**UNTARGETED METABOLOMICS PROFILING IN PREGNANT WOMEN REVEALS NUMEROUS METABOLIC PATHWAYS DISORDERS**

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**ABSTRACT**

Endocrine-disrupting chemicals (EDs) are used in numerous everyday products and due to human activity are released into the environment. Therefore, there has been an increasing interest in the impact of exposure to these chemicals on human health. Global untargeted metabolomics analysis was performed in a pregnant women cohort (Ν = 308) from three different countries (Spain, France and Norway). Plasma samples were analysed to integrate human biomonitoring with non-persistent endocrine disruptors and epidemiology for metabolic disorders. Moreover, the consequences of exposure to endocrine disruptors regarding the metabolic pathways and the development of adverse outcome pathways (AOPs), which aims in the correlation between biological changes and molecular modifications detected during the early chemical exposure have been examined. Samples were analyzed using Reversed phase liquid chromatography (RPLC) and hydrophilic interaction liquid chromatography (HILIC) methods coupled with mass spectrometry, in both positive and negative ionization (Electrospray Ionization, ESI +/-) modes, to increase the coverage of the detected metabolites. Data acquisition was followed by data pre-processing, batch effect correction and metabolites identification. The detected metabolites underwent pathway analysis, which resulted in pathways linked to various metabolic disorders, such as obesity and diabetes, different types of cancer (breast, colon) and other human diseases such as cardiovascular disease and hepatopathy, while a large number of the pathways is related to amino acids metabolism. These events have been linked to various AOPs, triggered by exposure to the EDs.

**KEYWORDS:** Endocrine disruptors, Untargeted metabolomics, Reversed Phase liquid chromatography, HILIC, Adverse Outcome Pathways