

Innovation from cell to society

Success Stories



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Making a Difference From cell to society

AllerGen NCE Inc. (AllerGen), the Allergy, Genes and Environment Network—one of Canada's Networks of Centres of Excellence (NCE)—proudly presents its ninth issue of *Success Stories*, showcasing the research and knowledge mobilization achievements of its researchers, students and partner organizations.

This Spring 2015 issue of *Success Stories* shares the accomplishments of several AllerGen-supported projects on the leading edge of health research and evidence-based outreach, and profiles the rising career path of a Network trainee. This issue's feature stories encompass:

- a vision for maximizing choice and minimizing risk for food allergic Canadians;
- an innovative peer-to-peer mentoring program for children with severe food allergies;
- a look at the epigenetic influences on allergic disease;
- a map of the molecules, interactions and pathways at play in allergies and asthma; and
- an AllerGen trainee connecting academic research, the pharmaceutical industry, and the medical community.

Since its inception, AllerGen has supported innovative research and development, capacity-building activities, stakeholder engagement and partnerships that foster research commercialization, social innovation and knowledge mobilization, enabling Canadians to better prevent, manage and treat allergy, asthma, anaphylaxis and related immune diseases.

Now more than a decade into its mandate, AllerGen pursues its goals with mature and globally-connected research teams; a balanced portfolio across investments in discovery, development, commercialization and knowledge mobilization; and an integrated research strategy spanning three Legacy Projects and three Enabling Platforms that build upon core research investments established in 2005.

Legacy Projects:

- **Canadian Healthy Infant Longitudinal Development (CHILD) Study**

This national birth cohort study collects biological samples and immunological, physiological and genetic data from over 3,300 Canadian children from pre-birth to age five in order to explore the root causes of asthma, allergies and other chronic immune and inflammatory diseases.

- **Clinical Investigator Collaborative (CIC)**

This multi-centre, Canadian-based Phase II clinical trials group offers biotechnology and pharmaceutical companies



an opportunity to evaluate promising new drug molecules for the treatment of allergic diseases in both the upper and lower airways.

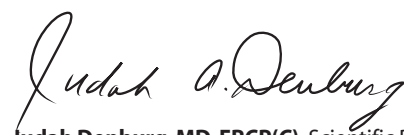
- **Canadian Food Allergy Strategic Team (CanFAST)**

This innovative, nationally-networked research team provides new knowledge about the origins, causes, prevalence and treatment of food allergy and anaphylaxis, and informs the development of improved clinical management strategies and public health measures.


Enabling Platforms:

- **Gene-Environment Interactions**
- **Biomarkers and Bioinformatics**
- **Patients, Policy and Public Health**

By sharing our stories of research success, we aim to keep Canadians up-to-date on advancements in the science of allergy and asthma. We hope you find this issue of *Success Stories* to be interesting and informative. [A](#)


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


Diana Royce, EdD, Managing Director and COO



Early in her career, Dr. Elliott noted the lack of Canadian data on the prevalence of food allergies. “We were relying on American or British estimates,” she recalls. To fill this gap, Dr. Elliott proposed a Canadian study, but to accomplish this she needed help from someone on the front line of clinical research.

More Choice, Less Risk for those with Food Allergies

Young Ryan has a choice to make. He can join his friends for dinner out and take pains to avoid any food that contains peanuts—or a plate or tongs that may have accidentally touched peanuts—or he can stay home. Missing out on dinner would simplify his life and put his parents at ease, but it would let his friends down and leave Ryan feeling lonely and “out of the loop.”

Dr. Susan Elliott believes that Canadians like Ryan should not have to make such choices. She maintains that people with food allergies should be less restricted when it comes to where they can dine, study, work and play, and should face fewer risks in their daily lives. They should all know how to avoid their allergic triggers, and anaphylactic reactions should be rare. If such reactions do occur—whether at a school, mall or restaurant—an Epinephrine Auto-Injector (EAI) should always be close at hand.



**Dr. Susan Elliott, Professor,
University of Waterloo**



**Dr. Ann Clarke, Professor,
University of Calgary**

Dr. Elliott has spent the better part of her career working toward realizing this vision. As a medical geographer in the departments of Geography and Public Health at the University of Waterloo, Dr. Elliott studies how our environment influences our health and well-being.

It's a “big-picture” job that entails observing communities for things like vulnerability to allergies, knowledge of allergy prevention strategies, and beliefs about health. What concerns Dr. Elliott above all is the “so what” of her work—how her findings can lead to improved public health policies and clinical care for Canadians. If food allergy is more prevalent in some populations, what do we do about it? If some groups do not have consistent access to EAI's, what do we do about that?

The Canadian food allergy landscape

Early in her career, Dr. Elliott noted the lack of Canadian data on the prevalence of food allergies. “We were relying on American or British estimates,” she recalls. To fill this gap, Dr. Elliott proposed a Canadian study, but to accomplish this she needed help from someone on the front line of clinical research. AllerGen stepped in with funding for the project and connected Dr. Elliott with clinical allergist and epidemiologist Dr. Ann Clarke. “She's what my kids would call a real doctor,” says Dr. Elliott with a chuckle.

As it turned out, Dr. Elliott's and Dr. Clarke's competencies fit hand-in-glove. “Ann had the knowledge and skills to study disease prevalence and progression, while I had experience looking at perceptions, experiences and implications,” says

Dr. Elliott. “As a team, we're unbeatable.”

In 2009, with funding from AllerGen and Health Canada, Drs Elliott and Clarke and their research team completed the first national study on the prevalence, perception, and impact of food allergy in Canada. The study, called SCAAALAR (Surveying Canadians to Assess the prevalence of common food Allergies and Attitudes toward food LABelling and Risk), focused on five food allergens: peanuts, tree nuts, fish, shellfish, and sesame. Among the 10,000 Canadians surveyed, roughly 7.5%—or one in 13 people—reported a serious allergy to one or more of these foods. The study also found higher self-reported allergies among educated Canadians and city dwellers.

There was just one thing missing from SCAAALAR: because the study was based on a national survey of randomly selected households, it did not fully represent minority populations considered to be especially vulnerable, such as low-income families, Aboriginal peoples and new Canadians. To obtain a more complete picture of the food allergy landscape, the Elliott-Clarke team embarked on a still more ambitious study, which they called SPACE (Surveying Prevalence of food Allergy in All Canadian Environments), to capture data for populations under-represented in the 2009 survey.

