

Using the Domestic Hen as a Model for Studying Ovarian Cancer

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Since BCERF joined Cornell's College of Veterinary Medicine in 2004, readers of this publication, visitors to our web site, and participants in the Regional Cancer and Environment Forums are hopefully becoming more aware of the ways in which the study of spontaneously arising cancers in wildlife and domesticated animals are increasing our understanding of human cancer. Below we highlight some very promising research, taking place within Cornell's Department of Animal Science, addressing ovarian cancer. Collaborations are currently underway between this lab and investigators at Roswell Park Cancer Institute.

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Background on human ovarian cancer

Ovarian cancer is the fifth leading cause of death from all cancers among women and it is a leading cause of gynecological malignancies. It is estimated that nearly 25,000 new cases of ovarian cancer will be diagnosed this year and more than half that many women die from this cancer each year (NCI, http://seer.cancer.gov/csr/1975_2002/results_single/sect_01_table.01.pdf). Ovarian cancer occurs with an approximate incidence of 1 out of 57 women. The estimated percentage of survival to five years is strongly influenced by the stage at which the cancer is diagnosed. The five-year survival for early stage tumors (stages I and II) is approximately 80-90 percent while that for later stage tumors (stages III and IV) is much less at 5-40 percent (Chi and Hoskins, 2000). Unfortunately, a large study (Pettersson et al., 1991) has indicated that a majority (approximately 65 percent) of tumors are not discovered until stages III or IV. This is likely related to the few symptoms experienced by women with ovarian cancer at early stages.

Ovarian tumors are believed to arise from several sites on the ovary. Most cases of ovarian cancer are termed "epithelial" and are believed to arise from the surface epithelium, or, the single layer of tissue covering the surface of the ovary. Seven to ten percent of cases are termed non-epithelial and arise from the germ cells or stroma of the ovary. Family history, including genetic mutations such as in the BRCA genes (Auersperg et al.,

2001), accounts for only about five percent of cases, while most cases are sporadic. The strongest risk factor for ovarian cancer is age, where the risk is low for young women and increases throughout reproductive life to plateau at about age 55 (Banks, 2000).

There are other factors that have been associated with alteration of risk for ovarian cancer. An important factor is pregnancy. A full-term pregnancy is associated with a risk reduction of approximately 40 percent (Banks, 2000). Moreover, each subsequent pregnancy confers an additional 10-15 percent reduction of risk. Use of the oral contraceptive pill for three years is associated with a 40 percent reduction of risk for ovarian cancer. Each additional year of use reduces the risk by five to ten percent (reviewed by Banks, 2000). Fathalla (1971) proposed that frequent ovulation contributes to increased risk for ovarian cancer. His hypothesis was termed "the incessant ovulation hypothesis." He proposed that repeated rupture and repair of the ovarian surface epithelium provides the opportunity for genetic aberrations. The single cell layer surrounding the ovary must be repaired after each ovulation. It is possible that areas of the surface epithelium become detached from the surface and become part of so-called inclusion cysts (reviewed by Auersperg, 2001). These "inclusion bodies" may provide an abnormal environment for the epithelial cells and are implicated in the origin of ovarian cancer. One study has indicated that women with ovarian cancer have been observed to have an increased incidence of

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inclusion cysts in the other ovary (Salazar et al., 1996). The incessant ovulation hypothesis is supported by the epidemiological data relating to pregnancy and oral contraceptive use. It is also possible that endocrine factors are involved in the genesis or progression of ovarian cancer.

Why is the domestic hen a good model for human ovarian cancer?

Most animals do not spontaneously develop ovarian cancer and this has made the study of the tumors difficult (MacLachlan, 1987). A variety of rodent models (Orsulic et al., 2002; Connolly et al., 2003) have been utilized as well as cell lines from human tumors (Langdon and Lawrie, 2000) and normal ovarian surface epithelial cells (Auersperg and Maines-Bandiera, 2000). These models have been useful but study of the origin and development of early tumors is limited. Generally, among domestic animals, the desired state is pregnancy and/or lactation and most wild animals are pregnant, lactating or seasonally sexually inactive. These physiological states are not associated with frequent ovulation or ovarian cancer. The one model that does exhibit ovarian cancer with a high incidence is the domestic hen (Campbell, 1951; Wilson, 1958; Fredrickson, 1987). This observation, along with the fact that the hen is a persistent ovulator, makes the hen a good model for the disease. Many commercial strains of laying hens ovulate almost daily through one or two years of egg production. This is similar to the pattern experienced by many contemporary women who ovulate monthly for 10-20 years, have one or two closely spaced pregnancies, and then resume ovulation for 10-20 more years.

