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A Newsletter of the Cornell University Program on Breast Cancer and Environmental Risk Factors (BCERF)

Perspectives on Approaches to Identify Cancer Hazards

By Suzanne Snedeker, Ph.D., Associate Director for Translational Research, BCERF

About 60,000 synthetic chemicals were in use when the Toxic Substances Control Act (TSCA) was passed in 1976 (1). About 700 to 2,300 new chemicals a year have been produced over the last three decades. Hence, it is estimated that 75,000 to 80,000 chemicals are in commercial use (2, 3). The EPA was given the charge of assessing health risks of chemicals. However, by the year 2005, the General Accountability Office (GAO) estimated the EPA had only assessed the toxicity of 2% of the chemicals in commerce (4). Federal agencies are faced with a daunting task: what are the best means to identify chemicals that may be a cancer risk to humans? And, can researchers take advantage of new advances in molecular biology to supplement or even replace current use of laboratory animal studies to more quickly screen large numbers of chemicals for their cancer-causing potential?

When the National Toxicology Program (NTP) was founded in 1978, part of its charge was to identify chemicals that could be cancer hazards for humans. The NTP animal cancer bioassay uses two-year studies in male and female mice and rats to assess the potential of chemicals to induce tumors. While the rodent bioassay was originally envisioned as a way to identify chemicals that would later be examined in human epidemiological studies, the NTP bioassay has become a primary means to identify chemicals that are considered to be a cancer hazard (5).

Because of the common biology between laboratory animals and humans, the NTP bioassay has been an extremely useful tool to predict cancer risk in humans. A number of chemicals were identified as carcinogens in these animal cancer bioassays long before human epidemiological data confirmed their carcinogenic potential. This includes 1,3-butadiene used in rubber and plastic manufacturing, the heavy metal cadmium, the pharmaceutical diethylstilbestrol, the medical instrument sterilizing agent ethylene oxide, the common solvent formaldehyde, and the chemical vinyl chloride, which is used in the manufacturing of many other compounds (6).

Conducting the cancer bioassay is a very complex process (7). It includes a review and selection process for the chemical or metabolites to be tested, a review of existing toxicological data, a series of preliminary studies to identify doses to be tested (90-day studies), conducting the actual two-year bioassay, followed by several years of scoring and reviewing the tumor data by pathologists. The study results are carefully evaluated in light of many considerations beyond tumor induction, including the presence of pre-cancerous lesions, the rarity of the tumor, ability of the chemical to induce multiple tumors in a tissue, and the various organ sites where the tumors were detected.

The cancer bioassay design is commonly misunderstood as not being relevant to the human exposure situation. It uses relatively high doses of the chemical administered to groups of 50 animals per dose. If this type of statistical model is not used, then it would mean unless the size of a study included thousands of animals per

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group, a study may show a false negative – e.g. no tumors observed if exposures were at very low environmental level – and the cancer hazard could be missed. For instance, a rate of one cancer in 1,000 humans is considered to be very high. Yet, several thousands of animals would have to be included at low levels of the chemical to detect this rate of tumor induction. Instead, fewer animals are used at a higher level of exposure to the chemical to identify whether a chemical has the ability to induce a tumor in this model system. This then allows researchers to identify a cancer hazard (6). Since multiple doses of the chemical are included in each animal bioassay study, mathematical models can be developed from the data. Scientists can then extrapolate down to environmentally relevant exposures to predict tumor induction rates without having to use thousands and thousands of animals in each study.

To date, over 600 chemicals have been screened by the NTP using the rodent cancer bioassay, and about half of these chemicals have shown some evidence of carcinogenicity. The NTP has identified 49 chemicals that have clear evidence of inducing mammary gland tumors (breast tumors) (8). The International Agency for Research on Cancer (IARC), headquartered in Lyon, France, has evaluated over 950 substances (chemicals and viruses or exposure situations), and has identified about 100 human carcinogens, with over 300 additional substances or mixtures as having some evidence of carcinogenicity (9).