To ensure they heard enough voices from these groups, the research team selected households within postal-code areas known to contain high proportions of vulnerable Canadians. In all, they recruited over 5,000 households—representing more than 15,000 individuals from low-income, immigrant, and Aboriginal populations across Canada—and asked them



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“Our previous studies provide a benchmark against which we can document trends over time,” she says. If it turns out that food allergies are indeed on the rise, “Canada will need to address this issue at the policy level with a national, coordinated food allergy strategy.” This could mean requiring restaurants to disclose potential allergens in all their dishes, or legislating the need for all schools to stock spare EAs for anaphylactic emergencies.

questions about current and past food allergies, eating habits, breastfeeding practices and household environments. They also pre-interviewed what Dr. Elliott calls “key informants”—directors of food banks, representatives from First Nations and Inuit organizations, and the heads of immigrant friendship and settlement centres—for guidance on culturally sensitive interview techniques.

SPACE study findings were published in the *Journal of Allergy and Clinical Immunology: In Practice* in September 2014. The study found that Canadians who had immigrated to Canada within the previous 10 years had fewer food allergies than the general population. This finding supports the “healthy immigrant” effect frequently observed in health research—that immigrants have a lower prevalence of several chronic conditions when they arrive in Canada, but their health status worsens over time, eventually converging with that of the Canadian-born population.

SPACE also revealed that Canadians with a lower education level reported having fewer food allergies, but Dr. Elliott has yet to uncover the reason.

In addition to documenting food allergies, the study asked participants to guess at the prevalence of food allergies in Canada. “On average, respondents estimated that 30% of Canadians have food allergies—a large gap from our SCAAALAR result of 7.5%,” says Dr. Elliott. “Clearly, people think it is a major public health problem.”

Some of this misperception comes from the popular media. One of Dr. Elliott’s former PhD students, Daniel Harrington, analyzed articles about food allergies from English and French newspapers across Canada over a 10-year period. He found that most articles quoted parents of allergic children far more often than physicians or policymakers. “A researcher or clinician may not be able to return a journalist’s call in time to be quoted for an article,” Dr. Elliott points out. While parents and advocacy

groups bring value to the conversation, “a lack of balanced reporting can skew the picture.” Dr. Elliott herself receives daily Google alerts about food allergies. “All the reports sound alarm bells about increasing prevalence,” she says. But is it true? “We think so, but we need good Canadian data before we can hope to influence Canadian policy.”

To get this data, Drs Elliott and Clarke plan to conduct another national survey in the fall of 2015. “Our previous studies provide a benchmark against which we can document trends over time,” she says. If it turns out that food allergies are indeed on the rise, “Canada will need to address this issue at the policy level with a national, coordinated food allergy strategy.” This could mean requiring restaurants to disclose potential allergens in all their dishes, or legislating the need for all schools to stock spare EALs for anaphylactic emergencies.

Pressing issues

In the meantime, Dr. Elliott has another pressing item on her agenda: helping vulnerable Canadians manage food allergies. “During our research, we heard stories of families that rely on food banks—organizations that don’t necessarily offer a range of allergen-free foods—having issues at school,” says Dr. Elliott. When a child brings a snack to school, it may be removed by school staff for containing allergens, even though “it might be the only food the child has to eat all day.”

According to Dr. Elliott, low-income families also struggle to purchase the three EALs—each costing \$120—recommended for children with severe allergies: one EAL for home, another for school, and a third one to be kept with the child at all times. Dr. Elliott says a black market for expired EALs has arisen as a result, and in some cases parents may simply give their child an inexpensive over-the-counter antihistamine like Benadryl in response to an allergic reaction.

As for new-immigrant families, Dr. Elliott says “they may have a lower rate of food allergies, but they also face challenges because many arrive from countries where food allergies are virtually nonexistent. Suddenly, these parents receive letters from the school telling them not to send peanut butter or other foods at lunchtime, which doesn’t make sense to them.” Ingredient listings and food labels may likewise confuse some new Canadians for whom English is not a first language, she points out.

If Dr. Elliott has her way, vague food labels and precautionary warnings will soon be a thing of the past. Health Canada has already used the original SCAALAR research to overhaul Canada’s food labelling requirements in 2012. Earlier regulations allowed manufacturers to mask some allergens


under umbrella terms such as “spices.” “The new labelling rules require all specific ingredients to be listed,” says Dr. Elliott. “If there is mustard seed in a product, it must appear as ‘mustard seed’ on the label.”

