LONGITUDINAL EXPOSOMICS FOR MATERNAL AND FOETAL HEALTH LINKED TO ADVERSE BIRTH OUTCOMES

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Introduction

The **exposome** is a novel public health paradigm that covers all environmental exposures across the life course, including chemical, physical, and behavioural/lifestyle factors, and how these exposures influence human health.[1,2] Environmental exposures, whether individually or in combination, can have a significant impact on human health, including **adverse health effects** that carry considerable **societal, economic, and ecological** costs.[3]

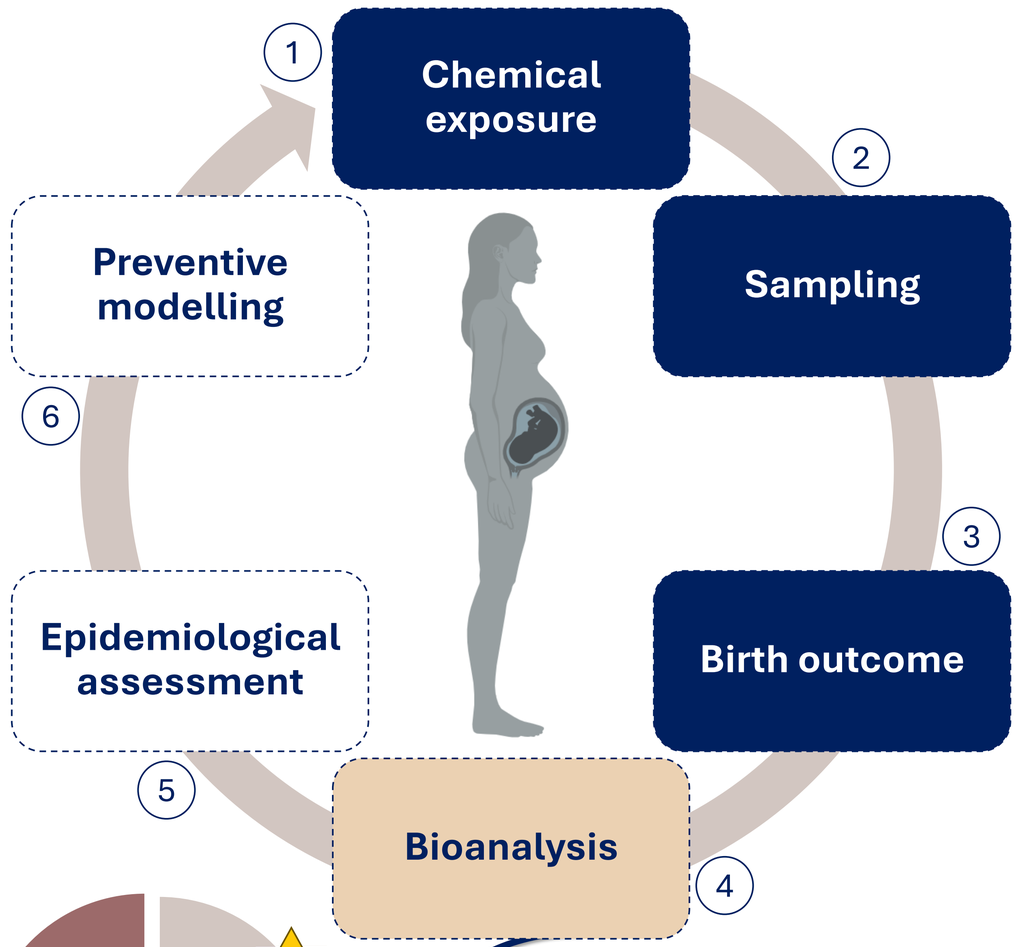
Aims and objectives

1 Develop an **analytical workflow** for exposure assessment of LECs.

2 Investigate **the longitudinal exposure patterns of LECs** and their influence on health outcomes.

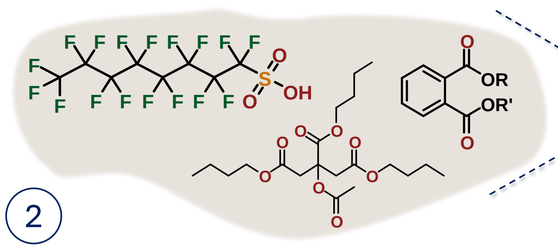
3 Develop **models for adverse birth outcomes** based on longitudinal exposomics data.

