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AllerGen

Innovation from cell to society



Success Stories

Networks of Centres of Excellence





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Making a Difference from cell to society

AllerGen NCE Inc. (AllerGen), the Allergy, Genes and Environment Network, is pleased to present its second issue of *AllerGen Success Stories*, featuring the research accomplishments of leading Canadian allergy, asthma, anaphylaxis, genetics and environment researchers, their students and partner organizations.

In this issue, the results of five AllerGen-supported projects are featured. These projects were undertaken in collaboration with partner organizations including Health Canada, The Asthma Society of Canada, Anaphylaxis Canada, the BC Lung Association, The Children's Asthma Education Centre, the Alberta Asthma Centre, the Karolinska Institute, the German Research Center for Environmental Health at Utrecht University, Groningen University and the University of Bristol. Each of these research initiatives ultimately aim to benefit patients and their families suffering from asthma and allergic diseases, including anaphylaxis.

Stories featured in this issue highlight research projects undertaken by pan-Canadian and international research teams in order to improve the lives of Canadians with anaphylaxis, asthma and allergies by:

- Strengthening Canada's food labelling regulations;
- Enhancing on-line access to asthma education tools;
- Offering asthma education tailored specifically for children
- Using geographical air pollution data to predict exposures; and,
- Developing novel medications.

Since 2005, AllerGen has worked to catalyze and support innovative research and discovery of causes, prevention and treatments of allergic and related immune diseases. As well, AllerGen contributes to the development, translation, mobilization, commercialization and policy use of research for the benefit of Canadians impacted by allergic disease, asthma, and anaphylaxis nationally and globally.

AllerGen invests in research in the following broad programmatic areas:

1. Gene-Environment Interactions

Strategic Focus: Genetics, environmental exposures and gene-environment interactions in allergy and asthma

2. Diagnostics and Therapeutics

Strategic Focus: Biomarkers, immune monitoring and drug development/discovery

3. Public Health, Ethics, Policy and Society

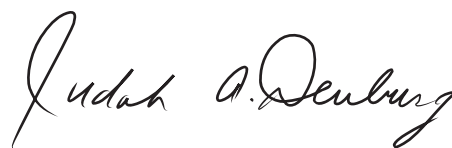
Strategic Focus: Allergic disease management and surveillance.

In addition, AllerGen supports four cross-programmatic, multi-disciplinary research teams:

- i. The Canadian Healthy Infant Longitudinal Development (CHILD) Study
- ii. Food Allergy and Anaphylaxis — the Canadian Group on Food Allergy Research (CanGoFAR) team
- iii. Mind-Body Interactions and Allergic Disease
- iv. Occupational and Work-related Allergy and Asthma.

Through its network of allergy and immune disease research experts and partner patient organizations, and with core support from the Networks of Centres of Excellence (NCE), a program of Industry Canada, AllerGen NCE hopes that these stories will accelerate dissemination, discussion and translation of research results.

With May being *National Asthma Awareness* month, and allergy season now upon us, we encourage all Canadians to take pride in the significant contributions that AllerGen NCE researchers are making to the global effort to more effectively understand, prevent, treat and manage asthma and other allergic diseases, which impact over 10 million Canadians per year. [A](#)



Judah Denburg, MD, FRCP(C), Scientific Director and CEO



Diana Royce, EdD, Managing Director and COO

A woman with long brown hair, wearing a pink short-sleeved shirt, is smiling and looking at a box of cookies she is holding in her right hand. She is standing in a grocery store aisle, with shelves of various food products visible in the background. A red shopping basket is in the foreground, containing some green leafy vegetables. The text is overlaid on the right side of the image.

“While it is commonly accepted that approximately 4% of Canadians have food allergies, this study found that 7.5% of Canadians believe that they have at least one food allergy and that the prevalence of food allergy differs between socio-economic groups and geographic regions” states Dr. Clarke.

AllerGen Food Allergy and Food Labelling Research Team Supports Policy Updates to Enhance the Protection of Food Allergic Consumers

Good government policy is based on strong scientific research. Without research, how can governments understand the nature and extent of a problem or know what is required to address it?

Drs. Ann Clarke, an Allergist at McGill University, and Susan Elliott, a Medical Geographer at the University of Waterloo, met through AllerGen NCE Inc. (AllerGen) and have since become a “dynamic duo” in Canadian food allergy research. In 2007, they embarked on a mission, in partnership with Health Canada, to establish the first national estimates of the number of Canadians with common food allergies. They were also curious about Canadians’ attitudes toward food allergy and whether or not product labels on food items adequately warned consumers about allergy-related ingredients.



Dr. Ann Clarke, McGill University



Dr. Susan Elliott,
University of Waterloo

Study data was obtained through telephone surveys with almost 10,000 adult Canadians, whose phone numbers were randomly selected from the White Pages. Survey questions, originally developed by Dr. Scott Sicherer at Mount Sinai Hospital in New York City, were adapted for use in Canada.

Research dependent upon public participation poses unique challenges for investigators. The general public is not always willing to participate in telephone surveys when contacted by a researcher. In the case of this project, 35% of those who answered the phone chose to participate. “Of course this wasn’t the participation rate we had hoped for, but realistically speaking, this is what you get now in most telephone surveys,” says Dr. Clarke. Nevertheless, the data obtained was reliable due to the survey design.

How Common Are Food Allergies in Canada?

Survey respondents were asked if they or any member of their household believed that they had a food allergy, particularly to peanut, tree nut, fish, shellfish or sesame. They were also asked if any of those food allergies had been confirmed by a doctor through allergy testing.

