

RESEARCH HIGHLIGHTS

AllerGen launches first globally-accessible allergy and asthma molecular database

AllerGen's <u>Allergy and Asthma Portal</u> (AAP)—a unique, web-accessible database that houses over 900 biomolecular interactions relevant to allergy and asthma—is now open to the public.

The AAP is the first resource of its kind and represents the most comprehensive database of the genes, proteins, biomolecular interactions and pathways associated with immunity and allergic diseases.

The AAP is built upon InnateDB, an AllerGenenabled database that has unravelled the network of all known molecular interactions in humans and mice. The AAP integrates allergy and asthma interactions from both the scientific literature and AllerGen researchers to produce a highly sophisticated database specifically geared to the study of allergy and asthma.

Both InnateDB and the new AAP were developed with AllerGen support by Network investigator <u>Dr. Fiona Brinkman</u>, a professor in the Department of Molecular Biology and Biochemistry at Simon Fraser University. Dr. Brinkman is an expert in the emerging field of bioinformatics—the use of computers to gather,

store, analyze and integrate biological and genetic information, which can then be used to study how diseases develop.

"The unique visualization tools available in the allergy and asthma portal allow users to quickly see things like molecular 'hubs' in an immune response," says Dr. Brinkman. "For example, instead of simply viewing a list of proteins involved in an allergic response, researchers will see how the proteins interact with each other, allowing for more integrated, advanced studies of allergic diseases."

The AAP is available for use by asthma and allergy researchers worldwide, with the most recently curated data accessible to AllerGen investigators only for a privileged period of two months.







Fewer food allergies among new immigrants and Canadians with low education

AllerGen researchers have published the first nationwide study to estimate the prevalence of food allergy among vulnerable Canadians, including those with low income/education, individuals of Aboriginal identity and new Canadians.

The study, "Surveying Prevalence of Food Allergy in All Canadian Environments (SPAACE)," was published in September in the Journal of Allergy and Clinical Immunology: In Practice. It concluded that Canadians with lower education and new Canadians (individuals who immigrated to Canada within the last 10 years) have fewer food allergies than the general population. The study also found that there were no differences in the prevalence of food allergy according to income or Aboriginal status.

The research was conducted by a team of AllerGen investigators and led by Drs Ann Clarke, a professor in the Department of Medicine at the University of Calgary, and Susan Elliott, a professor in the Department of Geography and Environmental Management at the University of Waterloo.

In a previous AllerGen-funded study, the authors found that 7.5% of Canadians self-report a food allergy and prevalence differs across socioeconomic groups and geographic regions.

The current study is based on data collected from 5,734 households, representing over 15,000 individuals from low-income, Aboriginal and immigrant populations across Canada. The

study measured food allergy prevalence as selfreported by respondents.

"This research enables us not only to better characterize the prevalence and experience of food allergy in Canada, but also to understand how the environment may influence its development," says Lianne Soller, first author of the study.

The reasons for the lower prevalence of food allergy among vulnerable Canadians are not clear; this difference could be due to a range of factors that require further research, according to the authors.

Although immigrants were less likely to experience food allergy, the odds of their self-reporting food allergy increased by 2% with each additional year of residence in Canada.

"These findings support the 'healthy immigrant effect,' which states that new Canadians tend to have a low prevalence of chronic conditions, but their health status worsens with time and eventually converges with that of the Canadian-born population," says Dr. Clarke.

The study's findings will help researchers to better understand the lived experiences of food allergies in vulnerable populations. The findings may also help to identify and address gaps in education, health care and public policy, and to ensure equal opportunity for all Canadians to seek and receive appropriate care related to food allergies.





Early-life shifts in gut microbes can increase susceptibility to inflammatory lung disease

Allergy researchers at The University of British Columbia (UBC) have found that antibiotic use in early life alters gut bacteria and enhances future susceptibility to inflammatory lung disease.

The study, led by Dr. Kelly McNagny, a professor in the Department of Medical Genetics at UBC, and Dr. Brett Finlay, a professor in the Departments of Biochemistry and Molecular Biology, and Microbiology and Immunology, was published in the *Journal of* Allergy and Clinical Immunology (JACI). It concluded that mice treated with the antibiotic streptomycin (but not vancomycin) early in life experienced a change in the composition of their intestinal microbiota, leading to an increased susceptibility to hypersensitivity pneumonitis (HP)—a disease in which the lungs become inflamed from breathing in substances such as moulds, dusts and chemicals.

