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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HPV Co-Infections Synergistically Increase Risk for Cervical Cancer

Helen Trottier, Ph.D.

Simultaneous infection with multiple types of human papillomavirus (HPV) appears to act synergistically to increase the risk of developing lesions that typically precede development of cervical cancer, according to research by **Helen Trottier, Ph.D., of McGill University**, and colleagues. This study is the first to document the higher risk of cervical cancer with multiple HPV infections.

The researchers studied 2,462 Brazilian women ages 18 to 40 who had repeated measurements of viral infection and lesion outcomes to assess the role of cumulative and concurrent infection with types of HPV in the development of cervical cancer. The greater the number of HPV types involved in the co-infection, the higher the risk of precancerous lesions. The excess risks for lesions from multiple-type infections remained after excluding women infected with HPV-16 and other high-risk HPV types, and women with persistent infections. Co-infections with HPV-16 and -58 appeared to be particularly prone to increase risk for precancerous lesions.

These findings have implications for the management of cervical lesions and prediction of the outcome of HPV infections. They also provide baseline data for analyzing the impact of the newly approved HPV vaccine. The researchers pointed out that the vaccine does not protect against HPV-58 and suggested that it be a target for the next generation of cervical cancer vaccines to be developed. The research was supported in part by an EGRP grant to **Eduardo Franco, Dr.P.H., of McGill University.**

Trottier H, Mahmud S, Costa MC, Sobrinho JP, Duarte-Franco E, Rohan TE, Ferenczy A, Villa LL, Franco EL. Human papillomavirus infections with multiple types and risk of cervical neoplasia. Cancer Epidemiol Biomarkers Prev. 2006 Jul;15(7):1274-80.

Avoiding Weight Gain Reduces Risk for Postmenopausal Breast Cancer

Heather Eliassen, Sc.D.

Women can reduce their risk of breast cancer, particularly after menopause, by avoiding weight gain in adulthood or by losing the extra pounds, suggest findings by **A. Heather Eliassen, Sc.D., of Brigham and Women's Hospital and Harvard Medical School,** and colleagues. Other studies have indicated that weight gain since early adulthood is associated with an increased risk of breast cancer in postmenopausal women, but weight change in middle-aged to older women has been studied less extensively.

The researchers analyzed data from the Nurses' Health Study (NHS) I on 87,143 postmenopausal women who were followed for up to 26 years to assess weight change since age 18. Weight change since menopause was assessed among 49,514 women who were followed up to 24 years. They found that women who gained 55 pounds or more since age 18 had a 45 percent increased risk of breast cancer compared with women who maintained their weight, with a stronger association among women who had never taken postmenopausal hormones. Women who gained about 22 pounds or more since menopause had an 18 percent increased risk of breast cancer. On the other hand, women who lost about 22 pounds or more since menopause, kept the weight off, and had never used postmenopausal hormones had a 57 percent reduction in risk of the cancer compared to women who simply maintained their weight.

"Women should be advised to avoid weight gain both before and after menopause to decrease their postmenopausal breast cancer risk," concluded the researchers. The study was supported in part by an EGRP grant to **Graham Colditz, M.D., Dr.P.H., of Brigham and Women's Hospital and Harvard Medical School**, who is principal investigator of the Nurses' Health Study I. EGRP has funded this cohort since 1973.

Eliassen AH, Colditz GA, Rosner B, Willett WC, Hankinson SE. Adult weight change and risk of postmenopausal breast cancer. JAMA. 2006 Jul 12;296(2):193-201.

Mammographic Density Reflects Exposure to Breast Cancer Risk Factors

Gertraud Maskarinec, M.D., Ph.D.

Mammographic densities have been hypothesized to reflect cumulative exposure to risk factors that stimulate the growth of breast cells and influence breast cancer incidence. **Gertraud Maskarinec, M.D., Ph.D., of the Cancer Research Center of Hawaii,** and colleagues, analyzed percent mammographic densities over time and explored predictors of density change in relation to age in the Hawaii component of the Multiethnic Cohort Study.