Several scientists have suggested, in a Commentary article published in the November 2008 issue of *Environmental Health Perspectives*, that the sensitivity of the animal cancer bioassay could be enhanced (10) by starting exposures earlier, when the animals are *in utero* (at the fetal stage), and then continue exposure throughout the lifetime of the animals, up to three years (rats typically live to about three years and mice two-and-one-half years). To date, only seven chemicals (1%) of the NTP rodent bioassays included exposure to the test chemical *in utero*. Because the developing fetus can be sensitive to the effects of hormonally active chemicals, earlier exposures to certain chemicals may be warranted. This may be important especially for identifying mammary gland carcinogens that may have the ability to "imprint" the developing mammary gland early in life, and leave it more susceptible to developing mammary cancer later in life. Carrying out animal studies beyond the two-year time point would allow identification of tumors that occur in very late life stages, even after a lifetime of exposure. The authors give two examples of chemicals that have been found to induce tumors that form late in life, the common solvent toluene, and the heavy metal cadmium.

In a February 2008 letter to the journal *Science*, Dr. James Huff, one of the founders of the NTP and the cancer bioassay program, stated, "the number of chemicals that have not yet been tested is staggering, and it becomes even more formidable when one considers mixtures of chemicals, together with the thousands of new chemicals that enter the marketplace every year" (11).

While Dr. Huff has called for more bioassays to be started each year (currently, only about five new bioassays are begun annually), the NTP is also moving to explore whether other means could be used to screen large numbers of chemicals for their toxicity. The NTP's vision and roadmap to use emerging technologies is summarized as follows:

> *"The NTP Vision for the 21st Century is to support the evolution of toxicology from a predominantly observational science at the level of disease-specific models to a predominantly predictive science focused upon a broad inclusion of target-specific, mechanism-based, biological observations. The intent of the NTP vision is to expand the scientific basis for making public health decisions on the potential toxicity of environmental agents" (12).*

The NTP first released its vision and roadmap, "A National Toxicology Program for the 21st Century," in 2004 (13). Since then, Francis Collins, the Director of the National Genome Project, George Gray, Assistant Administrator for the Office of Research and Development for the EPA, and John Bucher, Associate Director of the NTP, have expanded on this trajectory in a "Policy Forum" document written for *Science* in February 2008, including how to transform toxicology into a better tool for health protection (14). This article outlines the types of approaches that might be used, including high throughput screening (HTS) assays. Use of new approaches that can identify the genes, proteins (the workhorse of the cell), and metabolites induced or inhibited by chemical exposures are all cited for the HTS technologies (see also 15).

Data generated and collected by several federal agencies (e.g. EPA and NTP) could be linked, and relational databases developed to help interpret the data. The new data could also be tied to existing data on the

toxicology of the chemical. Still, part of this large undertaking is even prioritizing which chemicals should go through HTS, and the EPA is starting to evaluate HTS assays as tools for toxicological testing. Computational biology may also be used to yield more information on the relationship between the exposure to the chemical, the internal dose (actual dose that gets to the tissue being studied), and its toxic effect (called the pharmacodynamics).

These developments in toxicology are exciting and it is hoped that they will yield data-rich results and improve the ability to more expediently identify cancer hazards. But there are two barriers that must be overcome. First, while the HTS may generate voluminous data on tens of thousands of chemicals, interpretation of the data and adaptation of the data into a framework that can be used in cancer risk assessment will be a daunting task. Secondly, we will need to adapt HTS results into a regulatory framework to effectively use it for prevention of diseases such as cancer.

We currently heavily rely on human epidemiological data and animal cancer bioassays to assess cancer risk. Mechanistic studies and pharmacokinetics, as well as newly emerging gene-based assays, are used to support the human and animal cancer data. But these are rarely used by themselves to assess cancer risk and it is even rarer that federal agencies have used mechanistic data to regulate chemicals in consumer products or as the basis to limit exposures in the workplace. If we are able to use and take advantage of rapid screening assays, it will mean we will need a fundamental change in regulatory policy to make public health decisions based on predictive science. We ultimately need to use all of the tools available to assess cancer risk – human epidemiology, animal bioassays, and the emerging genomic-based methodologies – to apply the best science for regulatory decision-making. Abandoning any of our tools during this transition stage would be premature. Investing in ways to make public health decisions before widespread human exposure to chemicals occurs, however, is a goal that is important to support.