In a <u>previous study</u>, the authors found that infant mice treated with low doses of vancomycin (but not streptomycin) developed

an increased susceptibility to allergic asthmalike disease as adults.

"This work shows that altering the natural colonization of our gut with microbes early in life can have a long-term influence on the immune system and increase our chances of developing future allergic disease," says Dr. McNagny. "More importantly, we are beginning to get hints as to which types of bacteria are helpful and which are harmful in dampening susceptibility to allergic disease."

Dr. McNagny is an AllerGen NCE-funded investigator and co-first authors Shannon Russell and Matthew Gold are graduate students in the AllerGen Network. The research was supported by a Canadian Institutes of Health Research (CIHR) team grant.

The study's findings will help researchers to better understand the potential impact of antibiotic use on the gut microbiota and on future susceptibility to lung inflammation. The findings may also lead to the identification of probiotics that could lower the risk of developing allergic disease.





CIC confirms new drug reduces symptoms of allergic asthma

Researchers in AllerGen's Clinical Investigator Collaborative (CIC) have shown that a new drug (quilizumab) successfully blocks the production of an immune system protein, reducing symptoms of allergic asthma.

The <u>study</u>, led by <u>Dr. Gail Gauvreau</u>, associate professor in the Department of Medicine at McMaster University, was conducted by CIC investigators at six Canadian universities and one international site, and published in the July 2, 2014, issue of the journal *Science Translational Medicine*.

Quilizumab, manufactured by Genentech, is a new monoclonal antibody that targets a receptor on immature blood cells to block the production of immunoglobulin E (IgE), a key protein involved in the allergic response. While other drugs bind to circulating IgE, quilizumab acts by depleting the cells responsible for IgE production even before it occurs, according to Dr. Gauvreau.

"The reduction of IgE in the blood was sustained for at least six months after the last dose of quilizumab, suggesting a long-lasting effect on IgE production," says Dr. Gauvreau. "These findings may have implications for patients with severe asthma or other diseases

which are caused by high levels of circulating IgE."

The researchers tested the drug in a group of 29 subjects with mild asthma and another group of 36 subjects with allergic rhinitis (hay fever). Quilizumab reduced overall levels of IgE, and also reduced the amount of IgE that specifically targeted the allergens to which patients were exposed, the study found.

The Phase II study, conducted from December 2010 to March 2012, involved the work of AllerGen researchers Dr. Louis-Philippe Boulet (Laval University), Dr. Donald Cockcroft (University of Saskatchewan), Dr. Mark FitzGerald (The University of British Columbia), Dr. Beth Davis (University of Saskatchewan), Dr. Richard Leigh (University of Calgary), Dr. Irvin Mayers (University of Alberta), Dr. Barbro Dahlén (Karolinska Institute, Stockholm, Sweden) and the CIC's director, Dr. Paul O'Byrne (McMaster University).

A follow-up clinical trial involving a larger group of subjects with more severe asthma is underway according to Dr. Jeffrey Harris, principal medical director of immunology, tissue growth and repair for Genentech, and one of the study's co-authors.



International Obesity Journal of Obesity

New study links antibiotic use to overweight in children

A new study by AllerGen researchers has shown that children treated with antibiotics in the first year of life are more than twice as likely to be overweight later in childhood compared to children who were unexposed.

The <u>study</u>, published online in the *International Journal of Obesity*, linked provincial health records of antibiotic use with data from 616 children involved in a longitudinal birth cohort study. It found that 32.4% of children who received antibiotics in the first year of life were overweight by age 12 compared to 18.2% of children who did not receive antibiotics.

While antibiotic use during infancy increased the risk for overweight in all children, a strong association remained in boys but not girls after maternal overweight and other pregnancy factors were taken into account, according to the study's authors.

The study involved the work of AllerGen researchers Drs Anita Kozyrskyj, Meghan Azad

and Sarah Bridgman (University of Alberta), and Dr. Allan Becker (University of Manitoba), using data from the <u>Study of Asthma, Genesand the Environment (SAGE)</u> birth cohort.

