All together now: Exposome – linking different urban stressors

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Complementing the Genome with an ‘‘Exposome’’: The Outstanding Challenge of Environmental Exposure Measurement in Molecular Epidemiology

Recognizing the disparity in current knowledge between genes and environmental exposures, Chris Wild defined the “exposome”

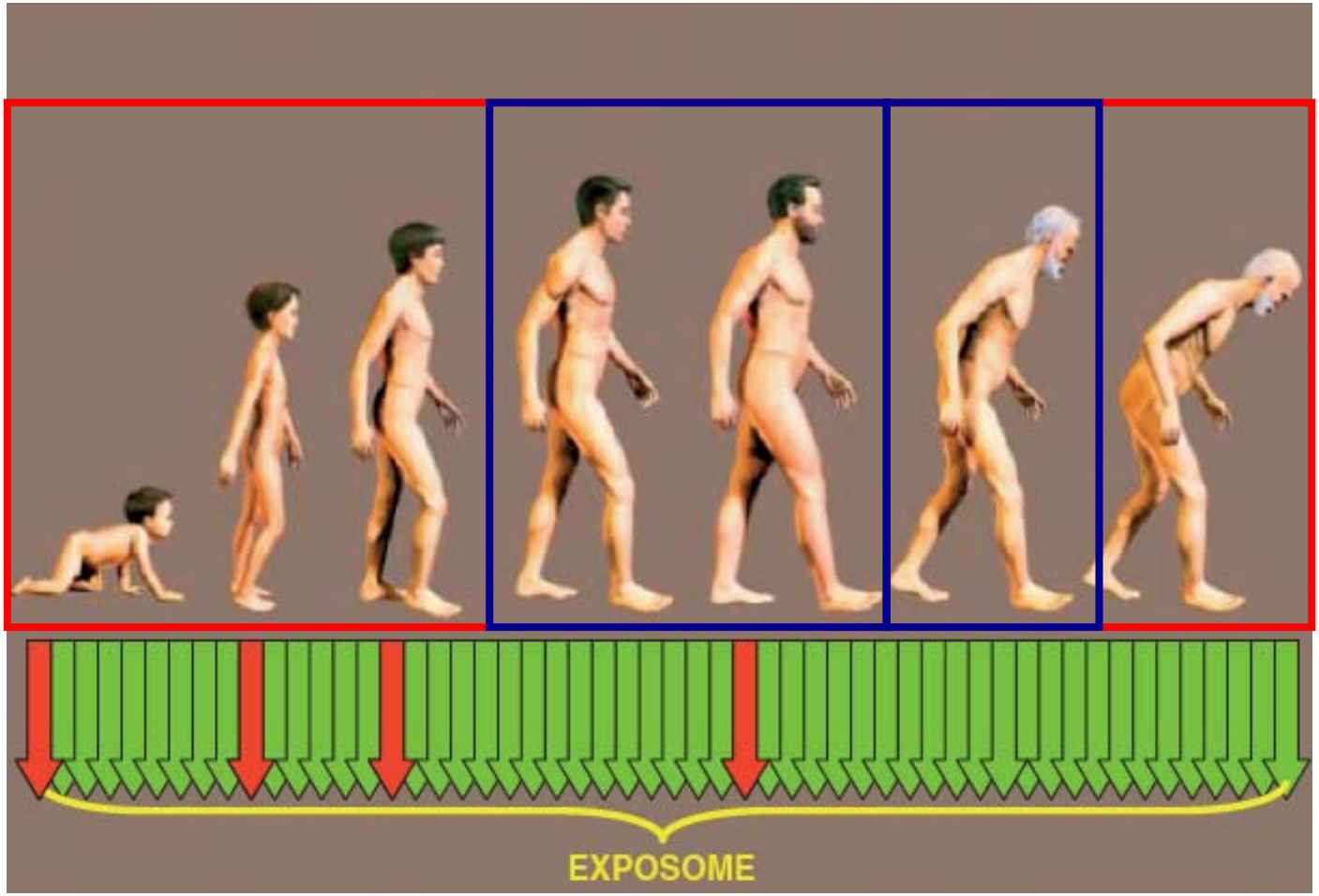
Representing all environmental exposures (including those from diet, lifestyle, and endogenous sources) from conception onwards, as a quantity of critical interest to disease etiology

Wild, C.P., Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer Epidemiol Biomarkers Prev 14 (8), 1847-1850 (2005).

