# Blood-Based Omics Profiling And Its Potential For The Study Of Environmental Carcinogenesis In Children And Adults

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Epidemiological investigations constitute the gold standard for the identification of environmental health hazards. However their relative insensitivity, and their post-hoc nature, underline the need for novel tools which, in addition to providing higher sensitivity, can detect early biological signals which can enable the prediction future disease. Such an approach, which has been made possible by the widespread application of global profiling technologies (omics), involves the identification of subtle perturbations of biological signals, induced by environmental exposures in readily accessible human tissues, and the characterisation of their relationship with disease pathogenesis. For example we have recently shown that perturbations in the global gene expression and epigenetic (DNA methylation) profile in peripheral blood leucocytes of healthy smokers predicts with remarkable efficiency diseases known to be caused by tobacco.

More recently we have followed up this paradigm by examining the impact on omic profiles in leucocytes in the peripheral blood of adults, as well as in cord blood, of polychlorinated persistent organic pollutants (POPs), including polychlorinated biphenyls (PCBs), a category of environmental chemicals over which there are substantial concerns concerning their health effects in adults and, especially, the fetus and young children. The evidence linking PCBs with human cancer has been evaluated by IARC as sufficient in connection with melanoma in adults, however for other types of cancer, e.g. B-cell lymphoma, the evidence is suggestive but inconclusive. In an epigenome-wide association study on 611 adults, free of diagnosed disease, we identified 650 CpG sites in blood leucocyte DNA whose methylation correlates strongly (FDR<0.01) with plasma concentrations of at least one of 6 PCBs, especially PCB156. The differentially methylated genes include many polycomb group protein target genes, almost all overmethylated with increasing exposure, a change considered as an early marker of carcinogenesis. Disease connectivity analysis of the differentially methylated genes points to multiple diseases potentially associated with PCB exposure, including melanoma. Importantly, the epigenetic exposure profile identified shows extensive, statistically highly significant and biologically plausible overlaps with published profiles associated with future CLL risk as well as clinical CLL. For all overlapping sites, the methylation changes are the same direction in subjects with higher exposure and with future or clinical CLL case status, supporting an causal link between exposure to PCBs and CLL.

An analogous investigation utilizing concentrations in the peripheral blood plasma of pregnant mothers and epigenetic profiles measured in cord blood leucocytes gave less significant associations relative to the study described above, probably due to the much lower exposure levels observed, in combination with additional protection to cord blood leucocytes provided by the placenta. Nevertheless sex-specific perturbations of the epigenetic profiles were detected in accordance with existing reports of the effects of PCBs.

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