Exploration of LC-MS approaches for DNA adductome mapping and modelling

Emma Van de Walle[1], Romel P. Dator[2], Valeria Guidolin[2], Marilyn De Graeve[1], Peter W. Villalta[2], Lynn Vanhaecke[1,3], Silvia Balbo[2], Lieselot Y. Hemeryck[1]

[1] *Department of Veterinary Public Health and Food Safety, Laboratory of Chemical Analysis, Salisburylaan 133, B-9820, Merelbeke, Belgium.*

[2] *Masonic Cancer Center, University of Minnesota, Minneapolis, MN 55455, USA.*

[3] *Institute for Global Food Security, School of Biological Sciences, Queen's University, University Road, Belfast, United Kingdom.*

The formation of DNA adducts following the exposure of DNA to genotoxic molecules can be the onset of chemically induced carcinogenesis. In recent years, interest in DNA adductome mapping has significantly grown and for DNA adductomics, which is considered a subbranch of metabolomics, liquid chromatography (LC) coupled to high resolution mass spectrometry (HRMS) is considered the gold standard. Due to ongoing technological advancements, the fields of LC and MS are continuously evolving. Accordingly, the fields of e.g. metabolomics and proteomics have strongly co-evolved, but DNA adductomics is however not yet fully up to speed. The scope of this research was to evaluate the use of Hydrophilic Interaction Liquid Chromatography (HILIC) vs. reversed phase C18 Ultra-High Performance Liquid Chromatography (UHPLC) coupled to HRMS, and two commonly used DNA adduct extraction procedures; i.e. thermal acidic (TA) vs. enzymatic (Enz) hydrolysis of DNA followed by DNA adduct purification and enrichment using solid phase extraction (SPE) or fraction collection (FC) in a 2x2 method matrix. The results demonstrate that HILIC compared to UHPLC allowed better modeling (highest number of valid models, average Q^2 = 0,786) of differences in the DNA adductome in tissues and according to diet in a rat feeding study, specifically so in combination with TA hydrolysis and SPE. Taking into account the need for a potent high-throughput methodology, the proposed approach demonstrates significant potential for DNA adductome mapping and modelling, and is therefore considered a good starting point for further exploration and optimization of LC-HRMS for DNA adductomics.