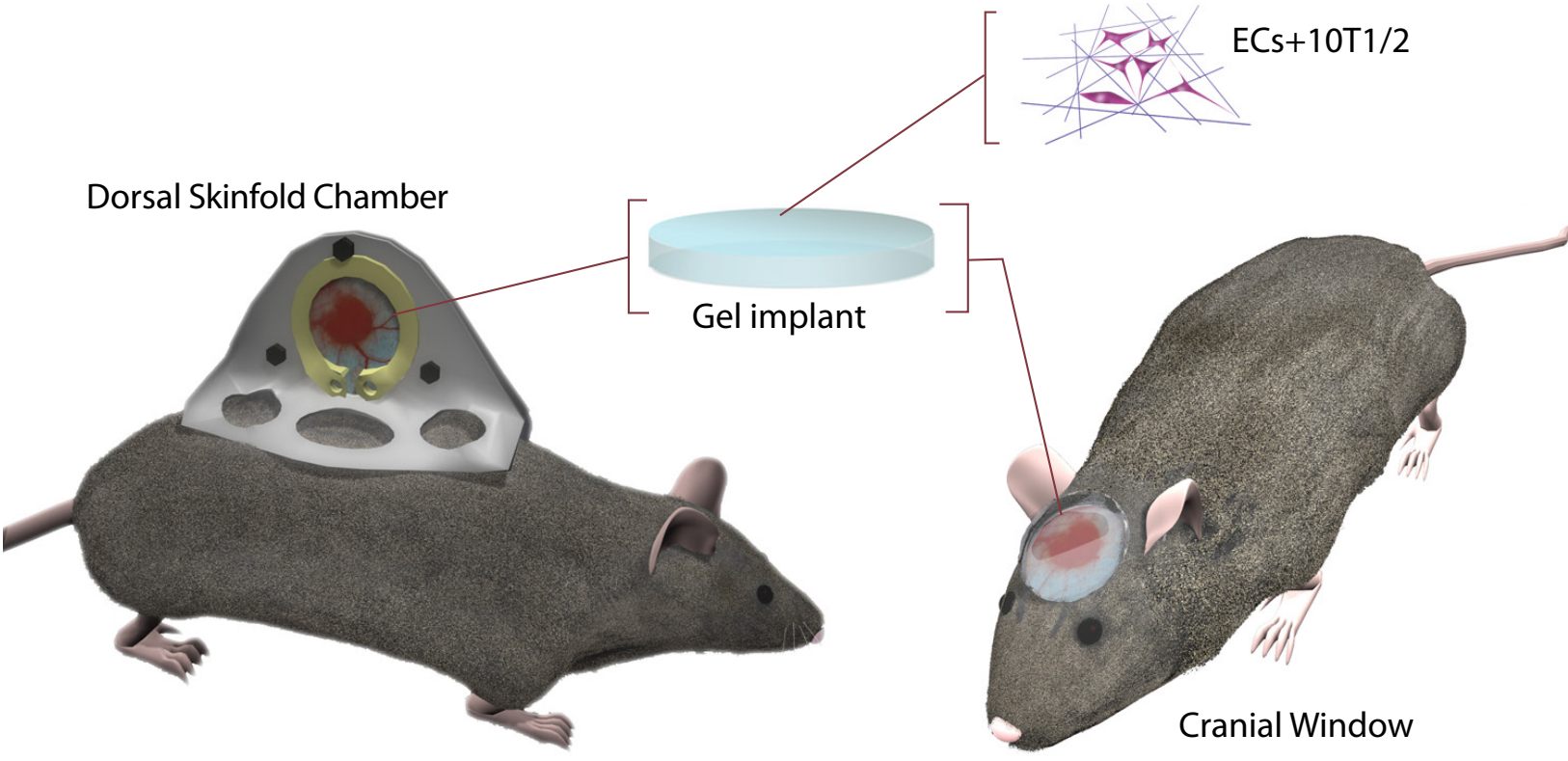


**Figure S1. Illustration of the engineered vessel model, in which ECs and 10T1/2 cells are embedded in collagenous gels and implanted into cranial window or dorsal skinfold chamber preparations**

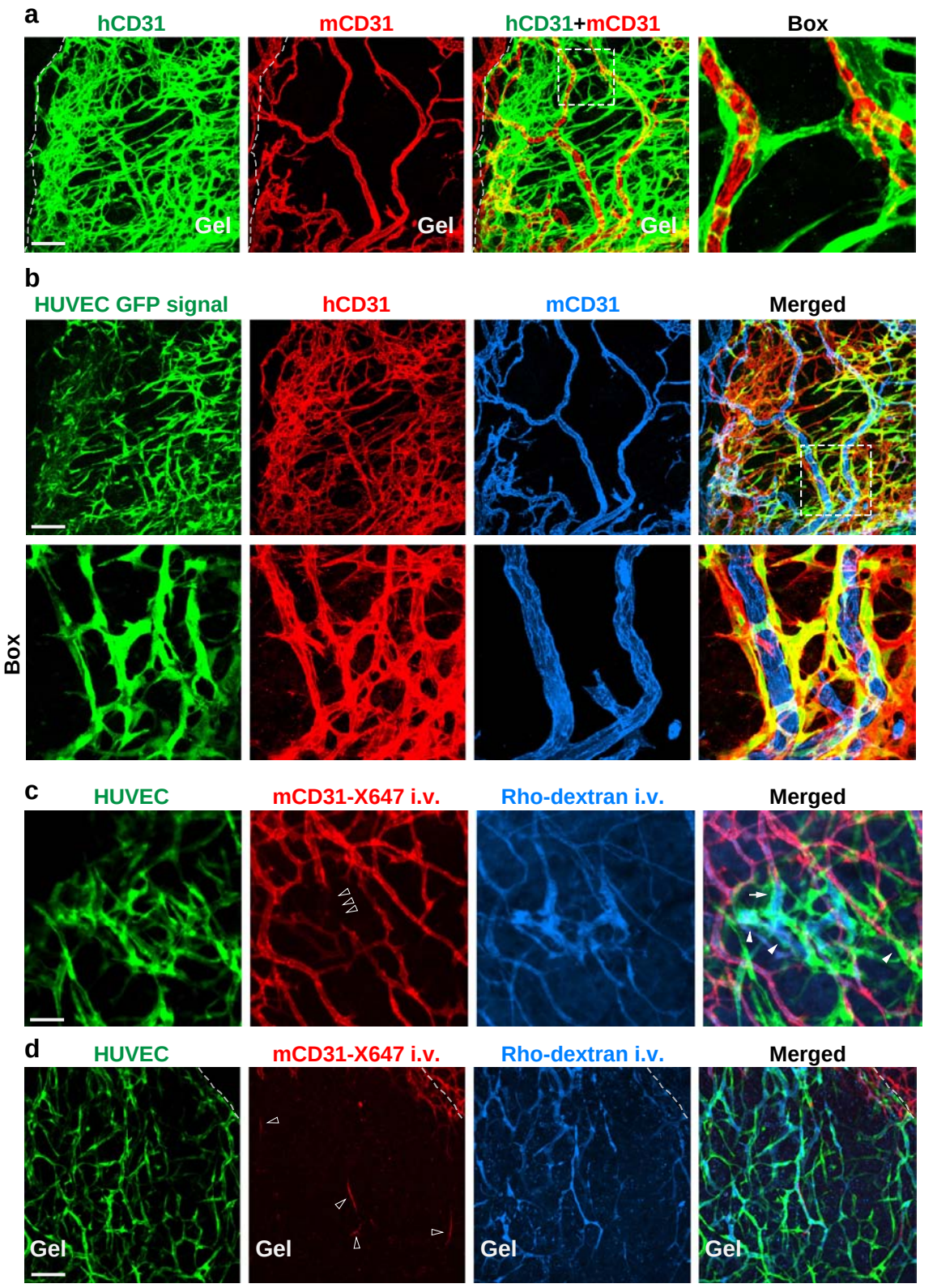


Figure S2. (**a**) Fourteen days after implantation in a cranial window, there is extensive association between the intricate network formed by the HUVECs (green, human specific CD31, hCD31) and the host vessels (red, mouse-specific CD31, mCD31), with the HUVECs ensheathing the host vessels in many regions. "Box" shows the detail of the area within the white box in the "hCD31+mCD31" panel. The white dashed curves indicate the edge of the engrafted gel. Note that wrapping only occurs near the host-implant interface (see Supplementary Movies 3 & 4 for 3D renderings). Whole-mount IHC stain; scale bar = 100 µm. (**b**) Implanted HUVEC population has high purity and its GFP expression can be used to monitor cell behaviour with intravital confocal imaging. The purity of GFP-transduced