EGRP Research Highlights

Epidemiology and Genetics Research Program

Division of Cancer Control and Population Sciences (DCCPS)
Web Site: *cancercontrol.cancer.gov*

Contents

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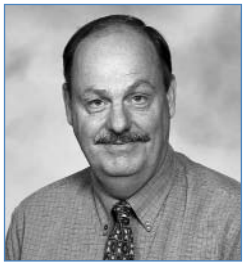
The Epidemiology and Genetics Research Program (EGRP) supports more than 400 grants and cooperative agreements annually. Investigators from throughout the United States and internationally are funded to conduct population-based research to increase our understanding of cancer etiology and prevention. Some recent research findings are highlighted in the following pages. The names of the Principal Investigators of the EGRP-supported grants cited in the published papers appear in boldface print.

Clues Found on Genetic Susceptibility for Aggressive Prostate Cancer



Stephen Thibodeau, Ph.D.

A variety of genetic epidemiologic studies are investigating how better to identify men at risk for aggressive prostate cancer. These studies have important implications for improving diagnosis and treatment and for identifying ways to prevent the disease. Previous research has suggested that chromosome 19q harbors a gene for prostate cancer aggressiveness. Research by **Stephen Thibodeau, Ph.D.**, of Mayo Clinic, and colleagues confirms this finding and provides strong evidence of the association. The scientists analyzed genome scan data from men in 161 families among whom there was a family history of prostate cancer. The study also suggested that chromosome 4q may be involved in tumor aggressiveness.

In other research, **Sara Strom, Ph.D.**, of The University of Texas M.D. Anderson Cancer Center, and colleagues found that the presence of a certain allele was strongly associated with younger age at diagnosis of prostate cancer. This "A" allele of the cell cycle regulating gene cyclin D1 also has been associated with early onset colorectal cancer and poorer prognosis for lung cancer. Still other research by **Richard Everson, M.D., Ph.D.**, of Wayne State University, and colleagues indicates that certain polymorphisms in the androgen receptor and in genes that influence androgen metabolism are associated with increased risk for being diagnosed with prostate cancer and with more aggressive disease.

Sara Strom, Ph.D.

Slager SL, Schaid DJ, Cunningham JM, McDonnell SK, Marks AF, Peterson BJ, Hebbring SJ, Anderson S, French AJ, Thibodeau SN. Confirmation of linkage of prostate cancer aggressiveness with chromosome 19q. Am J Hum Genet 2003 Mar;72(3):759-62.

Sanchez-Ortiz RF, Yamamura Y, Frazier ML, Babalan RJ, Troncoso P, Pettaway CA, Strom S. Relationship between cyclin D1 polymorphism and age at diagnosis of prostate cancer. Proc Annu Meet Am Assoc Cancer Res 2003.

Powell IJ, Land SJ, Zhou J, Sun Y, Dey J, Patel NP, Sakr WA, Hughes MR, Everson RB. Influence of androgen receptor and androgen metabolism polymorphisms on prostate cancer prognosis after prostactectomy in an ethnically diverse population. Proc Annu Meet Am Assoc Cancer Res 2003.

The Hunt for Prostate Cancer Susceptibility Genes Proves Difficult

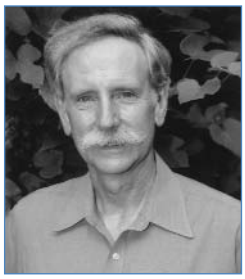
William Isaccs, Ph.D

Despite strong evidence for the existence of prostate cancer susceptibility genes, the search for such genes has been frustrating. The International Consortium for Prostate Cancer Genetics (ICPCG) demonstrates how difficult this research has been in a review of eight genome-wide linkage searches for chromosomal regions associated with development of the cancer. The ICPCG, with **William Isaacs, Ph.D.**, of Johns Hopkins University as principal investigator, is funded through a grant from EGRP. The review was based on 1,293 families with multiple cases of prostate cancer; but even with these numbers, no chromosomal region was found to be especially promising. Eleven linkage peaks with LOD scores in excess of 2 were identified, but no chromosomal region was reported as significant at this level by more than one study. Furthermore, only one of these linkage peaks corresponded to a peak previously suggested by another group.