This article can be found on our website at:
http://envirocancer.cornell.edu/newsletter/articles/v13Approaches.cfm

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Epigenetics and Breast Cancer: Update from the Baker Institute at Cornell

By Scott A. Coonrod, Ph.D., Associate Professor, Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University

In order to reduce the incidence of breast cancer, a major goal of human breast cancer research over the last several decades has been to determine how changes in DNA sequences cause normal breast cells to become cancerous. Results from these studies suggest that less than 25% of all breast cancers are actually due to heritable gene mutations, suggesting that the majority of mammary tumors actually arise from non-genetic factors.

As it turns out, new research shows that in addition to gene mutations, cancer can also be caused by changes in the amounts of small chemical groups, or modifications, that are either directly bound to DNA or are bound to histone proteins, which provide structural support for DNA molecules. These modifications do not change the DNA sequence and thus are called epigenetic modifications, which essentially means that these groups are near the DNA molecule but are not part of DNA itself. Surprisingly, these modifications, which are produced by a diverse group of enzymes called epigenetic modifiers, can be faithfully passed on from one cell generation to the next. Therefore, like DNA, epigenetic modifications can be inherited. Importantly, these epigenetic modifications are being found to play a critical role in regulating how our genes are expressed throughout development. Further, similar to genetic mutations, epigenetic researchers have found that different types of cancers may actually be caused by changes in the levels of epigenetic modifications at critical genes that regulate cell division and/or cell death, thereby causing a normal breast epithelial cell to begin to grow much faster than it should.

With these observations in mind, a primary long-term goal of my laboratory has been to establish whether the onset of breast cancer is caused by epigenetic phenomena. More specifically, we have found that members of an enzyme family called the peptidylarginine deiminases (PADs) are produced during estrus in mammary tissues and can place a novel epigenetic modification, called citrulline, on histone molecules that are associated with genes that are normally activated by estrogen. We have found that this citrulline modification actually represses the activity of these estrogen-responsive genes and that this repressive activity may also help to slow the rapid growth of breast cells following estrogen stimulation.

Based on our ongoing studies, we believe that PADs may represent a critical line of defense that mammary tissue utilizes to destroy estrogen-responsive cells in the mammary gland that begin to grow at abnormal rates. In the future we hope that our studies will lead to the development of new assays to detect breast cancers at very early stages and to the development of new breast cancer therapies.

This article can be found on our website at:
http://envirocancer.cornell.edu/newsletter/articles/vl3Epigenetics.cfm

Report on Carcinogens (RoC) Expert Panel for Styrene

By Suzanne Snedeker, Ph.D., Associate Director of Translational Research, BCERF

I was named to serve on the National Toxicology Program's (NTP)* Report on Carcinogens *expert panel for styrene earlier this year and participated in a series of meetings this summer as part of the review on styrene. Below is background information on the* Report on Carcinogens *and my experiences serving as a panel member.

First, what is the *Report on Carcinogens*? The *Report on Carcinogens* is prepared in response to legislation under the Public Health Service Act. The report contains a list of substances that "are either known to be human carcinogens or may reasonably be anticipated to be human carcinogens, and to which a significant number of persons in the United States is exposed" (Ref. *RoC*, 11th edition, 2004). The 12th edition of the *Report on Carcinogens* is under preparation.

The expert panel for styrene was composed of international experts from diverse fields, including epidemiology, toxicology, environmental fate, chemistry, and genotoxicity. The multi-step process used in determining whether a chemical is listed in the *Report on Carcinogens* includes the nomination of the chemical, followed by a process in which the evidence of its carcinogenicity and exposure is peer reviewed by several groups of scientists. One of the first steps is the preparation of a background document that contains a summary of the available data on 1) human exposure, 2) human cancer studies, 3) studies in experimental animals, 4) absorption, distribution, metabolism, and excretion, 5) genetic damage, and 6) mechanistic data. The background document is available to the public, and the expert panel reviews the document for its adequacy, accuracy, and completeness. The panel also reads comments on the background document submitted by the public, which includes manufacturers and industry groups.

The task is daunting. The background document for styrene was over 400 pages long and comments from the public filled several binders. Panel members were also give a CD with a PDF of every reference cited (over 450) in the background document. The panel members were assigned to one or more subgroups. Each panel member submitted an individual report on his or her review of the background document. They also submitted additional citations that should be included in the background document. Panel subgroups prepared written reports that were presented in a public forum. Every expert panel member reviewed each subgroup's comments.

