Other models

• Model with human liver

H. Suemizu, M. Hasegawa, K. Kawai, K. Taniguchi, M. Monnai, M. Wakui, M. Suematsu, M. Ito, G. Peltz, and M. Nakamura. 2008. Establishment of a humanized model of liver using NOD/Shi-scid IL2Rg(null) mice. *Biochem Biophys Res Commun* 377:248-252.

Severely immunodeficient NOD/Shi-*scid* IL2Rg^{null} (NOG) mice are used as recipients for human tissue transplantation, which produces chimeric mice with various types of human tissue. NOG mice expressing transgenic urokinase-type plasminogen activator in the liver (uPA-NOG) were produced. Human hepatocytes injected into uPA-NOG mice re-populated the recipient livers with human cells. The uPA-NOG model has several advantages over previously produced chimeric mouse models of human liver: (1) the severely immunodeficient NOG background enables higher xenogeneic cell engraftment; (2) the absence of neonatal lethality enables mating of homozygotes, which increased the efficacy of homozygote production; and (3) donor xenogeneic human hepatocytes could be readily transplanted into young uPA-NOG mice, which provide easier surgical manipulation and improved recipient survival.

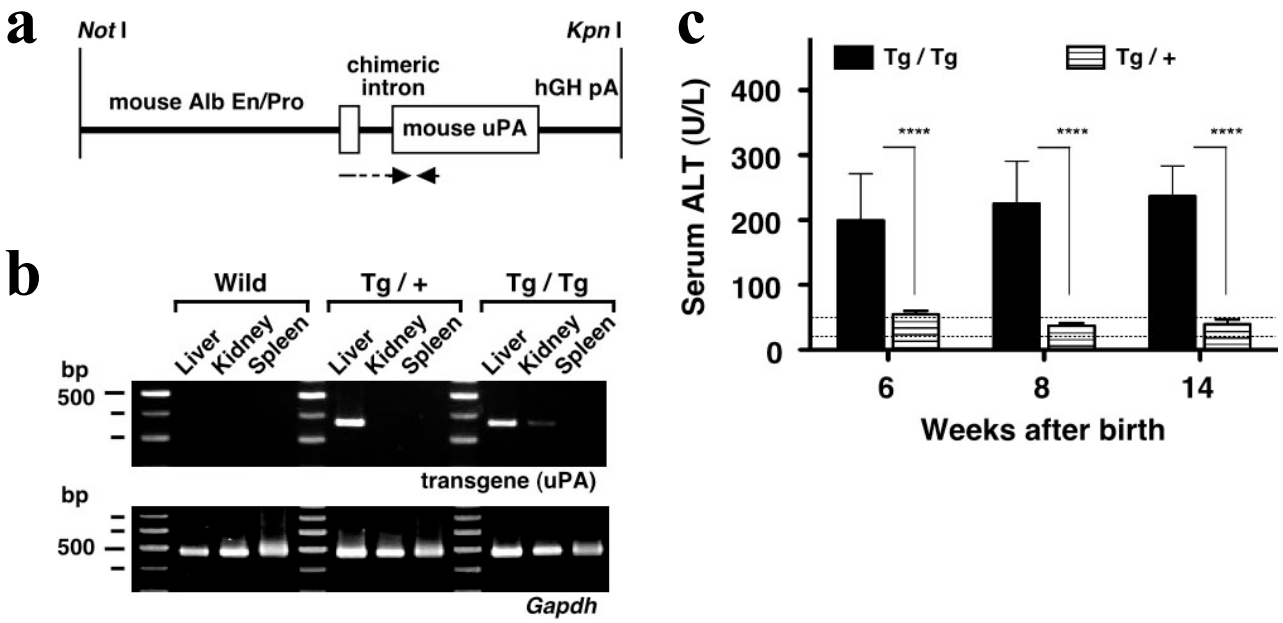

Figure 1. Establishment of the uPA-NOG mouse as a model of spontaneous hepatic injury.
(a) The uPA expression unit contains the mouse albumin enhancer/promoter (Alb En/Pro), the chimeric intron, mouse uPA cDNA, and the 3'-UTR of the human growth hormone gene with polyadenylation (pA) signal. Arrowheads depict the positions and directions of the RT-PCR primers. (b) RT-PCR analyses of uPA transgene expression. Wild, nontransgenic NOG; Tg/+, hemizygous; and Tg/Tg, homozygous uPA-NOG mice. *Gapdh* was used as an internal control. (c) ALT activities in uPA-NOG mice. All the values for the homozygous uPA-NOG (Tg/Tg) are significantly higher than those for the hemizygote (Tg/+) ($P < 0.0001$, unpaired t-test). Dashed lines indicate the two standard deviation ranges for the values for the nontransgenic NOG mice ($n = 7$). Each of the points for the hemizygous and homozygous uPA-NOG mice represent the mean ± SD of four to seven samples.