The main hurdle in this study was determining who, in fact, had a true food allergy. Many survey respondents, who believed

that they had a food allergy, had not seen their family doctor for allergy testing. Second, of the small group of survey respondents who had confirmatory tests, only some gave the researchers permission to access their medical file. Even then, only a few of the doctors’ offices contacted actually sent researchers the requested files.

In order to determine the prevalence of food allergies in Canada, Drs. Clarke and Elliott relied on food allergy symptoms as reported by survey respondents. “We asked very detailed questions about the foods that they had eaten, the symptoms that they had experienced, how long after they had eaten the food did they have these symptoms, and whether these symptoms occurred predictably each time after they ate the food. We then determined whether or not these symptoms suggested that they were truly having an allergic reaction,” explains Dr. Clarke.

Food allergy symptoms generally develop within an hour after eating. Symptoms may include an irritated mouth, swelling of the lips or the tongue, runny eyes or nose, itchy skin or hives, difficulty breathing, stomach cramps, vomiting, unconsciousness, and in some cases, even death.

“While it is commonly accepted that approximately 4% of Canadians have food allergies, this study found that 7.5% of Canadians believe that they have at least one food allergy and

that the prevalence of food allergy differs between socio-economic groups and geographic regions” states Dr. Clarke.

Dr. Elliott added, “Our research also shows that a large gap exists between Canadians’ perception of food allergy prevalence and actual food allergy prevalence. Food allergy is

“Health Canada has the benefit of all the data that we have collected. The government has made an informed decision about what sorts of labels will work on foods packaged to best benefit those suffering from food allergies,” states Dr. Elliott

the primary trigger of anaphylaxis, which we know can be life threatening. It is, therefore, essential that through research, we compile a comprehensive picture of food allergy prevalence and perception in Canada to appropriately inform regulatory decisions and reduce the overall burden.”

Do Canadians Take Food Allergies Seriously?

Survey respondents were asked to estimate what percentage of the population has a food allergy. On average, respondents believed that 33% of all Canadians, or one in three people, have a food allergy. This confirms that Canadians believe food allergies are more common than the evidence suggests. Researchers also found that Canadians typically rated the risk associated with having a food allergy as “very high.”

Dr. Clarke pointed out that while food allergy has to be taken seriously, the symptoms of the disease are completely preventable, which is not the case with most chronic diseases. “If you recognize food allergy early, and through proper education and food labelling you avoid the food, then you should never have any problems with the allergy,” she explains. “However, it can be very difficult to avoid foods containing allergens such as peanut and accidental exposures often occur.”

There are some notable exceptions when it comes to Canadian attitudes related to the dangers associated with food allergy. Seniors tend not to take food allergy seriously, which can cause friction with family members who have children with a food

allergy. “To older people, this is a relatively new thing, and it doesn’t make much sense,” says Dr. Elliott. Also, men who have a severe food allergy “tend to be more cavalier in their behaviour,” she advises. “The literature does tell us that familiarity with a risk lessens your perception of it.”



Drs. Clarke and Elliott suspect that the media plays a key role in creating the false perception that food allergy is both rampant and highly dangerous. Dan Harrington, a PhD student supervised by Dr. Elliott, conducted a media analysis of all the national and regional newspapers in Canada, a total of 18 English and French language newspapers, from the year 2000 onward. He looked at how often food allergy prevalence is reported, and who the media quotes as “experts” in their stories.

Mr. Harrington found that the media consistently exaggerates the prevalence of food allergy. It appears journalists typically rely on reports from affected individuals such as parents of allergic children and are not checking the facts with qualified allergy experts, patient associations or research networks like AllerGen NCE.

Do We Need to Improve Our Food Labels?

The answer is a resounding “yes!” and Health Canada has taken the first step in February 2011, by finalizing changes to *Canadian Food and Drug Regulations*, which will require the declaration in plain language of allergens in food products including almonds, Brazil nuts, cashews, hazelnuts, macadamia nuts, pecans, pine nuts, pistachios, walnuts, peanuts, sesame seeds, wheat and triticale, eggs, milk, soybeans, crustaceans, shellfish, fish and mustard seed. These rules will also limit instances where one of these ingredients will be “hidden” from declaration, because it is a secondary ingredient or component of ingredient. However,

at present, several different types of precautionary statements for allergy-related ingredients on Canadian product labels still exist, which is confusing for consumers. For example, a label could state: “may contain nuts,” or, “may be produced in a factory that manufactures nut products,” or “may be produced on equipment that has come into contact with nuts.” In some cases, the precautionary statement on the label is inappropriate. For example, there are labels on some 100% fruit-juice popsicles that state, “may contain nuts.” A consumer who is interested in avoiding nut products could be confused over which product is a safe purchase.

Health Canada aims to reduce the number of precautionary statements used on Canadian food labels and is looking to Drs. Clarke and Elliott’s research to provide guidance. Based on their research findings with respect to consumer choices and Canadians’ perception of risk when it comes to food allergy, the feedback to Health Canada is that the information on food packaging must be both simple and prominent.

Drs. Clarke and Elliott have also provided the data from this study to AllerGen investigators specializing in health economics at the University of British Columbia, who are brainstorming different ways to present precautionary statements to consumers, and are speaking to consumers about which of the options they like the best and why. For example, is it better to write “Peanut-free,” or have a symbol that denotes this?

