerGen's Mind-Body Research Thrust to the Next Level: Strategic Research Priorities 2009-2012 and beyond – How can we make the most of programmatic, networked mind-body research?	

	<ul style="list-style-type: none">• Where is our opportunity to make a unique contribution to science and society?• Who benefits?• Who are the potential research partners (nationally, internationally)?
3:00 – 3:15	Break
3:15– 4:00	Report back
4:00 – 4:20	Synthesis and prioritization of suggestions
4:20 – 4:30	Next Steps <ul style="list-style-type: none">• Priority outcome(s) of the workshop• Next steps and timeframes
4:30	Adjournment

Appendix B: Workshop Participants

	Name	Affiliation
1.	Arck, Petra	McMaster University
2.	Becker, Allan	University of Manitoba
3.	Befus, Dean	University of Alberta
4.	Bienenstock, John	McMaster University
5.	Chartier, Mariette	Healthy Child Manitoba Office, and Community Health Science, University of Manitoba
6.	Colman, Ian	University of Alberta
7.	Denburg, Judah	McMaster University
8.	Dreger, Lisa	University of Manitoba
9.	Forsythe, Paul	McMaster University
10.	Henley, Heather	University of Manitoba
11.	Heron, Darcy	University of Manitoba
12.	Kobor, Michael	University of British Columbia
13.	Kozyrskyj, Anita	University of Alberta
14.	Letourneau, Nicole	University of New Brunswick
15.	MacNeil, Brian	University of Manitoba
16.	Mignone, Javier	University of Manitoba
17.	Morris, Katherine	University of Alberta
18.	Peer, Miki	McMaster University
19.	Royce, Diana	Meeting Facilitator
20.	Subbarao, Padmaja	University of Toronto
21.	Szyf, Moshe	McGill University
22.	Vliagoftis, Harissios	University of Alberta
23.	Yager, Sarah	University of British Columbia
24.	Watt, Lynelle	AllerGen Research Coordinator