# Replication of Hepatitis B and C Virus in

# Human Liver Chimeric Mice

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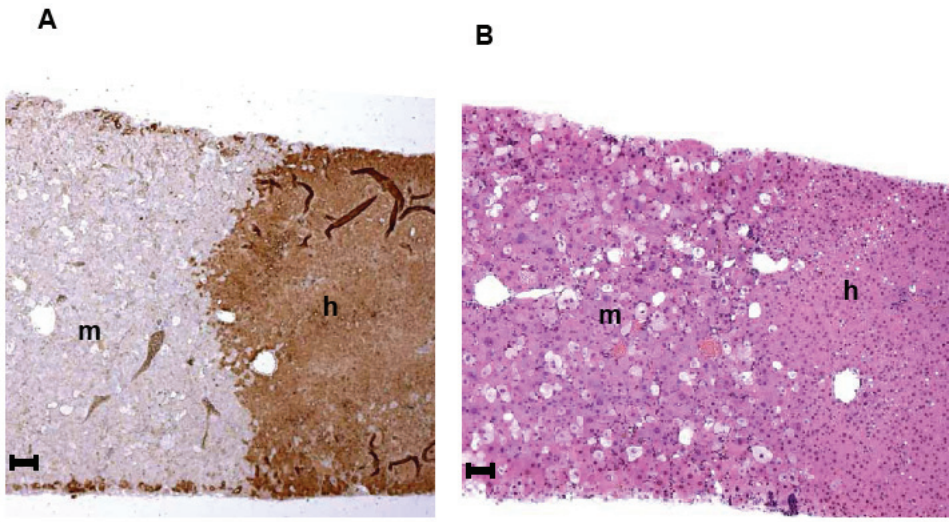
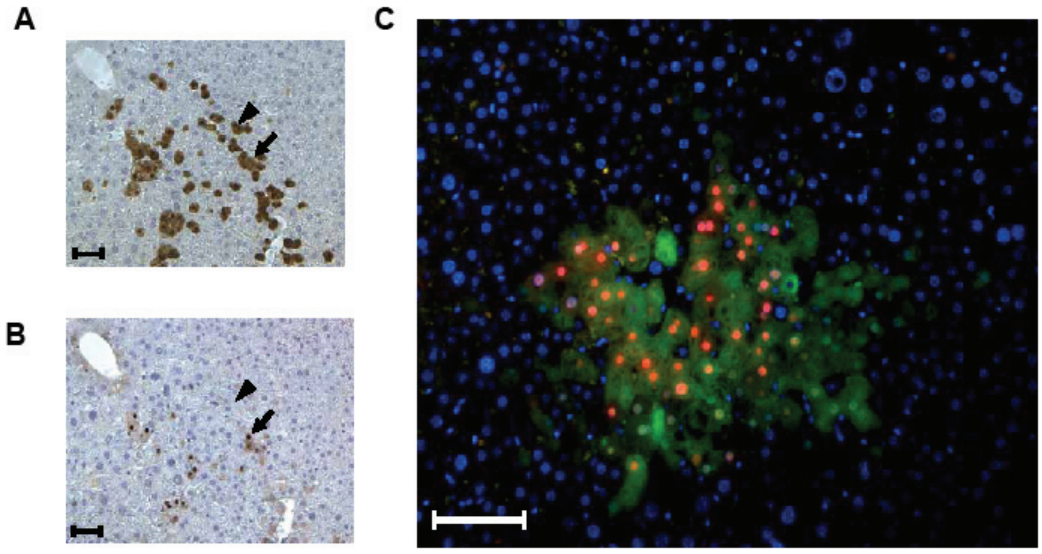
# Supplementary Material

