

Deciphering the placenta chemical exposome using non-targeted LC-HRMS

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BACKGROUND

The chemical exposome

- The **exposure of humans to chemical compounds** throughout their lifespan contribute to global burden of **chronic diseases** and **developmental disorders**^{1,2}.
- Essential to assess **the chemical exposome** during **the prenatal period** : Highly **critical window** of development, marked by a great vulnerability to any disturbance of biological balance³.
- Understanding and **monitoring the diversity of chemicals** that pregnant women are exposed to is crucial for **shaping future chemical use policies** and **reducing lifelong health risks for newborns**.

A unique matrix : the placenta

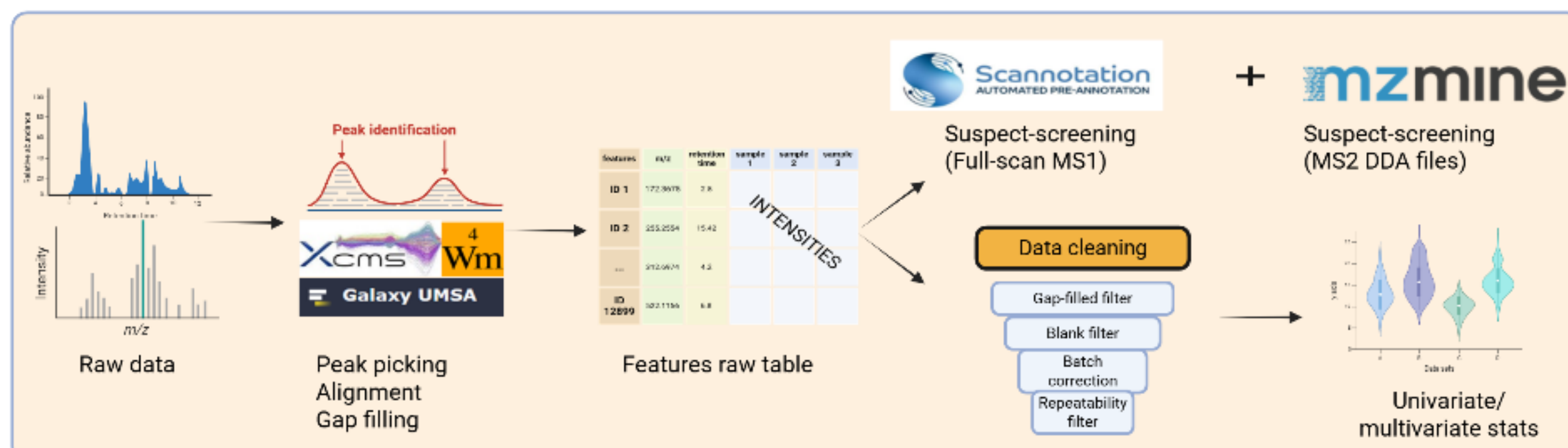
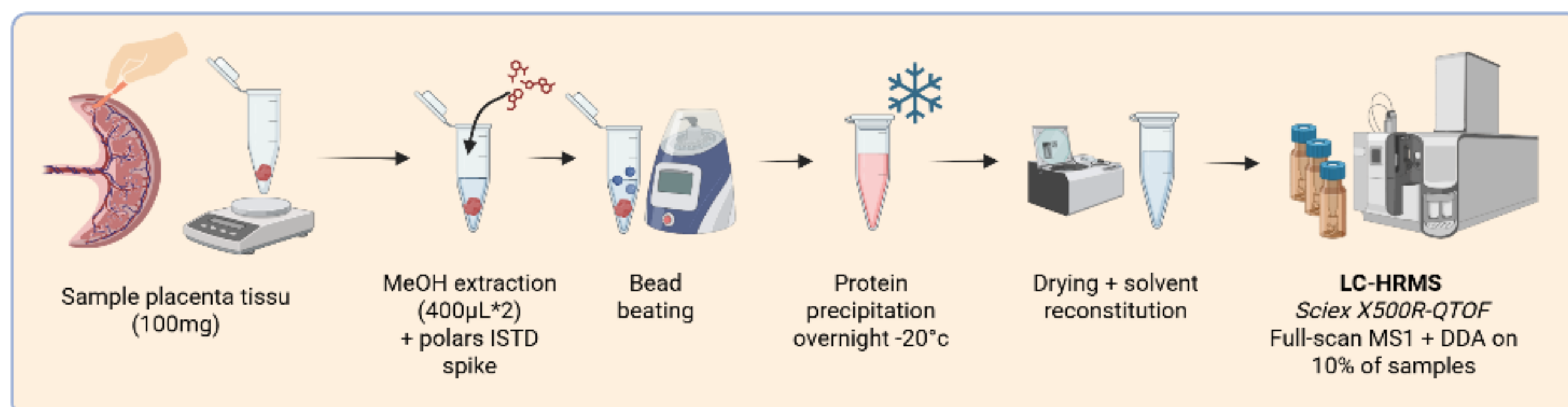
- **Easily accessible** after delivery, organ present during the entire pregnancy, provide **large amount of tissue** (>300g).
- More than **330 environmental chemicals were detected** in placenta, and a **large diversity** of endogenous metabolites^{4,5}.
- This is a non-exhaustive list, and **non-targeted analysis** using high-resolution mass spectrometry (**HRMS**) is the main solution to capture the wide jungle of chemicals.

