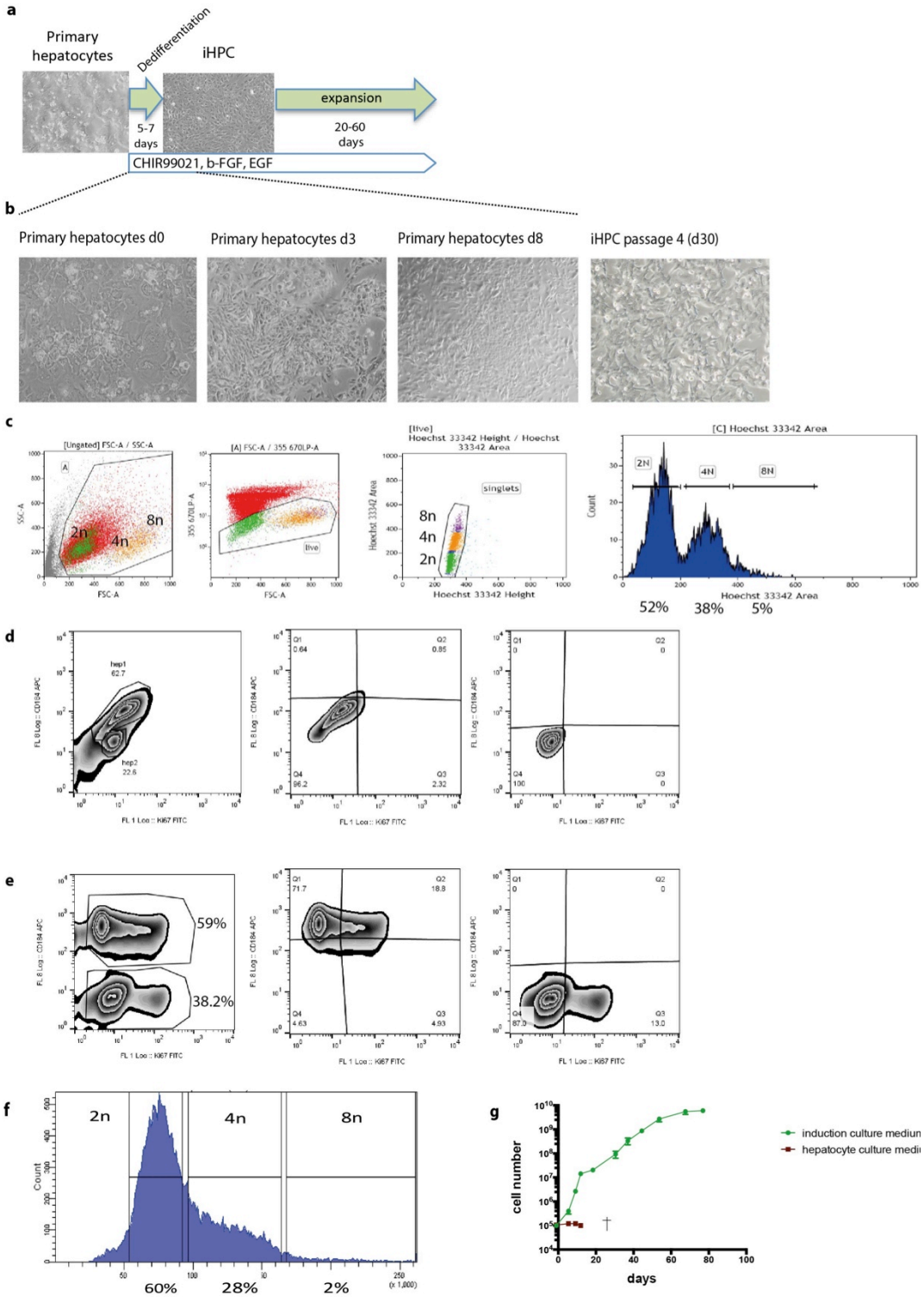


**Figure 1. Generation of induced hepatic progenitor cells (iHPC) from primary hepatocytes.** (a) Experimental protocol. (b) Morphological changes in primary hepatocytes during the first week of induction. (c) DNA Hoechst33342 staining of primary hepatocytes and sorting based on ploidy. Definitive endoderm 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.