Fredrickson (1987) conducted a three and one half-year study in which he evaluated the incidence of

reproductive tract tumors in 466 White Leghorn hens ranging from two to seven years of age. He found that 24 percent of all hens developed age-dependent malignant ovarian tumors. He also observed that these tumors were uncommon in hens less than two years of age and that ovulation rate was not associated with incidence. Hormonal imbalance did not appear to be a factor although the hormone levels were very variable.

Findings from the research analyzing characteristics of the chicken ovarian tumors suggest several features in common with the most typical type found in women. For example, one study has shown that hen ovarian tumors are cross-reactive with many antibodies used to detect several antigens in human ovarian cancers (Rodriguez-Burford et al., 2001). In our research we found that progesterone receptor is expressed in the cells lining the glands of hen ovarian cancers similar to women. We have also found that hen ovarian cancers are positive for expression of the oviductal protein, ovalbumin (Giles et al., 2004). The finding of ovalbumin expression suggested that hen ovarian cancer was similar to the most common type of ovarian cancer found in women which has oviduct-like characteristics.

Variations in ovarian cancer rates between different genetic strains

Studies have shown genetic differences in susceptibility to ovarian tumors among selected lines of hens with one flock having about a five-fold greater tumor incidence than another flock (Fredrickson, 1987). Here at Cornell, two closed strains of White Leghorn hens (Cornell C and K) have been maintained since 1935 and 1936, respectively (Cole and Hutt, 1973). These strains were derived from a

Ovarian cancer and immunotherapy: Dr. Kunle Odunsi's work at Roswell Park Cancer Institute

There is growing evidence for a link between the immune system and the control of cancer. Support for this link comes from observations that the immune system can protect against the development of spontaneous and chemically induced tumors in laboratory research. Further, a large number of targets for immune recognition of human cancer have been identified and characterized. Results of a large study published in *Proceedings of the National Academy of Sciences* (Sato et al., 2005) provide further evidence for the role of the immune system in controlling cancer. The research team, led by Dr. Kunle Odunsi, Associate Professor, Department of Gynecologic Oncology at Roswell Park Cancer Institute (RPCI), examined the precise location of subpopulations of immune cells [tumor infiltrating lymphocytes (TILs)] in 117 RPCI patients with epithelial ovarian cancer (EOC) to determine the interrelationship between subpopulations of TILs and overall survival. The results indicate that the presence of high numbers of killer immune cells (CD8+ TILs) is associated with favorable prognosis in ovarian cancer patients.

Based on these observations, Dr. Odunsi is currently conducting studies aimed at inducing or augmenting CD8+ immune cells, in order to improve outcome for ovarian cancer patients. The studies are testing the safety and effectiveness of a vaccine treatment derived from a protein, called NY-ESO-1, as immunotherapy for patients with ovarian, fallopian tube or primary peritoneal cancer.

This work is supported by a Cancer Vaccine Collaborative Grant from the Cancer Research Institute (CRI) and the Ludwig Institute for Cancer Research, and an Anna-Marie Kellen Clinical Investigator Award from the CRI to Dr. Kunle Odunsi.

similar genetic background and selected for disease resistance combined with selection for other important production traits. In recent years, they have been maintained with random breeding. Cole and Hutt (1973) observed differences in rate of reproductive cancer between the strains. In two separate studies, we found that two year old C strain of hens had a significantly ($p < 0.02$) increased rate of ovarian cancer compared to two year old hens of the K strain. In addition, we found that C strain hens had an overall significantly higher incidence ($p < 0.05$) of ovarian cancer compared to the K strain hens. A genetic association in human epithelial ovarian cancer is well documented; however, this accounts for only a small proportion of those with the cancer. Most cases of epithelial ovarian cancers occur in women with no family history of the disease.

