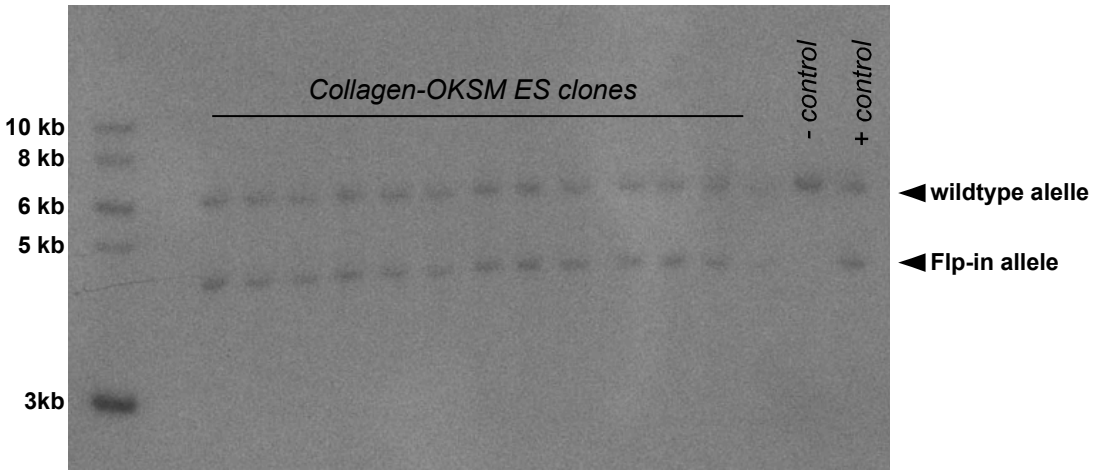
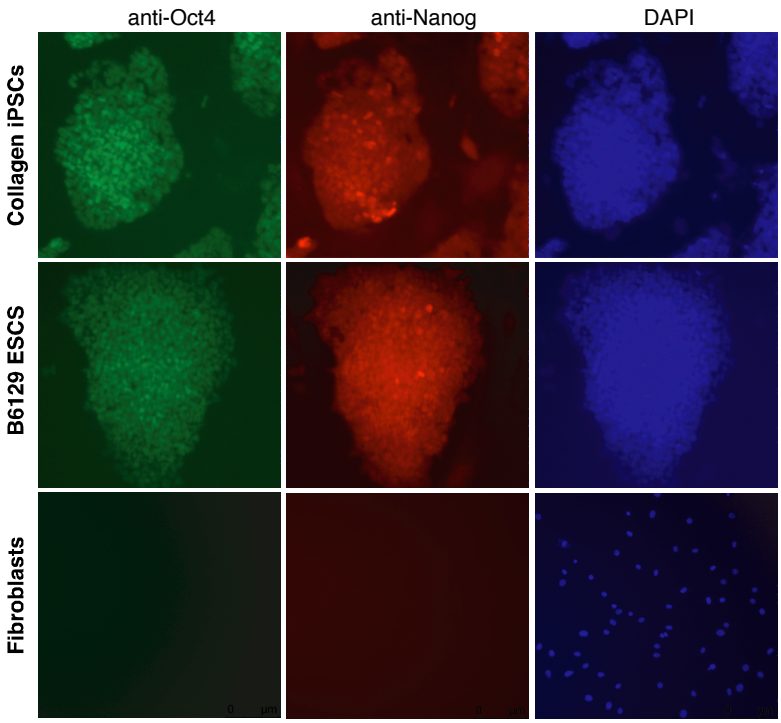
SUPPLEMENTARY INFORMATION:

Supplementary Figures:

