opment of lung cancer. Cigarette smoke can cause DNA damage through formation of Reactive Oxygen Species (ROS). 8-hydroxyguanine (8-OHG) is one of the major oxidative lesions and repaired by 8-oxoguanine DNA glycosylase (OGG1) which plays an important role in Base Excision Repair (BER) system. 8-OHG is highly mutagenic and, if not excised /repaired on DNA replication, can cause GC to TA transversion mutations. Several studies have been published on the association between lung cancer and OGG1 Ser326Cys polymorphism with conflicting results. Thus, in this study, it was aimed to investigate the relation between OGG1 Ser326Cys polymorphism and the risk of lung cancer and to measure the levels of urinary 8-OHdG as a biomarker of oxidative DNA damage. One hundred sixty-five subjects with lung cancer and 250 healthy control subjects were genotyped by Restriction Fragment Length Polymorphism-Polymerase Chain Reaction (RFLP-PCR) for OGG1 Ser326Cys polymorphism. No association between OGG1 Ser326Cys polymorphism and the risk of lung cancer was found. It was also measured urinary 8-OHdG levels by ELISA immunoassay in patients who did no received any chemotherapy and radiotherapy and healthy control subjects. There was no significant difference between patients and control subjects in urinary 8-OHdG levels.

405 GENE-ENVIRONMENT INTERACTION BETWEEN HOGG1 SER326CYS POLYMORPHISM AND SMOKING ON LUNG CANCER SUSCEPTIBILITY.

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The DNA repair enzyme human oxoguanine glycosylase 1(hOGG1) is responsible for repairing the oxidative DNA base damage 8-hydroxyguanine and recent studies have indicated that the Ser326Cys hOGG1 polymorphism may be associated with an increased risk of lung cancer. However, no interaction effect on lung cancer risk have ever been evaluated between the hOGG1 gene polymorphism and smoking. In the present study we investigated interaction between the hOGG1 Cys/Cys genotype and smoking on lung cancer susceptibility in 1568 Japanese lung cancer patients in a case-only study design. The patients were asked about smoking by means of a self-administered questionnaire, and blood samples were collected to determine their hOGG1 genotype. A statistically significant interaction odds ratio (ORi) between the hOGG1 Cys/Cys genotype and the smoking status of 40 or more pack-years was observed on the risk of squamous cell carcinoma plus small-cell carcinoma (ORi, 4.53, 95 % CI, 1.24-16.58) in women, but not in men (ORi, 0.73, 95 % CI, 0.43-1.26). Although it was not statistically significant, the ORi for all lung cancer was also higher in women than in men. These results suggest that excess risk in female smokers could result from reduced hOGG1 activity due to the hOGG1 Cys/Cys genotype.

406 GENETIC RISK FACTORS IN PROGRESSIVE MASSIVE FIBROSIS IN COAL MINERS.

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Progressive massive fibrosis (PMF) is a chronic interstitial lung disease with a complex etiology. Cytokines, growth factors and cell-surface adhesion molecules play crucial roles in the pathogenesis of pulmonary fibrosis by mediating inflammation, fibroblast proliferation, angiogenesis, and collagen synthesis. A case-control study was conducted to test the hypothesis that single nucleotide polymorphisms (SNPs) within genes involved in inflammatory and fibrotic processes modulate the risk of PMF development. The study population consisted of 648 underground coal miners with demographic information submitted to the National Coal Workers Autopsy Study (NCWAS). SNPs, which influence the regulation of interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha (TNFα), transforming growth factor beta-1 (TGFβ1), vascular endothelial growth factor (VEGF), intercellular cell adhesion molecule-1 (ICAM-1), and matrix metalloproteinase-2 (MMP-2) genes, were determined using a 5'-nuclease real-time PCR assay from autopsy lung tissue DNA. There were no significant differences in the distribution of any individual SNP or haplotype between the PMF and control groups. However, the polygenotype of VEGF +405/ICAM +241/-IL6 -174 (C-A-G) conferred an increased risk for PMF. These data suggest that single variants of cytokine and fibrogenic genes are unlikely to strongly influence susceptibility to PMF, although the role of VEGF, ICAM-1, and IL-6 polymorphisms in the development of PMF may require further investigation.

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407 RELATIONSHIP BETWEEN ARSENIC-SKIN LESIONS AND THE MET287THR POLYMORPHISM IN AS3MT GENE.

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AS3MT is the key enzyme in inorganic arsenic (iAs) metabolism. AS3MT catalyses the formation of methyl-As (MAs) and dimethyl-As (DMAs) metabolites from iAs. The exonic 14458 C>T (Met287Thr) and intronic 30585 C>T polymorphic variants of the AS3MT gene have been associated with altered profiles of iAs metabolism, specifically, with lower DMAs/MAs ratios in urine of individuals exposed to iAs or *in vitro* systems involving cultured cells or recombinant AS3MT variants. Previous studies have linked increased proportions of MAs in urine to a higher risk of adverse health effects. However, the direct association between the two AS3MT polymorphisms and susceptibility to iAs exposure has never been examined. We have conducted a cross-sectional study involving 122 residents of an iAs- endemic area in Mexico to investigate the potential association between the M287T and 30585 polymorphisms and the occurrence of skin lesions, the marker of chronic As toxicity. AS3MT polymorphisms were evaluated by real-time PCR and urinary As species were quantified by hydride generation atomic absorption spectroscopy (HG-AAS), using a cryotrap for trapping and separation of arsines. A marginally significant difference in the M287T genotype frequency was observed between individuals with and without skin lesions (P=0.07). The risk of developing skin lesions tended to be higher in subjects with the variant genotypes (14458 CT/TT) as compared to wild-type homozygote CC genotype: OR=4.04 (95% CI 0.95-17.3). However this difference was only marginally significant: p=0.055. The 30585 polymorphism was not associated with the presence of skin lesions. Our data suggest that the AS3MT-M287T polymorphism may be associated with an increased susceptibility to adverse effects of iAs exposures. However, further studies in larger populations are needed to study this association. This study was supported by Conacyt grant 50097

