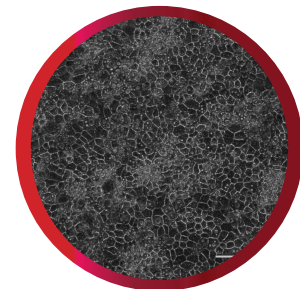


DefiniGEN human iPS-derived hepatocytes



DefiniGEN's human hepatocytes are highly functional cryopreserved cell products displaying many of the characteristics of primary human cells. Key hepatocyte functions include albumin production, glycogen storage and A1AT secretion. CYP450 mRNA expression and catalytic activities are also observed at comparable levels to primary human hepatocytes (PHH).

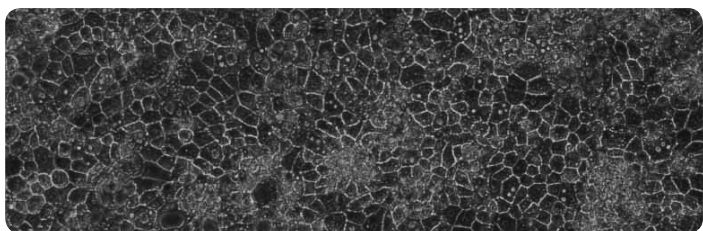


Figure 1. DefiniGEN hepatocytes display characteristic cell morphology. Def-HEP WT cells exhibit typical hepatocyte cobblestone morphology and bi-nucleation.

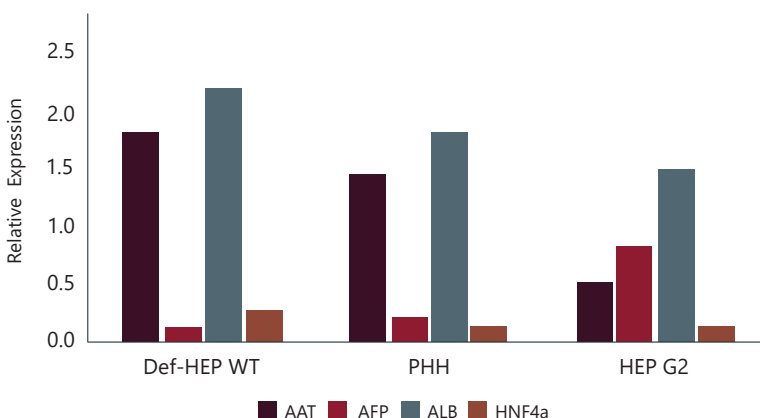


Figure 2. Gene expression analysis demonstrates that Def-HEP express key hepatocyte markers at similar levels to PHH. AFP levels are extremely low in Def-HEP indicating the cells have attained a functional mature status.

Hepatocyte maturation markers

Def-HEP cells display the functional characteristics of primary human hepatocytes including albumin secretion, A1AT production, glycogen storage and LDL uptake (Figure 3).

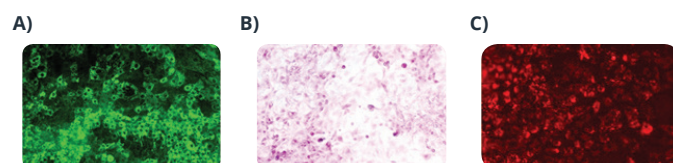


Figure 3. Functional analysis of Def-HEP WT hepatocytes. (A) Albumin secretion, 10x magnification (B) Glycogen storage shown by PAS staining (C) LDL cholesterol uptake shown by fluoresceinated LDL incorporation.

Specification

Catalog Number	Def-HEP WT
Format	Cryopreserved 3-6 million cells per vial
Viability	>70%
Applications	Research and Predictive Toxicology

In terms of general metabolism DefiniGEN hepatocytes generate ATP via mitochondrial oxidative phosphorylation and are thus suitable for mitochondrial toxicology applications. They do not exhibit the Crabtree Effect, the disadvantageous phenomenon observed in immortalized liver cell lines which generate their ATP via glycolysis.

Following a thaw and recovery protocol DefiniGEN hepatocytes have a 15-20 day window of use making them effective models for hepatitis lifecycle studies. The cells express key hepatitis markers such as CD81, SR-B1, Claudin-1 and Occludin at similar levels to primary human hepatocytes.