Is the exposure community not as smart?

- Possibly .....
- However, there is a fundamental difference being temporal variation in exposures versus constant properties for the Genome

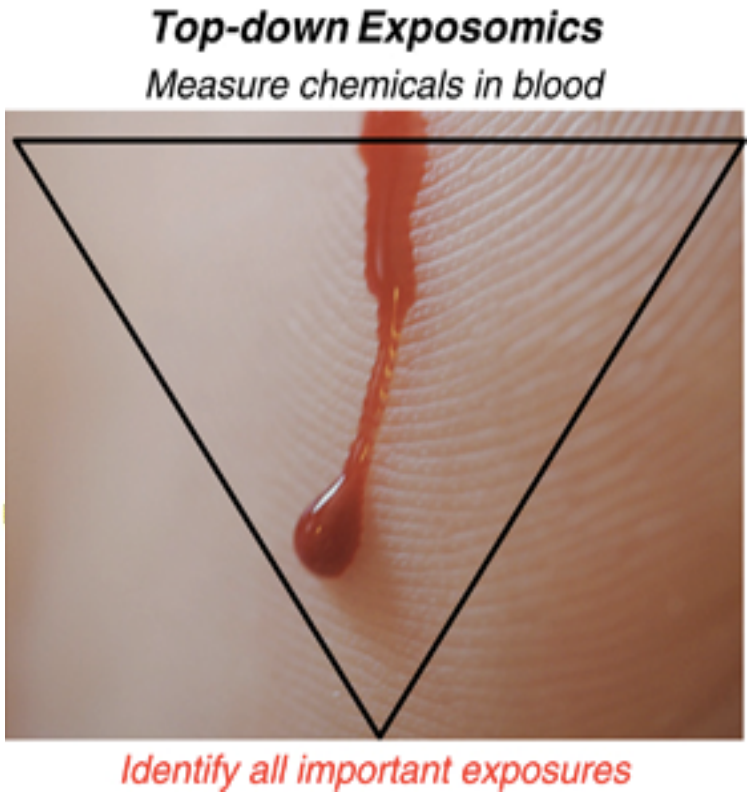
Lifecourse exposome



The Exposome; Discovering environmental causes of disease

- Environmental exposures are poorly characterized
- Epidemiologists have a fragmented view of exposures

