these subjects ranged from 3.5 to 90 ng/kg and were negatively associated with AhR mRNA in unstimulated peripheral blood mononuclear cells (p=0.03). When mitogen-induced lymphocytes were cultured with 10nM TCDD, all AhR-dependent genes were induced 1.2 to 3-fold. In these cells, plasma TCDD was associated with decreased EROD activity. In addition, there was a strong positive correlation between AhR and CYP1A1 expression (p=0.001) and between AhR and CYP1B1 expression (p=0.006). CYP1A1 expression was also strongly correlated with EROD activity (p=0.001). Four CYP1B1 polymorphisms and related haplotypes were studied. Both CYP1B1 genotypes, particularly the CYP1B1*3 allele, and CYP1B1 haplotypes significantly reduced CYP1B1 expression inducibility after cell culture with in vitro TCDD (p=0.04, t-test comparing CYP1B1 expression in the consensus genotype versus the expression in subjects with any CYP1B1 genotype variant; and chisquare=10.37, p=0.006, Pearson's analysis comparing the inducibility of CYP1B1 expression between all variant CYP1B1 haplotypes versus the CYP1B1*1 haplotype). CYP1A1, GSTM1, and GSTT1 genotypes were not significantly associated with CYP1A1 expression and EROD activity. The analysis of the expression of dioxin-inducible genes involved in carcinogenesis may help in determining dose-response relationships for human exposure to dioxin in vivo and in assessing the variability of human response, which may indicate the presence of subjects more susceptible to disease as a result of such exposures. We are grateful to Andrew Bergen , PhD, Core Genotyping Facility, NCI, for his contribution in the haplotype analysis.

#6399 *Myb*-DNA binding inhibited by herbicides *in vitro*. Larry W. Figgs and Jimmy D. Page. *Saint Louis University School of Public Health, St. Louis, MO and Biacore, Inc., Piscataway, NJ.*

Introduction: Although some herbicides are potential chemical carcinogens and epidemiologic evidence suggests that they are associated with lymphomas, the peripheral blood lymphocytes of people exposed to some herbicide show no evidence of chromosomal damage or mutations, but may show changes in cell cycle kinetics. To explore a potential pathway to herbicide-induced cell cycle deregulation, we examined changes in molecular interactions between *Myb*, a transactivating oncoprotein that regulates G1/S transition in dividing cells, and its DNA consensus-sequence binding site. *Methods* : We used electrophoresis mobility shift assays (EMSAs) to separate *Myb*-bound and free DNA from 30μl assays containing 1.0μg of custom 50mer oligonucleotides with a single *Myb* binding site sequence (AACGG), 2 ng of *Myb*, and varying dilutions ($1:10^2$ - $1:10^8$ assay dilution) of commercially available herbicides in phosphate buffered saline incubated overnight at 2 °C. Gels were stained with a fluorescent nucleic acid stain, exposed to ultraviolet radiation, and band luminosity was quantified by image analysis. Sigmoidal regression models were used to predict binding throughout each herbicide's dilution range. Using surface plasmon resonance (SPR) spectroscopy to observe herbicide-specific influences on dynamic *Myb*-DNA molecular interactions, we measured and compared association (k_a), dissociation (k_d), and equilibrium (K_D) rate constants of *Myb* and our custom oligonucleotide with herbicides (diluted 1:500) and without herbicide present. *Results* : Image analysis of EMSA gels showed that 2,4-DLV4® decreased *Myb*-DNA binding at a final assay dilution of $1:10^5$, Tordon RTU® decreased *Myb*-DNA binding at a $1:10^6$ final assay dilution, and Roundup® decreased *Myb*-DNA binding following a $1:10^3$ final assay dilution. SPR analysis of *Myb*-DNA interactions showed that the three herbicides modified the k_a, k_d, or K_D rate constants when present at a 1:500 assay dilution. *Conclusion* : Commercially available 2,4-D LV4®, Tordon RTU®, and Roundup® may modify *Myb*-DNA molecular interactions *in vitro* at concentrations ranging from $1:10^3$ to $1:10^6$ assay dilution.

