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P1: Assessment of Metabolism-Induced Hepatotoxicity on a 384-Pillar Plate

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Assessment of Metabolism–Induced Hepatotoxicity on a 384-Pillar Plate

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Abstract

Microarray bioprinting technology has been explored to create miniaturized 3D cell cultures on a 384-pillar plate, which were combined with drug metabolizing enzymes (DMEs) and test compounds in a 384-well plate for metabolism-induced toxicity assays. Our goal in this study was to demonstrate rapid assessment of metabolism-induced toxicity on the 384-pillar plate and obtain reliable and highly predictive information on compound's hepatotoxicity *in vivo*. Briefly, human cells including Hep3B human hepatoma cell line as well as human embryonic kidney 293 (HEK 293) cell were encapsulated in alginate-Matrigel on the 384-pillar plate. Test compounds and six different DMEs including cytochromes P450 (CYP450) and UDP-glucuronosyltransferase (UGT) were dispensed in the 384-well plate. By sandwiching the 384-pillar plate onto the 384-well plate, human cells were exposed to the compounds and their metabolites generated by DMEs. The cells were stained with luminescent and fluorescent dyes and IC_{50} values were calculated using the luminescence and fluorescence obtained. In summary, our approach allowed us to assess mechanisms of metabolism-induced toxicity in high throughput. Thus, the 384-pillar plate could be used as a high-throughput, early stage, microscale alternative to conventional *in vitro* multi-well plate platforms and provide a rapid and inexpensive assessment of metabolism-induced toxicity at early phases of drug development.