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Alix Sarah Aldehoff (MOLTOX) Advanced proteomics approaches hold potential for risk assessment of metabolism disrupting chemicals as omics-based NAM

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Authors: Alix Sarah Aldehoff, Isabel Karkossa, Helen Broghammer, Sontje Krupka, Juliane Weiner, Cornelius Goerdeler, Rima Nuwayhid, Stefan Langer, Martin Wabitsch, Ulrike Rolle-Kampczyk, Nora Klöting, Matthias Blüher, John T. Heiker, Martin von Bergen and Kristin Schubert

Abstract: The concept of metabolic disruption through exposure to chemicals has expanded our understanding of how environmental pollution can contribute to metabolic dysregulation and, ultimately, diseases like obesity, diabetes, and cardiovascular conditions. Current strategies for assessing the risks posed by chemicals need to break new ground. Omics technologies such as proteomics have proven to be powerful tools for investigating the molecular mechanisms of these metabolism disrupting chemicals (MDCs). Global proteomics, complemented by insights into the thermal stability of proteins and the profiles of post-translational modification (PTM), provides a near-phenotypic understanding of chemical modes of action. In addition, bioinformatics techniques enable the identification of hub protein candidates, modification sites and initiating events triggered by chemical exposure. One example of a potential MDC is diisononyl-cyclohexane-1,2-dicarboxylate (DINCH), a common alternative to legacy phthalates such as DEHP, which has been linked to the induction of adipogenesis and lipid accumulation. Here, we demonstrate the utility of advanced proteomics approaches in assessing the effects of potential MDCs such as DINCH and its metabolite MINCH by utilising the human Simpson-Golabi-Behmel syndrome (SGBS) adipocyte cell line and comparing it to primary human adipocytes and adipose tissue data from DINCH-exposed mice. The research sheds light on DINCHs molecular effects including protein interactions beyond its primary target, PPARγ. The results emphasize the potential of omics-based approaches to enhance risk assessment frameworks for emerging contaminants.

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