The study population included 607 breast cancer cases and 667 controls. Eighty-two percent of the women had more than one mammogram, and almost half of the women had three or more mammograms. The researchers used a computer-assisted method to assess densities of mammograms performed over more than 20 years and before a diagnosis of breast cancer. The effects of ethnicity, status (whether the woman was diagnosed with breast cancer or not), reproductive characteristics, hormonal therapy, body mass index, and soy intake on initial status and longitudinal change were assessed using multilevel modeling. They found that cumulative percent mammographic densities and age-specific breast cancer rates increased at similar rates. Japanese ancestry, being overweight, estrogen/progestin therapy, and to a lesser extent, estrogen-only therapy, predicted a slower decline in mammographic densities with age. Case status and adult soy intake were related to higher densities, whereas being overweight and having any children were associated with lower densities at initial status. Age at menarche was not related to density.

The findings agree with the hypothesis that cumulative breast density reflects exposure to risk factors that predict age-specific breast cancer incidence. Risk factors that influence the decline in mammographic densities over time may be important in breast cancer prevention, said the researchers. The study was supported in part by EGRP grants to **Dr. Maskarinec and Laurence Kolonel, M.D., Ph.D., also of the Cancer Research Center of Hawaii.** EGRP has funded the Multiethnic Cohort Study since 1993, with Dr. Kolonel as principal investigator.

Maskarinec G, Pagano I, Lurie G, Kolonel LN. A longitudinal investigation of mammographic density: the multiethnic cohort. Cancer Epidemiol Biomarkers Prev. 2006 Apr;15(4):732-9.

Hormone Use Increases Breast Cancer Risk Among Black Women

Lynn Rosenberg, Sc.D.

Epidemiologic studies have shown a link between recent long-term hormone use among women, particularly the use of estrogen with progestin, and an increased risk of breast cancer. Research also has indicated an increased risk of breast cancer among leaner women who use these hormones, but most participants in these studies were white women.

Lynn Rosenberg, Sc.D., of Boston University, and colleagues focused on women in the Black Women's Health Study (BWHS) and found that recent long-term hormone use increased the risk of breast cancer in this population, also. The risk increased with duration of use and was strongest among leaner women, agreeing with previously published results for white women. The study included 32,559 black women who were 40 years of age or older. It was supported by an EGRP grant to Dr. Rosenberg.

The BWHS is a cohort study that has been funded by EGRP since 1994, with Dr. Rosenberg as principal investigator.

Rosenberg L, Palmer JR, Wise LA, Adams-Campbell LL. A prospective study of female hormone use and breast cancer among black women. Arch Intern Med. 2006 Apr 10;166(7):760-5.

Eight Genetic Variants in DNA Repair Pathway Ruled Out as Important in Breast Cancer


Yawei Zhang, M.D., Ph.D.

Epidemiologic studies have suggested that polymorphisms in genes encoding components of the DNA base-excision repair (BER) function are associated with cancer risk. Impaired BER function can lead to accumulation of DNA damage and initiation of cancer. **Yawei Zhang, M.D., Ph.D., of Yale University,** and colleagues evaluated the association between variation in six BER pathway genes (*XRCC1*, *ADPRT*, *APEX1*, *OGG1*, *LIG3*, and *MUTHYH*) and breast cancer risk in large population-based case-control studies in the United States and Poland. Eight single nucleotide polymorphisms (SNPs) were assessed; the researchers preferentially selected coding SNPs in the candidate genes.

No significant association was found between breast cancer risk and the SNPs analyzed in samples from the U.S. study.

Meta-analyses of the researchers' data and published data from studies of two SNPs in *XRCC1* showed no evidence of association between breast cancer risk and homozygous variants versus wild type for *Q399R*; there was a suggestion of an association for this polymorphism in Asian populations (Odds Ratio (OR) = 1.6).

The researchers concluded that the polymorphisms evaluated in this study do not play a significant role in breast carcinogenesis. The research was supported in part by EGRP grants to **Amy Trentham-Dietz, Ph.D., of the University of Wisconsin; Polly Newcomb, Ph.D., of Fred Hutchinson Cancer Research Center; and Linda Titus-Ernstoff, Ph.D., of Dartmouth.**

Zhang Y, Newcomb PA, Egan KM, Titus-Ernstoff L, Chanock S, Welch R, Brinton LA, Lissowska J, Bardin-Mikolajczak A, Peplonska B, Szeszenia-Dabrowska N, Zatonski W, Garcia-Closas M. Genetic polymorphisms in base-excision repair pathway genes and risk of breast cancer. Cancer Epidemiol Biomarkers Prev. 2006 Feb;15(2):353-8.

