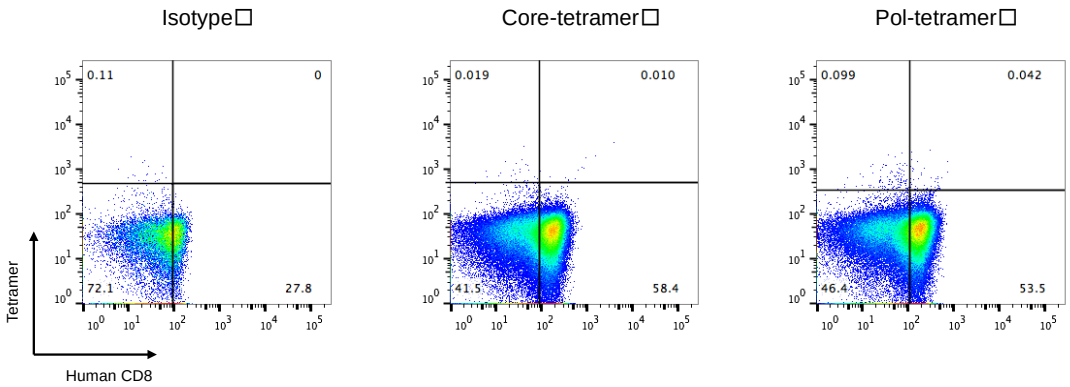
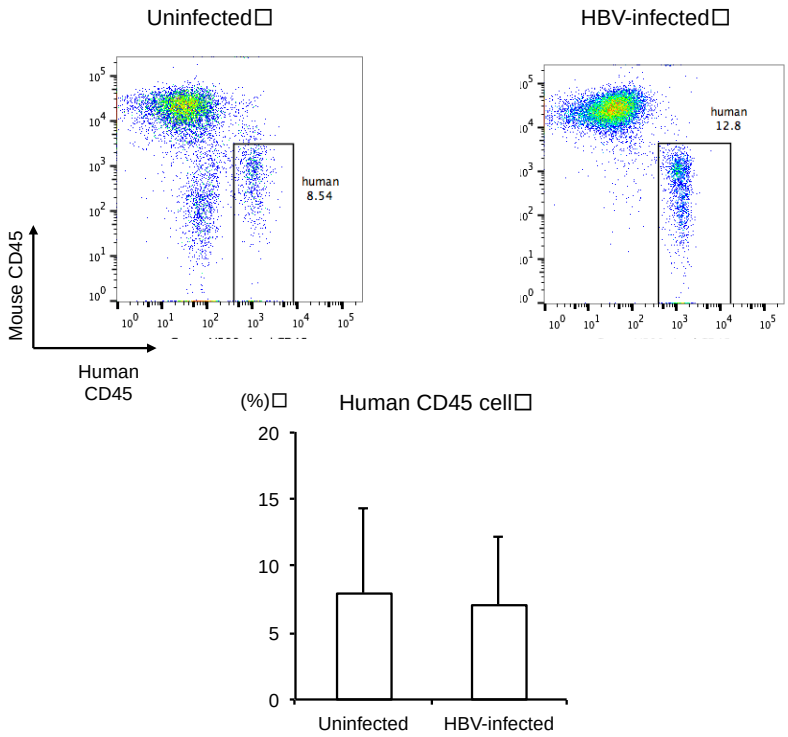


Supplementary Fig. 1. Flow cytometry analysis of liver mononuclear cells in fulminant hepatitis B patients. Liver transplantation was performed 9 days after clinical onset in this patient (peak ALT levels of 17280 IU/ml). Liver infiltrating cells were collected using ex vivo perfusion of the liver allograft through the portal vein after hepatectomy. Human liver mononuclear cells were separated by human-CD8 and HLA-A24 tetramer (Pol and Core).