HUVEC population (green) is confirmed by IHC staining with human CD31 antibody (hCD31, red). Host vessels are stained with mouse CD31 (mCD31, blue). "Box" shows the detail of the area within the white box in the "Merged" panel. Wrapping of host vessels by yellow (i.e., positive for both GFP and hCD31) HUVECs is extensive. Whole-mount IHC stain; scale bar = 120 µm. (**c**) Detail of the area within the white box in "Day 14" images of Figure 1b. Wrapping of host vessels (red, mCD31-X647 i.v.) by implanted HUVECs (green, GFP transduction) is evident (arrowheads). Vessel perfusion is shown by Rhod-dextran (light blue) injected i.v. A segment of host vessel appears to have been degraded and replaced by a segment of HUVEC vessel (empty arrowheads). Blood flow is now diverted to a HUVEC vessel (arrow points to the junction). See Supplementary Movie 5 for a view of this confocal stack. Intravital confocal images; scale bar = 50 µm. (**d**) Regressing host vessel segments (red, mCD31-X647 injected i.v.; empty arrowheads) inside HUVEC networks (green, GFP transduction) in the gel shown in Figure 1b, Day 28. Perfused vessels are visualized by i.v. injection of Rho-dextran (light blue). The white dashed curves indicate the edge of the engrafted gel. Intravital confocal images; scale bar = 100 µm.

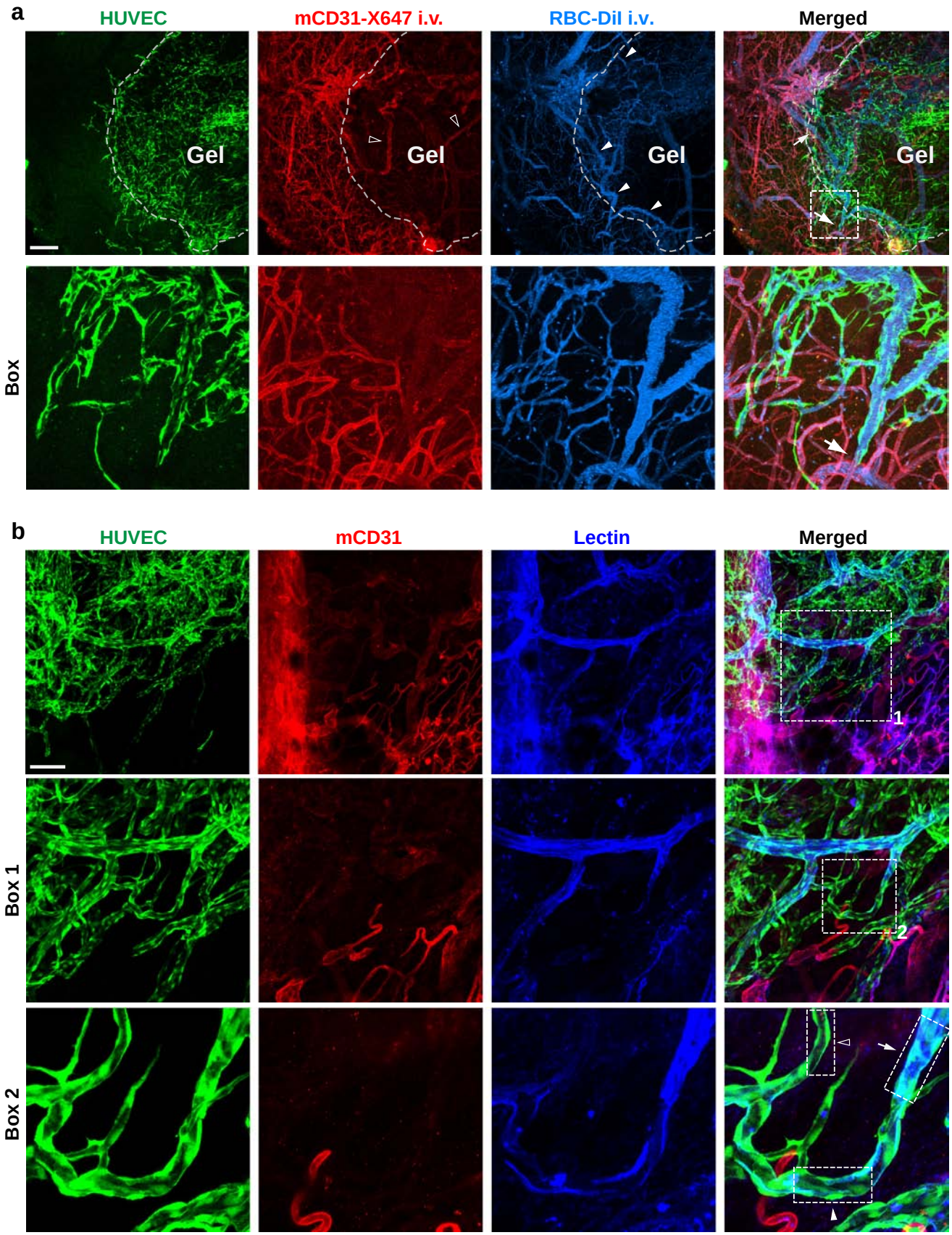


Figure S3. (**a**) Perfusion of HUVEC networks in the mouse cranial window 40 days after implantation. Many HUVEC vessels (green, GFP transduction) at the host-implant interface have connected to the host vasculature (red, mCD31-X647 injected i.v.) and are now perfused (filled arrowheads, blue panel which shows DiI-labeled RBCs, denoted RBC-DiI, injected i.v.). This has allowed HUVECs in the bulk of the gel to "tap" into the existing blood flow. White dashed curves indicate the edge of the engrafted gel. "Box" shows the detail of the area within the white box in the "Merged" panel. Arrows indicate host-implant junctions. Some pre-existing host vessels underneath the gel are also visible (empty arrowheads). Intravital confocal images; scale bar = 500 µm. (**b**) HUVEC vessels (green, GFP