The challenge is agreeing on a set of precautionary statements that are consistent, universally understandable, and prominently displayed on food packaging. Canada is a nation of immigrants, which means that researchers designing precautionary statements need to take into account the fact that English or French may not be the first language for many Canadians, and that there may be cultural differences when it comes to interpreting symbols. An additional challenge is the visual clutter created as a result of having to include precautionary statements and ingredient lists in both English and French. Similarly, the smaller font size required to accommodate the additional information may make labels harder to read. As a result, precautionary statements can be easily missed by seniors, people with impaired eyesight, or by hurried shoppers.

The good news for Canadians is that results from this nationwide study have already been used by Health Canada to change food labeling regulations and the next step is to improve precautionary statement labeling on food products containing


common allergens. “Evidence-informed policy is important,” states Dr. Elliott and “Health Canada has the benefit of all the data that we have collected. The government has made an informed decision about what sorts of labels will work on foods packaged to best benefit those suffering from food allergies.”

Filling the Knowledge Gaps

As a clinical allergist and epidemiologist, Dr. Clarke studies the natural history of a disease, describes its frequency and identifies factors influencing its outcomes. Dr. Elliott, on the other hand, as a medical geographer, studies the influence of environment on health and well-being.

It was AllerGen NCE that encouraged Dr. Clarke and Dr. Elliott to work together and as a result, a highly successful research partnership was born and continues to thrive. “Without AllerGen, our paths would not have crossed,” says Dr. Clarke. “The partnership would not have happened, and AllerGen helps us to nurture that relationship.”

Drs. Clarke and Elliott have clearly benefited from their affiliation with AllerGen NCE, and will in turn benefit Canadian consumers by passing their findings on to Health Canada. They have also been working closely with Canadian patient advocacy groups like Anaphylaxis Canada; Association Québécoise des allergies alimentaires (AQAA) — Quebec’s food allergy association; and the Allergy/Asthma Information Association (AAIA), so that people living with food allergies have access to the most current information.

Drs. Clarke and Elliott aim to ensure that this AllerGen NCE - Health Canada study improves the everyday lives of Canadians, and to date they have had a direct impact on Canadian public policy. As of August 2012, the mandatory changes on all Canadian food labels for allergen ingredient declaration will take full effect. Other changes using these research results are being contemplated by Health Canada in the months ahead. Dr. Samuel Godefroy, Director General, Food Directorate with Health Canada says, “Health Canada’s Food Directorate has had a very fruitful collaboration with AllerGen.” Dr. Godefroy adds, “Health Canada’s Food Directorate will continue to partner with AllerGen to fill the knowledge gaps associated with food allergies and anaphylaxis in support of its actions to enhance the protection of food allergic consumers in Canada.” 



Researchers have a better understanding of a disease when there are one or two “misbehaving” genes to isolate and study. However, asthma is a complex disease that involves many genes interacting with the environment and lifestyle.

Using the World-Wide Web to Drive Asthma Genes Research Forward at High Speed

Imagine a world where medicine has evolved beyond the 'one size fits all' approach, with family physicians prescribing asthma treatments based on a patient's genetic profile.

A team of researchers at AllerGen NCE are working to turn this possibility into reality. They recognized, however, that in order for asthma gene studies to advance rapidly and reach the point where genetic testing is widely available, the large amount of data that these studies generate needs to be organized in a user-friendly database, accessible to researchers everywhere. The potential for genetically based asthma "break-through" treatments generated by global knowledge-sharing inspired a group of AllerGen NCE researchers, led by Dr. Denise Daley at the University of British Columbia, to create an innovative website called "Genapha," short for *genomic applications for humanity*.



Dr. Denise Daley, University of British Columbia

This web-site provides easy global access to a complex database of asthma-related genes studied by the AllerGen NCE team. Genapha has been extremely well received by the global asthma research community, which shares AllerGen's vision for asthma diagnosis and treatments tailored specifically to patient needs.

This initiative has been a resounding success. As of April 2011, the Genapha website has had 7,555 individual users from 88 countries. Of those visiting the site, 51.5% returned to access more information.

Why We Need Genapha

Researchers have a better understanding of a disease when there are one or two "misbehaving" genes to isolate and study. However, asthma is a complex disease that involves many genes interacting with the environment and lifestyle. Genetic research produces an enormous amount of data. Traditionally, results from scientific studies are shared with other researchers

through publication in peer-reviewed journals and presentations at conferences. While these are important forums, the limitation is that only significant results are shared. AllerGen NCE researchers wanted to go beyond publishing only significant results. They believed that researchers locally and internationally could instantly benefit from accessing all the genetic data arising from their asthma study. In addition, due to the nature and similarity of asthma genes, a public database of asthma-related genes studied would also be a valuable resource for researchers studying other types of inflammatory and immunological diseases.

The Birth of Genapha

AllerGen NCE recognized a global need for an asthma-related genetic database and, as such, invested \$175,000 into the development of the Genapha website. "Science is now a global enterprise, and AllerGen has provided us with the funding



Dr. Daley and her team are currently in the process of improving Genapha's search tools and expanding the capabilities of their 'Path' software. In the near future, Path2 will be launched and the team will be expanding Genapha's links to patient education and advocacy group websites. Dr. Daley and fellow AllerGen NCE researchers are also studying asthma genes that span the entire human genome. The results of this study will be added to the Genapha website when completed. "We are just at the beginning of where Genapha can go," says Dr. Daley.

support to develop global network connections," says Dr. Daley. Additional funding was provided by the Canadian Institutes of Health Research (\$25,000) and the BC Lung Association (\$22,500). Genapha brought together four separate AllerGen NCE-sponsored asthma studies involving 5,565 individuals in Canada and Australia. These individuals have been genotyped for 162 genes that researchers suspect are involved in asthma, generating more than 12.3 million genotypes. Genotyping is the process of determining the genes (genotype) of an individual by examining their DNA sequence using a type of scientific experiment (biological assays). "Genapha is a wonderful platform to showcase what AllerGen researchers have accomplished," says Dr. Daley.

