The Exposome concept and its future potential

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Non communicable diseases

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

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Innovative methods to assess the external/internal exposome

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
Combining Birth Cohorts at the EU level

Stressors combination

Epigenomics and long term effects

In utero exposure to PM$_{10}$

In utero development
Avon Longitudinal Study of Parents and Children (ALSPAC)

Birth

Infancy

Cord blood samples

Samples Blood @ 7 y

Samples Blood @ 15 y

450K methylation array

450K methylation array

450K methylation array

Not significant

significant (Bonferroni)

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.