408 AMINOLEVULINIC ACID DEHYDRATASE (ALAD) POLYMORPHISM IS ASSOCIATED WITH BLOOD LEAD LEVEL AND HYPERTENSION IN THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY (NHANES III).

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Background: Environmental lead exposure has been associated with an increased risk of hypertension. Few studies have addressed the role of aminolevulinic acid dehydratase (ALAD) polymorphism to influence the effect of lead exposure on hypertension. Methods: We examined the role of ALAD polymorphism in the relationship between hypertension and lead exposure using the data of the National Health and Nutrition Examination Survey (NHANES III). Results: The prevalence of hypertension was 22.8% (n=1695). Among persons with and without hypertension the mean blood lead was 3.72 and 2.78 ug/dl, respectively. The prevalence of ALAD2 carriers was 14.7% and 13.4% for people with and without hypertension, respectively. The mean blood lead of ALAD2 carriers was 3.77 ug/dl and 2.53 ug/dl, whereas ALAD1 homozygous carriers had a mean blood lead of 3.73 ug/dl and 2.81 ug/dl in people with and without hypertension, respectively. Regression analysis stratified by lead quartile showed that in the highest lead quartile (>3.8 ug/dl) ALAD 2 carriers had a higher prevlence of hypertension than ALAD1 homozygous carriers (p= 0.0208). The adjusted odds ratios (by race, sex, age, education, smoking status, alcohol intake, body mass index, serum creatinine, serum total calcium and glycated hemoglobin) for ALAD2 carriers was 1.83 (95%CI; 1.11-3.03). Conclusions: Our findings suggest that genetic variation of ALAD is associated with the effect of lead on hypertension.

409 GENETIC VARIANTS IN FOUR METAL-REGULATORY GENES IN AUTISM.

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Autism is a common neurodevelopmental disorder with both genetic and environmental components. Genetic susceptibility to mercury (Hg) toxicity has been advanced as an explanation for autism in a subset of children and has become a widely held public belief. In this model, even "safe" Hg levels could be implicated in the

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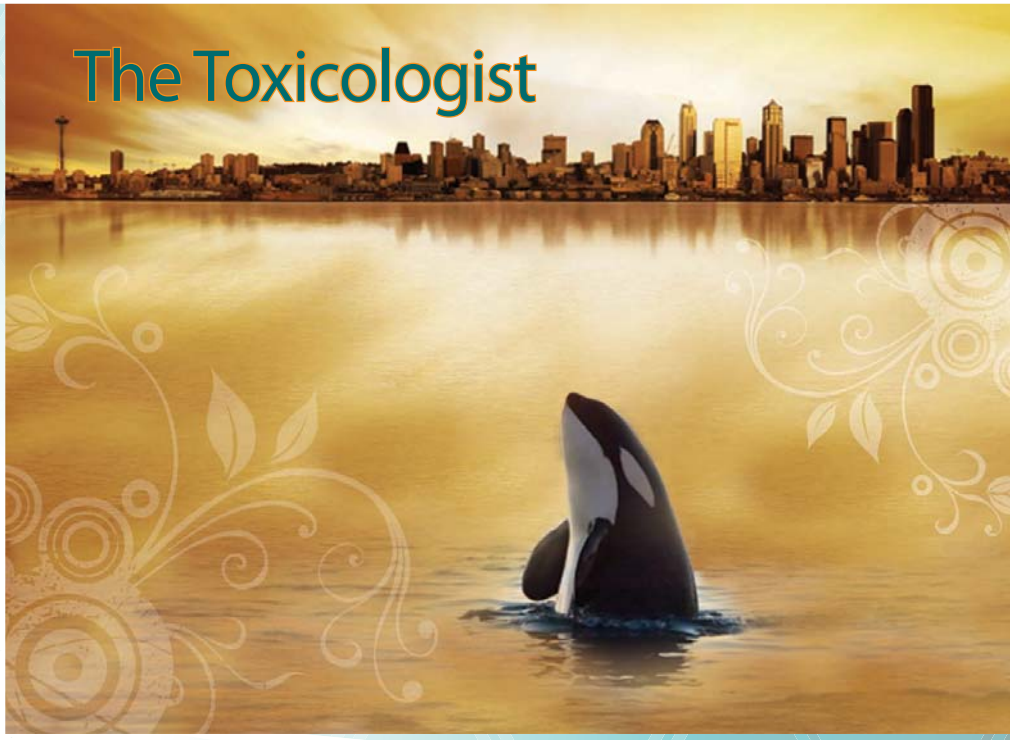

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