The ICPCG's review shows that prostate cancer is genetically complex and that combined analyses of large family sets will be needed to evaluate reliably the linkage evidence. The consortium plans such analyses with a combined dataset on more than 2,000 families; which will provide the statistical power to detect genes of much smaller effect and allow a more reliable evaluation of subsets based on family history, disease aggressiveness, and co-occurrence of other types of cancer.

Easton DF, Schaid DJ, Whittemore AS, Isaacs WJ. Where are the prostate cancer genes?—A summary of eight genome wide searches. Prostate 2003 Dec 1;57(4):261-9.

More Evidence of Lycopene's Protective Effect in Prostate Cancer



Walter Willett, M.D.

Lycopene, a carotenoid in tomato products, may be more protective against sporadic prostate cancer than those cancers with a stronger familial or hereditary component, according to research by **Walter Willett, M.D.**, and **Edward Giovannucci, M.D., Sc.D.**, of Harvard School of Public Health, and colleagues. The strengths of this study include its prospective design, large sample size, and the combining of data on diet and plasma concentrations of various carotenoids for analyses. Previous studies have relied largely on estimated dietary intake or on single blood measurements of carotenoids. In this study, scientists found a statistically significant inverse association between higher plasma lycopene concentrations and lower risk of prostate cancer that was restricted to men who were over age 65 and men who did not have a family history of the cancer. The findings also suggested that diets rich in ß-carotene may protect against prostate cancer in younger men. The analyses are from a nested case-control study within the Health Professionals Follow-up Study (HPFS), which is a large cohort of male health professionals that was established in the 1980s. EGRP has funded the cohort since its beginning.

Edward Giovannucci, M.D., Sc.D.

Wu K, Erdman JW Jr, Schwartz SJ, Platz EA, Leitzmann M, Clinton SK, DeGroff V, Willett WC, Giovannucci E. Plasma and dietary carotenoids, and the risk of prostate cancer: A nested case-control study. Cancer Epidemiol Biomarkers Prev 2004 Feb 1;13(2):260-9.

Aspirin Use May Increase Risk for Pancreatic Cancer

Charles Fuchs, M.D., M.P.H.

Extended periods of aspirin use appear to be associated with increased risk for pancreatic cancer among women, according to a study by **Charles Fuchs, M.D., M.P.H.**, and **Graham Colditz, Dr. P.H., M.D.**, of Brigham and Women's Hospital and Harvard Medical School, and **Walter Willett, M.D.**, of Harvard School of Public Health, and colleagues. Women who had reported regularly taking aspirin for more than 20 years had a 58 percent increased risk, compared with women who never regularly consumed more than two aspirin tablets per day. Risk for the cancer increased with increasing aspirin dose. The finding is from the Nurses' Health Study, a large cohort of female nurses that was established in the 1970s and has been funded by EGRP since its beginning.

Schernhammer ES, Kang JH, Chan AT, Michaud DS, Skinner HG, Giovannucci E, Colditz GA, Fuchs CS. A prospective study of aspirin use and the risk of pancreatic cancer in women. J Natl Cancer Inst. 2004 Jan 7;96(1):22-8.

Electromagnetic Fields Not Associated With Risk for Breast Cancer

M. Cristina Leske, M.D., M.P.H.

M. Cristina Leske, M.D., M.P.H., of Stony Brook University, and colleagues found no indication that electromagnetic fields (EMFs) increase risk for breast cancer in a study that included comprehensive measurements of EMFs in and around the outside of the homes of study participants and data collected by interview. The findings offer reassurance to individuals who have been concerned about a possible link between EMFs and risk for breast cancer. The results are consistent with an earlier NCI-funded study of EMFs and breast cancer that included in-home measurements, adding further weight to the strength of the evidence.