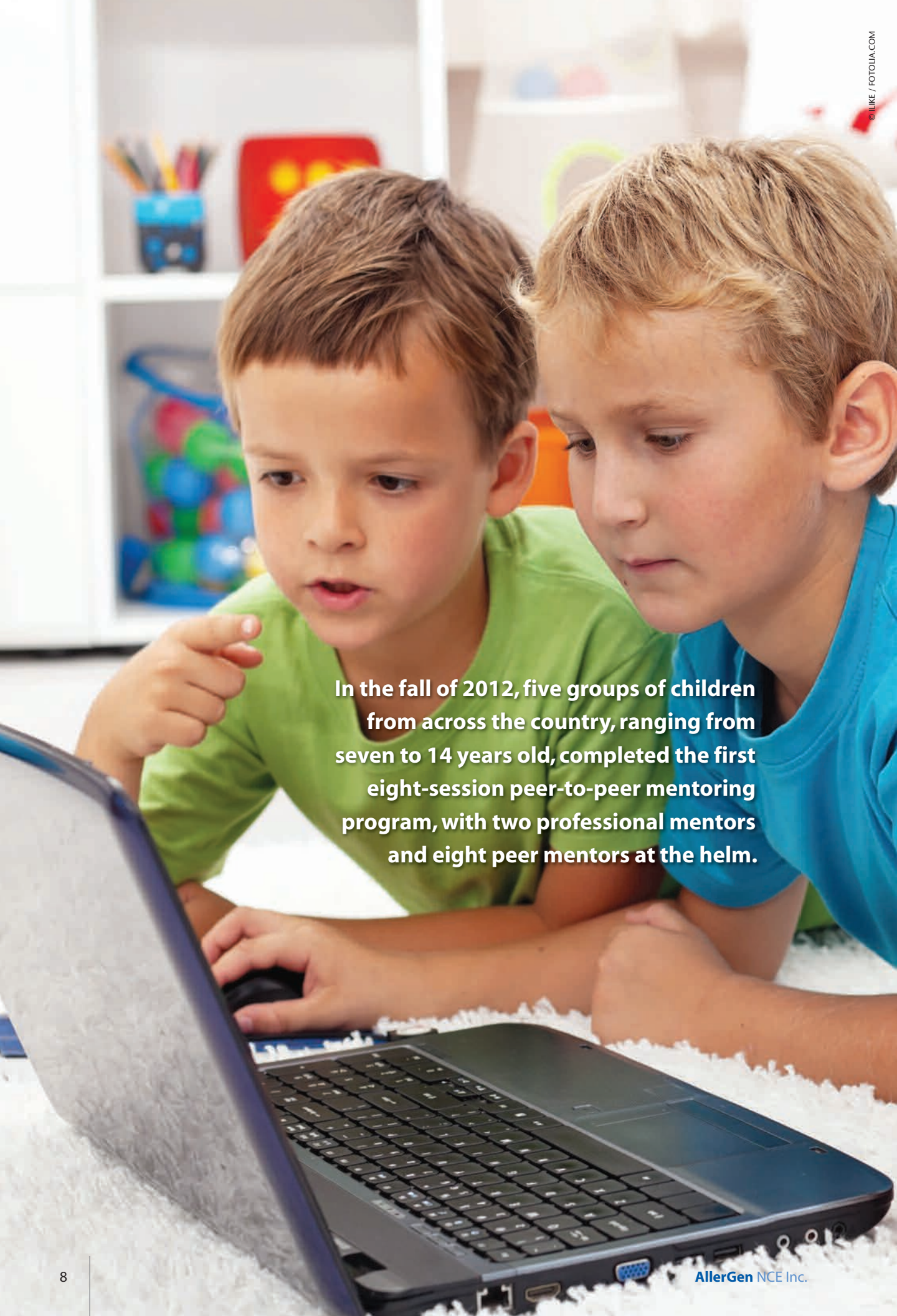
There is still ample room for improvement in labelling practices, though. For example, “may contain” precautionary labels that warn customers about possible traces of allergens in packaged foods are voluntary in Canada—and they leave many consumers scratching their heads, especially families that do *not* live with food allergies. “Parents of allergic children tend to have more experience with precautionary statements and know which products are safe to consume,” says Dr. Elliott. “Other parents have no way to gauge the risk.” Consumers have indicated that they would like to see ambiguous statements about allergens replaced with yes-or-no messaging, along with pictograms (such as a red line across a peanut) displayed more prominently on packaging. “It’s what people want,” she says. In order to address these pressing issues, however, it’s important to get buy-in from all stakeholders, including the food industry. Dr. Elliott takes heart that “Health Canada appears to be on board.”

Toward a national strategy

That’s a good thing, because Dr. Elliott’s long-range vision, which she shares with many colleagues and other food allergy stakeholders, requires the government’s full support. Their big aspiration: a national food allergy strategy for Canada. To this end, she will be hosting a meeting for food allergy stakeholders, including those in government, in 2015. AllerGen has provided funding, support and resources for the event.

Dr. Elliott maintains that a coordinated national strategy would help to “maximize choice and minimize risk” for Canadians, like Ryan, with food allergies. “We also need standards for dealing with murky ethical issues,” she says. For example, what happens if a child has an anaphylactic reaction at school and is not carrying an EAL? “If such an emergency were to happen today, school administrators would have to decide whether or not to use another child’s autoinjector, which puts them in an impossible bind.”

In the meantime, small signs of progress give Dr. Elliott hope for the future. “The other day, I walked past a chocolate shop in my neighbourhood and saw a sign in the window that read: ‘Epipens® on the premises,’” she says. “That’s encouraging. But there is still a lot of work ahead to maximize choice and minimize risk for Canadians affected, both directly and indirectly, by food allergies.” 



In the fall of 2012, five groups of children from across the country, ranging from seven to 14 years old, completed the first eight-session peer-to-peer mentoring program, with two professional mentors and eight peer mentors at the helm.

Peer Power: Helping Allergic Kids to Help Each Other

If you have ever faced a major life challenge, you probably know that people who have been through the same thing can offer a unique brand of “been there, done that” understanding and support. This is why peer support groups have become a mainstay of self-help programs in our society. In today’s high-tech world, many of these support communities have moved online.

Having lived with severe asthma and multiple allergies all her life and studied the needs of families affected by chronic health conditions, Dr. Miriam Stewart knows that kids with asthma and allergies can face social isolation and miss out on activities with their peers. She also knows that these children have few avenues to connect with other kids facing the same challenges. This led her to wonder: might children with asthma or allergies enjoy meeting online to trade stories and coping strategies?



**Dr. Miriam Stewart, Professor,
University of Alberta**



**Kyle Dine,
Youth Project Coordinator,
Anaphylaxis Canada**

A running start

Dr. Stewart, a health researcher and a professor in the Faculty of Nursing at the University of Alberta, began by asking parents, teens and kids what they thought of the idea, and got a chorus of “yes!” responses. Next, she conducted two AllerGen-supported pilot studies to get a read on the needs of young people with severe allergies, and to design and test online peer support programs to meet those needs.

In total, Dr. Stewart and her research team consulted with nearly 100 children and teens, and 50 parents. Peer mentors and health professionals moderated the pilot sessions over a period of several months. The upshot? “The kids made friends, gained confidence, and reported feeling more like other children,” says Dr. Stewart. Perhaps the greatest benefit of all: the kids developed more supportive relationships with their families and friends.

The success of these pilot studies confirmed for Dr. Stewart that a full-fledged online “peer-to-peer” mentoring program could work. To make it happen, she and her team reached out to national patient organizations like the Asthma Society of Canada, the Canadian Lung Association, and Anaphylaxis Canada. From these consultations, a working group emerged, which included Sharon Anderson and Kim Kara from the Social Support Research Program at the University of Alberta, Heather Cruikshank of Anaphylaxis Canada, and Rupinder Chera of the Asthma Society of Canada. “Rather than reinvent the wheel, we adapted what we learned from our pilot studies to our partners’ needs,” says Dr. Stewart. One thing everyone agreed on: “The

program would have to be sustainable. We didn’t want to start something grand and then have it flame out.”

With funding from AllerGen and Alberta Innovates-Health Solutions, the group began by refining the program toolkit—a framework of resources that includes online materials and tools, as well as a training package for peer mentors. Anaphylaxis Canada and the Asthma Society of Canada hand-picked and trained the peer mentors, all of whom had severe allergies and/or asthma themselves. “The involvement of trained peers is a distinguishing feature of our program,” says Dr. Stewart, adding that peer mentors take an online training program and meet with health professionals before and after the group sessions with the children.

Next, Dr. Stewart consulted groups of seven-to-11-year-old children—the age range for the program’s first run—and asked them: “What do you think is important to include? What would you like to talk about?” Parents also had the opportunity to weigh in. Dr. Stewart learned that kids and parents wanted to talk not only about the nuts and bolts of asthma and allergy management—how to recognize and avoid triggers—but about the social implications of their condition. Also high on their wish lists: celebrity role models who lived with the same challenges.

