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The SCREENPEST project:

Development and implementation of an innovative large-scale screening approach for extended characterisation of human exposure to pesticides

Margaux HEURTÉ¹, Fatima-Zahra Alem¹, Tarek Moufawad², Elodie Mirmont³, Jean-Philippe Antignac², Julia Baudry⁴, Emmanuelle Bichon², Nathalie Bonvallot¹, Cécile Chevrier¹, Ingrid Guiffard², Emilien Jamin³, Emmanuelle Kesse-Guyot⁴, Arthur David¹, Laurent Debrauwer³

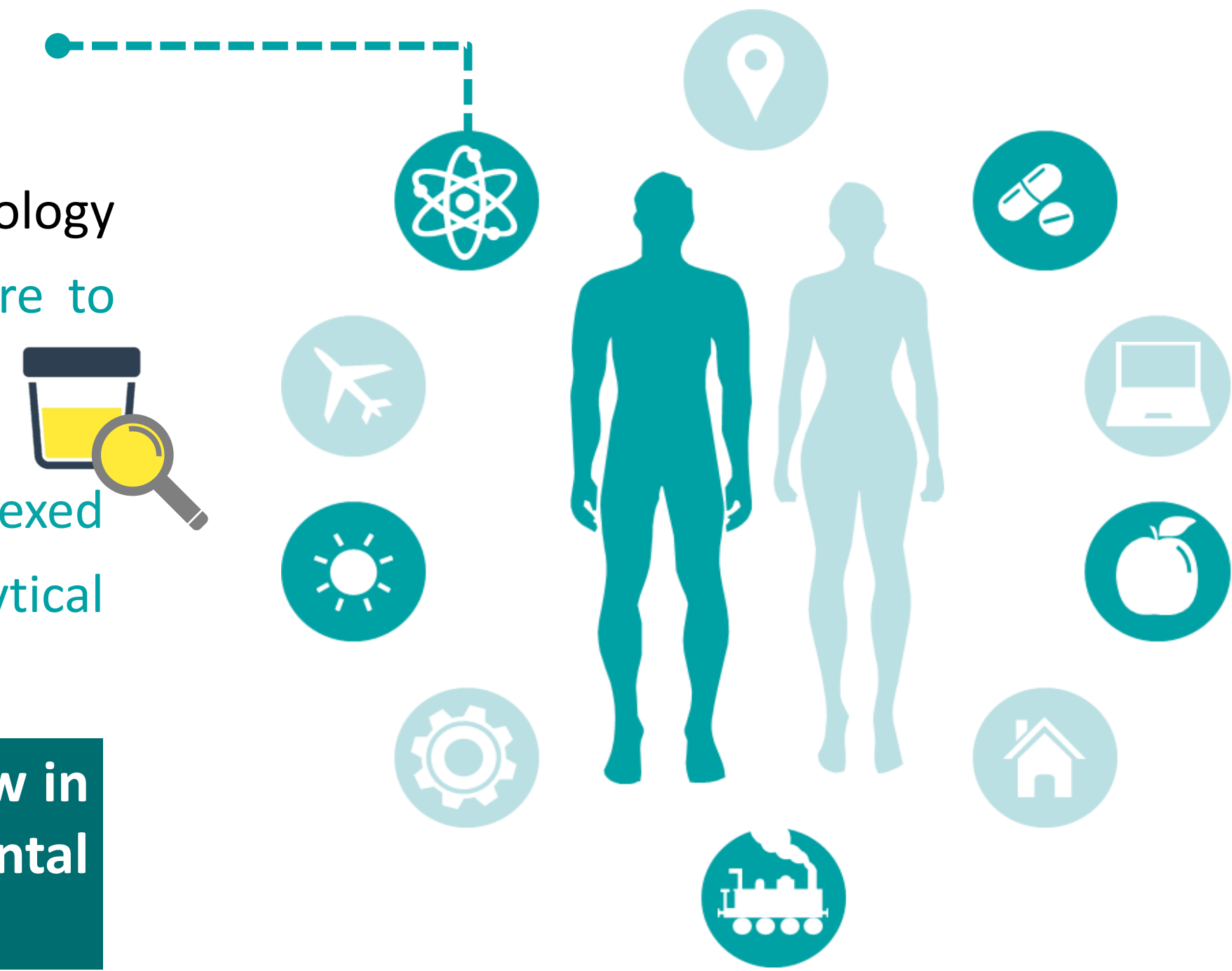
¹Univ Rennes, Inserm, EHESP, Irset (Institut de recherche en santé, environnement et travail), UMR_S 1085, Rennes, France
²LABERCA – ONIRIS/INRAE, UMR 1329, Route de Gachet, La Chantrerie, CS 50707, 44307 Nantes
³TOXALIM – INRAE, INRAE UMR 1331, 180 chemin de Tournefeuille, BP 93173, 31027 Toulouse Cedex 3
⁴CRESS – EREN – INRAE, EREN, Université Paris13 – Sorbonne Paris Nord, SMBH, 74 rue Marcel Cachin, 93017 Bobigny cedex