"Our results are consistent with research that shows a stronger intrauterine effect of pregnancy overweight on daughters than sons, but of a stronger postnatal environmental influence on sons than daughters," explains Dr. Kozyrskyj.

"Given the current epidemic of childhood obesity and the relatively frequent prescription of antibiotics for infants, this is a promising area for further research," says Dr. Azad, first author of the publication. "Next, we would like to study the role of gut microbes in this process: antibiotic use during infancy may cause disruption of the gut microbiota during a critical period of development, with negative consequences for metabolism and weight gain later in life. We will be curious to learn whether antibiotics have gender-specific effects on gut microbes."





Canadian newborns are routinely exposed to antibiotics

In a new study published August 13, 2014, by The Journal of Maternal-Fetal & Neonatal Medicine, AllerGen trainee Ryan Persaud and a team of AllerGen researchers found that Canadian newborns are routinely exposed to antibiotics immediately before or after birth.

The <u>article</u>, "Perinatal antibiotic exposure of neonates in Canada and associated risk factors: a population-based study," describes direct and indirect (*via* the mother) in-hospital antibiotic exposures and their associated risk factors. From a review of the hospital charts of 449 mother-newborn pairs enrolled in AllerGen's <u>CHILD Study</u>, the authors concluded that 45% of newborns were exposed to antibiotics during the perinatal period. The main indication for direct antibiotic treatment of newborns was a suspected infection, while the main reason for maternal antibiotic use was routine treatment for a caesarean section delivery.

Mr. Persaud, a 4th-year pharmacy student at the University of Manitoba and lead author on the paper, participated in the research with support from an AllerGen *Summer Studentship* award. Co-authors of the article include AllerGen researchers Dr. Meghan Azad, Radha Chari, Dr. Malcolm Sears, Dr. Allan Becker, Dr. Anita Kozyrskyj and the CHILD Study Investigators.

"The AllerGen Summer Studentship (matched with a Manitoba Institute of Child Health Undergraduate Summer Studentship) allowed me to work with expert pediatric allergy and microbiome researchers, and provided training, networking and experience that were critical to the success of my first academic publication," says Mr. Persaud.

Previous research indicated that infant antibiotic use is a risk factor for childhood asthma, allergy and obesity, and suggested that a disruption of the gut microbiota may be at play. Ongoing research in the CHILD Study will examine the impact of antibiotic use on the development of infant gut microbiota and immunity, and address the long-term consequences of the perinatal antibiotic exposure documented in this study.



CIC investigators test promising treatment for patients with hard-to-treat asthma

Researchers in AllerGen's Clinical Investigator Collaborative (CIC) have shown that the drug mepolizumab can successfully block the production of an immune system protein, reducing the dose of prednisone required to treat patients with severe asthma who are dependent on it.

Mepolizumab is a monoclonal antibody that binds to and inactivates interleukin-5 (IL-5), a key protein involved in the allergic response.

The <u>study</u>, published in the *New England Journal of Medicine (NEJM)*, concluded that mepolizumab blocked IL-5, decreasing asthma exacerbations and reducing the dose of corticosteroids needed to control asthma in a subgroup of patients with high levels of eosinophils (white blood cells) in their sputum and blood.

The multi-centre, global study, led by Dr. Elizabeth Bel from Amsterdam, involved the work of Canadian researchers, including AllerGen CIC investigators Drs Parameswaran Nair (McMaster University), Louis-Philippe Boulet (Laval University), Catherine Lemière (Université de Montréal) and James Martin (McGill University). Dr. Nair's Hamilton-based study site recruited the largest number of patients for the international trials. The research was sponsored by GlaxoSmithKline, the manufacturer of mepolizumab.

The study's results confirm <u>previous research</u> led by Dr. Nair and published in the *NEJM* in 2009.



GRANT AWARDS

AllerGen researcher funded to lead worldwide study of air pollution and disease

Pr. Michael Brauer, an AllerGen investigator and a professor in the School of Population and Public Health at The University of British Columbia (UBC), is leading a new study that will provide an unparalleled worldwide analysis of the relationship between air pollution and cardiovascular and respiratory disease.