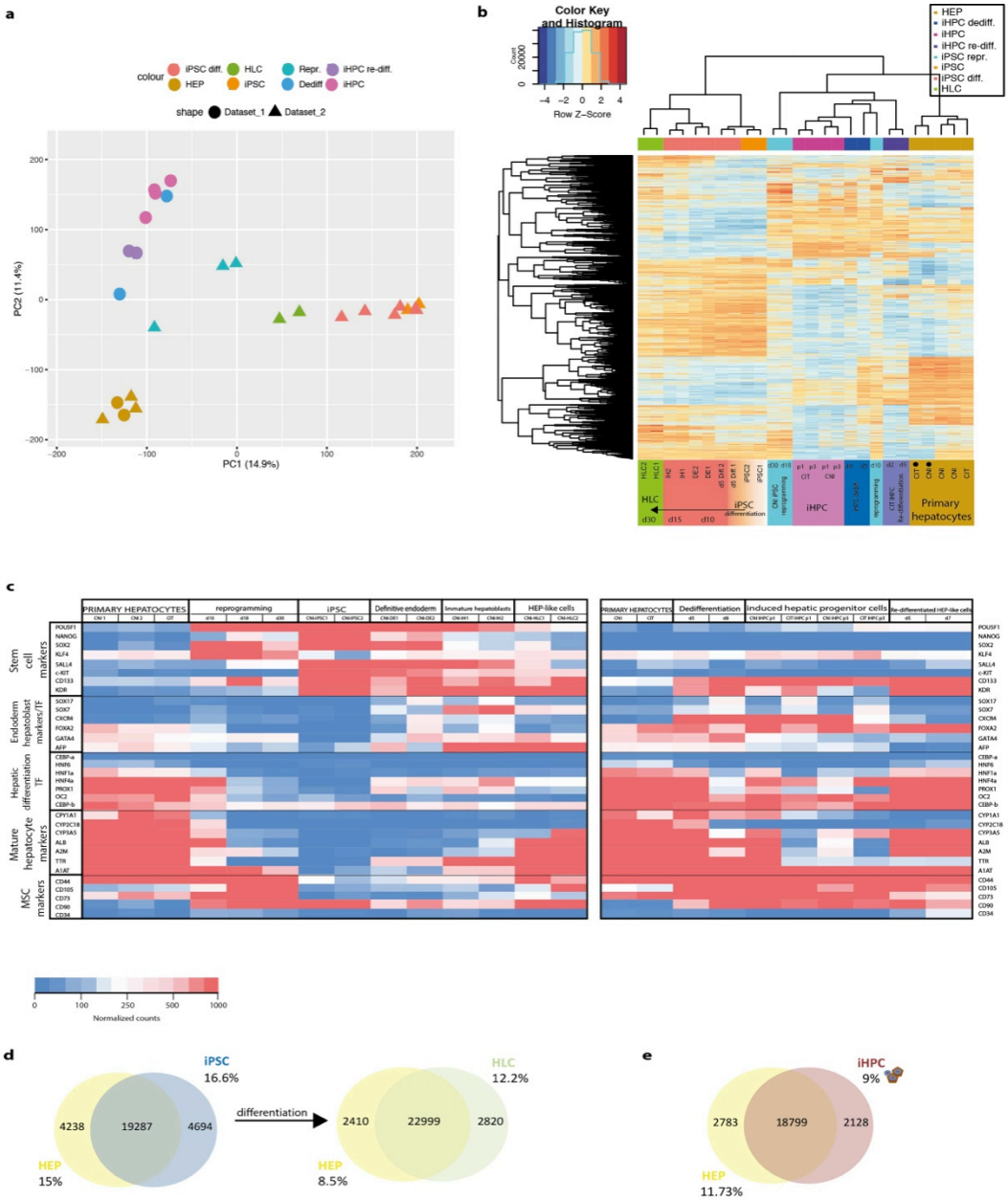


**Figure 2. Comparing the protein-coding transcriptome of iHPC and iPSC, and products differentiated therefrom.** (a) Principal component analysis of protein-coding genes combining dataset 1 (dedifferentiation of hepatocytes into iHPC and *in* vitro 2D re-differentiation, circles). and dataset 2 (iPSC 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.