To maximize the usefulness of the website, <http://genapha.icapture.ubc.ca> Dr. Daley and her team have integrated knowledge from 11 different public databases into Genapha. The challenge was then navigating the sheer volume of available information. To meet this challenge, the team developed new,

innovative tools and software titled "Path" and "SLIMS" to make searching for information easier and allowing users to interact with the data. These tools have been incorporated into the Genapha website. Software packages have been developed and can be used by any researcher studying complex traits whether they are in humans, animals or even plants.

Genapha's Global Impact

This initiative has been a resounding success. As of April 2011, the Genapha website has had 7,555 individual users from 88 countries. Of those visiting the site, 51.5% returned to access more information. In addition, "Path" software has been downloaded over 3,000 times. The "SLIMS" research software, released on July 2010, has also had more than 1,850 hits and has over 1,000 registered users.

In addition to a positive response by the international research community to Genapha, 54 organizations have requested permission to link to the Genapha website, including



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“Genapha is a wonderful platform to showcase what AllerGen researchers have accomplished,” says Dr. Daley.

asthma education and advocacy groups. The Genapha site also makes available sophisticated animations developed by University of British Columbia’s Dr. Scott Tebbutt, Assistant Professor in the Department of Medicine, Division of Respiratory Medicine, which can be used to assist asthma patients and their families seeking to learn more about the genetic factors associated with asthma.

Future Developments

Dr. Daley and her team are currently in the process of improving Genapha’s search tools and expanding the capabilities of their ‘Path’ software. In the near future, Path2 will be launched and the team will be expanding Genapha’s links to patient education and advocacy group websites. Dr. Daley and fellow AllerGen NCE researchers are also studying asthma genes that span the entire human genome. The results of this study will be added to the Genapha website when completed. “We are just at the beginning of where Genapha can go,” says Dr. Daley. Ultimately, Genapha’s capacity to better manage scientific data and promote global networking will culminate into the development of focused genetic testing, better diagnostic tools and personalize management of asthma for Canada’s 3.4 million asthmatics. [A](#)



When asked what he wants you, the reader, to know about this project, Dr. Becker responds: "It's all about education. Education, education, education! Education is a critical component in healthcare and in changing behaviours of children and their families."

Teaching Kids with Asthma

How to Take Charge of Their Health

Asthma, a common chronic inflammatory disease of the airways is a major health problem, affecting up to one in five children in Canada, or 20% of the population under the age of 18. Asthma is the leading cause of children missing school and parents missing work for associated emergency room visits. Asthma has a negative impact on the quality of life of our children; it is no fun sitting on the sideline during team sports. It takes an enormous emotional toll on both children and their families. During an asthma attack, children are often terrified as they labour to breathe. Some kids say they feel as though they are being suffocated.

Until there is a cure for this disease, it is imperative to control symptoms and reduce the frequency of flare-ups and full-blown attacks. This is why asthma education programs are important.



Dr. Allan Becker, University of Manitoba

The Roaring Adventures of Puff: A School-Based Asthma Education Program

Dr. Allan Becker is a passionate advocate for children's asthma education. "Education can be extremely positive. It may be the single best approach to therapy that we have."

In addition to being a Professor in the Department of Pediatrics & Child Health at the University of Manitoba and a consultant allergist, Dr. Becker is also Director of The Children's Asthma Education Centre (CAEC) at the Children's Hospital of Winnipeg. The CAEC provides education delivered by Certified Asthma Educators to children and their families, and develops and assesses new strategies for asthma education.

One of the new educational strategies that Dr. Becker was interested in assessing was a school-based asthma education program for children aged 7 to 12 developed by Ms. Shawna McGhan and her team at the Alberta Asthma Centre at the University of Alberta.

The program — called *The Roaring Adventures of Puff*, or RAP, stars a "cool" dinosaur named Puff who, like the children, has asthma. With the help of Puff, a Certified Asthma Educator teaches children about asthma, its triggers, how to cope with symptoms, how medications work, and proper use of asthma medication and devices. Within the small group setting, kids with asthma are encouraged to talk about coping skills and begin

addressing their feelings of anxiety, loneliness, embarrassment and other personal challenges that get in the way of reaching their potential. The program consists of six one-hour sessions that use games, crafts and puppetry to teach lessons in a fun, interactive manner. The lessons are taught at school, typically during lunch break. RAP involves not only the kids with asthma, but also the larger school community and their families. Consequently, the program develops multiple support systems for the child and has positive effects on self-esteem and confidence. The aim of RAP is to equip children and their peers with the knowledge, as well as the confidence, skills and tools to control their asthma, that can keep them healthier over their life time.

The program has been proven successful in primary schools in Alberta and Ontario and as such, Dr. Becker wanted to launch the program in Manitoba. He was interested in whether or not schools that offered this asthma education program in Manitoba experienced a subsequent decline in absenteeism and an improvement in health outcomes as was the case in Alberta and Ontario. He was also keen to launch the program in rural and inner-city schools – settings in which the program had not yet been delivered and are more difficult to reach with conventional health services.



Puff the *Asthmasaurus* Visits Manitoba

With core funding from AllerGen NCE (\$62,000) and partnership support from the Children's Hospital Foundation (\$20,000), the RAP program has now run in 23 schools in Winnipeg (including inner-city schools) and in four schools in rural Manitoba (one of which is in a First Nations community). To date, a total of 178 children in Manitoba have completed the program.

