21st century Ecotoxicology and Human toxicology: Applications and perspectives for the use of OMICs data

Bruno Campos, Jinhee Choi, Xiaowei Zhang, Geoff Hodges

May 10, 8:35 - 16:00, Hall 300

There are currently in the region of 100,000 chemicals in commercial use, making it impossible to monitor and assess the biological effects of exposure to each individual compound, much less mixtures given the finite scientific resources available. Historically, regulatory requirements on chemical risk assessments are largely based upon in vivo toxicity testing of individual substances on "representative" single species, supported by some in vitro and in silico approaches. Thus extrapolation to more relevant endpoints in relevant species is required. Many traditional (eco)toxicological studies use lab-based tests with apical endpoints as a proxy for more relevant exposure scenarios, and while these studies are useful and have provided valuable insights, they are inherently flawed and cannot provide deep mechanistic insights into the biological significance of exposure.

It is analytically, physically, and financially impractical to detect and test the chronic toxicity and sub-lethal endpoints (relevant to better understand population effects) of all of the man-made chemicals in the environment. Therefore, better methods must be developed and validated to quantify biologically relevant endpoints of chronic toxicity. OMICs technologies (genomics, transcriptomics, proteomics, lipidomics, epigenomics and metabolomics, etc) are gaining increased prominence in human and environmentaltoxicology because they can provide insights into the biological significance of chemical exposure. However, this mechanistic knowledge is currently rare and difficult to obtain, especially given the purpose of predicting adverse effects to individuals and populations (of all species, including human) from these early indicators of toxicity. Recognizing that this knowledge gap stems from the lack of useful experimental data, an innovative and coordinated scientific approach is needed. Current breakthroughs of molecular and OMICS biology revealed major toxicity and stress response pathways are often conserved in various species, from model organisms for human health studies to wildlife species used for ecotoxicity testing. Moreover, some model species, such as, the nematode, C.elegans and zebrafish, D. rerio, are frequently being used both in human biology, as well as in ecotoxicology. From this context, in this session, we attempt to address OMICS in cross-species extrapolation aspect, by focusing on common molecular level response of various species, including model species for human health, aiming at integration of ecotoxicity and human toxicity.

This session aims to assemble environmental and human health scientists for discussions on how omics technologies can advance the field of (eco)toxicology, while providing data relevant for risk assessment.

We invite presentations of research in both human health and environmental science that use omics technology to gain a better understanding of the adverse effects from chemicals and natural stressors on organisms. These may include examples of omics-based predictions of apical endpoints, cross-species extrapolations, studies integrating chemical monitoring and omics, biomonitoring, exposure biomarker development, chemical risk assessment and non-invasive omics applications.

Both field- and laboratory-based research is welcome, along with research studies utilizing novel methodologies.

We propose to bring together scientists and regulators from around the globe with different perspectives to discuss novel approaches and applications for integrating omics and (eco)toxicology together to advance our understanding of the molecular underpinnings of toxicity. Such discussion will increase the value and robustness of this data-driven knowledge and its applications in risk assessment to better protect the environment. It has become apparent that a better understanding of the molecular events leading to adverse effects can improve both human health and environmental risk assessment and OMICs approaches provide unbiased approaches that can help achieve this goal.

Alternative approaches to animal testing for (eco)toxicity, and the regulatory application of the 3Rs in chemical risk assessments

Adam Lillicrap, Marta Sobanska, Teresa Norberg-King, Marlies Halder

May 9, 8:35 - 16:00, Silver Hall

Within this session, new and novel approaches to the use of vertebrate species (e.g. fish, amphibians, and birds) for (eco)toxicity tests will be explored, with a focus on understanding the role that animal alternatives have in supporting environmental hazard and risk assessments of chemicals. Numerous technical and regulatory challenges need to be considered during the future integration of the traditional 3Rs (reduction, refinement, and replacement of animal tests). These challenges include consideration of the additional 3Rs (6Rs), which requires that any alternative approach is robust/reliable, repeatable and most importantly gains regulatory acceptance. In Europe, the need for alternative approaches has been primarily driven by certain legislations such as the EU Directive on the protection of animals used for scientific purposes, the UK Animals (Scientific Procedures) Act, the 7th Amendment to the EU Cosmetics Directive, selected legislation in Germany and the European chemical legislation REACH. As an example, in REACH it is possible in principle to fulfil so-called 'standard information requirements' by other means than new experimental studies by using existing non-GLP and non-guideline data; weight of evidence (WoE); (Q)SAR predictions; in vitro methods; grouping of substances and read-across approaches. Some of the adaptations may also be based on novel approach methodologies such as Adverse Outcome Pathways (AOPs) and/or OMICs. This session will explore new approaches towards developing and adopting efficient chemical assessments and also the hazard assessments of effluents for both acute and chronic ecotoxicity endpoints. Advances in read-across, enhanced predictive models (e.g. QSARs) and new developments for in vitro and in vivo models to support environmental risk assessments are encouraged. Additionally, progress relating to the generation of new bioaccumulation data using alternative approaches, particularly for PBT assessments, or how the various approaches or methods could be accepted into a regulatory framework and/or integrated test strategy are also encouraged. Furthermore, we welcome discussions on how to address uncertainties, challenges, advances and needs for further development for alternative approaches, particularly in support of understanding potential limitations/advantages. This session is organised by the SETAC Animal Alternatives in Environmental Science Advisory Group (AAAG) and the European Chemicals Agency (ECHA).