"PURE AIR: A Global Assessment of Air Pollution and Respiratory and Cardiovascular Disease within the Prospective Urban and Rural Epidemiological Study" has received a four-year, \$753,000 operating grant from the CIHR Institute of Population and Public Health.



Dr. Michael Brauer

The award will support Dr. Brauer and a team of seven researchers, including AllerGen's CIC research leader Dr. Paul O'Byrne, to conduct the first worldwide health study on the impacts of both outdoor and

household air pollution on cardiovascular and respiratory disease.



The study will use an existing international cohort: the Prospective Urban and Rural Epidemiological Study (PURE), led by Dr. Salim Yusuf of the Population Health

Research Institute at McMaster University.
PURE has recruited 155,000 individuals
residing in 628 communities in 17 countries
and 5 continents, with follow-up completed for
four years and continuing for a further six.

PURE AIR will use novel satellite-based approaches to estimate outdoor air pollution levels, as well as targeted air pollution monitoring for all communities. Household air pollution will be estimated using detailed information already collected on the heating and cooking methods, fuel types and ventilation practices used in the PURE study participants' homes.

The results will help to determine the relationship between outdoor and household air pollution exposures and cardiovascular and respiratory diseases, as well as key relevant risk factors, such as blood pressure and lung function.



CHILD research team awarded five-year CIHR grant

Pr. Malcolm Sears, an AllerGen research leader and a professor of medicine at McMaster University, together with a team of CHILD researchers from across Canada, has received a five-year operating grant, valued at over \$1 million, from the Canadian Institutes of Health Research (CIHR) Institute of Circulatory and Respiratory Health. The CHILD Study application was ranked highest among 65 proposals reviewed by the respiratory committee in the March 2014 competition.

The project, titled "Early Life Determinants of Asthma," will use data from over 3,300 infants in the CHILD birth cohort study to explore how selected environmental factors affect allergies

and asthma in children with different genetic backgrounds, as reflected in their Genetic Risk Scores (GRS).

A GRS for asthma has recently been developed: the higher an individual's score, the more likely is life-long asthma; however, it is not known how environmental exposures influence this genetic risk.

AllerGen investigators Drs Sonia Anand (McMaster University), Jeffrey Brook (Environment Canada, University of Toronto) and PJ Subbarao (The Hospital for Sick Children) are also Principal Investigators for the project.

Grant supports further exploration of C-section impact on infant gut microbiota

Allan Becker (University of Manitoba), together with other CHILD Study researchers, were awarded a \$100,000 one-year grant from CIHR's Human Development, Child and Youth Health Institute for their project: "Cesarean section: impact on infant gut microbiota, childhood obesity and allergic disease."

This project will build on earlier SyMBIOTA findings, published in journals such as the *British Medical Journal, Allergy, Asthma & Clinical Immunology and Canadian Medical Association Journal,* using the CHILD Study data as a research platform.



KNOWLEDGE MOBILIZATION



New online course helps educators keep allergic kids safe at school

Anaphylaxis Canada has launched a new online course to help teachers, administrators and educational staff to keep allergic students safe at school.

Anaphylaxis in Schools: What Educators Need to Know is a free, bilingual resource available to schools across the country. The course incorporates graphics, audio narration, practice scenarios, and step-by-step visual guides to help educators prevent and manage emergency situations at school.

This course is the first in a series of three anaphylaxis training programs developed in collaboration with Leap Learning Technologies Inc. and the Canadian Society of Allergy and Clinical Immunology (CSACI), with support from AllerGen NCE and McMaster University.

Additional courses targeted to members of the community, including parents, caregivers, childcare centres and the general public will be released in 2015.



Inside AllerGen's Success Stories (Fall 2014)

- the ethics of biobanking;
- the launch of a much-needed asthma clinic in El Salvador:
- how uncontrollable asthma contributes to the burden of workplace productivity loss;
- new ways to conduct clinical research trials for hayfever; and
- a young allergy researcher's study of the infant microbiome.

Read the Fall 2014 issue



SyMBIOTA website up and running

The SyMBIOTA (Synergy in Microbiota Research) project now has its own website.

Led by AllerGen investigators Dr. Anita Kozyrskyj (University of Alberta) and Dr. James Scott (University of Toronto), the project uses AllerGen's CHILD Study data as a research platform to investigate the environmental determinants of infant microbiota. Launched in June 2014, the site provides an overview of the SyMBIOTA project—its objectives, procedures, team members, publications and other achievements, including media coverage—and a brief introduction to gut microbiota development in infants.

Dr. Paul O'Byrne organizes "Managing Respiratory Disease" event

Paul O'Byrne, an AllerGen research leader, professor in the Division of Respirology and Chair of the Department of Medicine at McMaster University, is organizing and will speak at a Continuing Medical Education (CME) event hosted by the Firestone Institute for Respiratory Health.

The event, titled "Managing Respiratory Disease in Primary Care Practices," will take place October 17-18, 2014. Its target audience includes FP/GPs, internists, respirologists, nurse practitioners, RNs, respiratory therapists, students and residents.





TRAINEE ACCOMPLISHMENTS

Record high employment rate for AllerGen HQP

n the past year, over 40 AllerGen trainees secured employment. This is the highest single-year employment figure for AllerGen HQP in the past decade.

Trainees found employment across various sectors, including academia (22), industry and the private sector (12), provincial and federal governments (6) and hospitals (2).

Examples of areas where AllerGen graduates are employed include: the Ontario Ministry of the Environment, the Ontario Ministry of Transportation, British Columbia Centres for Disease Control, Public Health Ontario, The Hospital for Sick Children, Tekmira Pharmaceuticals, Naegis Pharmaceuticals, STEMCELL Technologies and GlaxoSmith Kline.

In 2013-2014, five obtained faculty appointments:

Dr. Meghan Azad, an AllerGen trainee and postdoctoral fellow at the University of Alberta, was appointed Assistant Professor at the University of Manitoba and the affiliated George & Fay Yee Centre for Healthcare Innovation.

Dr. Jeremy Hirota, an AllerGen trainee and postdoctoral fellow at the James Hogg

Research Centre at The University of British Columbia (UBC), was appointed Assistant Professor in the Division of Respiratory Medicine, Department of Medicine, at The University of British Columbia.

Dr. Yuka Asai, an AllerGen trainee and PhD candidate at McGill University, joined the Division of Dermatology at Queen's University in Kingston, ON. She also provides consultation services to the Kingston General Hospital and outpatient services at the Hotel Dieu Hospital.

Dr. Elinor Simons, an AllerGen trainee and PhD candidate at the Hospital for Sick Children, was appointed Assistant Professor/Clinician Scientist in the Section of Allergy, Department of Pediatrics and Child Health, at the University of Manitoba.

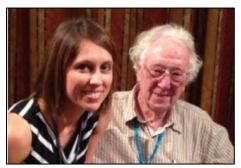
Dr. Victoria Arrandale, an AllerGen trainee and recent PhD graduate from the University of Toronto's Gage Occupational & Environmental Health Unit, was appointed Senior Research Associate in the Occupational Cancer Research Centre at Cancer Care Ontario and Assistant Professor in Occupational and Environmental Health at the University of Toronto's Dalla Lana School of Public Health.

reAction June 2014



Trainees rub shoulders with Nobel Laureates, talented science writers

Read **Dr. Meghan Azad**'s informal <u>report</u> on her participation in the 64th Lindau Nobel Laureate Meeting in Lindau, Germany.



Dr. Azad with Nobel Laureate Oliver Smithies: "an unforgettable, once-in-a-lifetime experience"

Dr. Azad thanks the Canadian Institutes of Health Research (CIHR) for nominating her for inclusion in the event and for sponsoring her participation. Read **Dr. Jeremy Hirota**'s informal <u>report</u> on his participation in the <u>2014 Banff Centre</u> <u>Science Communications Workshop</u>, which took place in Banff, Alberta.



Dr. Hirota at the Banff event:"a truly transformative experience"
(Photo: Nick Davila)

Dr. Hirota thanks AllerGen for the Research Skills Acquisition Award that facilitated his attendance.



PEOPLE & PARTNER NEWS

AllerGen investigator named one of "World's Most Influential Scientific Minds"

An AllerGen investigator is among 90 Canadians named in Thomson Reuters' new compilation of "The World's Most Influential Scientific Minds: 2014."

Dr. Fiona Brinkman, a professor in the Department of Molecular Biology and Biochemistry at Simon Fraser University, was ranked as a top influencer in the category of "computer science" for her work in the area of bioinformatics.