The team responsible for implementing the RAP program in Manitoba, as well as assessing its effectiveness, are Dr. Becker, Ms. Catherine Gillespie and Ms. Lesley Stewart (both from Winnipeg Health Sciences Centre) with the support of Ms. Shawna McGhan (Alberta Asthma Centre) and Dr. Dean Befus (University of Alberta). The Certified Asthma Educators who delivered the program were provided by Manitoba's Ministries of Health and Education, and the CAEC.

One outcome of the RAP program is to reduce school absenteeism, which can impact school performance, parental work absenteeism and quality of life. The team has compared the number of school absences of children with asthma at baseline (before the start of the program), to the number of absences recorded after the program was delivered (at 6 and 12 month follow-up intervals). A sustained decline in school absenteeism will indicate a positive change in the behaviours of children with asthma. "You can change knowledge quite quickly, but that doesn't necessarily convert into a change in behaviour, and it definitely may not convert into change over time," states Dr. Becker.

The team used the 'Pediatric Asthma Specific Quality of Life' (ASQoL), "Parental ASQoL" as well as the "Parental Lost Productivity" questionnaires to assess how the RAP program

impacted asthma control. The questionnaire is self-reported (*i.e.*, children and parents are asked to complete it). The questionnaire was given to the children during the first and last class of the RAP program, then 6-months and 12-months after the program ends. Parents and caregivers also received their self-reported questionnaires to complete at the same intervals.

The research team hopes to see positive behavioural changes and effective problem solving skills in RAP program graduates that include avoiding asthma triggers (*e.g.*, pets), changing their environment (*e.g.*, a smoke free home), and using

is increased potential to have more trained personnel,” says Dr. Becker.

“Education, Education, Education!”

When asked what he wants you, the reader, to know about this project, Dr. Becker responds: “It’s all about education. Education, education, education! Education is a critical component in health-care and in changing behaviours of children and their families.”

He also acknowledges that in order to have the best educational practices, there is a need for additional research in the field of


The RAP program and Puff the Asthmasaurus have been warmly welcomed by Manitobans and according to Dr. Becker, this project has received “very positive feedback” from all stakeholders in school health (*i.e.*, school administrators, teachers, parents, students and regional health authorities). This is an important step in the right direction in assisting children to have better control over their asthma symptoms. In addition, thanks to grants from AllerGen NCE and the National Lung Health Framework, and the support of Dr. Becker’s team, there is now an online training program to become a qualified RAP instructor.

medications as directed. These behaviour changes should lead to a reduction in asthma flare-ups and asthma-related school absences. Dr. Becker and his team hope to complete the data analysis by late 2011.

The RAP program and Puff the Asthmasaurus have been warmly welcomed by Manitobans and according to Dr. Becker, this project has received “very positive feedback” from all stakeholders in school health (*i.e.*, school administrators, teachers, parents, students and regional health authorities). This is an important step in the right direction in assisting children to have better control over their asthma symptoms. In addition, thanks to grants from AllerGen NCE and the National Lung Health Framework, and the support of Dr. Becker’s team, there is now an online training program to become a qualified RAP instructor. AllerGen’s investment in this online training program provided a critical base to build upon and disseminate the program. The experience gained from this study will inform modification to the RAP instructor’s training course and in particular, how to engage and mentor remote and aboriginal communities with limited formal healthcare backgrounds. “This means that there

healthcare education. There are many and varied factors at play, from the way a program is planned and delivered, to how you involve the family and healthcare team, to individual and population learning styles and cultures. The RAP program encourages each instructor to adapt the program to meet group needs, but more research is needed to understand best implementation strategies.

The problem is getting the necessary funding to support education research and program delivery. “It’s nearly impossible to get funding for education programs,” sighs Dr. Becker. “Without support from organizations like AllerGen, you can’t convince governments, school boards and hospitals that the investment is worthwhile.”

Asthma education can potentially result in a reduction in school and work absenteeism, unclog our emergency rooms, lower healthcare costs and improve the quality of life for an overwhelming number of Canadians. Can we afford not to support it? 

Air pollution maps are useful tools for any study looking at the effects of traffic generated air pollution on human health. “One of the advantages of the maps is that they become very flexible in their use once they are developed,” states Dr. Allen.



Mapping Air Pollution to Predict Asthma

It is well documented in the research literature that traffic-generated air pollution irritates the airways of individuals living with asthma. Emerging evidence now suggests that traffic-generated air pollution also contributes to the development of asthma — a chronic disease affecting 3.4 million Canadians. Exposure to traffic-generated air pollution, while in the womb and during childhood, could also be an independent risk factor promoting the development of asthma.

In order to investigate the relationship between traffic-generated air pollution and asthma further, AllerGen NCE committed \$79,480 to the research program of Dr. Ryan Allen (Simon Fraser University) and Dr. Michael Brauer (University of British Columbia) to develop air pollution maps for the cities of Edmonton and Winnipeg. These maps complement those already developed for a number of other Canadian cities and can be used to estimate the extent to which city residents are exposed to air pollution. This tool paves the way for Canadian scientists to further explore the connection between air pollution and the development of asthma.



Dr. Michael Brauer,
University of British Columbia



Dr. Ryan Allen, Simon Fraser University

Using Telephone Poles to Make Maps

Drs. Allen and Brauer set out to determine and map the concentrations of nitrogen dioxide (a tell-tale gas found in traffic-related air pollution) in relation to the road system and land use in Edmonton and Winnipeg. Their team included Dr. Moira Chan-Yeung, Dr. Chris Carlsten (both from University of British Columbia), Dr. Allan Becker (University of Manitoba), and university students working as field technicians.