Maternal exposome concept



The DOHaD (Developmental Origins of Health and Disease) hypothesis proposes that early life exposures, particularly during fetal development, can permanently alter an individual's metabolism and physiology, increasing their risk of developing chronic diseases later in life.

1 Exposure to legacy and emerging contaminants (LECs)



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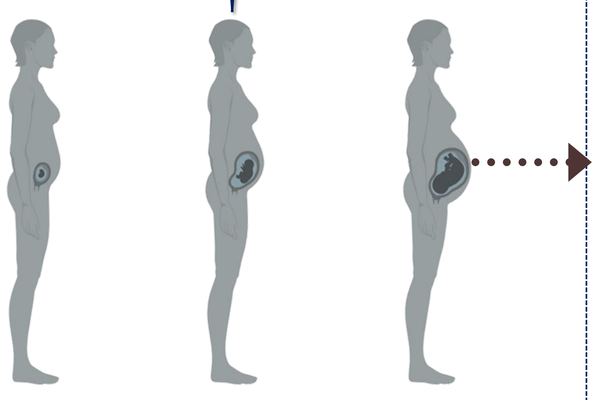
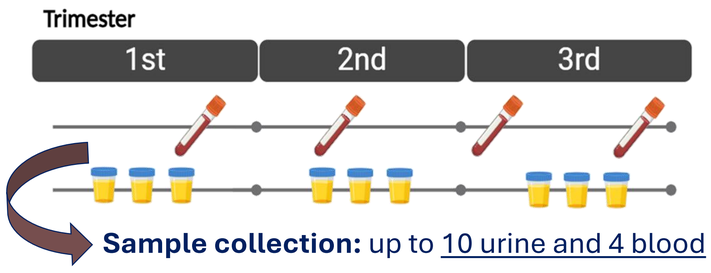
Towards Improved Maternal and Foetal Health via Multi-point Exposure Monitoring (TIMFEM) Chinese Birth Cohort

- longitudinal monitoring
- multi-matrix and multi-timepoint strategy
- women between the ages of 18 and 40, who reside in Hefei, China (>10 weeks pregnant)
- large number of participants (over 2,000 pregnant women)

- Exclusion: multiple pregnancies, major infectious diseases, serious mental health issues, inability to understand the nature of the study





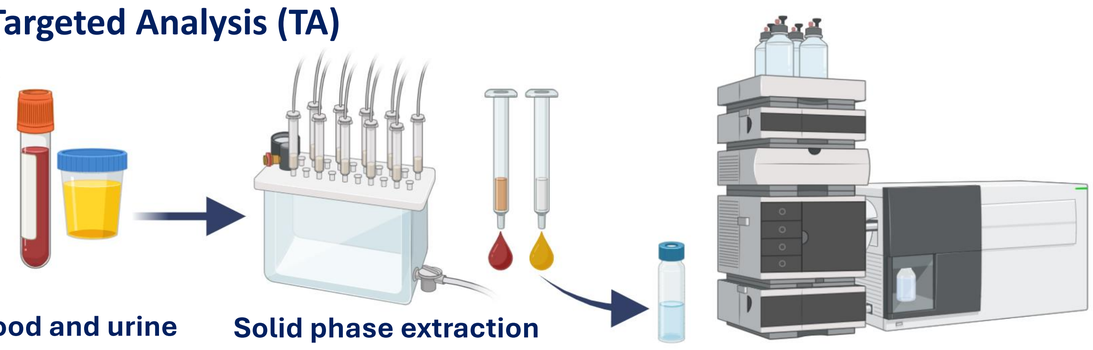
Sample collection: up to 10 urine and 4 blood

3

Mother
- Gestational diabetes
- Preeclampsia
- Pregnancy-induced hypertension

Child
- Low birth weight
- Macrosomia
- Preterm birth
- SGA
- LGA

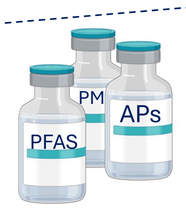
4 Targeted Analysis (TA) — A



Blood and urine

Solid phase extraction
- OASIS MAX (phthalates)
- OASIS WAX (PFAS)