Cost effective and ecological relevant testing using invertebrate species: new insights for environmental risk assessment

Bruno Campos, Dick Roelofs, Susana Loureiro, Carlos Barata

May 11, 8:35 - 12:45, Meeting Studio 311 & 312

Invertebrate species are commonly used in ecotoxicity testing to investigate the impact of chemicals on the environment. A range of regulatory guidelines (OECD, ISO, EPA) are available, combining different invertebrate species and toxicological endpoints. However these guidelines and studies are mainly prescriptive and limited to relatively few species. Model and non-model invertebrate species from the three compartments of the biosphere (air, water and soil), offer a far greater range of interest for research, spanning from classical toxicological characterization to modern holistic approaches, with potential to substitute vertebrate testing. The small size, ease of maintenance and short life cycles of most invertebrate species commonly used in environmental sciences make them also very suitable for evaluating effects at different levels of organization within single and combined exposures with other chemicals or with other natural/anthropogenic stressors. Automated high throughput screening application possibilities and linkage to ecosystem functions make them good models for assessing toxic effects in the laboratory and the field using micro, mesocosms and transplant experiments. The emergence and accessibility to advanced molecular based technologies are allowing ever more complex research involving genome studies while recent tools for genome editing are greatly facilitating our understanding of the molecular cascades triggered in response to stress and its phenotypic consequences. Molecular based technologies combined with systems biology approaches offer the possibility to assess effects from the transcriptome, metabolome, organ or individual as well as the linkage to higher ecological levels up to population level. Within this session we intend to show the latest breakthroughs and new directions in toxicological research using invertebrates, focusing on novel systems, endpoints, assays and testing strategies. We invite presentations focusing on lab and field studies addressing impacts across several levels of biological organization considering molecular, life-history, demographic and/or behavioural endpoints; studies focused on a mechanistic understanding of toxic effects and/or on risk assessment of chemical pollutants alone or interacting with natural and anthropogenic stressors (temperature, food, nutrients, etc). We also invite industry to show latest high-throughput approaches using invertebrate species. Finally, we invite regulatory agencies members to discuss the latest developments and perspectives for invertebrate testing with regulatory impact.

Environmental endocrine compound concentrations and human and ecosystem health effects

Joan Grimalt

May 10, 11:05 - 12:45, Copper Hall

Pollutants of endocrine disrupting activity may generate health effects at very low concentrations. Some of these compounds are persistent and bioaccumulative and their environmental occurrence is hazardous for human health, organisms and ecosystems because it magnifies through the food chain. Others are labile to chemical degradation but in some cases their widespread use, namely in agriculture applications, involve a permanent baseline environmental occurrence which also translates toxic risks to organisms and humans. In the context of the current European Union debate between regulations based on hazards (compound properties) or risk assessment (environmental occurrence) of these exogenous substances with potential endocrine disruption more data are needed for assessment of their health impacts at the present environmental concentrations in agricultural areas, remote and pristine continental ecosystems. This information is needed to correlate environmental occurrences of specific compounds with effects such as thyroid dysfunctions, decreased fertility, decreased hatching success and deformities in birds and fish, metabolic disfunctions in birds, fish and mammals, abnormal behavioral patterns in birds, demasculinization and feminization of male fish, birds and mammals, defeminization and masculinization of female fish and birds, and others. Cohort results associating environmental exposures to human health effects are also welcome. We invite current researchers from the scientific community to contribute to this session presenting their current research work in this topic. Their information is needed for assessment of the regulation criteria to be implemented to protect the ecosystems and health of organisms and humans, either based on hazards or risk assessment considerations.

