The Exposome concept and its future potential

European Health Forum
Gastein
Session: Environment and Health:
Building the Evidence Base for Policy

October 5th, 2017

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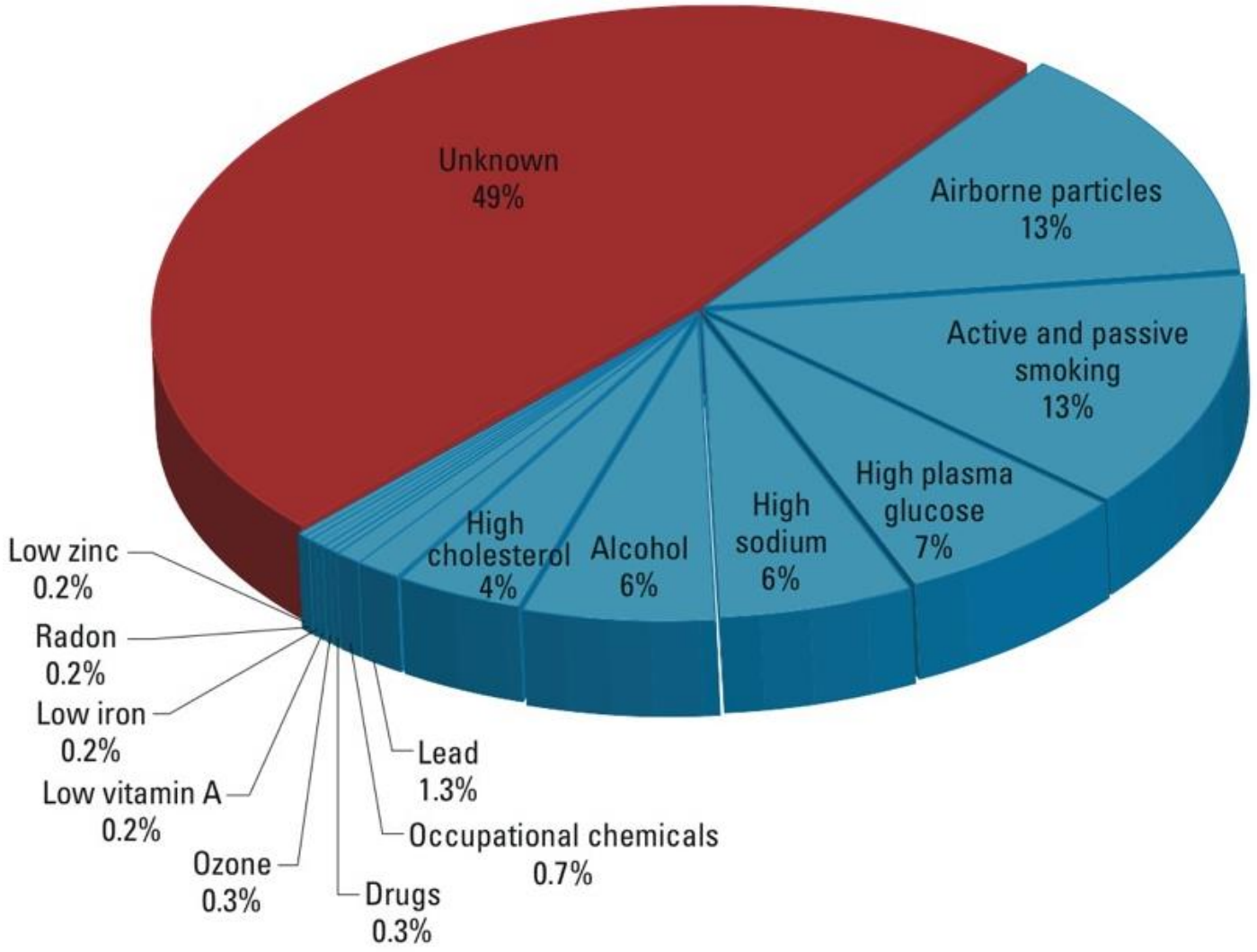
Non communicable diseases



Rappaport et al, EHP, 2014, based on Lim et al, Lancet 2012

The definition of the exposome

"The Exposome (Chris Wild, IARC): The totality of environmental exposure an individual is subjected to from conception to death…"

Health and disease are influenced by the genome and the exposome, including lifestyle factors.