After incorporating input from the kids and their parents, Dr. Stewart and her working group created different versions of the toolkit tailored by disease (asthma *versus* allergy) and age group (children *versus* teens).

Success Stories: Innovation from cell to society

Next came the challenge of designing an online interface that would appeal to kids. The group had successfully used *GoToMeeting*, an interactive online platform, and *Club Penguin™*—a virtual world created by the Disney company—in the pilot studies, so they decided to proceed with these technologies. The result was an immersive program that allowed participants to view *PowerPoint* slides, answer questions using drawing tools, and use a highlighter for word searches. They were also able to talk or type-chat with their new friends while learning about dealing with their allergies or asthma and sharing personal experiences.

Testing positive

In the fall of 2012, five groups of children from across the country, ranging from seven to 14 years old, completed the first eight-session peer-to-peer mentoring program, with two professional mentors and eight peer mentors at the helm. Peer mentors “used their personal experiences to break the ice and help participants feel more comfortable sharing their own stories,” Dr. Stewart explains. After each session, the peer mentors stayed online together to debrief. “They discussed what went well, what to change, and what they observed about the group dynamic.”

The young participants also had a chance to evaluate the program, and they gave it an emphatic “thumbs up.” One child enjoyed making “new friends you can only meet on the Internet”—that, and the “scribbling.” Another child appreciated “knowing that I’m not the only one who has allergies.” In fact, several participants touched on this theme: after the program, they felt “no longer alone,” “not left out,” and “included.” The program also helped participants improve the day-to-day management of their allergies and asthma. “Children with allergies reported that they were more likely to carry their epinephrine autoinjectors with them after completing the program,” says Dr. Stewart.

A follow-up analysis reinforced the program’s value. The children’s perception of being supported rose significantly after the program, in tandem with improvements in their disease-related quality of life. “Participants were also more likely to seek further support after they completed the program,” Dr. Stewart noted.

Dr. Stewart’s team used the feedback to make final program adjustments, notably more visuals and games, less text and instruction. “We also decided to develop a guide for program coordinators, create graphics for branding, and make fuller use of interactive tools to increase participation.” Also in the works: “An adapted version of the program toolkit, supported by the Canadian Institutes of Health Research and AllerGen, that is more relevant to Aboriginal and low-income families affected by asthma and allergies.”

In the meantime, follow-up funding from the private sector enabled Anaphylaxis Canada to move the program toward becoming the “sustainable initiative” that Dr. Stewart’s team hoped for from the outset. With administrative help from AllerGen and its business accelerator partner, TEC Edmonton (a joint venture of the University of Alberta and the Edmonton Economic Development Corporation), Anaphylaxis Canada became the first organization to secure a license to run the program independently. “Our main role was to create a document setting out the terms of a business agreement between Anaphylaxis Canada and the University of Alberta, which owns the program,” says Joanna Preston, a senior manager in TEC Edmonton’s Health Sciences Technology Management division.

Chatting, clicking and doodling

Allergy Pals, the Anaphylaxis Canada version of the program, launched in April 2014, under the supervision of Kyle Dine, the organization’s youth project coordinator. “Our membership had been asking for something like this time and time again, so I was excited to lead the project,” he says. And he is just the guy to do it: diagnosed at age two with allergies to peanuts, tree nuts, eggs, fish, shellfish, and mustard, Dine “gets” what life with severe allergies is all about, and is passionate about his work as an educator and entertainer promoting allergy awareness.

The eight-session *Allergy Pals* program offers education and support to seven-to-11-year-old children with severe food allergies. Each group is led by a peer mentor, with a health support and education specialist working behind the scenes.



Where do you keep your auto-injector at school?

Backpack

Desk

Office

Around my waist

With a teacher

Other

Write your initials in one (or more) of the bubbles

Are people allowed to bring things to school that you're allergic to?

Yes!

No!

Write your initials in the "yes" or "no" bubble!

Allergy Pals Session 7 program slides facilitate group conversation and participation.

"The peer mentors are young—between 15 and 25—and know what it's like to live with severe allergies, so the kids can relate to them," says Dine.

Just like the pilot version of the program, *Allergy Pals* has kids talking, clicking, scribbling and doodling. Each session starts with a few minutes of group sharing. Then, the peer mentor presents a series of slides devoted to a particular theme, such as birthday parties or travelling. Some slides offer tips, others ask questions that can be answered with a click, and still others prompt the kids to set goals. The session wraps up with an Antarctic mission on the *Club Penguin™* website—not surprisingly, a major highlight for participants. "The one thing the kids can't do is see each other," says Dine. "A webcam is too distracting and can intimidate the shyer participants, so we simply include a slide each week with everyone's picture on it. The kids do better when just hearing each other."


The program sparkles with colour, energy, and optimism. "That's no accident," says Dine. Anyone who has dealt with kids knows that "walls of text and preachy messages don't cut it with this group," he says. "They have to be doing something, not just sitting and watching."

The topics for each *Allergy Pals* session came out of Dr. Stewart's pilot studies assessing what young people wanted to discuss. As it turned out, school life ranked high on their list. In session seven, a slide prompts participants to share where they keep their epinephrine autoinjectors at school, while another asks them if their allergy triggers are allowed on school

premises. "It's a tricky subject to tackle," says Dine. "Schools are working to develop effective policies for allergic students and there is often a debate over how to accommodate them."

Another *Allergy Pals* session deals with outings. Bad experience with a waiter? Left out at a birthday party? "The kids have a chance to swap stories and role-play scenarios," says Dine, noting that "a big part of having a severe allergy is the effect it has on one's social life, so we put a lot of emphasis on social strategies."

The program has been "a complete and utter success," says Dine. In the first three programs alone, *Allergy Pals* mentored 113 Canadian kids with allergies, and sessions slated for 2015 were full within the first eight hours of registration. Without exception, surveyed parents said they would recommend the *Allergy Pals* program to others, and over 90% maintained that they would enroll their child in a follow-up program. Anaphylaxis Canada has already created Level 2 and Level 3 programs to allow previous participants to continue sharing. Dine says that *Allergy Allies*, a new mentorship program geared to teens (aged 12–15 years), will launch in spring 2015.

For her part, Dr. Stewart is "delighted that children and teens across Canada are benefitting from these online peer support programs." She hopes that a similar sustainable peer mentoring program for kids with asthma—currently under discussion with the Asthma Society of Canada—will lead children to conclude, as did an *Allergy Pals* graduate, that "living with allergies and asthma is a lot easier when you know you're not alone." 