transduction) at various stages of perfusion 48 days after implantation in a cranial window. Host vessels are red (mCD31 staining) and vessel perfusion is shown by biotin staining (blue) of lectin injected i.v. before tissue fixation. Arrows, filled arrowheads and empty arrowheads point to fully, partially and not-yet-perfused HUVEC vessels, respectively. Whole-mount IHC stain; scar bar = 200 µm.

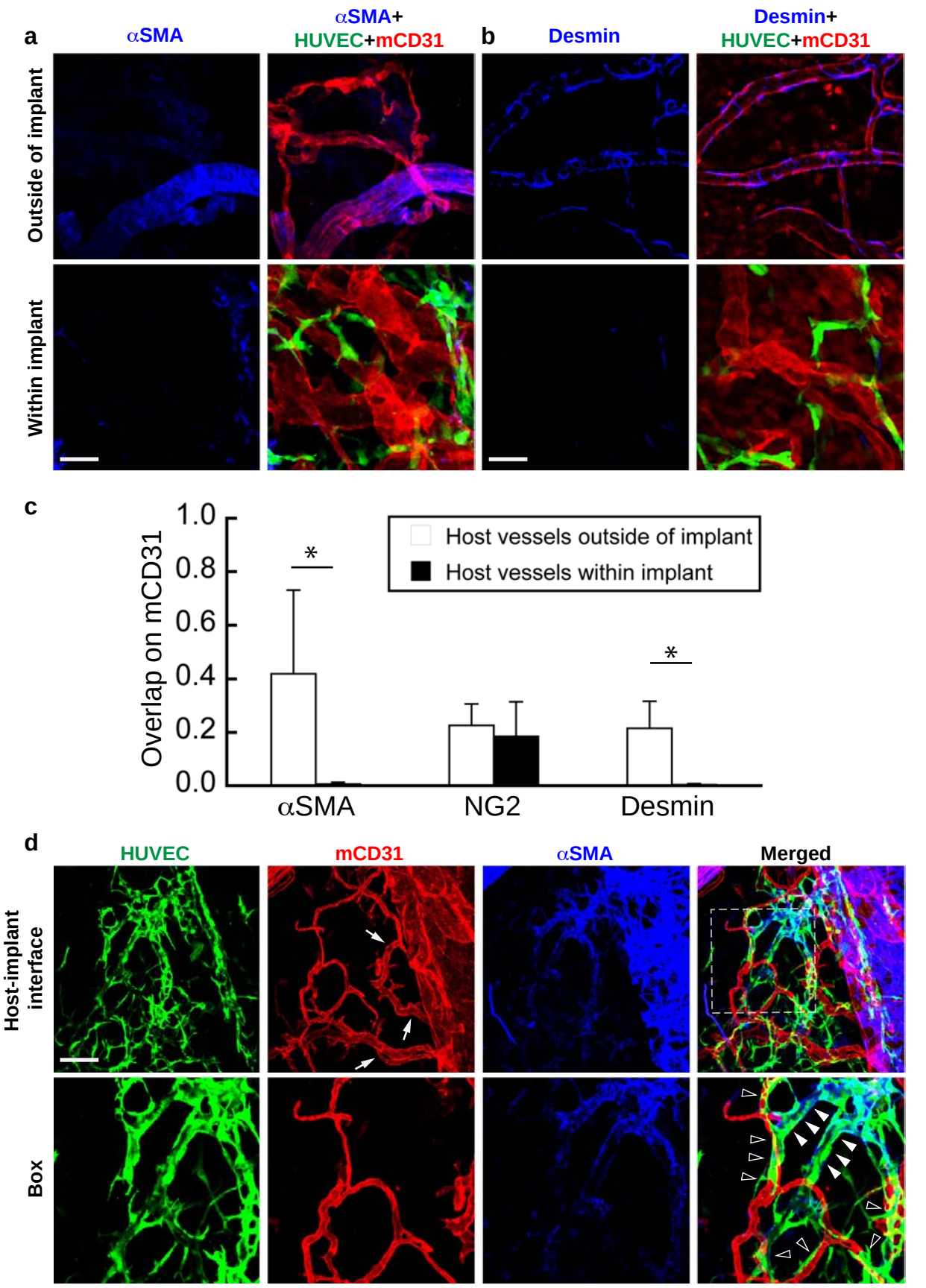


Figure S4. **αSMA- and desmin-positive pericytes in regions of WAT anastomosis.** IHC staining was performed on gels that had been implanted in cranial windows for two weeks. (**a**) αSMA staining (blue) appears normal on host arteries and arterioles (all host vessels are red, mCD31 staining) located in the host tissue ("Outside of implant"), but is lacking on practically all host vessels that have grown into the implant through angiogenesis ("Within implant"). Whole-mount IHC stain; scale bar = 40 μm. (**b**) Desmin staining (blue) is more sparse compared to αSMA staining, but is present on most host vessels –not just arteries and arterioles– outside of the implant. Similar to αSMA, however, demin is also almost completely missing on host vessels within the implant. Whole-mount IHC stain; scale bar = 40 μm. In contrast, NG2-positive pericytes are prevalent around host vessels both outside and within the implant (see Figure 2). Colocalization between the three pericyte markers and mCD31 is quantified in (**c**), and shows no difference in NG2 levels inside vs. outside the gel. (**d**) The heterogeneous αSMA distribution is especially striking at the host-implant interface where even some rather large host vessels lack αSMA-positive pericytes (arrows). In addition, some wrapping HUVECs seem to be associated with αSMA-positive pericytes. Closer examination ("Box") reveals that the more mature HUVEC segments (i.e., forming a larger lumen and a smoother surface; filled arrowheads) appear to have stronger αSMA staining than those that are more primative (empty arrowheads). Similar results were observed for desmin staining (data not shown). Whole-mount IHC stain; scale bar = 60 μm.