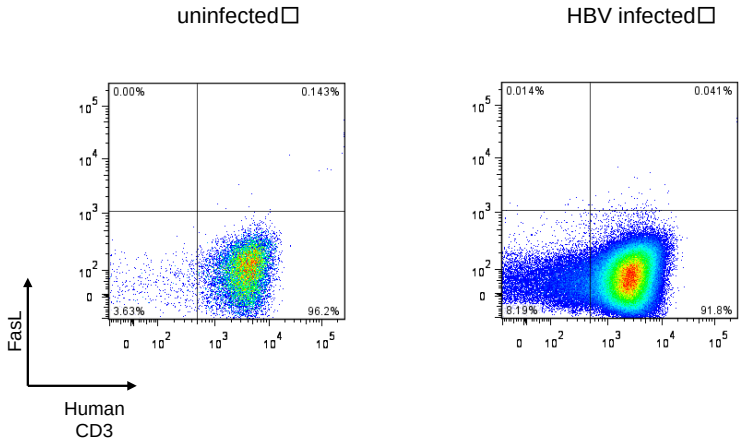
Supplementary Fig. 2



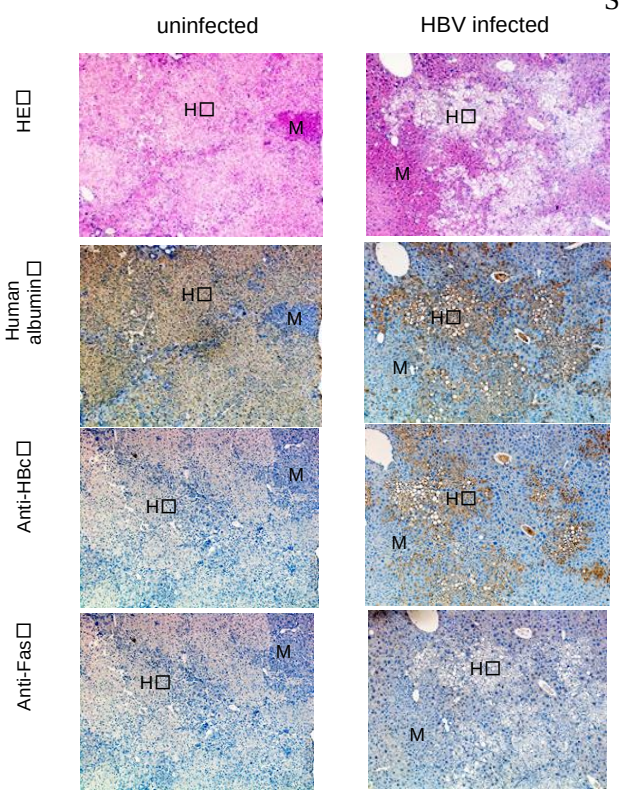
Supplementary Fig. 2. Analysis of human mononuclear cells in the liver in TK-NOG mice one week after PBMC transplantation.

Liver mononuclear cells isolated from mice one week after treatment with human PBMCs were stained with antibodies against human CD45 and mouse CD45 and analyzed by flow cytometry (upper panel). Percentages of human mononuclear cells in PBMC-treated mice were similar between uninfected and HBV-infected mice (lower panel).