The main thrust of our laboratory is reproductive endocrinology and therefore, our interest relates to possible hormonal correlates of ovarian cancer. Estrogen-only replacement therapy has been indicated as a risk factor for ovarian cancer (Lacey et al., 2002) and this has led us to examine plasma estradiol in our two strains of hens. Preliminary analysis showed that basal plasma estradiol was elevated in the C strain of hens as compared to the K strain hens (Davignon and Johnson, unpublished). Furthermore, plasma estradiol was higher at all ages examined (one, two and three years of age) in C strain hens as compared to K strain hens, suggesting that the C strain may be exposed to chronic, higher levels of estradiol. Egg production, as a reflection of ovulation rate, and plasma progesterone, were not different between the strains. The biological basis for the difference in plasma estradiol may be due to a significantly larger ovary in C strain hens ($p < 0.02$), with the result of more small follicles capable of estradiol production (Robinson and Etches, 1986).

Another hormone that has been implicated in the development or progression of ovarian tumors is the gonadal hormone inhibin. Matzuk and co-workers (Matzuk et al., 1992) have demonstrated that inhibin may be a tumor suppressor factor in mice. We hypothesized that inhibin may be expressed at a lower level in the hens more prone to ovarian cancer (C strain) as compared to the K strain hens. For this reason, we examined inhibin in the plasma and messenger RNA expression in the granulosa layer of the C and K strain hens. In two separate trials, plasma immunoreactive inhibin was significantly lower ($P < 0.02$ and $P < 0.05$ for trial 1 and 2, respectively) in C strain hens compared to K strain hens. We found that inhibin messenger RNA was expressed at a lower level ($P < 0.02$) in the C strain as compared to the K strain. The role of inhibin in ovarian cancer in the hen warrants further study.

Prostaglandins have been implicated in a variety of cancers and the enzymes responsible for their production (COX-1 and COX-2) have been targeted as potential therapies. In many tumors such as colon and lung, COX-2 has been implicated. Recent studies suggest that COX-1 may be selectively increased in human ovarian cancer (Gupta, et al., 2003) and this has also been found to be the case in the hen (Urlick and Johnson, in press). These findings may implicate COX-1 inhibitors (such as non-steroidal anti-inflammatory drugs) as suitable targets for the prevention or treatment of ovarian cancer.

In summary

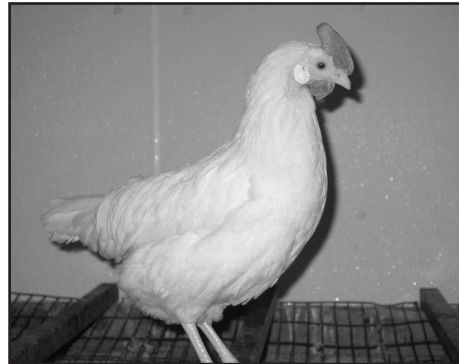
The etiology of ovarian cancer in humans is poorly understood, in part from a lack of animal models. One animal that has been shown to spontaneously develop the disease is the domestic hen. Similar to women, the incidence of ovarian tumors in hens increases with age and exhibits metastases to similar abdominal tissues. A genetic component has been shown in hens with the incidence influenced by strain. Ovarian tumors are more common in the C strain of White Leghorn hens compared to the K strain. Interestingly, C strain hens also have greater plasma estradiol levels and larger ovaries than K strain hens. Furthermore, blood plasma inhibin levels were reduced for C strain hens compared to K strain hens. Finally, ovarian tumors in hens show increased expression of COX-1 similar to humans, suggesting a possible therapy and further validating the hen as a good model for humans. In conclusion, analysis of genetic differences in hens and the relationship of these factors to the incidence of ovarian cancer may be very helpful in learning more about the etiology of the disease in the chicken and hopefully, can be applied to this very lethal disease in humans.

Acknowledgments

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The domestic hen, a persistent ovulator, producing an egg almost every day.

