



Do Early Life Environmental Exposures Work with Genes to Modulate Immune Development?

Childhood diseases of the immune system such as leukemia have become more prevalent in recent decades. While survival rates of leukemia have also increased, scientists do not fully understand the underlying causes of this disease. Results of past studies suggest that factors leading to increased prevalence of leukemia are both genetic and environmental. For instance, genetic mutations that affect an important regulatory protein (Notch-1) have been identified in about 70% of adult acute lymphoblastic leukemia (T-ALL) patients, suggesting that this mutation plays a significant role in this disease. Likewise, effects on the Aryl Hydrocarbon Receptor (AhR), an important regulator of gene expression, have been observed in about 30% of T-ALL patients. These results may be an indication that exposure to environmental pollutants that affect immune system development and function plays a role in leukemia risk. Moreover, the observations associated with Notch-1 and AhR in leukemia show a potential interaction between genes and the environment. If such a gene-environment interaction is an explanation for the increase leukemia rate, the key question is when does that interaction need to occur to lead to disease?

Dr. Michael D. Laiosa, research assistant professor of Environmental Medicine, emphasizes that maternal exposure to dioxin and other related environmental contaminants may be contributing to the rise in immune diseases such as leukemia. To test this hypothesis, Dr. Laiosa is seeking to find out if a mother's exposure to environmental pollutants while pregnant or breast feeding can impact development of immune diseases. This study uses mice to specifically examine whether inappropriate AhR activation by maternal exposure to the environmental contaminant dioxin affects Notch-1 activity and/or Notch-1 dependent T-ALL (leukemia) in offspring. This study will contribute to a larger body of research aimed at understanding the underlying causes of diseases such as leukemia and whether there are ways to mitigate the risk. For instance, Dr. Laiosa suggests that the same developmental sensitivities that increase a child's vulnerability may also cause their bodies to be more receptive to interventions or treatments. Thus, a better understanding of which environmental factors affect immune system development has the potential to help researchers develop early life treatments as well.

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Immune Development, continued...

Dr. Laiosa's long-term goal is to identify the environmental factors which influence immune system development through maternal and early life exposures, and to better understand how the interaction between environmental factors and genetic susceptibility factors affect later-life diseases. If this relationship is better understood, it may be possible to identify at-risk populations using biomarkers (the presence or absence of a molecule in the body) and target these populations with potential early interventions. Better understanding of the mechanisms by which these changes occur might also allow researchers and clinicians to develop improved treatments for immune disease, and potentially develop novel disease prevention strategies, particularly for at-risk individuals and populations.



Bisphenol A Exposure May Pose a Greater Risk to Humans than Previously Thought

Bisphenol A (BPA), an industrial chemical with estrogenic properties, is used to produce many plastics and consumer products. Whether BPA can cause human health effects is a matter of some debate. Past research has demonstrated potential adverse effects in the development of the nervous, reproductive, endocrine, and immune systems.

Until recently, it was believed that exposure was primarily through food, with rapid clearance from the body within 24 hours. Based on this assumption, the Food and Drug Administration (FDA) considered BPA to pose a low threat to human health.



Drs. Rick Stahlhut, Wade Welshons (University of Missouri-Columbia) and Shanna Swan conducted a study examining the rate of BPA elimination from the body. They analyzed data from the CDC's National Health and Nutrition Examination Survey (NHANES) data. The research resulted in a paper, titled "Bisphenol A data in NHANES suggest longer than expected half-life, substantial non-food exposure, or both," which was recently published in *Environmental Health Perspectives*.

Results of their study demonstrated that the current views regarding sources of exposure of humans to BPA and rapid elimination rates may be inaccurate. Although BPA is rapidly cleared by mice after they are given an experimental oral dose of the chemical, in the CDC's NHANES data, human research subjects who reported fasting 10-20 hours still had significant levels of BPA in their bodies. The levels of BPA in those who fasted were only moderately lower than those who had just eaten. This research may indicate that humans are exposed to BPA through sources other than food, or that BPA has a longer half-life in humans, perhaps due to temporary storage of BPA in body fat. Inconsistencies between this study and past research have left scientists puzzled. For a long time researchers have thought they understood the pathways of human BPA exposure and clearance, but now "it's back to the drawing board," says Dr. Stahlhut, "we've got to figure out why these data are not consistent."

Immunotoxicology Specialty Section Paper of the Year

A paper co-authored by Michael D. Laiosa, Kevin G. Eckles, Margaret Langdon, Allen J. Rosenspire and Michael J. McCabe Jr. was awarded Paper of the Year by the Immunotoxicology Specialty Section of the Society of Toxicology. The award is given annually to papers that significantly contribute to the field of Immunotoxicology. The paper, titled "Exposure to inorganic mercury *in vivo* attenuates extrinsic apoptotic signaling in *Staphylococcal aureus* enterotoxin B stimulated T-cells," summarizes the researchers' discovery of a new way that low levels of mercury (Hg) may contribute to autoimmunity.