Matchbox-sized nitrogen dioxide monitors were attached to telephone and power poles at 40 different locations in Edmonton and Winnipeg and left to collect data over a two-week period. These monitors were strapped to the poles during two different seasons (summer and winter) to account for temperature variations.

Drs. Allen and Brauer extracted data from the monitors and were then able to calculate the average nitrogen dioxide concentration, or traffic-generated air pollution concentration,

for each location. Their goal was to determine the air pollution concentrations across the entire city, not just at the 40 locations where the monitors were placed. To do this, the research team used a technique called land use regression analysis to predict the relationships between levels of air pollution, road systems/ distances to the nearest major roads; and land use, including quantities of land zoned for industrial use in the surrounding areas. Dr. Allen explained, "The power of this technique is that while we don't know the air pollution concentrations everywhere, we know where all the roads are, and where the industrial lands are. So, if we can understand the relationship between pollution and land use, then we can predict pollution concentrations everywhere." This technique has resulted in maps for Edmonton and Winnipeg that depict the concentrations of traffic-generated air pollution across those cities.

On further examination of these maps, AllerGen NCE researchers discovered that a difference in air pollution



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concentration exists between distances of as little as 75 metres. Thus, people living in close proximity to a major road are exposed to different concentrations of air pollution than those living just 75 metres away.

Does Every City Need an Individualized Air Pollution Map?

Researchers using land use regression analysis have long pondered whether or not an air pollution model for one city can be transferred to another. For example, can geographical predictors of air pollution in one city be applied to another city with the same predictors? Dr. Allen's team was one of the first to actually study this question. "This was the novel aspect of our study, given that land use regression has been done in other places in North America and Europe," he said. Their research led to the conclusion that a model for one city has limited use for another city. The model provides a rough picture of what is

going on in terms of concentrations of air pollution (a useful first step), however, for optimal results, it is more beneficial to develop a customized model for each city.

How Air Pollution Maps Contribute to Asthma Studies

The purpose of the research team's maps is not simply to document air pollution concentrations across the cities of Edmonton and Winnipeg. They are essential tools for a number of important, AllerGen NCE-funded asthma studies. AllerGen researchers are using these maps together with previously generated data to accurately predict the amount of air pollution a child has been exposed to, once it is known where the child lives or spends most of his or her time.

Drs. Allen and Brauer credit AllerGen NCE with encouraging them to think of practical uses for their maps. "AllerGen forces you to get the most out of your research," says Dr. Allen. The

maps were initially produced to support the *Canadian Asthma Primary Prevention Study* (CAPPS) conducted in Vancouver and Winnipeg — where a link between traffic-related air pollution and asthma was recently demonstrated, as well as the Winnipeg-based *Study of Asthma, Genes and Environment* (SAGE). These maps will also be used as pollution exposure assessment tools in the *Canadian Healthy Infant Longitudinal Development* (CHILD) Study, a multidisciplinary study of 5,000 Canadian children enrolled ‘pre-birth’ and followed for five years.

Drs. Allen and Brauer are currently collaborating with a Health Canada research group that is using the maps to see if air pollution is associated with stroke. Their data and models are also being used in a CAREX Canada project titled *Surveillance of Environmental and Occupational Exposures for Cancer Prevention*. These maps, and the health studies they serve, could one day result in major changes in urban planning *i.e.*, how cities are designed, where schools are built and where major roads are constructed.

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The CHILD Study is by far Canada’s largest study on how genes and environmental factors interact and influence the development of allergic disease.


In addition to the CHILD Study, these maps are being used in the AllerGen NCE-funded *Traffic Pollution, Asthma and Genetics* (TAG) study led by Drs. Brauer and Carlsten, a major international partnership undertaken in collaboration with researchers at the Karolinska Institute, The German Research Center for Environmental Health, Utrecht and Groningen Universities in The Netherlands, and the University of Bristol (UK). The aim of this project is to combine high-quality air pollution and genetic data from birth cohort studies to better understand the role of traffic-generated air pollution and its interaction with genetic factors on the development of asthma and allergy in children.


Multiple Uses for Air Pollution Maps

Air pollution maps are useful tools for any study looking at the effects of traffic generated air pollution on human health. “One of the advantages of the maps is that they become very flexible in their use once they are developed,” states Dr. Allen.

AllerGen NCE Promotes Applied Networked Research

Drs. Allen and Brauer agree that AllerGen NCE played an instrumental role in their success. “There is no way that this project would have happened without AllerGen funding,” states Dr. Brauer, who adds “it is notoriously difficult to get funding for projects that apply already existing knowledge.” Perhaps more importantly, AllerGen NCE encouraged the use of the maps in multiple Canadian asthma studies and other health research.

AllerGen NCE also helps young researchers develop their careers. A case in point is provided by Dr. Allen. “AllerGen has been incredibly helpful to me,” he says. “Not only am I a relatively new investigator, I am also a newcomer to the Canadian research landscape. It has been a tremendous resource for me to learn who is doing what, and who is the “go-to” person for specific information. It has also given me valuable learning opportunities. One of the nicest things about AllerGen NCE is that you are exposed to numerous people doing different types of work and you have an opportunity to interact with people that you would not otherwise interact with.” 

A person is shown from the waist down, sitting in a meditative pose (Padmasana) on a light-colored surface. They are wearing a white tank top and white shorts. Their hands are held in front of them in a mudra, with the index and thumb fingers touching. The background is plain white.