Chemical and data analysis

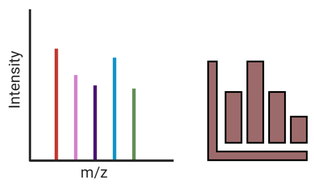


LECs standard solutions
(phthalates, alternative plasticisers, PFAS)

LC-MS/MS
Target Analysis

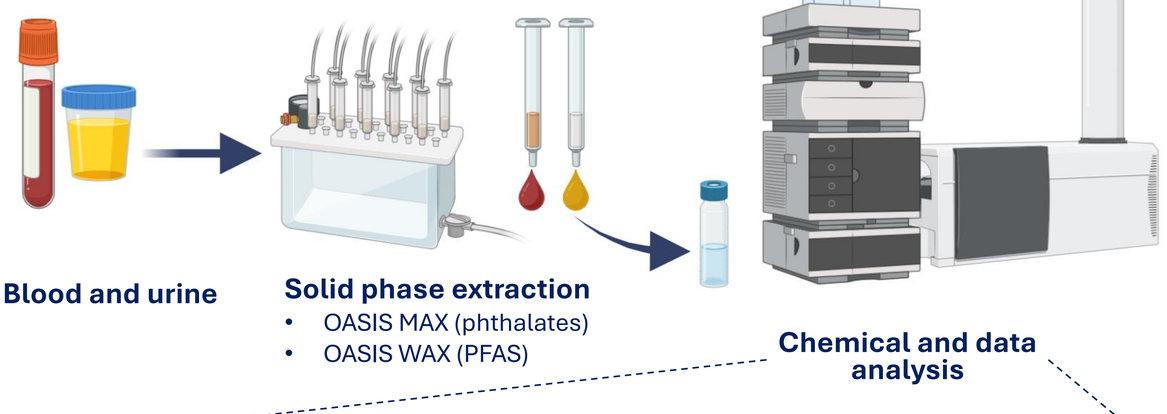
Mobile phases:
A= Water + 0.1 % FA
B= MeOH + 0.1 % FA

Column:
Kinetex Biphenyl 100x2.1 mm, 2.6 µm



Targeted identification and quantification

4 Suspect and non-targeted screening (SS/NTS) — B



Blood and urine

Solid phase extraction
- OASIS MAX (phthalates)
- OASIS WAX (PFAS)

Chemical and data analysis

Sample preparation

conjugation vs. deconjugation

QA/QC analysis

EU-PARC interlaboratory tests
-81 spiked compounds (urine/blood)

LC-QTOF-MS
- full scan analysis m/z range 50-1200
- high accuracy (mass error < 5 ppm)

Mobile phases:
A= Water + 0.1 %FA
B= MeOH + 0.1 %FA

Column:
Kinetex Biphenyl 100x2.1 mm, 2.6 µm

Data analysis using Mzmine
- Peak alignment
- Deisotoping
- Gap filling
- baseline correction
- Blank filtering

Suspect list
in-house MS2 database, MassBank, MetFrag

Confidence level
- Comopunds to be taken for further analysis (L2-L3)

Data analysis - Qualitative Mass Hunter:
Visual check of matching compounds:
- peak shape
- RT plausibility
- isotope pattern
- exact mass match

Characterization and Semi-quantification

of statistically relevant and frequently detected compounds
- Statistical significance ($P < 0.05$) significantly up/downregulated in case vs. control
- High detection frequency (DF >50%)

5 Chemical exposure profiles and trajectory analysis

- Comparing chemical exposure profiles from TA and SS/NTS associated with health outcomes (stat. method: ICC, MER, RCS)
- Trajectory analysis with mixed modeling → sensitive developmental window periods

6 Prediction modeling and risk assessments for adverse birth outcomes

- Mixture effect modeling approaches for compounds DF>50% (stat. method: BKMR, QGC, WQS) → identifying the top contributors to the observed health effects
- Risk assessment and toxicity risk evaluation

References
[1] Miller, G. et al. (2025) 'Integrating exposomics into biomedicine.' Science, 388(6745), pp.356-358.
[2] Vermeulen, R. et al. (2020) 'The exposome and health: Where chemistry meets biology.' *Science*, *367*(6476), pp.392-396.
[3] Landrigan, P.J. et al. (2018) 'The Lancet Commission on pollution and health.' *The Lancet*, *391*(10119), pp.462-512.

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