Outcomes from EFSA’s Scientific Colloquium on omics in risk assessment

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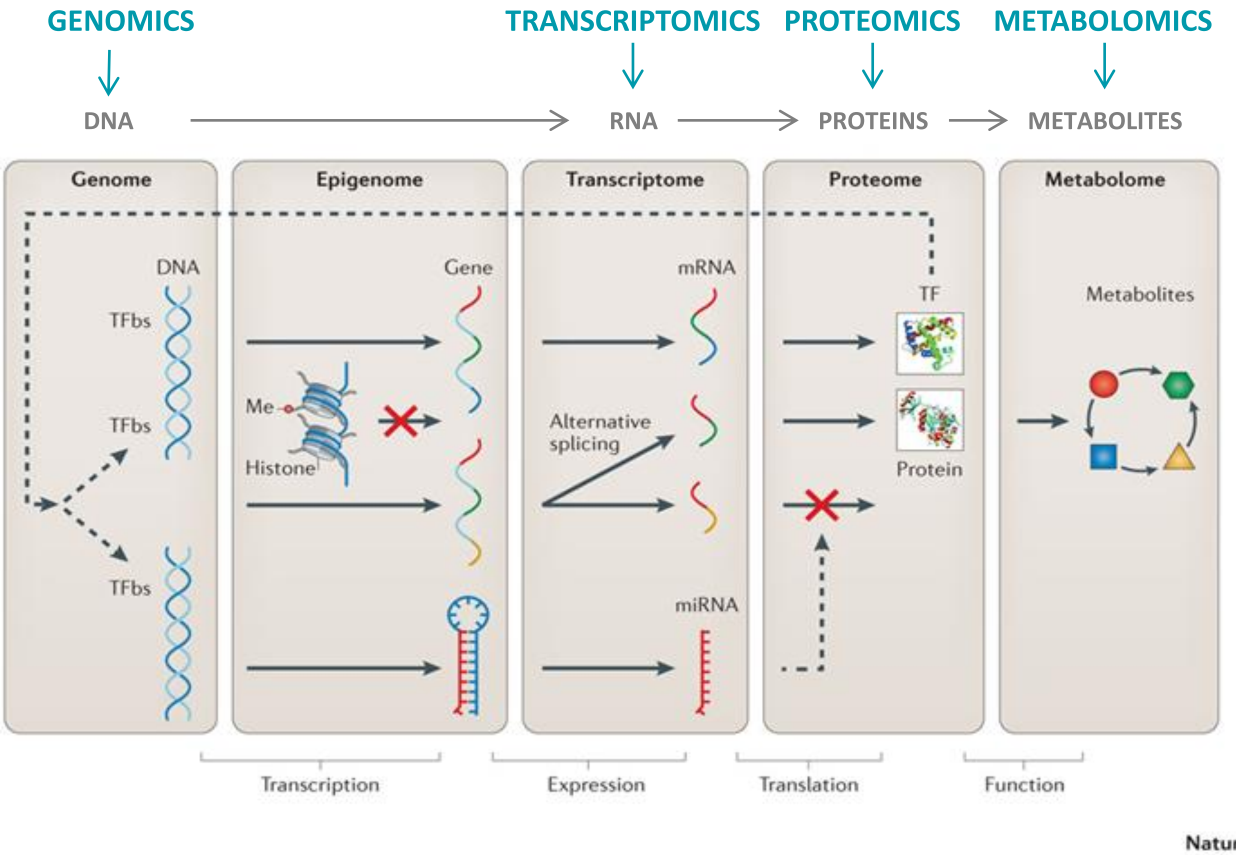
European Food Safety Authority

“OMICS” studies

Omics studies are used to characterise and quantify the roles and relationships of large sets of different types of molecules in an organism to get information on the functional status of or the impact of environmental factors on an organism

"OMICS" studies



- Information on functional status of an organism
- Information on impact of external factors on an organism

Adapted from Ritchie et al., 2014, Nature review Genetics, 16, 85-97

OMICS in basic and applied science

- Genomics benefitted from next-generation sequencing technologies to study genomes in more detail, e.g.
  - Single nucleotide polymorphism (SNP) analyses have helped to understand the basis of disease and disease resistance
  - Rapid and accurate sequencing of full genomes can be used in determining food borne pathogens
  - Comparative genomics and evolution

- Transcriptomics provides information on the transcription of genes, e.g.
  - RNA sequencing to determine chemically induced changes in gene expression (e.g. Cadmium stress in plants)

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OMICS in basic and applied science

- Proteomics provides information on proteins and their interaction in a cell, e.g.
  - The proteome reflects on the dynamic state of a cell, tissue or organism and provides the possibility to identify biomarkers in toxicology
  - High-throughput proteomics can identify the molecular signature of a disease

