

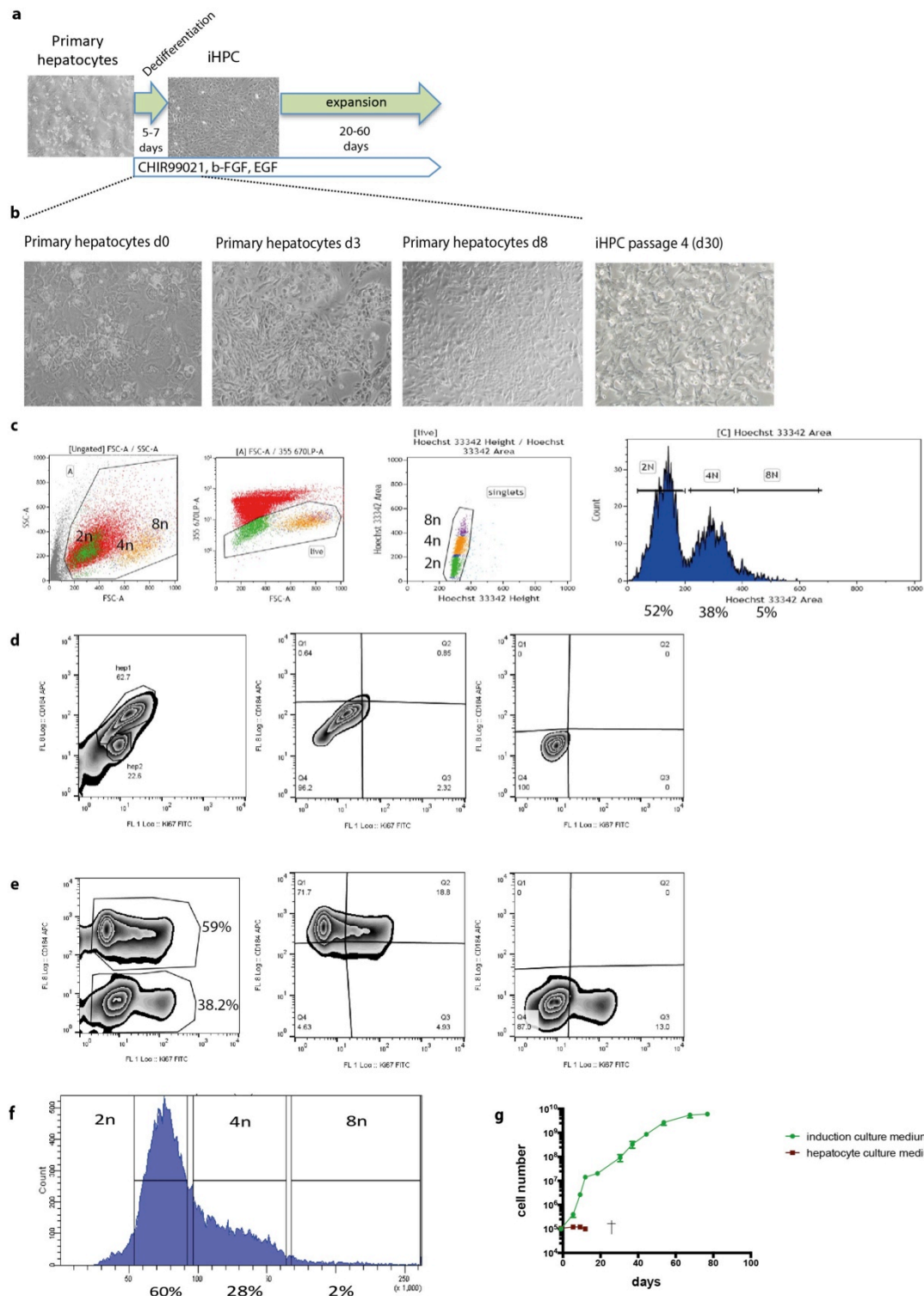


Figure 1. Generation of induced hepatic progenitor cells (iHPC) from primary hepatocytes.

(a) Experimental protocol. (b) Morphological changes in primary hepatocytes during the first week of induction. (c) DNA Hoechst33342 staining of primary hepatocytes and sorting based on ploidy. Definitive endoderm C-X-C chemokine receptor type 4 (CXCR4) and proliferative marker Ki67 expression by flow cytometry of (d) primary hepatocytes and (e) iHPC. (f) DNA Hoechst staining of iHPC (passage 2). (g) Comparative rates of *in vitro* expansion of iHPC and primary hepatocytes.