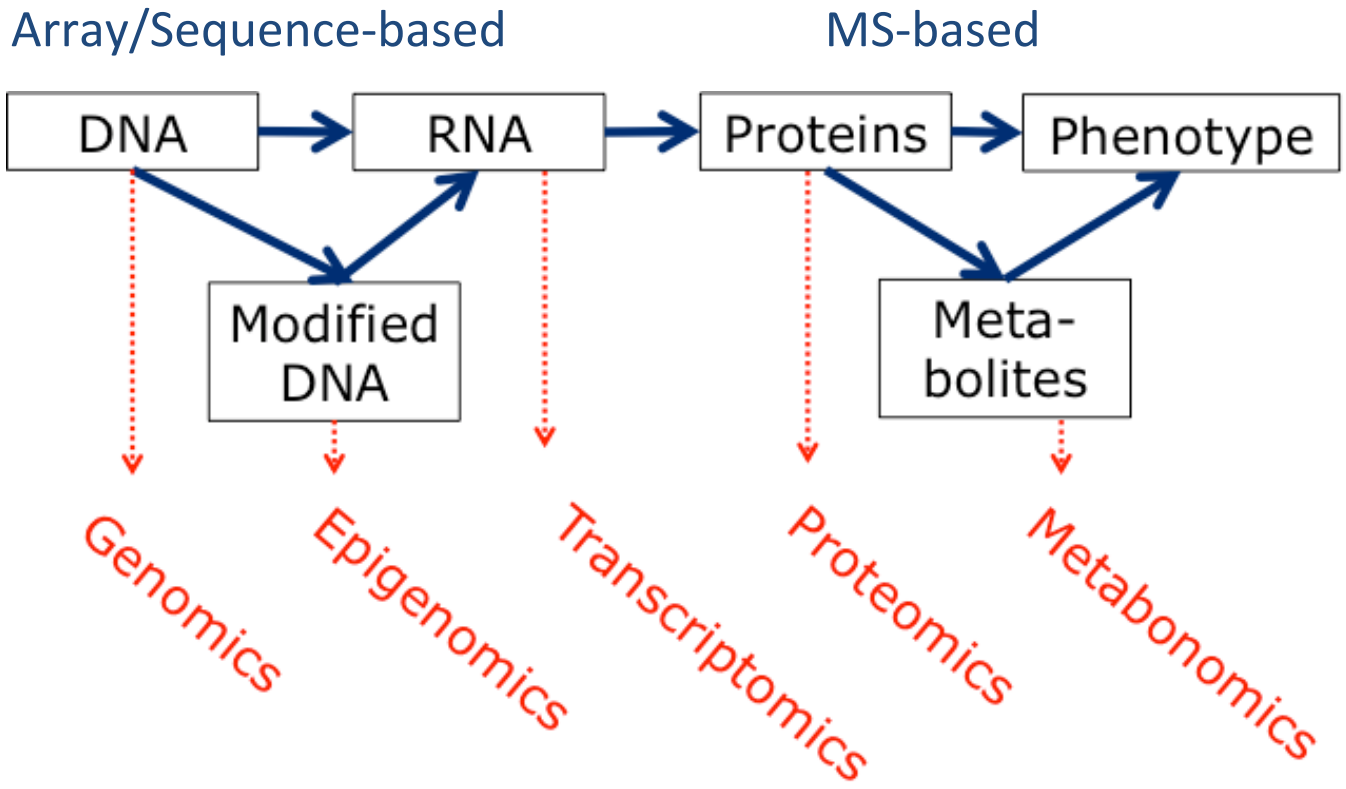
- Tools for exposure assessment are limited and are ill suited for (quantitative assessment) of thousands of potentially causative exposures
- Argued for an 'agnostic' top-down approach
  - OMIC profiles
    - Identify particular 'exposures' (Signals)
    - Develop high-throughput biomarkers
    - Determine sources of external and internal exposure



Modest claim

- So far we all did it wrong
- We = exposure assessors and especially epidemiologists
- Not individual enough
- Not comprehensive enough in terms of components and time points
- Probably not the most relevant components for major diseases

OMIC Analyses of the exposome



Traces of exposure occurrence in terms of a particular pattern of gene methylation and expression, proteins, or metabolites

Omics

- Omics used for disease mechanisms, only recently explored for exposure assessment
- Large number of components measured
- Broad patterns instead of specific chemical
- Reflect exposure plus biological responses -> no perfect correlation with external exposure

Evidence?

- There is indeed evidence of fingerprints of specific exposures e.g radiation, smoking, benzene, soy diet change
- How specific are they?