The concept of epigenetics has been around for many years, but interest in the topic surged in 2004 with the publication of a study that linked the quality of mothering behaviour in rats to the activity of specific genes.

An Epigenetic Lens on Allergy and Asthma

The word “epigenetics” is everywhere these days. A Google search of the term generates over three million hits, magazine articles on the topic abound, and epigenetics conferences and scientific meetings are being held all over the world. It’s a hot new line of research that has the science world all fired up.

So, what does the word mean, anyway? In simple terms, epigenetics looks at how genes are turned on and off, and how this process influences health and disease. The Greek prefix “epi,” which means “above” or “beyond,” is fitting: epigenetics looks above and beyond our genes to the environmental factors that influence them.



**Dr. Michael Kobor, Professor,
The University of British Columbia**

The concept explains a lot from a biological point of view: genes affect our appearance, temperament, and vulnerability to disease, but we have only about 25,000 of them. How can such a small number create such tremendous variety among humans? Epigenetics—the way genes express themselves in different bodies and at different times in a lifespan—makes it possible.

Dr. Michael Kobor, a professor in the Department of Medical Genetics at The University of British Columbia (UBC) and Canada Research Chair in Social Epigenetics, offers a simple analogy: “Think of a gene as the lightbulb,” says Dr. Kobor. “Epigenetics is the dimmer switch that turns the light on or off, or dials it up or down to varying degrees.”

Dr. Kobor, who also works as a scientist at the Centre for Molecular Medicine and Therapeutics, a UBC facility housed within the Child and Family Research Institute, suspects that the study of epigenetics may solve some of the mysteries of asthma and allergies—a hunch he intends to put to the test.

Setting the dimmer switch

The concept of epigenetics has been around for many years, but interest in the topic surged in 2004 with the publication of a study that linked the quality of mothering behaviour in rats to the activity of specific genes. The study found that mother rats who licked and groomed their pups produced female offspring that grew up to become sensitive and attentive mothers themselves. Similarly, mother rats who deprived their babies of this attention produced female offspring that were neglectful mothers in adulthood. While the babies of “low-

licking” mothers had the same genetic makeup as those of “high-licking” mothers, some of their genes were “dimmed down”—suggesting that the lack of maternal care actually affected their genes.

Since then, a growing body of evidence has suggested that the environment in early life, and even before birth, can affect the activity of specific genes. “It appears that childhood poverty or maltreatment, as well as nutrition during pregnancy, may set these ‘dimmers’ in a certain way,” says Dr. Kobor. What’s more, “the dimmer setting may become lodged in that position for part or all of an organism’s life.”

Dr. Kobor has reason to suspect that epigenetic modifications may be the link between heredity and the immune system “glitches” responsible for allergies. In a 2009 study, he and his collaborators showed that childhood poverty can boost the activity of genes that promote inflammation. The net result: an increased susceptibility to allergy. “This vulnerability persists even if the individuals move out of poverty in adulthood,” he says. On an encouraging note, Dr. Kobor’s research has also shown that warm maternal care can “dial down” the immune malfunctions resulting from a poor start in life.

Dr. Kobor also participated in a study that linked chronic stress to the overexpression of genes associated with inflammation. The study followed 33 adults caring for a family member with a brain tumour—a situation that placed them under considerable stress—and compared them to 47 adult “controls” with no major stressors in their lives. Dr. Kobor and his co-investigators discovered that the stressed caregivers had



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their “dimmer switch” set to “high” in a key inflammation-promoting gene. “This gave us a clue as to how chronic stress may increase vulnerability to diseases related to inflammation,” says Dr. Kobor, adding that he and his wife took these findings to heart when their son was born. “As new parents, we made a conscious effort to create a calm, low-stress atmosphere in our home,” he recalls.

Scaling up with birth cohorts

To date, most research studying the epigenetic influences on allergy have involved animal studies or small-scale human trials. Dr. Kobor says there’s an urgent need to ratchet the research up a notch. That’s where his current AllerGen-funded research

project comes in: REEGLE (Rapid Environmental Effects on Genes: the Lens of Epigenetics) is gathering data from over 3,000 children. “That’s a huge number for this type of study,” he says. “We’re very excited.”

REEGLE hopes to establish whether environmental factors turn specific genes on and off, and whether these epigenetic alterations contribute to the development of pediatric asthma and allergy. “We’re working with the hypothesis that environmental exposures early in life can ‘get under the skin’ to regulate the activity of genes involved in allergic diseases and asthma,” says Dr. Kobor.

REEGLE is accessing biological samples from two large birth cohort studies to conduct its analyses: AllerGen’s Canadian

Healthy Infant Longitudinal Development (CHILD) Study and the Kingston Allergy Birth Cohort. Dr. Kobor's research team is analyzing DNA from the umbilical cord blood of children participating in these studies to find out if environmental influences, such as maternal stress and childhood poverty, can switch off the genes that protect against allergy and asthma—or switch on those that promote inflammation.

Unlike a lightbulb, a gene's inner workings cannot be seen with the naked eye. So, how do researchers know if a gene is turned on or off? Dr. Kobor explains that molecular structures called methyl groups interfere with a gene's activity by attaching to various places on the DNA strand, akin to knots along the length of a rope. As a rule, "methylation clogs up the works, so the more methylation, the less gene activity," he says. The degree of methylation can also change over time, which could help explain why allergies may come and go through the life cycle. "That's why the REEGLE study is analyzing biological samples from children at ages one and five—to find out whether genes are becoming more or less active over time."

REEGLE is also looking at the epigenetic impact of short-term exposure to allergens and airborne contaminants such as traffic-related air pollution. Might a blast of car fumes, for example, cause certain genes to switch off? The answer appears to be yes: in a recently published study, Dr. Kobor and his AllerGen colleague Dr. Chris Carlsten (Associate Professor of Medicine at UBC) demonstrated that just two hours of inhaling diesel exhaust fumes triggered DNA methylation changes among patients with asthma, potentially silencing or dimming a gene that produces a protective protein.

"Our research also has the potential to demonstrate the *reversibility* of epigenetic effects," says Dr. Kobor—an idea he views as rich with possibility. "If we can pinpoint the environmental factors that turn on protective genes and turn off harmful ones, then we can take steps to provide a safe environment for vulnerable people," he says.

