Deciphering the human prenatal chemical exposome using high resolution mass spectrometry and placenta

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Context

Human biomonitoring

- **Chemical pollution by xenobiotics** (such as plasticizers and pesticides) are suspected of contributing to **global burden of chronic diseases**[1]
- Need to develop new methodologies to identify relevant cocktails of xenobiotics (i.e. the **chemical exposome**) accumulating in humans
- Human biomonitoring : focus on one of the most critical periods of development: the **prenatal period.**

Prenatal period

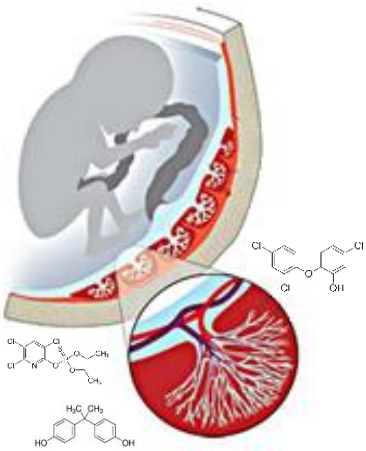
- Highly **critical period** of development in humans, marked by a great vulnerability and a strong sensitivity to **any disturbance of biological balance**
- Exposure to chemical pollutants during these periods may therefore have consequences on the health status of the fetus, but more generally throughout its life[2]

Placenta

- Unique **fetal-maternal unit**, easily accessible
- Promising matrix to study the prenatal exposome : **accumulation of xenobiotics/pollutants** throughout pregnancy[3]
- Large organ with tissues of different origins. The **spatial distribution of exogenous chemicals** remains unknown.
- No existing standardized methodology for placenta sampling

A comprehensive and complementary analytical workflow

- Most studies of the impact of prenatal exposure have targeted a small number of chemicals in placenta samples
- **Suspect-screening** and **non targeted analysis** permits screening of a very broad spectrum of chemicals
- Need for analytical sensitivity and optimized annotation workflow to detect and identify low-abundant xenobiotics
- Use of **multiple** chromatographic modes combined to mass spectrometry to **enhance the coverage** of chemical diversity of exposome.



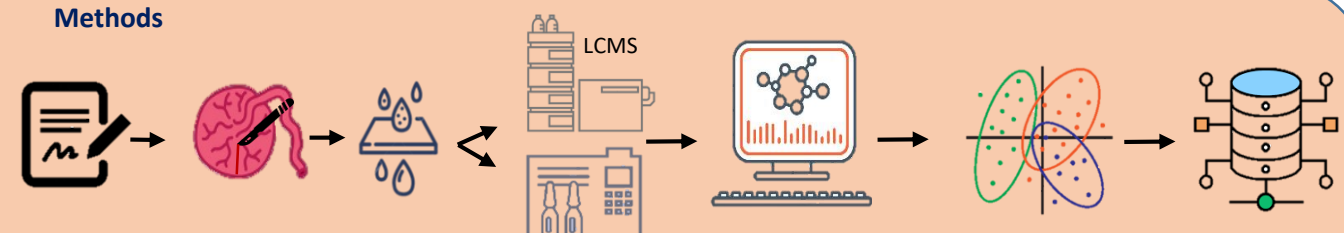
Objectives

Develop a robust **standardized methodology** to apply suspect screening and non-target analyses based on high-resolution mass spectrometry to profile placenta samples from large mother-child cohort studies

Tasks:

- Study the **intra-placenta and inter-placentas variability**: determine the variations of analytical response of all detected biomarkers
- Provide the **first online library** of xenobiotics, biotransformation products and endogenous metabolites that can be detected by HRMS in placentas

Methods



Protocol
- Sampling conditions
- Inclusion criteria

Placenta tissue collection
- n=28 placentas
- 18 samples/placenta

Sample preparation
- Extraction with organic solvents
- Protein/PL depletion
- Spiking with IS

Non-targeted Data acquisition
- UHPLC-ESI-QTOFMS
- GC-HRMS-Orbitrap

Data processing
- Peak detection
- Annotation workflow
- Prioritization via XenoScreener

Multivariate Statistical analysis
- PCA
- OPLS-DA
- Intra-class correlation coefficient

Database creation

References

1. Prüss-Ustün, A., Vickers, C., Haefliger, P., & Bertollini, R. (2011). Knowns and unknowns on burden of disease due to chemicals: a systematic review. *Environmental health : a global access science source*, *10*, 9. **2.** Mandy, M., & Nyirenda, M. (2018). Developmental Origins of Health and Disease: the relevance to developing nations. *International health*, *10*(2), 66–70. **3.** Jeong, Y., Lee, S., Kim, S., Park, J., Kim, H. J., Choi, G., Choi, S., Kim, S., Kim, S. Y., Kim, S., Choi, K., & Moon, H. B. (2018). Placental transfer of persistent organic pollutants and feasibility using the placenta as a non-invasive biomonitoring matrix. *The Science of the total environment*, *612*, 1498–1505.