Schoenfeld ER, O'Leary ES, Henderson K, Grimson G, Kabat GC, Ahnn S, Kaune WT, Gammon MD, Leske MC. Electromagnetic fields and breast cancer on Long Island: A case-control study. Am J Epidemiol 2003 July 158(1):47-58.

Estrogen Associated With Increased Risk for Breast Cancer in Asian Women

Herbert Yu, M.D., Ph.D.

Most epidemiologic studies on estrogen and breast cancer have been conducted in white populations. **Herbert Yu, M.D., Ph.D.**, of Yale University, and **Wei Zheng, Ph.D.**, of Vanderbilt University, and colleagues assessed the association in Asian women whose levels of estrogen are substantially lower than those of white women. They found that elevated sex hormones in the circulation, both estrogen and androgen, were associated with increased risk for breast cancer even in the Asian population with relatively low sex hormone levels. The finding suggests that the role of endogenous sex hormones in breast cancer is the same in the Asian population as in white women.

Wei Zheng, Ph.D.

Yu H, Shu XO, Shi R, Dai Q, Jin F, Gao YT, Li BD, Zheng W. Plasma sex steroid hormones and breast cancer risk in Chinese women. Int J Cancer 2003 May 20;105(1):92-7.

Obesity, Tamoxifen, and Outcomes With ER-Positive, Early Breast Cancer Examined

James Dignam, Ph.D.

James Dignam, Ph.D., of The University of Chicago, and colleagues have found that obesity is not associated with an increased risk of recurrence among women with early stage, hormone-responsive breast cancer and does not appear to decrease the effectiveness of the drug tamoxifen. The finding supports use of tamoxifen for women of all body types. Earlier studies suggested that risk for breast cancer recurrence and death was increased for obese women compared with lean women, but these studies included women with different stages of breast cancer. Obesity was found to be associated with increased risk for contralateral breast cancer, other new primary cancers, and overall mortality. The findings are from analysis of data on 3,385 women enrolled in a National Surgical Adjuvant Breast and Bowel Project (NSABP) randomized, placebo-controlled clinical trial (B-14) evaluating the effectiveness of tamoxifen following surgery for lymph node-negative, estrogen receptor (ER)-positive breast cancer.

Dignam JJ, Wieand K, Johnson KA, Fisher B, Xu L, Mamounas EP. Obesity, tamoxifen use, and outcomes in women with estrogen receptor-positive early-stage breast cancer. J Natl Cancer Inst 2003 Oct 1;95(19):1467-76.

Lobular Breast Carcinoma on the Increase

Janet Daling, Ph.D.

Research has suggested that combined estrogen and progestin hormone replacement therapy (CHRT) may be associated with increased risk for breast cancer, particularly invasive lobular breast carcinoma. The finding is noteworthy because lobular carcinoma is more difficult to detect by physical examination and mammography. **Janet Daling, Ph.D.**, of Fred Hutchinson Cancer Research Center, and colleagues report that incidence rates for lobular carcinoma increased steadily from 1987 to 1999 (the proportion increasing from 9.5 to 15.6 percent of all breast cancer cases), while rates for ductal carcinoma remained constant. The increase in rates for lobular carcinoma was most pronounced for women ages 50 and older.

In further research focusing on postmenopausal women, Daling and others found that the risk for invasive lobular breast carcinoma and other histologic types of breast cancer increased among women who were currently taking CHRT. Unopposed estrogen replacement therapy (ERT) was not associated with increased risk for any histologic type of

breast cancer. Neither CHRT nor ERT substantially increased the risk for ductal breast carcinoma. They also found that incidence rates for lobular carcinoma in situ have steadily increased over the past 25 years among postmenopausal women. These findings suggest the need for further research to explore reasons for these trends.

Li CI, Anderson BO, Daling JR, Moe RE. Trends in incidence rates of invasive lobular and ductal breast carcinoma. JAMA 2003 Mar 19;289(11):1421-4.

Daling JR, Malone KE, Doody DR, Voigt LF, Bernstein L, Coates RJ, Marchbanks PA, Norman SA, Weiss LK, Ursin G, Berlin JA, Burkman RT, Deapen D, Folger SG, McDonald JA, Simon MS, Strom BL, Wingo PA, Spirtas R. Relation of regimens of combined hormone replacement therapy to lobular, ductal, and other histologic types of breast carcinoma. Cancer 2002 Dec 15;95(12):2455-64.

Li CI, Anderson BO, Daling JR, Moe RE. Changing incidence of lobular carcinoma in situ of the breast. Breast Cancer Res Treat 2002 Oct;75(3):259-68.

Some Breast Cancers May Be Due to Inherited Susceptibility to Hormones at Puberty

Thomas Mack, M.D., M.P.H.

Thomas Mack, M.D., M.P.H., and Ann Hamilton, Ph.D., of the University of Southern California at Los Angeles, have found that certain breast cancers may be linked to an unusual inherited sensitivity to the ovarian hormones that flood the body at puberty. Among identical female twins who both were diagnosed with breast cancer, the twin who began menstruating earlier was more than five times as likely as the other twin to develop breast cancer first. Females who started menstruating before age 12 were especially susceptible to getting breast cancer first within the pair. In contrast, some of the well-known risk factors for breast cancer, such as late age at first pregnancy and at menopause, were associated with increased risk for breast cancer only among pairs of identical and fraternal twins in which one twin had breast cancer, but not among those in which both twins had the disease. These findings suggest that there may be another pathway to development of breast cancer that is related to genetic susceptibility. In some genetically susceptible women, elevated ovarian hormone levels at puberty might affect breast cells when they are still immature and vulnerable, and the damage may manifest itself as cancer decades later.

Hamilton AS, Mack TM. Puberty and genetic susceptibility to breast cancer in a case control study in twins. N Engl J Med 2003 Jun 5;348(23):2313-22.

Breast Cancer Receptor Status Varies by Risk Factor

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

Studies of risk factors for estrogen receptor (ER) status of breast cancer patients typically have considered only age or age and other risk factors one at a time. Many of these studies did not classify cases jointly for both ER and progesterone receptor (PR) status. **Graham Colditz, M.D., Dr.P.H.**, of Brigham and Women's Hospital and Harvard Medical School, and colleagues found that risk factors vary by hormone receptor expression of the breast cancer. They found heterogeneity among the four estrogen receptor and progesterone receptor categories (ER+/PR+, ER+PR-, ER-/PR-, ER-/PR+) for some breast cancer risk factors (e.g., age, menopausal status, body mass index after menopause) but not for others (e.g., benign breast disease, family history). Overall, the four categories of tumors based on receptor status showed different associations with age, pregnancy, history, postmenopausal hormone use, and body mass index after menopause. The findings argue for dividing breast cancer cases by tumor receptor status in estimating breast cancer risk. The analysis was based on data from the EGRP-funded Nurses' Health Study.

Colditz GA, Rosner BA, Chen WY, Holmes MD, Hankinson SE. Risk factors for breast cancer according to estrogen and progesterone receptor status. J Natl Cancer Inst 2004 Feb 4;96(3):218-28.

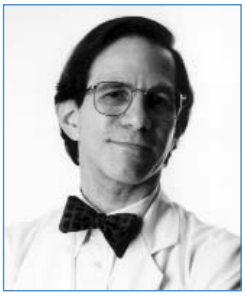
Loss of DNA Repair Capability in Colorectal Cancer Patients Increases With Age


Noralane Lindor, M.D.

The frequency of loss of expression of the DNA repair gene hMLH1 in colo-rectal cancer patients is strongly associated with increasing age, according to research by **Noralane Lindor, M.D.**, of Mayo Clinic, and colleagues. The loss was most pronounced in tumors of female patients and in tumors that originated on the right side of the colon. Loss of gene expression in right-sided tumors occurred in almost 50 percent of patients who were more than 90 years of age. The age-related trend also was seen in males and in tumors that originated in the left colon. The findings suggest the need for additional research on possible environmental or genetic reasons for the damage and the possibility of developing a non-invasive method to screen for the disease. The study population was drawn from the EGRP-funded Colon Cancer Family Registries.