Autoimmunity can occur when the body is unable to distinguish between host and foreign cells. This causes T-cells, which attack foreign cells and play a significant role in regulating the immune system, to react to the body's own cells resulting in inflammation and tissue damage. Causes of autoimmunity are still largely unknown, but researchers have made great progress in recent years. For instance it is suspected that certain interactions between genetic and environmental factors are involved in the development of autoimmune disorders or contribute to their progression.

Dr. Laiosa and colleagues studied mice to determine the effect of low-level exposure to inorganic Hg in the body, or *in vivo*, with respect to its impact on a regulatory protein called CD95. CD95 is an essential component of the immune system that is responsible for regulating the death of cells in a process called apoptosis. The results of their study demonstrated for the first time that inorganic Hg may affect T-Cell activation and survival by altering CD95 activity *in vivo*. This finding has potential implications for understanding the establishment and progression of autoimmunity as it relates to environmental contaminants such as mercury.

EHSC News

The Rochester Young Men's Study, conducted in conjunction with researchers in Denmark, Copenhagen and Murcia, Spain, is currently underway. This study seeks to understand how prenatal factors such as mothers' smoking and beef consumption while pregnant may affect the future fertility of their sons. Enrollment began in February 2009 and 50 subjects have already been enrolled in the first 7 weeks (projected sample size 300).

The University of Rochester recently received a VHA, Inc. Leadership Award for Community Benefit Excellence. This award is given to health care providers that exhibit excellence in serving the community by providing services that extend beyond the regular course of care. These organizations demonstrate an overall community benefit strategy, and effectively communicate this strategy to the community.

Rochester's Healthy Home, a partnership between the Community Outreach and Education Core of the UR Environmental Health Sciences Center and the SouthWest Area Neighborhood Association, was highlighted as a prominent example of collaboration between the University and community groups in Rochester. This resource provides hands-on training to help reduce environmental health hazards in the home.

To view the full press release, please visit: <http://www.urmc.rochester.edu/pr/news/story.cfm?id=2527>

For more information on the Healthy Home, please visit: <http://www2.envmed.rochester.edu/envmed/ehsc/outreach/CommunityPartners/CommunityPartnersHH.html>

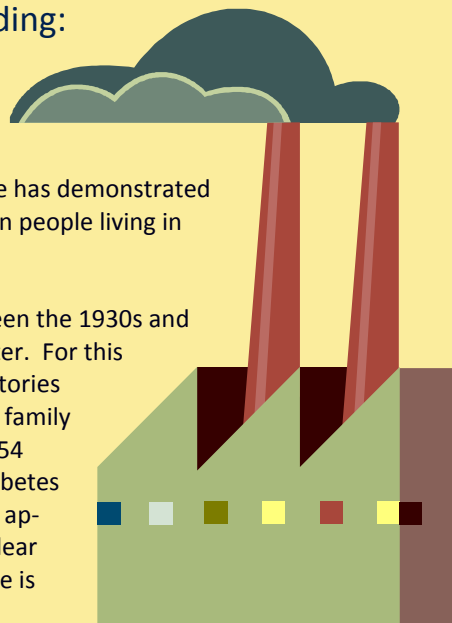
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Community Connections

The Environmental Health Sciences Center recently hosted several community talks by scientists and community members, including:

Dr. Alan Silverstone, professor of Microbiology and Immunology at SUNY Upstate Medical School, gave a talk at our December 2008 EHSC Community Advisory Board meeting. Dr. Silverstone discussed his research in Anniston, Alabama, where he has demonstrated a possible correlation between diabetes and PCB concentrations in people living in areas contaminated by industrial PCB pollution.

Over 1.3 billion pounds of PCBs were produced in Anniston between the 1930s and 1970s, resulting in high concentrations of PCBs in the soil and water. For this study, blood PCB concentrations were measured and diabetes histories recorded for Anniston residents. After correcting for age, obesity, family history and other risk factors, it was found that people aged 35 – 54 with high concentrations of PCBs were more likely to develop diabetes than those with lower concentrations. Likewise, higher PCB levels appear to also increase the risk of heart disease and stroke. It is unclear whether timing of exposure (late or early life) is a factor, and there is much more research needed in this field.



