ABSTRACTS
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The following are the 16 highest-scoring abstracts of those submitted for presentation at the 32nd Annual ASPO meeting to be held March 16-18, 2008 in Bethesda, MD.

DNA Hypermethylation Phenotypes and One Carbon Metabolism Genetic Variants in Breast Tissues from Normal Healthy Women

Dumitrescu RG, Marian C, Krishnan SS, Spear SL, Kallakury BVS, SeillierMoiseiwitsch F, Ressom H, Freudenheim J, Shields PG

One common alteration in breast tumors is hypermethylation of tumor suppressor gene promoters. In this study, we examined potential determinants of DNA hypermethylation in normal breast tissue, including genetic variants for genes important to one-carbon metabolism in relation to hypermethylation. We recruited 141 women without a history of breast or other cancers, who were undergoing reduction mammoplasty. Hypermethylation phenotypes for p16 INK4, BRCA1, ERα and RAR-β in normal breast tissues were determined by MSP and Pyrosequencing assays. Genetic variants of MTHFR and MTR genes were determined by TaqMan assays. Chi-square, *t* tests and logistic regression model were used to determine the association between promoter hypermethylation of these genes and genotypes and other characteristics of these women. The mean age of women was 35+/−12 years. p16 INK4, BRCA1 and ERα promoter hypermethylation was identified in 31%, 16% and 9% of women respectively. Hypermethylation of the RAR-β gene was not detected for any of the women. The mean age for women with p16 INK4 hypermethylation was 37.3+/−15 and those without was 33.8+/−11. p16 INK4 hypermethylation was significantly associated with race (*P*-value = 0.02), alcohol consumption during lifetime (*P*-value = 0.05) and marginally associated with the number of children (*P*-value = 0.07). Family history of cancer was associated with p16 INK4 and BRCA1 hypermethylation (*P*-value = 0.03 and *P*-value = 0.009 respectively). Furthermore, family history of breast cancer was associated with BRCA1 and ERα hypermethylation (*P*-value = 0.09 and *P*-value = 0.01). There was a weak association of MTR 2756G allele with p16 INK4 hypermethylation status (*P*-value = 0.08). The presence of hypermethylation of important tumor suppressor genes was a common finding in healthy women without history of breast cancer. Several known risk factors for breast cancer increase the risk of hypermethylation, as do genetic variants for MTR gene. Understanding the determinants of hypermethylation in normal breast tissues can provide insight into a potentially significant mechanism for breast carcinogenesis.

Risk of Second Breast Cancer According to Hormone Therapy Use Among Women with carcinoma *in situ* of the Breast

Trentham-Dietz A, Newcomb PA, Nichols HB, Hampton JM

Women diagnosed with breast carcinoma *in situ* (BCIS) often face difficult decisions regarding use of postmenopausal hormone replacement therapy (HRT) and anti-estrogen therapy. Although relative survival after a diagnosis of BCIS is nearly 100%, BCIS is a strong risk factor for a subsequent invasive breast cancer. We examined HRT and tamoxifen use in a cohort of women diagnosed with BCIS during 1997-2004. All women (N = 1,293) were interviewed by telephone after diagnosis and also every 2 years during 2003-2006. Interviews collected risk factor, breast diagnosis, and treatment information. Pathology reports were obtained to confirm subsequent *in situ* and invasive breast cancer diagnoses. The median age at the initial diagnosis of BCIS was 56.0 years (range 26-74). Risk of a subsequent breast cancer diagnosis was evaluated by hazard ratios (HR) and 95% confidence intervals (CI) from proportional hazards models adjusted for age, education, mammography use prior to diagnosis, family history of breast cancer, and type of surgery at the initial diagnosis. After an average follow-up of 5.8 years, 94 (7%) second breast cancer diagnoses were confirmed including 52 (55%) BCIS and 42 (45%) invasive breast cancers. Compared to women that used neither HRT nor tamoxifen, use of both pre-diagnosis HRT and post-diagnosis tamoxifen was associated with a reduced risk of subsequent breast cancer (HR = 0.24, 95% CI 0.10-0.58). Other combinations of use (HRT prior to the initial diagnosis without tamoxifen after diagnosis; tamoxifen use without pre-diagnosis HRT use; HRT both before and after the initial diagnosis) were not strongly associated with risk of subsequent breast cancer (HR = 0.63, 95% CI 0.35-1.13; HR = 0.72, 95% CI 0.33-1.54; and HR = 0.78, 95% CI 0.27-2.22, respectively). Although HRT use increases risk of a first BCIS diagnosis, these results suggest that pre-diagnosis use of HRT followed by tamoxifen use after diagnosis is strongly associated with disease-free survival.