Expert panel members then voted on whether styrene should be listed in the *Report on Carcinogens*; the majority voted yes. The expert panel's overall recommendation was that styrene should be listed in the *Report on Carcinogens* as "reasonably anticipated to be a human carcinogen based on limited evidence of carcinogenicity in humans and sufficient evidence in animals." (Ref: http://ntp.niehs.nih.gov/files/Styrene_expert_panel_report_B_final_508.pdf)

There are many more layers of scientific review before the NTP makes its final recommendation on whether styrene will be listed in the *Report on Carcinogens*. If you would like to find out more about the process, see the NTP's *Report on Carcinogens* website at: http://ntp.niehs.nih.gov/index.cfm?objectid=DFAFC5A1-F1F6-975E-766CD2956416305E. This page includes links to all documents reviewed by the expert panel for styrene, as well as the panel's peer review comments on the background document, its recommendation for listing in the *Report on Carcinogens*, and its scientific justification for the listing recommendation.

It was a privilege to serve on the styrene panel. The dedication of the panel members during the review process, as well as that of the NTP's staff and others involved in the preparation of the background document, was remarkable.

This article can be found on our website at:
http://envirocancer.cornell.edu/newsletter/articles/vl3ROCStyrene.cfm

New European Education Materials on Hormonally Active Chemicals and Breast Cancer Risk

The Chemicals Health Monitor Project, based in Brussels, Belgium, released a set of educational materials addressing breast cancer last spring.

MATERIALS AVAILABLE

Breast cancer and exposure to hormonally active chemicals: An appraisal of the scientific evidence

This report reviews the scientific evidence that certain chemicals may be implicated in breast cancer, focusing on the role of hormone-disrupting chemicals. Early life and multiple exposures receive particular attention. Dr. Andreas Kortenkamp of the University of London authored the report, and peer reviewers include Dr. Julia Brody, Executive Director of the Silent Spring Institute in Newton, Massachusetts. Kortenkamp states in the report, "...in view of the proven natural and therapeutically used oestrogens, it is biologically plausible that less potent hormonally active chemicals may also contribute to risks...." He goes on to conclude, "preventative action should be based on evidence available from experimental laboratory studies, and should not wait for the outcome of human epidemiological studies because confirmatory data from epidemiological studies will take decades to materialise." The report is fully referenced and available in English only at this time.

Factors influencing the risk of breast cancer – established and emerging

This briefing, also fully referenced, was designed as a plain-language overview of known and hypothesized breast cancer risk factors. It contains two sections, one on established risk factors and the second addressing "the current thinking regarding the involvement of certain chemical exposures in breast cancer, and in particular, the concerns about man-made chemicals which mimic the female hormone oestrogen." As of this writing, the briefing is available in English, Spanish, French, Italian, Russian, and German.

Breast Cancer: Preventing the preventable

This tri-fold brochure briefly summarizes the evidence that hormonally active chemicals may be implicated in breast cancer, and serves as a 'teaser' for the two reports described above. It includes six steps addressing what to do to minimize exposure and also emphasizes the policy actions needed for widespread reduction in exposures to hormonally active chemicals. As of this writing, the brochure is available in English, Spanish, French, Italian, Russian, and German.

Portfolio of papers that highlight how chemical exposures may be implicated in breast cancer

From the publicity materials: "The portfolio is a selection of peer-reviewed, published papers presenting the scientific case for chemical exposures playing a role in breast cancer. (It)... includes two principal strands of compelling research.

- Firstly, large ongoing epidemiological studies and other epidemiological studies suggesting an association between certain chemical exposures and breast cancer that have not been contradicted by other studies.
- Secondly, papers illustrating demonstrable changes in mammary tissue due to low level *in utero* exposures to certain chemicals in experimental animals."

The portfolio is intended to provide a useful resource for "clinicians, scientists, breast cancer charities, and other health professionals." Gwynne Lyons of CHEM Trust, a charitable organization in the United Kingdom, compiled the report for the Health and Environment Alliance (HEAL). The Chemicals Health Monitor Project was launched by HEAL in collaboration with partner European organizations in March 2007.

All four publications can be downloaded at http://chemicalshealthmonitor.org/spip.php?rubrique100

This article can be found on our website at:
http://envirocancer.cornell.edu/newsletter/articles/v13ActiveChem.cfm

Reaching Out to Emergency Responders: In Person, on the Web, and in Print

By Suzanne Snedeker, Ph.D., Associate Director for Translational Research, BCERF

Dr. Suzanne Snedeker addressing women firefighters in Montour Falls.