Further contributions to the exposome concept

Wild	• **All life-course environmental exposures** from prenatal period onwards; includes internal body processes, external exposures, and lifestyle factors.
Rappaport and Smith	• **The Chemical exposome.** Total exposures throughout life, where the "environment" is the body's internal chemical environment and "exposures" are all the **biologically active chemicals in this internal environment**.
Buck Louis	• **Mixture of environmental exposures**, including man-made and naturally occurring chemicals, physical agents (e.g., noise, vibration, temperature), **macro level factors** (e.g., population density, sanitation), and **lifestyle factors**.
NRC Report	• "**Eco-exposome**" extends concept from point of contact between stressor and receptor, **inward into organism and outward to general environment**.

Courtesy of D Balshaw, NIEHS

The complexity of exposures

What type of Stressor?
Physical, Chemical, Biological, Psycho-social

Which Source?
Air, Water, Soil, Food, Consumer Products, Drugs

Where?
Home, School, Work, Neighborhood, City, Region

What type of effect?
Organs, Tissues, Biological pathways, Adverse pathways

When?
Fetal, Child, Adolescent, Adult, Elderly

The EU exposome and HBM landscape

project	topic	origin	Start/end
Exposomics	exposome	EU	2012/2016
Helix	exposome	EU	2012/2017
Heals	exposome	EU	2013/2018
HBM4EU	Human biomonitoring	EU	2017/2021

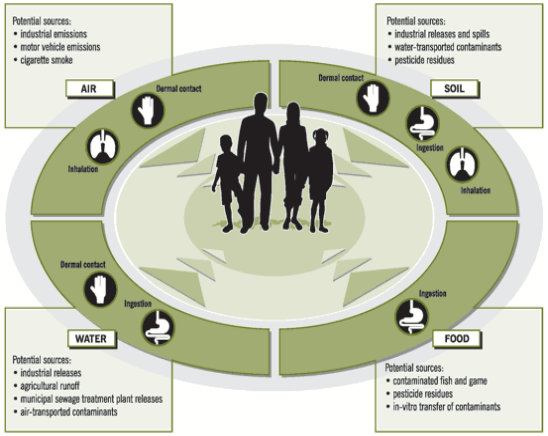
Innovative methods to asses the external/internal exposome