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Do Aspirin and Other NSAIDs Lower Risk of Breast Cancer?
Bardia A, Ebbert JO, Vierkant RA, Wang AH, Olson JE, Limburg P, Anderson K, Cerhan JR

Purpose: To examine the association of aspirin and other NSAID use with breast cancer incidence and its ER and PR subtypes.

Methods: Iowa Women's Health Study is a prospective cohort study of postmenopausal women. Aspirin, and other NSAID use was reported on a self-administered questionnaire (1992; N = 26,577). Breast cancer incidence (including ER/PR status) through 12 years of follow-up was ascertained by annual linkage to the Iowa SEER Cancer Registry. Cox proportional hazards models were used to estimate multivariate relative risks (RRs) and 95% confidence intervals (CIs) of breast cancer incidence, adjusting for other breast cancer risk factors.

Results: During 288,864 person-years of follow-up, 1492 incident cases of breast cancer were observed. Compared to aspirin never users, women who regularly consumed aspirin had a lower risk of breast cancer (RR = 0.80, 95% CI: 0.71-0.91). Higher frequency of use was associated with lower risk (RR = 0.73, 95% CI: 0.62-0.86, for aspirin use 6 or more times/week versus never use; *P* trend = 0.0007). The inverse association was virtually identical across all subtypes defined by ER or PR status. In contrast, use of other NSAIDs was not associated with breast cancer incidence (RR = 1.00, 95% CI: 0.89-1.12), irrespective of frequency of use or ER or PR status of the tumor.

Conclusions: Aspirin, but not other NSAID use, was associated with a lower risk of breast cancer, irrespective of it's ER/PR subtype, suggesting that the protective effects of aspirin are not directly related to estrogen or progesterone signaling pathways.

Obesity, Weight Gain, and CML Risk
Strom SS, Gruschkus SK, Rivas SD, Cortes JE

Little is known regarding the etiology of chronic myelegenous leukemia (CML). Some evidence suggests that obesity influences risk of other myeloid malignancies. We conducted a hospital-based case control study of 253 cases and 270 controls to determine the impact of obesity and weight gain on CML risk. Cases were diagnosed at MD Anderson Cancer Center from 1999-2006. Controls matched on age, sex, and ethnicity were recruited among individuals accompanying patients to outpatient clinics (excluding leukemia/lymphoma clinics). The mean age of cases was 48 years (range 16-83); 52% were male. The ethnic distribution was 82% white, 10% Hispanic, 7% African American, and 1% Asian. A multiple logistic regression analysis adjusting for family history and ionizing radiation/agrichemical exposure demonstrated an independent dose-response effect for mild (BMI 30-35 kg/m2) and moderate/severe obesity (BMI>35 kg/m2) (OR 2.05; 95%CI 1.20-3.50 and OR 3.24; 95%CI 1.64-6.37, respectively, *P*-trend <0.001). In a separate model evaluating weight gain, gaining > = 1 kg/year from age 25-40 was associated with increased risk (OR 3.63; 95% CI 1.46-9.04) after adjusting for weight at age 25 and other confounders. Results from this study suggest that obesity and weight gain during early adulthood may modulate CML risk.

Physical Activity, White Blood Cell Count, and Lung Cancer Risk in a Prospective Cohort Study
Sprague BL, Trentham-Dietz A, Klein BEK, Klein R, Cruickshanks KJ, Lee K, Hampton J