The *BCERF Alert for Women Firefighters* gives emergency responders information on chemical exposures encountered in all phases of firefighting, from fighting house fires and brush fires, to inspection activities long after a fire has been extinguished. Many of the chemicals generated in a fire may increase the risk of breast cancer. Most have been identified as cancer hazards by the National Toxicology Program. These include chemicals released from smoldering polyurethane foam found in upholstery and mattresses, and benzene released from vinyl shower curtains and plastic plumbing. The *BCERF Alert* stresses the importance of wearing Self-Contained Breathing Apparatus (SCBA) from the moment of arrival at a fire scene until departure from the scene, to protect emergency responders from these chemical exposures.

In Person

We were invited by the Fire Service Women of New York State (NYS) to conduct two workshops for women firefighters at the Fire Science Academy in Montour Falls, NY. BCERF staff Chris Batman-Mize, Outreach Coordinator for this project, Nellie Brown, Director of Workplace Health and Safety Programs, ILR Extension, and I conducted the workshops on September 20, 2008. The workshops focused on three areas: understanding how breast cancer occurs, illustrating how chemicals can be generated from fires through thermal decomposition, and the importance of wearing SCBA to protect against inhaling chemicals generated during fires that can still be present long after fires are put out.

The women firefighters attending the workshops discussed the challenges they face in protecting themselves. Volunteer firefighter departments are often challenged by economics. Limited funding may mean not having the ability to provide properly fitting protective breathing apparatus to all personnel at the fire site. One size does not fit all. Fortunately, the culture of fighting fires has changed from accepting going into a fire without protective gear, to supporting being in full "turn out" gear that includes protective clothing and the proper respiratory protection. We are finding that many firefighters are also emergency medical technicians (EMTs), especially in rural areas. We are excited to partner with them to extend our outreach and brochure distribution to other emergency responders.

To learn more about the Fire Service Women of NYS, visit their website at: http://www.fswnys.org/.

On the Web

The *BCERF Alert* is now available as a downloadable brochure and also online with full references in both English and Spanish:

- Full-color brochure in English (PDF format, requires Acrobat Reader) http://envirocancer.cornell.edu/learning/alert/fire08.pdf
- HTML English http://envirocancer.cornell.edu/learning/alert/fire08.cfm
- HTML Spanish (Español) http://envirocancer.cornell.edu/learning/alert/fire08_espanol.cfm

In Print

We are now in the third printing of the *BCERF Alert for Women Firefighters* brochure. We have

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Fall Forum at Stony Brook University on Long Island: Regional Activity and Outreach to Young Women

On Monday, November 3, 2008, BCERF returned to Long Island to host its Fall Regional Cancer and Environment Forum at Stony Brook University. Meeting in the beautiful Charles B. Wang Center, we offered a new program schedule, starting in the afternoon and including an evening program with dinner, to help accommodate high school students and their families. We particularly sought young women's participation in our effort to share and hear reactions to our Estrogen Connection project. We thank Karen Miller of the Huntington Breast Cancer Action Coalition and Laura Weinberg of the Great Neck Breast Cancer Coalition for their enthusiasm and support in planning and publicizing this program.

Contaminants Emerging in Our Water: Don't We Have Enough to Worry About?

Dr. Henry J. Bokuniewicz, a Professor of oceanography at the Marine Sciences Research Center in the School of Marine and Atmospheric Sciences at Stony Brook University also serves as Director of the University's Long Island Groundwater Research Institute. We invited him to speak on reports of emerging contaminants, particularly pharmaceuticals, in water supplies. Dr. Bokuniewicz suggested a perspective that recognizes that there is "contamination all around us." He cited the 2002 US Geological Survey (USGS) report on US streams containing pharmaceuticals and personal care products. Despite the term "emerging contaminants" becoming a recognized way of describing these contaminants, most of them are not new. "Emerging" refers rather to our increased ability to detect them, at more and more minute levels. We can detect parts per trillion or even quadrillion, and, Dr. Bokuniewicz explained, can distinguish compounds down to one electron in some cases. He also cited the "explosion of pharmaceuticals," with prescription drug use going up and percentages seven times the rate of population growth. The Associated Press report this past year alerted the country to pharmaceuticals in the water supplies of major metropolitan areas (see also *Ribbon* article in the Volume 13, Number 2, Spring 2008 issue, "Following the News on Pharmaceuticals in Drinking Water," or online at http://envirocancer.cornell.edu/Newsletter/articles/v13DrinkingWater.cfm).