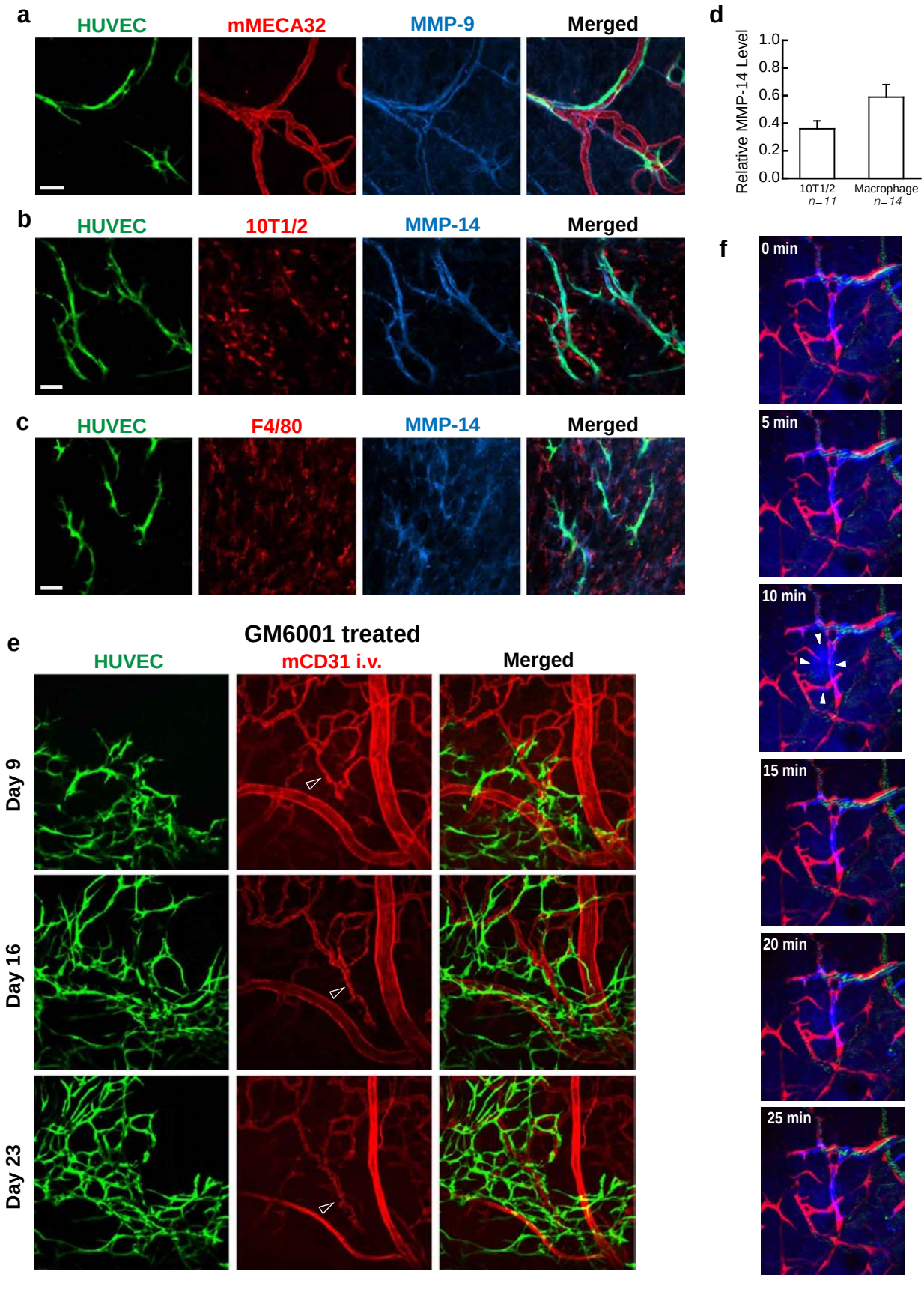


Figure S5. (**a**) MMP-9 (blue) expression on wrapping HUVECs (green, GFP transduction) and host vessels (red, mMECA32 staining). Whole-mount IHC stain; scale bar = 50 µm. (**b**) MMP-14 (blue) expression by non-wrapping HUVECs (green, GFP transduction) and 10T1/2 cells (red, dsRed transduction). Whole-mount IHC stain; scale bar = 60 µm. (**c**) MMP-14 (blue) expression by non-wrapping HUVECs (green, GFP transduction) and F4/80-positive host macrophages (red). Whole-mount IHC stain; scale bar = 60 µm. (**d**) Quantification of the relative levels of MMP-14 expression by 10T1/2 cells and host macrophages normalized to the level on non-wrapping HUVECs. (**e**) GM6001 treatment (100 mg/kg, daily intraperitoneal injection, 2 weeks) inhibits HUVEC (green, GFP transduction) WAT anastomosis with host vessels (red, mCD31-X647 injected i.v.). Empty arrowheads point to a host vessel that was wrapped by HUVECs at the start of the treatment and had not been degraded by the end of the treatment. Intravital confocal images; scale bar = 50 µm. (**f**) Time series of images showing the transient leakiness (filled arrowheads) on host vessels wrapped around by HUVECs (red, dsRed transduction). Vessel perfusion and blood flow are respectively shown by CB-dextran (blue) and fluorescently-labeled red blood cells (green) injected i.v. Intravital confocal images; scale bar = 60 µm.

