High throughput microscopy of mechanism-based reporters in druginduced liver injury

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Stellingen

Behorende bij het proefschrift

High throughput microscopy of mechanism-based reporters in drug-induced liver injury

1. Fluorescently labeled reporter cell lines are a perfect tool to study the live cell dynamics of adaptive stress response activation (this thesis).
2. HepG2 cells are an excellent model system to make GFP reporters, with applications in the first stages of pharmaceutical hepatotoxicity screening (this thesis).
3. Precision safety assessment should involve the expression and function of enhancers and repressors of Nrf2 signaling (this thesis).
4. The application of HepG2 adaptive stress response GFP reporters provide additive value in primary pharmaceutical hepatotoxicity screening (this thesis).
5. There is not just one Cmax value per drug, as individuals will have their own Cmax value; a Cmax range is therefore more relevant than a single Cmax value (Based on Regenthal et al, Journal of clinical monitoring and computing, 1999).
6. A systematic physiological, pharmacological and toxicological evaluation of cell models is essential to define what model is fit for a particular purpose and where it fits in a tiered testing strategy (Based on Sison-Young et al, Toxicological Sciences, 2015).
7. Culturing cells in vitro causes a strikingly similar perturbation pattern as a toxicant in vivo (Based on Sutherland et al, PLOS Computational Biology, 2016).
8. In order to stop the increase in costs per drug pharmaceutical companies need to increase productivity of research and development departments by re-focusing on full mechanistic biological understanding to optimize target discovery (Based on Paul et al, Nature Reviews Drug Discovery, 2010).
9. A simple statistical significance score that reduces the cell biological complexity to a black and white effect oversimplifies the complete change in biology introduced by a (chemical) perturbation.
10. Trends in biological research are very much like fashion: when the technique is fully optimized and used by research groups worldwide, the next best thing is already prone to replace the ‘old’ technique.
11. Improvements in predictive pharmaceutical toxicity screening have a long lag phase.