EGRP Research Highlights

Epidemiology and Genetics Research Program

Web Site: epi.grants.cancer.gov

The Epidemiology and Genetics Research Program (EGRP) supports about 450 grants and cooperative agreements annually. Investigators from throughout the United States and internationally are funded to conduct population-based research to increase our understanding of cancer etiology and prevention. Some of their recent research findings are highlighted in the following pages. The names of the first authors and of the EGRP-supported Principal Investigators whose grants are credited in the published papers appear in boldface print. Also visit EGRP's Web site to view a special section with highlights from many other studies: *epi.grants.cancer.gov*.

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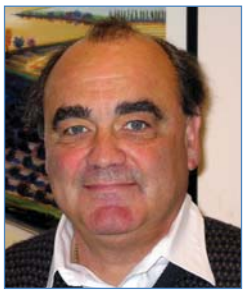
Molecular Features of Adult Glioma Detailed



John Wiencke, Ph.D.

Malignant gliomas in adults represent a highly heterogeneous group of tumors with unknown etiology. Mutations in the *TP53* gene, most likely arising from DNA alkylation, are common in these brain cancers and are associated with various demographic risk factors including age and ethnicity. Inactivation of the DNA repair protein O^6-methylguanine-DNA-methyltransferase (MGMT), which repairs alkylation damage, is associated with *TP53* mutations in human cancers, and several heritable polymorphisms in MGMT have been defined. **John Wiencke, Ph.D., of the University of California at San Francisco** (UCSF), and colleagues conducted molecular analyses of 556 glioma tumors (astrocytic) and collected information on *TP53* status, epidermal growth factor receptor (*EGFR*) gene and murine double minute-2 (*MDM2*) gene amplification, and *MGMT* germline genotype data.

Patients with tumors bearing *TP53* mutations tended to be younger than those whose tumors did not have this mutation, and they were more likely to be nonwhite (African American and Asian) than Latino and non-Latino white. In addition, *EGFR* gene amplification was associated with an older age of onset (68 years vs. 48 years); carriers of the *MGMT* variant 84Phe allele were less likely to have tumors with *TP53* overexpression; and *EGFR* gene amplification and protein overexpression were inversely associated with the variant *MGMT* allele. An inverse relationship between *TP53* mutation and *MDM2* or *EGFR* amplification was observed. The findings indicate that age, race/ethnicity, and inherited genetic factors are linked to molecular features of glioma, and it seems likely, say the researchers, "that applying these markers in molecular epidemiology studies holds promise in searching out the underlying causes of these cancers." The study was supported in part by EGRP grants to **Dr. Wiencke** and **Margaret Wrensch, Ph.D.,** also of UCSF.

Wiencke JK, Aldape K, McMillan A, Wiemels J, Moghadassi M, Miike R, Kelsey KT, Patoka J, Long J, Wrensch M. Molecular features of adult glioma associated with patient race/ethnicity, age, and a polymorphism in O^6-methylguanine-DNA-methyltransferase. Cancer Epidemiol Biomarkers Prev 2005 Jul;14(7):1774-83.

Oophorectomy Confirmed As Protecting Against Breast Cancer in *BRCA1* Mutation Carriers

Andrea Eisen, M.D.

Findings from a large study by **Andrea Eisen, M.D., of Toronto Sunnybrook Regional Cancer Centre**, and colleagues demonstrate that bilateral oophorectomy is an effective means of reducing risk for breast cancer in *BRCA1* gene mutation carriers, and may be effective for *BRCA2* mutation carriers as well. Oophorectomy was found to be associated with a 56 percent reduction in breast cancer in *BRCA1* carriers. A similar but nonsignificant reduction in breast cancer risk was found for *BRCA2* carriers (Odds Ratio (OR): 0.57). The strongest effects were observed with oophorectomies performed in *BRCA1* carriers before 40 years of age (OR: 0.36) and for breast cancers that were diagnosed before 40 years of age (OR: 0.53). The protective effect for carriers of both the *BRCA1* and *BRCA2* mutations may be limited to a period of 15 years following surgery (OR: 0.39). Data were analyzed on 1,439 patients with breast cancer and 1,866 controls from a registry of *BRCA1* and *BRCA2* carriers. These results confirm previously reported findings from smaller studies of women with hereditary susceptibility to breast and ovarian cancer, but go further. Earlier studies were not sufficiently large to estimate the magnitude of risk reduction by age of oophorectomy or by *BRCA1/BRCA2* mutation status, or to measure the duration of the effect. This research was supported in part by an EGRP grant to **Susan Neuhausen, Ph.D., of the University of California at Irvine.**