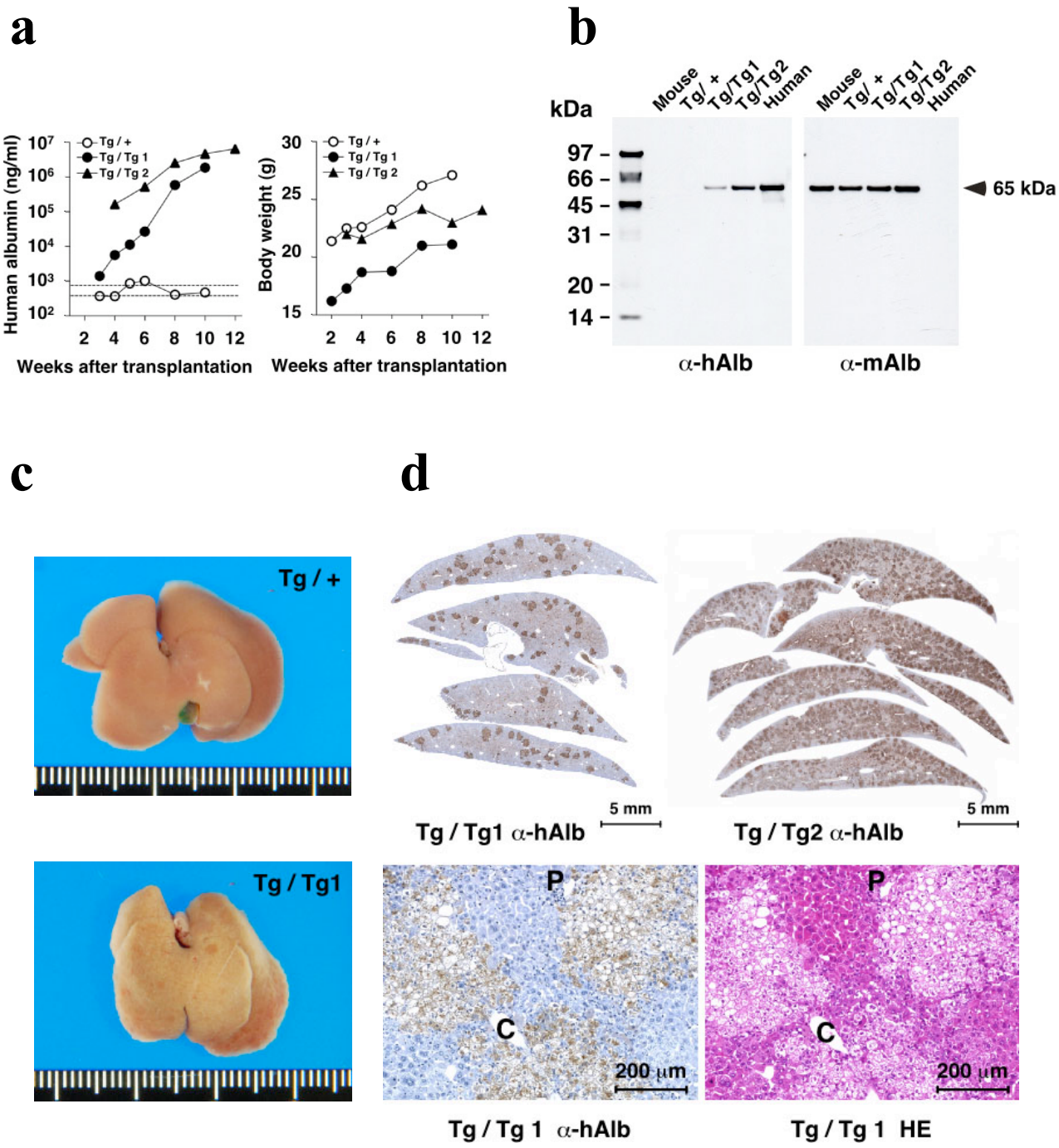

Figure 2. Engraftment and repopulation of human hepatocytes in uPA-NOG mice.
(a) Blood albumin concentrations in human cell recipients were assayed by ELISA. Dashed lines indicate the two standard deviation ranges for the values for the untransplanted uPA-NOG mice (n = 6). Body-weight changes after human hepatocyte transplantation are shown. (b) Immunoblot analysis shows human albumin (α-hAlb) and mouse albumin (α-mAlb) production in hemizygous (Tg/+) or homozygous (Tg/Tg) uPA-NOG transplant recipient mice. (c) Gross appearance of the uPA-NOG mouse liver 10 weeks after human hepatocyte transplantation. Tg/+, hemizygous; Tg/Tg, uPA-NOG homozygote. (d) Histology and immunohistochemistry of livers from uPA-NOG mice that were repopulated with human hepatocytes. Immunohistochemical staining for human albumin (top and lower left) and H&E staining (lower right). P, portal tract; C, central vein.