Ovarian Carcinogens Identified by the National Toxicology Program (NTP)

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

Breast cancer and ovarian cancer share many similarities. The incidence of both cancers increases as women age, and a relatively small percentage of ovarian and breast cancer cases are explained by inherited genes such as the BRCA genes. As with breast cancer, there is an increased interest in identifying preventable causes of ovarian cancer. Because ovarian cancer has so few symptoms, it has been relatively difficult to study, and very few epidemiological studies have been able to address whether environmental factors play a role in ovarian cancer. Most of our data identifying chemicals that may increase the risk of ovarian cancer has come from animal modeling studies. And, many of the chemicals identified as inducing ovarian tumors have also been found to induce mammary tumors in the National Toxicology Program's (NTP) cancer bioassay studies. The table on the facing page lists the ten substances (environmental chemicals as well as pharmaceutical drugs) that the NTP has identified as having "clear evidence" of causing ovarian tumors in female mice. Five of the ten substances also induce mammary tumors in one or more species of laboratory animals. This illustrates the importance of using a variety of approaches and models to understand both the biology of cancer (for example, see accompanying article *Using the Domestic Hen as a Model for Studying Ovarian Cancer*) as well as other models to identify preventable cancer hazards. It also illustrates that cancers hold some factors affecting etiology in common. 

References

- Dennis, M.J., Howarth, N., Key, P.E., Pointer, M., Massey, R.C. (1989). Investigation of ethyl carbamate levels in some fermented foods and alcoholic beverages. *Food Additives and Contaminants* 6(3), 383-389.
- DHHS (2004). Report on Carcinogens, Eleventh edition, Carcinogen Profiles, 2004, (Research Triangle Park, NC, U.S. Dept. of Health and Human Services, Public Health Service and National Toxicology Program).
- Dunnick, J.K and Hailey, J.R. (1996). Phenolphthalein exposure causes multiple carcinogenic effects in experimental model systems. *Cancer Research* 56, 4922-4926.
- FDA (2006). Drugs@FDA; approved prescription, over-the-counter and discontinued drugs (Food and Drug Administration) searchable database accessible at <http://www.accessdata.fda.gov/scripts/cder/drugsatfda/>, cited April 13, 2006.
- FDA (2006). Database of Approved Animal Drug Products (Food and Drug Administration Center for Veterinary Medicine, VMRCVM Drug Information Lab) on line database available at <http://dil.vetmed.vt.edu/>, cited 4/24/06.
- Hiraku, Y., Sekine, A., Nabeshi, H., Midorikawa, K., Murata, M., Kumagia, Y., and Kawanishi, S. (2004). Mechanism of carcinogenesis by a veterinary antimicrobial drug, nitrofurazone, via oxidative DNA damage and cell proliferation. *Cancer Letters* 215, 141-150.
- Kim, Y.K, Koh, E., Chung, H.J. and Kwon, H. (2000). Determination of ethyl carbamate in some fermented Korean foods and beverages, *Food Additives and Contaminants* 17(6), 469-475.
- National Toxicology Program's (NTP) websites (cited 4/13/06):
a. General NTP web site. <http://ntp.niehs.nih.gov/>
b. Long-term study reports and abstracts. <http://ntp.niehs.nih.gov/index.cfm?objectid=084801F0-F43F-7B74-0BE549908B5E5C1C>
c. Organ sites associated with neoplasia (cancer); searched on "ovary." <http://ntp.niehs.nih.gov/index.cfm?objectid=0723D2CE-D417-1004-8F2FFBCFE702A2B7>
- PDR, Physicians' Desk Reference (2005). 59th edition (Montvale, New Jersey, Thompson PDR).
- Plumb, D.C. (2005). *Plumb's Veterinary Drug Handbook* (5th edition) (Ames, Iowa, Blackwell Publishing).

