Advanced in vitro models for studying drug induced toxicity

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Stellingen

behorende bij het proefschrift

Advanced *in vitro* models for studying drug-induced toxicity

1. HepG2 cells transform from a highly proliferative state in monolayer culture to non-proliferating spheroids in 3D culture (this thesis).

2. HepG2 spheroids show increased expression of albumin, urea, xenobiotic transcription factors, phase I and II drug metabolism enzymes and transporters (this thesis).

3. Cell cycle regulation, xenobiotic metabolism pathways such as PXR/RXR, complement system, bile-acid biosynthesis and coagulation system are significantly upregulated and show a close similarity to the human liver gene expression compared to other hepatocyte cell models (this thesis).

4. Genes in the Nrf2 pathway are important markers for hepatocellular injury (this thesis).

5. Liver buds created using 3D cell cultures show close resemblance to *in vivo* liver buds (Takebe, T. *et al.*, Nature; 2013).

6. Repeated dosing (in *in vitro* cultures) increases sensitivity without loss of specificity (Khetani, S. R. *et al.*, Toxicological Sciences; 2013).

7. High content screening allows simultaneous assessment of pre-lethal cytotoxic effects and different mechanisms of toxicity on a high-throughput screening platform (Tolosa, L. *et al.*, Toxicological Sciences; 2012).

8. Sub-chronic toxicogenomic studies improve the determination of mode-of-action of compounds (Jackson, A.F. *et al.*, Toxicology and Applied Pharmacology; 2014).

9. Simple yet robust designs endure.

10. The Karma of a cell is re-defined in a 3D environment.

11. We used to think life existed on a flat surface; only later did we realize it is supported on a mighty spherical object. Now that we realized the same in cell biology, should we still trust the life on a flat surface?

12. 3D cultures exemplify the importance of teamwork in achieving extraordinary success.

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