Pesticides exposure assessment

The aim of the SCREENPEST project is to provide a methodology for large-scale characterisation of human internal exposure to pesticides, via a "suspect profiling" approach, using urine.

To gain access to this variety of compounds a novel multiplexed approach by profiling a single sample using different analytical platforms is needed.

Development of a harmonised analytical workflow in terms of sample preparation, instrumental measurement and data processing.



Cohort studies

PELAGIE

- Mother-child cohort (France, 2002-2006)
- Association between the exposure to pesticides of pregnant women and biometric data at birth
- Access to 200 samples

NutriNet-Health

- General population (France, since 2009)
- Association between the exposure to pesticides and the onset of type 2 diabetes
- Access to 200 samples

Methodology & Sample Preparation

Elaboration of a large list of suspects, around 200 pesticides and phase I/II metabolites, covering a wide range of physicochemical properties for methodological developments. (logKow:[-4.71;8.38], MM/g.mol⁻¹: [72;720])

Commercial availability, bibliography, pesticide used in France in 2019, epidemiologists expertise and available data from the HMB4EU project.

10.1021/acs.analchem.2c00061

Optimisation of the 3 HRMS techniques to get the best separation and detection of the suspects (selected for development) by LC and GC.

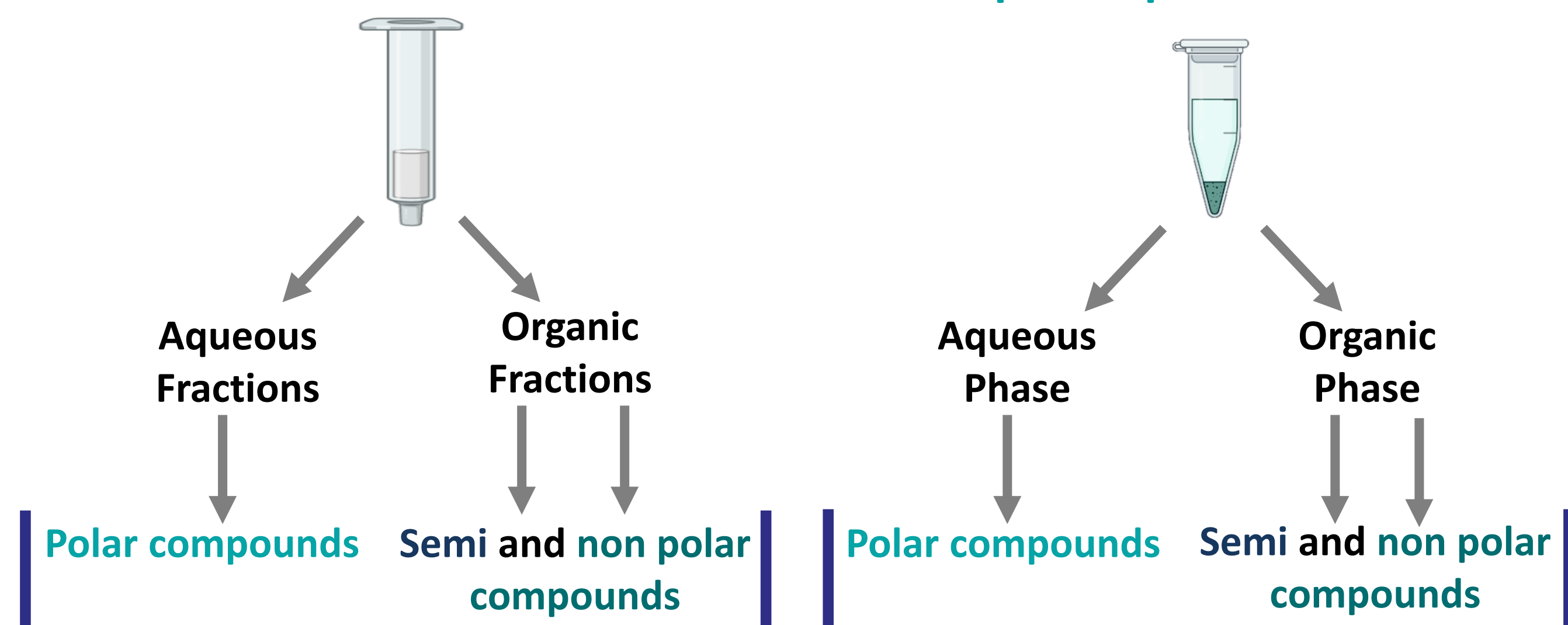
Characterisation of the suspects by HRMS.

Optimisation of sample preparation: methodological developments at various concentration levels (20, 50 and 100 ng.mL⁻¹) in pooled urine in 5 replicates.

Performance comparison of two non discriminating extraction techniques (recovery and matrix effect)

Solid-Phase Extraction

Liquid-Liquid Extraction



Extracts from one unique sample

Analysis of polar compounds

Analysis of semi and non polar compounds

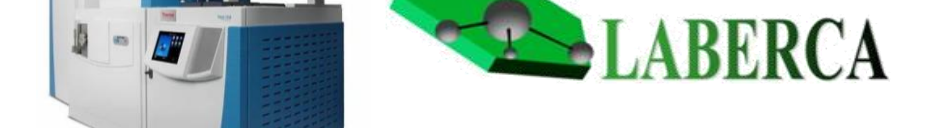
HILIC – LTQ-Orbitrap XL
 Acquity UPLC® BEH Amide
 (1.7µm, 1.0x100mm)
 ESI+ and ESI-



