

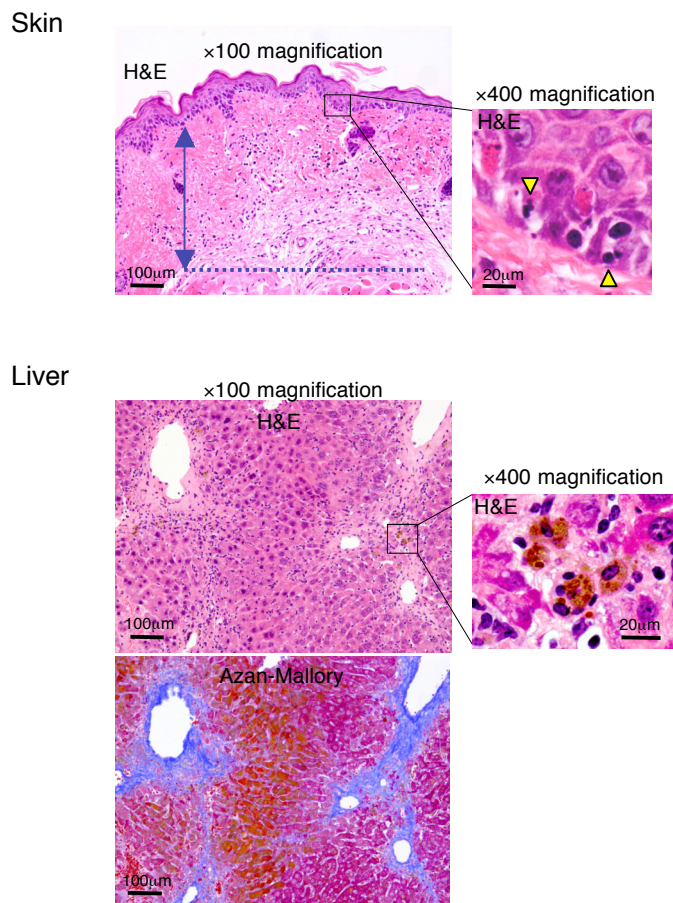
**Figure S1. Survival and engraftment of human CD45<sup>+</sup> cells of recipient mice.**

NOG mice were irradiated at sublethal dose (200cGy) and the next day were transplanted with  $1 \times 10^5$  CD34<sup>+</sup> cells purified from human umbilical cord blood cells (HuCB) (CD34<sup>+</sup> transplant) or with  $1 \times 10^7$  mononuclear cells (MNCs) isolated from HuCB (whole CB transplant).

**(A)** Survival curve (each group n=10). The *p* value was calculated by log-rank test.

**(B)** Engraftment of human leukocytes in recipient mice. Peripheral blood of recipient mice was harvested at the indicated time points, and population of human CD45<sup>+</sup> cells was analyzed using flow cytometry. Data are shown as mean $\pm$ SEM of human CD45<sup>+</sup> cells among total PBL (each, n=10 in CD34<sup>+</sup> transplant group, and n=10 at 0-6 weeks, n=8 at 8 weeks, n=7 at 10 weeks and n=3 at 12 weeks in whole CB transplant group).