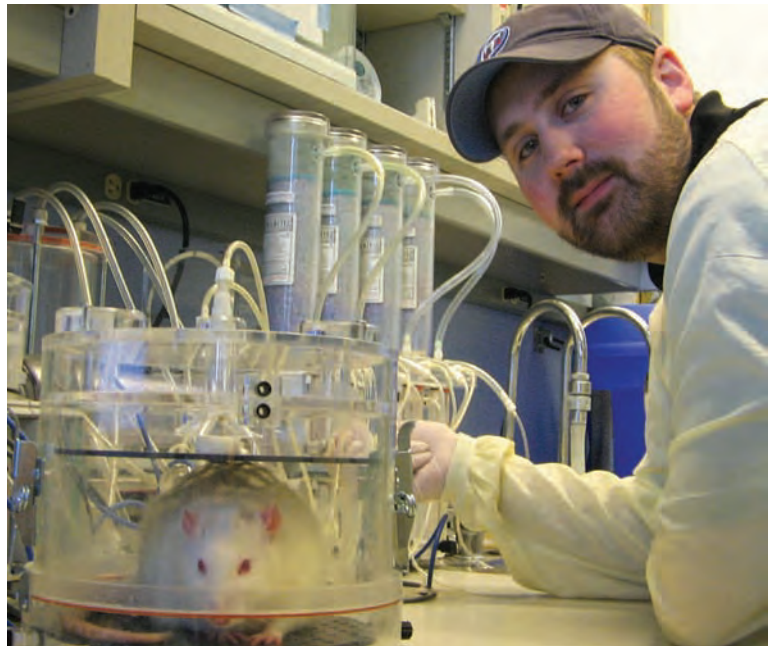
Modern science is just beginning to understand how the pathway and molecules work in the human body to regulate allergic responses and inflammation. Dr. Befus predicts that advancing knowledge of pathways and molecules will lead to the development of better diagnostic tools.

Unlocking the Secrets of Mind-Body Connections to Revolutionize Inflammatory and Allergic Disease Diagnosis, Treatment and Prevention

Science is finally catching up with ancient wisdom; there is a powerful connection between our minds and bodies.

Dr. Dean Befus, a professor at the University of Alberta, and his colleagues Dr. Ronald Mathison and Dr. Joseph Davison, from the University of Calgary, have been on a 25 year quest for the mind-body pathway that naturally regulates allergic and inflammatory diseases. These researchers embarked on a mission to understand how the nervous system controls allergic and inflammatory responses at a cellular and molecular level. In doing

this, they hope to develop novel treatment and prevention strategies for a wide variety of allergic and inflammatory conditions such as asthma and other airway diseases, food allergies, skin allergies, septic shock and spinal cord injury.



Chris St. Laurent, University of Alberta

This ambitious research project has faced many obstacles over the past two decades; from finding that human bodies work differently from their animal models, to struggles with securing funding essential to sustain the project. Thanks to the perseverance of this research team and AllerGen NCE (which provided funding and helped build valuable partnerships with research experts across disciplines), new novel, anti-inflammatory and anti-allergy medications have been developed that may soon be ready for human clinical trials. "If the research is correct, then it will be a significant success story in Canada of fundamental scientific discovery that has been successfully translated into new applications," states Dr. Befus.

On the Path to Understanding How Inflammation Works

Over two decades ago, Drs Befus, Mathison and Davison first aspired to increase knowledge about a poorly understood pathway in the nervous system that regulates the body's immune and inflammatory responses. They selected an inflammatory

response that they understood very well through experience — inflammation in the lungs (*e.g.*, asthma) and in the intestine (*e.g.*, food allergies) and set out to find the responsible cells and molecules.

After years of studying rats, the researchers identified the nerve pathway involved with inflammation. They discovered that the salivary gland is an important part of this pathway that has "dramatic, anti-inflammatory effects," says Dr. Befus. The nerve pathway controls the release of a hormone that regulates inflammation. Researchers not only identified the nerve pathway involved, but also found the large hormone involved, called a prohormone, as well as the specific part of the prohormone that is responsible for this biological activity.

Different parts of this prohormone promote different biological activities. For example, other research groups have found that one part of this prohormone plays a role in both pain control and erectile dysfunction. The entire prohormone is approximately 146 amino acids long. The section of this prohormone that interests AllerGen NCE researchers is very small, at only three

amino acids long. This tiny piece of the prohormone is most abundant in the rat's salivary glands, but can also be found in other places in the rat's body, for example, in male reproductive organs and in the lungs.

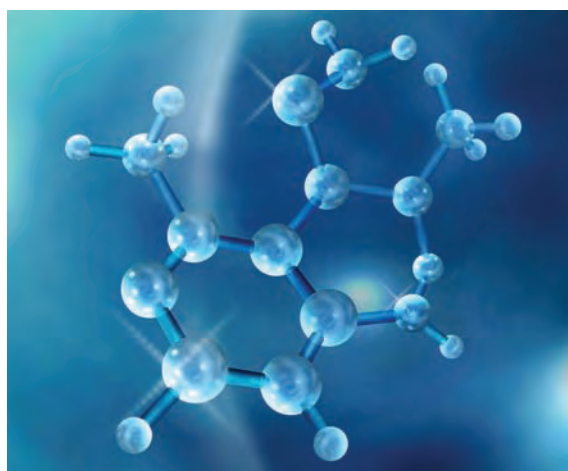
After identifying the portion of the prohormone involved in wound-healing in rats, the team's next step was to determine if the same prohormone exists in humans. Facilitated by AllerGen NCE, the team partnered with Dr. Mark Wilkinson, an expert in bioinformatics research at the Department of Medical Genetics, University of British Columbia (UBC).