Hepatitis marker analysis

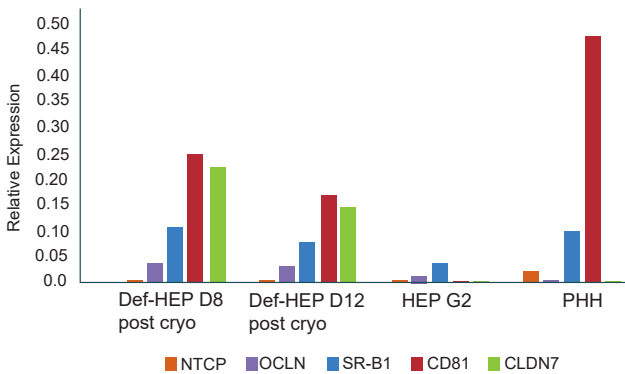


Figure 4. Gene expression analysis demonstrating the presence of key Hepatitis markers in Def-HEP including NTCP, Occludin, SR-B1, CD81 and CLDN7.

Multiple inducible CYP450 activities

Def-HEP cells display CYP450 induced activity profiles that are comparable to PHH (CYP1A2 EROD assay, inducer - omeprazole), (CYP3A4 PGlo assay, inducer - rifampicin) (Figure 6).

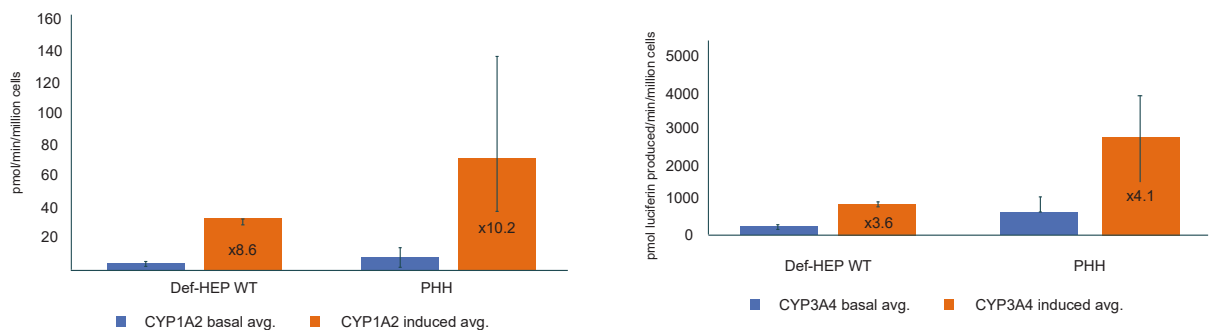


Figure 6. Def-HEP cells have comparable CYP activity to PHH and induced activity profiles that are highly similar to PHH (CYP1A2 EROD assay, inducer - Omeprazole), (CYP3A4 PGlo assay, inducer - rifampicin).

Extended culture time

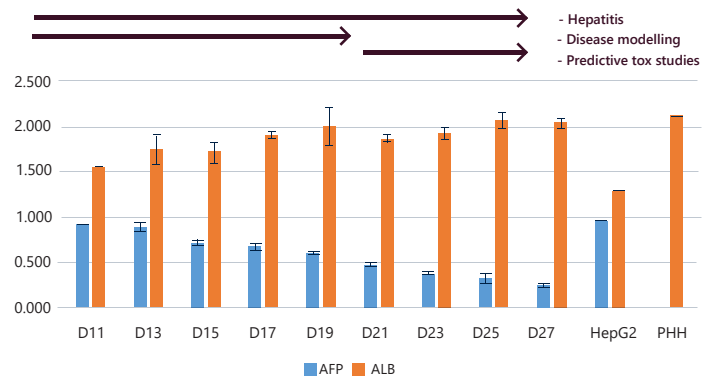


Figure 5. Cryopreserved Def-HEP cells are thawed, plated, and recovered over 7 days to ensure a functional hepatocyte monolayer forms. Subsequently the cells have a +20 day functional window to enable hepatitis, disease modelling, and toxicology studies to be undertaken over a longer timeframe than is possible with PHH.