Large Study Supports Prophylactic Oophorectomy for *BRCA1* and *BRCA2* Gene Mutation Carriers


Steven Narod, M.D., Ph.D.

In a large-scale prospective study, **Amy Finch, M.Sc., of Toronto-Sunnybrook Regional Cancer Centre,** and colleagues estimated the absolute risks for developing ovarian, fallopian tube, and peritoneal cancers among women with *BRCA1* and *BRCA2* gene mutations, and the reduction in risk associated with the removal of ovaries and fallopian tubes.

The study included 1,828 *BRCA1* and *BRCA2* gene mutation carriers (mean age = 47.3 years) participating in an international registry of 32 centers in Canada, the United States, Europe, and Israel. The women were followed for an average of 3.5 years. A total of 555 (30%) women had prophylactic bilateral salpingo-oophorectomy (removal of the ovaries and fallopian tubes) prior to study entry, and 490 (27%) had the surgery after entry. Prophylactic bilateral salpingo-oophorectomy reduced the risk of ovarian and fallopian tube cancer by 80 percent. A residual risk of 4.3 percent for peritoneal cancer remained at 20 years after oophorectomy, but the researchers believe the risk was not sufficiently high to recommend against the surgery.

"It is important that both fallopian tubes and ovaries be removed because either site may be the origin of cancer, and both organs should be examined in fine detail to rule out the presence of microscopic disease," said the researchers. The study was supported in part by an EGRP grant to **Steven Narod, M.D., Ph.D., of Toronto-Sunnybrook Regional Cancer Centre.**

Finch A, Beiner M, Lubinski J, Lynch HT, Moller P, Rosen B, Murphy J, Ghadirian P, Friedman E, Foulkes WD, Kim-Sing C, Wagner T, Tung N, Couch F, Stoppa-Lyonnet D, Ainsworth P, Daly M, Pasini B, Gershoni-Baruch R, Eng C, Olopade OI, McLennan J, Karlan B, Weitzel J, Sun P, Narod SA; Hereditary Ovarian Cancer Clinical Study Group. Salpingo-oophorectomy and the risk of ovarian, fallopian tube, and peritoneal cancers in women with a *BRCA1* or *BRCA2* mutation. JAMA. 2006 Jul 12;296(2):185-92.

High Glycemic Index and Load May Increase Risk for Colorectal Cancer Among Obese Women

Mary McCarl, M.P.H.

The colorectal cancer risk factors of obesity, greater energy consumption, and low physical activity modulate circulating levels of insulin, which may have growth-promoting effects on the colorectum and thus influence carcinogenesis. Dietary glycemic index (GI) and glycemic load (GL) directly affect circulating insulin levels, and the consumption of foods with high GIs leads to more rapid increase in blood insulin levels than foods with low GIs.

Mary McCarl, M.P.H., of the University of Minnesota, and colleagues conducted a prospective study to examine associations of GI and GL with colorectal cancer among 35,197 participants in the Iowa Women's Health Study. They found that neither GI nor GL were major colorectal cancer risk factors among older women (ages 55–69). However, among obese women (baseline body mass index (BMI) > 30 kg/m^2), colorectal cancer incidence was increased for women in the highest versus lowest quintiles of GI (Relative Risk (RR) = 1.66) and GL (RR = 1.79). The increase was observed for both colon and rectal cancer and for women with and without diabetes. For women with a BMI below 30 kg/m^2, no statistically significant associations between GI or GL and colorectal cancer risk were found.

The results indicate that although neither GI nor GL are major colorectal cancer risk factors among older women in general, high GI or GL may increase risk for the cancer among obese women. The Iowa Women's Health Study has been funded by EGRP since 1985, with **Aaron Folsom, M.D., M.P.H., of the University of Minnesota,** as the principal investigator.

McCarl M, Harnack L, Limburg PJ, Anderson KE, Folsom AR. Incidence of colorectal cancer in relation to glycemic index and load in a cohort of women. Cancer Epidemiol Biomarkers Prev. 2006 May;15(5):892-6.

Occupational Exposures Associated With Risk for Esophageal and Stomach Cancer

Karen Wernli, Ph.D.

Karen Wernli, Ph.D., of Fred Hutchinson Cancer Research Center, and colleagues analyzed associations between occupational exposures in the Shanghai, China, textile industry and risk of esophageal and stomach cancer. Few occupational exposures have been associated with these highly lethal cancers, which account for a substantial proportion of the cancer burden in developing countries.