The EHSC co-sponsored a visit by **Dr. Sandra Steingraber**, an ecologist, author and cancer survivor, to the Breast Cancer Coalition of Rochester in March. Dr. Steingraber's talk focused on the mutually beneficial relationship between activism and science. After introducing data on the rate of change in cancer trends, Dr. Steingraber discussed the ability of activists and scientists to work cooperatively toward the goal of saving [women's] lives. Specifically with respect to pharmaceutical estrogens, BPA and atrazine, Dr. Steingraber suggested ways in which advocacy is able to shape culture and "make room" for science. Likewise, she discussed the role of research in bringing health and environment-related issues to light for the public, which in turn generates the demand for further research.



Deepa Premnath, a paralegal with Farmworker Legal Services, presented an introduction to farmworkers and pesticides at our May 2009 EHSC Community Advisory Board meeting. Her talk focused on the barriers that face migrant and seasonal farmworkers, and how these barriers tie into the health and safety of farmworkers. Ms. Premnath focused on her local work with migrant farmworkers in the Rochester region.

In New York State, farmworkers do not have the right to form unions, receive no overtime pay and have no mandatory rest days. Employers are not required to provide disability insurance and there are fewer restrictions on child labor.

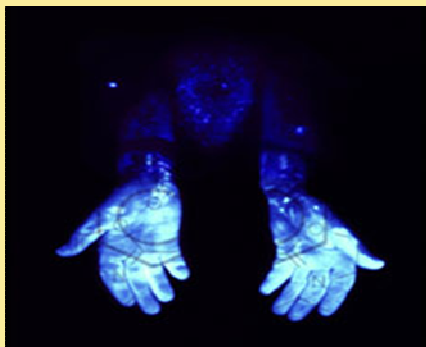


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Connections, continued...

Migrant and seasonal workers face a number of barriers that extend beyond those facing farmworkers in general, including language, education, isolation and poor access to health care and other resources. Such barriers result in a “vulnerable workforce that is hesitant to complain,” giving employers disproportionate power over employees.

These barriers are particularly significant in situations that pose a health risk to farmworkers. The US Environmental Protection Agency estimates 10 to 20 thousand pesticide-related injuries each year, which is a particularly serious issue in the case of migrant workers who may not understand the language of warning labels or may be too fearful of employer retaliation (e.g., firing the employee) to request medical assistance when symptoms arise. Pesticides are particularly dangerous for children and pregnant women who work in the fields, but are also commonly carried home on workers’ clothing. Organizations such as Farmworker Legal Services are reaching out to migrant farmworkers to help them better understand their rights and be comfortable demanding a safe work environment without fear of retaliation.



EHSC News, continued...

The Community Outreach and Education Core serves to strengthen connections between EHSC researchers and the local communities. We are encouraging our local partners to invite EHSC researchers to give community lectures. Our partners have in turn requested a list of volunteer speakers and topics from which to choose. Several EHSC scientists have already offered to give talks:

- ✦ Dr. Alison Elder
Effects of air particulates on asthma
- ✦ Dr. Rick Stahlhut
Relationship of PCBs, obesity and diabetes
- ✦ Dr. Edwin Van Wijngaarden
Introductory lectures in epidemiology, cancer clusters, and public health and sustainability
- ✦ Dr. Jim Campbell
Lead poisoning and environmental exacerbations of asthma

Please contact Valerie George (valerie_george@urmc.rochester.edu) or Katrina Korfmacher (katrina_korfmacher@urmc.rochester.edu) if you are interested in these or other topics.

Dr. Alison Elder received a Young Investigator Award from the Society of Toxicology’s Inhalation and Respiratory Specialty Section. The award is given out to researchers with less than 15 years of experience following their highest degree. Recipients are selected based on their scientific contributions, originality, creativity, and impact on the field of inhalation or respiratory toxicology.

If you have questions or comments about this newsletter, please contact Valerie_George@urmc.rochester.edu

EHSC News, continued...

Dr. Katrina Korfmacher and Valerie George in the Community Outreach and Education Core are conducting a study this summer to characterize local fish consumption. A University of Rochester undergraduate student, Annalise Kjolhede, and one intern with Action for a Better Community have been hired as summer interns to interview anglers and survey the general Rochester population. The purpose of this study is to quantify the extent of local fish consumption in the Rochester area, generate a rapid protocol that is applicable to similar cities, and to gauge general knowledge of the consumption advisories. This project is supported by the Great Lakes Research Fund.



The Uniqueness of Women's Health September 15-16, 2009

Women's health has progressed from a focus solely on the reproductive tract to a diverse set of concerns such as depression, heart disease, osteoporosis, breast disease, and dermatologic disorders. The common thread is that many health conditions affect women differently than men.