With their UBC colleague, the team discovered that humans do not have the exact gene that rats do for producing the prohormone. However, it is likely that there are one or more

can no longer sit in an ivory tower and not consciously think about what impact your research has upon society," says Dr. Befus.

This research team is diligently working to translate its discoveries about the pathway and prohormone segment involved in inflammation, into tangible benefits for Canadians. An exciting potential benefit is the development of novel medications to treat allergic diseases such as hay fever, asthma, eczema and food allergies, which have reached unprecedented levels in the Western world and are among the fastest growing diseases reported by Canadians. There is also the potential for this research to translate into new medications to treat other inflammatory conditions such as spinal cord injury and sepsis,

Researchers are beginning to understand the biology of a pathway involved in human allergy responses and inflammation, and are on the cusp of human clinical trials for novel medications that offer hope to patients around the world who suffer from allergic diseases, sepsis and spinal cord injuries.



genes in humans that produce a similar molecule with anti-allergic functions. This tiny piece of prohormone is found in many different places throughout the human body. It has many forms, some of which appear to be unique to the tissue of origin and likely relate to the unique functions of the site of its production.

The AllerGen NCE research team is still trying to discover exactly how this small piece of prohormone works in humans. Dr. Befus states, "I hope that 20 years from now, people appreciate the biology of this pathway very differently from the way they do at this early stage."

Laboratories No Longer in 'Ivory Towers'

This research team credits AllerGen NCE with inspiring them and researchers across Canada to think about science in terms of how it can directly benefit Canadians, socially and economically. "You are forced to think about that all the time in an NCE. You

which is a very serious medical condition where infection caused by bacteria, virus or fungus leads to a whole-body inflammatory state. Better anti-inflammatory medications could save the lives of patients with sepsis, and improve both the recovery time and the extent of spinal cord injuries, provided they are administered quickly.

This research team has partnered with AIM Therapeutics, a Canadian company based in Toronto, to test the anti-allergy and anti-inflammation potential of new medications derived from their AllerGen-supported prohormone research. AIM Therapeutics has invested significantly in further developing the team's research findings. Results so far are promising. Human clinical trials are anticipated to occur in the near future.

Better medications will improve the health of many Canadians and the quality of their lives. Also, better medications could mean huge economic cost savings for Canada. AllerGen NCE notes that Canadians currently spend \$15 billion annually on allergic

diseases related to ambulance transportation, hospital stays, emergency department visits, doctor's visits and medications.

According to the Rick Hansen Foundation, the annual cost to Canadian healthcare of spinal cord injuries is \$750 million. The lifetime cost per injured person to the Canadian health system is estimated to be between \$1.25 million and \$25 million, depending on the severity of the injury. An anti-inflammatory medication capable of reducing the extent of spinal cord injury and recovery time will significantly reduce national healthcare costs.

With respect to sepsis, a recent study by the Canadian Institute for Health Information found that 30,500 patients were hospitalized with sepsis in Canada (excluding Quebec) in 2008-2009, of which 30% died. Besides the human toll, there is a large financial cost due to the average length of stay for sepsis patients, which is an average of nine days longer than for those admitted for other conditions. A better anti-inflammatory medication treating sepsis will save lives and may also reduce the length of hospital stays and associated healthcare costs.

In addition, the AllerGen NCE research team has entered into a licensing agreement with an American company that specializes in veterinary science. This company aims to use the team's discoveries of the inflammation pathway and molecules to develop novel medications for animals with allergic and inflammatory conditions. Better medications would be welcomed by both pet owners and farmers.

Modern science is just beginning to understand how the pathway and molecules work in the human body to regulate allergic responses and inflammation. Dr. Befus predicts that advancing knowledge of pathways and molecules will lead to the development of better diagnostic tools. Asthma, for example, is currently a difficult disease to diagnose because it rests heavily on the patient's reporting ability and the doctor's experience with the disease. Dr. Befus also predicts that advancing pathway and molecular knowledge will assist in developing disease prevention and management tools that extend beyond medications, such as tools that address the impact stress has on the immune system and tools that enhance coping skills. In his words, "Maybe there are future strategies that are very different from the typical pharmaceutical approaches. These could be behavioral, societal and involve social development and the way we raise our children. At least now we are beginning



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to shed some light on how social interactions influence health and disease."

It Takes a Village to Translate Science

Countless students have been associated with this research project over the years. Approximately 65% have stayed with academia in some way, while others have gone into medicine or industry. Not only have these students gained invaluable critical thinking and research skills, they have taken with them the philosophy that it is important to consider your work's impact upon society. AllerGen NCE is a strong supporter of capacity building for up and coming scientists and researchers in the field of allergy, asthma and anaphylaxis.

The success of this research team is made possible because of collaborations with other Canadian researchers and industry. Dr. Befus gives all the credit to AllerGen, an "NCE that is remarkably well-placed" to foster "tremendously valuable" partnerships.

Researchers are beginning to understand the biology of a pathway involved in human allergy responses and inflammation, and are on the cusp of human clinical trials for novel medications that offer hope to patients around the world who suffer from allergic diseases, sepsis and spinal cord injuries. Further advancing our knowledge of human biology at a molecular level could, in the long-term, lead to a complete revolution in disease prevention, diagnosis and management. [A](#)

Success Stories: *Innovation from cell to society*



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Success Stories

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