Influence of Genetic Variance on an Occupational Exposure Assessment Model of 1,6-Hexamethylene Diisocyanate

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Significant differences in systemic response to xenobiotic exposure result from inter-individual genetic variation, but this variation is not included as a predictor of outcome in exposure assessment models. We developed an approach to investigate and identify individual differences in genetic variation that influence biomarkers of exposure levels. Urine biomarker 1,6-hexamethylene diamine (HDA) was measured as a quantitative biological phenotype in a well-characterized population of 33 automotive spray painters exposed to 1,6-hexamethylene diisocyanate (HDI). A total of 25 SNPs were significantly associated with measured biomarker levels in urine and blood after adjusting for multiple comparisons at a false discovery rate p<0.20. The genetic marker most associated with urine biomarker levels, rs169, was also a significant predictor in linear mixed-effects models that accounted for personal HDI exposure across multiple visits per worker (p<0.05). Our results indicate that the incorporation of genetic markers in exposure assessment models can be informative of biomarker levels.

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