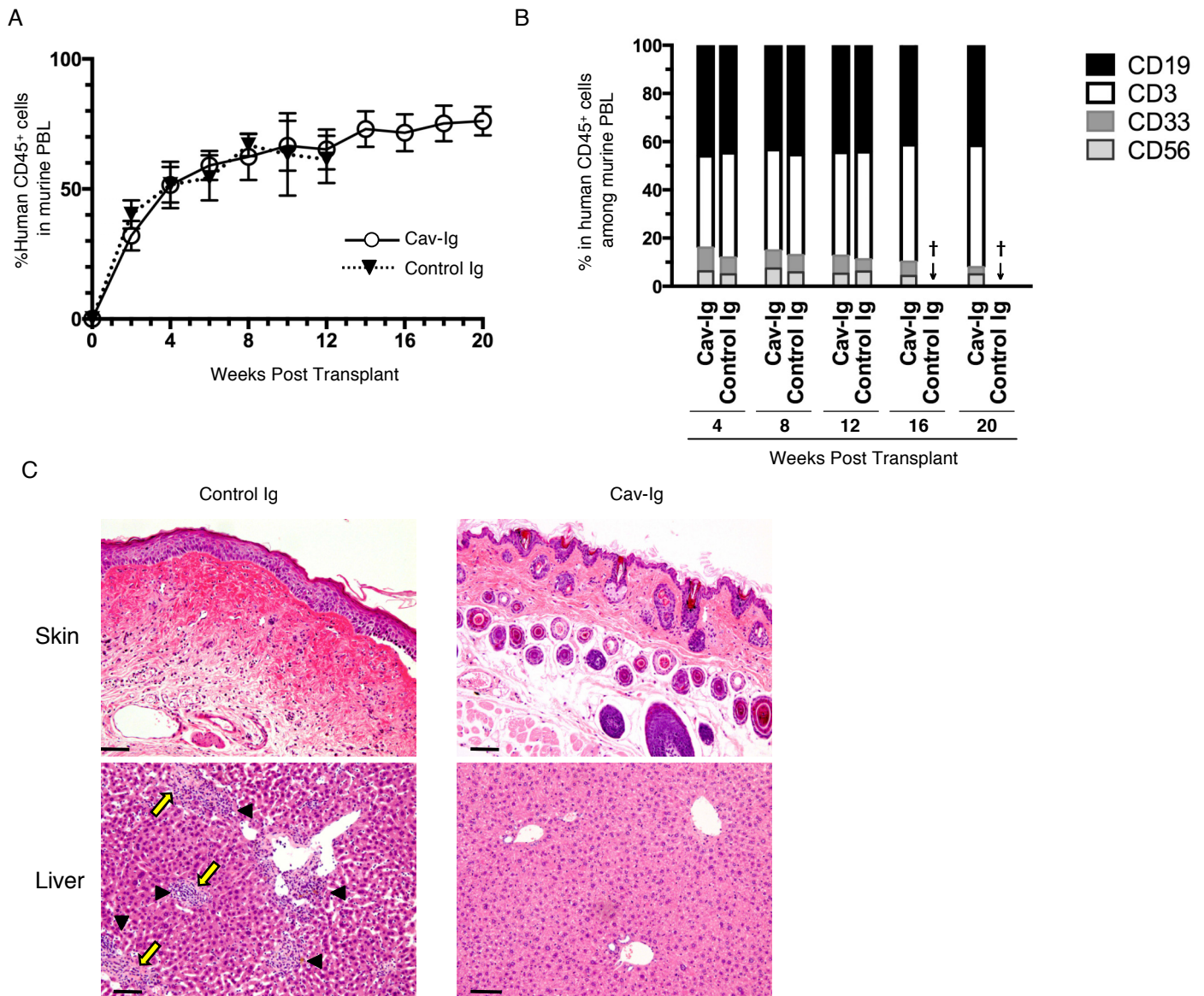
**(C)** Sustained composition of human leukocyte populations in recipient PBL. PBL harvested from each group were stained for human CD3, CD19, CD33 or CD56 among human CD45<sup>+</sup> cells. Data are presented as mean percentages of human CD45<sup>+</sup> cells (each, n=10 in CD34<sup>+</sup> transplant group, and n=10 at 0-4 weeks, n=8 at 8 weeks and n=3 at 12 weeks in whole CB transplant group). Cross indicates death of all mice in whole CB transplant group.



**Figure S2. Sclerodermatous change and portal fibrosis in whole CB transplant mice.**

*Skin*, H&E staining of the skin tissue of whole CB transplant mice (8 weeks post transplantation). The skin specimen shows homogenization (sclerosis) of most of the reticular dermis (blue two-way arrow) with fat loss and follicular drop-out (dotted line indicates the boarder between the hypodermis and muscle layer). In the stratum basale, vacuolar degeneration is presented with apoptotic bodies (yellow arrow heads). Representative histology is shown from 3 independent experiments (each, n=10).

*Liver*, H&E and Azan-Mallory staining of the liver tissue of whole CB transplant mice (8 weeks post transplantation). A low-power magnification shows portal fibrosis and a high-power magnification, cholestasis. Representative histology is shown from 3 independent experiments (each, n=10).