Studies have suggested that physical activity may lower lung cancer risk. The association of physical activity with reduced chronic inflammation provides a potential mechanism. We evaluated the relation between physical activity, inflammation, and lung cancer risk in a prospective cohort of 4,831 subjects, 43-86 years of age, in Beaver Dam, Wisconsin. A total physical activity index was created by summing episodes of sweat-inducing physical activity per week, city blocks walked per day, and flights of stairs climbed per day, as ascertained by interview. Two inflammatory markers, white blood cell count and serum albumin, were measured at the baseline examination. During an average of 12.8 years of follow-up, 134 cases of lung cancer were diagnosed. Risk of lung cancer was reduced by over 40% among participants with a total activity index greater than 13 (OR = 0.56, 95% CI: 0.35-0.90) compared to inactive participants. Participants with white blood cell counts in the upper tertile (≥8000/uL) were 2.81 (95% CI: 1.58-5.01) times as likely to develop lung cancer as those with counts in the lowest tertile (<6400/uL). Serum albumin was not related to lung cancer risk. There was no evidence that inflammation mediated the association between physical activity and lung cancer risk, as the physical activity risk estimates were essentially unchanged after adjustment for white blood cell count. These data suggest that physical activity and white blood cell count are independent risk factors for lung cancer.

Smoking Susceptibility Predicts Experimentation Among Mexican-American Girls and Boys
Spelman A, Spitz M, Kelder S, Frankowski R, Wilkinson A

Susceptibility to smoking is defined as the lack of a firm commitment not to smoke in the future or if offered a cigarette by a friend. Few studies have examined the risk factors of susceptibility and experimentation among Hispanic adolescents, although they are twice as likely to be susceptible compared to other racial/ethnic groups. This study examined susceptibility at baseline as a predictor of experimentation after one year of follow-up, along with several psychosocial variables, among 1,035 Mexican-American (MA) adolescents age 11-13 who had never smoked. The overall susceptibility and experimentation rates at follow-up were 28% and 9%, respectively. Girls and boys who were susceptible at baseline were 4.2 and 3.1 times more likely to experiment after one year compared to their non-susceptible peers. Girls were more likely to experiment if they lived with someone (other than a parent or sibling) who currently smokes. Boys were more likely to experiment if they had a high level of acculturation, had a father who currently smokes, endorsed ''kids think smoking is cool'' and had received at least one detention in school. Based on these data, susceptibility is the best marker for experimentation for MA adolescents. Identifying risk factors associated with susceptibility will aid in the development of more effective and targeted smoking prevention programs in this population. NCI, R01CA105203, M Spitz, PI.

The Influence of Polymorphisms in Cytokine Genes on Response to Analgesia in Lung Cancer Patients Referred for Palliative Treatment: TNF- -308 G/A, IL-6 -174 G/C, and IL-8 -251T/A

Reyes-Gibby CC, El Osta B, Spitz M, Parsons H, Kurzrock R, Shete S, Bruera E

We previously reported the importance of polymorphisms in cytokine genes in the epidemiology of cancer-related pain. We now explore the extent to which functional variations in cytokine genes, e.g.,tumor necrosis factor-alpha (TNF á-308 G/A), interleukin (IL) -6 -174G/C, and IL-8 -251T/A, could explain variability in analgesic response in patients referred to palliative care specialists for pain treatment and control. Pain severity (0 = no pain; 10-worst pain) was assessed at initial consultation and at first follow-up visit in 140 white patients with non-small cell lung cancer of all stages and histologies. Total dose of opioids taken over the past 24 hours at the time of first-follow up visit was converted to an equivalent dose of parenteral morphine. We genotyped TNF á-308 G/A, IL 6 -174G/C, and IL-8 -251T/A and determined their associations with opioid consumption. Results showed 41% (57/140) reported severe pain (score >7/10) at initial consultation (mean = 5.5; median = 6; mode = 7), which significantly decreased to 25% (mean = 4; median = 4; mode = 2) at first follow-up visit (McNemar tests = $P < 0.01$). Univariate analyses showed IL6 was significantly associated with high Morphine Equivalent Daily Dose (75th percentile >120 mg/24H; $P < 0.004$). Controlling for demographic and clinical variables, logistic regression analyses showed that carriers of the IL6-174C/C [Odds Ratio = 4.7; 95% CI = 1.2; 15.0] received higher doses of morphine. We found preliminary evidence of the influence of cytokine genes on response to analgesia in lung cancer patients. Our findings need to be validated in large prospectively accrued populations with incorporation of additional genetic markers in the cytokine pathway.

Racial Differences in Pancreatic Cancer Sood P (1), Henson DE (2), Schwartz AM (3), Grimley PM (4), Patierno S (5) Department of Epidemiology and Biostatistics (1), Cancer Insitute (2, 5), and Department of Pathology (3), The George Washington University, Washington DC, and Department of Pathology (4), Uniformed Services University of the Health Sciences, Bethesda MD.