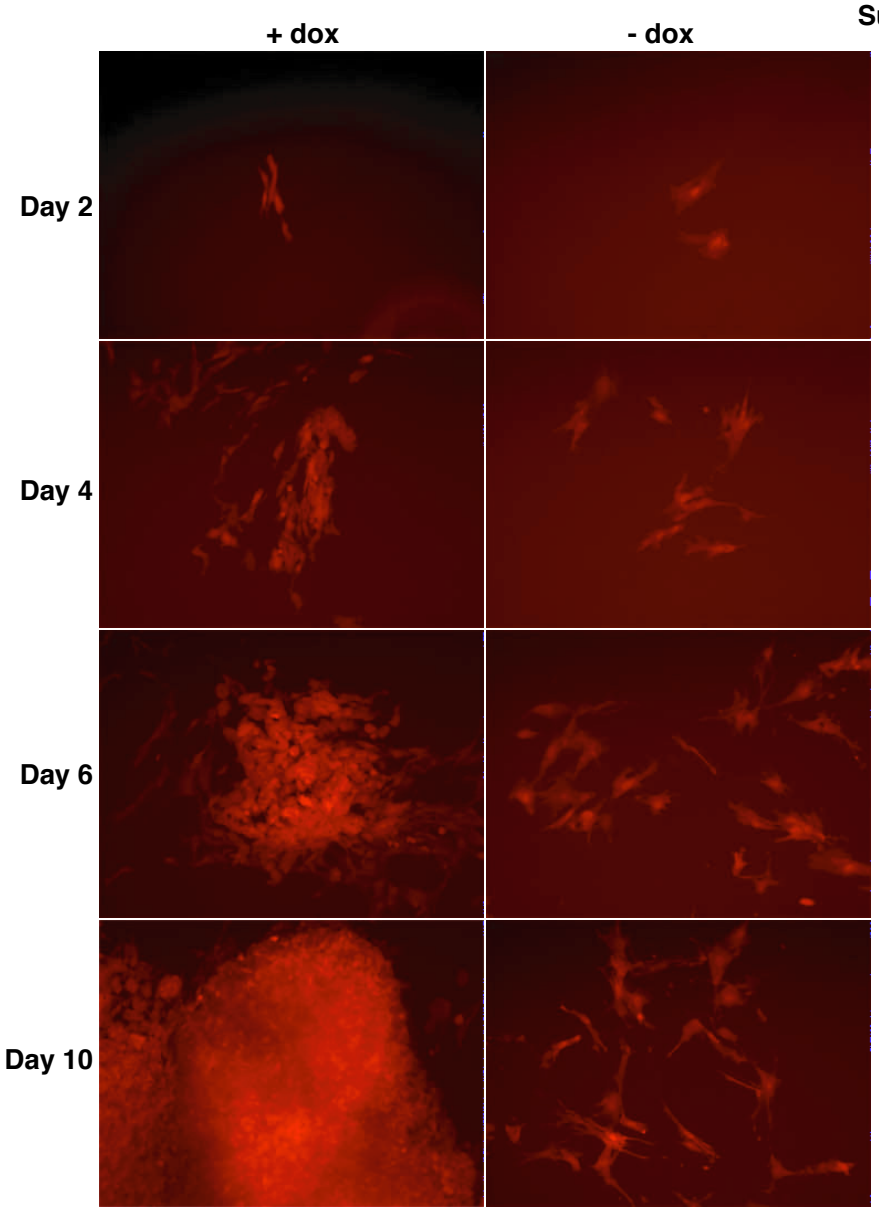
Supplemental Figure 1



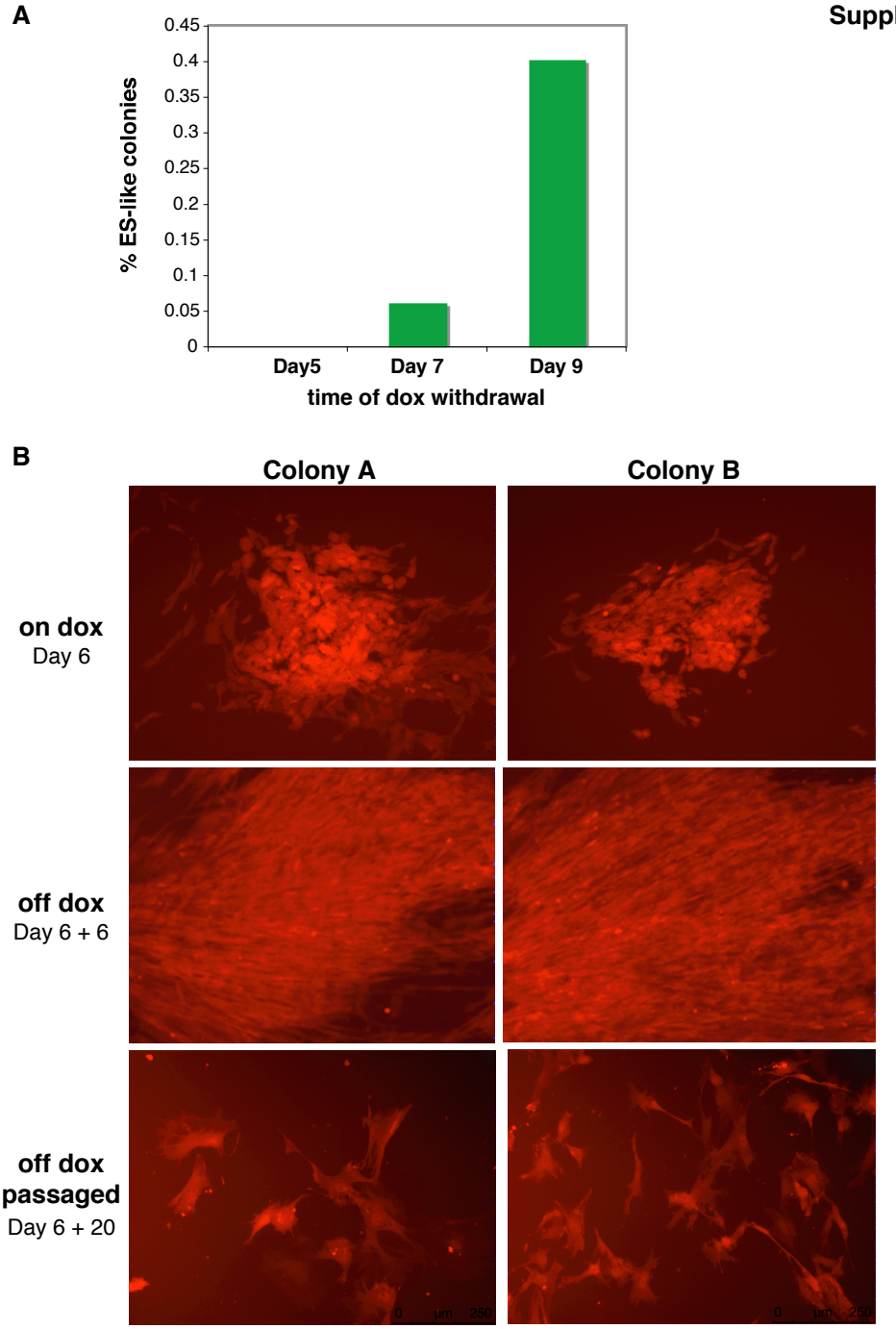
Supplementary Figure 1. Confirmation of correct targeting of Col1a1. Southern blot using genomic DNA extracted from 12 individual Collagen-OKSM ESC clone as well as a negative (iPSC clone with Col1a1 locus in wildtype configuration) and positive (iPSC clone with Oct4 cDNA in Col1a1) control DNA.



Supplementary Figure 2. Expression of pluripotency markers in Collagen-OKSM iPSCs. Immunofluorescence images after staining iPSCs cultured for several weeks in the absence of doxycycline (upper panel), ESCs (middle panel) and Collagen-OKSM fibroblasts cultured in the absence of doxycycline (lower panel) with antibodies against Oct4 and nanog. Nuclei were counterstained with DAPI.