HEALS

Remote sensing

Environmental sensors

personal sensors

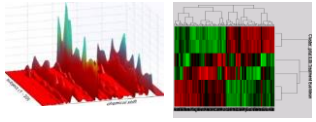


Exposure modelling

Exposure and Effect biomarkers

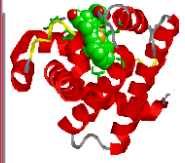
Human bio-monitoring

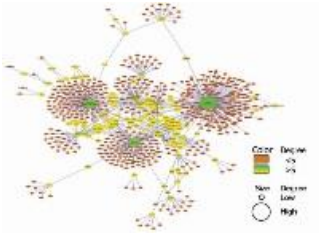
OMICS



PBTK

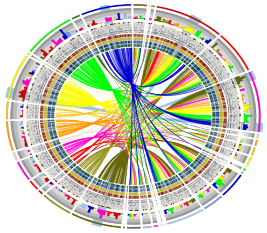
Causality: mechanistic studies





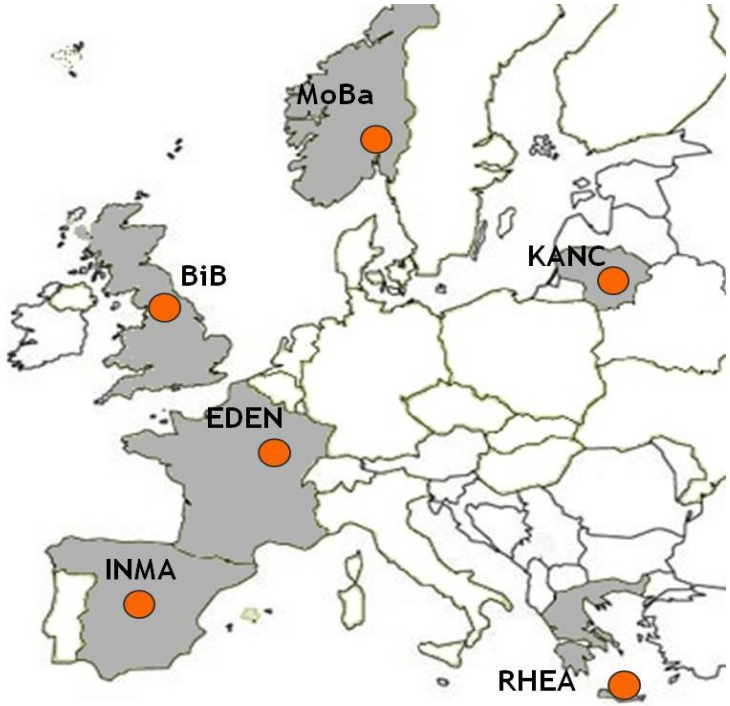
EWAS: Environment wide association studies

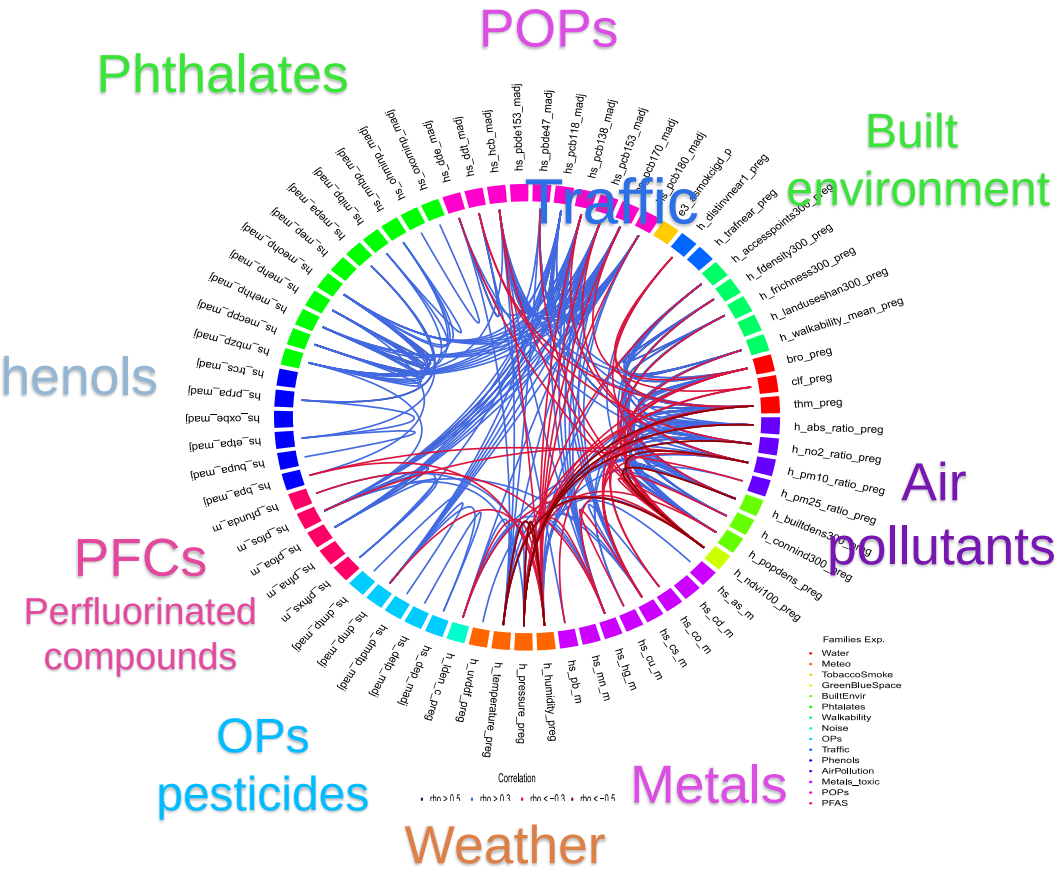
GEWIS: Genome-Environment wide interaction studies