In a case-cohort study nested in a cohort of female textile workers in Shanghai, the researchers analyzed and compared data on 102 workers with esophageal cancer and 646 workers with stomach cancer diagnosed between 1989 and 1998 with data from a subcohort of 3,188 workers. Risk for esophageal cancer was increased 15.8-fold with 10 or more years of exposure to silica dust and 3.7-fold with long-term exposure to metals (welding dust, lead fumes, and steel). Risk increased with increasing duration of exposure. In addition, the researchers unexpectedly found that cumulative exposure to endotoxin, a cotton dust contaminant, was inversely related to risk of esophageal and stomach cancer. Endotoxin is known to elicit a systemic inflammatory response after inhalation and somehow may have a protective effect against cancer.

The researchers pointed out that silica, metals, and endotoxin exposures are not unique to the textile industry and might influence the risk of esophageal and stomach cancer in other industries. The study was supported in part by an EGRP grant to **Harvey Checkoway, Ph.D., of the University of Washington.**

Wernli KJ, Fitzgibbons ED, Ray RM, Gao DL, Li W, Seixas NS, Camp JE, Astrakianakis G, Feng Z, Thomas DB, Checkoway H. Occupational risk factors for esophageal and stomach cancers among female textile workers in Shanghai, China. Am J Epidemiol. 2006 Apr 15;163(8):717-25. Epub 2006 Feb 8.

Pancreatic Cancer Genetic Epidemiology Consortium Focuses on Familial Susceptibility

Gloria Petersen, Ph.D.

Organized in 2002 with grant support from EGRP, the Pancreatic Cancer Genetic Epidemiology (PACGENE) Consortium is a foundation for investigating the genetic etiology of familial pancreatic cancer susceptibility. PACGENE has seven data collection centers, a statistical genetics core, and a pathology/archival genotyping core.

In a published paper, Principal Investigator **Gloria Petersen, Ph.D., of the Mayo Clinic**, and colleagues describe the Consortium and their observations on age at diagnosis of pancreatic cancer among 466 participating probands and 670 affected relatives. (Probands have at least two first-degree relatives with pancreatic cancer.) Probands and affected relatives were diagnosed with the cancer at a significantly younger mean age (64) than pancreatic cancer patients in the general population (70), a finding consistent with other studies. The age for the general population was determined using data from NCI's population-based Surveillance, Epidemiology, and End Results (SEER) Program. The researchers also found that age at diagnosis among the affected relatives did not decrease with increasing number of affected family members.

PACGENE now is conducting linkage analyses to pursue the genetic basis of familial pancreatic cancer. Because pancreatic cancer is relatively rare and rapidly fatal, it is difficult for any single research center to recruit sufficient numbers of study participants and collect sufficient biospecimens from informative families to perform linkage analyses and other research. The research was supported in part by EGRP grants to Dr. Petersen.

Petersen GM, de Andrade M, Goggins M, Hruban RH, Bondy M, Korczak JF, Gallinger S, Lynch HT, Syngal S, Rabe KG, Seminara D, Klein AP. Pancreatic cancer genetic epidemiology consortium. Cancer Epidemiol Biomarkers Prev. 2006 Apr; 15(4):704-10.

New Biomarker Proposed for Lung Cancer Risk

Randa El-Zein, M.D., Ph.D.

The cytokinesis-blocked micronucleus (CBMN) assay in human lymphocytes is one of the most commonly used methods for measuring DNA damage. **Randa El-Zein, M.D., Ph.D., of The University of Texas M.D. Anderson Cancer Center,** and colleagues modified the CBMN assay to evaluate susceptibility to the nicotine-derived nitrosamine 4-(methlynitrosamino)-1-(3-pyridyl)-1-butanone (NNK), which is a carcinogen and a strong inducer of lung cancer.

They measured the frequency of NNK-induced chromosomal damage endpoints (micronuclei, nucleoplasmic bridges, and nuclear buds) per 1,000 binucleated lymphocytes. Spontaneous and NNK-induced chromosomal damage was significantly higher in lung cancer patients compared to controls. Forty-seven percent of patients compared with 12 percent of controls had greater than four spontaneous micronuclei; 66 percent of patients compared with none of the controls had greater than four spontaneous nucleoplasmic bridges; and 25 percent of patients compared with 5 percent of controls had greater than one spontaneous nuclear bud. The study included 139 cases and 130 controls.

