Second (Virtual) Summer School 2021_7-8 June 2021

Title of the lecture: How much complexity is enough ? In vitro phototoxicity case.

ABSTRACT
Author Dr. Helena Kandarova, ERT

Centre of Experimental Medicine, Institute of Experimental Pharmacology and Toxicology, Slovak Academy of Sciences
Institute of Biochemistry and Microbiology, Faculty of Chemical and Food Technology STU

Phototoxicity is defined as a toxic response that is elicited after the first exposure of skin (or other organs) to certain chemicals and subsequent exposure to light, or that is induced similarly by skin (or other organs) irradiation after systemic administration of a chemical.

In vitro test for phototoxicity testing (the 3T3 NRU PT), performed with a mouse fibroblast cell line was one of the first tests implemented into the European regulations, and later on also OECD guidelines as EU B.41 (2000) and OECD TG 432 (2004)

Information derived from the in vitro 3T3 NRU phototoxicity test serves to identify the phototoxic potential of test substances, i.e. the existence or absence of possible hazards likely to arise from a test substance in association with exposure to UV and visible light.

Despite extensive validation, when used across the various industrial sectors, scientist found out, that the method has several limitations. Testing of water poorly soluble materials or formulations is difficult and (especially for the pharmaceuticals), the 3T3 NRU OT provided too many false positive results, not confirmed in in vivo studies. Another drawback of this method is a lack o the prediction o the phototoxic potency.

To overcome these problems, scientists have already in 1994 suggested to use reconstructed tissue models, either as stand alone, or as second tier in the phototoxicity testing strategy. The use o the 3D skin models have however been implemented into the ICH S10 guideline on the phototoxicity testing of pharmaceuticals only in 2015 – i.e. 21 years later. A new OECD TG on the phototoxicity guideline has been endorsed at the OECD WNT in April 2021 and will be published in due course.

The presentation summarises the long way to the development and acceptance of a testing concept utilising 2D and 3D in vitro models and will discuss the benefits as well as drawbacks of models and testing strategies with various levels of complexity.