Dr. Fiona Brinkman

Thomson Reuters identified the most influential scientists by analyzing citation data over the last decade. Roughly 3,200 researchers worldwide earned the distinction by ranking among the top 1% "most cited" in 21 fields of science and social science.

Timothy Caulfield one of Alberta's "50 Most Influential People"

AllerGen investigator Professor Timothy Caulfield, Professor in the Faculty of Law and the School of Public Health at the University of Alberta and Canada Research Chair in Health Law and Policy, was named one of "Alberta's 50 Most Influential People" by Alberta Venture magazine.

The magazine's profile of Professor Caulfield refers to him as "quite possibly the world's most scientific lawyer," noting how well he "cuts through the murk and translates meaningful



Prof. Timothy Caulfield

health information to the public, all while promoting sound, science-based health policy."

Professor Caulfield is currently producing an AllerGen-supported White Paper Series analysing the legal and

ethical dimensions of allergy and asthma research, including the ethics of biobanking.



AllerGen and CRRN partner in early-career grant program



AllerGen is partnering with the Canadian Respiratory Research Network (CRRN) in the Emerging Research Leaders Initiative (ERLI)—a grant program for researchers as they transition from a post-doctoral fellow to early-career professional in the areas of cardiovascular, cerebrovascular, and/or respiratory health research.

This multi-partnered initiative is led by the Canadian Lung Association and the Heart and Stroke Foundation, and includes organizational partners from non-profit, government, industry,

and emerging/existing Networks of Centres of Excellence.

The grant, valued at \$150,000 (\$50,000/year for three years), is intended to assist new investigators to establish independent health research programs and achieve the research productivity necessary to obtain funding from national and other external granting agencies. A successful CRRN applicant whose research aligns with AllerGen's mission and research scope is eligible for additional funding of \$12,000/year for the duration of the award.

AllerGen investigator, partner organization help launch epinephrine auto-injector pilot project in Hamilton

Apilot project, led by the City of Hamilton and involving McMaster University and AllerGen partner Anaphylaxis Canada, was launched in Hamilton on September 8, 2014.

The project will analyze the impact of stocking epinephrine auto-injectors at Jackson Square shopping mall, and of training mall security

guards to recognize an anaphylactic reaction and to administer the auto-injectors. The analysis will be conducted by a research team headed by AllerGen investigator Dr. Susan Waserman, Professor of Medicine at McMaster University.

For more information, read the <u>press release</u>.





AllerGen partners recognized for business acceleration, entrepreneur mentorship

Tec Edmonton, an AllerGen partner organization, was named "runner-up Canadian business accelerator of the year" in the 2014 Startup Canada Awards (Prairie Region). It was also ranked number 10 globally by the 2014 UBI (University Business Indicator) Index.

Dr. Randy Yatscoff, an AllerGen RMC and NSIP committee member, a mentor in AllerGen's KTEE Mentorship Program, and Executive Vice-President of Business Development for TEC Edmonton, was named "Entrepreneur mentor of the year" for the Prairie Provinces by Startup Canada.

MEDIA

AllerGen investigators in the news

Two recent studies conducted by AllerGen researchers have generated international media coverage.

In August 2014, **Dr. Kelly McNagny** and coauthors found that antibiotic use in early life alters gut bacteria and enhances future susceptibility to inflammatory lung disease. The study was published in the *Journal of Allergy and Clinical Immunology*, producing 25 media hits, including interviews with *Global News*, *CTV*, and the *Delhi Daily News* (India), within 48 hours.

In May 2014, researchers in AllerGen's Clinical Investigator Collaborative (CIC) successfully tested an antibody (mepolizumab) that may lead to an improvement in asthma

control by reducing inflammation in the lungs. The study, which appeared in the *New England Journal of Medicine*, generated 27 print articles and radio/TV interviews worldwide in 48 hours.

AllerGen investigator **Dr. Susan Waserman** (McMaster University) was <u>interviewed</u> on *CTV* on the topic of "allergy-free peanuts."

AllerGen investigator **Professor Timothy Caulfield**'s opinion piece, "Who owns your tissue? You'd be surprised," was published in the *Globe and Mail*. He was also interviewed in the *National Post* on the same topic.

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