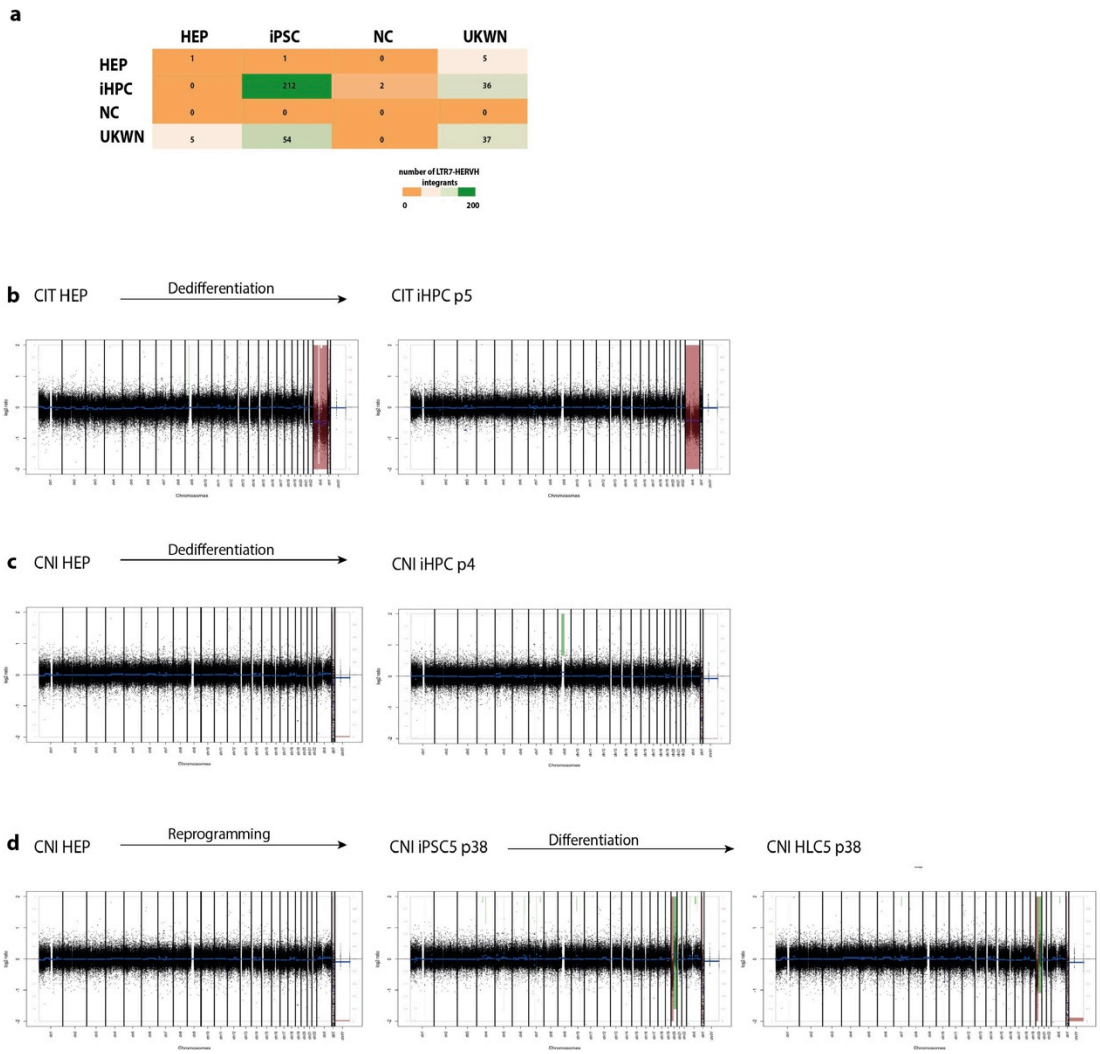


**Figure 3. Genomic stability during iHPC and iPSC generation and differentiation.** a) Table showing the number of LTR7-HERVH non-coding transcripts in common between iPSC and iHPC. **HEP**: integrants with foldChange>2 and pval < 0.05 in HEP vs iPSC and HEPvs iHPC. **iPSC**: integrants with foldChange>2 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.

