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WP3 DigiOmica collaborative learning in Integrated omics for environmental sustainability

Module 10: *Air pollution genomics*

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- **Educational goals**: the aim of this module is to present knowledge about the
  - 'Omics' (especially, genomics and epigenomics) approaches to study the negative effects of air pollutant exposure
  - Genome-wide association studies (GWAS) Genome-wide interaction studies (GWIS) of air pollution exposure
  - Impact of epigenomic modifications in air pollution research

Summary

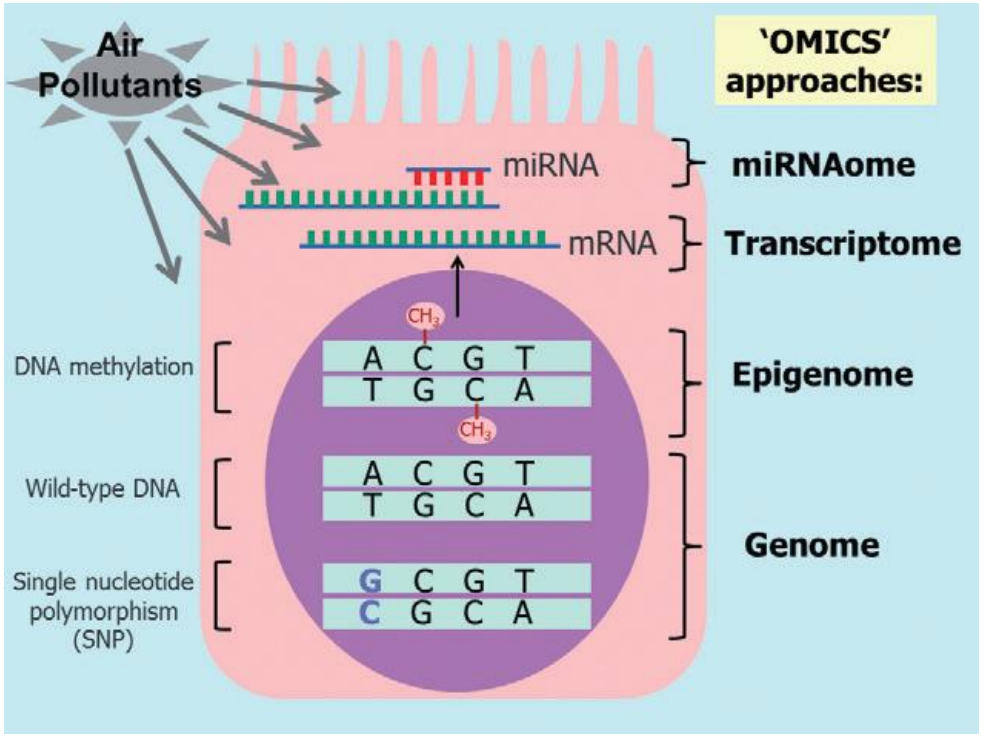
Omics approaches to study the air pollutant exposure's health effects comprise systematic investigations at the genomic level. Genomics and epigenomics contribute to the assessment of the response to air pollutant exposure through studies based on single-nucleotide polymorphisms (SNP) in DNA (genome-wide) and epigenomic changes like differences in DNA methylation and post-translational histones modifications (epigenome-wide). The genome/epigenome changes that result from gene-environment interaction influence protein expression and function at the metabolic level, thus impacting cellular functions in response to air pollution. The appraisal of these changes through genomics/epigenomics tools facilitates the adverse effects of air pollutants' understanding. This case study presents data about the state-of-the-art in genome-wide association studies of SNP, changes in DNA methylation, and post-translational histone modifications that occur with air pollutant exposure. The material also reveals GWIS and conceptual models for air pollution epigenetic epidemiologic studies as advantageous research perspectives.