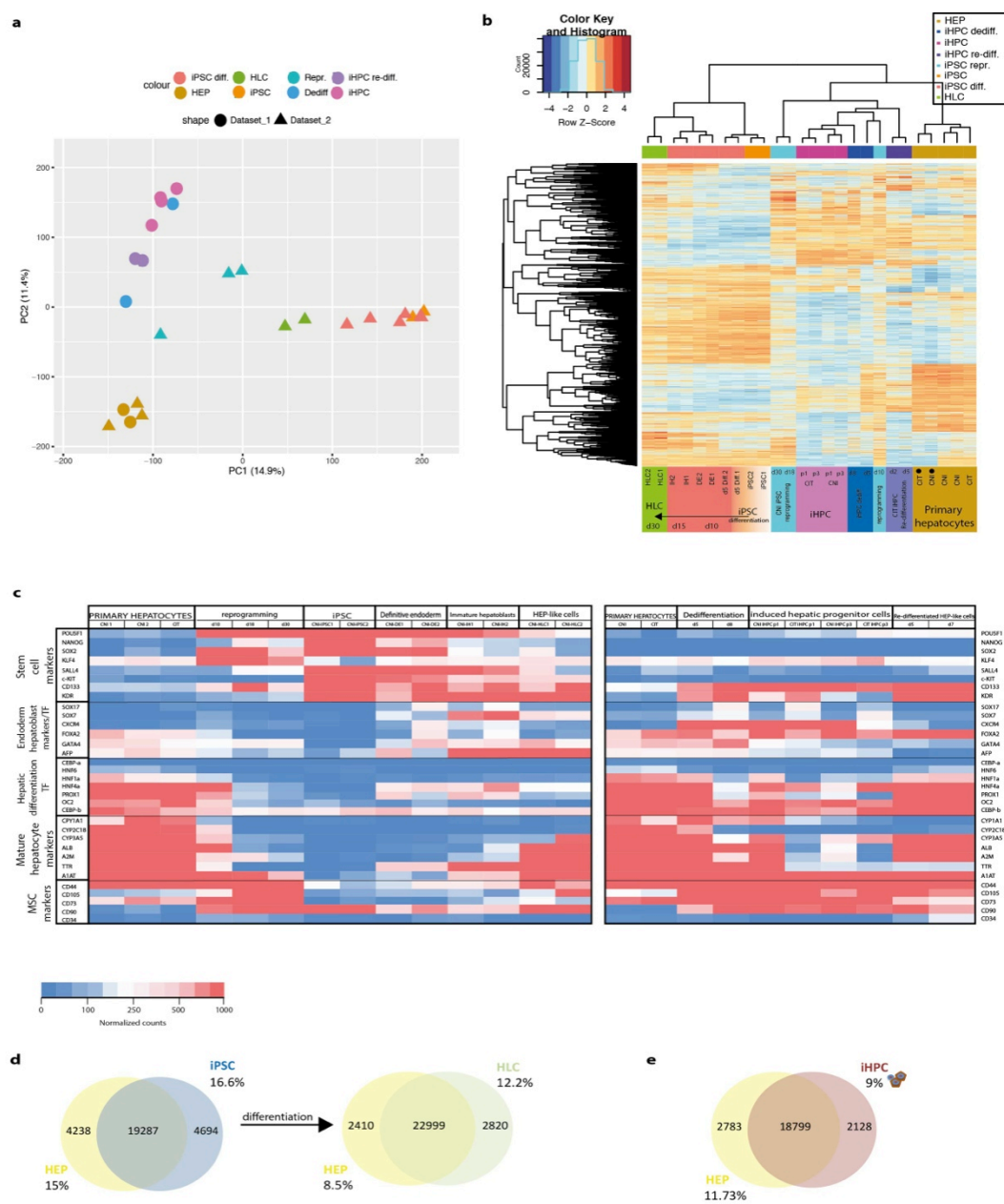


Figure 2. Comparing the protein-coding transcriptome of iHPC and iPSC, and products differentiated therefrom. (a) Principal component analysis of protein-coding genes combining dataset 1 (dedifferentiation of hepatocytes into iHPC and *in vitro* 2D re-differentiation, circles). and dataset 2 (iPSC generation from primary hepatocytes and differentiation to HLC, triangles). (b) Heatmap illustrating levels of 5,000 protein-coding transcripts with the highest standard deviation (SD) among samples combining dataset 1 (HEP dedifferentiation, iHPC at different passages and re-differentiation) and dataset 2 (iPSC generation from primary hepatocytes and differentiation to HLC, triangles). RNA from primary hepatocytes sequenced in dataset 1 are labelled with circles. (c) Heatmap representation showing RNA-seq normalized counts of a selection of cell-stage specific genes during generation and re-differentiation of iPSCs (left) and iHPCs (right). Venn diagrams illustrating protein-coding transcripts detected in (d) hepatocytes, iPSC and HLC, and (e) hepatocytes and iHPC.