AIM

Develop a standardized methodology to apply non-targeted LC-HRMS methods to profile placenta at large cohort scale.

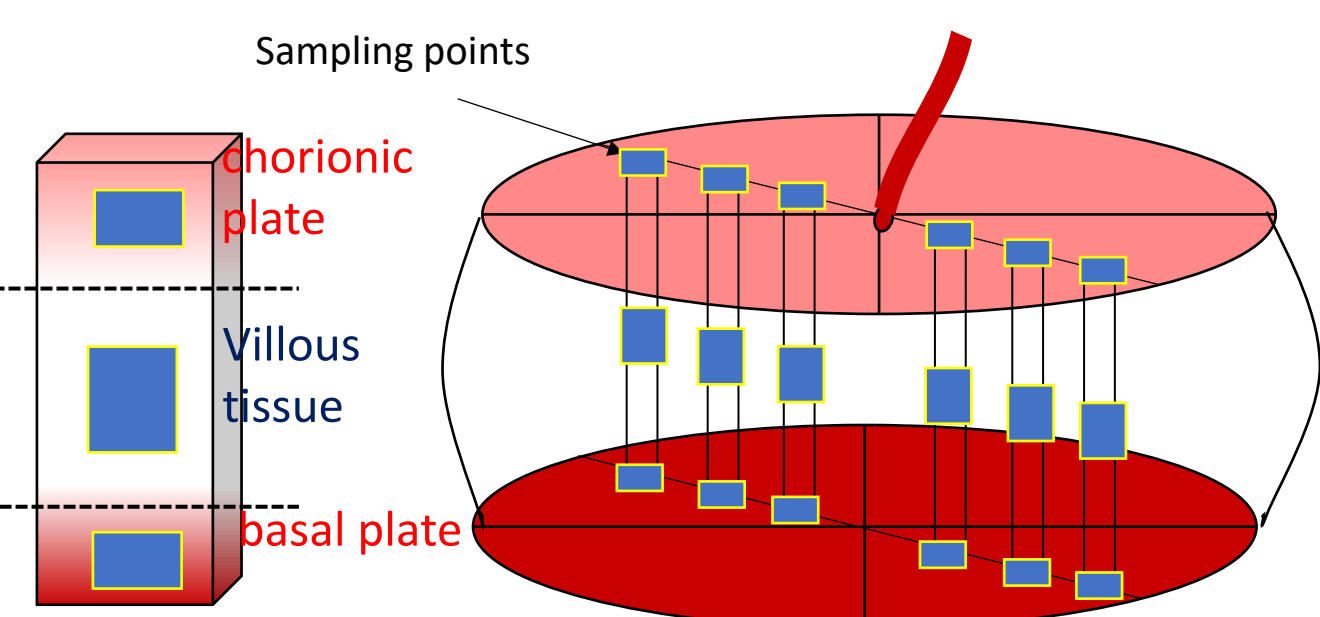
Tasks

- Set-up a **standardized protocol** enabling to compare several zones of the placenta
- **Collect samples** from uncomplicated pregnancies to obtain >25 placentas
- Study the **intra-placenta** and **inter-placentas variability**: determine the variations of biomarkers (xenobiotics and metabolites)
- Generate and share **the most exhaustive annotation** of the placental exposome and metabolome to date : 'Placenta Atlas'