Fish model species in human and environmental toxicology

Jessica Legradi, Riccardo Massei, Marek Pípal

May 11, 8:35 - 12:45, Hall 400

Fish models are commonly used in human and eco-toxicity testing to investigate the impact of chemicals on whole organisms. Many important biological functions are conserved between fish species and humans. Therefore fish have a wide utility domain, spanning from basic developmental biology, neurobiology, endocrinology to immunology. The small size of some available fish species including the zebrafish (Danio rerio) or medaka (Oryzias latipes) and their robust nature makes them ideally suited for application in automated high throughput screens. Furthermore, early life stages of these species offer all the key attributes of a complex in vivo system (e.g. including metabolism), as well as attributes of in vitro assays, as tests can be carried out in multiwell plates formats with small sample volumes and run in comparatively short periods of time. These attributes make them well suited for toxicity testing of environmental extracts and in effect directed analysis (EDA) to detect unknown contaminants in complex samples. Research on fish over the last decade has been greatly facilitated by the availability of sequenced genomes, which are available for over twelve species with more pending. This facility together with advances in genetic and epigenetic studies, including gene knockout and transgenesis technologies, is greatly facilitating understanding of the molecular mechanisms of toxicology. Due to the large similarity with other vertebrates, there is also a growing interest in the application of fish model species in human disease and development. Fish early life stages have been recently used in several cancer genetics studies and drug discovery tests. In the ecotox field fish are also studied outside of the laboratory in their native environment. Prominent models for native fish models are roach (Rutilus rutilus) and rainbow trout (Oncorhynchus mykiss). Studying fish in their natural habitat allows to go further than simple dose-effect assessments. Within this session we intend to show recent developments in toxicological research using a variety of different fish model species, focusing on novel systems, endpoints, assays and testing strategies. Results of toxicity studies of single compounds as well as complex environmental samples are of interest. Effects on individual fish, multigenerational exposure effects, and population level impacts will be considered. We especially welcome presentations highlighting new analytical methods and techniques for contaminants or their metabolites in exposure media or fish. The session will be interdisciplinary and bring together researchers across a wide range of research areas with the view to enhance approaches in human and ecotoxicity testing.

Interplay between nutritional factors and chemical toxicity

Patrick Kestemont

May 9, 14:20 - 16:00, Hall 300

The session will focus on the interactions between the nutritional status of organisms and their responses to chemicals (or vice versa) in the broadest possible way. The session aims to include presentations on the influence of nutritional conditioning of, for instance, algae (e.g. P, or N, or Si in the environment) and zooplankton or fish (e.g. P, fatty acids, vitamins in their diet) on their sensitivity to various substances (organics, metals, etc.), either at mono- or multispecies level. The session also aims to include presentations on how chemical exposure may affect the nutritional composition of species (e.g. P, fatty acid, vitamins, sterols) at lower trophic levels, and what the indirect consequences could be for species from higher trophic levels via the diet, including dietary chemical exposure.

Marine and freshwater ecotoxicology

Ketil Hylland, Ionan Marigomez

May 9, 11:05 - 16:00, Hall 400

Freshwater, coastal and marine areas are crucial for food production, recreation and transport, but also function as recipients of industrial and public waste. However there is still surprisingly limited knowledge about how toxic substances affect aquatic organisms and processes. Our understanding of possible impacts is limited to a few model species and a limited number of endpoints, nearly always studied in isolation from possibly modulating factors. This session wishes to contribute to increasing the knowledge base of how toxic substances affect aquatic organisms and to improve on the risk assessment of such substances in marine and freshwater ecosystems. The session will particularly welcome presentations on immunotoxicity and developmental toxicity, but will include studies on other mechanisms of toxicity, such as neurotoxicity, genotoxicity and reproductive toxicity. Toxic substances are never present in isolation and the session will address how other environmental factors such as temperature, salinity and organic matter content modulate responses to toxicants. This session aims to address the above issues with platform and poster contributions from academia, industry and institutions that manage the marine and freshwater environment. Presentations on the following topics will be particularly welcome: - Comparative studies of effects of toxic substances in different aquatic organisms - Studies of immunotoxicity, neurotoxicity, genotoxicity, reproductive toxicity and developmental toxicity of aquatic organisms - Studies on how environmental factors may modulate effects of toxic substances - Interactions between contaminants and other environmental pressures in marine and freshwater ecosystems - Comparison of sublethal responses to contaminants in freshwater, estuarine and marine organisms.

