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Predicting Allergies and Asthma in Babies — Pioneering Canadian Scientists Discover that Stem Cells are "Crystal Balls"

Parents envision their newborn baby developing from a beautiful, active child into a healthy, happy and productive adult. They wonder what traits their son or daughter will inherit or develop. Parents who suffer from asthma and/or allergies worry about their child also developing these conditions as they grow up. New evidence from AllerGen-funded research shows that it may be possible to predict the risk of developing allergies and asthma much earlier in childhood — even at birth.

Dr. Judah Denburg, Scientific Director and CEO of AllerGen NCE and Professor of Medicine at McMaster University

An international team of scientists led by Dr. Judah Denburg, Scientific Director and CEO of AllerGen NCE and Professor of Medicine at McMaster University, has discovered that hemopoietic stem cells (*i.e.*, those giving rise to blood), found in abundance in a baby's umbilical cord blood, can help predict susceptibility to developing allergies and/or asthma later in life. Early diagnosis of allergic disease provides greater opportunity for medical and lifestyle interventions that may alter disease progression and ultimately increase a child's quality of life while growing up. Successful development of an early-life predictive test would revolutionize both diagnosis and management of allergies and asthma, resulting in the best possible health outcomes for children.

From Observation to Experimentation

Even though Dr. Denburg is the leader of an asthma and allergy research centre, he was trained in hematology, which is the study of blood, blood-forming organs, and blood diseases. In searching for a diagnostic test for a certain type of leukemia that involves many inflammatory cells also present in allergic inflammation (mast cells, basophils and eosinophils), Dr. Denburg used his own blood sample as the *control*, and found, to his astonishment, that it was replete with many hemopoietic stem cells that become mast cells, basophils and eosinophils. Since he did not have leukemia, Dr. Denburg began to wonder if his allergies were responsible for the increased presence of stem cells in his blood, and if so, if this condition was common to all people with allergies. Years of further research by Dr. Denburg proved that his initial hypothesis was correct, and that hemopoietic stem cells, and the bone marrow where they are produced, are in fact highly involved in allergies and asthma in older children and adults with these conditions.

Cord Blood Stem Cells as Allergy Predictors

Over the past few years, Dr. Denburg has been preoccupied with determining whether or not hemopoietic stem cells in a newborn baby's cord blood contribute to, or predict, the development of allergic disease. With funding from AllerGen NCE, the Canadian Institutes of Health Research, as well as several industry partners, Dr. Denburg assembled a team of pan-Canadian and international scientists to help investigate this possibility using data from several longitudinal birth cohort studies undertaken in Canada and Australia in which information on a baby's allergic risk, based on parental history and skin testing as well as maternal environmental exposures, was available.

In all, Dr. Denburg and his collaborators collected the cord blood of several hundred babies and then tracked them over several years. The cord blood samples were cultured in the laboratory and observations were conducted. The team confirmed a strong relationship between the levels and types of hemopoietic stem cells found in the babies' cord blood and the level of risk for developing allergies, as well as some early manifestations of allergic disease in the babies as they were growing up. For example, the team found that certain changes in cord blood hemopoietic stem cells are indicative of the extent to which a child will develop a fever and wheezing when battling a viral infection, and the development of eczema, an allergic skin condition, in the first years of life.

As a result of Dr. Denburg's research, we now know that the hemopoietic stem cells in the cord blood of *at risk* babies are programmed to generate inflammatory cells that are the key actors in allergies. "The cord blood really does have an imprint of allergy risk embedded in the profile of the stem cells. That's a really surprising discovery," says Dr. Denburg. The implications of this research are two-fold. First, there is an opportunity to develop a blood test that identifies hemopoietic stem cell programming for early diagnosis of allergies. Second, it provides a window of opportunity for development of novel treatments that go beyond managing allergy symptoms, such as a runny nose and wheezing, to actually modifying allergic risk early in life.

Dr. Denburg and his colleagues from McMaster University, several other AllerGen-associated Canadian universities, and institutions in Europe and Australia continue to examine the impact that maternal nutrition, smoking and exposure to chemicals during pregnancy have on a baby's hemopoietic stem cell programming. On the current AllerGen research team are also world-renowned scientists with different areas of expertise, including: Drs Guy Delespesse (Centre hospitalier de l'Université de Montréal – Research Centre); Mark Larché and Gail Gauvreau (McMaster University); Kelly McNagny (University

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of British Columbia); and, Anne Ellis (Queen's University). This team, called "STEM" (Stem-cell Team for Emerging Markers) is financially supported by AllerGen NCE, the Canadian Institutes of Health Research (CIHR), the National Research Council (NRC) and industry partners.

STEM is now poised to apply stem cell analyses to cord blood samples from AllerGen's own Canadian birth cohort study, the *Canadian Healthy Infant Longitudinal Development* (CHILD) *Study* collected at The Hospital for Sick Children site (led by Dr. Padmaja Subbarao). The CHILD Study, directed nationally by Dr. Malcolm Sears (McMaster University) is the largest birth cohort study ever undertaken in Canada to uncover the causes of allergic disease and asthma. The CHILD Study is a joint initiative between AllerGen NCE and CIHR, with several federal and provincial partners, and will provide abundant biological samples for future study.

The Benefits of a Research Network

AllerGen NCE is known in the scientific community for promoting team-building across multiple research disciplines. "Having a whole network approach has been invaluable," states Dr. Denburg. "It brought me together with other leading researchers from around the world, and provided added-value funding for networking and collaboration. We are now part of a team. These are the windfalls of having a network."

To most parents, having Canada's best scientific minds working together to tackle the growing problem of allergic disease is comforting, particularly when newer and better options for diagnosis, management and treatment are found. Results arising from the STEM team's efforts are leading the way forward to that end, providing us with a valuable new stem cell "crystal ball" with which to predict allergies and asthma in early life.