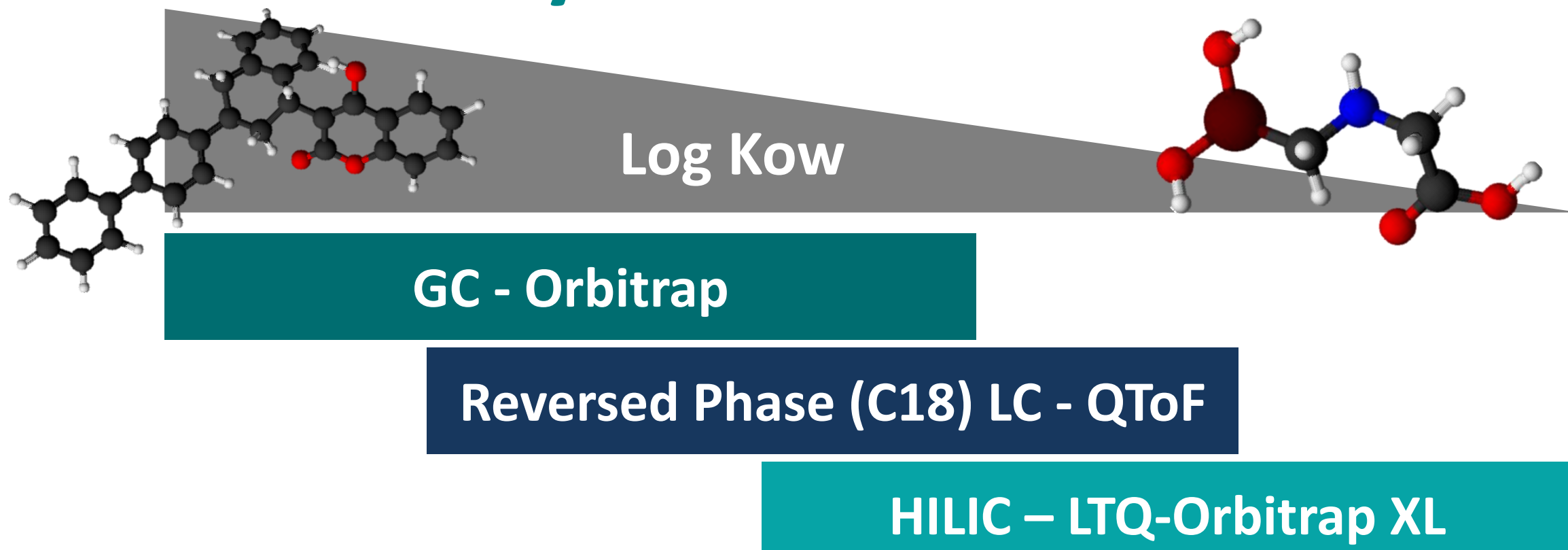
C₁₈ polymeric phase – QTOF
 ACQUITY UPLC® HSS T3
 (1.8µm, 1.0x150mm)
 ESI+ and ESI-



GC – Q Exactive Orbitrap
 DB-5MS
 (0.25µm, 0.250mmx30m)



HRMS Analysis



Analytical challenges to cover a wide range of compounds with:

- Different physicochemical properties from a unique sample
- Poorly characterised biotransformation products
- Low levels concentration

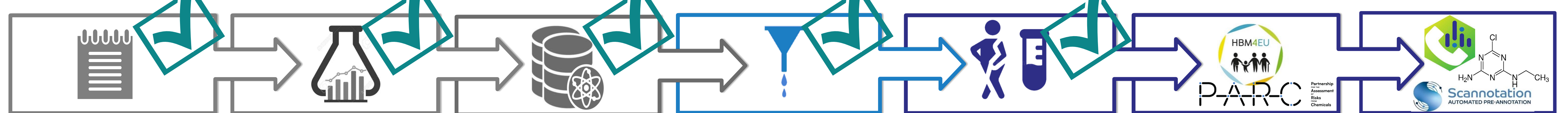
Data treatment - Bioinformatic tools

Extending the HR spectral library of reference pesticides and their metabolites.

Complementing bioinformatic tools in non-targeted and suspect screening approaches using in house developed softwares (Galaxy, Scannotation).

