ENVIRONMENTAL EPIGENETICS

From Mechanisms to Regulation

21–22 February 2019 | Örebro University
Bilbergska huset, Lecture Hall B

1999–20YEARS–2019
ÖREBRO UNIVERSITY

Programme – Thursday 21 February

08:30–09:00	Registration
09:00–09:10	*Welcome and Introduction* – **Steffen Keiter,** MTM Research Centre, Örebro University, Sweden
09:10–09:30	*Long-term and transgenerational effects in zebrafish – why do we need epigenetics information?* – **Xavier Cousin**, IFREMER, France
09:30–10:10	*Transgenerational Epigenetic Inheritance: Past Exposure, Future Diseases* – **Carlos Guerrero Bosagna**, Department of Physics, Chemistry and Biology (IFM), Linköping University, Sweden
10:10–10:30	*Investigating the mitotic inheritance of biological effects caused by environmental chemicals in the Zebrafish Liver (ZF-L) cell line* – **Mélanie Blanc**, MTM Research Centre, Örebro University, Sweden
10:30–11:00	Fika (Swedish coffee break)
11:00–11:20	*Epigenetics and environmental origins of cancer* – **Zdenko Herceg**, Head, Section of Mechanisms of Carcinogenesis, Head, Epigenetics Group, International Agency for Research on Cancer (IARC), 150 Cours Albert Thomas, F-69008, Lyon, France
11:20–12:00	*Current approaches to analysing (environmental) epigenetics data* – **Philipp Antczak,** Institute of Integrative Biology, University of Liverpool, UK
12:00–13:00	Lunch
13:00–13:20	*Epigenetic changes as biomarkers for EDC (mixture) exposures and adverse health outcomes* – **Joëlle Rüegg**, Karolinska Institutet, Stockholm, Sweden
13:20–13:50	*Epigenetic effects of environmental stress in zebrafish* – **Jorke Kamstra**, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Netherlands
13:50–14:10	*Epigenetic mechanisms as drivers for environmental stress response, a case study with daphnia* – **Jana Asselman**, Department of Animal Sciences and Aquatic Ecology, Ghent University, Belgium

14:10–14:30	*Epigenetic research for understanding toxicity of environmental contaminants* – **Oskar Karlsson**, SciLifeLab & Department of Environmental Science and Analytical Chemistry, Stockholm University, Sweden
14:30–15:00	Fika (Swedish coffee break)
15:00–15:40	*Enhancing systematic review and evidence mapping with shared ontologies and semantic matching; an example from epigenetic research* – **Michelle Angrish**, US Environmental Protection Agency (EPA)
15:40–16:20	*Potential regulatory applications of epigenetics: how can we improve the epigenetic data quality needed for regulatory purposes?* – **Miriam Jacobs**, Public Health England, United Kingdom
16:20–16:50	*Future directions in environmental epigenetics* – **Juliette Legler**, Institute for Risk Assessment Sciences (IRAS), Utrecht University, Netherlands
16:50–17:00	Wrap up first day
17:00	Bus to the hotels
18:30–	Drinks and dinner at the Castle of Örebro

Programme – Friday 22 February

08:00–08:30	Registration
08:30–08:45	Briefing and dividing in discussion groups
08:45–11:15	Discussion groups (including Fika at 9:45): 1. Epigenetics in Regulation and AOPs, Miriam + Michelle 2. Test approaches and Biomarkers - pros and cons, Jorke + Steffen 3. When is an epigenetic change adverse? Joelle + Melanie 4. High content techniques and bioinformatics, Xavier + Philip
11:15–12:00	Short summaries of the discussion groups (each 5 min) and final remarks
12:00–13:00	Lunch

Abstracts

Michelle Angrish: *Enhancing systematic review and evidence mapping with shared ontologies and semantic matching; an example from epigenetic research*

Epigenetic data may be important for hazard identification during chemical risk assessment by providing mechanistic weight of evidence for chemical effects on life-stage disease susceptibility correlated with adverse health outcomes. Confidently describing those adverse outcome pathway linkages depend upon finding all the evidence relevant to a problem formulation and then grouping and integrating that information in such a way that ensures multiple studies are evaluating the same thing. Chemical risk assessments are increasingly adapting systematic review (SR) and systematic mapping methods that minimize risk of bias and maximize transparency. Epigenetics poses a challenge because data are frequently discordant, correlative, and use terms that inconsistently describe broad categories of experimental data and methodology. A solution to this challenge is semantic ontology concept matching. Ontologies facilitate systematic methods for assessing health risks, and permit data-driven AOPs, both of which will improve accuracy of a chemical assessment.

Philipp Antczak: *Current approaches to analysing (environmental) epigenetics data*

As with many of the large dataset generating OMICs techniques, epigenetics is subject to generating large amounts of data that need to be analysed using computational tools. To address the biological questions at hand, the right experimental design needs to be paired with the right computational analysis. Here we will explore the current state of analytical techniques available to epigenetics, the applied experimental designs (and their limitations), the utilised computational approaches, and how we can design and analyse better experiments in the future.

Jana Asselman: *Epigenetic mechanisms as drivers for environmental stress response, a case study with daphnia*

Understanding how organisms respond to environmental changes is a key question in environmental and human toxicology. The ecotoxicological model crustacean Daphnia has been recently put forward as a new model organism in environmental epigenetics due to its recently sequenced genome and methylome, its clonal reproduction cycle and its importance as a model organism in environmental toxicology. Here, we highlight the advantages of this model system for environmental epigenetics.