This two-day conference, hosted by the University of Rochester Medical Center, is divided into two sections focusing on women's health. On September 15th there will be a post-clinical graduate course to increase awareness of culturally appropriate prevention, diagnostic and treatment services. This will be followed by a day-long workshop on the 16th that will revolve around discussions on improving the communication of health information to consumer interest groups and health professionals.

For more information or to register, please contact:

Office of Continuing Professional Education
University of Rochester Medical Center
Phone: 585.275.4392
E-mail: CMEOffice@urmc.rochester.edu
Web: www.urmc.rochester.edu/cpe

Healthy Buildings September 13-17, 2009

For the first time in 12 years, this international conference and exhibition showcasing innovations in indoor environmental quality and healthy and sustainable environmental technology will be held in the United States. The event will provide a unique setting for sharing information on research and technology, and new products and services. International experts in indoor air quality and healthy built environments will also have the opportunity to network and connect with colleagues. This annual conference is organized by the International Society of Indoor Air Quality and Climate and will be hosted by Syracuse University and the Syracuse Center of Excellence in Environmental and Energy Systems.

For more information or to register, please visit: <http://hb2009.org/>

Congratulations Toxicology Students and Graduates!

We would like to congratulate this year's toxicology graduates! The Center's most recent PhD graduates are:

Na Li, who will be attending pharmacy school at St. John Fisher; Zhengyu Yin, a postdoctoral fellow at NIEHS in North Carolina; Sophia Fang, now living in Seattle, WA; Sara Saperstein, now a postdoctoral fellow at Vanderbilt University; Jamie J. O'Brien-Bernard, who recently accepted a postdoctoral fellowship at University of California, San Diego; and Brent Kobiush, now a Toxicologist at General Mills in Minneapolis, Minnesota. Fanny Casado, Samuel Caito, David Adenuga, Michael Madejczyk, Ming Kung, Jennifer Head, Xianglu Han, Sarah Latchney, and Jonathan Holz all achieved their Master's degrees this year, marking the "halfway point" of the PhD tracks.

A number of these students and others also received awards for their outstanding achievements in the field of toxicology:

- ✘ Jamie J. O'Brien-Bernard received the Harold C. Hodge Award for "especially meritorious research." This award is given to the best PhD thesis in the Environmental Health Sciences.
- ✘ Lisa Bottalico was recognized as a Rochester Toxicology Scholar.
- ✘ Whitney Christian and Melissa Badding received Bristol-Meyers Squibb Research Awards
- ✘ Samuel Caito received the William F. Neuman award for his exemplary citizenship and scholarship in the Toxicology Training Program.
- ✘ Ph.D. student Jamie J. O'Brien-Bernard and postdoctoral fellow Dr. Rick Stahlhut received the Robert F. Infurna award. This award was started in 1998 to recognize authors of the "best research paper[s] in toxicology." Their respective papers are:

O'Brien JJ, Spinelli SL, Tober J, Blumberg N, Francis CW, Taubman MB, Palis J, Seweryniak KE, Gertz JM, Phipps RP. 15-deoxy-D12,14-PGJ2 enhances platelet production from megakaryocytes. *Blood* 112:4051-60, 2008.

Stahlhut, R.W., Welshons, W.V. & Swan, S.H. Bisphenol A Data in NHANES Suggest Longer Than Expected Half-Life, Substantial Non-Food Exposure, or Both. *Environmental Health Perspectives* 117:784-789, 2009.

- ✘ Amber Rinderknecht (postdoctoral researcher), Jessie Shi, Sarah Latchney, Xianglu Han, Fanny Casado, Samuel Caito, Kurt Bertram, Randi Benson all received travel grants for various toxicology conferences/events.
- ✘ Jennifer Head was awarded a Bristol-Meyers Squibb/University of Rochester collaborative initiative research award for her work investigating the relationship between AhR, iNOS and neutrophil recruitment during Influenza A virus infection. Jennifer is also recognized as authoring a review article that has been published in *Biochemical Pharmacology* and was featured in the NIEHS newsletter this May.
- ✘ Sarah Latchney attended the 25th International Neurotoxicology Conference and received first place in the Graduate Student Poster Competition.
- ✘ Jamie O'Brien received the 1st place Society of Toxicology Drug Discovery Specialty Section's Emil A. Pfizer award at the annual SOT meeting in Baltimore.
- ✘ Bethany Winans received the URM Graduate Alumni Fellowship Award. This award is designed to recognize students just entering the graduate program at URM who show promise for exceptional accomplishment in the program.
- ✘ Betina Lew received an Outstanding Postdoctoral award from the Women in Toxicology special interest group of the Society of Toxicology. The award recognizes academic achievement, leadership, and service.