Making meaningful connections


As the REEGLE project forges ahead, Dr. Kobor plans to look deep into the biochemistry of epigenetics. "How does a life experience like growing up in poverty actually end up changing the activity of our genes?" he asks. In the best-case scenario, findings from REEGLE could lead to what Dr. Kobor calls

REEGLE hopes to establish whether environmental factors turn specific genes on and off, and whether these epigenetic alterations contribute to the development of pediatric asthma and allergy. "We're working with the hypothesis that environmental exposures early in life can 'get under the skin' to regulate the activity of genes involved in allergic diseases and asthma," says Dr. Kobor.

"epigenetic screening." For example, if his team discovers that certain protective genes are turned off in the bronchial tissues of certain babies, children with these "epigenetic red flags" could be monitored more closely for asthma.

Dr. Kobor says REEGLE is "a great example of how interdisciplinary research can come together," and he credits AllerGen for bringing the project to life. "The AllerGen Network operates on a peer-reviewed funding system, which is critical to the advancement of quality allergic disease research in Canada," he says. In fact, Dr. Kobor envisions REEGLE becoming a core resource for epigenetic work across AllerGen's research spectrum. "The knowledge gained through this project will be freely available to other researchers, who can use it to advance their own work," he says. Looking beyond AllerGen, he hopes REEGLE will catalyze the development of a pan-Canadian network of scientists and clinicians united in their interest in the environmental regulation of allergic disease.

Eventually, the REEGLE team plans to integrate sociological data collected by the CHILD Study—information about maternal socioeconomic status, mental health, and reported stress—into the project.

Dr. Kobor looks forward to making those "meaningful connections" that ultimately improve lives. "The data are getting better and better," he says. "It's an exciting time to be doing this sort of work." 



“Allergic responses are not straightforward and linear—they are complicated networks impacted by both the genetics of the individual and their environment.”

Molecular Mysteries of Allergies and Asthma: Uncovering Simplicity within Complexity

The human organism is complicated. The more we learn about the biology that governs our bodies, brains and behaviour, the more complexity we find—especially when we get down to the molecular level.

“Our genes make proteins that create and interact with other molecules in many ways,” says Dr. Fiona Brinkman, a biochemistry and molecular biology professor at Simon Fraser University. “Essentially, humans are a complex network of different molecules interacting with each other to form a system,” she says. “The majority of the molecular pathways in this system have remained a bit of a mystery.”



**Dr. Fiona Brinkman, Professor,
Simon Fraser University**

Named by Thomson Reuters in 2013 as “one of the world’s most influential scientific minds,” Dr. Brinkman is working hard, along with many other researchers across the globe, to bring these molecular mysteries to light. Along the way, she has become an expert in the emerging specialty of bioinformatics—a field that uses computers to gather, analyze and integrate vast amounts of biological information that can be used to illuminate, among other things, how diseases develop.

Dr. Brinkman is particularly interested in creating a map of the molecules, interactions and pathways at play in allergies and asthma. “It would make our research much easier if these molecular interactions were simple,” she says. In fact, however, “allergic responses are not straightforward and linear—they are complicated networks impacted by both the genetics of the individual and their environment.”

To collect and integrate what is known about these molecular interactions, Dr. Brinkman has masterminded a database that is generating a lot of “buzz” in the medical research community. The *Allergy and Asthma Portal*, or AAP, catalogues not just the genes and proteins involved in allergy and asthma, but all of their known interactions and connections to other key molecules.

The first tool of its kind, the AAP will boost researchers’ ability to look more holistically at our human molecular system, enabling a better understanding of how allergy, asthma and other immune diseases develop, and, ultimately, how to treat and prevent them.

Perceiving the whole elephant

Most previously established databases consider molecules and molecular pathways in isolation, rather than as part of a system. Dr. Brinkman likens this approach to the parable of the blind men describing an elephant, where each man describes only the part he can feel, out of context. The man touching the trunk proposes it’s a snake: the man touching a tusk proposes it’s a spear. Only by pooling their observations together can they perceive the whole elephant. Dr. Brinkman employs another animal analogy: “If you watch a flock of birds flying overhead,” she says, “you see patterns that you would not detect by focusing on just one bird. We find the same thing when we analyze complex molecular interactions in the human body—by looking at them holistically—elegant yet simple patterns emerge.”

Systems biology—an emerging branch of human disease research—takes this wide-angle view. “The premise is that disease doesn’t arise just from a change in a gene, but from changes or disruptions in the network of interactions it impacts,” Dr. Brinkman explains. “Cracking the human genome was just the beginning: now we need to generate a map of how genes and proteins change and how they operate in networks (the human interactome) to get to the endgame.”

According to Dr. Brinkman, researchers know much more about those components of the human interactome associated with the development of cancer than those involved in the development of allergy and asthma. She hopes the AAP will

“The premise is that disease doesn’t arise just from a change in a gene, but from changes or disruptions in the network of interactions it impacts,” Dr. Brinkman explains. “Cracking the human genome was just the beginning: now we need to generate a map of how genes and proteins change and how they operate in networks (the human interactome) to get to the endgame.”

help rectify this and provide “new insight into the key molecular players in allergy and asthma, which may lead to new ideas for therapies.”

A mountain of data

The AAP officially opened its “digital doors” to the global research community in September 2014. “We are adding new interactions to the portal every day,” says Dr. Brinkman. She works closely with the project’s co-lead, Dr. David Lynn, a former postdoctoral student in Dr. Brinkman’s research lab now based at Flinders University in Adelaide, Australia. The AAP research team also includes bioinformatics experts, software and database developers, and data curators.

While the term “curation” may usually be associated with museum displays, it also applies to the scientific work of Dr. Brinkman and her bioinformatics team: they find molecular interactions reported in the biomedical literature, select relevant ones, and organize them into the AAP database. As Dr. Brinkman explains it, curation is an arduous process that requires precision and patience. Not only is there “an ever-increasing mountain of data to collect from the literature,” but “the information has to be organized carefully and brought down to a common vocabulary.”

Even naming the items to be entered in the database can be challenging, she notes. For example, the same protein can have several different names. Or a food involved in nut allergy could be referred to as a peanut or as a nut, “but the computer doesn’t know that peanuts are nuts unless you tell it so.” Curating information from the literature using standardized terms and recording relationships between terms is an essential step toward enabling more sophisticated analyses.

Fortunately, Dr. Brinkman was able to link the AAP to an existing database called *InnateDB*—a project she had completed with AllerGen support—which has made the capture and integration of the AAP data “more manageable than it might otherwise have been.” *InnateDB* integrates information about immune pathways and interactions in humans, mice and other organisms, toward the goal of mapping the immune interactome. “You might say that AAP expands *InnateDB* in the direction of allergy and asthma,” she says. “It’s a natural fit, because both allergy and asthma involve immune responses gone awry.”