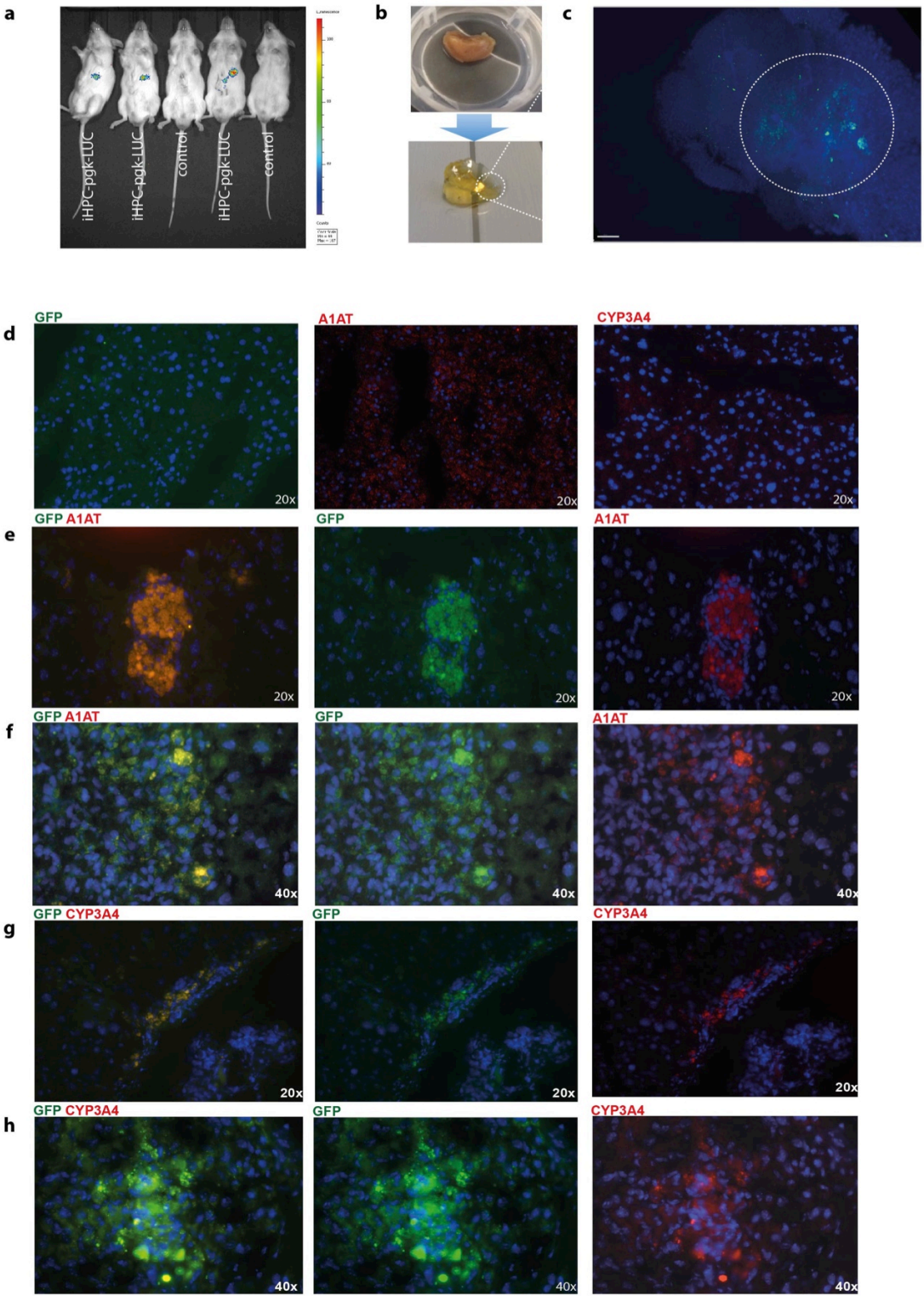


**Figure 4. iHPC re-differentiation *in vivo* upon transplantation.** (a) Luciferase-based detection of LV-PGK-Luc-transduced iHPCs transplanted into the liver of NSG mice. (b) Lipid-cleared liver lobe for 3D imaging of transplanted iHPC. (c) 3D imaging of GFP-positive TTR-GFP-transduced iHPC. (d) Immunoflourescence-based 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.