These results provide strong evidence that the modified CBMN assay is extremely sensitive to NNK-induced genetic damage, and that the test's simplicity, speed, and sensitivity make it valuable for screening and possibly for prioritizing potential cases for early detection. This research was supported in part by EGRP grants to **Dr. El-Zein and Margaret Spitz, M.D., M.P.H., of M.D. Anderson Cancer Center.**

El-Zein RA, Schabath MB, Etzel CJ, Lopez MS, Franklin JD, Spitz MR. Cytokinesis-blocked micronucleus assay as a novel biomarker for lung cancer risk. Cancer Res. 2006 Jun 15;66(12):6449-56.

Prostate Cancer Aggressiveness Appears To Be Influenced by Several Genes


Susan Slager, Ph.D.

Several independent genome scans have reported evidence of linkage using the Gleason score as a measure of prostate cancer aggressiveness, but with inconsistent results. **Susan Slager, Ph.D., of the Mayo Clinic,** and colleagues conducted an independent genome-wide scan using the Gleason score as a quantitative trait on brothers participating in the University of Michigan Prostate Cancer Genetics Project.

The researchers genotyped 405 highly polymorphic microsatellite markers in 175 brother pairs from 103 families. The strongest evidence of linkage was to chromosome 6q23 at 137 cM. Other evidence of linkage was found on chromosomes 1p13–q21 and 5p13–q11. Altogether, three interesting regions ($P<0.005$) and two modest regions of linkage ($P<0.05$) were identified. For all but one of these regions, there is previous evidence of linkage to tumor aggressiveness.

The findings provide further evidence that tumor aggressiveness has a genetic component, said the researchers, and that the genetic component may be influenced by several independent genes. The study was supported in part by EGRP grants to **William Isaacs, Ph.D., of The Johns Hopkins University, and Kathleen Cooney, M.D., of the University of Michigan.**

Slager SL, Zarfas KE, Brown WM, Lange EM, McDonnell SK, Wojno KJ, Cooney KA. Genome-wide linkage scan for prostate cancer aggressiveness loci using families from the University of Michigan Prostate Cancer Genetics Project. Prostate. 2006 Feb 1;66(2):173-9.

Chromosome 8 Region Associated With Prostate Cancer Risk in African Americans


Matthew Freedman, M.D.

Matthew Freedman, M.D., of Dana-Farber Cancer Institute, Broad Institute of Harvard, and Massachusetts Institute of Technology, and colleagues have identified an area of chromosome 8q24 as a major risk factor for prostate cancer, especially in African-American men. The researchers used their newly developed "admixture mapping" method to screen through the genome of African Americans (who have both African and European ancestry) searching for the differences in inherited DNA from ancestral backgrounds.

They studied 1,597 African Americans with prostate cancer and 873 controls and found that the genetic risk factor nearly doubled the likelihood of prostate cancer in younger African-American men. This finding may explain why younger African Americans have a greater risk of prostate cancer than other populations and why the increased risk attenuates with older age, said the researchers.

The study also shows that admixture mapping can be a powerful and practical way to map genetic variants for complex diseases, they reported. Additional research will be needed to identify the specific gene involved at 8q24. The study was supported in part by grants to **Brian Henderson, M.D., of the University of Southern California; Kathleen Cooney, M.D., of the University of Michigan; and Alice Whittemore, Ph.D., of Stanford University.**

Freedman M, Haiman CA, Patterson N, McDonald GJ, Tandon A, Waliszewska A, Penney K, Steen RG, Ardlie K, John EM, Oakley-Girvan I, Whittemore AS, Cooney KA, Ingles SA, Altshuler D, Henderson BE, Reich D. Admixture mapping identifies 8q24 as a prostate cancer risk locus in African American men. Proc Natl Acad Sci USA. 2006 Sep 19;103(38):14068-73. Epub 2006 Aug 31.

InterLymph Identifies Genetic Variants Associated With Non-Hodgkin's Lymphoma

Nathaniel Rothman, M.D., M.P.H.

Increased risk of non-Hodgkin's lymphoma (NHL) has been observed in individuals with a family history of the disease or other hemopoietic cancers, suggesting that genetic susceptibility plays a role. In a study by the InterLymph Consortium, **Nathaniel Rothman, M.D., M.P.H., of NCI's Division of Cancer Epidemiology and Genetics** (DCEG), and colleagues hypothesized that single-nucleotide polymorphisms (SNPs) in genes important in lymphoid development and pro-inflammatory or anti-inflammatory pathways may be associated with increased risk of NHL.