Eisen A, Lubinski J, Klijn J, Moller P, Lynch HT, Offit K, Weber B, Rebbeck T, Neuhausen SL, Ghadirian P, Foulkes WD, Gershoni-Baruch R, Friedman E, Rennert G, Wagner T, Isaacs C, Kim-Sing C, Ainsworth P, Sun P, Narod SA. Breast cancer risk following bilateral oophorectomy in BRCA1 and BRCA2 mutation carriers: an international case-control study. J Clin Oncol 2005 Oct 20;23(30):7491-6.

Exercise and Weight Control Associated With Decreased Breast Cancer Risk

Alecia Malin, Ph.D.

Women who exercise more and control their weight may significantly reduce their risk of developing breast cancer, according to research by **Alecia Malin, Ph.D., of Meharry Medical College,** and colleagues. In their study, the researchers found a strong link between "energy balance"—the difference between energy intake (eating) and energy expenditure (physical activity)—and breast cancer risk. This association was stronger in postmenopausal women than in premenopausal women, and postmenopausal women with higher body mass index measurements who did not exercise were found to be at substantially increased risk of breast cancer (Odds Ratio (OR): 4.74). The findings support current breast cancer prevention efforts that encourage increased physical activity levels and discourage age-related weight gain. The population-based study included 1,459 breast cancer cases and 1,556 controls participating in the Shanghai Breast Cancer Study. The research was supported in part by an EGRP grant to **Wei Zheng, M.D., Ph.D., M.P.H., of Vanderbilt University.** The Shanghai Breast Cancer Study is a cohort that has been funded by EGRP since 1996.

Malin A, Matthews CE, Shu XO, Cai H, Dai Q, Jin F, Gao YT, Zheng W. Energy balance and breast cancer risk. Cancer Epidemiol Biomarkers Prev 2005 Jun;14(6): 1496-501.

Folate Intake Associated With Decreased ER$^-$ Breast Cancer Risk

Shmin Zhang, M.D., Sc.D.

Folate plays an important role in DNA methylation, and aberrant methylation of the estrogen receptor (*ER*) gene may be related to the loss of *ER* gene expression in breast tumors. Deficiency in folate has been hypothesized to be associated with ER$^-$ breast cancer, but data have been sparse. In new research, **Shumin Zhang, M.D., Sc.D., of Harvard School of Public Health**, and colleagues found that higher total folate intake was associated with a lower risk of developing ER$^-$ but not ER$^+$ breast cancer. Women in the highest quintile of total folate intake had a 20 percent reduction in risk for ER$^-$ breast cancer compared to women in the lowest quintile of intake. The inverse association between total folate intake and ER$^-$ breast cancer was particularly strong in women who regularly consumed alcohol (15 grams per day [0.5 oz.] or more). Ensuring adequate folate intake seems especially important for women at higher risk of breast cancer because of alcohol consumption, the researchers say. The analysis is from the Nurses' Health Study I. During 20 years of followup, 2,812 ER$^+$ and 985 ER$^-$ breast cancer cases were documented among the cohort of 88,744 women. The research was supported in part by an EGRP grant to **Graham Colditz, M.D., Dr.P.H.,** of the same institution. NHS I has been funded by EGRP since 1973.

Zhang SM, Hankinson SE, Hunter DJ, Giovannucci EL, Colditz GA, Willett WC. Folate intake and risk of breast cancer characterized by hormone receptor status. Cancer Epidemiol Biomarkers Prev 2005 Aug;14(8):2004-8.

Pooled Analysis Shows Dietary Fiber Not Associated With Decreased Colorectal Cancer Risk

Yikyung Park, Sc.D.