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References

- Auersperg N., and Maines-Bandiera, S.L. (2000). Culture and characterization of human ovarian surface epithelium. In *Ovarian Cancer Methods and Protocols*. J. M. S. Bartlett, ed. (Totowa, NJ: Humana Press), pp. 169-174.
- Auersperg, N., Wong, A. S. T., Choi, K. C., Kang, S. K., and Leung, P. C. K. (2001). Ovarian surface epithelium: Biology, endocrinology, and pathology. *Endocrine Reviews* 22, 255-288.
- Banks E. (2000). The epidemiology of ovarian cancer. In *Ovarian Cancer Methods and Protocols*, J. M. S. Bartlett, ed. (Totowa, NJ: Humana Press), pp. 3-11.
- Campbell, J.G. (1951). Some unusual gonadal tumours of the fowl. *British Journal of Cancer* 5, 69-82.
- Chi and Hoskins, (2000). Primary surgical management of ovarian cancer. In *Ovarian Cancer Methods and Protocols*. J. M. S. Bartlett, ed. (Totowa, NJ: Humana Press), pp. 75-87.
- Cole, R. F., and Hutt, F.B. (1973). Selection and heterosis in Cornell white leghorns: A review, with special consideration of interstrain hybrids. *Animal Breeding Abstracts* 41,103-118.
- Connolly, D., Bao, R., Nikitin, A.Y., Stephens, K.C., Poole, T.J., Hua, X., Harris, S.S., Vanderhyden, B.C., and Hamilton. T.C. (2003). Female mice chimeric for expression of the simian virus 40 Tag under control of the MISIR promoter develop epithelial ovarian cancer. *Cancer Research* 63, 1389-1397.
- Fathalla M.F. (1971). Incessant ovulation-a factor in ovarian neoplasia? *Lancet* 2, 163.
- Fredrickson, T.N. (1987). Ovarian tumors of the hen. *Environmental Health Perspectives* 73, 35-51.
- Giles, J. R., Shivaprasad, H. L., and Johnson, P. A. (2004). Ovarian tumor expression of an oviductal protein in the hen: a model for human serous ovarian adenocarcinoma. *Gynecologic Oncology* 95, 530-533.

Chemical Name (NTP Technical Report #)	Chemical's Major Uses
Benzene* (TR 289)	Used in the synthesis or production styrene plastics, synthetic styrene rubber, nylon, detergents (alkylbenzene detergents), drugs, dyes, and insecticides. Formerly widely used as a solvent; many of these uses have been replaced by less toxic chemicals. Benzene is present in non-leaded gasoline at 1-2% by volume.
1,3-butadiene* (TR 288)	Used in production of synthetic rubber and latex adhesives. Detected in cigarette smoke, motor vehicle exhaust, and gasoline.
N-methylolacrylamide (TR 352)	Acts as a cross-linking agent used in adhesives, resins, textiles, and latex film.
5-nitroacenaphthene* (TR 118)	No commercial use reported in the U.S. Has been used Japan for the synthesis of naphthalamide dyes used as whitening agents in laundry detergents and in paper products.
Urethane* (TR 510) also called Ethyl Carbamate	Found in foods treated with dimethyl pyrocarbonate (beer, wine, orange juice, and some soft drinks). Also detected in fermented foods (yogurt, soy sauce, kimchi [fermented cabbage], and olives) and beverages (whiskey, fruit brandy, sherry, port, wine, and beer). Used in the production of pesticides, fumigants, various pharmaceuticals, and cosmetics (no information on specific products was located). Used in treating fabrics to give them "wash and wear" permanent press qualities. Formerly used as a drug to treat human cancers, varicose veins, and topically to treat bacterial infections. Formerly used in veterinary medicine as an anesthetic. Found as a contaminant in certain anticonvulsant drugs (trimethadione and paramethadione) used to treat epilepsy.
4-vinylcyclohexene (TR 303)	Released in off-gassing from rubber tire curing.
4-vinyl-1-cyclohexane diepoxide (TR 362)	Used commercially in epoxy resins used in coatings and adhesives, and also in the production of other diepoxides and epoxy resins.

Chemical Name (NTP #)	Pharmaceutical's Major Uses
Nitrofurantoin (TR 341)	Used as a drug in the treatment of certain types of bacterial urinary tract infections in human and veterinary medicine. Currently available by prescription.
Nitrofurazone* (TR 337)	Used as a drug in human and veterinary medicine, primarily as a topical anti-bacterial to treat skin infections and to a lesser extent orally to treat African trypanosomiasis (a sleeping sickness). Currently available by prescription as a topical ointment.
Phenolphthalein (TR 465)	Used in over-the-counter laxative preparations for 91 years (since 1906); FDA prohibited its use in laxatives in 1997 based on the NTP cancer bioassay results. Also used in the laboratory as an acid-base indicator.
Urethane* (TR 510)	See notes above for use in veterinary practice as an anesthetic and in human medicine, as a contaminant of certain anti-convulsive drugs.