**Figure S3. Survival and engraftment of human CD45<sup>+</sup> cells in whole CB transplant mice after administration of Cav-Ig or control Ig.**

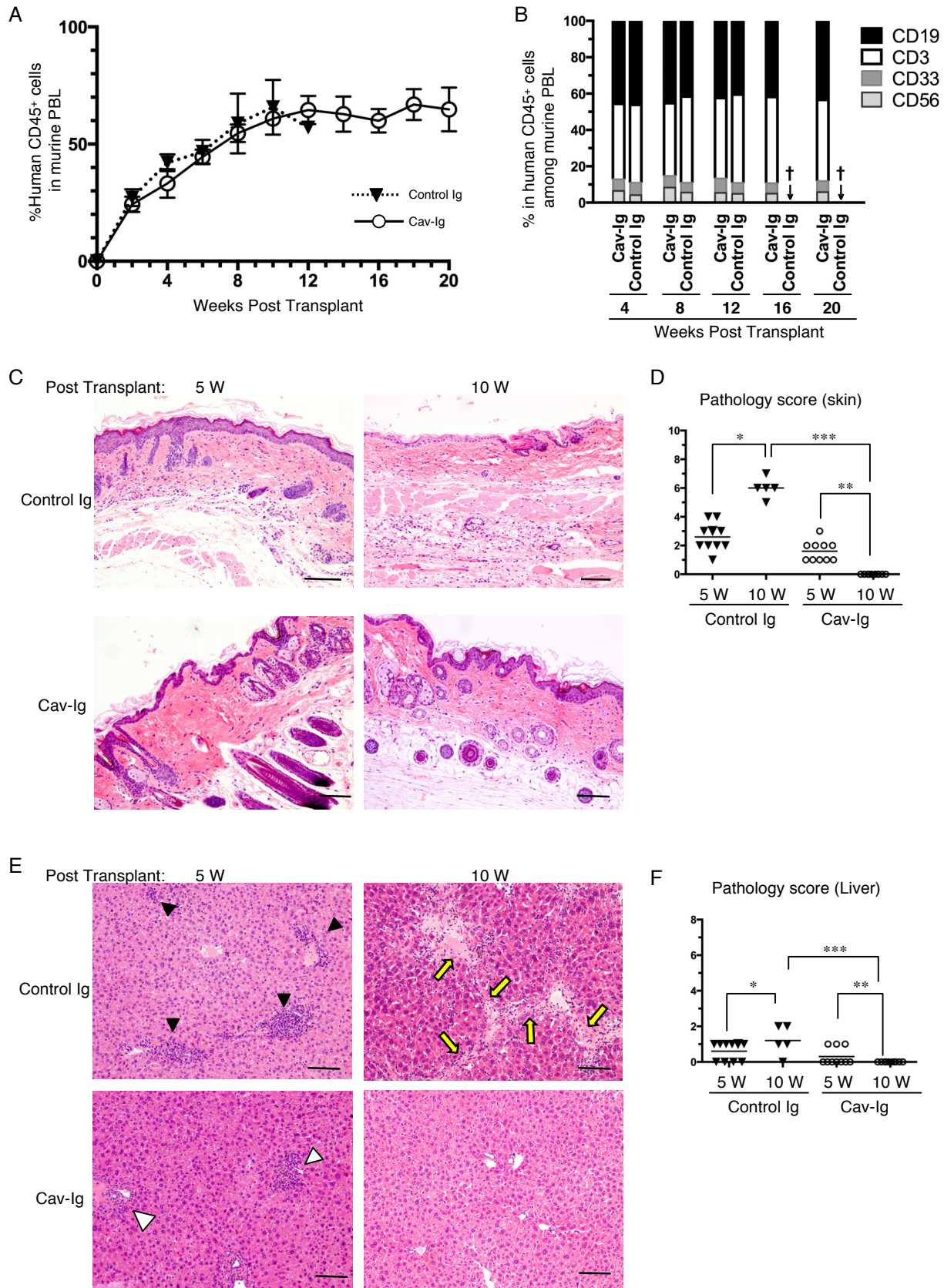
Sublethally irradiated NOG mice were transplanted with  $1 \times 10^7$  MNCs isolated from HuCB. Cav-Ig or control Ig (each 100 $\mu$ g/dose) was administered intraperitoneally thrice a week, beginning at day +1 after transplantation until day +28.

**(A)** Engraftment of human leukocytes in recipient mice. Peripheral blood of recipient mice was harvested at the indicated time points, and population of human CD45<sup>+</sup> cells was analyzed using flow cytometry. Data are shown as mean $\pm$ SEM of human CD45<sup>+</sup> cells among total (each, n=10 in Cav-Ig group, and n=10 at 0-6 weeks, n=9 at 8 weeks, n=7 at 10 weeks and n=2 at 12 weeks in control Ig group).