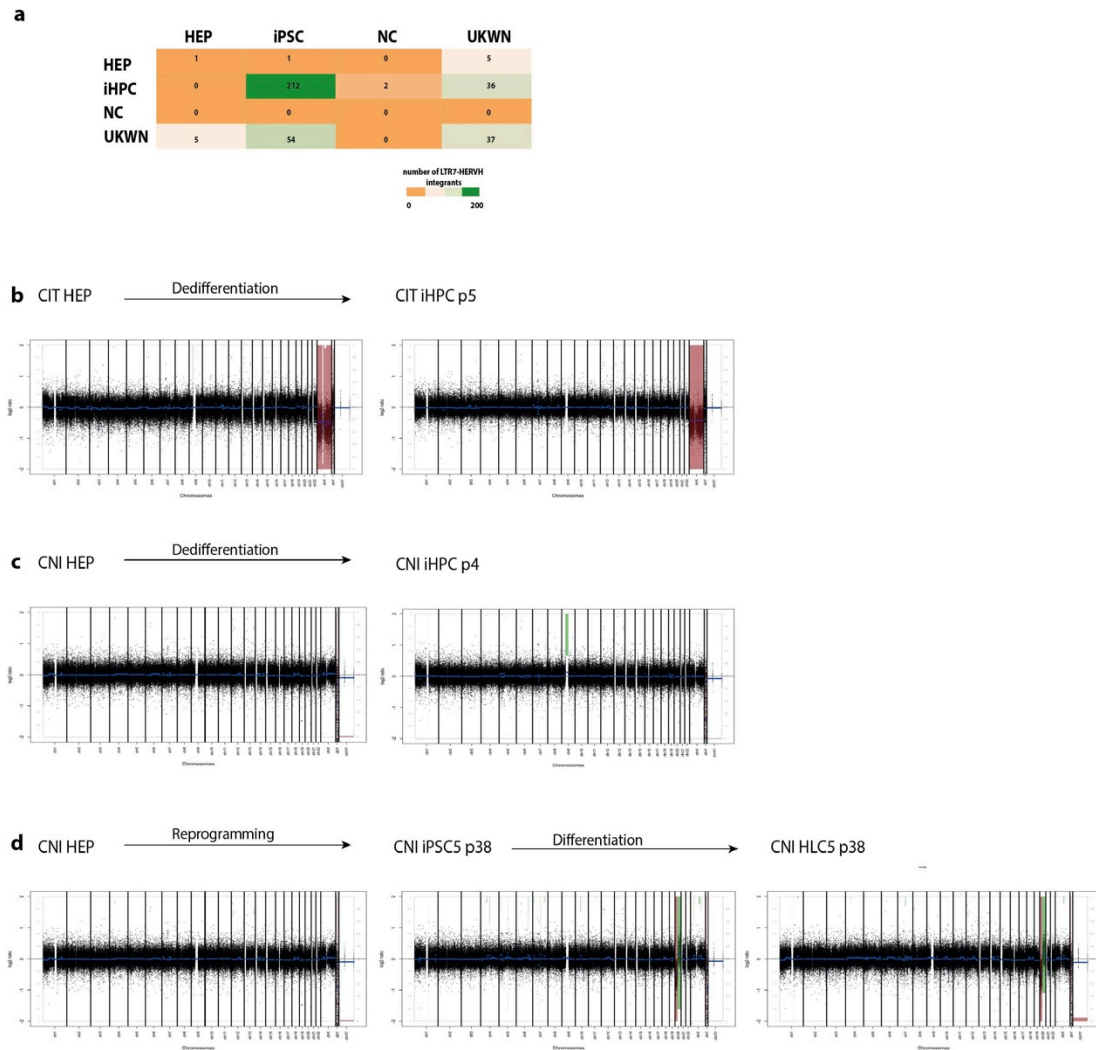


Figure 3. Genomic stability during iHPC and iPSC generation and differentiation. a) Table showing the number of LTR7-HERVH non-coding transcripts in common between iPSC and iHPC. **HEP**: integrants with foldChange>2 and pval < 0.05 in HEP vs iPSC and HEPvs iHPC. **iPSC**: integrants with foldChange>2 and pval < 0.05 in iPSCvsHEP. **iHPC**: integrants with foldChange>2 in iHPCvsHEP. **NC**, not changing: integrants with foldChange<1.1 in both conditions. **UKWN**, integrants with foldChange between 2 and 1.1 or pval>0.05. (b) DNA array showing mutations, amplifications and deletions across the chromosomes in de-differentiation of citrulinemia primary hepatocytes to iHPC. (c) Dedifferentiation of Crigler-Najjar primary hepatocytes to iHPC. (d) Reprogramming to iPSC and differentiation to HLC of Crigler-Najjar primary hepatocytes.