*These five chemicals also induced benign and/or cancerous mammary tumors in one or more rodent species in the NTP cancer bioassay.

Compiled by Suzanne Snedeker, Ph.D. and Katarzyna (Kasia) Fertala, undergraduate research assistant.

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Gupta R.A., Tajada, L.V., Tong, B.J., Das, S.K., Morrow, J.D., Dey, S.K., and DuBois, R.N. (2003). Cyclooxygenase-1 is overexpressed and promotes angiogenic growth factor production in ovarian cancer. *Cancer Research* 63, 906-911.

Johnson, P. A., Wang, S.-Y. and Brooks, C. (1993). Characterization of a source and levels of plasma inhibin during the ovulatory cycle of the domestic hen. *Biology of Reproduction* 48, 262-267.

Lacey, J.V., Mink, P.A., Lubin, J.H., Sherman, M.E., Troisi, R., Hartge, P., Schatzkin, A., and Schairer, C. (2002). Menopausal hormone replacement therapy and risk of ovarian cancer. *JAMA* 288, 334-341.

Langdon S. P., and Lawrie, S. S. (2000). Establishment of ovarian cancer cell lines. In *Ovarian Cancer Methods and Protocols*. J. M. S. Bartlett, ed. (Totowa, NJ: Humana Press), pp.155-159.

MacLachlan N.J. (1987). Ovarian disorders in domestic animals. *Environmental Health Perspectives* 73, 27-33.

Matzuk, M.M., Finegold, M.J., Su, J.G., Hsueh, A.J., and Bradley, A. (1992). Alpha inhibin is a tumour-suppressor gene with gonadal specificity. *Nature* 360, 313-319.

Orsulic, S., Li, Y., Soslow, R.A., Vitale-Cross, L.A., Gutkind, J.S., and Varmus, H.E. (2002). Induction of ovarian cancer by defined multiple genetic changes in a mouse model system. *Cancer Cell* 1, 53-62.

Pettersson F. (1991). Annual report on the results and treatment in gynecological cancer. International Federation of Gynecology and Obstetrics. *Panorama Press AB*, vol. 21.

Rodriguez-Burford C., Barnes, M. N., Berry, W., Partridge, E. E., and Grizzle, W. E. (2001). Immunohistochemical expression of molecular markers in an avian model: A potential model for pre-clinical evaluation of agents for ovarian cancer chemoprevention. *Gynecologic Oncology* 81, 272-279.

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BCERF Staff Brief Senator Hillary Clinton

BCERF played a central role in Senator Hillary Clinton's March 3, 2006 visit to the Cornell College of Veterinary Medicine (CVM). While being connected by videoconference with several of our colleagues at Roswell Park Cancer Institute, we had the opportunity to discuss new approaches, recent findings, and emerging issues in cancer and environment research.

BCERF staff shared a roundtable with the Senator, Sprecher Institute Director Dr. Rodney Page, CVM Dean Donald Smith, Cornell President Hunter R. Rawlings, President and CEO of Cayuga Medical Center Dr. Rob Mackenzie, and several other members of the CVM community.

We presented the Senator with a packet updating her on BCERF activities, accomplishments, and feedback from the public, and Drs. Suzanne Snedeker and Carol Devine of BCERF shared information about several current BCERF projects.

Dr. Snedeker described the rationale and process of doing translational research, the basis of BCERF's public health education projects. She outlined the BCERF approach: evaluating the current scientific research and translating those evaluations into risk reduction programming, while being responsive to the current needs of individuals and groups, and tailoring all risk communication messages and resources. She illustrated this process with examples of current activities, such as the Envirocancer Connections Long Distance Learning workshops (see related article), the Teachers and Breast Cancer Risk Communication project (see Volume 11, Number 1, Winter 2006), and the Cancer Risk of Turf Grass Pesticides project. This project includes a database currently under development,

tailored to meet the needs of turf grass professionals who want accessible information on the cancer risk of over 3,000 pesticide products used on turf in NYS.