- Metabolomics captures data for a large pool of metabolites, e.g.
  - Metabolomics to dissect plant responses to abiotic stress
  - Metabolomics to dissect the nutritional profile of food and feed
  - Metabolomics for the discovery of new biomarkers

William C.S. Cho, 2007

"OMICS" in risk assessment

- **OMICS technologies in research**
  - has been used for more than a decade to study basic biological problems
  - vast amounts of analytical data are being collected and shared
- **OMICS technologies in support of risk assessment**
  - is still in an initial phase
  - However, OMICS datasets are starting to be used in some risk assessment areas and have been accepted as a powerful tool to substitute or complement "classical" studies

EFSA activities in relation to OMICS

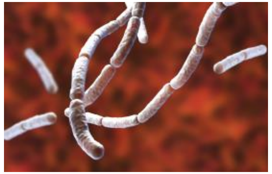
- In 2014 EFSA has published a review of modern methodologies and tools for human hazard assessment of chemicals

- In April 2018, EFSA held its 24th colloquium focusing on omics and aiming to
  - Explore the potential use of OMICS datasets to support the scientific safety evaluation
  - Advance further on concrete paths of implementation to support risk assessors in the process of incorporating OMICS tools into the risk assessment of food and feed products

Programme of the 24th EFSA colloquium

- 4 Plenary talks introducing the topics addressed in the different discussion groups
- 4 Discussion groups addressing challenges for the implementation of OMICs in the risk assessment
- Feed back from the discussion group to all participants in a final plenary session

Discussion groups



- **DG1:** Genomics for identification and characterisation of microbial strains in food and feed products

- **DG2**: The use of Metabolomics in the comparative risk assessment of GM plants

- **DG3**: The use of OMICS in human risk assessment of chemicals

- **DG4**: The use of OMICS in environmental risk assessment

Event report

- Summary of the outcomes of the different discussion groups and the overall messages from the colloquium will be presented in the colloquium's event report

- The event report is expected to be published by the end of October 2018

Discussion group 1: Genomics of Microorganisms

- **Setting:** microbes (bacteria, yeasts, fungi) are extensively used in food and feed chain
  - added as viable organisms to the food chain (e.g probiotics, novel food of microbial origin)
  - serve as production organisms for food and feed products (e.g. food enzymes, feed additives…)
- **Issue discussed**: Comprehensive analysis and functional characterisation of microbes is necessary
  - to properly identify the microbe taxonomically
  - to identify undesirable properties, such as potential for toxin production or antimicrobial resistance
  - To properly characterise genetic modifications
- Genomics, i.e Whole Genome Sequencing (WGS) is a powerful tool to address this issue

Discussion group 1: Genomics of Microorganisms

- **Outcomes:**
  - **WGS** particularly useful for **taxonomic classification** of not well known species or species with pathogenic strains. Quality standards, algorithms and similarity threshold values were recently published for bacteria but do not yet exist for eukaryotic microorganisms.
  - **WGS** can provide information on the **presence of** genes encoding **virulence factors** and **toxic compounds**.
    - Main limitation is knowledge of those genes and their regulation.
    - WGS data should be complemented with additional evidence.
  - **WGS** has some predictive value to identify and characterise **antimicrobial resistance**, but cannot substitute phenotypic testing.
  - **WGS** enables **characterisation of genetic modifications**, in particular long insertions
- **Development needs for use of WGS data**:
    - Quality standards for laboratory work and data analysis
    - Expertise and supporting knowledge for data interpretation
    - Reference data sets and curated databases of microbe sequences

DG2: Metabolomics in risk assessment of GM plants

- **Setting:** Comparative approach - GM plants are compared to their non-GM counterpart and non-GM commercial varieties by analysing a set of compositional endpoints
  - internationally agreed standard set of key compounds is analysed
  - each compound is compared individually between GM and non-GM plants
- **Issue discussed:** Can metabolomics add to or substitute the current approach?
  - Basis for discussion was an approach developed in research projects (group E. Kok and collaborators, RIKILT Institute, Netherlands)
    - uses omics data to generate „general profiles" of the plants
    - The profiles of commercial varieties are used to establish a safe „one class" against which the GM plant profile is tested

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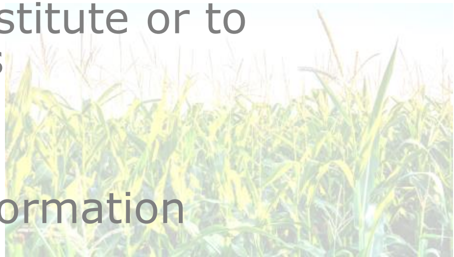
DG2: Metabolomics in risk assessment of GM plants