Purpose: To describe the epidemiology of racial differences in pancreatic cancer.

Methods: Data were obtained from NCI's SEER Program for the years 1973-2004. There were 8,245 cases of pancreatic cancer in Blacks and 63,903 in Whites. Cases were compared by linear and by log-log plots of the age specific incidence rates versus the age of diagnosis. The two main histological tumor types of the pancreas, ductal epithelial carcinomas and endocrine tumors, were considered. Rates are expressed as cases per 100,0-00 persons.

Summary: Of the two main pancreatic tumor types, ductal epithelial carcinomas comprise >97% and endocrine tumors <3%. The rate of ductal epithelial carcinoma was significantly higher in Black men (19.1) than in White men (13.2) and significantly higher in Black women (14.8) than in White women (9.7). These higher rates have been consistent for 31 years. The median age of diagnosis was 68 for Blacks and 72 for Whites. In every age group, the age specific rate was higher in Blacks than in Whites. Log-log plots revealed parallel linear rate patterns for both racial groups. The rate of endocrine tumors, which have a different etiology than ductal carcinomas, was also higher in Blacks (0.30) than in Whites (0.23).

Conclusions: Blacks are more susceptible to pancreatic ductal epithelial carcinomas and to endocrine tumors than are Whites. Cancers of the same histological pattern and cell of origin having similar log-log graphical patterns among Blacks and Whites suggest a similar age related carcinogenesis. Reasons for the greater susceptibility of Blacks to pancreatic cancer relative to Whites are unclear.

Is Stroke a Late Effect of Chemotherapy?

Geiger AM, Camacho F, Krajenta R, Buist DSM, Bernstein L, for the Cancer Research Network Chemo-Stroke Study Team, Wake Forest University, Henry Ford Health System, Group Health Cooperative

Purpose: To examine the association of chemotherapy with stroke one year or more after cancer diagnosis.

Background: Chemotherapy is a critically important, life-saving cancer treatment, yet has been associated with adverse effects, such as stroke, long after treatment ends. However, available data are inadequate to support adjustments to treatment or risk reduction efforts in cancer survivors.

Methods: We used the Cancer Research Network's Virtual Data Warehouse to gather cancer registry, utilization, pharmacy and enrollment data at four integrated healthcare delivery systems for adults diagnosed with hematopoietic or invasive solid cancer (bladder, female breast, colorectal or ovary). Cox proportional hazards models were used to explore the association of chemotherapy with stroke one year or more after the cancer diagnosis, adjusting for demographic characteristics and delivery system; cancer type and treatment; and history of thromboembolic disease, hypertension and diabetes.

Results: Of 37,355 eligible patients, 44.1% were aged 65 years or older, 74.5% were female and 23.5% were non-white. The overall multivariable adjusted hazard ratio (HR) for the association between chemotherapy and stroke was 0.89 (95% confidence interval [CI] = 0.77-1.04). The association differed for hematopoietic (HR = 1.38, CI = 1.05-1.81) and solid tumors (HR = 0.76, CI = 0.63-0.90). Specifically, chemotherapy for non-Hodgkin's lymphoma appeared to increase stroke risk (HR = 1.5, CI = 1.05-2.39), while chemotherapy appeared to be unassociated with or decrease stroke risk when given for colorectal (HR = 0.78, CI = 0.60-1.01), ovarian (HR = 0.51, CI = 0.24-1.10), or breast cancer (HR = 0.67, IC = 0.51-0.89).

Conclusions: These results suggest that the association between chemotherapy and stroke is complicated and likely varies by chemotherapeutic agent. Healthier individuals may be more likely to receive chemotherapy for some conditions, and this may explain the associations that appear protective.