#6400 Farm exposure to individual pesticides and glioma in men. Avima M. Ruder, Martha A. Waters, Tania Carreon, Mary Ann Butler, Geoffrey M. Calvert, Karen E. Davis-King, Paul A. Schulte, Wayne T. Sanderson, Elizabeth M. Ward, L. Barbara Connally, Ellen F. Heineman, Jack S. Mandel, Roscoe F. Morton, Douglas J. Reding, Kenneth R. Rosenman, and Glenn Talaska. *National Institute for Occupational Safety and Health, Cincinnati, OH, National Cancer Institute, Rockville, MD, University of Minnesota, Minneapolis, MN, Mercy Medical Center, Des Moines, IA, Marshfield Clinic National Farm Med. Ctr., Marshfield, WI, Michigan State University, East Lansing, MI, and University of Cincinnati, Cincinnati, OH.*

An excess incidence of brain cancer in farmers has been noted in several studies. The Brain Cancer Collaborative Study Group conducted the Upper Midwest Health Study to evaluate associations between rural exposures and brain cancers among adult (18-80) male and female rural residents in Iowa, Michigan, Minnesota and Wisconsin, where brain cancer incidence is significantly elevated. Histologically confirmed intracranial glioma cases (458 men) diagnosed January 1, 1995, through January 31, 1997, were identified from hospitals, medical practices, and cancer registries. Controls (648 men) were stratified samples of licensed drivers (ages 18-64) and Health Care Finance Administration enrollees (ages 65-80) residing in rural counties of each state. In-person interviews with participants or proxies collected farm, occupational, and other exposure information. Participants who lived on a farm where a pesticide was used were classified as exposed to that pesticide; those who reported personally handling a pesticide on the farm were classified as users. A NIOSH reference database, with over 800 trade names whose active ingredients have been identified, was used to convert pesticide trade name responses to generics. The frequency of farm use of generics was used to identify pesticides to which at least 100 participants (men and women) reported exposure. Multivariate logistic regressions controlled for farm residence and for age since controls were older. Those exposed to or using farm pesticides were compared with the 128 controls and 125 cases who had no farm, home and garden, or occupational pesticide exposure. Exposure to any farm pesticide was associated with lower glioma risk: adjusted odds ratio (OR) 0.54, 95% confidence interval (CI), 0.36-0.83. There was no association between farm residents' exposure to alachlor, cyanazine, diazinon, dicamba, glyphosate, metolachlor, pendimethalin, or trifluralin, and glioma risk. There were negative statistically significant associations between glioma risk and farm residents' exposure to 2,4-D, atrazine, DDT, and malathion. Use of any farm pesticide also was associated with lower glioma risk: OR 0.51, CI, 0.33-0.80. Personal use of pesticides on the farm was significantly lower among cases than controls for 2,4-D, alachlor, atrazine, cyanazine DDT, dicamba, malathion, and metolachlor. Results for analyses excluding proxy respondents (47% of cases) did not differ significantly. Evidence has been shown for pesticides crossing the blood-brain barrier and for pesticide central nervous system neurotoxicity. However the evidence for pesticide carcinogenicity in the brain is not strong. In our study, no positive association of farm pesticide exposure or use and glioma risk was found. Other farm exposures, which will be analyzed in future papers, may explain the excess brain cancer risk seen in previous studies of rural residents.

#R6401 Farm exposure to pesticides and glioma in women. Tania Carreon, Mary Ann Butler, Avima M. Ruder, Martha A. Waters, Karen E. Davis-King, Geoffrey M. Calvert, Paul A. Schulte, L. Barbara Connally, Elizabeth M. Ward, Wayne T. Sanderson, Ellen F. Heineman, Jack S. Mandel, Roscoe F. Morton, Douglas J. Reding, Kenneth R. Rosenman, and Glenn Talaska. *National Institute for Occupational Safety and Health, Cincinnati, OH, National Cancer Institute, Rockville, MD, University of Minnesota, Minneapolis, MN, Mercy Medical Center, Des Moines, IA, Marshfield Clinic, Marshfield, WI, Michigan State University, East Lansing, MI, and University of Cincinnati, Cincinnati, OH.*

An excess incidence of brain cancer in male farmers has been noted in several studies, but few studies have focused on women. This study evaluated the association between pesticide exposure and brain cancer among adult (18-80) female rural residents in Iowa, Michigan, Minnesota and Wisconsin, states where brain cancer incidence is significantly elevated. Since hormonal factors may play a role in the development of brain tumors, the effect of pesticides reported as endocrine disruptors was also evaluated. Histologically confirmed intracranial glioma cases (n=341) were identified from hospitals and medical practices. Controls (n=528) were stratified samples of rural residents who were licensed drivers (ages 18-64) and Health Care Finance Administration enrollees (ages 65-80). In-person interviews collected farm, occupational and other exposure information. Participants exposed to pesticides resided on farms where pesticides were used; participants who used pesticides personally handled them. A National Institute for Occupational Safety and Health database was used to convert pesticide trade name responses to generics. Pesticides to which ≥100 participants (either gender) reported exposure were identified. Logistic regression models adjusted for farm residence and