- **Outcome**: Metabolomics could be used to either fully substitute or to complement the existing approach on a case-by-case basis
- **Advantages:**
  - More compounds can be analysed, increased level of information
  - **focus on pathways** rather than individual endpoints, providing a more holistic picture of the metabolism
  - in the **"profile – one class" approach**, there is **no endpoint-by-endpoint** comparison but a holistic comparison of the GM plant profile against a safe class of commercial varieties
  - Could be cost-efficient, if the approach is globally accepted and depending on exact conditions
- **Development needs:**
  - Standardisation of experimental protocols and data analysis (statistics)
  - Global regulatory harmonisation and frame for interpretation in the risk assessment

DG3: OMICS in human risk assessment of chemicals

- **Setting:** to discuss the relevance and use of various types of OMICS in toxicology
- **Issue discussed/outcome:** Types of information that can be gained from OMICS
  - Use of OMICS to identify points of departure (NOAEL, BMD) in chemical risk assessment for deriving health-based guidance values (ADI)
  - Identification of novel biomarkers for prognosis, effect or exposure
  - Support for hypothesis generation and Adverse Outcome Pathway (AOP) development
  - Support for the grouping of chemicals according to toxicological profile

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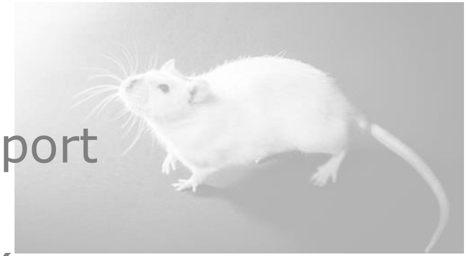
DG3: OMICS in human risk assessment of chemicals



Overall outcome:

- Currently, OMICS data **provide added value** to support chemical risk assessment and
- Usful to address challenging questions in toxicology (e.g. endocrine effects, nanotoxicology, mixture toxicity)

Gaps and development needs:

- Establishment of standards for **data processing and interpretation**
- Knowledge on the **variability of omics baseline values** (humans and experimental animal models)
- To provide data in a **reproducible** manner so they can be used in the regulatory decision-making processes

DG4: OMICS in environmental risk assessment

Setting: to discuss the use of OMICS and OMICS derived endpoints in environmental hazard assessment

Issues discussed/outcomes:

- OMICS is **most useful in development** of robust and well supported **AOPs and MoAs** that can inform hazard identification.
- Comparison of **OMICs derived endpoints** to conventional endpoints
  - OMICS focuses on sub-lethal endpoints rather than lethality
  - Only a low number of OMICS derived endpoints can be linked to conventional life history metrics that are measured in ERA
- OMICs can help in some cases to **identify sensitive** (non-target) **species or endangered species** where standard eco-toxicity tests fail , e.g
  - For RNAi based regulated products: transcriptomics can be used to verify RNAi binding sites (target and non-target genes) in different species

DG4: OMICS in environmental risk assessment

Gaps and development needs:

- high quality data sets and dose response modelling to derive ERA standards
- high quality reference data associated with OMICS data to describe natural variation
- Support in translation of the outcome of the OMICS data analysis to a functional impact on adverse outcome / hazard identification
  - Needed: Data packages/tools that link chemical structure, biological pathways and life history outcomes
- Most needed: Developing a 'confidence' framework for use of OMICS data to close the gap between 'what we can measure' and 'what we want to protect'

OMICS in risk assessment-where are we today?

The EFSA colloquium highlighted that

- OMICS data are **an important tool,** e.g in **elucidating mechanisms** and **determining MOA, AOP**
- OMICS data **can be integrated into the risk assessment** in several of the areas discussed even though there are **development needs**
  - Reference data sets
  - Information on baseline variability
  - quality and reporting standards
    - ECETOC project for metabolomics and transcriptomics reporting framework. OECD OMICS reporting framework (projects initiated)
  - Develop expertise

OMICS in risk assessment-where are we today?

- OMICS data are **already part of risk assessment data** at EFSA
  - WGS data in analysis of food borne diseases
  - WGS data in dossiers for genetically modified plants
- **Challenges** are linked to
  - storage → cloud based storage
  - data analysis → software tools and expertise development
  - setting quality standards → guideline development
  - Interpretation in risk assessment → guideline development
    - Technical Note on the quality of DNA sequencing for the molecular characterisation of genetically modified plants (EFSA Journal 2018;16(7):534)
    - Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA Journal 2018;16(3):5206)

OMICS in risk assessment

Change the mindset: OMICS data are not the future, they are the present

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  - Matthew Ramon, European Food Safety Authority, Italy
  - Reinhilde Schoonjans, European Food Safety Authority, Italy
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