Although several mechanisms have been proposed for the ability of dietary fiber to reduce colorectal cancer risk, observational and epidemiologic studies and randomized controlled trials of dietary fiber supplements have failed to show a strong effect. To clarify the relationship, **Yikyung Park, Sc.D., while at Harvard School of Public Health,** and colleagues conducted a pooled analysis of 13 prospective cohort studies included in the Pooling Project of Prospective Studies of Diet and Cancer. Data from each cohort were re-analyzed using a standard approach. An age-adjusted model showed a significant inverse association between dietary fiber intake and colorectal cancer risk (16% reduction in risk). This association was slightly weakened after adjustment for nondietary risk factors, multivitamin use, and total energy intake. In the final model, however, which adjusted for other colorectal cancer risk factors, such as red meat and total milk and alcohol intake, only a nonsignificant, weak inverse association was observed. The researchers concluded that "although high dietary fiber intake may not have a major effect on the risk of colorectal cancer, a diet high in dietary fiber from whole plant foods can be advised because this has been related to lower risks of other chronic conditions such as heart disease and diabetes."

The analysis encompassed 725,628 men and women, followup times of 6 to 20 years, and 8,081 colorectal cancer cases. Several of the cohort studies included in this analysis are funded by EGRP: Health Professionals Follow-up Study, with **Walter Willett, M.D., M.P.H., Dr.P.H., Harvard School of Public Health**; Iowa Women's Health Study, with **Aaron Folsom, M.D., M.P.H., University of Minnesota;** and Nurses' Health Study I and II, with **Graham Colditz, M.D., Dr.P.H., of Harvard School of Public Health,** and **Dr. Willett,** respectively.

Dr. Park is now a visiting research fellow in NCI's Division of Cancer Epidemiology and Genetics (DCEG), the intramural epidemiology research component of the Institute.

Park Y, Hunter DJ, Spiegelman D, Bergkvist L, Berrino F, van den Brandt PA, Buring JE, Colditz GA, Freudenheim JL, Fuchs CS, Giovannucci E, Goldbohm RA, Graham S, Harnack L, Hartman AM, Jacobs DR Jr, Kato I, Krogh V, Leitzmann MF, McCullough ML, Miller AB, Pietinen P, Rohan TE, Schatzkin A, Willett WC, Wolk A, Zeleniuch-Jacquotte A, Zhang SM, Smith-Warner SA. Dietary fiber intake and risk of colorectal cancer: a pooled analysis of prospective cohort studies. JAMA 2005 Dec 14;294(22):2849-57.

NSAIDs May Protect Against Colon Cancer in African Americans

Leah Sansbury, Ph.D.

African Americans have the highest rates of colon cancer incidence and mortality among all U.S. ethnic groups, and this discrepancy is not accounted for by differences in screening rates. Epidemiologic studies have shown that nonsteroidal anti-inflammatory drug (NSAID) use can reduce the risk of colon cancer, but no studies have specifically examined NSAID use and colon cancer risk in African Americans. **Leah Sansbury, Ph.D., of NCI's Center for Cancer Research,** and researchers at the University of North Carolina at Chapel Hill conducted a population-based case-control study to determine whether the protective effects of NSAIDs on colon cancer risk are comparable for African Americans and white Americans. They found a similar degree of protection for both groups, with Odds Ratios for regular NSAID use of 0.41 for African Americans and 0.48 for white Americans. The protective effect was stronger for women than for men. The study enrolled 731 African Americans (294 cases and 437 controls) and 960 white Americans (349 cases and 611 controls). The research was funded by EGRP grants to **Robert Sandler, M.D., M.P.H., of the University of North Carolina at Chapel Hill.**

Dr. Sansbury is at NCI as a Cancer Prevention Fellow, a program providing postdoctoral training opportunities in cancer prevention and control. Information on research training opportunities at NCI (intramural) and sponsored by NCI (extramural) is located at: *www.cancer.gov/researchandfunding/training*.

Sansbury LB, Millikan RC, Schroeder JC, Moorman PG, North KE, Sandler RS. Use of nonsteroidal antiinflammatory drugs and risk of colon cancer in a population-based, case-control study of African Americans and Whites. Am J Epidemiol 2005 Sep 15;162(6):548-58.

NSAIDs May Protect Barrett's Esophagus Patients From Esophageal Cancer

Thomas Vaughan, M.D., M.P.H.

Aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs) may significantly reduce risk of esophageal cancer in people with Barrett's esophagus, a precancerous condition that affects 1 million to 2 million Americans, according to findings by **Thomas Vaughan, M.D., M.P.H., of Fred Hutchinson Cancer Research Center,** and colleagues. In the largest and longest observational study of its kind, the researchers examined the relationship between duration, frequency, and recency of NSAID use and risk of esophageal cancer. They found that people with Barrett's esophagus who regularly took NSAIDs had a substantially reduced risk of developing esophageal cancer and did not develop the cancer as soon as people who did not take them regularly. Current NSAIDs users had one-third the risk of developing esophageal cancer compared to those who had never used them. The protective effect of NSAID use disappeared rapidly after usage stopped, however. This prospective, longitudinal observational study involved a cohort of 350 people with Barrett's esophagus. The findings lend support to previous observational studies and animal studies that have shown that NSAIDs might protect against cancer in people with Barrett's esophagus. The research was supported in part by an EGRP grant to **Brian Reid, M.D., Ph.D.,** of the same institution.

Vaughan TL, Dong LM, Blount PL, Ayub K, Odze RD, Sanchez CA, Rabinovitch PS, Reid BJ. Non-steroidal anti-inflammatory drugs and risk of neoplastic progression in Barrett's oesophagus: a prospective study. Lancet Oncol 2005 Dec;6(12):945-52.

Striking Ethnic Discrepancies Seen in Smoking-Related Lung Cancer Risk

Christopher Haiman, Sc.D.

Lung cancer is more likely to develop in cigarette smokers who are African American or Native Hawaiian than in smokers who are white, Japanese American, or Latino, according to research by **Christopher Haiman, Sc.D., of the University of Southern California**, and colleagues. The findings are especially noteworthy because of the study's large size and its far broader ethnic and racial representation than other studies. The research team analyzed lung cancer incidence among 183,813 African-American, Japanese-American, Latino, Native-Hawaiian, and white men and women from the Multiethnic Cohort Study (MEC) of more than 215,000 individuals in California and Hawaii. In the analysis, 1,979 lung cancer cases were identified between baseline (1993-96) and 2001.

Among those who smoked less than 30 cigarettes per day, risks for African Americans and Native Hawaiians were significantly greater than for the other groups. The difference between groups was particularly evident among those who smoked 10 or fewer cigarettes per day. Among those who smoked 10 cigarettes or fewer a day, whites had a 55 percent lower risk of lung cancer than African Americans; and among those who smoked 11 to 20 cigarettes a day, a 43 percent lower risk. For Latinos and Japanese Americans, the percentages were lower still. However, once smoking rates reached 30 cigarettes a day—the equivalent of a pack and a half—or more, the risk difference was minimal. The differences in risk were observed for both sexes and all histologic types of lung cancer. Environmental measures looked at—occupation, diet, and education (as a proxy for socioeconomic status)—could not explain what the researchers called "the striking racial and ethnic differences in the risk of lung cancer associated with cigarette smoking."

The findings do not change the public health message on the hazards of smoking. Individuals are far more likely to get lung cancer if they smoke, and they can reduce their risks by quitting. The research was supported by an EGRP grant to **Laurence Kolonel, M.D., Ph.D., University of Hawaii, Manoa**, for the MEC, which has been funded since 1993.

Haiman CA, Stram DO, Wilkens LR, Pike MC, Kolonel LN, Henderson BE, Le Marchand L. Ethnic and racial differences in the smoking-related risk of lung cancer. N Engl J Med 2006 Jan 26;354(4):333-42.

Vitamin D and Surgery Season Associated With Improved Survival in Early Lung Cancer

Wei Zhou, M.D., Ph.D.

Vitamin D has anti-proliferative and anti-invasive properties *in vitro* and in animal studies and may induce apoptosis of cancer cells. In humans, dietary vitamin D intake, regional ultraviolet light B levels, and sunlight exposure all contribute to vitamin D levels. **Wei Zhou, M.D., Ph.D., of Harvard School of Public Health**, and colleagues examined the association of surgery season, as a marker for sunlight exposure, and vitamin D intake with recurrence-free and overall survival in 456 patients with early-stage non-small cell lung cancer. Patients undergoing surgery in the summer had a higher recurrence-free survival rate than patients undergoing surgery in the winter (Hazard Ratio (HR): 0.75). No association between vitamin D intake and survival was found. However, analysis of the joint effects of vitamin D and surgery season showed that patients with the highest vitamin D intake who had surgery in the summer had a 5-year recurrence-free survival rate of 56 percent, compared to 23 percent for patients with low intake who had surgery in the winter. These findings should be confirmed in a prospective study to assess the serum vitamin D levels at time of surgery, say the researchers; if confirmed, dietary vitamin D supplementation may be advisable for early-stage lung cancer patients, particularly during the winter and in groups that tend to be deficient in vitamin D. This research was supported in part by an EGRP grant to **David Christiani, M.D., M.P.H., M.S.**, of the same institution.