Kakar S, Burgart LJ, Thibodeau SN, Rabe KG, Petersen GM, Goldberg RM, Lindor NM. Frequency of loss of hMLH1 expression in colorectal carcinoma increases with advancing age. Cancer 2003 Mar 15;97(6):1421-7.

Another Lead Found on Genetics of Familial Colorectal Cancer


Sanford Markowitz, M.D., Ph.D.

Research points to a chromosomal region responsible for forms of familial colorectal cancer unrelated to well-known hereditary forms of the disease. Familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC) account for about 5 percent of colorectal cancers, but an additional 20 percent of individuals with the cancer report having a first-degree relative with the disease. Whole genome scans were conducted to test for genetic linkage in 53 kindreds in which two or more siblings were diagnosed with colorectal cancer by age 65 or younger, or who had advanced colon adenomas of greater than 1 centimeter, or showed high-grade dysplasia. Kindreds with FAP, HNPCC, or other known hereditary forms of the cancer were excluded.

Sanford Markowitz, M.D., Ph.D., of Case Western Reserve University, and colleagues found that a single locus (9q22.2-31.2) can contribute to susceptibility in patients with familial colorectal cancer unrelated to known syndromes. Additional research is needed to determine whether the findings can be generalized to larger populations.

Wiesner GL, Daley D, Lewis S, Ticknor C, Platzer P, Lutterbaugh J, MacMillen M, Baliner B, Willis J, Elston RC, Markowitz SD. A subset of familial colorectal neoplasia kindreds linked to chromosome 9q22.2-31.2. Proc Natl Acad Sci 2003 Oct 28;100(22):12961-5.

Searching for Reasons for Elevated Rates of Colon Cancer Among African Americans


Jessie Satia-Abouta, Ph.D.

African Americans have the highest incidence rate for colon cancer among U.S. racial ethnic groups, and the reasons are largely unknown. The North Carolina Colon Cancer Study, which is a large case-control study with similar numbers of African Americans and whites, provides a unique opportunity to search for clues. **Jessie Satia-Abouta, Ph.D.**, and **Robert Sandler, M.D., M.P.H.**, of the University of North Carolina at Chapel Hill, and colleagues found that total energy intake consistently was positively associated with increased risk for colon cancer for both whites and African Americans. However, associations with individual macronutrients (fat, carbohydrate, protein) varied somewhat by race and adjustment for energy intake.


Robert Sandler, M.D., M.P.H.

For African Americans, saturated fat was associated with increased risk for colon cancer when risk estimates were not

adjusted for total energy intake, and dietary fiber was statistically significantly associated with reduced risk both with and without adjustment for total energy intake. These findings, coupled with those from an earlier study specific to African Americans, suggest that a high-fiber, low saturated fat diet may decrease risk for colon cancer for this group. For whites, when risk estimates were not adjusted for total energy, high intakes of total energy and most macronutrients were positively associated with increased risk for colon cancer, but the associations largely disappeared when total energy was taken into account. Alcohol intake was not associated with increased risk for colon cancer in either racial group.

In other analyses on this study population, vitamins E and C from food sources were associated with a reduction in risk for colon cancer among African Americans when comparing individuals with intake in the highest quartile to those in the lowest quartile. Beta-carotene, vitamin C, and calcium were associated with a reduction in risk for colon cancer among whites when comparing individuals in the highest to the lowest quartile. This research suggests that micronutrients may be independently associated with 30–70 percent reductions in risk for colon cancer in the two groups.

Satia-Abouta J, Galanko JA, Potter JD, Ammerman A, Martin CF, Sandler RS; North Carolina Colon Cancer Study. Associations of total energy and macronutrients with colon cancer risk in African Americans and whites: Results from the North Carolina Colon Cancer Study. Am J Epidemiol 2003 Nov 15;158(10):951-62.

