**Molecular Mechanisms of Food Contaminants Toxicity**

**Course Leader:** **Joseph Rafter**
Department of Medical Nutrition, Karolinska Institutet, Stockholm, Sweden

09.00 – 09.15 **Introduction**
**Joseph Rafter**, Professor, Department of Medical Nutrition, Karolinska Institutet, Stockholm, Sweden.
*Research interests: Nutrition and cancer; environment – gene interactions; role of gut microflora in health and disease*

09.15 – 10.00 **General overview of persistent organic pollutants in food**
**Per Ola Darnerud**, Assistant Professor, Senior Toxicologist at National Food Administration, Uppsala, Sweden.
*Research interests: POPs in food and breast milk - distribution and effects in experimental models*

10.00 – 11.00 **Infections and food contaminants**
**Nils-Gunnar Ilbäck**, Professor, Senior Toxicologist at National Food Administration, Uppsala, Sweden.
*Research interest: Role of infection in distribution and effects of environmental contaminants.*

11.00 – 11.15 Pause

11.15 – 12.00 **Molecular mechanism of dioxin action**
**Ingemar Pongratz**, Assistant Professor, Department of Biosciences, Karolinska Institutet, Stockholm, Sweden.
*Research interests: Crosstalk between bHLH-PAS transcription factors and nuclear receptors, endocrine disruption*

12.00 – 12.45 **Similarities and differences in dioxin and PBDE toxicity and mechanisms of action**.
or
**Risk-benefit from consumption of Baltic herring; molecular aspects.**

12.45 – 13.00 Summary/conclusions, discussion with lecturers

**Toxicology of Nanoparticles - emerging issues in risk assessment**

**Course Leaders:** **Kirsi Vahakangas**
SC Education EUROTOX
**Anthony Seaton**
University of Aberdeen, UK

## Background

Nanomaterials are generated for different technical purposes in technology, medicine, consumer products or are released into the environment by engine exhaust. They are generally < 100 nm in size and involve a variety of chemicals, shapes and physicochemical properties. It is likely that exposure to nanomaterials has complex toxicological implications. Nanomaterials are proposed for many different applications and there is a great potential for consumers exposure. However, the understanding of health risk is limited and the lack of information may lead to under- as well as overestimation of the impact of nanomaterials on human health.

## Objectives

The course will strengthen the educational side in the discussion and will enable a deeper understanding of the nature of nanomaterials. The context of potential exposure will be explained and the strengths and limits of existing strategies for toxicological testing will be clarified. The main goals are to strengthen the understanding of facts in the discussion on nanomaterials.

## Speakers

Introduction: Introduction into the keywords and main goals of the course
**Kirsi Vahakangas**, Oulu, Finland

1. Physico-chemical characteristics of nanoparticles. Fields of application. New challenges
Speaker TBD

2. Existing models to study the effects. Are they suitable for acute and long-term effects? Technical options to modify models. Open questions – uncertainties
**Uwe Heinrich**, Hannover, Germany

3. Biological responses: Facts and fears. Nanoparticles are more like dust or more like liquids?
Speaker TBD

4. Summary addressing existing problems, and open questions
**Anthony Seaton**, University of Aberdeen

**New strategies to determine the toxicological risk of chemicals by molecular modelling**

**Course Leader:** **Heidi Foth**
SC Education EUROTOX

## Background

Computational Toxicology has recently gained more and more attention especially in industry and regulatory agencies. Several systems are in daily use to predict the safety of chemicals and drugs.
The new chemical safety program of the EU, REACH (registration, evaluation and authorisation of chemicals) seeks to increase the knowledge on existing chemicals in order to identify harmful compounds for human health in advance to marketing and to care for ecosystemic stability ("no data – no market"). The general strategy is very ambitious and will pose new demands on toxicological expertise in terms of overview on existing data from experimental testing or modelling systems. In order to increase efficiency in the acquisition of basic data for regulatory decisions and to decrease the need for animal testing, traditional testing can be waived if validated in vitro testing or computational modelling is available.
Several strategies in computational toxicology have already been established for prediction of drug safety. They are mainly used to prioritize toxicological testing for interesting drug candidates and aid in the selection process during early stages in development. It is an open question how and when modelling of exposure and prediction of effects can be used to support safety decisions in drug development.