Zhou W, Suk R, Liu G, Park S, Neuberg DS, Wain JC, Lynch TJ, Giovannucci E, Christiani DC. Vitamin D is associated with improved survival in early-stage non-small cell lung cancer patients. Cancer Epidemiol Biomarkers Prev 2005 Oct;14(10):2303-9.

InterLymph Consortium Investigates Alcohol Consumption and Non-Hodgkin's Lymphoma

Lindsay Morton, Ph.D.

InterLymph, short for the International Consortium of Investigators Working on Non-Hodgkin's Lymphoma Epidemiologic Studies, is an open scientific forum for epidemiologic research in non-Hodgkin's lymphoma (NHL) comprised of international researchers who have completed or ongoing case-control studies. The investigators discuss and undertake research projects that pool data across studies or otherwise undertake collaborative research.

For a recent pooled analysis, InterLymph researchers obtained original data from nine case-control studies totaling 15,175 individuals (6,492 cases and 8,693 controls) from the United States, United Kingdom, Sweden, and Italy to study the association between alcohol consumption and risk for NHL. They found that individuals who drank alcohol had a lower risk of NHL than nondrinkers. Risk estimates were lower for current drinkers than former drinkers compared to nondrinkers. Risk did not decrease with increasing alcohol consumption, nor did the protective effect vary by type of alcohol consumed, although it did change by subtype of NHL. The lowest risk estimates were for Burkitt's lymphoma. Other studies on alcohol consumption and risk for NHL have yielded inconsistent results, as have studies that have investigated type of alcoholic beverage or subtype of NHL. Further study is warranted to confirm their findings and to determine the biological mechanism for the association, suggest the researchers.

The study's lead author is **Lindsay Morton, Ph.D., of NCI's Division of Cancer Epidemiology and Genetics Research** (DCEG), which is the intramural epidemiology research component of the Institute. Some of the case-control studies included in the analysis are supported through EGRP grants to **Elizabeth Holly, Ph.D., M.P.H., of the University of California, San Francisco; Alexandra Levine, M.D., of the University of Southern California; Mads Melby, M.D., Ph.D., of Statens Serum Institute, Denmark;** and **Tongzhang Zheng, M.D., Sc.D., of Yale University.**

Support for InterLymph's logistical needs is provided by EGRP and DCEG; the International Agency for Research on

Cancer (IARC), Lyon, France; and the Leukaemia Research Fund, London, England.

Lymphoma researchers without case-control data to pool may participate in InterLymph's annual meetings and working groups. The next conference is Friday, March 31, 2006, in Washington, D.C., with NCI investigators as hosts. Contact Geoffrey Tobias, DCEG: *tobiasg@mail.nih.gov*. The InterLymph Web site is: *epi.grants.cancer.gov/InterLymph.*

Morton LM, Zheng T, Holford TR, Holly EA, Chiu BC, Costantini AS, Stagnaro E, Willett EV, Dal Maso L, Serraino D, Chang ET, Cozen W, Davis S, Severson RK, Bernstein L, Mayne ST, Dee FR, Cerhan JR, Hartge P; InterLymph Consortium. Alcohol consumption and risk of non-Hodgkin lymphoma: a pooled analysis. Lancet Oncol 2005 Jul;6(7):469-76.

Pooled Analysis Indicates Fruits and Vegetables Not Associated With Decreased Ovarian Cancer Risk


Anita Koushik, Ph.D.