## Supplementary Methods

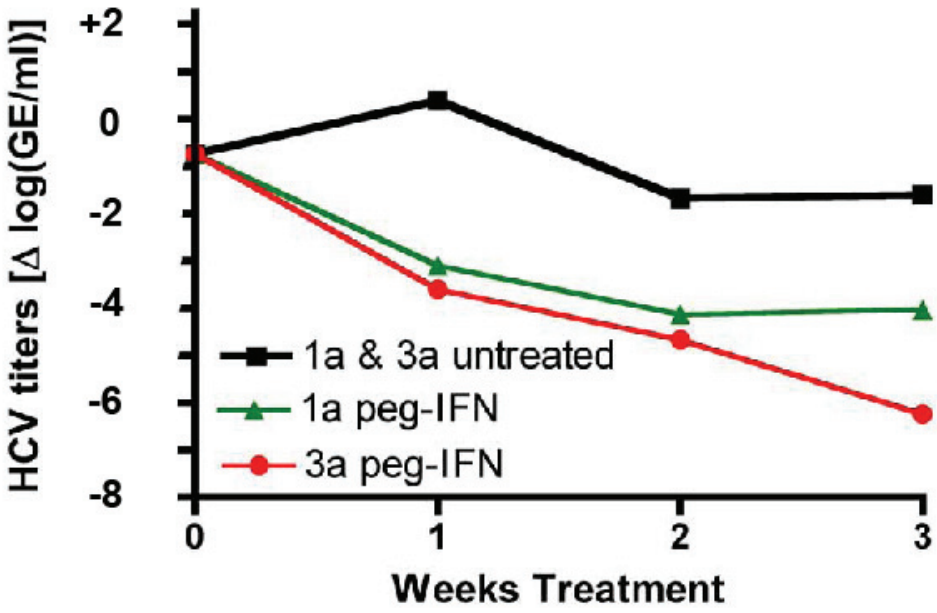
**Treatment of HBV infected human liver chimeric mice with adefovir dipivoxil:**
Chimeric fah-/-/rag-2-/-/il-2rg-/- mice were injected with $1x10^8$ GE HBV, genotype D (serotype ayw) into the tail vein. The inoculum was derived from the serum of an HBV-infected chimpanzee and diluted in PBS to a volume of 200 μ.
After 6 weeks when plateau phase of HBV DNA in the serum was reached, animals were treated with adefovir dipivoxil (4mg/kg/day in 0.05 M citric acid, oral gavage once daily) or citric acid only.



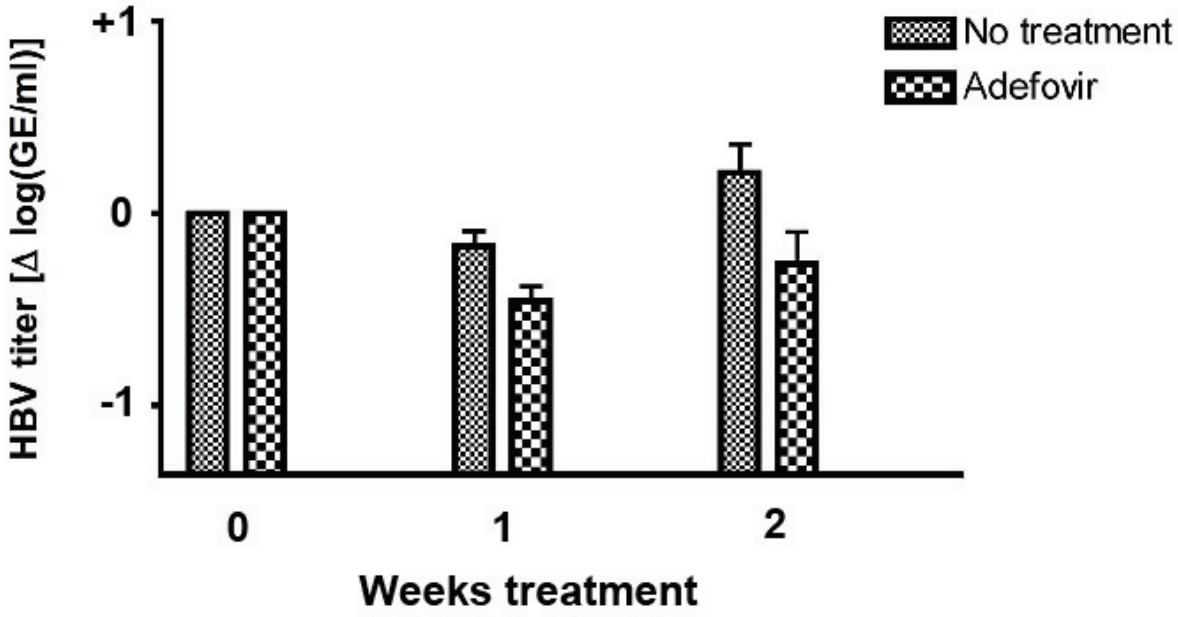

**Supplemental Figure 1.** Histological appearance of HBV infected chimeric mouse liver. (**A**) Immunostaining for FAH showing positive human (h) tissue and nonreactive mouse (m) tissue. (**B**) Serial section of (**A**) with H&E staining showing infiltration and cell death of mouse tissue, while the human counterpart shows normal liver tissue. Scale bar is 50 μm.