Supplementary Fig. 3A□



Supplementary Fig. 3B□

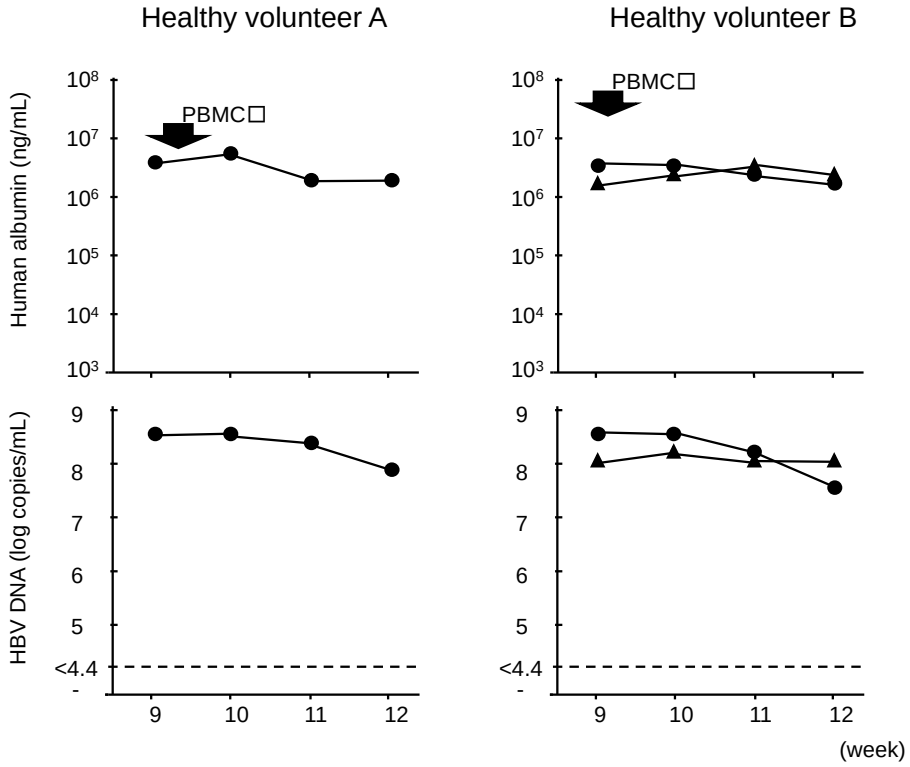


Supplementary Fig. 3. Analysis of the Fas/FasL system in human hepatocyte chimeric TK-NOG mice injected with human PBMCs.

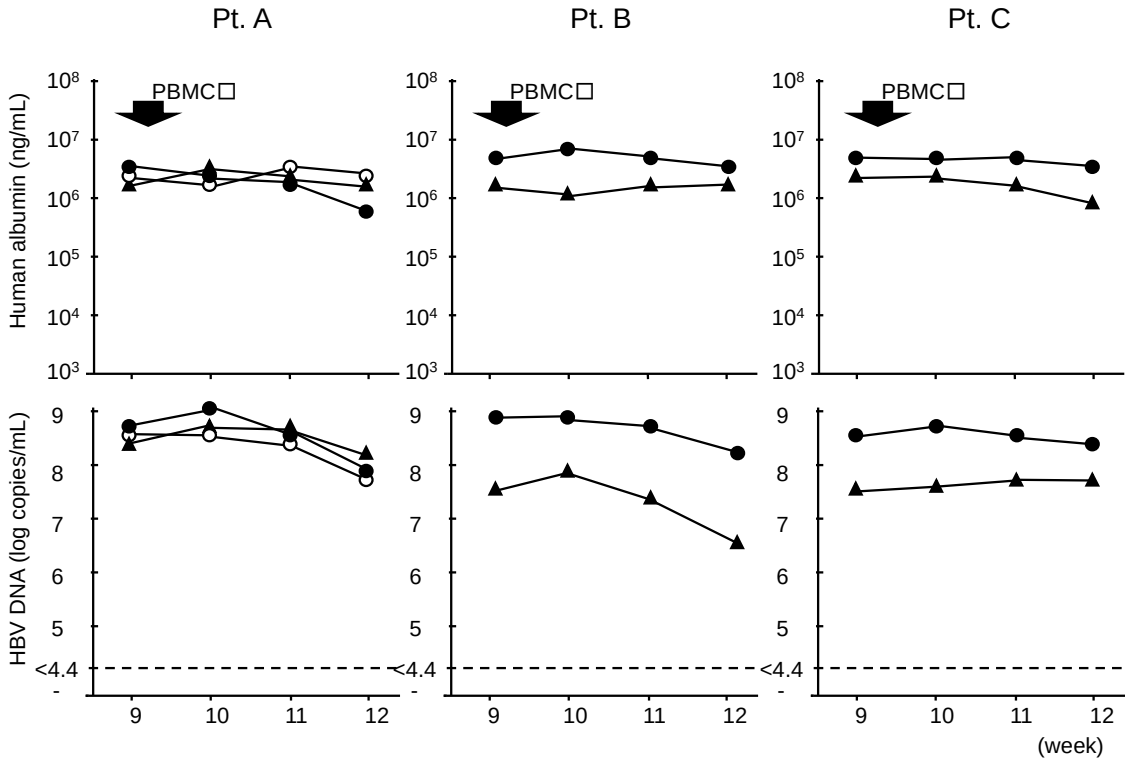
(A) Flow cytometry analysis of liver mononuclear cells in uninfected and HBV-infected mice. Fas-L positive cells were almost undetectable in these mouse livers.

