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High-Content, 3D Cell Culture Assays on a Micropillar/Microwell Chip Platform

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Abstract

High content imaging (HCI) is a multi-parametric assay using multiple fluorescent dyes that are relevant to specific cell functions. The HCI assays provide an insight into the mechanisms of toxic drug responses, thus enhancing predictability of drug toxicity. However, current HCI assays are performed on 2D cell monolayer cultures which are physiologically irrelevant, creating a new opportunity for better predictable 3D HCI assays. The goal of this research is to develop HCI assays on 3D cellular microarrays that can be implemented for various toxicity screening, leading to classification of drug toxicity via investigating profiles of cell injury. As a model system, Hep3B human liver cells were dispensed onto a micropillar chip with a microarray spotter, which were exposed to various concentrations of model drugs. The chip containing the cells was then stained with multiple fluorescent dyes and scanned with a chip scanner to measure different end points. Conclusively, HCI assays performed on the 3D cellular microarrays showed a capability to identify several mechanisms of toxic drug responses. The mechanisms including DNA and mitochondrial impairment, calcium homeostasis, and glutathione conjugation were successfully demonstrated on the micropillar/microwell chip platform. Computational algorithms along with additional assays will be developed for enhanced predictability.