

ing. On the other hand, ALIs generated with a mixture of cells from several individuals give a snapshot of global reaction of a small population when exposed to a chemical compound.

This talk will describe the *in vitro* upper and lower respiratory tract models currently available to simulate the structure and function of human lung epithelial tissues, such as organoids, lung-on-a-chip, transwell inserts ALI cultures. The use of these models for diverse applications will also be discussed, including the evaluation of the barrier function, local tolerance, airway inflammation, sensitization, as well as the respiratory diseases (lung fibrosis, cancers), etc.

<https://doi.org/10.1016/j.toxlet.2025.07.013>

CEC01-04

AOP and development of test methods to predict the respiratory sensitisation potential of substances

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Asthma is one of the most prevalent lung diseases in developed countries and is induced by exposure to sensitizing agents. Respiratory sensitization is a complex immunological process that is a result of continued or long-term exposure to agents which can eventually lead to hypersensitivity. Although respiratory hypersensitivity has been known for decades, there are currently no validated approaches available for the identification of suspect agents. This is largely due to the different classifications for respiratory sensitizers, as well as complexity of the response and the late manifestation of symptoms. Additionally, it has been challenging to make a clear distinction between respiratory reactions triggered by sensitization of the respiratory tract and those triggered by other factors, including type and duration of exposure and concurrent exposure to other agents that may amplify the symptoms.

The causal linking of events at different levels of biological organization in adverse outcome pathway (AOP) concepts has evolved as important approach in chemical hazard and risk assessment. While this has been conducted for skin sensitizers, efforts to understand and assess the effect of respiratory sensitizers have been stagnant for over a decade, and no AOP has been established.

Due to the urgent need for accurate and reliable test methods for the identification of respiratory sensitizers, various testing methods are being explored. This presentation will discuss the most recent information on respiratory sensitization and key events potentially relevant in the AOP concept.

<https://doi.org/10.1016/j.toxlet.2025.07.014>

CEC01-05

An integrated human-*in vitro* approach to explore the role of miRNAs in occupational asthma

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Asthma resulting from sensitization of the respiratory tract to chemicals and defined allergic asthma, is associated with significant morbidity, and is clearly an important health concern with serious clinical consequences. Occupational allergic asthma resulting from sensitization of the respiratory tract to chemicals is clearly an important health concern with serious clinical consequences. The main pathological feature of allergic asthma is due to the complex interactions between immune cells and immunological mediators. Basically, Th1/Th2 ratio imbalance is one of the essential immunological mechanisms of asthma

but also Th17/Tregs imbalance form an extreme complex interactive network. Recent evidences reported alterations in miRNA expression in a variety of lung diseases, including allergic asthma. Several miRNAs have been associated with asthma and airways inflammation but target identification remain not yet determined for the majority of the studies. Despite research for more than three decades, there are still no validated methods for the assessment of respiratory sensitizing potential of LMW compounds. The main idea of this project is based on the assessment of a new *in vitro* approach to better study and investigate the allergic asthma pathology. The central hypothesis of this project is that miRNAs play a key role in the activation and maintenance of the allergic asthma through the active involvement of the immune system. The specific aim of this project, that is entirely based on human cells, is to identify miRNA patterns and consequently which specific targets are involved in the interaction between the respiratory system and the immune system in the allergic asthma disease. The project could be ideally divided in two parts: the *in vitro* part (Part I) and the human part (Part II). Part I – For the *in vitro* approach the human lung epithelial cells, namely Calu-3, will be exposed to 5 respiratory sensitizers (hexamethylen, methylene diphenyl, and toluene diisocyanate; ammonium hexachloroplatinate; trimellitic anhydride), 1 skin sensitizer (2,4-dinitrochlorobenzene) and 1 irritant (sodium dodecyl sulphate) through a liquid aerosols system (Cloud Alpha System – VITRO-CELL® Systems). A microRNA panels will be performed in control conditions and exposed conditions. A bibliographic research will be made to investigate miRNAs possibly involved in allergic asthma and/or immune system activation/de-regulation. Part II – in collaboration with Dott. Liviero (Occupational Unit of Padova University) a broad miRNA evaluation in asthmatic patients will be conducted, through the analysis of miRNA expression in blood microvesicles and in exhaled breath condensate obtained from healthy and asthmatic patients. The translational potential of the project is due to the use of a primary cell culture model as well as human samples. Furthermore, implementation of miRNA patterns could be useful as prevention tool (biomarkers for diagnosis) of allergic asthma.

CEC02 | Developmental Neurotoxicity (DNT): Bridging from Mammal to Cellular Behavior

CEC02-01

Brief Session Introduction on DNT

E. Fritsche

SCAHT, Switzerland

No abstract has been submitted.

<https://doi.org/10.1016/j.toxlet.2025.07.015>

CEC02-02

Current regulatory (*in vivo*) neurotoxicity testing

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An overview will be given on the applicable guidelines and the implementation thereof in general toxicity and reproductive and developmental toxicity studies. The DNT endpoints and their methodology as well as the results they provide will be discussed, together with the challenges/limitations that are faced.

<https://doi.org/10.1016/j.toxlet.2025.07.016>

Toxicology Letters

*An International Journal for the Rapid Publication of Short Reports on all Aspects
of Toxicology Especially Mechanisms of Toxicity*

Editor-in-Chief

Angela Mally

Associate editors

Timothy W. Grant, Scott Garrett, Emanuela Testai, and Alicia Paini

Abstracts of the
59th Congress of the European Societies of Toxicology
(EUROTOX 2025)
TOXICOLOGY ADDRESSES SOCIETY'S REAL LIFE RISKS
FOR SUSTAINABLE HEALTH AND WELL BEING

Athens, Greece, 14–17 September 2025

Publication of this supplement is supported by EUROTOX.



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