conferenceseries.com

Porreca Immacolata et al., J Clin Toxicol 2016, 6:6(Suppl)
http://dx.doi.org/10.4172/2161-0495.C1.022

Pesticide toxicogenomics across scales: Gene expression profiling *in vitro* predicts mechanisms of thyroid toxicity and other exposure outcomes *in vivo*

Porreca Immacolata, D'Angelo Fulvio, De Franceschi Lucia, Mattè Alessandro, Ceccarelli Michele, Iolascon Achille, Russo Filomena, Ravo Maria, Scarfò Marzia, Weisz Alessandro, Mario De Felice, Massimo Mallardo and **Concetta Ambrosino**
Biogem Research Institute, Italy

The recent advances in biological techniques, from the Omics technologies to the most innovative cellular models, are proposed as methods of modern toxicology. Particularly, the application of the toxicogenomic approach to cell cultures has been suggested for chemical testing to reduce animal use and to identify molecular targets extrapolable to humans. Despite this promise, the studies showing the validation of *in vitro* toxicogenomics results in animal models are limited. The present work is a proof of the concept that toxicogenomics data obtained in cellular models can recapitulate impairments occurring *in vivo* and predict cell-type unrelated outcomes. We generated gene expression profiles by multiple-dose and co-exposure testing of 2 pesticides, ethylene-thiourea (ETU) and chlorpyrifos (CPF), in immortalized rat follicular cells ($PCCl_3$) by high-throughput RNA sequencing. The deregulated pathways/mechanisms were highlighted by a multi-leveled bioinformatics approach, based on gene clustering analyses. Different techniques were applied to confirm molecular data and bioinformatics suggestions in mice exposed in utero and lifelong to different dose of both pesticides and their mixtures. We highlighted specific and common mechanisms of toxicity for ETU and CPF, the last exerted throughout the inhibition of transcripts (Egr1, Hmga1, Zfp36l2) controlling proliferation/survival of thyroid and blood cells. *In vitro* expression data, mechanisms and unexpected outcomes were verified *in vivo*. Thyrocytes damage was confirmed by the reduction of circulating T4 and of Bcl2 transcript. Hematopoietic injury, involving several compartments, was confirmed with a more severe phenotype for the red cells. Indeed, a reduction of the reticulocyte count was retrieved in mouse co-exposed to CPF and ETU, both 0.1 mg/kg/die, below the CPF and ETU NOAEL. In conclusion, although *in vitro* systems cannot entirely replace the animal models because not fully recapitulating adaptation processes, our approach shows that *in vitro* toxicogenomics is a powerful tool in identification of signature/mechanisms of toxicity or unpredicted outcomes verifiable in rodents and hopefully, in humans, a point that should be further addressed.

Biography

Porreca Immacolata has completed her PhD from University of Naples "Federico II" working in the developmental biology field. After that, she started her Postdoc in the Genes and Environment Laboratory of Biogem Research Institute. She is responsible of studies aiming to dissect the mechanisms of toxicity of pesticides on the endocrine system using *in vitro* and *in vivo* model systems. Combining toxicogenomics with classical toxicology approaches, she aims to generate new strategies for human risk assessment.

immacolataporreca@gmail.com

Notes: