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Inverted Culture Plate Insert for Cellular Co-Culture

Summary

Lack of metabolic competence is a major limitation for the majority of current high throughput screening (HTS) assays used for screening drugs, environmental chemicals and industrial compounds for toxicity. As many compounds are metabolically transformed in vivo, toxicity assays should reflect physiologically-relevant metabolism to accurately predict their in vivo safety. Human primary hepatocyte (HPH)-target cell co-culture has been the in vitro standard for testing xenobiotics and toxicity. However, current methods are limited by the short-term viability of liver slices or low expression of drug-metabolizing enzymes in immortalized cell lines. To address these challenges, UMB researchers have developed a novel inverted HPH-target cell co-culture system that can be used with current cell-based screening assays. The inverted co-culture system uses HPHs to provide functional metabolism to the co-cultured target cells and allows both the HPHs and the target cells to be evaluated for gene expression, toxicity, or any experimental endpoint, maximizing the information gained through each experiment. In addition to improving the assessment of chemical toxicities, this new system can be scaled up to an HTS format by retrofitting it onto current HTS systems. This simple and low cost method is an attractive approach for in vitro HTS of chemical toxicity in a metabolically-competent environment.

Key Investigator

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Field

Research tools

Technology

Inverted cell co-culture system

Advantages

Allows basic cellular co-culture to be cost-effectively added to existing plates and assays

Easier co-culture of HPH with better metabolite exposure than current methods

Can be scaled up for HTS

Status

Available for licensing
Available for sponsored research

Patent Status

Pending

UMB Docket Reference

BM-2017-002

Market

The inverted co-culture system is designed to integrate into existing HTS assays and provide a simple, cost-effective solution to the complex problem of cellular co-culture with physiologically relevant parameters. Compared with the most commonly used available product, Transwell® culture plates, the inverted co-culture design significantly facilitates attachment and morphology of HPH, while allowing the HPH and target cells to directly face each other and enhance the exchange of medium and metabolites in the same chamber. Transwell® plates are priced between $90 and $300, depending on pore size and membrane material. The inverted co-culture system would have a more competitive price, as the insert can be made with polystyrene, the same material as a typical cell culture plate, and does not require a membrane.

Technology

As depicted in the schematic diagram (Fig. 1, exemplified in a 96-well platform), HPH is plated in the top chamber of the 96-well inverted co-culture insert. This is in contrast to existing HTS assays, where cells are plated on the bottom of the 96-well plate. After cell attachment, the HPH-containing co-culture inserts are flipped over into the plate containing target cells to complete the inverted co-culture model (middle panel). After seeding, hepatocytes are overlaid with Matrigel to form an HPH sandwich culture configuration, which improves their metabolic function. Immortalized cells are then plated in 96-well plates and HPH-containing co-culture inserts transferred to the cell line-seeded 96-well plate and treated with test compounds. The 96-well plates can then undergo HTS assay readouts.

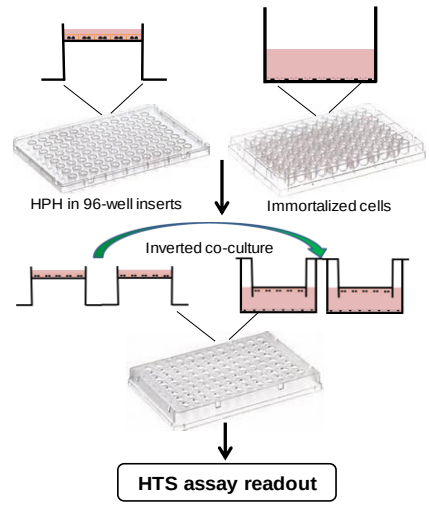

Fig 1. Schematic illustration of HPH-cell line co-culture. The inverted design will maximize the exposure of metabolites to target cells.

Technology Status

This technology has been tested with proof-of-concept experiments, including 1) the design and 3D printing of the inverted co-culture insert; 2) an assay to determine the metabolic capacity of HPHs in this culture model using common metabolism probes; 3) functionally characterized this co-culture model by determining the metabolic-dependence of the toxicity of 3 model compounds.

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