Global DNA Methylation Level in Normal Breast Tissue: Associations with Demographics, Lifestyle Exposures and One Carbon Metabolism Genes SNPs
Marian C*, Dumitrescu RG*, Seillier-Moiseiwitsc F, Millen A, Nie J, Freudenheim J, Shields PG

Global DNA hypomethylation is thought to be a common and early epigenetic event in breast carcinogenesis. There are few data regarding global DNA methylation in normal breast tissue and what factors are associated with it. We investigated the association with demographic factors, smoking and alcohol drinking and polymorphisms in two genes of the one carbon metabolism pathway. Tissue was collected from 57 Caucasian and 53 African American women without history of breast cancer, undergoing reduction mammoplasty surgery. Data on demographics (age, race, BMI, menopausal status, age at first birth, number of children, number of pregnancies, income, and family history of cancer) and life style exposures (smoking and alcohol drinking) were collected. SNPs genotyping for MTHFR C677T and A1298C, and MS A2756G was done by real time PCR allelic discrimination. Global DNA methylation was assessed by LINE-1 pyrosequencing. Comparisons were made with non-parametric one-way analyses of variance by ranks. Global methylation level range was 65.34-82.78%, mean 73.87%, median 73.30% and SD 4.60%. Global methylation was positively associated with current smoking status, a history of drinking, family history of cancer, income level, and the presence of the variant allele of the MS (A2756G) genotype and marginally associated with race and being ever pregnant. When stratified by race, the associations were not significant for African-Americans. For Caucasians there were significant associations with family history of cancer, income and with variant alleles in MS (A2756G) and MTHFR (A1298C), and a marginal association with current smoking status. Our study suggests that lifestyle factors may influence the level of DNA methylation especially in Caucasian women. Further, genetic variation in one-carbon metabolism may also have an influence on DNA methylation in Caucasians. The association with family history of cancer could possibly be an indicator of a heritable epigenetic trait. Understanding factors related to DNA methylation may provide insight into the prevention and etiology of breast cancer.
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African American and Caucasian Women's Knowledge and Attitudes toward BRCA1/2 Genetic Counseling and Testing
Graves KD, Sheppard VB, Denis-Cooper LC, Montalvo BK, Boisvert ME, Schwartz MD

We evaluated the impact of individual, socio-cultural, and systemic variables on knowledge and attitudes about BRCA1/2 counseling/testing to explore factors related to BRCA1/2 testing disparities between African Americans and Caucasians. We conducted telephone interviews with 105 women with a negative breast biopsy history and 1 or more relatives with breast/ovarian cancer (n = 75 Caucasian, n = 30 African American). We assessed demographics, cancer history, perceived risk, worry, medical mistrust, cancer fatalism, family/physician communication, race- and SES-based experiences, and knowledge and attitudes toward BRCA1/2 testing. We examined predictors of knowledge and attitudes with backward linear regressions, entering variables associated at the bivariate level with each outcome. The initial model for knowledge included: education, income, perceived risk, medical mistrust, cancer fatalism, family communication, and race. Final predictors of knowledge were higher: education (β = 0.21, P = 0.03), perceived risk (β = 0.24, P = 0.02) and family communication (β = 0.23, P = 0.02). Race did not predict knowledge. The initial model for attitudes included: family communication, perceived risk, income, and race. Final predictors of a more positive attitude toward BRCA1/2 testing were lower perceived risk (β = −0.26, P = 0.02) and higher family communication (β = 0.20, P = 0.05). Race did not predict attitudes. Relationships among knowledge, attitudes, and BRCA1/2 testing uptake have been explored in prior research, and disparities exist between African Americans and Caucasians in testing uptake. Present results indicate knowledge and attitudes did not differ between African American and Caucasian women after controlling for demographic and socio-cultural variables. Family communication and perceived risk were predictive of both knowledge and attitudes. Continued exploration of the impact of individual, socio-cultural, and systemic variables on actual BRCA1/2 counseling/testing uptake will further elucidate reasons for testing disparities between African Americans and Caucasians.

Promoter Methylation of Prostate Cancer Specific Genes in low-income African American Adults
Papaiahgari S, Ford JG, Lee M, Brait M Loyo, Begum S, Hoque MO

Purpose: Aberrant promoter hypermethylation of several known or putative tumor suppressor genes (TSGs) occurs frequently in the pathogenesis of several cancers, including prostate cancer. African Americans and individuals of low socioeconomic status (SES) are at increased risk of developing prostate cancer. Promoter methylation in GSTP1, APC, CCND2, MGMT, p16 and RARβ has been associated with an increased probability of developing prostate cancer. We conducted a pilot study to determine the prevalence of promoter hypermethylation in these genes in a sample low SES African Americans.

