GERMAN FEDERAL INSTITUTE FOR RISK ASSESSMENT

Metabolic Effects of Endocrine-Disrupting Chemicals: Novel Testing METhods and Adverse Outcome Pathways (EDCMET)

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Background

The term "**endocrine disrupting chemical**" (ED) mostly refers to compounds that interfere with hormone-related signalling pathways, thereby causing adverse health effects. Recently, the concept of endocrine disruption has been extended to **alterations at the metabolic level**, which may result for example in obesity, fatty liver disease or diabetes, diseases which represent an increasing worldwide health concern. Currently, no validated methods exist to assess metabolic effects of EDs. Thorough understanding of the molecular mechanisms that lead to adverse metabolic effects of EDs is presently lacking.

The EURION Cluster

Starting in early 2019, the **European Union has funded the "EURION" cluster** of eight projects on the overarching topic 'New testing and screening methods to identify endocrine disrupting chemicals' within the Horizon 2020 (H2020) framework, in order to address this unmet need and other gaps in the context of ED testing.

EURION – European Cluster to Improve Identification of Endocrine Disruptors

EDCMET - Metabolic effects of endocrine disrupting chemicals: novel testing methods and adverse outcome pathways. (11 partners)

GOLIATH - Beating Goliath: Generation of novel, integrated and internationally harmonised approaches for testing metabolism disrupting compounds. (15 partners)

OBERON - An integrative strategy of testing systems for identification of EDs related to metabolic disorders. (11 partners)

ATHENA - Assays for the identification of thyroid hormone axis-disrupting chemicals: elaborating novel assessment strategies. (10 partners)

SCREENED - A multistage model of thyroid gland function for screening endocrine-disrupting chemicals in a biologically sex-specific manner. (9 partners)

ERGO - Breaking down the wall between human health and environmental testing of endocrine disrupters: EndocRine Guideline Optimisation. (15 partners)

ENDpoiNTs - Novel testing strategies for endocrine disruptors in the context of developmental neurotoxicity. (16 partners)

FREIA - Female reproductive toxicity of EDCs: a human evidence-based screening and identification approach. (11 partners)

EURION Cluster Activities

- Foster project integration and synergies
- Joint working groups on scientific and regulatory topics
- Common annual meetings
- Workshops & trainings
- International Advisory Panel for regulatory matters

- Communication & dissemination:
  - Webpage: www.eurion-cluster.eu
  - Twitter: @EurionCluster

EDCMET – Basic Facts

- Funded by the EU Horizon 2020 research and innovation programme
- Duration: 01/01/2019 – 12/31/2023
- Total funding: € 5,980,408.75
- Full title: Metabolic Effects of Endocrine-Disrupting Chemicals: Novel Testing METhods and Adverse Outcome Pathways

EDCMET – Aims & Goals

The main objective of EDCMET is to **develop validated in silico, in vitro and in vivo methods to assess metabolic effects of EDs**.

EDCMET will apply the **adverse outcome pathway** (AOP) paradigm to identify molecular initiating events (MIE) that can be used for the prediction of emergent adverse biological phenotypes. A strong focus is put on **energy and fat metabolism**, as well as on **nuclear receptors as molecular targets** that regulate these processes.

EDCMET – Expected Impact

Results from EDCMET are expected to substantially contribute to our **mechanistic knowledge** related to metabolic EDs. Moreover, a **tiered strategy** for the **testing of metabolic effects of EDs** will be developed for future implementation in regulatory toxicology.

EDCMET – Approaches & Methodology

EDCMET will achieve its goals by utilising a wide variety of methodologies. The approach comprises computational tools for the prediction of biological activities and interactions, cell culture-based screening tools, up-to-date animal models, multi-layer omics technologies for the identification of molecular mechanisms, and also epidemiological data, in order to associate the exposure to chemicals to ED-related metabolic effects and to identify human biomarkers of exposure to metabolic EDs.

EDCMET – Partners

University of Eastern Finland: project coordination & management

Funding Acknowledgement

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EDCMET – Research Strategies

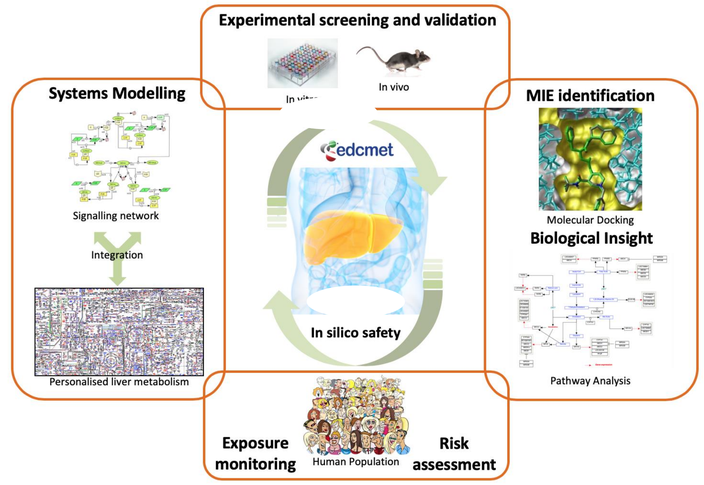

Figure 1: Overview of the EDCMET approach. Development and improvement of methods for the detection of metabolic EDs comprises in silico bioinformatic and modeling approaches, in vitro testing, optimisation of rodent in vivo study protocols, as well as the use of epidemiological data from human cohort studies. By closely working together, the different approaches will

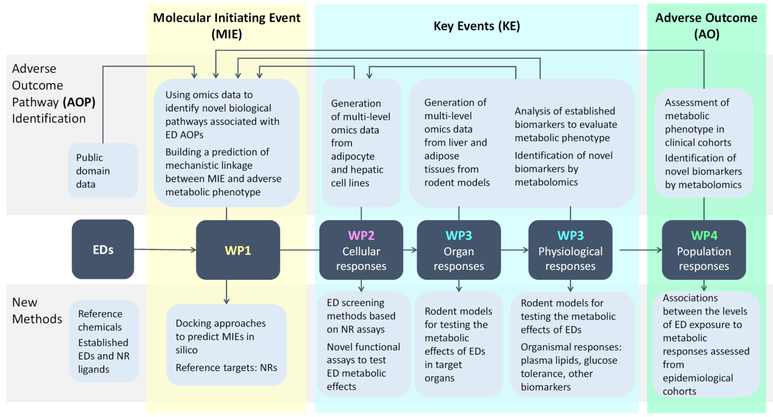

Figure 2: Structure of the EDCMET project. WP1 is dedicated to in silico analyses aimed at identifying metabolic ED compounds and critical molecular initiating events in metabolic ED-related adverse outcome pathways (AOP). WP2 comprises in vitro analyses in order to establish and validate an in vitro ED screening battery, and also profiling of ED chemicals for mode of action and AOP development. WP3 will focus on establishing standardised metabolic endpoints for rodent in vivo tests to complement existing testing strategies. Moreover, WP3 carries out in vivo validation of in vitro data and in silico computational predictions. WP4 links to human exposure and adverse metabolic effects by population-based approaches using human cohort studies. All WPs will contribute to the development of novel testing methods and to mechanistic understanding of metabolic ED.

Contact & Communication

- EDCMET webpage: **www.uef.fi/en/web/edcmet**
- Twitter: **@edcmet.eu**
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Reference: Braeuning, A., Lampen, A., Levonen A.-L. (2019). Investigating the metabolic impact of endocrine disrupting chemicals. www.rdworldonline.com