

Coming 2012

## iCell® Hepatocytes

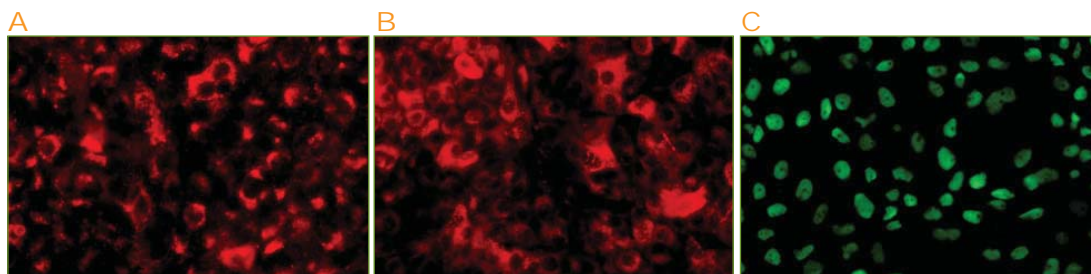
Cellular Dynamics International (CDI) is developing iCell® Hepatocytes, human induced pluripotent stem (iPS) cell-derived hepatocytes. iCell Hepatocytes will provide, for the first time, access to commercial quantities of high quality, high purity human liver cells for preclinical drug discovery, hepatotoxicity testing, and disease research.

Liver toxicity and alterations of hepatic physiology are frequently occurring reasons for preclinical failure during drug development. In addition, drug-induced liver injury is the most common reason for market withdrawal of approved drugs due to safety concerns. Liver diseases associated with drug toxicity can be attributed, in large part, to the lack of biologically relevant and predictive model systems. Current hepatocyte model systems include primary human hepatocytes harvested from cadavers, immortalized cell lines, and animal models. Each of these models presents limitations in functionality, reproducibility, and/or availability. iCell Hepatocytes will overcome these limitations and provide a reliable source of well-characterized, highly reproducible, and readily available human hepatocytes for preclinical drug development and safety testing.

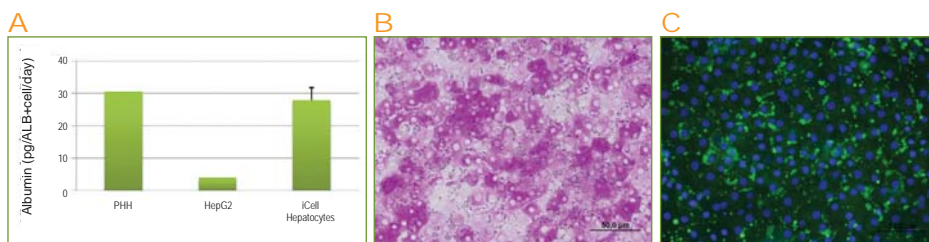
### Applications

iCell Hepatocytes will be amenable to a variety of biochemical and cellular assays to study:

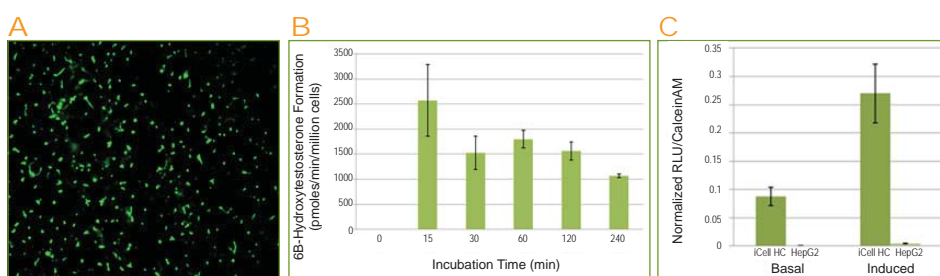
- Hepatotoxicity
- Gene regulation
- Intrinsic metabolism
- Cytochrome P450 induction/inhibition
- Transporter function



▲ **Figure 1: iCell Hepatocytes Express Characteristic Hepatocyte Proteins**  
*iCell Hepatocytes were immunostained for (A) alpha-1-antitrypsin, (B) albumin, and (C) hepatocyte nuclear factor 4-alpha. Characteristic cytoplasmic staining is observed for alpha-1-antitrypsin and albumin (red), and nuclear staining is observed for hepatocyte nuclear factor 4-alpha (green).*



**▲ Figure 2: iCell Hepatocytes Display Intrinsic Hepatocyte Functions**  
*iCell Hepatocytes were assayed for (A) albumin production, (B) glycogen storage, and (C) lipid storage. iCell Hepatocytes produce albumin protein at levels similar to primary human hepatocytes (PHH) and greater than HepG2 cells, as measured by ELISA. Storage of glycogen and lipid is demonstrated by staining with Periodic Acid Schiff and 4,4-difluoro-1,3,5,7-tetramethyl-4-bora-3a,4a-diaza-s-indacene (BODIPY® 505/515), respectively.*



**▲ Figure 3: iCell Hepatocytes Exhibit Functional Bile Canaliculi and P450 Metabolism**  
*iCell Hepatocytes exhibit (A) functional bile canaliculi, (B) CYP3A basal activity, and (C) CYP3A4 induction activity. Formation of bile canaliculi was assayed 3 days post-plating using 5(6)-carboxy-20,70-dichlorofluorescein diacetate (CDFDA) (photo courtesy of Qualyst, Inc.). CYP3A basal activity (metabolism of testosterone substrate) was assayed by mass spectrometry in suspended iCell Hepatocytes at the indicated time-points. CYP3A4 induction activity in response to 10  $\mu$ M dexamethasone was assayed using the P450-Glo 3A4 assay (Promega) in plated iCell Hepatocytes and HepG2 cells, as indicated.*

## ADVANTAGES

### Quality, Quantity, Purity

- Characteristics and functions required for in vitro hepatotoxicity, metabolism, and transporter studies
- Well-characterized and reproducible for consistent results
- Readily available in cryopreserved format
- High purity (>90%) provides biologically relevant results

### For More Information

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