Editorial. The Predict-IV project: Towards predictive toxicology using in vitro techniques

Abstract:
This special Issue of Toxicology in Vitro covers the most relevant findings of a large scale integrating Project on “Profiling the toxicity of new drugs: a non-animal based approach integrating toxicodynamics and biokinetics”, funded by the European Commission (Grant No. 202222, Predict-IV), which started in May 2008 and was finalised in October 2013. To prevent events like the Elixir Sulfanilamide scandal in 1937 in the USA or the Thalidomide disaster in the 1950s and early 1960s in Germany, almost all regulatory authorities have introduced safety testing for new or previously untested chemical entities (Limonciel, 2014). The consequence was the establishment of a battery of animal-based tests for specific toxicological endpoints. However, we now know that there are large species differences in xenobiotic handling and thus there is a drive to use human derived models. New developments in cell culture and molecular biology provide a unique opportunity to meet regulatory requirements while improving on the predictivity of pre-clinical test systems, as already suggested by Russell and Burch (1959). In addition to in vitro models the use of in silico predictions of toxicity as well as the use of physiologically-based biokinetics has matured over the last decades (Blaauboer, 2010; Blaauboer et al., 2012). The utilisation and integration of in vitro and in silico techniques promise to increase the speed of drug safety testing, decrease the costs incurred thereby having more drugs on the market. Also by using human-derived models we aim to improve on the predictivity of animal-based models (Jennings, 2015), thus these drugs will likely be safer than ever before. In the Predict-IV project we divided the problem into four main aspects: (1) cell culture models suitable for repeat dose exposures, (2) mechanistic toxicology based on “omic” analysis, (3) biokinetics, and (4) quantitative in vitro to in vivo extrapolation. Here we provide a short overview of the project outcomes, the majority of which are published in this issue.

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