Dr. Devine described the project "Small Steps are Easier Together." This collaboration

increase the number of healthy foods offered at community events. Through small steps like these the community hopes to prevent excess weight gain among women. (This project is funded by a grant from the Cooperative State Research, Education and Extension Service of the US Department of Agriculture.)


In the same session, Senator Clinton was also able to hear about the various ways in which research at Cornell on spontaneously occurring cancers in wild and domesticated animals are increasing our understanding of



Dr. Rodney Page presents Senator Clinton with a steps log from BCERF's "Small Steps are Easier Together" project

between BCERF, Cornell Cooperative Extension of Delaware County and the communities of Stamford and Hobart, New York is testing a new environmental model of ways that communities can work together to address the critical public health issues of obesity and breast cancer risk. Currently 63% of the adult women in the pilot community signed up for teams to increase daily walking steps and to

the disease (see lead article this issue). Dr. Page informed the group that Cornell is one of only two universities to have a veterinary school working closely with a cancer center.

Senator Clinton said at a press conference later that afternoon. "I am incredibly impressed with the work that is occurring ... with the potential for breakthroughs in public health ... the work being done here is essential." 

Two Collaborative Long-Distance Learning Workshops Held in February

Margaret Carey, M.P.H., BCERF Environmental Health Educator

Ms. Carey coordinates BCERF's EnviroCancer Connections – Long-Distance Learning Programs.

BCERF was very excited to offer two long-distance learning workshops this past February in collaboration with New York State Breast Cancer Support and Education Network (NYSBCSEN). On February 3, the topic was Biomonitoring and on February 10, the topic was Endocrine Disruptors. The NYSBCSEN, with twenty-three member organizations across New York State chose both topics and worked with BCERF in the planning of the workshops.

Dr. Suzanne Snedeker, BCERF Associate Director for Translational Research, led both of these workshops from the Cornell-Ithaca campus to Cornell Cooperative Extension facilities in New York City and Albany. Most participants were able to attend both workshops, with a total of 41 individual participants. Dr. Snedeker presented several mini-talks at each workshop, each followed by lively discussions between the three viewing sites. Laura Weinberg, President of the Great Neck Breast Cancer Coalition, assisted BCERF by facilitating the session at the New York City site.

First workshop focused on Biomonitoring.

Biomonitoring is the direct measurement of chemicals or metabolites found in humans. Dr. Snedeker presented results from the Center for Disease Control and Prevention's (CDC) 'Third National Report on Human Exposure to Environmental Chemicals,' published in 2005. The study includes an assessment of exposures to 148 chemicals in a cross-section of the U.S. population. The report included the results of blood and/or urine levels across different age ranges (6-11, 12-19 and 20 years and older) and three different ethnic groups (Mexican Americans, non-Hispanic blacks and non-Hispanic whites). As Dr. Snedeker explained, this type of environmental health tracking programs helps identify the chemical body burden from all sources of exposure, track trends in exposure, identify at-risk populations, establish 'reference ranges' for chemicals for which we have little or no data, helps evaluate whether prevention efforts work, and provides direction on further research and monitoring efforts.

Next, the Biomonitoring workshop covered approaches currently being used to study emerging environmental contaminants. The 'Sister Study,' funded by the National Institute of Environmental Health Science, is an ongoing

study that will follow 50,000 sisters of women with diagnosed with breast cancer to explore linkages between genetics, biology, and the environment (see Volume 9, Number 4, Fall 2004 issue of *The Ribbon* and www.sisterstudy.org). Dr. Snedeker also presented new data on levels of polybrominated diphenyl ethers (PBDEs), which have been detected globally in wildlife. This class of chemicals, used extensively as flame retardants, have been detected in human breast milk, blood, and fat samples in humans. Recent evidence suggests rising levels in the U.S. population. Data on possible health effects is emerging. Animal models have identified areas of concern, including effects on cancer risk and neurological development.

Second workshop addressed endocrine disruptors.

Endocrine disruptors, which may be synthetic or from natural sources, may interfere with a variety of endocrine functions and can cause adverse health effects. This includes effects on sexual development; fertility; cancer incidence; limb, bone and organ development; cognitive development; or neurological development. Some types of endocrine disruptors are "estrogen mimics," and include certain pesticides, plasticizers, and industrial chemicals.