(B) Histological analysis of livers of uninfected and HBV-infected mice. Liver samples obtained from mice with or without HBV infection were stained with hematoxylin-eosin staining (HE), anti-human albumin antibody, anti-hepatitis B core (HBc) antibody and anti-human Fas antibody. Labeled regions indicate human (H) and mouse (M) hepatocytes, respectively (original magnification 40x).

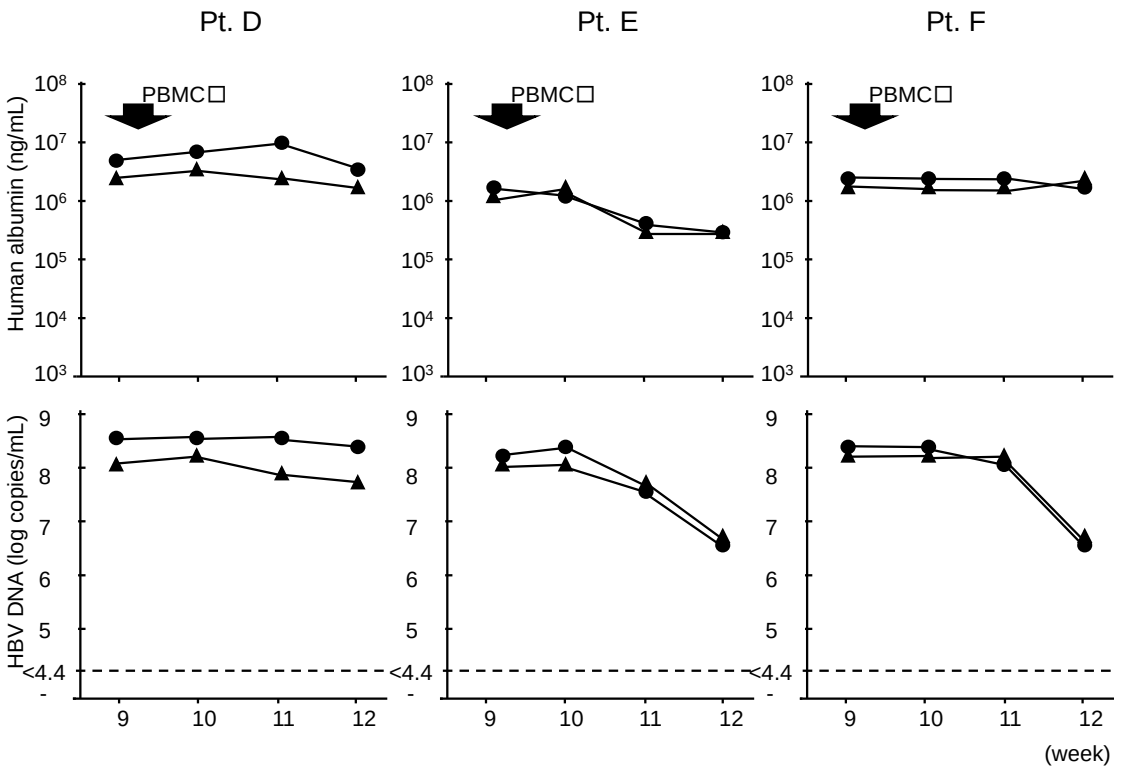
Supplementary Fig. 4A



Supplementary Fig. 4B



Supplementary Fig. 4C

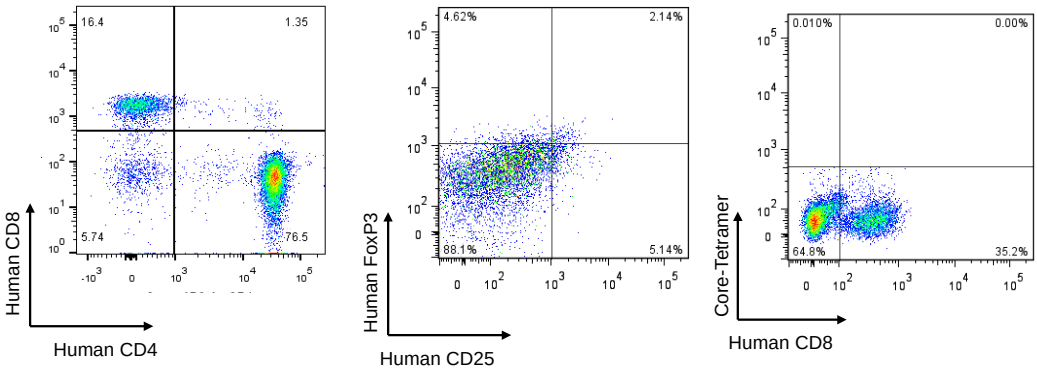


Supplementary Fig. 4. Time course of HBV-infected chimeric TK-NOG mice after human PBMC injection.

Human PBMCs obtained from two healthy volunteers (A) and six chronic HBV-infected patients (Pt) (B and C) were injected