This study included 3,586 cases of NHL and 4,018 controls from eight case-control studies participating in InterLymph. The researchers analyzed 12 SNPs in nine genes selected on the basis of previous functional or association data: *IL1A*, *IL1RN*, *IL1B*, *IL2*, *IL6*, *IL10*, *TNF*, *LTA*, and *CARD15*. They found that *TNF-308→A* and *IL10-3575T→A* were associated with an increased NHL risk, particularly diffuse large B-cell lymphoma. Other NHL studies that have investigated this *TNF* polymorphism and *IL10* polymorphisms were small and not population-based.

The research, which underscores the value of large consortia in identifying genetic associations, was supported in part by EGRP grants to **William Isaacs, Ph.D., of The Johns Hopkins University, and Kathleen Cooney, M.D., of the University of Michigan.**

InterLymph, short for the International Consortium of Investigators Working on Non-Hodgkin's Lymphoma Epidemiologic Studies, is an open scientific forum for NHL epidemiologic research that is comprised of international researchers with completed or ongoing case-control studies. Its Web site is *epi.grants.cancer.gov/InterLymph*.

Rothman N, Skibola CF, Wang SS, Morgan G, Lan Q, Smith MT, Spinelli JJ, Willett E, De Sanjose S, Cocco P, Berndt SI, Brennan P, Brooks-Wilson A, Wacholder S, Becker N, Hartge P, Zheng T, Roman E, Holly EA, Boffetta P, Armstrong B, Cozen W, Linet M, Bosch FX, Ennas MG, Holford TR, Gallagher RP, Rollinson S, Bracci PM, Cerhan JR, Whitby D, Moore PS, Leaderer B, Lai A, Spink C, Davis S, Bosch R, Scarpa A, Zhang Y, Severson RK, Yeager M, Chanock S, Nieters A. Genetic variation in TNF and IL10 and risk of non-Hodgkin lymphoma: a report from the InterLymph Consortium. Lancet Oncol. 2006 Jan;7(1):27-38.

Vaginal Washing Associated With Increased Risk of HIV

R. Scott McClelland, M.D., M.P.H.

Women who perform vaginal washing are at increased risk for acquiring HIV-1 compared to women who do not perform vaginal washing, according to a study by **R. Scott McClelland, M.D., M.P.H., of the University of Washington**, and colleagues. The researchers analyzed data from a 10-year study of risk factors for contracting HIV-1 among 1,270 sex workers in Kenya.

The increased risk applied to women who used either water or soap for vaginal washing. Women who used water to cleanse had a 2.6-fold increased risk for contracting HIV-1 compared to women who did not perform vaginal washing, and women who used soap had a 3.8-fold increased risk of infection. Furthermore, women who used soap or other substances were at greater risk (1.47-fold increased risk) of infection compared to women who used only water.

The researchers concluded that vaginal washing may be important in promoting the spread of HIV-1 and that intervention strategies aimed at modifying intra-vaginal practices should be evaluated as a possible female-controlled HIV-1 prevention strategy. The research was supported in part by an EGRP grant to **King Holmes, M.D., Ph.D., of the University of Washington.**

McClelland RS, Lavreys L, Hassan WM, Mandaliya K, Ndinya-Achola JO, Baeten JM. Vaginal washing and increased risk of HIV-1 acquisition among African women: a 10-year prospective study. AIDS. 2006 Jan 9;20(2):269-73.

Lessons Learned: MSI Testing Inconsistencies Reported by Six-Laboratory Consortium

Noralane Lindor, M.D.

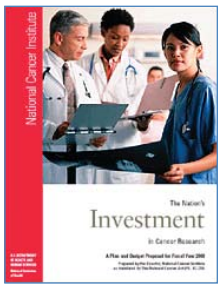
Microsatellite instability (MSI) testing is almost a standard part of the clinical evaluation of individuals who develop colorectal cancer at young ages or who have family histories suggestive of hereditary nonpolyposis colon cancer syndrome (HNPCC). Despite the high volume of MSI testing conducted clinically, no reports have been published on the agreement of MSI results among laboratories.