Mélanie Blanc: *Investigating the mitotic inheritance of biological effects caused by environmental chemicals in the Zebrafish Liver (ZF-L) cell line*

Within environmental science, in vitro testing using cell lines is widely used to screen for chemical toxicity. However, not much is known when it comes to its usefulness in regards to epigenetic toxicity. This study investigated the mitotic inheritance of biological effects caused by environmental chemicals in the Zebrafish Liver (ZF-L) cell line and subsequent unexposed passages. Metabolomics together with global DNA methylation and qPCR experiments were used in order to try to relate long-lasting biological effects to stable changes in DNA methylation.

Carlos Guerrero Bosagna: *Transgenerational Epigenetic Inheritance: Past Exposure, Future Diseases*

Early exposures to environmental toxicants during fetal development are fundamental to explain recently observed impairments in the reproductive system of humans and wild animals. These environmental exposures, which include daily practices, occupational exposures and contact with contaminants, are known to produce epigenetic changes related to impaired fertility in humans. Exposure to environmental toxicants can also induce epigenetic transgenerational inheritance of disease phenotypes. The mechanism involves exposure of pregnant females and induction of germ line epigenetic alterations in their developing embryos. This early developmental exposure generates phenotypic variation in the adults and in the unexposed individuals of subsequent generations. The germ line plays a fundamental role in this transgenerational process because it will transmit acquired epigenetic modifications between generations. Epigenetic modifications in the germ line take place during developmentally sensitive periods undergoing major DNA methylation reprogramming. Recent findings show that early developmental exposures to a variety of environmental toxicants can induce epigenetic transgenerational inheritance of phenotypes associated with increased apoptosis in spermatogenetic cells in males, and incidence of polycystic ovary syndrome in females. Germ line epigenetic alterations are observed three generations after the initial exposure and are mainly exposure-specific. In addition, somatic epigenetic and transcriptome alterations are observed in somatic cells three generations after the exposure occurred.

Xavier Cousin: *Long-term and transgenerational effects in zebrafish – why do we need epigenetics information?*

In the course of several projects, zebrafish were exposed at various stages to pollutants which resulted in multi and trans-generational effects. Molecular analyses suggest the triggering of epigenetics pathways which should be investigated to have a full understanding of mechanisms.

Zdenko Herceg: *Epigenetics and environmental origins of cancer*

The epigenome can be viewed as an interface between the genome and environment, therefore aberrant epigenetic events associated with environmental stressors are likely to play an important role in the onset and progression of different human malignancies. There is also growing evidence that epigenetic changes may be risk factor-specific ("fingerprints") that should prove instrumental in the discovery of new biomarkers in cancer. I will review the state of the science of epigenetics associated with environmental stressors and cancer risk, highlighting key developments in the field.

Miriam Jacobs: *Potential regulatory applications of epigenetics: how can we improve the epigenetic data quality needed for regulatory purposes?*

Epigenetic mechanisms have integral roles in toxicological modes of action for human health regulatory endpoints. Whilst publications in the field indicate rapid expansion, the studies reported rarely reinforce each other in identifying key epigenetic markers that could be applied to test methods developed for chemical regulatory purposes. With respect to carcinogenicity, clinical oncology epigenetic biomarkers provide useful starting points, but application to in vitro and vertebrate in vivo regulatory assays is not at all straight forward. Case studies of ongoing collaborative work exploring how to approach this within the OECD test guidelines programme, and what is needed to expedite epigenetic applications for regulatory needs, will be discussed.

Jorke Kamstra: *Epigenetic effects of environmental stress in zebrafish*

Following exposure of different antropogenic sources to zebrafish epigenetic effects were assessed. I will present results from exposure experiments of industrial chemicals, pharmaceuticals, and ionizing radiation asessing effects at the level of DNA methylation, small RNAs, histones and chromatin structure and how this relates to phenotype.

Oskar Karlsson: *Epigenetic research for understanding toxicity of environmental contaminants*

There has been a rapidly increasing interest in whether environmental factors modulate the establishment and maintenance of epigenetic modifications, and thereby affect gene expression and phenotype in humans and wildlife. We combine experimental model systems, omics tools and molecular epidemiological research to study gene-environment interactions and epigenetic basis of disease.

Juliette Legler: *Future directions in environmental epigenetics*

The presentation will be about the exciting possibilities in epigenetic research, and how newly developed techniques can bring us one step closer in our understanding of how the environment interacts with the epigenome. It will propose how we can use this new knowledge to advance the field of toxicology and risk assessment.

Joëlle Rüegg: *Epigenetic changes as biomarkers for EDC (mixture) exposures and adverse health outcomes*

In my presentation, I will discuss the potential value of epigenetic changes as biomarkers for adverse health outcomes induced by early life exposure to EDCs and mixtures thereof. I will address the need for linking experimental findings in animal studies both to mechanistic understanding as well as to relevance for human exposure and health, and how we address this need in our research.

Scientific organization committee

Mélanie Blanc – Örebro University, Örebro, Sweden (local host)

Xavier Cousin – IFREMER, La Rochelle, France

Jorke Kamstra – Norwegian University of Life Sciences (NMBU), Oslo, Norway

Steffen Keiter – Örebro University, Örebro, Sweden (local host)

Joelle Rüegg – Institute of Environmental Medicine (IMM), Karolinska Institute, Stockholm, Sweden

Additional information

Location

The Workshop takes place in Lecture Hall B in Bilbergska Huset on Campus Örebro, Fakultetsgatan 1, 701 82 Örebro

Getting here

You can travel to campus from the main station by bus 2 and 3 (Brickebacken), 9, 10 and 20 (University). For further information, see www.oru.se/english/about-us/getting-here/

Contact

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For questions about the conference content, contact Steffen Keiter: steffen.keiter@oru.se or +46 (0)19 30 36 04.

Hotels

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