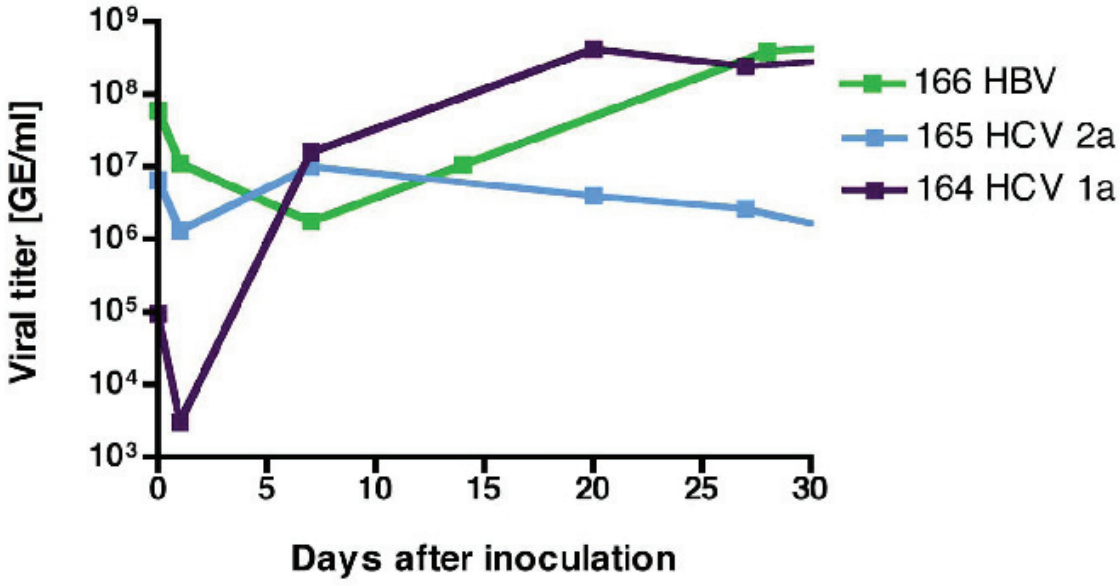

**Supplemental Figure 2** HBV infection of mice with low human chimerism. (**A**) Immunostaining of the liver for FAH and/or HBcAg. Serial sections of the same cluster of human hepatocytes stained for FAH (**A**) and HBcAg (**B**). The arrow points to cells that are stained by both antibodies and the arrowhead to cells that are stained by FAH only. (**C**) Fluorescent co-staining of a hepatocyte cluster for FAH {green} and HBcAg {red}. The cellular distribution of FAH is mainly cytoplasmic while HBcAg shows a strong nuclear and faint cytoplasmic staining.




**Supplemental Figure 3.** Treatment of HCV genotype 1a and 3a with peg-IFN. Data points represent normalized, mean HCV titers of HCV-1a (n=3), HCV-3a (n=2) treated with peg-IFN and untreated control group (n=4 HCV genotype 1a & 3a).




**Supplemental Figure 4.** Treatment of HBV infected human chimeric mice with adefovir dipivoxil. Histograms represent normalized mean values of treated (n=3) and untreated group (n=3)




**Supplemental Figure 5.** Viral titers in the serum of HBV and HCV (genotype 1a and 2a) infected chimeric mice. All three mice have been repopulated with hepatocytes of the same donor.

**Supplemental table 1**
Donor information for human hepatocyte transplantation

| Donor | Age | Race | Sex | BMI [kg/m$^2$] |
|---|---|---|---|---|
| A | 44 | Caucasian | female | normal |
| B | 67 | Caucasian | female | normal |
| C | 20 | African American | female | normal |
| D | 48 | Caucasian | female | normal |
| E | 61 | African American | female | normal |
| F | 4 | Caucasian | male | not analyzed |
| G | 64 | Caucasian | female | normal |
| H | 47 | Caucasian | female | 19 |
| I | 24 | Caucasian | female | 27 |
| J | 44 | Caucasian | female | normal |
| K | 58 | Caucasian | male | 26 |
| L | 18 | Caucasian | female | obese |

**Supplemental table 2**
Repopulation rates of different donors and viruses

| Animal # | IHC[a] | Donor | Virus |
|---|---|---|---|
| 164 | 80% | A | HCV-1a |
| 195 | 40% | D | HCV-1a |
| 165 | 20% | A | HCV-2a |
| 179 | 30% | B | HCV-2a |
| 184 | 30% | B | HCV-2a |
| 187 | 40% | B | HCV-2a |
| 193 | 80% | C | HCV-2a |
| 205 | 70% | E | HCV-1a/2a |
| 206 | 70% | F | HCV-1b/2b |
| 166 | 30% | A | HBV |
| 170 | 70% | A | HBV |
| 172 | 20% | B | HBV |
| 197 | 80% | F | HBV |

[a] IHC with anti-FAH, percentage reflect human chimerism in mouse liver