SEVENTH FRAMEWORK PROGRAMME

Combining Birth Cohorts at the EU level



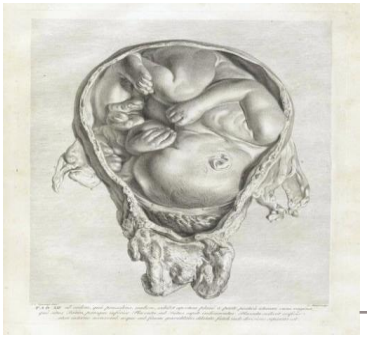


Stressors combination

Vrijheid et al, Environ Health Perspect 2015;122(6):535-44.

Epigenomics and long term effects

***In utero* exposure to PM_{10}**



450K methylation array

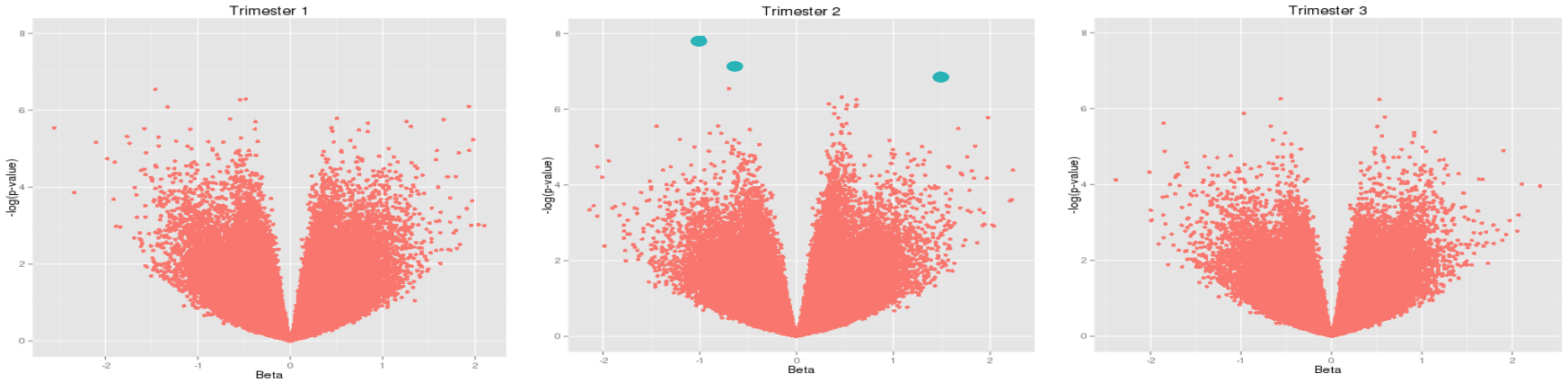
450K methylation

450K methylation

Cord blood samples → Samples Blood @ 7 y → Samples Blood @ 15 y

In utero development | Birth | Infancy

Avon Longitudinal Study of Parents and Children(ALSPAC)



Courtesy: P Vineis

First implications of the exposome studies

- **Considerable development of methodologies supporting global assessment of exposures, health effects, causality:**
  - **Sensors (general and personal)**
  - **Monitoring**
  - **Modeling: exposure, environment and health effects**
  - **Effect markers**
  - **Assessment of combined effects: systems medicine**

- **Implications in public health:**
  - **regulation,**
  - **vulnerable populations,**
  - **public health messages supporting general prevention**

- **Implications at the individual level: Precision Prevention (ex: asthma, diabetes, elderly, newborns, etc.)**

What is Precision medicine?