- **Expected learning outcomes**: Upon completion of this Module the learners will be able to:
  - Describe how the genome-wide association studies can improve our understanding of the adverse effects of air pollutants
  - Understand the links between air pollutant exposure and the epigenome
  - Present the principles of ‘candidate gene’ and the ‘genome-wide’ (‘hypothesis-independent’) approaches as tools for assessment of the biological response to air pollutants exposure
  - Examine the causative role for the epigenome in the adverse effects of environmental exposures, using air pollution as a model
  - Know the essence of the approach for use of GWAS to measure controlled air pollutants exposures in healthy individuals

Provisional Table of contents:

Presentation of the learning content

1. Introduction



Source: J.W. Holloway et al., Respirology (2012) 17, 590–600

- **Genomics** – systematically studying the response to air pollutant exposure
- **Epigenomics** – studying the differences in DNA methylation and post-translational histones modifications

Presentation of the learning content

2. Findings

2.1 Biological response to air pollutants exposure: genomic approaches

- **Candidate gene approach** – measurement of the genetic variation in individual genes and the data association with disease phenotype of air pollution injury
- **Genome-Wide Association Studies (GWAS)** - independent association studies in case-control or population-based samples for studying genetic factors in disease due to air pollution
- **Measurement of the results of controlled exposures in healthy individuals** for identification of genetic factors that modulate the biological responses to air pollution exposure

Presentation of the learning content

2. Findings

2.2 Epigenome-wide approaches for study epigenetic processes

- Exposure to air pollution and changes in gene-specific methylation – exemplary human studies for global methylation profiling using microarrays:
  - Animal models of exposure, air pollution exposure human studies, and combined epigenomic and genomic (GWAS) studies
- Post-translational histone modifications following air pollution exposure
  - Air pollution exposure-associated changes in histone modifications at specific loci

Presentation of the learning content

3. Alternatives

3.1 Genome-wide interaction studies (GWIS)

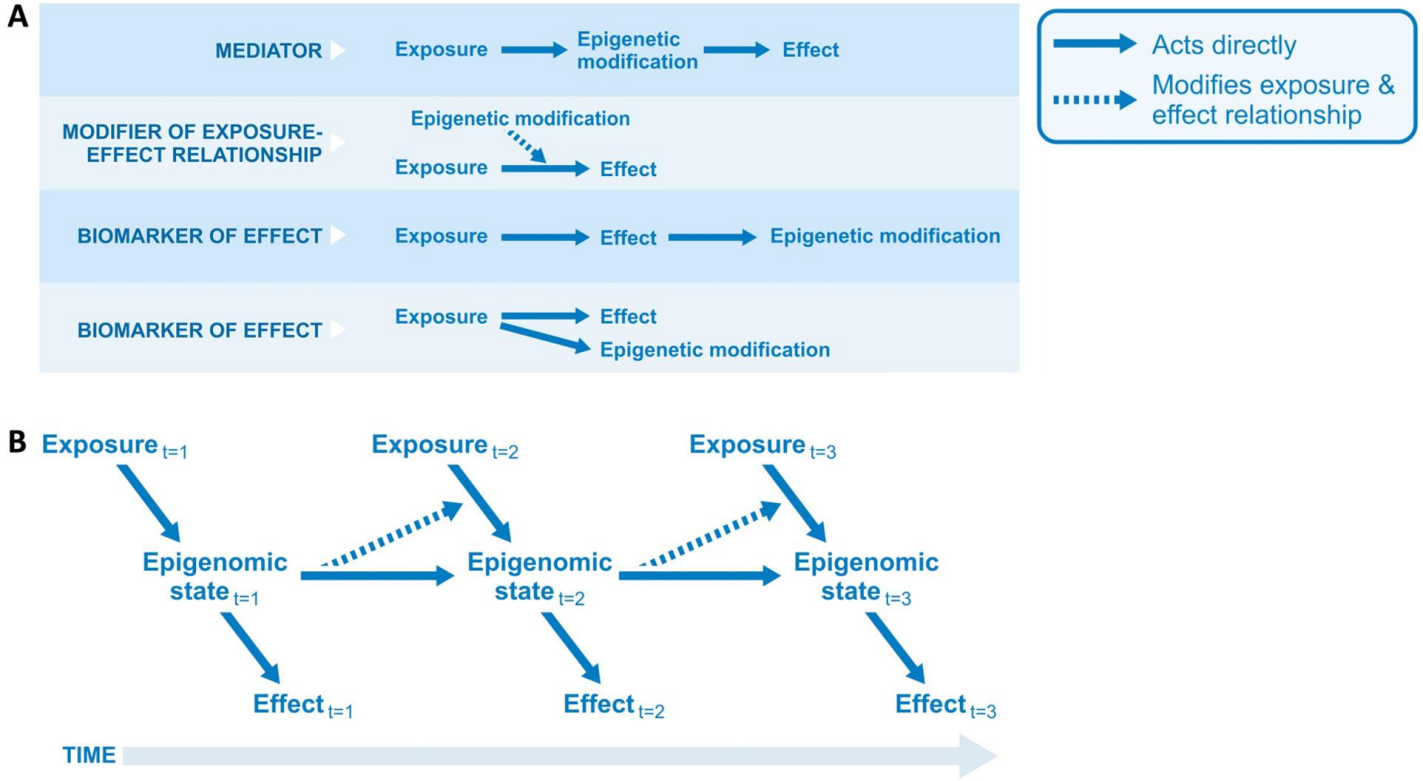
- Importance of gene – environment interactions and complex pathways comprising multiple genes and exposures
- Genome-wide interaction studies (GWIS) – advantages and challenges
- Exemplary GWIS