Dr. Snedeker explained the importance of timing of exposure to endocrine disrupting chemicals. There are critical windows of susceptibility in the human breast, especially during early phases of breast development. She presented animal model data on how atrazine (a herbicide) and dioxin can affect early development of the mammary gland, and ongoing work to assess how early exposures may influence breast cancer risk later in life. Dr. Snedeker reviewed how the Breast Cancer and Environmental Research Centers (BCERC), funded by the National Institute of Environmental Health Sciences, have utilized biomonitoring pilots in their efforts to understand if particular chemicals are detectable in young girls, and plans to study whether interactions between genetics and environmental chemicals may affect the onset of puberty in young girls.

Workshops received positive feedback. Participants were very pleased with the information that was provided both during the presentations and as handouts. As one participant reported, the workshop was "worthwhile for the excellent materials, alone!" The discussions among all the participants were informative to all, they reported, and many asked for additional resources. We are pleased that the feedback was so positive, and that the topics requested by the NYSBCN were so pertinent to current activities in breast cancer research. *web sites of interest on back cover*

Save the Date

**Next Regional Cancer and Environment Forum
Thursday, Sept. 28, 2006**

to be held on Long Island, location to be announced.

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- Robinson, F.E. and Etches, R. J. (1986). Ovarian steroidogenesis during follicular maturation in the domestic hen (*Gallus domesticus*). *Biology of Reproduction* 35, 1096-1105.
- Salazar, H., Godwin, A., Daly, M., Laub, P., Hogan, W., Rosenblum, N., Boente, M., Lynch, H., and Hamilton, T. (1996). Microscopic benign and invasive malignant neoplasms and a preneoplastic phenotype in prophylactic oophorectomies. *Journal of the National Cancer Institute* 88, 1810-1820.
- Sato, E., Olson, S.H., Ahn, J., Bundy, B., Nishikawa, H., Quian, F., Jungbluth, A.A., Frosina, D., Gnjatic, S., Ambrosone, C., Kepner, J., Odunsi, T., Ritter, G., Lele, S., Chen, Y.-T., Ohtani, H., Old, L.J., and Odunsi, K. (2005). Intraepithelial CD8+ tumor-infiltrating lymphocytes and a high CD8+/regulatory T cell ratio are associated with favorable prognosis in ovarian cancer. *Proceedings of the National Academy of Sciences*, 102(51), 18538-18543.
- Urick, M.E., and Johnson, P.A. Cyclooxygenase 1 and 2 mRNA and protein expression in the *Gallus domesticus* model of ovarian cancer. *Gynecologic Oncology*, in press.
- Vale, W., Rivier, C., Hsueh, A., Campen, C., Meunier, H., Bicsak, T., Vaughan, J., Corrigan, A., Vrldin, W., Sawchenko, P., Petraglia, F., Yu, J., Plotsky, P., Spiess J., and, Rivier, J. (1988). Chemical and biological characterization of the inhibin family of protein hormones. *Recent Progress in Hormone Research* 44, 1-34.
- Wilson, J.E. (1958). Adeno-carcinoma in hens kept in a constant environment. *Poultry Science* 37, 1253(abs.). 

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Web sites of interest regarding biomonitoring and endocrine disruptors

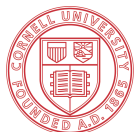
- <http://www.cdc.gov/exposurereport/> for the CDC's Third National Report on Human Exposure to Environmental Chemicals
- <http://www.cdc.gov/nceh/publications/factsheets.htm> for Fact Sheet list for the National Center for Environmental Health (NCEH)
- <http://www.epa.gov/scipoly/ospendo/edspoverview/primer.htm> for the Environmental Protection Agency's web site on Endocrine Disruption
- <http://envirocancer.cornell.edu/presentations/endocrine.cfm> for BCERF's slide show on "Breast cancer – Is there a link to endocrine disrupting chemicals?"
- <http://envirocancer.cornell.edu/Bibliography/cENDOCRINE.cfm> for BCERF's Endocrine Disruption Bibliography Collection
- <http://envirocancer.cornell.edu/FactSheet/cENDOCRINE.cfm> for BCERF's Endocrine Disruption Fact Sheet Collection 



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