“an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person” (*PMI NIH*)

Until now, precision medicine has primarily focused on the use of genomics to improve diagnosis and therapy at the individual clinical level

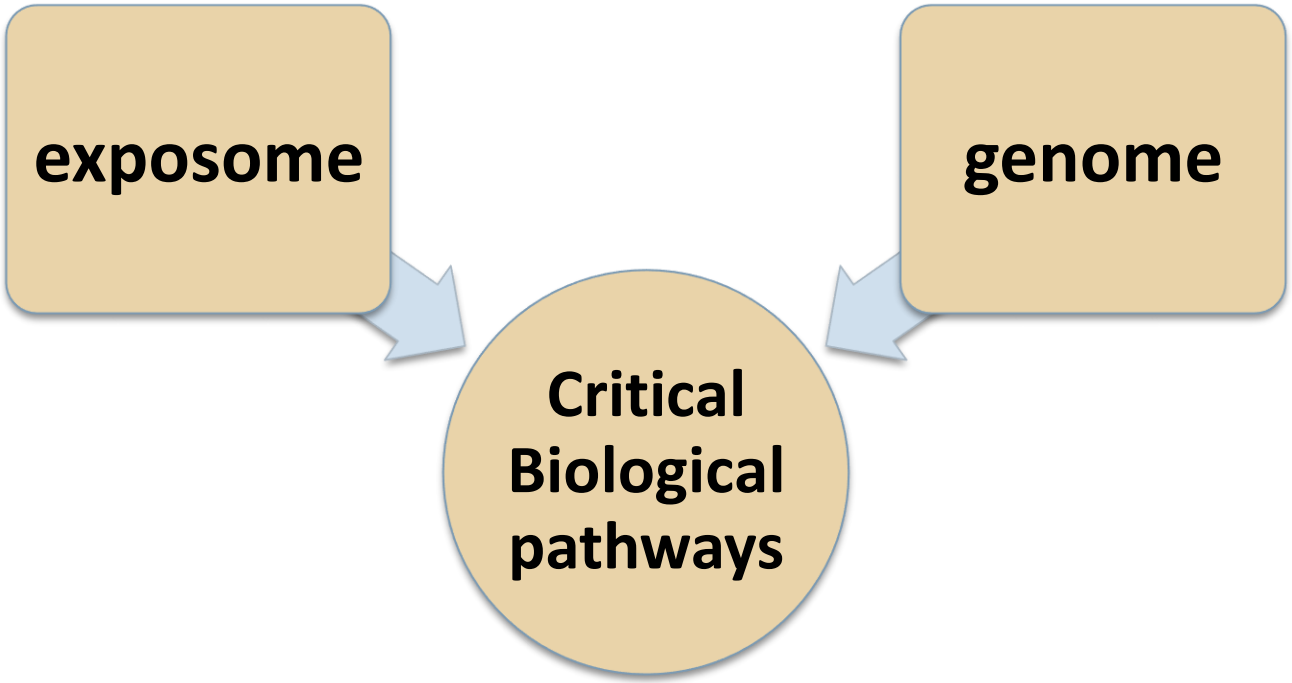
Precision medicine: beyond genomics

- ✓ **Translating large scale epidemiological studies into individual risk factors is not obvious for most diseases**
- ✓ **Social and environmental health determinants should be considered: poverty, education, stress, pollution, etc.**
- ✓ **There are different causes for vulnerability that are not captured by genomics**

Khoury and Galea, JAMA, 2016

Paving the way for Precision Prevention

Integrating genomics and exposomics will lay the foundation of the precision and preventive medicine of the future



Why is the exposome concept relevant?

In the Gene X Environment paradigm, we now need to increase our knowledge on the E (including social, economic and physical effects.

Public policies should take into consideration the multiplicity of stressors and their possible interactions (ex: diet and contaminants, poverty, stress and exposure to pollutants, etc.)

Combination of genomics and exposomics should target prevention and therapeutic strategies

An improved assessment of vulnerability will also allow to target prevention: developmental, genetic, associated disease, diet, social, economic, etc

Precision Prevention : general implications

Precision medicine should be combined with more general public health interventions aiming at decreased exposure when relevant

Based on G x E assessment, intervention can be through changes in lifestyle, diet, decreased exposure, in addition to targeted therapies

Such ambition should stimulate innovation in environmental health science and technology, in ubiquitous sensing, in high throughput biological analysis technologies and in big data analysis

They should promote trans-disciplinary education and training