Smoking: Irreversible and reversible genes

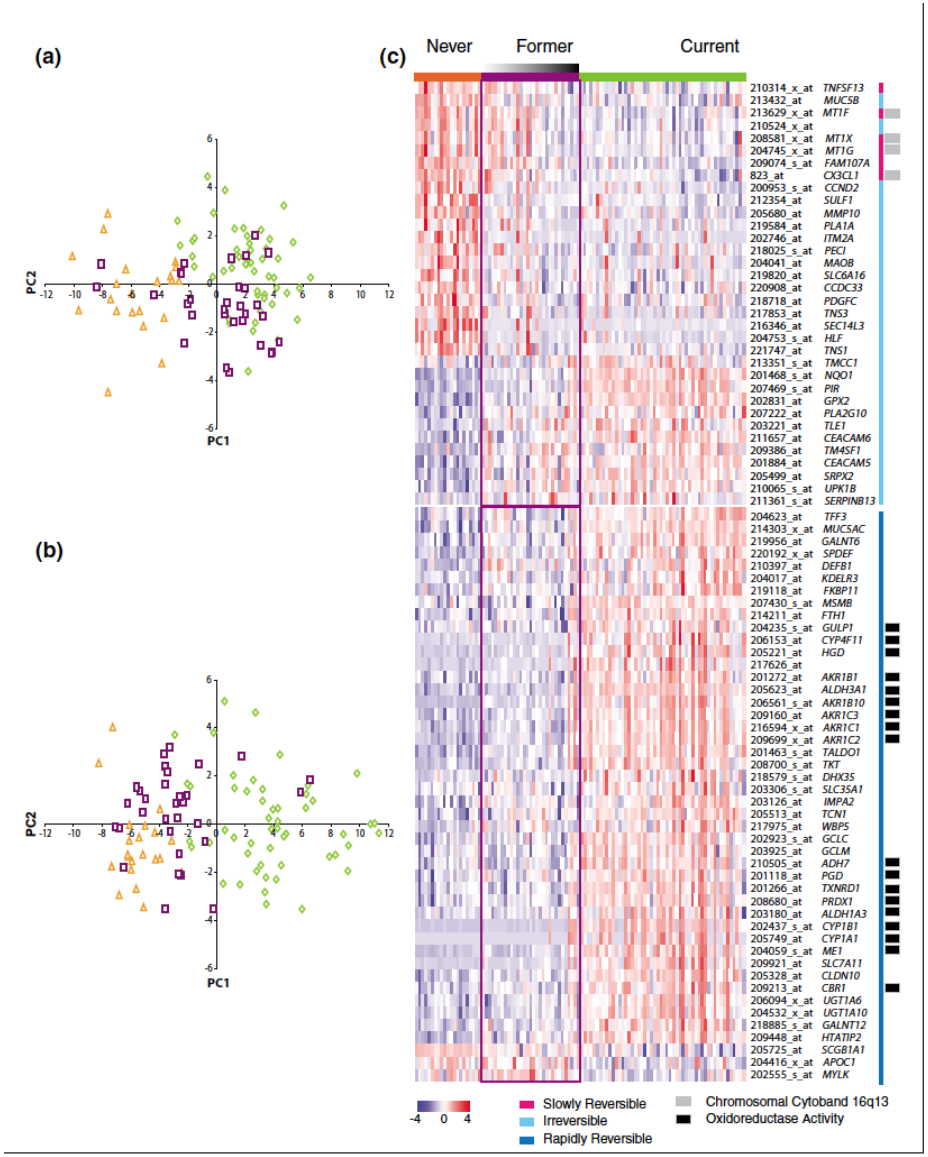


Figure 4 *(see legend on previous page)*

- Data shows current, former and never smokers can be identified by pattern of reversible and irreversible altered genes
- Specific to tobacco smoke?
- Specific to particle toxicity?
  - Diesel exhaust
  - Indoor air pollution
- A reflection of exposure or disease?

Beane et al., Genome Biology, 2007

REVIEW

The exposome: from concept to utility

Christopher Paul Wild

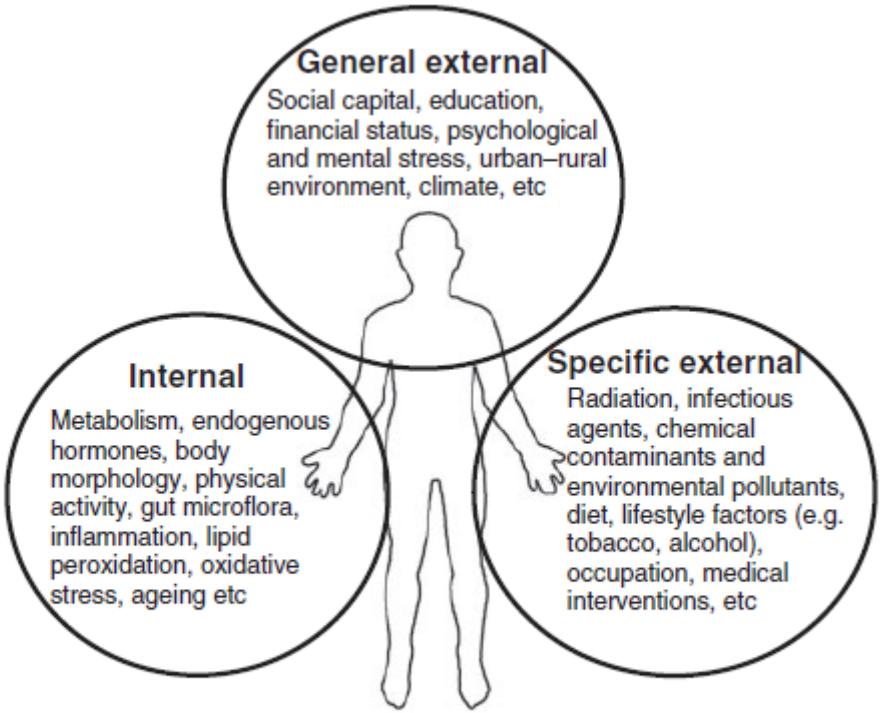


Figure 1 Three different domains of the exposome are presented diagrammatically with non-exhaustive examples for each of these domains

Table 1 Some examples of approaches and tools to measure the exposome

Approach	Tools
Biomarkers (omics)	
General	Genomics, transcriptomics, proteomics, metabolomics, epigenomics
Targeted	Adductomics, lipidomics, immunomics
Sensor technologies (including mobile phones)	Environmental pollutants, physical activity, stress, circadian rhythms, location [global positioning systems (GPS)]
Imaging (including mobile phones, video cameras)	Diet, environment, social interactions