Mechanistic ecotoxicology of engineered nanomaterials: lessons learnt from human models

Teresa Fernandes, Iseult Lynch

May 9, 8:35 - 10:15, Gold Hall

The interest in the ecotoxicological effects of engineered nanomaterials (ENMs) in the scientific literature is rapidly growing along with the increasing number of applications of nanotechnology. This session focus on the state of the art of ENMs mechanistic ecotoxicology, considering effects and responses at different levels of biological organization, from genes to populations and including aspects of ENM toxicokinetics and toxicodynamics. Interest in the mechanistic toxicology of ENMs is driven from both a scientific curiosity perspective, but also by practical needs related to material categorization, read across and mixture effects. This includes the need to establish whether there are ENM specific effect mechanisms. A key aspect of this session is to explore how much studies on human models, which have a longer track record, originally arising from students on air pollution, might inform effects on environmental models. This session will provide a summary of the state of the art on the occurrence of specific ENM effects in biological systems; differentiate cells/tissue injuries due to nano and non-nano materials and between ENMs with similar chemistry but different physical properties. Specifically the session will focus on ENM (pristine and aged) bioavailability, testing procedures and biomarkers, results from topdown molecular approaches such as transcriptomics, proteomics and metabolomics. An important aspect in mechanistic toxicology of ENMs is represented by ENM imaging and tracking in biological systems. This session will aim to include recent results in this area in the illustration of mechanistic pathways. Therefore, this session will include studies of uptake, distribution, toxicokinetics and toxicodynamics, using imaging and localization into cells and biological tissues including highthroughput molecular techniques (transcriptomics, proteomics, metabolomics), to provide links between lower and high organisation effects and address systems toxicology of nanomaterials. Derivation of read-across, extrapolation and QNAR development will also be included.

Multigenerational, epigenetic and evolutionary effects in human and environmental toxicology: from mechanisms to risk assessment

Jana Asselman, Michael Eckerstorfer, Elias Oziolor, Arnaud Chaumot

May 8, 8:35 - 10:15, Hall 300

Scientific evidence is indicating that environmental pollutants, including chemicals, biocides and plant protection products, may influence organisms beyond exposed generations by affecting the regulation of epigenetic mechanisms and triggering rapid micro-evolutionary processes. Yet, the disruptive potential in environmental toxicology remains to be further characterized, due to the limited fundamental knowledge of epigenetic, evolutionary and multigenerational effects in ecotoxicological model organisms. Furthermore, while these effects in humans and animal models are increasingly studied and the relevance of such effects for toxicological mechanisms is generally appreciated, their incorporation in the regulation of chemicals remains limited. Indeed, they present new challenges for risk assessment as their adverse outcomes may occur long after the exposure to certain environmental stressors and pollutants. Such delayed effects can significantly affect future generations, which are either exposed only during germline development or even not exposed to the initiating stressor at all (inter- and transgenerational effects). Scientific research reporting of multigenerational effects and evidence of trans-generational effects of pollutants is accumulating across a diversity of systems, however, little is known on the natural variation of epigenetic traits defining non-adversity. Furthermore, biological responses may also depend on population standing genetic variation and evolutionary history, and on phylogenetic constraints. It is thus difficult to extrapolate toxicological responses of natural and genetically diverse populations and communities from laboratory assays based on inbred or clonal organism/species. Therefore, it becomes urgent to acquire tools and methods to measure, anticipate, and even predict (epi)genetic and evolutionary ecotoxicological effects, the genetic of adaptation/maladaptation to environmental stress and the adaptive potential of natural populations, as well as to understand their consequences for ecosystems. Further research is needed to address a series of key questions: When can a chemical or a class of chemicals be classified as hazardous by causing significant (epi)genetic or evolutionary effects on humans and animals? Is it possible to develop standard test guidelines to assess such effects? Could effective and cost-efficient screening methods perform in model organisms be used to predict epigenetic and evolutionary effects of chemicals in higher organisms including humans for? How can multigenerational effects be assessed at the (epi)genetic level? In addition, epigenetic and evolutionary studies supported by new technologies, may provide substantial insight in how chemicals can alter regulatory processes at levels that do not necessarily result in overt toxicity but may significantly affect subsequent unexposed generations Answering these questions and developing guidelines for the inclusion of epigenetic and evolutionary effects in risk assessment ideally requires a dialog from the early stages between scientists and stakeholders (see EVOGENERATE Work Group of the SETAC ERA AG). Therefore, this session, proposed by the EVOGENERATE Work Group, will address the development of new methods and model systems for the characterization of the (epi)genetic, evolutionary and multigenerational effects, hazard identification, both at short- and long-term, and the integration of epigenetic and evolutionary data in ecological and human health risk assessment. These methodologies and model systems should provide scientific guidance to support optimized decision making, through a sustainable trade-off between human demand on, and conservation of natural resources.