Experimental Design: The promoter methylation status of the above genes was examined by high throughput quantitative fluorogenic real-time polymerase chain reaction (PCR) using serum DNA from a convenience sample of 98 African Americans from Baltimore City (32 current smokers; 30 former smokers and 36 lifetime nonsmokers; 50% of participants reported < 16,000 family income for the past 12 months).

Results: The promoter methylation frequency of these genes was GSTPi 2 (2%) APC 8 (8.2%), CCND2 25 (25.5%), MGMT 10 (10.2%), P16 9 (9.2%) RARb 33 (33.7%). Methylation of at least one gene was detected in 46/98 (47%), two genes 15/98 (15%), three genes 7/98 (7.4%) and four 4/98 (4%). Our initial analysis identified the gene P16 has 12% of methylation in smokers compared to 3% of methylation in non-smokers.

Conclusion: The high prevalence of promoter hypermethylation in the above TSGs in a high-risk study population raises the question about the potential utility of this panel of methylation markers in prostate cancer detection.

Ovarian as a Subsequent Primary Cancer Among Women Cancer Survivors, 1973-2004
Rim S, Berkowitz B, Peipins L

Background: Ovarian cancer is the leading cause of mortality among gynecological malignancies. Identifying persons at increased risk of ovarian cancer can be important for early detection and better chances of survival. Studies have shown certain cancer survivors may be at increased risk of developing a subsequent primary ovarian cancer. We examined the risk of ovarian cancer as a second primary diagnosis among women cancer survivors using data from the Surveillance, Epidemiology and End Result (SEER) program.

Methods: Cancer incidence data from 9 SEER registries were used to identify women diagnosed with a first primary invasive cancer from 1973 to 2004. We calculated the relative risk [observed (O)/expected (E)] of a second primary ovarian cancer by first cancer site, age at first cancer diagnosis (<50, 50+), and latency (0 to <5, 5 to <10, 10 to <20, 20+ years) since the first primary cancer.

Results: Among 3,341 cancer survivors, more than 40% were diagnosed with a subsequent primary ovarian cancer within the first 5 years since their first primary cancer diagnosis. Women <50 years of age at first primary diagnosis had significantly (P < 0.05) increased risk of ovarian cancer 0 to <5 years after initial diagnosis with cancers of the breast (O/E = 2.5, 95% CI: 2.1-3.0), corpus uteri (O/E = 6.8, 95% CI: 5.1-9); colon (O/E = 5.9, 95% CI: 3.7-8.9); and cervix uteri (O/E = 3.4, 95% CI: 2.2-5.1). Breast cancer survivors had continuously higher than expected risk of ovarian cancer beyond 5 years (O/E ≥ 2.0). For women diagnosed with breast cancer, increased risk was also observed among those age ≥ 50 years within 5 years after diagnosis (O/E = 1.1, 95% CI: 1-1.2). However, older women (age ≥ 50) were at a significantly decreased risk following cancers of the corpus uteri (O/E = 0.2, 95% CI: 0.1-0.3) and colon (O/E = 0.7, 95%).

The Importance of Updating the Family History of Cancer Survivors
Madlensky L, Wasserman L, Parker B, Pierce JP; for the WHEL study group

Purpose: To determine how the prevalence of ''high risk'' cancer family histories changes over time in cancer patients.

Methods: Breast cancer survivors in the WHEL study provided detailed family history data at baseline and again at study closure. The Myriad prevalence tables were used to categorize survivors as ''high risk'' or ''not high risk''.

Results: At baseline, 8.2% of 2508 survivors were classified as high risk. At follow-up (avg. 7.5 years later), an additional 5.8% of women became high risk due to new cancers in their families. Among high-risk survivors, 15% reported that they had never heard of BRCA testing. Of the 85% who had heard of testing, 23% reported that they had been tested.

Conclusions: The prevalence of ''high risk'' cancer family histories increased by 70% in a cohort of breast cancer survivors over 7.5 years. It is important for clinicians to identify high-risk families not only at initial diagnosis, but to update the family history periodically. A substantial proportion of high-risk women had never heard of BRCA testing, and could benefit from genetic counseling to discuss the cancer risk in their families.