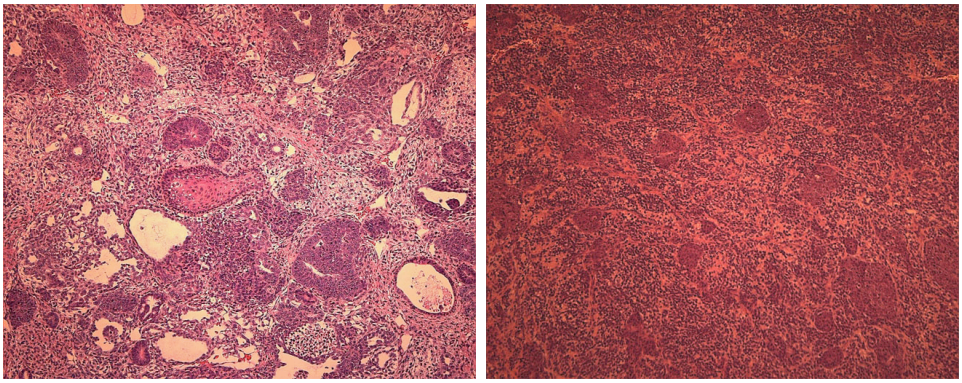


Supplementary Figure 3. Morphological changes of reprogramming fibroblasts. RFP^{+} MEFs isolated from midgestation chimeras derived after blastocyst injections with Collagen-OKSM ESCs transduced with a lentivirus expressing tdTomato were cultured either in the presence (+ dox, left panel) or absence (no dox, right panel) of doxycycline. Images were taken after the indicated days of culture.

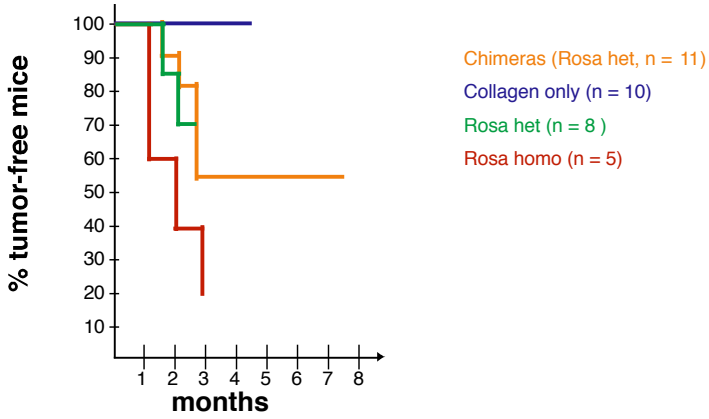


Supplementary Figure 4. Effect of premature dox withdrawal. (A) Reprogramming efficiencies of Collagen-OKSM MEFs after culture for 5, 7 and 9 days in the presence of doxycycline.. (B) RFP fluorescence images of two representative intermediate colonies formed after culturing MEFs for 6 days in the presence of doxycycline (upper panel). After withdrawal of doxycycline cells (Day 6 + 6, middle panel) cells stopped reprogramming, reverted to an elongated fibroblast-like morphology (compare to Supplementary Figure 3) and upon passaging stopped dividing (Day 6 + 20, bottom panel).