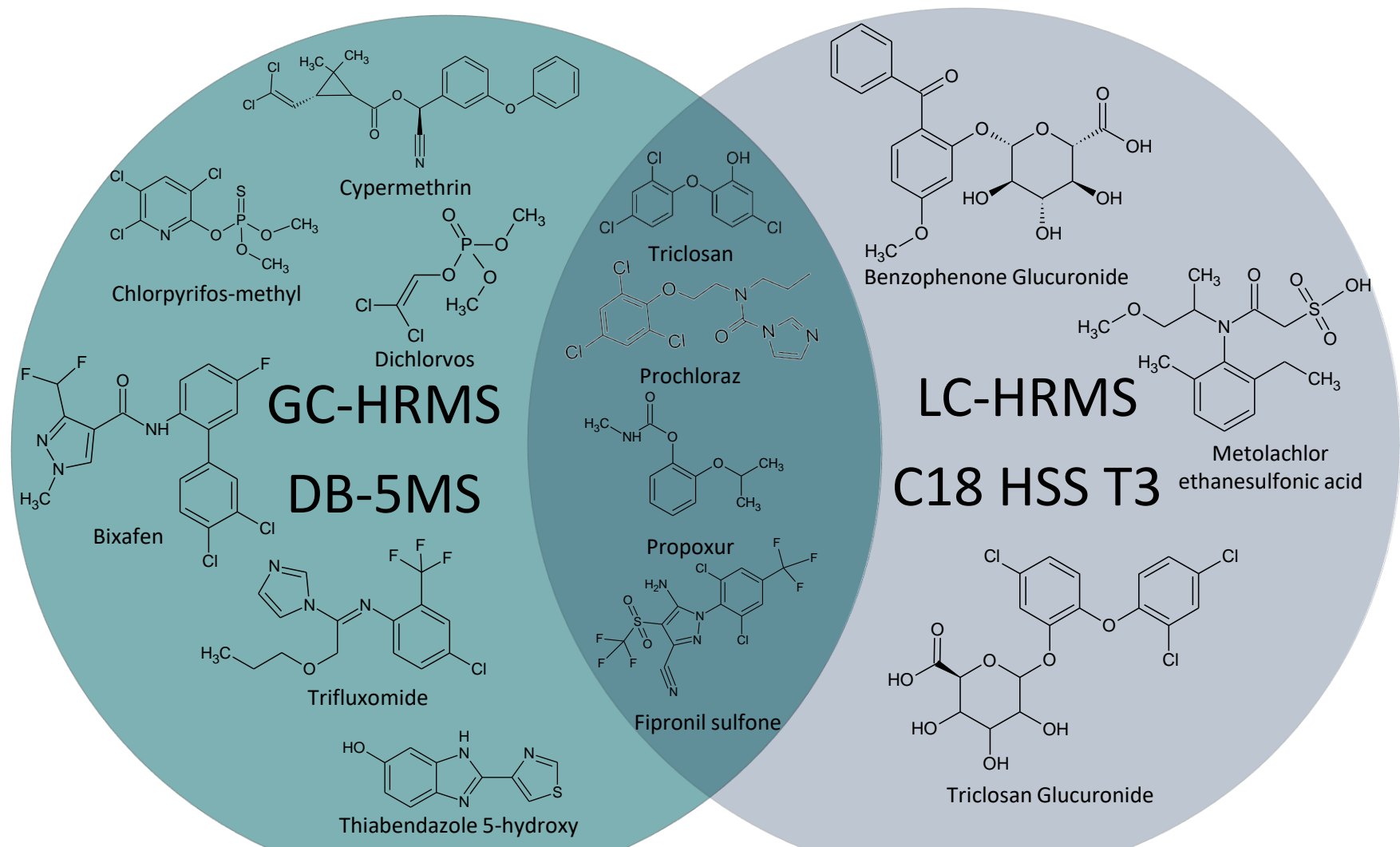
Statistical analysis and data interpretation

