

High-Throughput-Screening: Challenges and Opportunities in food safety risk assessment

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High-throughput *in vitro* screening plays an important role in next generation (non-animal) toxicity testing strategies. The ILSI Europe ToxCast Expert Group aimed to explore how mechanistic insights in the biological targets of food-relevant chemicals can be obtained from high-throughput ToxCast results. Starting point are the 556 direct additives that have been identified in the ToxCast database. These different chemicals were subdivided into structurally related chemical groups and functional use classes according to EU regulation (e.g. E-numbers, nutrients, flavourings, regulatory-restricted chemicals). Relevant biological targets of a chemical group were considered those toward which a high percentage of chemicals within a group are active. The most obvious activity identified was the estrogen receptor-mediated actions of the chemical group containing parabens and structurally related gallates, as well the chemical group of pyranones, containing genistein and daidzein. In a second step, the possibilities of using the ToxCast data of the defined chemical groups

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for read-across purposes were evaluated. These results revealed that Tox21/ToxCast are particularly useful to discriminate out-of-domain structural relatives (i.e. structural relatives that are active towards a certain target vs those that are not). Despite the opportunities of utility of HTS for read-across purposes, challenges exist with respect to linking the activated pathways towards apical toxicological endpoints. Examples of these possibilities and challenges will be presented.

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