Anita Koushik, Ph.D., of Harvard School of Public Health, and colleagues conducted a pooled analysis of 12 prospective studies in North America and Europe to learn if increased fruit and vegetable consumption decreased risk for ovarian cancer. They found that neither total fruit or vegetable intake in adulthood, intake of specific fruit or vegetable groups, nor intake of individual fruits or vegetables were associated with risk for the cancer. This large study of more than 2,000 ovarian cancer cases also enabled the researchers to conduct analyses by main histologic type and levels of risk factors for the cancer. The researchers point out that the findings may not generalize to fruit and vegetable intake at an earlier time in life, and regardless of their findings, fruit and vegetable consumption remain important components of a healthy diet. A previous evaluation by the International Agency for Research on Cancer (IARC) of eight published case-control and cohort studies conducted through early 2003 had concluded that vegetable intake might reduce risk for ovarian cancer, but inconsistent results precluded drawing a firm conclusion. This new pooled analysis included data from several cohorts supported by grants from EGRP: Iowa Women's Health Study, with **Aaron Folsom, M.D., M.P.H., of the University of Minnesota;** and Nurses' Health Study I and II, with **Graham Colditz, M.D., Dr.P.H., and Walter Willett, M.D., M.P.H., Dr.P.H., respectively, of Harvard School of Public Health.**

Koushik A, Hunter DJ, Spiegelman D, Anderson KE, Arslan AA, Beeson WL, van den Brandt PA, Buring JE, Cerhan JR, Colditz GA, Fraser GE, Freudenheim JL, Genkinger JM, Goldbohm RA, Hankinson SE, Koenig KL, Larsson SC, Leitzmann M, McCullough ML, Miller AB, Patel A, Rohan TE, Schatzkin A, Smit E, Willett WC, Wolk A, Zhang SM, Smith-Warner SA. Fruits and vegetables and ovarian cancer risk in a pooled analysis of 12 cohort studies. Cancer Epidemiol Biomarkers Prev 2005 Sep;14(9):2160-2167.

Red and Processed Meat Associated With Increased Pancreatic Cancer Risk


Ute Nöthlings, Dr.P.H.

Consumption of meat has been associated with risk of pancreatic cancer, but previous findings were inconsistent. An analysis of pancreatic cancer cases in a multiethnic population by **Ute Nöthlings, Dr.P.H., of the University of Hawaii, Manoa,** and colleagues found that red and processed meat are strong risk factors for the disease. Red and processed meats were associated with 50 percent and 70 percent increases in risk, respectively, across quintiles, independent of energy intake. Data from the Multiethnic Cohort Study (MEC) were analyzed for associations between intake of meat, other animal products, fat, and cholesterol and pancreatic cancer risk. No link was found between the disease and consumption of poultry, fish, dairy products, or eggs. Fat and saturated fat were found to be unlikely contributors to the underlying carcinogenic mechanism. Carcinogenic substances related to meat preparation methods might be responsible for the risk, say the researchers, and they suggest that future research focus on meat preparation methods and related carcinogens. The analysis was based on data on 482 cases of pancreatic cancer diagnosed over a 7-year period. The research was supported in part by an EGRP grant for the MEC to **Laurence Kolonel, M.D., Ph.D.**, of the same institution. EGRP has funded the MEC since 1993.

Nöthlings U, Wilkens LR, Murphy SP, Hankin JH, Henderson BE, Kolonel LN. Meat and fat intake as risk factors for pancreatic cancer: the multiethnic cohort study. J Natl Cancer Inst 2005 Oct 5;97(19):1458-65.

Insulin-Like Growth Factor Polymorphisms Associated With Body Size


Carol Sweeney, Ph.D.

Insulin-like growth factor (IGF) regulatory molecules mediate growth hormone signaling and affect cell proliferation and apoptosis, influencing weight gain, body fat distribution, and risk of obesity-related diseases, including cancer. **Carol Sweeney, Ph.D., of the University of Utah,** and colleagues examined associations of polymorphisms affecting IGF, IGF binding proteins (IGFBP), insulin receptor substrates, and the vitamin D receptor (VDR) with body size and fat distribution in Hispanic and non-Hispanic white women. Two associations were observed in both groups of women: *IGF1* CA repeat alleles greater than 19 repeats in length were associated with higher waist-to-hip ratios, and women with an *IGFBP3* A allele more often reported higher birth weights. In Hispanic women only, the *IGFBP3* A allele was associated with taller height, the *IRS*1R allele was associated with smaller waist-to-hip ratio, and the *VDR Fok*I ff genotype was associated with larger waist-to-hip ratio. The researchers say that the findings support the thinking that genetic variation in IGF pathway molecules has functional consequences for growth and central obesity, and that genotype-phenotype relationships are ethnic specific. The study included 462 Hispanic women and 1,702 non-Hispanic white women. It was funded in part by an EGRP grant to **Martha Slattery, Ph.D.,** of the same institution.