Workflow

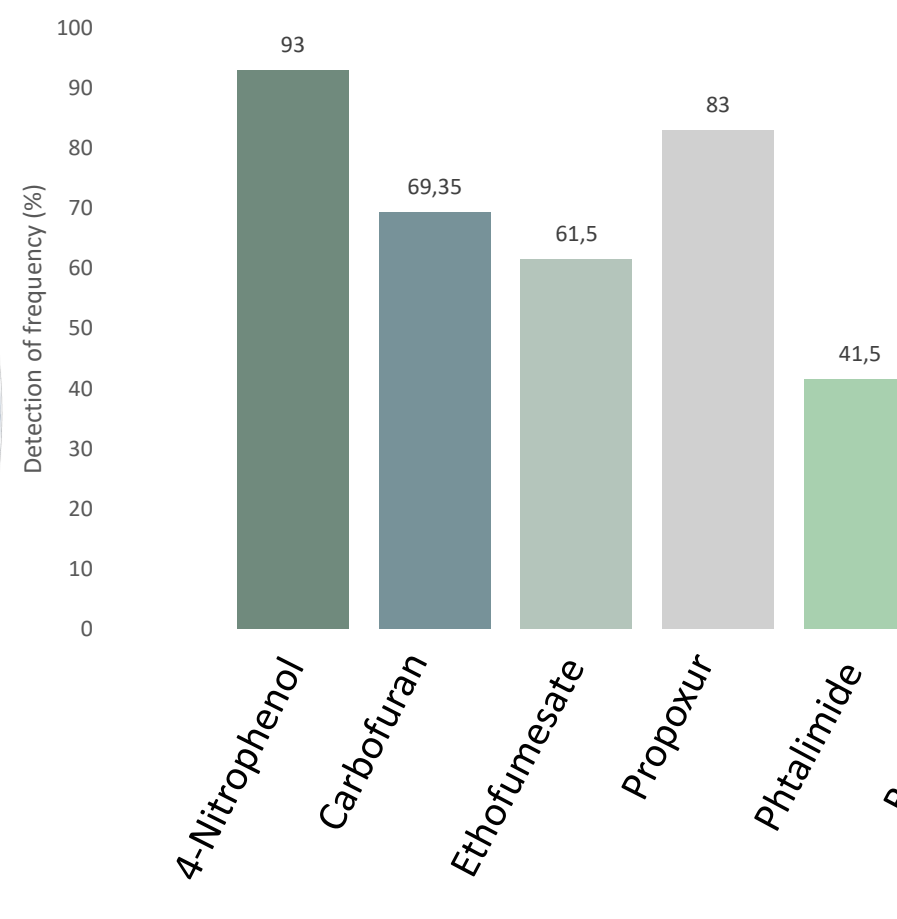


Elaboration of a list of suspects → Optimisation of the analytical methods → Generation of a HR spectral library → Development of non discriminating extraction techniques → Application on urine samples from PELAGIE and NutriNet-Health cohorts → Study of QA/QC for NTA/SS (2 levels of concentration 20-100 ng.mL⁻¹) → Pre-Annotation of exposure biomarkers with open source software