Noralane Lindor, M.D., of the Mayo Clinic, and colleagues compared MSI testing performed by six laboratories, all of which are part of the Colon Cancer Family Registry (CFR), and found discordant results with no evident systematic trends. Two laboratories with the longest experience in MSI testing showed a 99 percent concordance of the 100 loci tested, demonstrating that MSI scoring potentially is reproducible. After analysis of possible reasons for the discordance, each laboratory repeated its testing. Agreement of readings improved dramatically, which was attributed in large part to cleaner PCR products. Disregarding mononucleotide single base pair gains, concordance also was improved by greater use of equivocal readings, duplicate readings, and general refinement of MSI reading skills. DNA quality was not an issue.

The researchers proposed five key rules that laboratories should observe when conducting MSI testing. Dr. Lindor is principal investigator of one of the Registry sites. The Colon CFR is an EGRP-funded resource for investigators interested in conducting population- and clinic-based interdisciplinary studies on the genetic and molecular epidemiology of colon cancer. Its Web site is *epi.grants.cancer.gov/CFR*.

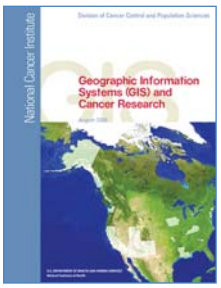
Lindor NM, Smalley R, Barker M, Bigler J, Krumroy LM, Lum-Jones A, Plummer SJ, Selander T, Thomas S, Youash M, Seminara D, Casey G, Bapat B, Thibodeau SN. Ascending the learning curve—MSI testing experience of a six-laboratory consortium. Cancer Biomarkers. 2006 Jul;2(1-2):5-9.

New NCI Publications



The Nation's Investment in Cancer Research: A Plan and Budget Proposal for Fiscal Year 2008. This publication describes NCI's strategies and plans to decrease the burden of cancer. It highlights scientific accomplishments and opportunities—from broad analyses of research trends to examples of targeted projects—and trends affecting current and future research, progress on NCI objectives, a description of NCI's infrastructure for implementing its objectives, and a proposed budget for Fiscal Year 2008. The annual document has been called the "Bypass Budget" because NCI submits its budget request directly to the President for review and transmittal to Congress. This report is available online at *plan.cancer.gov*. Print copies may be ordered from NCI's Publications Locator at *https://cissecure.nci.nih.gov/ncipubs*.

Geographic Information Systems (GIS) and Cancer Research. This publication provides information about how GIS can be used in cancer research, including to gain information about environmental exposures, monitor emerging trends for cancer control, look at health disparities, conduct research on behaviors, and provide the basis for health policy.



It describes applications for GIS technology in various areas of cancer research, describes GIS tools and resources, landmark GIS studies, and current funding opportunities in GIS with NCI's Division of Cancer Control and Population Sciences. The document is expected to be available in December via NCI's Publications Locator: *https://cissecure.nci.nih.gov/ncipubs*.

NCI Cancer Bulletin. New each week, NCI's online newsletter provides information about Institute programs and initiatives. Regular features include the NCI Director's update, information on funding opportunities, research highlights, legislative updates, interviews with important people in cancer research, and a calendar of meetings and presentations. Access the *Bulletin* and subscribe at *www.cancer.gov/ncicancerbulletin*.

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  Paul Brennan, Ph.D., M.S., International Agency for Research on Cancer

Sources of Information on Grant Policies, Funding, and Training

- Our NCI Division of Cancer Control and Population Sciences (DCCPS) Home page: *cancercontrol.cancer.gov* for grant policy alerts and information on funding opportunities.
- NCI Division of Extramural Activities (DEA): *deainfo.nci.nih.gov*
- *Grants.gov* (central resource to find and apply for U.S. grants)
- NIH Electronic Submission of Grant Applications Web site: *era.nih.gov/ElectronicReceipt/index.htm*
- Subscribe to:
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  - **NIH Extramural Nexus** (bimonthly newsletter for grantees, new in 2006): *grants.nih.gov/grants/nexus.htm*
  - **EGRP's Listserv** (occasional Bulletins, News Flashes) contact: *andersoL2@mail.nih.gov*
- NCI Research Resources (directory of more than 100 products and services): *resresources.nci.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** (2005). Access online at *www3.cancer.gov/admin/gab* or order a print copy via NCI's online Publications Locator: *https://cissecure.nci.nih.gov/ncipubs*. **(The publication 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*.)**