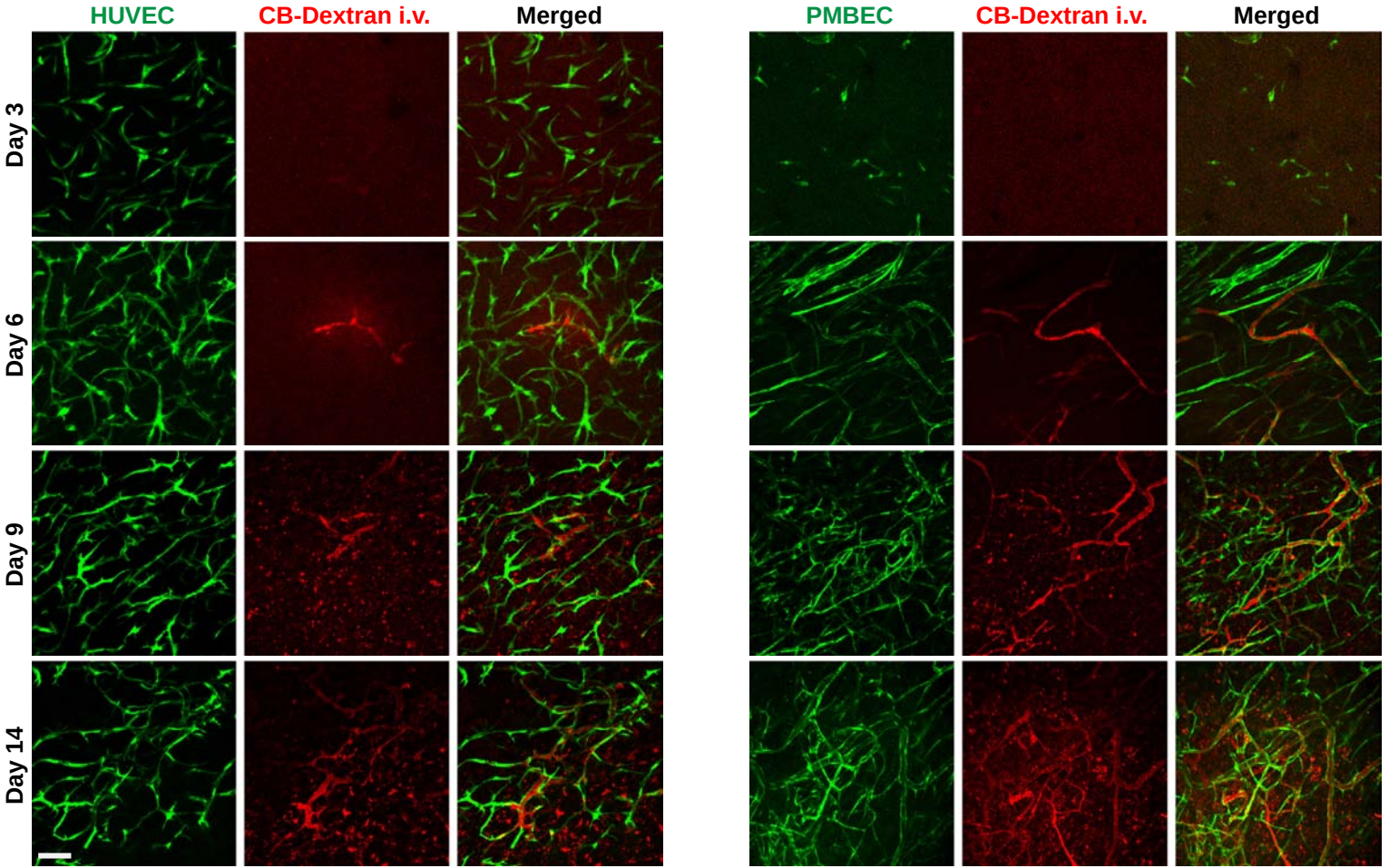


**Figure S6. Perfusion of vascular networks made by HUVECs (green, GFP transduction) implanted into SCID mice and by Tie2-GFP/Rag1$^{-/-}$ PMBECs (green, Tie2-promoted GFP expression) implanted into Rag1$^{-/-}$ mice**. Vessel perfusion was visualized by i.v. injection of CB-dextran (red). Intravital confocal images; scale bar = 100 µm. Quantitative results are shown in Fig. 5a.