**(B)** Sustained composition of human leukocyte populations in recipient PBL. PBLs harvested from each group were stained for human CD3, CD19, CD33 or CD56 among human CD45<sup>+</sup> cells. Data are presented as mean percentages of human CD45<sup>+</sup> cells. Cross indicates death of all mice in control Ig group (each, n=10 in Cav-Ig group, and n=10 at 0-4 weeks, n=9 at 8 weeks and n=2 at 12 weeks in control Ig group).

**(C)** H&E staining of the skin and liver tissues for control Ig group or Cav-Ig group evaluated at 6 weeks post transplantation. The skin specimen of control Ig group showed sclerotic changes including acanthosis, loss of rete ridge, fat loss, follicular drop-out and homogenized collagen deposition, in contrast to the normal appearance of the skin of Cav-Ig group. The liver specimen of control Ig group showed portal inflammation (arrow heads) and portal collagen deposition (yellow arrows), which were not observed in Cav-Ig group. Representative histology is shown from 3 independent experiments (each, n=10). Original magnification  $\times 100$ . Scale bars indicate 100 $\mu$ m.





**Figure S4. Administration of Cav-Ig during early GVHD development impedes lethal GVHD without adverse effect on engraftment of human CD45<sup>+</sup> cells in peripheral blood of recipient mice.** Sublethally irradiated NOG mice were transplanted with  $1 \times 10^7$  MNCs purified from HuCB. Cav-Ig or control Ig (each 100 $\mu$ g/dose) was administered intraperitoneally thrice a week, beginning at day +29 after transplantation until day +56.

**(A)** Peripheral blood of recipients was harvested at the indicated time points, and populations of human CD45<sup>+</sup> cells were analyzed using flow cytometry. Data are shown as mean±SEM of human CD45<sup>+</sup> cell among total PBL (each, n=10 in Cav-Ig group, and n=10 at 0-6 weeks, n=9 at 8 weeks and n=2 at 10-12 weeks in control Ig group).

**(B)** Sustained composition of human leukocyte populations in recipient PBL. PBLs harvested from each group were stained for human CD3, CD19, CD33 or CD56 among human CD45<sup>+</sup> cells. Data are presented as mean percentages of human CD45<sup>+</sup> cells. Cross indicates death of all mice in control Ig group.

**(C)** H&E staining of the skin tissues of control Ig group or Cav-Ig group at 5 weeks or 10 weeks post transplantation. Normal skin histology was observed in recipient mice with Cav-Ig administration, in contrast to sclerodermatous changes developed in recipient mice with control Ig administration. Representative histology is shown from 3 independent experiments. Original magnification ×100. Scale bars indicate 100µm.

**(D)** Pathologic damage in the skin of recipients administered with Cav-Ig or control Ig was examined at 5 and 10 weeks post transplantation using a semiquantitative scoring system. Recipients of control Ig developed progression of GVHD pathology (\*,  $p<0.0001$ ). In contrast, recipients of Cav-Ig showed significant reduction in GVHD pathology at 10 weeks rather than at 5 weeks post transplantation (\*\*,  $p<0.0001$ ), and also as compared to recipients of control Ig group at 10 weeks (\*\*\*,  $p<0.0001$ ). Each dot indicates individual value and horizontal bars indicate mean value. Data are cumulative results from 3 independent experiments.

**(E)** H&E staining of the liver tissues of control Ig group or Cav-Ig group at 5 weeks or 10 weeks post transplantation. In recipient mice with Cav-Ig administration, portal inflammation was observed at 5 weeks post transplantation (white arrow heads), with restoration to normal appearance at 10 weeks post transplantation. In contrast, portal inflammation was observed in recipient mice with control Ig administration at 5 post transplantation (black arrow heads) and portal fibrosis, at 10 weeks post transplantation (yellow arrows). Representative histology is shown from 3 independent experiments. Original magnification ×100. Scale bars indicate 100µm.

**(F)** Pathologic damage in the liver of recipients administered with Cav-Ig or control Ig was examined at 5 and 10 weeks post transplantation using a semiquantitative scoring system. Recipients of control Ig developed progression of GVHD pathology (\*,  $p<0.05$ ). In contrast, recipients of Cav-Ig showed significant reduction in GVHD pathology at 10 weeks rather than at 5 weeks post transplantation (\*\*,  $p<0.0001$ ), and also as compared to recipients of control Ig group at 10 weeks (\*\*\*,  $p<0.0001$ ). Each dot indicates individual value and horizontal bars indicate mean value. Data are cumulative results from 3 independent experiments.