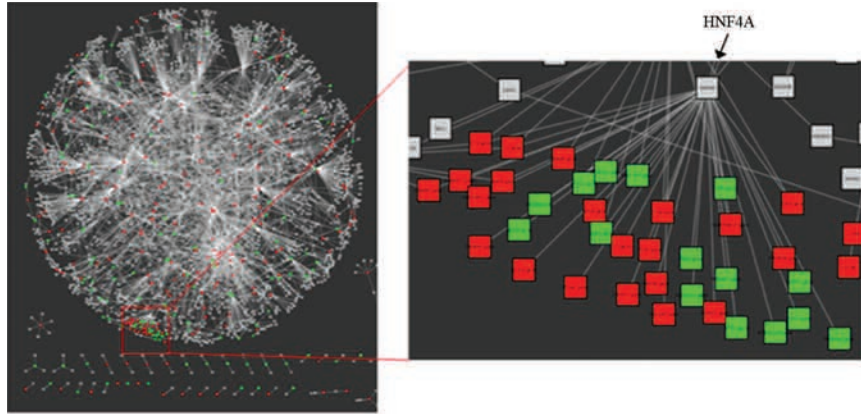
Dr. Brinkman credits AllerGen with making the AAP possible: in addition to funding the development of the public portal itself, AllerGen has provided support for the data gathering and curation processes. She applauds AllerGen for its foresight in “appreciating the value of taking our time to properly gather together data and properly curate it.”

Real world, real results

All this may seem far removed from the real-life struggles of sneezing and wheezing patients. Quite the opposite, says Dr. Brinkman. As a case in point, researchers using the AAP’s parent database, *InnateDB*, made a molecular discovery that led to a new medication, currently undergoing clinical trials, for patients suffering from a severe inflammatory disease.

AAP and the *InnateDB* have spurred other discoveries that could help suffering patients. “Take a look at this commonly-termed ‘hairball’ of a molecular network,” says Dr. Brinkman, referring to an image on the AAP website that maps molecular interactions and genetic information from patients with an immune disease. “The red dots indicate overactivity of certain key genes, while the green dots show underactivity.”

Dr. Brinkman goes on to explain that “you often get a whole bunch of proteins upping their activity in response to an allergen. If you just look at these proteins as a list, it doesn’t tell



you much. But if you look at them within a network context and see how they interact with each other, you often discover that the response is simpler than originally thought—that many of the genes involved in a response are actually linked to a key regulator.” In fact, the database was able to link the overactive genes in the ‘hairball’ network to a regulator protein called HNF4A. “This may eventually lead to an immune-modulating therapy that targets this protein,” she says.

“The AAP can help researchers go beyond therapeutic target discovery. Such analyses could also help tease out the molecular interactions that predict a more severe allergic response,” says Dr. Brinkman. The database may further shed light on “which groups of patients are more likely to respond to an allergy or asthma therapy, and which ones may need closer follow-up.”


Beyond the molecule

Dr. Brinkman now has her sights set on expanding the AAP beyond the molecular level. “The AllerGen Network has rich clinical and epidemiological data regarding other key players in the development of allergy and asthma, such as microbes in people’s bodies, and environmental data about where people live in relation to pollution sources,” she points out. “We’re initiating an assessment of this data to see how we can expand our curation and integration further, capitalizing on the exceptional data that AllerGen researchers have generated.”

As the AAP attempts to make sense of even more complicated inter-relationships, it will become an even more valuable research, discovery and development tool. “Such a powerful tool is crucial, considering the potential for uncovering new insights from the rich, integrated data within

Fortunately, Dr. Brinkman was able to link the AAP to an existing database called *InnateDB*—a project she had completed with AllerGen support....

“*InnateDB* integrates information about immune pathways and interactions in humans, mice and other organisms, toward the goal of mapping the immune interactome.” You might say that AAP expands *InnateDB* in the direction of allergy and asthma,” she says. “It’s a natural fit, because both allergy and asthma involve immune responses gone awry.”

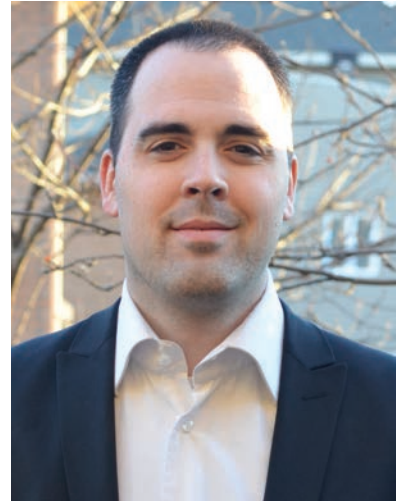
the AllerGen network,” says Dr. Brinkman. “We must pull AllerGen data together so, like the analogy of the blind men, we can move closer to a true understanding of what allergy and asthma are—and potentially uncover novel, possibly even simple, ways in which these conditions can be avoided or controlled.” 

As therapeutic specialists—often with training in pharmacy or holding a science-based PhD like Dr. Préfontaine—medical science liaisons act as “messengers” between the pharmaceutical industry and healthcare providers.



HQP Profile—David Préfontaine: From Research Lab to Industry Liaison

Bench science, big pharma: separate spheres attracting two different types of people? Not according to Dr. David Préfontaine, a scientist who straddles both worlds. Dr. Préfontaine transformed from a laboratory or “bench” researcher into a rising star in the pharmaceutical industry, bringing his passion for science to bear on his current position as Medical Science Liaison at Novartis Pharmaceuticals Canada Inc.



**Dr. David Préfontaine,
Medical Science Liaison,
Novartis Pharmaceuticals Canada Inc.**

Science that matters

Dr. Préfontaine has always chosen to follow his heart. Raised on the south shore of the island of Montreal, he began university with a clear vision: “To do science that matters.” While completing an undergraduate biology degree at Université Laval, Dr. Préfontaine took a physiology course that sparked his interest in the harmful effects of the nearly 5,000 chemicals found in cigarette smoke. He later pursued this topic in a Master’s thesis on the toxicology of tobacco smoke at the Université du Québec à Montréal (UQÀM).

