A GENE-ENVIRONMENT INVESTIGATION OF MERCURY BIOMARKERS VIA EPIDEMIOLOGICAL AND IN VITRO APPROACHES

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The risk assessment of Hg is complicated due to innate variation underlying mercury biomarkers. Recent findings suggest that gene-environment interactions may help explain some of this variation given that several genes mediating the toxicokinetics and toxicodynamics of Hg are highly polymorphic in humans. Here we hypothesize that single nucleotide polymorphisms (SNPs) in key glutathione, metallothionein, and selenoprotein genes underlie inter-individual differences in Hg body burden as assessed by analytical biomarker analysis of urine and hair. Associations were explored in two cohorts and in an *in vitro* model. First, a population of 515 dental professionals was recruited during the 2009 and 2010 Michigan Dental Association (MDA) Annual Conventions. Samples of urine (biomarker for inorganic Hg) and hair (organic Hg) were collected, and total Hg content was measured. Average urine (1.1±1.2 μg/L) and hair (0.5±0.7 μg/g) Hg levels were similar to national averages from the National Health and Nutrition Examination Survey (NHANES). Information on dietary fish consumption and potential confounders were obtained from questionnaires. Taqman assays were used to genotype DNA from buccal swab samples at 20 polymorphic sites in genes implicated in Hg metabolism (e.g. GCLC-129, SEPP1-234, MT1A-27). An initial analysis of this dataset using t-tests reveals that GSTP1-105 and SEPP1-234 may significantly impact the Hg biomarker results (i.e., modify the relationship between fish consumption and hair mercury levels). Second, ~400 mother-child pairs were sub-sampled from the 16+ year ELEMENT (Early Life Exposure in Mexico to Environmental Toxicants) cohort study. Mean children's blood Hg (1.65μg/L) was about 3x higher than values reported in NHANES, though hair Hg (0.50μg/L) and urine Hg (0.96μg/L) was similar. Blood and hair Hg were about 2-fold higher in individuals that carried two GSTP1 minor allele SNPs. Results from another 20 SNPs will be summarized. For both human cohorts, trends were observed concerning genetic influences on hair-blood ratios and the relationship between fish consumption and hair biomarkers, and these are currently being subjected to in-depth multilinear regression modeling. Third, we have developed an in vitro (*E. coli*) model that harbors two common GSTP1 polymorphisms to help tease apart mechanisms of action, and this model will be described. By considering gene-environment interactions using *in vitro* and epidemiological approaches, the outcome of this work is expected to enhance our ability to assess the human health risks of mercury and help identify vulnerable groups.