Portable computerized devices (including palmtop computers)	Behaviour and experiences (ecological momentary assessment), stress, diet, physical activity
Improved conventional measurements (combined with environmental measures)	Job-exposure matrices; dietary recall (e.g. EPIC-Soft)

Understanding the link between environmental exposures and health: does the exposome promise too much?

Annette Peters,[1,2] Gerard Hoek,[3] Klea Katsouyanni[4]

- Biomarkers describing changes of physiological states upon exposure to environmental agents are often indicators of internal effective dose and early physiological responses

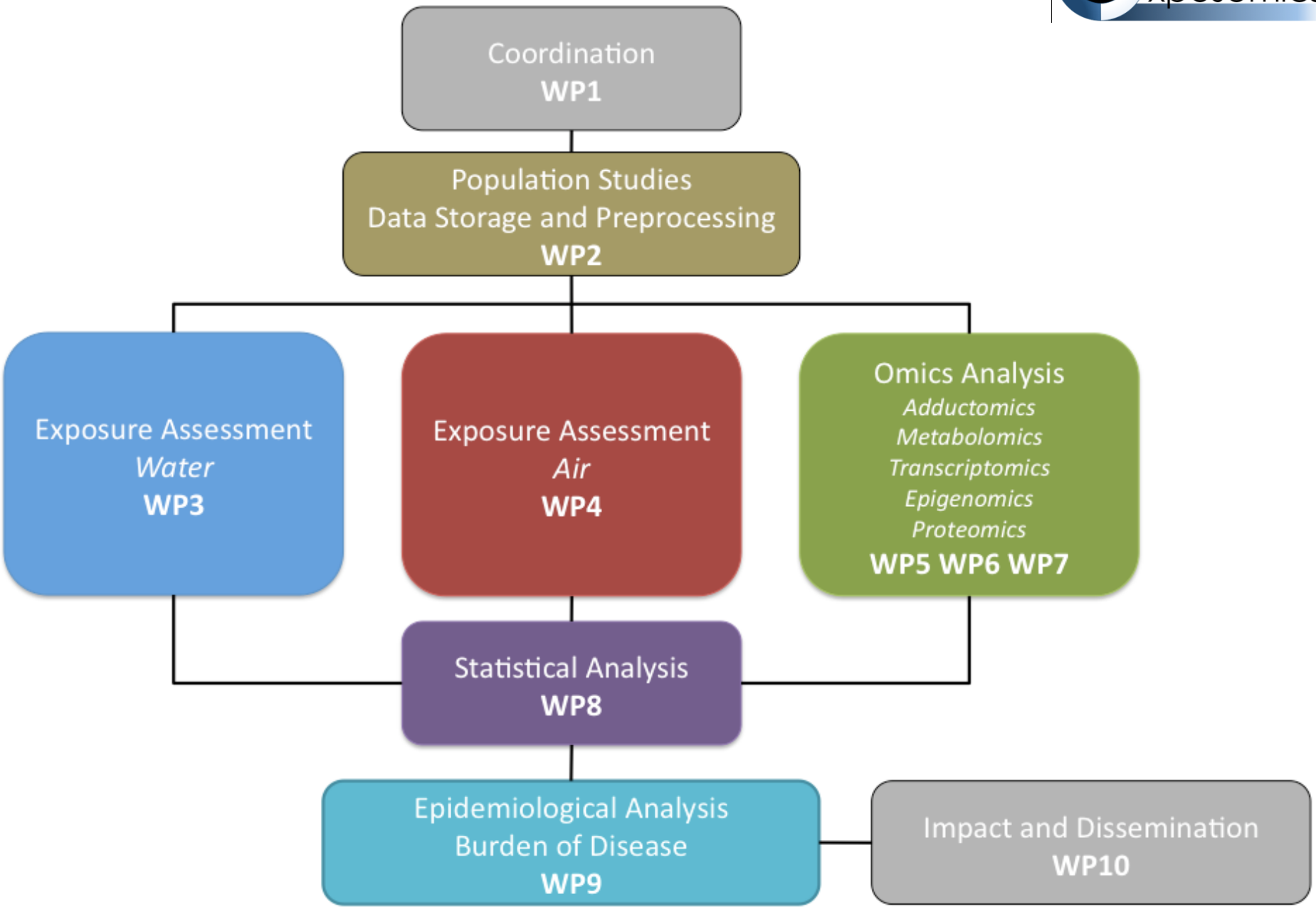
- Internal dose measurements of environmental exposures might have lost the distinct signature of the relevant sources