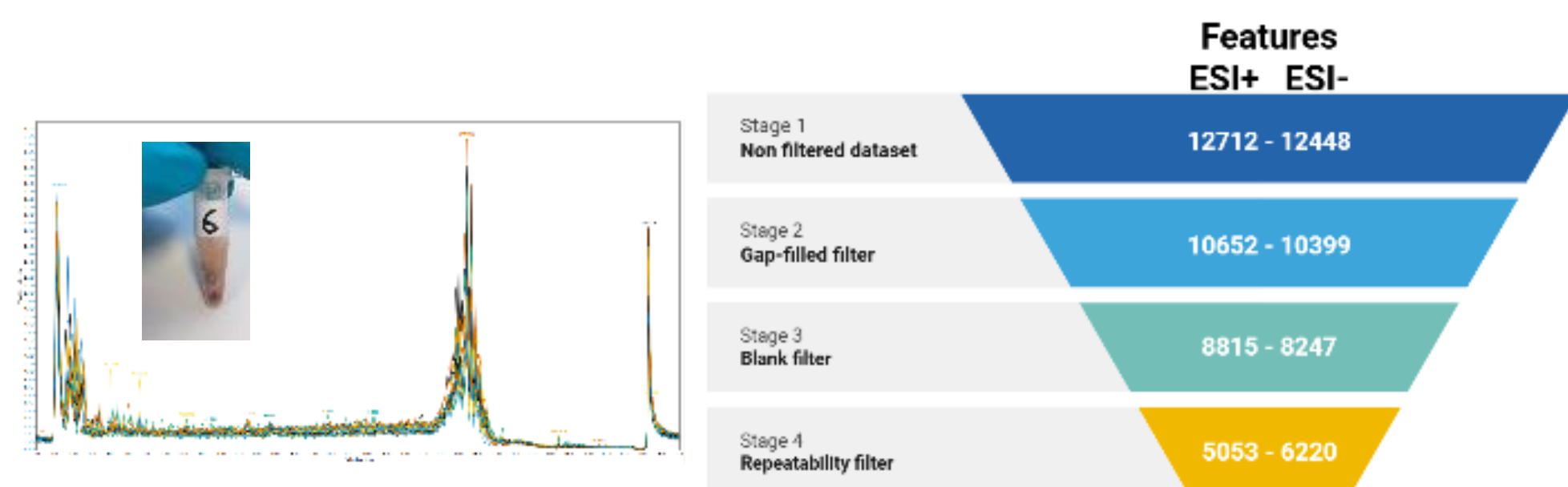
RESULTS

Sampling protocol & collection



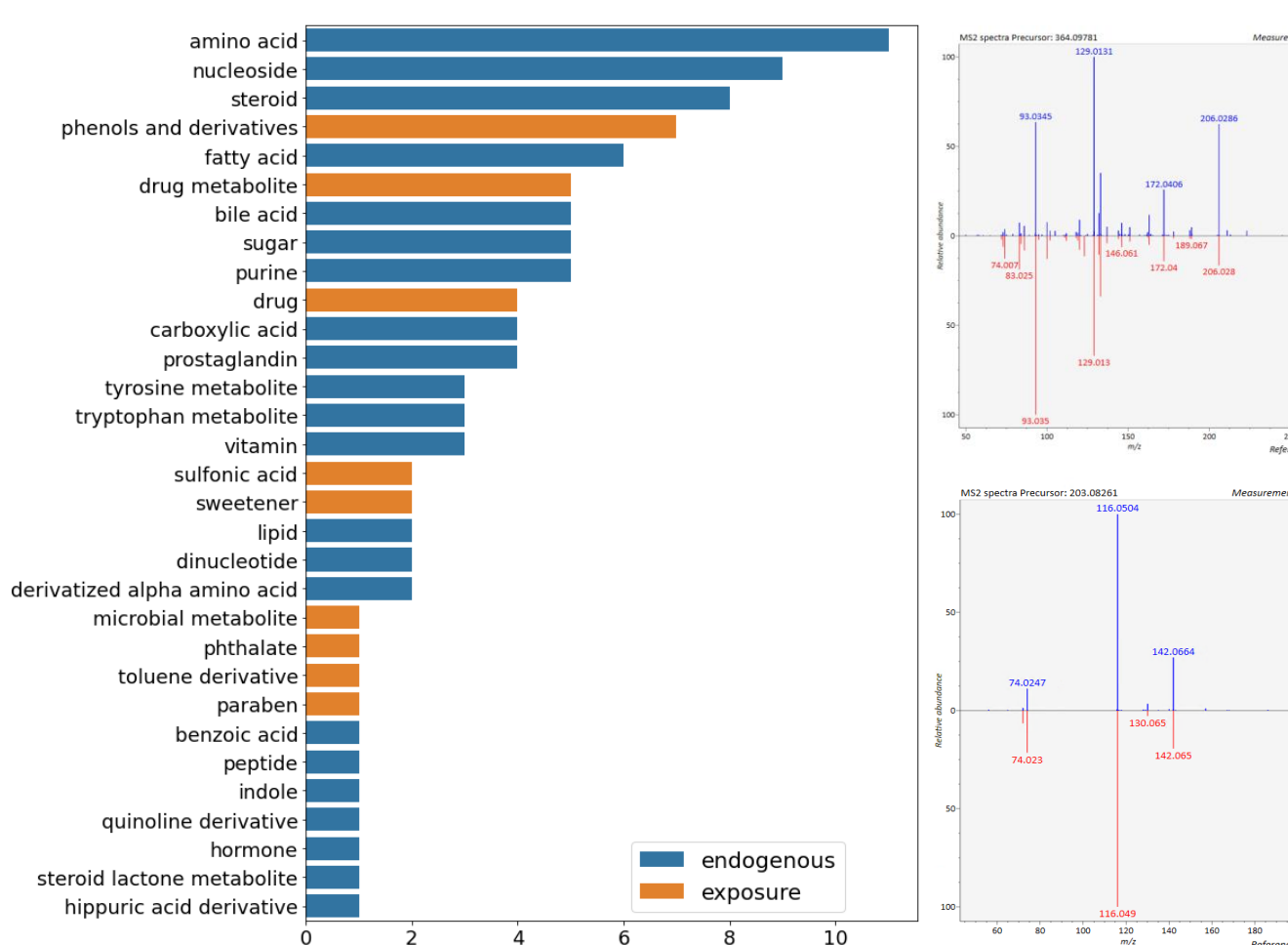
Clinical parameters	Boys (n=14)	Girls (n=11)
Maternal Age (yrs)	30.2 ± 4	32.1 ± 5
Gestational age at delivery (weeks)	39.3 ± 1	40 ± 1
Maternal BMI (kg/m ²)	24.5 ± 4	20.4 ± 4
Vaginal delivery (%)	100	100
Delay between placenta expulsion/dissection (min)	30.8 ± 23	46.7 ± 35
Antibiotics administration (%)	21	45
Foetal weight / Placental weight	5.81 ± 1	6.07 ± 0.7