Dr. Bokuniewicz used caffeine as a case study for some of the perspectives he wanted to share. The USGS found 100 parts per trillion of caffeine on average in their samples. Caffeine "comes right through" sewage treatment plants, which are not designed to remove this nor any of the other chemicals discussed. Dr. Bokuniewicz provided examples of local Long Island work exploring these issues, such as that of Bruce Brownawell and Mark Benotti, whose samples found levels of caffeine in treated water slightly lower but similar to those that the USGS found.

Dr. Bokuniewicz provided very helpful technical information about the Long Island aquifers, which supply all of the public drinking water. Benotti analyzed samples from one of the main aquifers on Long Island and found some of the compounds at levels as high as 67 parts per trillion, but not in many samples. Dr. Bokuniewicz explained that this may "represent degradation"; that the chemicals "didn't survive the 50-year trip through the aquifer."

Dr. Bokuniewicz suggested a comparison of a therapeutic dose to these amounts found in water, but also pointed out that these are compounds that are designed to work at very low levels. He reviewed some of the data on changed sex in fish populations, but also commented that fish "change their sex easily." Nevertheless, he said that the ecological impact is not to be dismissed lightly. Dr. Bokuniewicz's perspective was that there is "little we can do about medications not absorbed by the waste stream," but that we must make it a point to properly dispose of all expired and unused prescription and over-the-counter drugs by, for example, taking them to a local hazardous waste collection event, or if none exist, disposing of them in household trash rather than flushing or pouring down the drain. See the handout from the NYS Department

Left to right, top row: Karen Miller, Huntington Breast Cancer Action Coalition; Laura Weinberg, Great Neck Breast Cancer Coalition; Elsa Ford, Brentwood/Bayshore Breast Cancer Coalition; Maria Gonzalez, Brentwood/Bayshore Breast Cancer Coalition; Stephen Boese, Learning Disabilities Association of New York State; Suzanne Snedeker, BCERF; Colette Thaw, Great Neck Breast Cancer Coalition; Mary Joan Shea, Huntington Breast Cancer Action Coalition. Center: Miriam Goodman, Huntington Breast Cancer Action Coalition. Kneeling: Mallika Kumar and Karolina Kworoniecka, Great Neck South High School.

of Environmental Conservation from which Dr. Bokuniewicz adapted his own handout at the Forum, available at: http://www.dec.ny.gov/chemical/45083.html.

Children's Environmental Health Centers of Excellence: Partnerships Making a Difference

This talk was given by two collaborators on a very exciting project. Stephen Boese, the Executive Director of the Learning Disabilities Association of New York State (LDANYS), and Karen Joy Miller, the President of Huntington Breast Cancer Action Coalition (HBCAC) and the founder of Prevention Is The Cure (PITC), described their respective organizations and their mission of working together.

Boese began by outlining HBCAC and LDANYS. HBCAC was founded over 20 years ago on Long Island to raise visibility of the breast cancer epidemic, provide forums to encourage open dialogue, and to create opportunities for transdisciplinary research. Their strong focus on prevention evolved into the PITC campaign. LDANYS is affiliated with LDA of America, a nationally recognized children's environmental health initiative, and is a statewide not-for-profit membership association of parents, professionals, and service organizations. LDANYS is concerned with the increases in learning and developmental disabilities – one in six children is affected – and Boese

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says that "a modest investment in prevention can reap huge benefits for the state." Both organizations are acutely interested in the growing body of research on exposure to environmental toxins during critical periods of development increasing the risk of both cancers and neurological problems.