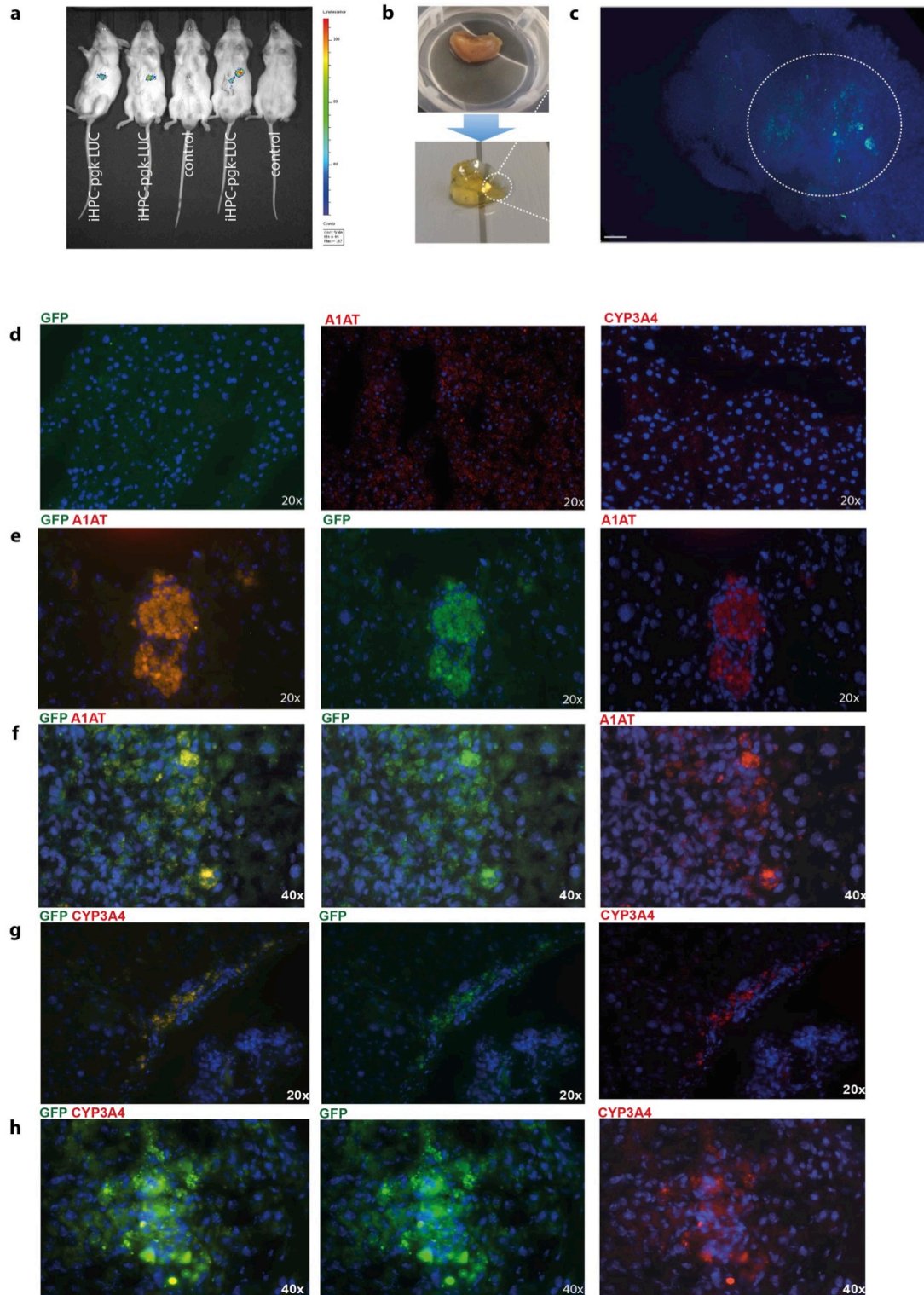


Figure 4. iHPC re-differentiation *in vivo* upon transplantation. (a) Luciferase-based detection of LV-PGK-Luc-transduced iHPCs transplanted into the liver of NSG mice. (b) Lipid-cleared liver lobe for 3D imaging of transplanted iHPC. (c) 3D imaging of GFP-positive TTR-GFP-transduced iHPC. (d) Immunofluorescence-based detection of GFP, human CYP3A4 and human A1AT in the liver lobe of sham NSG mice. Co-detection of (ef) GFP and human A1AT and (gh) GFP and human CYP3A4 in the liver mice injected with LV-TTR-GFP-transduced iHPCs.