Sweeney C, Murtaugh MA, Baumgartner KB, Byers T, Giuliano AR, Herrick JS, Wolff R, Caan BJ, Slattery ML. Insulin-like growth factor pathway polymorphisms associated with body size in Hispanic and non-Hispanic white women. Cancer Epidemiol Biomarkers Prev 2005 Jul;14(7):1802-9.

Perspectives: *Nature Reviews Cancer*

Three articles were published recently by EGRP grantees and EGRP staff in the "Perspectives" section of *Nature Reviews Cancer.*

Consortium Hunts Low-Penetrance Breast and Prostate Cancer Genes


David Hunter, M.D., Sc.D.


Michael Thun, M.D.


Elio Riboli, M.D., M.Sc.


Brian Henderson, M.D.

The research team testing the principle that pooling data and biospecimens across large-scale studies through consortial arrangements is an effective approach to research on genes and the environment describes its approach to searching for low-penetrance breast and prostate cancer genes of the hormone-regulated pathway in the December 2005 issue of *Nature Reviews Cancer*. The Breast and Prostate Cancer Cohort Consortium, also known as the BPC3 Study, is characterizing variations in about 50 genes that mediate two pathways associated with these cancers—the steroid-hormone metabolism pathway and the insulin-like growth factor signalling pathway—and are associating these variations with cancer risk. The BPC3 Study combines the resources of 10 large prospective cohorts; three genomic facilities; and epidemiologists, population geneticists, and biostatisticians from multiple institutions. Data and biospecimens are being pooled on more than 8,000 cases of prostate cancer and 5,000 cases of breast cancer.

Participation of eight of the cohorts is funded through four EGRP grants to: **David Hunter, M.D., Sc.D., of Harvard School of Public Health,** for the participation of the Physicians' Health Study I and II, Nurses' Health Study, Health Professionals Follow-up Study, and Women's Health Study; **Michael Thun, M.D., of the American Cancer Society** (**ACS**), for the ACS Cancer Prevention Study II; **Elio Riboli, M.D., M.Sc., of the Imperial College, London,** for the European Prospective Investigation into Cancer and Nutrition (EPIC); and **Brian Henderson, M.D., of the University of Southern California/Norris Comprehensive Cancer Center,** for the Multiethnic Cohort Study. Two cohorts from NCI's Division of Cancer Epidemiology and Genetics (DCEG), the intramural epidemiology research component of the Institute, also participate: the Prostate,

Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, directed by Richard Hayes, D.D.S., Ph.D., and the Alpha-Tocopherol, Beta-Carotene Cancer Prevention (ATBC) Study, directed by Demetrius Albanes, M.D.

The BPC3 Study is the first research project initiated by the Consortium of Cohorts, a group formed by NCI to address the need for large-scale collaborations in the genetic and molecular epidemiology of cancer. The Consortium is a joint initiative of NCI's Division of Cancer Control and Population Sciences (DCCPS), of which EGRP is a part, and DCEG. The Consortium and BPC3 Study Web site is: *epi.grants.cancer.gov/Consortia/cohort.html.*

Hunter DJ, Riboli E, Haiman CA, Albanes D, Altshuler D, Chanock SJ, Haynes RB, Henderson BE, Kaaks R, Stram DO, Thomas G, Thun MJ, Blanche H, Buring JE, Burtt NP, Calle EE, Cann H, Canzian F, Chen YC, Colditz GA, Cox DG, Dunning AM, Feigelson HS, Freedman ML, Gaziano JM, Giovannucci E, Hankinson SE, Hirschhorn JN, Hoover RN, Key T, Kolonel LN, Kraft P, Le Marchand L, Liu S, Ma J, Melnick S, Pharaoh P, Pike MC, Rodriguez C, Setiawan VW, Stampfer MJ, Trapido E, Travis R, Virtamo J, Wacholder S, Willett WC; National Cancer Institute Breast and Prostate Cancer Cohort Consortium. A candidate gene approach to searching for low-penetrance breast and prostate cancer genes. Nat Rev Cancer 2005 Dec;5(12):977-85.

Long Island Breast Cancer Study Project: Research on Environmental Exposures and Breast Cancer

Debbie Winn, Ph.D.

