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PROTEOMIC ANALYSIS OF SERUM FROM WORKERS EXPOSED TO BENZENE

Roel Vermeulen¹, Qing Lan¹, Laura Gunn², Marielena McGuire³, Diane McCarthy³, Guilan Li⁴, Luoping Zhang², Nathaniel Rothman¹, Martyn T. Smith²

¹Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, DHHS, Bethesda, MD; ²University of California at Berkeley, Berkeley, CA, ³Ciphergen Biosystems, Inc., Fremont, CA, and ⁴National Institute of Occupational Health and Disease Control, CDC, Beijing, China

Study of proteomes in humans exposed to potentially toxic compounds may facilitate the identification of new biomarkers of exposure and early biologic effects. Benzene is an established human hematotoxin and leukemogen and readily forms protein adducts. As such, it is an excellent candidate to explore possible exposure - related proteome changes. We carried out a pilot study among 10 workers exposed to benzene and 10 controls to determine if their proteome patterns differed. Serum samples were selected from a cross-sectional study in China among workers in a shoe manufacturing factory with mean benzene air levels > 20 ppm and from unexposed controls. Serum samples were fractionated over anionic exchange spin columns coupled to robotic preparation. Six fractions were collected and the three fractions with the majority of the protein/peptides were (fraction 1: 50 mM Tris-HCL, 0.1% OGP pH 9, fraction 4: 100 mM Na Acetate, 0.1% OGP pH4, and fraction 6: 33.3% isopropanol/16.7% acetonitrile/0.1% trifluoroacetic acid). The three fractions were profiled on the following ProteinChip® array surfaces: WCX, H50 and IMAC-Cu with SELDI-TOF-MS detection. Differences in average peak intensity were tested using the non-parametric test of mean (Mann Whitney statistic). In total about 1000 protein peaks were identified. After manual relabeling (re-labeled 300 peaks) 18 peaks were identified with final p-values of less than 0.01 for the differences in mean ranks between the exposed and unexposed subjects. Given the high likelihood of false positive findings due to low prior probabilities that any given protein would be affected by benzene exposure and multiple comparisons, only proteins with a p-value less than or equal to 0.0001 were considered possibly associated with benzene exposure (N=3). The three identified proteins were relatively small (< 8 kDA) and average intensity was decreased among exposed subjects for all three proteins. If these proteins can be successfully identified and are shown in a larger sample size to be correlated with benzene exposure, this will provide support for the use of proteomics to further understanding of the potentially toxic effects of exposure to xenobiotic compounds.