LC-HRMS analysis



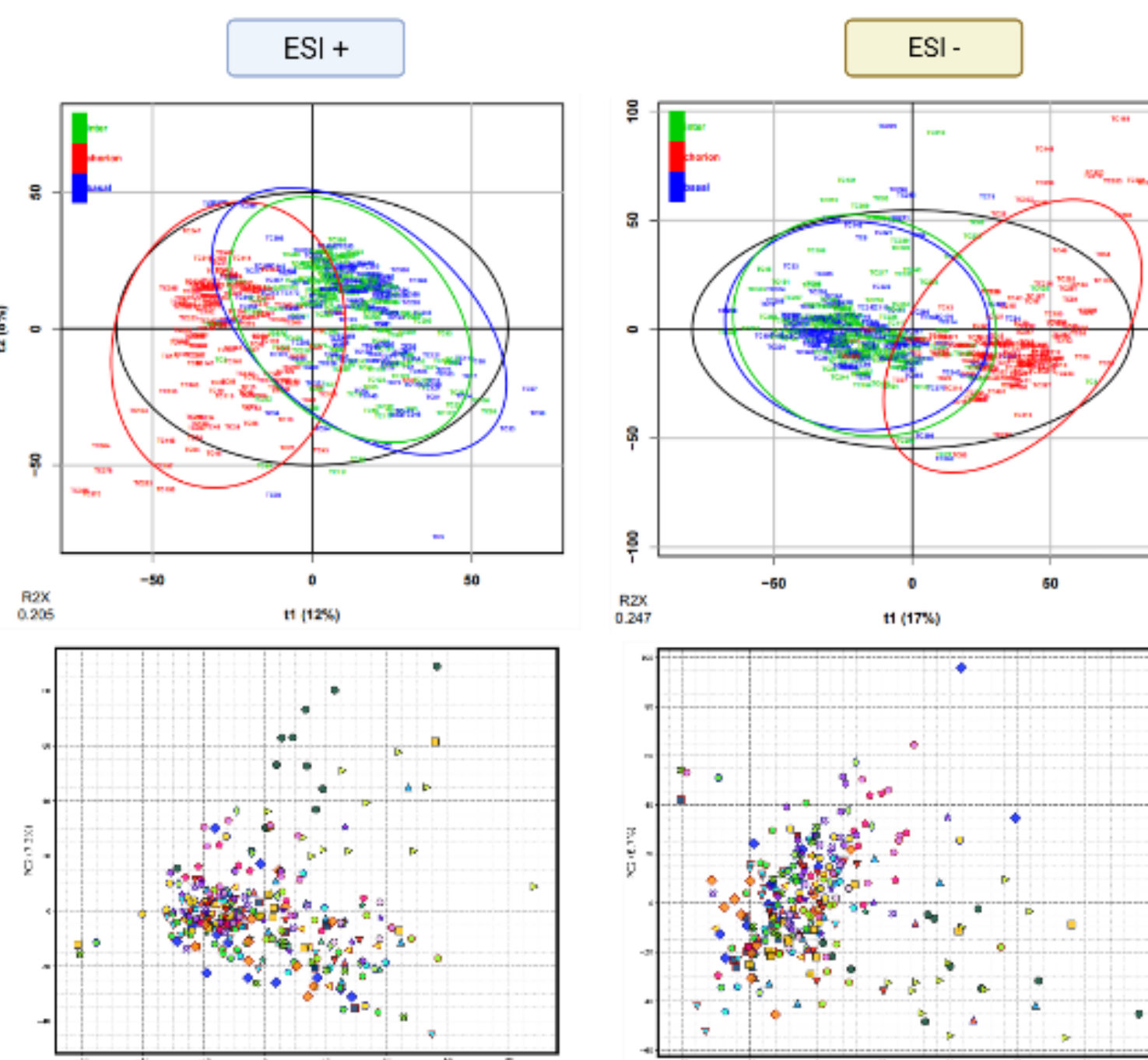
Statistics

Annotations



tissue discrimination

inter-placentas discrimination



References

- (1) 10.1016/S0140-6736(17)32345-0; (2) 10.1016/j.envint.2021.106616; (3) 10.1210/en.2015-1394; (4) 10.1080/10643389.2022.2104075; (5) 10.1021/acs.est.3c04845; (6) 10.1016/j.ica.2022.339983.

Conclusion & Outlook

- Results indicate that **the distance to cord insertion is not significant, whereas the tissue type is**. Particularly, the **chorionic plate distinguishes over 70% of the features**.
- Inter-placentas discriminative patterns for **active exposures (i.e., drugs)**. Difficulties to capture passive environmental exposure – **low abundance and low detection frequency** – unlikely to be selected for MS2-DDA fragmentation.
- A reproducible methodology for placenta sampling was developed and used in Rennes (France) hospital to collect **(18*25)=450 placenta samples**.
- The method (sample preparation & LC-HRMS analytical conditions) was optimized in a previous study⁶. Focus was placed on ensuring **robust analytical QA/QCs, reproducible data (pre)processing and effective data filtering** for statistical analyses.
- Complementary results via **GC-HRMS analysis** (2-steps derivatization for metabolites; LLE for volatile xenobiotics) are currently underway.