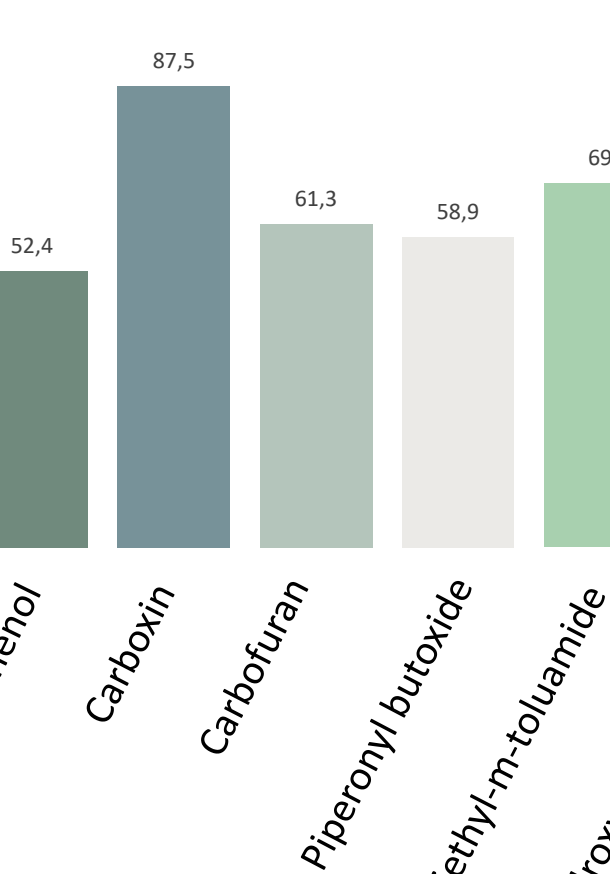
PRE-ANNOTATION BIOMARKERS EXPOSITION*



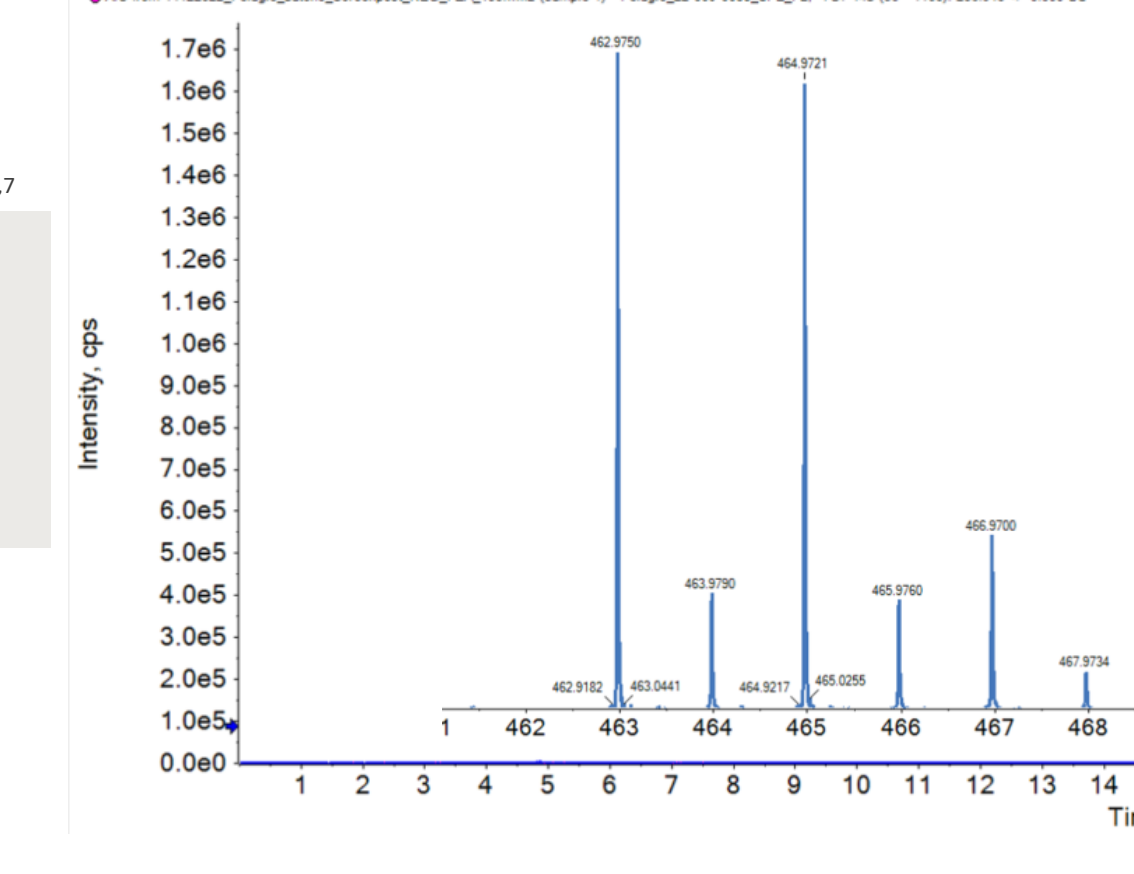
GC-HRMS Annotation (Cohort Nutrine)



GC-HRMS Annotation (Cohort Pelagie)



GC-HRMS Annotation (Cohort Pelagie)



*The annotation are currently being validated through the study of MSMS results (annotation level 1 to 5) for LC-HRMS.

Conclusion: This multi-complementary project has demonstrated the complementarity of analytical methods for describing the large-scale chemical exposome using a single optimized analytical workflow. Multiple SS analysis highlights the presence of pesticides in their parent or metabolized form in LC-HRMS.