## Objectives

The course will pay attention to the basic elements of the use of modelling in new strategies for exposure assessment and toxicology. QSAR models are well established as supportive systems to plan drug testing strategies. There will be a certain emphasis of this course regarding safety prediction of chemicals, especially because the EU legislation (REACH) will create some factual pressure on toxicologists to use alternative test systems. Therefore, the concept of REACH will be explained and the strengths and limits of existing strategies for toxicological testing will be clarified. The main goals are to strengthen the understanding of the main arguments and to discuss the future challenges for toxicological expertise.

## Speakers

Introduction: New challenges for toxicology and toxicological expertise under REACH
**Heidi Foth**, Halle, Germany

1. Modelling of exposure Speaker TBD
2. Kinetic modelling Speaker TBD
3. TOPKAT

**B. Simon Hettich**, Darmstadt, Germany

4. DEREK and MULTICASE

**A. Rothfuß**, Berlin, Germany

**High throughput assays in toxicological testing**

**Course Leader: Prof. Jaroslaw Dastych**
Centre for Medical Biology, Polish Academy of Sciences, Poland

**Background**

High-throughput testing of potential drug toxicity is necessary in the early stage of drug development. Proper *in vitro* toxicity screening systems allow for assessment of an early safety profile of the new chemical entity. This is a part of the optimization process and an important component of the discovery phase of drug development. Because the number of compounds tested reaches tens of thousands, the toxicity assays have to conform to the high-throughput format.

**Objectives**

The course is focused on the techniques that are currently applied for this purpose in the industry as well as the new emerging technologies that facilitate prediction of the more subtle forms of toxicity such as neurotoxicity, developmental toxicity and immunotoxicity. During the course we will also discuss the process of assay automation and the methods for data handling.

**Speakers**

1. Cell-based *in vitro* toxicity screening in drug discovery research
   **Jelic Dubravko**
   PLIVA Research Institute Ltd, Zagreb, Croatia

2. Automation of *in vitro* toxicity screening for development of high-throughput capacities
   Speaker TBD
   Comesa Poland/Beckman Coulter

3. Application of molecular biology techniques for *in vitro* toxicity screening
   **Jaroslaw Dastych**
   Centre for Medical Biology, Polish Academy of Sciences, Poland

4. Data handling in the process of high-throughput toxicity screening
   Speaker TBD

**Basic concepts in immunology and immunotoxicology**

**Course Leaders:** **Emanuela Corsini**
University of Milan, Italy
**Ian Kimber**
Syngenta, UK

## Background

The immune system has evolved to protect us from pathogenic microorganisms and malignant diseases. Immunity is a series of delicately balanced, complex, multi-cellular, and physiological mechanisms that allow mammals to distinguish foreign materials and transformed cells from "self" and to neutralize or eliminate them. The immune system provides the means to initiate rapid and highly specific responses against a myriad of potentially pathogenic organisms.

Over the past 25 years, immunotoxicology has emerged as an important area of toxicology. Immunotoxic and allergic effects are unequivocally a significant cause of morbidity and even mortality. Immunotoxic effects are best divided into three main categories, namely immunosuppression, allergy and autoimmunity. Decreased immunocompetence may result in repeated, more severe, or prolonged infections as well as the development of cancer, while undesirable immunostimulation may lead to immune-mediated diseases such as hypersensitivity responses and autoimmune diseases. Overall, the nature of immunotoxic effects induced by drugs and chemicals has been extensively investigated and efforts have been made to design animal models and assays suitable for immunotoxicity safety evaluation.

## Objectives

This course will provide a grounding in fundamental and clinical aspects of immunology, and will describe the basic elements of immunotoxicity, allergy and autoimmunity. The main objective is to deliver an accessible guide to the immune system and immunotoxicology for general toxicologists.

## Speakers

1. An Introduction to Immunology: Fundamental and Clinical Aspects
**Ian Kimber**, Syngenta, UK

2. New and Emerging Approaches to the Assessment of Immunotoxic Potential
**Emanuela Corsini**, University of Milan, Italy

3. Practical Considerations in the Assessment of Immunotoxic Activity
**Rebecca Dearman**, Syngenta, UK

4. Immunologic and Allergic Responses to Drugs and Drug Hypersensitivity Reactions
**Raymond Pieters**, University of Utrecht, Holland