Satia-Abouta J, Galanko JA, Martin CF, Potter JD, Ammerman A, Sandler RS. Associations of micronutrients with colon cancer risk in African Americans and whites: Results from the North Carolina Colon Cancer Study. Cancer Epidemiol Biomarkers Prev 2003 Aug;12(8):747-54.

BRCA1/2 Gene Mutations Do Not Increase Risk for Colorectal Cancer

Stephen Gruber, M.D., Ph.D., M.P.H.

People who have the BRCA1 and/or BRCA2 gene mutations that have been associated with increased risk for breast and ovarian cancer do not carry the same elevated level of risk for colorectal cancer, according to a study by **Stephen Gruber, M.D., Ph.D., M.P.H.**, of the University of Michigan Comprehensive Cancer Center, and colleagues. The scientists studied blood samples from patients with colorectal cancer and found the same number of BRCA gene mutations as found among controls without colorectal cancer. There also did not appear to be a link between family history of breast cancer and an individual having colorectal cancer. The study used a kin-cohort design to compare the incidence of colon cancer among relatives of BRCA1/2 founder mutation carriers among relatives of non-carriers.

Niell BL, Rennert G, Bonner JD, Almog R, Tomsho LP, Gruber SB. BRCA1 and BRCA2 founder mutations and the risk of colorectal cancer. J Natl Cancer Inst 2004 Jan 7;96(1):15-21.

GST Detoxifying Gene Variant Linked to Lung Cancer in Men, Younger Individuals

Xifeng Wu, M.D., Ph.D.

Research suggests that polymorphisms of glutathion transferases (GST), which are involved in detoxification of carcinogens, may alter the ability to detoxify and increase risk for certain cancers. Research by **Xifeng Wu, M.D., Ph.D.**, **Margaret Spitz, M.D., M.P.H.**, and **Waun Hong, M.D.**, of The University of Texas M.D. Anderson Cancer Center, and colleagues indicates that the GSTP1 exon 6 polymorphism is associated with increased risk for lung cancer especially in men, younger individuals, and ever smokers. This finding suggests that having the polymorphism may be an important genetic susceptibility factor. The scientists did not find the exon 5 polymorphism, which also has been implicated in lung cancer, to be associated with increased risk for the disease.

Wang Y, Spitz MR, Schabath MB, Ali-Osman F, Mata H, Wu X. Association between glutathione S-transferase p1 polymorphisms and lung cancer risk in Caucasians: A case-control study. Lung Cancer 2003 Apr;40(1):25-32.

DNA Repair Gene Polymorphisms and Cigarette Smoking Interaction Found


David Christiani, M.D.

David Christiani, M.D., of Harvard School of Public Health, and colleagues have published the first report demonstrating gene-smoking interaction between the joint effects of the DNA repair genes XRCC1 and ERCC2 and cumulative cigarette smoking exposure in risk for lung cancer. The magnitudes of these interactions appear to be associated with the number of variant alleles of the ERCC2 polymorphisms Asp312ASN and Lys751Gln and the XRCC1 Arg399Gln polymorphism. How cigarette smoking changes the DNA repair capability of the polymorphisms is not known.

Zhou W, Liu G, Miller DP, Thurston SW, Xu LL, Wain JC, Lynch TJ, Su L, Christiani DC. Polymorphisms in the DNA repair genes XRCC1 and ERCC2, smoking, and lung cancer risk. Cancer Epidemiol Biomarkers Prev 2003 Apr;12(4):359-65.

XPA Polymorphism Associated With Decreased Risk for Lung Cancer


Margaret Spitz, M.D., M.P.H.

Margaret Spitz, M.D., M.P.H., and **Waun Hong, M.D.**, of The University of Texas M.D. Anderson Cancer Center, and colleagues have shown that an XPA polymorphism modulates nucleotide excision repair (NER) capacity and is associated with decreased risk for lung cancer, particularly among ever smokers. Individuals with the A→G substitution in the 5´-end of the non-coding region had a reduced risk of lung cancer. This pattern was statistically significant for Caucasians and Mexican Americans, but not for African Americans.