The Long Island Breast Cancer Study Project (LIBCSP) was initiated in the early 1990s in response to a congressional mandate to investigate possible environmental factors that may be responsible for high rates of breast cancer in Nassau and Suffolk counties (Long Island) and two other counties. More than 10 studies were conducted through grants to investigators, and a geographic information system (LI GIS) was developed under contract that presently is available to researchers to explore relationships between environmental exposures and breast cancer risk.

The LIBCSP has played an important role in efforts to understand the high rates of breast cancer in some regions of the United States. In the December 2005 issue of *Nature Reviews Cancer,* **EGRP's Debbie Winn, Ph.D.**, reviews its accomplishments and provides a broad overview of NCI's extramural epidemiologic research initiatives on the environment and breast cancer that have been supported since the early 1990s, including the presently funded Breast Cancer and Environment Research Centers (BCERCs). EGRP manages NCI's extramural research program in epidemiology. Funding for the LIBCSP and BCERCs has been in collaboration with the National Institute of Environmental Health Sciences (NIEHS). LIBCSP Web site: *epi.grants.cancer.gov/LIBCSP*; LI GIS Web site: *www.healthgis-li.com*; and BCERCs Web site: *epi.grants.cancer.gov/BCERC.html*

Winn DM. Science and society: the Long Island Breast Cancer Study Project. Nat Rev Cancer 2005 Dec;5(12):986-94.

What Have We Learned Since Doll and Peto's Analysis on Risk and Preventability of Cancer?

Graham Colditz, M.D., Dr.P.H.

"Epidemiology—identifying the causes and preventability of cancer?" reviews studies of cancer incidence using different epidemiologic techniques that have been conducted in the 25 years since Professor Sir Richard Doll and Professor Sir Richard Peto published their landmark comprehensive analysis of evidence on the risk and preventability of cancer. "These studies revealed expanded opportunities for cancer prevention through approaches that include vaccination, increased physical activity, weight control, and avoidance of post-menopausal hormone therapy," write **Graham Colditz, M.D., Dr.P.H., of Brigham and Women's Hospital and Harvard School of Public Health,** and **Thomas Sellers, Ph.D., H. Lee Moffitt Cancer Center & Research Institute**, and **EGRP's Edward Trapido, Sc.D.,** in the January 2006 issue of *Nature Reviews Cancer.* The authors make some suggestions for future directions in epidemiologic research, including in method development and method incorporation, and for studies of interactions between behavior, psychological and social mechanisms, and risk indicators to fill gaps in etiology and survivorship studies.

Colditz GA, Sellers TA, Trapido E. Epidemiology—identifying the causes and preventability of cancer? Nat Rev Cancer 2006 Jan;6(1):75-83.

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Sources of Information on Grant Policies, Funding, and Training

- Our Division of Cancer Control and Population Sciences (DCCPS) Home page: *cancercontrol.cancer.gov* for grant policy alerts and information on funding opportunities.
- DCCPS Tobacco Control Research Branch: *cancercontrol.cancer.gov/tcrb*
- NCI's Division of Extramural Activities (DEA): *deainfo.nci.nih.gov*
- NCI's Research Resources (directory of more than 100 products and services): *resresources.nci.nih.gov*
- Subscribe to:
  - **NCI Cancer Bulletin** (weekly newsletter): *cancer.gov/ncicancerbulletin*
  - **NIH Guide for Grants and Contracts**: *grants1.nih.gov/grants/guide/listserv.htm*
  - **NIH's eRA for Partners** (The Commons) newsletter: *era.nih.gov/eranews/latestpartners.cfm*
  - **NIH Extramural Nexus** (Newsletter for grantees, new in 2006): *grants.nih.gov/grants/outsider/0106Nexus.htm*
  - **EGRP's Listserv** (occasional Bulletins, News Flashes) contact: *andersoL2@mail.nih.gov*
- NCI-Sponsored Training Opportunities: *www.cancer.gov/researchandfunding/training*
  EGRP's training Web site: *epi.grants.cancer.gov/training*
- **Everything you wanted to know about the NCI Grants Process...but were afraid to ask**. Access online at *www3.cancer.gov/admin/gab/index.htm* or order a print copy via NCI's online Publications Locator: *https://cissecure.nci.nih.gov/ncipubs*. (Newly updated August 2005, but **does not include information about NIH's mandatory transition to electronic submission of applications and the new form; see: *era.nih.gov/ElectronicReceipt/index.htm*.)**