Boese described his and Miller's history of participating in a working group, organized by Dr. Philip Landrigan of the Mount Sinai School of Medicine, developing and promoting the concept of the Children's Environmental Health Center of Excellence. The many objectives of the Centers include evaluating, diagnosing, and treating children with diseases of environmental origin, along with various community education, support, and outreach objectives. Boese and Miller working together on the Centers corresponds well with the joint mission of HBCAC and LDANYS: promoting preventive and precautionary ideals, providing science-based information in understandable formats to those with limited science background, promoting informed decision making, influencing policy that reduces exposure to environmental toxins, and promoting community wellness. Boese described progress made to date, including the development of advisory boards and ensuring a statewide commitment. He informed the group of the toll-free number available for speaking with an environmental health expert: 1-866-265-6201.

Karen Miller shared the wonderful educational materials that they are developing for the Center, which include a coloring book, brochure, reference cards, and a game addressing lead contamination, endocrine disruptors, air pollution, and pesticides (or L.E.A.P., resulting in the project slogan, "Look before you LEAP"). Through this game children might learn, for example, to avoid bus fumes and not to put plastic toys in their mouths. She solicited the group's feedback on the resources, and explained the approach used for their content and features. Reference cards are packed with information on what to avoid and what to choose in order to reduce exposures in the home, community, and broader environment, and in one's lifestyle and diet. Even so, she explained, it's always a challenge to determine the simplest wording and most important information.

For more information, see their websites: www.ldanys.org and www.hbcac.org.

Genetic variation, environmental factors, and breast cancer risk

Dr. Mia Gaudet, Assistant Attending Epidemiologist at Memorial Sloan-Kettering Cancer Center in New York, provided an extremely useful background talk focusing on genetics and environment in breast cancer risk. She has co-authored several papers in this area, including the paper that investigated the relationship of breast cancer risk to exposure to polyaromatic hydrocarbons (PAHs), using the Long Island Breast Cancer Study Project data. In this talk, she provided background statistics, an overview of breast cancer risk factors, an explanation of the interaction of non-genetic and genetic factors, and directions for future research. She very much shares BCERF's enthusiasm, saying, "it is an exciting time for the translation of research for the public."

Dr. Gaudet provided the estimates for US breast cancer incidence for 2008: 125 new cases per 100,000 women, totaling 178,000 cases. New York State has the 13th highest state rate in the nation at 131 cases per 100,000, or 13,800 new cases this year. She described how incidence rose in the 80s, leveled off a little in the 90s, and is decreasing in the 00s. The decrease is found in those over the age of 50, with the decline in the use of hormone replacement therapy (HRT) largely responsible. Women are at risk of breast cancer throughout adulthood: from age 25 to 55 risk increases sharply, then increase occurs at a slower rate, and by age 80 there is a decline in breast cancer incidence. Incidence in African American women is higher in younger women than it is in white women, and lower later. Mortality is higher in African American than in white women at every age group.

Dr. Gaudet defined the term risk factor, emphasizing that risk factors are based on studies of populations, and that it is impossible to give an individual woman her risk of breast cancer. Importantly, having any given risk factor does not guarantee breast cancer in an individual. Risk factors are based on estimates and provide a guide of who is at higher or lower risk. Breast cancer has no "smoking gun" like lung cancer, but rather has a myriad of factors. Most of these weakly increase risk, and a few known factors strongly increase risk. Family history is one of the strongest risk factors: two or more first-degree relatives having had breast cancer increases one's risk four-fold; one first-degree relative increases risks two- to three-fold. Family history is an indicator of shared genetics *and* environment.

Dr. Gaudet provided a brief lesson in "Genetics 101" before moving on to explain what science has accomplished in breast cancer genetics. An important graphic in her presentation showed that "genetic factors vary by frequency of variation and magnitude of breast cancer risk." Eight genes have been verified to

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increase breast cancer risk, and there likely are additional genetic variations related to risk. Early work in the field located the rare genetic mutations that cause a high risk of breast cancer, BRCA 1 and 2. Other known variations carry moderate risk and are somewhat rare, and now, Dr. Gaudet explained, "work is focused on the end of the curve that is common/low risk," and on African American women.

Questions of the identification of genetically susceptible individuals are becoming more and more important. Private companies are offering expensive testing. Dr. Gaudet emphasized that there is no government oversight of these tests and that there is uncertainty and concern about this among physicians and scientists. She continued in her talk to state that, "genetic variation is only a small fraction of the story," and that "your genetic variation and environment act in concert." She described some of the gene-environment interaction research underway, posing questions such as these: "How does the known genetic variation related to breast cancer risk alter the effect of environmental factors?" "Are early interventions of the environment possible to lower risk of genetically susceptible women?" Dr. Gaudet also outlined important research questions that are not yet being addressed and urged women to consider joining breast cancer research studies, particularly those with biological sample collection.