Wu X, Zhao H, Wei Q, Amos CI, Zhang K, Guo Z, Qiao Y, Hong WK, Spitz MR. XPA polymorphism associated with reduced lung cancer risk and a modulating effect on nucleotide excision repair capacity. Carcinogenesis 2003 Mar;24(3):505-9.

Some Medications Associated With Decreased Risk of Non-Hodgkin's Lymphoma


Elizabeth Holly, Ph.D., M.P.H.

The incidence of non-Hodgkin's lymphoma (NHL) has been increasing steadily worldwide, and little is known about risk factors for the disease. Some studies have suggested that certain medications may have a protective effect against the cancer, but drug exposures were assessed in different ways in the studies. In research drawing upon the drug-dispensing records from community pharmacies and hospital records in the Netherlands, **Elizabeth Holly, Ph.D., M.P.H.**, of the University of California at San Francisco, and colleagues report an inverse relationship between occurrence of NHL and use of antihistamine medications (histamine2 blockers) and analgesics among women. They also found reductions in risk among women that were not statistically significant and may have been due to chance for other drugs studied. However, the inverse associations tended to increase with increasing duration of use of the drugs, suggesting reason for further study. The other drugs studied included nonsteroidal anti-inflammatory drugs, cholesterol-lowering drugs, and antibiotics.

Beiderbeck AB, Holly EA, Sturkenboom MC, Coebergh JW, Stricker BH, Leufkens HG. Prescription medications associated with a decreased risk of non-Hodgkin's lymphoma. Am J Epidemiol 2003 Mar 15;157(6):510-6.

Long-Term Use of Hair Dye Increases Risk of Non-Hodgkin's Lymphoma

Tongzhang Zheng, M.D., Sc.D

Long-term users of hair coloring products have an increased risk of developing non-Hodgkin's lymphoma (NHL), according to a study by **Tongzhang Zheng, M.D., Sc.D**., of Yale School of Medicine, and colleagues. The researchers found that women who used darker permanent hair coloring products for more than 25 years showed the highest increased risk. They also found that the risk of NHL associated with hair coloring product use appears to vary based on subtype of the disease. Previous studies on hair dye use and NHL have been contradictory and inconclusive. This is the first study to examine the impact of hair dye use with time period of use as a key factor.

Zhang Y, Holford TR, Leaderer B, Boyle P, Zahm SH, Flynn S, Tallini G, Owens PH, Zheng T. Hair-coloring product use and risk of non-Hodgkin's lymphoma: A population-based case-control study in Connecticut. Am J Epidemiol 2004 Jan 15;159(2):148-54.

Sunlight-Induced DNA Damage Associated With Increased Risk for Melanoma

Qingyi Wei, M.D., Ph.D.

Qingyi Wei, M.D., Ph.D., of The University of Texas M.D. Anderson Cancer Center, and colleagues have found that reduced DNA repair capability caused by ultraviolet light is associated with increased risk for melanoma. They also found a dose-response relationship between the DNA damage and risk for melanoma. This hospital-based case-control study is the largest and first epidemiologic study to show that reduced DNA repair capability may play a role in causation of sunlight-induced melanoma. Sunlight exposure, particularly intermittent bursts of exposure early in life, is directly associated with risk for melanoma. A relatively small proportion of individuals exposed to sunlight develop melanoma, however, suggesting that genetic susceptibility plays a role in causation of the cancer.

Wei Q, Lee JE, Gershenwald JE, Ross MI, Mansfield PF, Strom SS, Wang LE, Guo Z, Qiao Y, Amos CI, Spitz MR, Duvic M. Repair of UV light induced DNA damage and risk of cutaneous malignant melanoma. J Natl Cancer Inst 2003 Feb 19;95(4):308-15.

Explanation Found for HPV 16's Strong Association With Cervical Cancer

Howard Strickler, M.D., M.P.H.

Human papillomavirus (HPV) 16, which is responsible for about one-half of all cervical cancers, appears to be more successful in escaping immune surveillance than other HPV types. The findings may explain why HPV 16 plays a major role in causing cervical cancer. **Howard Strickler, M.D., M.P.H.**, of the Albert Einstein College of Medicine, and colleagues compared the prevalence and incidence of different HPV types among HIV-positive women who had varying levels of T cells, an indicator of immune status.