intraperitoneally into HBV-infected chimeric mice. The upper panel shows the time course of human albumin concentration, and the lower panel shows HBV DNA titer in mouse serum.

Supplementary Table 1. Characteristics of the chronic hepatitis patients whose PBMC were injected into mice .

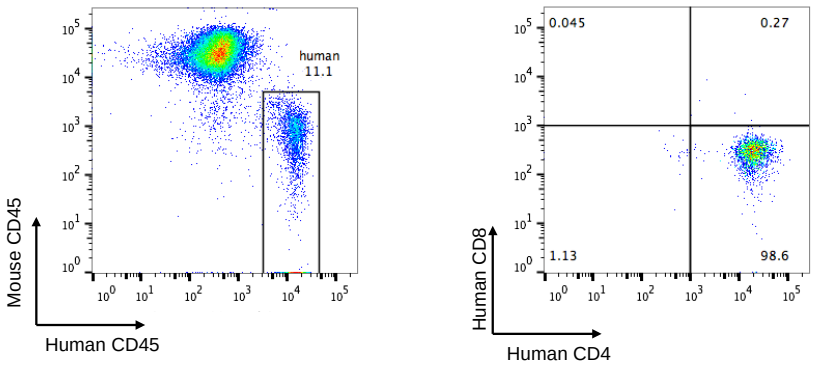
Patient	Pt. A	Pt. B	Pt. C	Pt. D	Pt. E	Pt. F
Age	30	42	33	36	42	42
HBV DNA (log copies/ml)	3.5	Not detected	>9.1	7.0	6.2	2.2
ALT (IU/l)	29	32	23	66	25	23
HBeAg (S/CO)	342	0.308	23	3.7	8.193	0.33
HBeAb (%)	0	99.5	0	43	44.9	98.5
Treatment	LAM+ADV	ETV	-	-	-	-
HLA-A haplotype	2/26	11/26	24/26	2/24	24	24/31



Supplementary Fig. 5. Flow cytometry analysis of human PBMCs obtained from a donor who recovered from severe acute hepatitis.