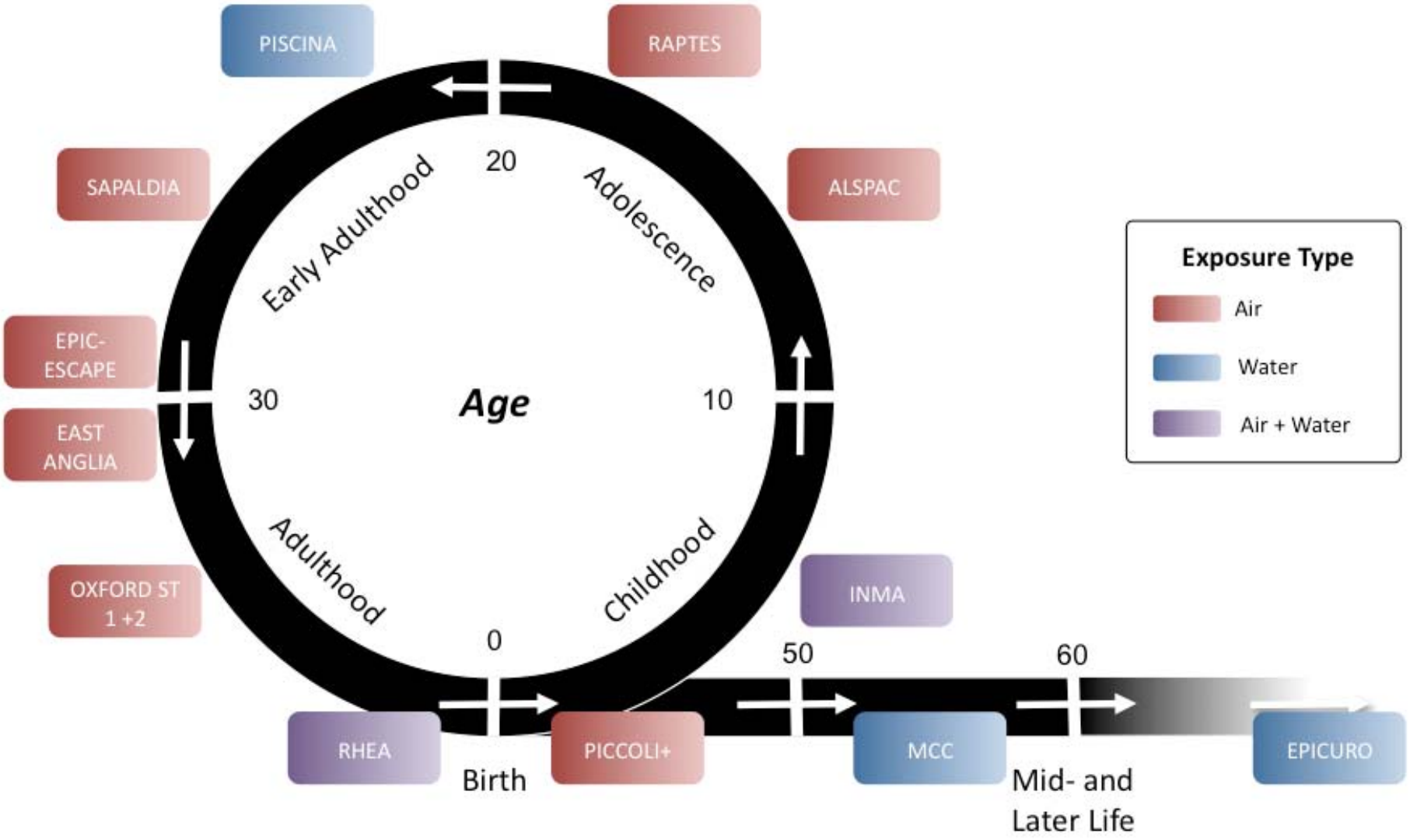
Observations

- External and internal exposome
- Some empirical evidence that the approach can be made to work
- Temporal and inter-individual variability
- Statistical challenges (patterns, fals positives)
- Interest in funding agencies

FP7 multi-center study
Coordinated by Prof Paolo Vineis (Imperial College)

Partners: Imperial College, IRAS, CREAL, Swiss TPH, Kings College, CRIC, Genedata, Rappoport, Smith, Krystopolous


Coordination
WP1
Population Studies
Data Storage and Preprocessing
WP2
Exposure Assessment
Water
WP3
Exposure Assessment
Air
WP4
Omics Analysis
Adductomics
Metabolomics
Transcriptomics
Epigenomics
Proteomics
WP5 WP6 WP7
Statistical Analysis
WP8
Epidemiological Analysis
Burden of Disease
WP9
Impact and Dissemination
WP10


PISCINA
RAPTES
SAPALDIA
ALSPAC
EPIC-ESCAPE
EAST ANGLIA
OXFORD ST 1 +2
INMA
RHEA
PICCOLI+
MCC
EPICURO
Early Adulthood
Adolescence
Adulthood
Childhood
Age
0
10
20
30
50
60
Birth
Mid- and Later Life
Exposure Type
Air
Water
Air + Water

Basic components of the EXPOsOMICS project

1. Select subjects from 3 types of existing studies: Experimental Short-Term Studies (STS), Mother-Child Cohorts (MCO) and Adult Long-Term Studies (ALTS), reflecting all life stages from conception to old age

2. Measure the external exposome component for air and water contaminants by performing extensive, repeated Personal Exposure Monitoring (PEM).

Fresh blood samples will be collected from all the individuals undergoing PEM.

In these new plus stored samples (~ 1,000 samples), EXPOsOMICS will conduct untargeted omic analyses. The aim is to look for new biomarkers of exposure to chemicals or mixtures and evaluate intra-individual variation of the internal exposome.

3. The strongest signals from the above will be measured in approximately 2,000 stored samples from cohorts, using targeted omic analysis methods, with the aim to evaluate them as predictive of risk by examining their association with health effects.

4. Combine external and internal exposome data, Land Use Regression models (LUR) and satellite data to calibrate exposure estimates obtained using traditional methods in MCO/ALTS and use these refined estimates for risk assessment and burden of disease evaluations.

Exposome solves it all?

- Bit too early yet ....
- Concept interesting for calling for better EA incorporating multiple stressors
- More experimental work needed to demonstrate utility
- Link with sources / external exposures remains vital