For his PhD in pathology, which he completed at McGill University’s Meakins-Christie Laboratories under the supervision of AllerGen investigators Drs Bruce Mazer and Qutayba Hamid, Dr. Préfontaine broadened his focus to study the triggers and root causes of respiratory diseases, including allergies, asthma and chronic obstructive pulmonary disease (COPD). Although different in many respects, both asthma and COPD are chronic conditions causing airway obstruction, coughing, wheezing and shortness of breath. In the Meakins-Christie Laboratories, Dr. Préfontaine spent his days—and many nights—mastering a variety of research techniques while identifying immune pathways associated with the development of respiratory diseases. “Although it was pure ‘bench science’ where you are in the laboratory 24/7, I was collaborating with clinicians and working on human tissues, which kept reminding me that what I was doing could one day help asthma patients,” he recalls.

The desire to contribute to “science that matters” continued to drive Dr. Préfontaine’s career choices, including his decision to join the AllerGen Students and New Professionals Network (ASNPN) in 2007. The ASNPN offers AllerGen trainees and young professionals working in allergic disease research opportunities for networking, knowledge exchange and professional skill development. Within AllerGen’s supportive milieu, and at its conferences and other trainee capacity-building and networking events, Dr. Préfontaine found himself very much at home. “Sharing information with asthma and allergy researchers and students across the country came naturally to me,” he says. “I’ve always enjoyed the process of making knowledge available to different groups of people.”

Dr. Préfontaine’s leadership qualities soon became apparent, and in 2009 he assumed the role of ASNPN regional director for Quebec and the Atlantic region. That same year, Dr. Préfontaine advanced to the position of ASNPN Vice-President, in which capacity he oversaw ASNPN training activities and fostered relationships with heads of other AllerGen committees.

Clinical crossroads

Dr. Préfontaine’s experiences ended up broadening his horizons in unexpected ways. “All the networking activities at AllerGen were exposing me to new opportunities outside the lab,” he says. “I was beginning to feel a pull toward other career possibilities.” His work with AllerGen was also leading him to



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He credits AllerGen for providing the ideal training ground for young allergic disease professionals—whether they are pursuing a career in industry, government, clinical practice or academia. “When you are involved in AllerGen, you can’t help but improve your networking and negotiating skills,” he says, noting that “these skills helped me both to get the job and to do the job.”

discover new talents in himself, such as organizing, decision-making, and distilling complex information into easily digestible concepts—a process known as knowledge translation.

When he completed his PhD in 2010, Dr. Préfontaine reached a crossroads: more lab research as a postdoctoral fellow, or something else? After much consideration, Dr. Préfontaine chose to pursue a career outside of academia, noting “I wanted to deepen my knowledge of respiratory, but not in the lab. I wanted to get closer to people.”

When the opportunity to work as a clinical research associate in respiratory diseases at Montreal’s Mount Sinai Hospital came his way, Dr. Préfontaine leapt at “the chance to look at diseases such as asthma and COPD through a new lens.” The job put him in touch with allergists, respirologists, surgeons and other clinicians “who knew and taught me a lot about the healthcare system, which was new territory for me.”

Dr. Préfontaine found himself collaborating on large-scale clinical trials of new pharmacological and non-pharmacological treatments for COPD, a line of work he found especially rewarding. “It got me closer to the reality of patients who live with this disease,” he says. “I worked on a couple of very interesting projects.” One of his published studies uncovered the value of an exercise capacity screening tool as a predictor of prognosis in COPD, while another described the changing profile and journey of patients admitted for sub-acute COPD care throughout the prior decade, changes likely due to “demography, as well as different discharge strategies, home care, and self-management strategies over time.”

All the while, Dr. Préfontaine continued to nurture the relationships he had initiated through AllerGen. “I made sure I attended AllerGen’s conferences both regionally and nationally,” he says, describing the Network as a “very fertile networking environment. You never know who you’ll meet and connect with.”

Novartis comes knocking

Dr. Préfontaine met a representative of his current employer, Novartis Pharmaceuticals Canada Inc., at an AllerGen meeting in 2013. “It just goes to show that exciting opportunities can arise even at local events,” he says. His future colleague got right to the point: “He had a position to fill, and my background and skill set made me an interesting candidate.”

Interesting indeed. Dr. Préfontaine’s experience as a laboratory scientist, a clinical researcher, and an accomplished communicator made him custom-fit for the position of Medical Science Liaison within Novartis’s respiratory diseases portfolio. As therapeutic specialists—often with training in pharmacy or holding a science-based PhD like Dr. Préfontaine—medical science liaisons act as “messengers” between the pharmaceutical industry and healthcare providers. For his part, Dr. Préfontaine felt a new kind of excitement at the thought of bringing novel healthcare solutions to people suffering from respiratory diseases.


After close to two years on the job, Dr. Préfontaine describes himself as a “scientific consultant in the respiratory field,” as opposed to a salesperson for pharmaceutical products. “Pharmaceutical companies have a lot to offer the patient, but therapies penetrate the community *via* doctors,” he says.

“That’s the role of a medical science liaison—to make sure that prescribing physicians understand the science behind the medications.”

Specifically, Dr. Préfontaine communicates with physicians and other health providers about therapies for asthma, COPD, and cystic fibrosis within the province of Quebec, ensuring that “they are aware of everything Novartis is doing in respiratory medicine.” The job also has him travelling to conferences and attending advisory board meetings, where he asks key opinion leaders in respiratory medicine to weigh in on the significance of clinical trial results. The physicians, in turn, share with him their views on the data, as well as their clinical challenges. “This helps pharmaceutical companies meet physicians’ and patients’ needs, and improve both clinical development and corporate strategy,” he says.

Dr. Préfontaine’s liaising duties don’t end there. In addition to facilitating collaborations between Novartis and the research and medical communities, he reports back from the medical trenches to company scientists working on new therapies. Internally, he also swaps scientific and strategic insights with the medical affairs, medical education, marketing, regulatory and legal departments.

All of this makes for a “highly variable, challenging, and exciting job,” he says, adding that “people skills are a big part of it.” In this regard, he credits AllerGen for providing the ideal training ground for young allergic disease professionals—whether they are pursuing a career in industry, government, clinical practice or academia. “When you are involved in AllerGen, you can’t help but improve your networking and negotiating skills,” he says, noting that “these skills helped me both to get the job and to do the job.”

Looking back on his career path, Dr. Préfontaine would not change any part of it. “I loved the challenge of the PhD—not just the research, but the questioning it led to,” he reflects. While he enjoyed the scientific rigour of academia, “I had to ask myself some hard questions about the impact of my work.” The conclusion he ultimately reached is that “I’m a big-picture guy, and discussing the clinical relevance of trial data with physicians helps me to stay grounded and contribute to making a difference for patients—today with the existing pharmaceutical portfolio, tomorrow with new products in the pipeline.” 

Success Stories: *Innovation from cell to society*



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Success Stories

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