The Estrogen Connection: Estrogenic Chemicals in Plastics, Personal Care Products, and Electronics

Dr. Suzanne Snedeker, BCERF's Associate Director for Translational Research, provided an updated version of her "Estrogen Connection" talk that she gave at BCERF's Spring Forum in Rochester (summary in Volume 13, Number 3, Summer 2008 issue of *The Ribbon* or online at http://envirocancer.cornell.edu/Newsletter/articles/v13Spring08.cfm). For this Forum, the talk bridged to an evening dinner program, to which younger women were especially invited to view and share their thoughts about the three videos produced as part of the Estrogen Connection project. The videos address environmental estrogens in everyday products including plastics, cosmetics, detergents, and electronics.

An update to the earlier version of the talk included the recent federal agency activities and controversies surrounding bisphenol-A (BPA), one of the chemicals of concern in the project, that can leach out of canned foods, polycarbonate bottles, and dental sealants. Dr. Snedeker summed up new developments this way: the National Toxicology Program (NTP) recently reviewed the developmental and reproductive effects of BPA and regards the concern for the mammary gland as "minimal." Meanwhile, the Food and Drug Administration (FDA) had released a report stating that the levels of BPA in the US food supply are not of concern. However, there is a controversy ensuing as to whether members of the FDA panel have conflicts of interest that may not have allowed unbiased contribution to the FDA's review. Dr. Snedeker also mentioned that a scientific peer review of FDA's draft assessment of BPA has recently been released. They cite problems in the FDA report, calling for a reassessment. In addition, the FDA has recently requested more information on medical devices that may contain and leach BPA. (This talk was videotaped and will be featured on CornellCast in the near future. CornellCast – found at http://www.cornell.edu/video/ – hosts video and audio recordings of lectures, discussions, and performances featuring members of the Cornell community and guests.)

Following the lecture and over dinner, Heather Stone, Program Manager for the Estrogen Connection project, and Dr. Snedeker then provided an informal setting to view the videos and collect reactions and action strategy ideas from participants. They brought along many examples of products and labels to examine with regard to their possibilities for containing estrogenic chemicals and four handouts overviewing the basics on avoiding estrogenic chemicals in makeup, plastics, canned food, laundry detergent, and electronics. The high school student participants provided a wealth of valuable input on strategies for reaching their peers and practical approaches for reducing exposures among younger people. They provided many suggestions on the next step in the Estrogen Connection project: developing credit-card-sized market guides on ways to avoid environmental estrogens in cosmetics, as well as "DOs" and "DON'Ts" for choosing alternatives to avoid environmental estrogens in plastics, household detergents, and electronics.

This article can be found on our website at: http://envirocancer.cornell.edu/newsletter/articles/vl3ForumFall08.cfm

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http://envirocancer.cornell.edu/newsletter/pdf/vl3i4.pdf

Reaching Out to Emergency Responders: In Person, on the Web, and in Print *continued from page 7*

distributed over 10,000 copies to firefighters throughout NYS and have just ordered 5,000 more copies to meet the demand for distribution to other emergency responders, including EMTs and police. Our special thanks to Cheryl Hine, Fire Protection Specialist, and Chief Rocky Jones, for all of their help disseminating the brochure to firefighters across NYS. To those of you that would like to distribute the brochure in your community, you can order print copies of the *BCERF Alert* brochure by contacting Chris Batman-Mize, Outreach Coordinator, at (607) 253-3805 or cgb62@cornell.edu.

This article can be found on our website at:
http://envirocancer.cornell.edu/newsletter/articles/vl3Emergency.cfm

Chris Batman-Mize, MSW, joined BCERF in September as Outreach Coordinator. Chris is providing outreach to New York State female firefighters in an effort to supply information about the various carcinogenic chemicals they come into contact with on a regular basis through their invaluable service work to the communities they call home. She has worked in numerous social work roles including child abuse investigator, probation officer, substance abuse counselor, and educational counselor. Most recently Chris worked with organizations with a focus on social justice issues regarding worker's rights and benefits. She is enjoying connecting with the female firefighter population and providing information that could help them protect their health and safety.

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