Predictors of Prostate and Colorectal Cancer Screening Adherence Among Men Registered for Prostate Cancer Screening
Red S, Davis KM, Schwartz MD, Williams RM, Ahaghotu C, Taylor KL

Colorectal cancer screening (CRCS) is recommended for those >50, while prostate cancer screening (PCS) remains controversial. However, national surveys have shown that men are more likely to undergo PCS than CRCS, and that this difference is associated with demographics, history of cancer, and health behaviors. We assessed whether this differential screening rate existed among men registered for free PCS, and whether the predictors of adherence were similar to national samples. We included baseline variables from a trial of a PCS decision aid: demographics, health behaviors, psychological factors (e.g., perceived risk, QOL, knowledge). Participants included men over 50 registered for PCS at Georgetown University (GU; N = 259) and Howard University (HU; N = 114). Across both samples, average age was 59.3 (SD = 5.4), 55% were African American, 51.7% had > a college degree, and 67.8% had a regular doctor. PCS adherence was defined as having a PSA/DRE in the past 13 months and CRCS adherence was defined as having had one of four screening exams within the recommended timeframe. More men were adherent for CRCS (50.4%) than PCS (44.5%; P < 0.001); however, more men reported ever having PCS (82%) than CRCS (55.5%; P < 0.001). Significant bivariates were included in logistic regression analyses. PCS adherence was greater among men who: were adherent for CRCS (OR = 2.3, CI 1.4, 3.8), had a regular doctor (OR = 1.9, CI 1.1, 3.5), were from GU (OR = 2.7, CI 1.5, 4.8), and had never smoked (OR = 2.1, CI 1.02, 4.3). CRCS adherence was greater among men who: were adherent for PCS (OR = 2.5, CI 1.5, 4.1), had a regular doctor (OR = 3.6, CI 2.0, 6.4), had health insurance (OR = 2.0, CI 1.04, 3.9), and had a previous cancer diagnosis (OR = 4.2, CI 1.02, 17.5). Compared to several national samples, we found slightly lower PCS adherence and higher CRCS adherence. However, predictors of both PCS and CRCS adherence were consistent with previous studies. We did not find evidence that psychological factors played a role in adherence among this group of men seeking PCS in a mass screening setting.

Mitochondrial DNA Somatic Mutations and Content Change in Buccal Cells of Smokers

Tan DJ, Chen JG, Goerlitz DS, Dumitreascu R, Orden RA, Goldman R, Shields PG

mtDNA is particularly susceptible to damage by mutagens. mtDNA alterations are believed to play a role in carcinogenesis, and are found in smoking-related cancers. Thus, we hypothesize that mtDNA damage would be a good biomarker of tobacco smoke exposure. We sought to replicate earlier findings for the association of smoking with increased mtDNA content in buccal cells, and further hypothesized that there would be an increased number of somatic mtDNA mutations in smokers. Buccal cells and blood lymphocytes were studied from 42 healthy smokers and 30 non-smokers. temporal temperature gradient electrophoresis screening and sequencing was used to identify mtDNA mutations. The relative mtDNA content was determined by real-time PCR. Assuming that mtDNA in lymphocytes represent the inherited sequence, it was found that 31% of smokers harbored at least one somatic mtDNA mutation in buccal cells with a total of 39 point mutations and 8 short deletions/insertions. In contrast, only 23% of nonsmokers possessed mutations with a total of 10 point mutations and no insertions/deletions detected. MtDNA somatic mutation density was higher in smokers (0.68/10,000 bp/person) than in nonsmokers (0.2/10,000 bp/person). There was a statistically significant difference in the pattern of homoplasmy and heteroplasmy mutation changes between smokers and non-smokers. While nonsmokers had the most mutations in D-loop region (70%), smokers had mutations in both mRNA encoding gene (36%) and D-loop region (49%). The mean ratio of buccal cells to lymphocytes of mitochondrial DNA content in smokers was increased (2.81)when compared with nonsmokers (0.46). In addition, a low positive correlation between ratio of buccal cells/lymphocytes mtDNA content and smoking status has been observed. These results suggest that cigarette smoke plays an important role in the increase in mtDNA mutation in the buccal cells of smokers. The estimation of an individual's risk could be perhaps improved by coupling of mitochondrial mutations to other markers for tobacco smoke associated disease risk. [Supported by NCI contract HHSN261200644002 and in part by FAMRI Clinical Innovator Award 052444 to RG].