Presentation of the learning content

3. Alternatives

3.2 Air pollution exposures and epigenome alterations

- Conceptual models for air pollution epigenetic epidemiologic studies



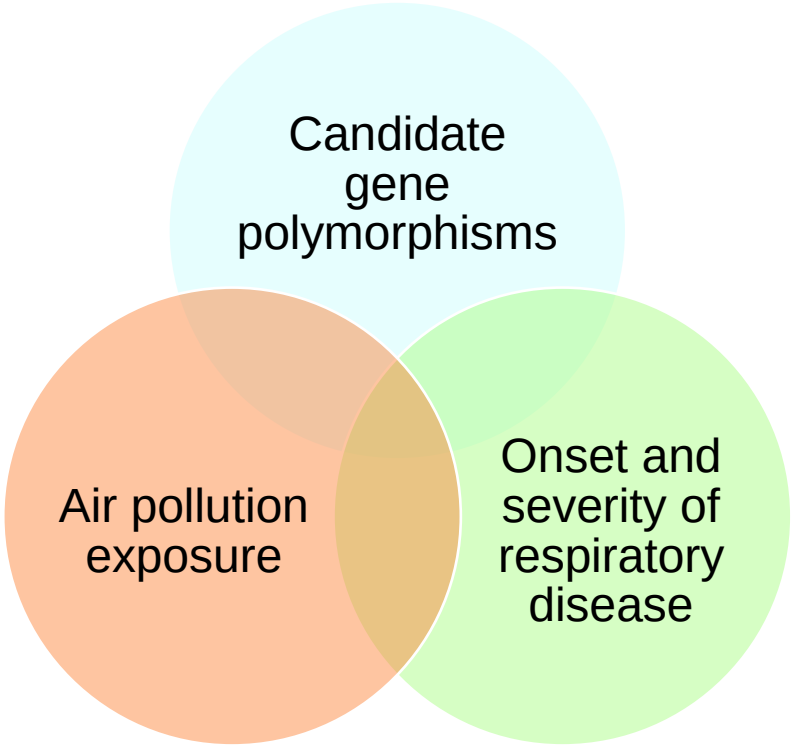
Source: Perera et al., Curr Opin Toxicol. 2019;18:27-33. doi: 10.1016/j.cotox.2019.02.008

Presentation of the learning content

4. Solutions

4.1 Genes - environment interaction study

- Implementing the principles of genes - environment interactions
- Exemplary implementation: the role of antioxidant gene polymorphism



Presentation of the learning content

4. Solutions

4.2 Exploring the epigenomic modifications in air pollution research

- Epigenome mapping and publicly- available epigenome browsers - visualization of the global distribution of histone modifications

- Application of locus-specific epigenetic editing using clustered regularly interspaced short palindromic repeat (CRISPR) technology

Presentation of the learning content

5. Recommendations

- Future utilization of GWIS approach – revealing the mechanisms by which air pollution exposure causes respiratory disease
- Clarifying how air pollution interacts with genetic variants (genomics approach), methylation and other gene regulation mechanisms, e.g., histone and chromatin changes (epigenomics approach)
- Use of microarray and NGS techniques

Presentation of the learning content

6. References

- McCullough SD, Dhingra R, Fortin MC, Diaz-Sanchez D. Air Pollution and the Epigenome: A Model Relationship for the Exploration of Toxicoepigenetics. Curr Opin Toxicol. 2017 Oct 1;6:18-25. doi: 10.1016/j.cotox.2017.07.001. PMID: 33869910; PMCID: PMC8048108.
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