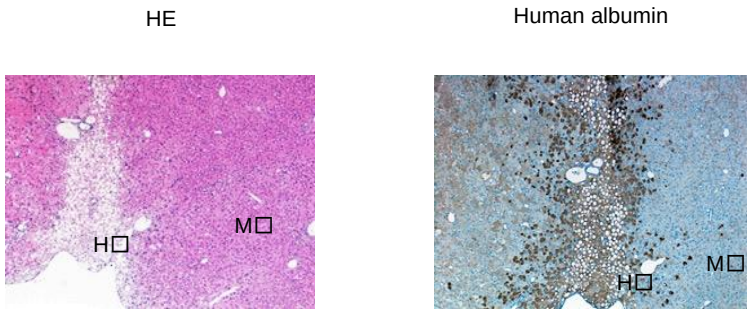
Human PBMCs were analyzed by flow cytometry. Cells were stained with antibody as described in the Methods.

Supplementary Fig. 6 ☐



Supplementary Fig. 6. Analysis of liver mononuclear cells from mice injected with CD8-depleted human mononuclear cells.

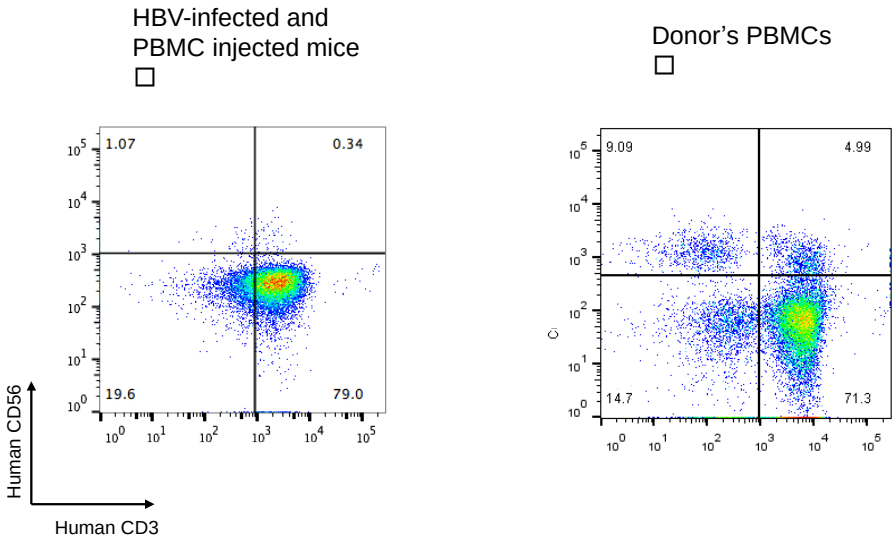
Cells from the CCD8-negative fraction were injected intraperitoneally into HBV-infected mice (n=3). Flow cytometry analysis of liver mononuclear cells in HBV-infected mice injected with CD8-depleted human mononuclear cells. CD8-positive cells were almost completely removed.



Supplementary Fig. 7. Histological analysis of livers of uninfected mice.

Liver samples obtained from uninfected mice were stained with hematoxylin-eosin staining (HE) and anti-human albumin antibody. Labeled regions indicate human (H) and mouse (M) hepatocytes, respectively (original magnification 40x).