Strickler HD, Palefsky JM, Shah KV, Anastos K, Klein RS, Minkoff H, Duerr A, Massad LS, Celentano DD, Hall C, Fazzari M, Cu-Uvin S, Bacon M, Schuman P, Levine AM, Durante AJ, Gange S, Melnick S, Burk RD. Human papillomavirus type 16 and immune status in human immunodeficiency virus-seropositive women. J Natl Cancer Inst 2003 Jul 16;95(14):1062-71.

Mononucleosis Related to Epstein-Barr Virus and Risk for Hodgkin's Lymphoma

Mads Melbye, M.D., Ph.D.

Infectious mononucleosis related to infection with Epstein-Barr virus (EBV) is associated with an increased risk for Hodgkin's lymphoma in young adults. This finding is from a study of more than 60,000 young adults in two Danish cohorts of patients who tested positive for infectious mononucleosis. **Mads Melbye, M.D., Ph.D.**, of the Statens Serum Institut in Copenhagen, and colleagues found no evidence of an increased risk of EBV-negative Hodgkin's lymphoma following infectious mononucleosis. However, there was a 4-fold increased risk of EBV-positive Hodgkin's lymphoma after infectious mononucleosis. The estimated median incubation time from mononucleosis to diagnosis of EBV-positive Hodgkin's lymphoma was 4.1 years.

This study makes a convincing connection among infectious mononucleosis, EBV, and the development of Hodgkin's disease. The risk of Hodgkin's disease after infectious mononucleosis is low—about 1 case per 1,000 persons with EBV-related mononucleosis—suggesting that other cofactors are involved.

Hjalgrim H, Askling J, Rostgaard K, Hamilton-Dutoit S, Frisch M, Zhang JS, Madsen M, Rosdahl N, Konradsen HB, Storm HH, Melbye M. Characteristics of Hodgkin's lymphoma after infectious mononucleosis. N Engl J Med 2003 Oct 2;349(14):1324-32.

Oncogenic Human Papilloma Virus Infection and Progression to Cervical Cancer

Eduardo Franco, Dr.P.H.

Precursor lesions of the cervix detected by cytology persist longer and are more likely to progress in women who have oncogenic types of human papilloma virus infections (HPV) than in women with non-oncogenic types of HPV infections or in uninfected women. These findings reported by **Eduardo Franco, Dr.P.H.**, of McGill University, and colleagues suggest that testing for HPV in women who have abnormal PAP smears may help identify patients who would benefit from more intensive follow-up and chemopreventive treatment. Other patients might be followed at longer intervals and potentially could avoid invasive diagnostic and therapeutic procedures.

Schlecht NF, Platt RW, Duarte-Franco E, Costa MC, Sobrinho JP, Prado JC, Ferenczy A, Rohan TE, Villa LL, Franco EL. Human papillomavirus infection and time to progression and regression of cervical intraepithelial neoplasia. J Natl Cancer Inst 2003 Sep 3;95(17):1336-43.

Clinic-Based Designs Give More Accurate Penetrance Estimates

Alice Whittemore, Ph.D.

Alice Whittemore, Ph.D., and Gail Gong, Ph.D., of Stanford University School of Medicine, used computer simulations to compare the performance of two study designs based on family data for estimating the disease risk associated with mutations of known disease-susceptibility genes. The scientists found that clinic-based designs, where families are ascertained because they meet certain criteria for multiple disease occurrence in the family, yielded more accurate estimates than did population-based designs, where families are sampled through population-based registries of affected individuals. The reason may be that clinic-based designs include more identified mutation carriers. The study was conducted with assistance from the EGRP-funded Cancer Family Registries.

Gong G, Whittemore AS. Optimal designs for estimating penetrance of rare mutations of a disease susceptibility gene. Genet Epidemiol 2003 Apr;24(3):173-80.