

VALIDATION OF SIGNATURE BIOMARKERS BY HIGH-THROUGHPUT TAQMAN® LOW DENSITY ARRAY (TLDA) IN PCB-EXPOSED SLOVAK POPULATION

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Background and Aims: Valid biomarkers that link environmental exposures to the pathogenesis of human disease can enhance health risk assessment and contribute to effective new disease prevention policies in environmental and occupational settings. This presentation concerns results of a large scale evaluation of changes in gene expression in relation to body burdens of PCBs (polychlorinated biphenyl ethers) using microarrays, combined with a primary validation through high-throughput TLDA in a NIEHS project to SKD.

Methods: The microarray results of global gene expression in peripheral blood for individuals with varying levels of PCBs, and in PBMC cells (*in vitro*) with Slovak human median equivalence concentrations of PCBs were analyzed by GeneSpring GX 10.0. The Ingenuity Pathway Analysis retrieved the top biofunctions, networks, and major molecules to establish these signature biomarkers relative to disease and developmental processes occurring after exposure to these chemicals. The high-throughput qRT-PCR by TLDA studies were done on ABI platform. Data analysis was done through DataAssist™ and StatMiner®.

Results: The potential signature biomarkers (RRAD, MYC, CD3, CYP1A2, PON1, CYP2D6, ARNT, BCL2, LEPR, LPR12, ENTPD3, ITGB1, NPPB, and TRAP1) identified in the PCB-exposed population and in *in vitro* studies, involved relevant biological pathway signatures leading to major abnormalities and disorders in the PCB-exposed population (viz., Cardiovascular, Developmental Disorders, Neurobehavioral, Cancer). The analyses of global expression on validating the genes have indicated that the subjects are grouped into different clusters (high and low PCB exposure groups) depending upon the quantitative expression of the candidate genes. These gave a hint that these gene fingerprints could lead to identification of groups at risk through specific pathways based upon the PCB exposure.

Conclusion: Upon validation, this high-throughput biomarker-based method will be capable of identifying high-risk individuals with specificity & selectivity, through therapeutically relevant genomic classifiers, as a measure of biological responses to environmental stressors.

Comentario [IH1]: did you look at multiple samples from the same person? if not, then 'changes in' does not appear to be the correct description of what you did.