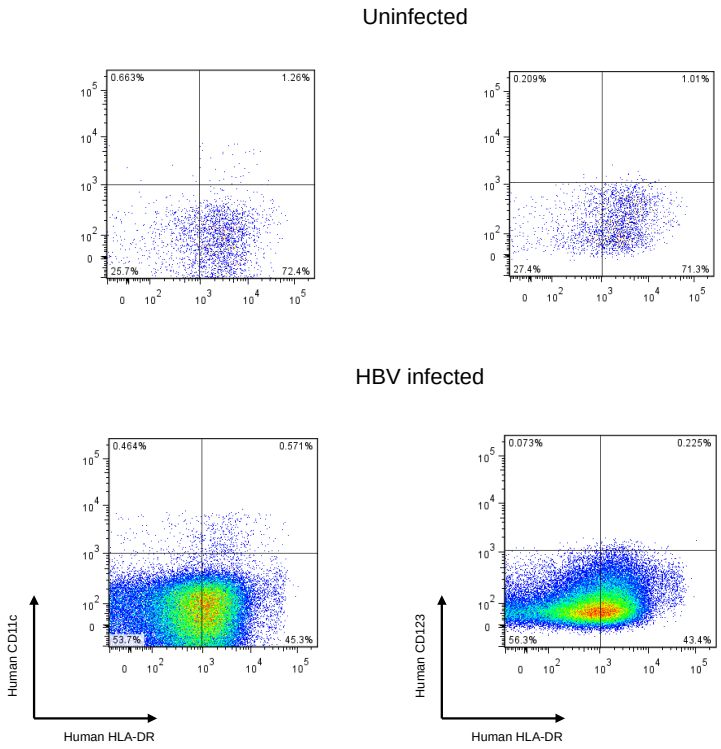
Supplementary Fig. 8□



Supplementary Fig. 8. Flow cytometry analysis of liver mononuclear cells in HBV-infected chimeric TK-NOG mice and donor PBMCs.

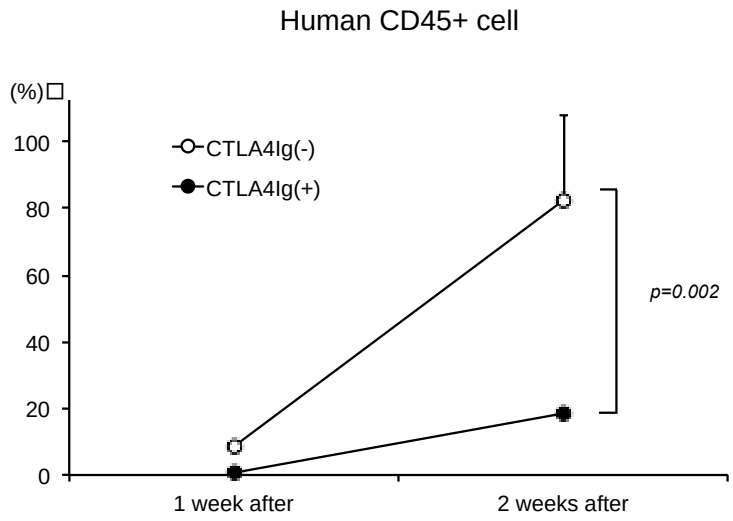
After defining human PBMCs as cells negative for mouse CD45 and positive for human CD45, we further analyzed the phenotypes of these cells. Liver mononuclear cells were separated with antibodies against CD3 and CD56. Human NK cells were defined as CD45+CD3-CD56+ cells.

Supplementary Fig. 9☐



Supplementary Fig. 9. Flow cytometry analysis of liver mononuclear cells in uninfected and HBV-infected chimeric TK-NOG mice.

After defining human PBMCs, we further analyzed the phenotypes of these cells. Mouse liver mononuclear cells were separated with antibodies against anti-human HLA-DR and CD123 (left panel) and HLA-DR and CD11c (right panel). Human plasmacytoid DCs were defined as CD45+Lin-1-HLA-DR+CD123+ cells, while human myeloid DCs were defined as CD45+ Lin-1-HLA-DR+CD11c+ cells.



Supplementary Fig. 10. Comparison of the populations of human CD45-positive cells between CTLA4Ig-treated and untreated mice.

Liver infiltrating cells in human PBMC-injected and HBV-infected mice with or without CTLA4Ig were analyzed by flow cytometer. Cells were stained with antibody as described in the Methods. There was no difference in human CD45-positive mononuclear cell chimerism between untreated and CTLA4Ig-treated mice one week after transplantation. However, CTLA4Ig treatment resulted in significantly less human CD45-positive mononuclear cell chimerism than untreated mice after two weeks.