Abstract

[Research Title]

Proposition of a comprehensive human biomonitoring method to assess co-exposure to chemicals

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[Abstract]

Exposure characterization is an indispensable component of chemical risk assessment. To facilitate exposure characterization, a technique that measures metabolites or parent chemicals directly in human urine and blood has been introduced into the risk assessment process in environmental and occupational health settings to evaluate chemical exposure at the individual level. This technique, human biomonitoring (HBM), originally involved targeted analyses of parent compounds of concern or their metabolites, but non targeted or comprehensive analyses are theoretically desirable to elucidate combined exposure to multiple chemicals, which remain to be developed. One primary bottleneck is the absence of chemical libraries that provide accurate information on mass, retention time and MS2 spectra of chemical metabolites. The absence of such libraries makes it difficult to annotate chemical metabolite candidates detected in biospecimens. For most relevant metabolites, their standard reagents are not commercially available. In this project, we chose chemicals that have been highly prioritized by ministries, listed under the following categories: (a) Initial Environmental Risk Assessment of Chemicals, (b) Priority Assessment Chemical Substances designated by Japan's Chemical Substance Control Law, and (c) biocides or other chemicals in prevalent outdoor/ indoor use to which attention has been paid in a risk assessment context. We administered parent standards to mice, collected urine containing the metabolites, and constructed a suspected metabolite MS2 spectral library. A total of 5915 accurate masses and retention times of urinary metabolites/parent compounds derived from 120 chemicals were exported and registered in MSP format in the MassBank public domain. (MassBank of North America (MoNA) https://mona.fiehnlab.ucdavis.edu). The library was applied to urine samples from pregnant women and adult female students in Japan. This screen revealed exposure to 12 and 15 of the represented parent compounds/candidate chemicals in these respective populations. Our approach, using our constructed library, is useful for suspect screening in HBM. It may be applied to various ongoing HBM projects as a screening tool to select chemicals to be measured by quantitative targeted analyses with an understanding of the limitations of the developed

approach.

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