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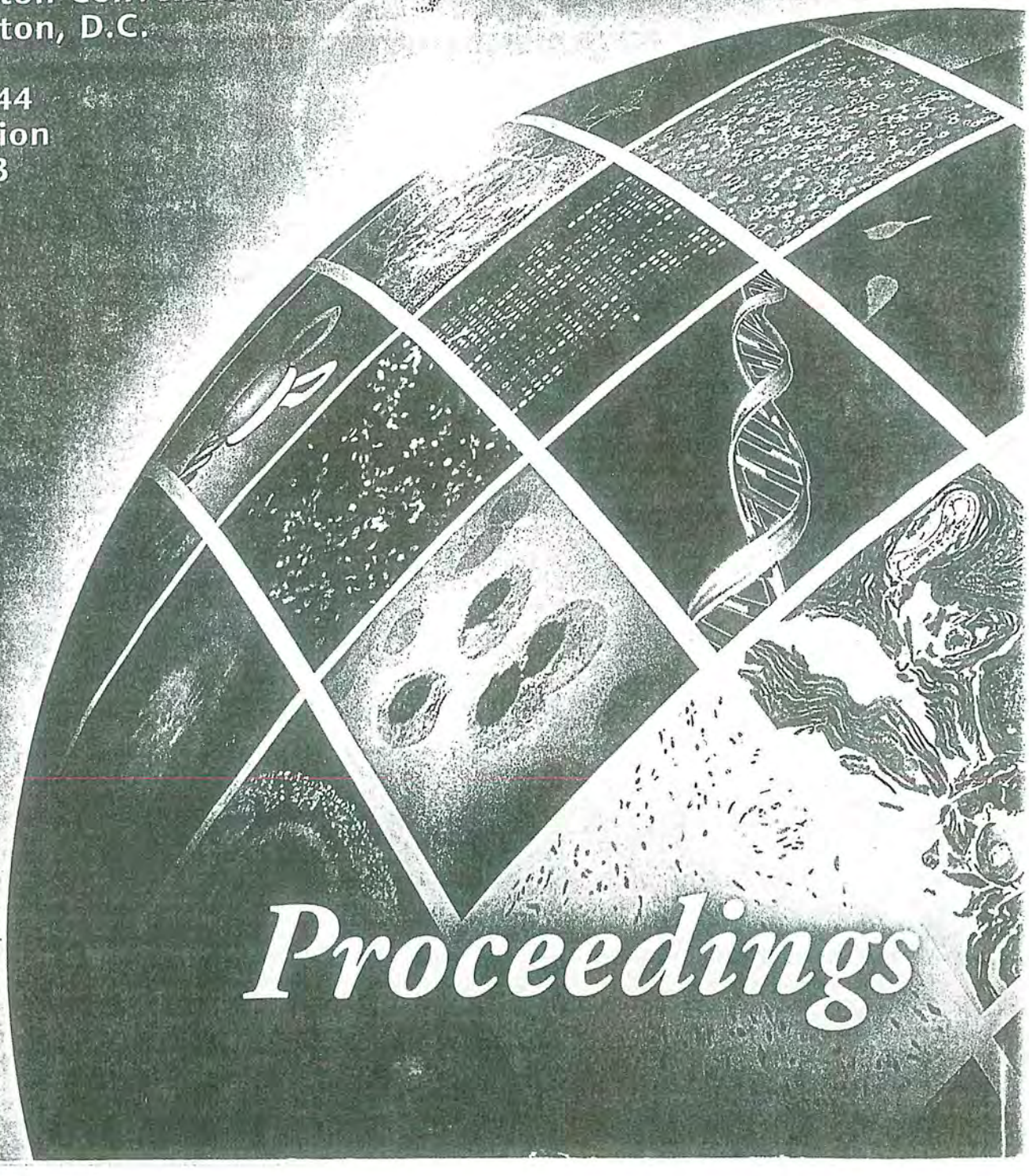
Volume 44
2nd Edition
July 2003



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