A **Supplemental Figure 5**

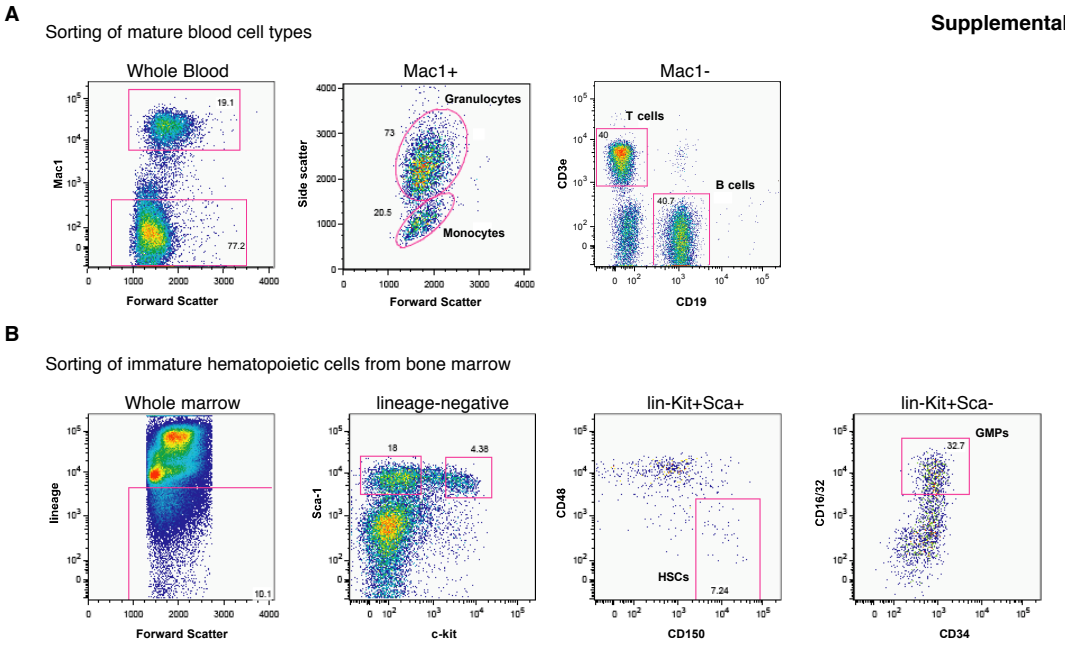


B

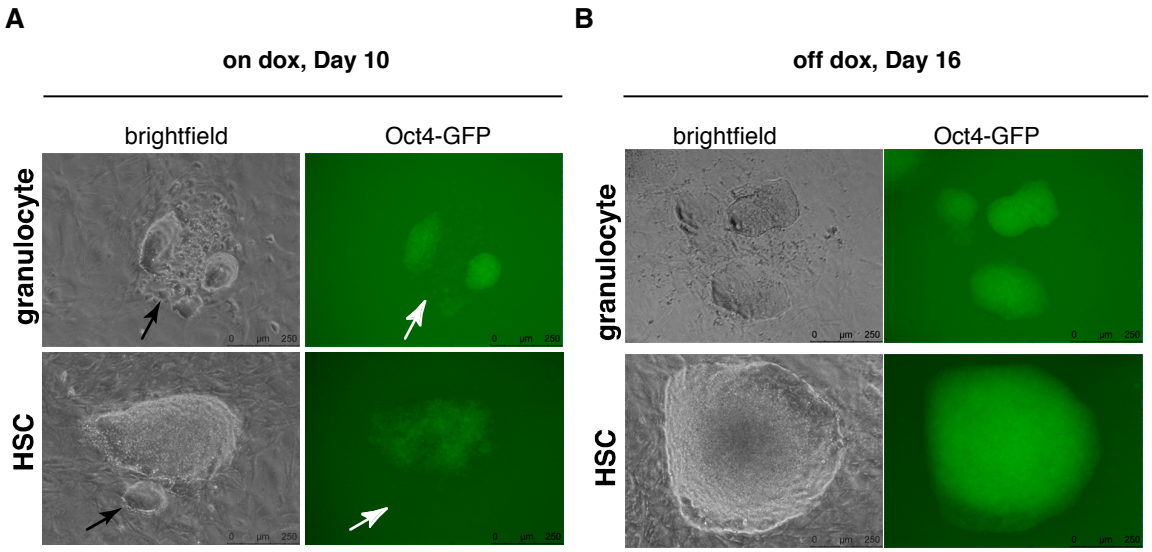


Supplementary Figure 5. Tumor formation in Collagen-OKSM mice. (A) Histological sections through two tumors found in adult chimeras derived after blastocyst injection of Collagen-OKSM ESCs. (B) Curve showing percentage of tumor-free mice at the indicated timepoints.

Supplemental Figure 6



Supplementary Figure 6. Isolation of hematopoietic cells. Gating logic for the isolation of four different mature hematopoietic cell types from blood (upper panel) as well as two immature cell types from bone marrow (lower panel). Cells were defined by the following criteria: Monocytes ($Mac1^{+}$ SSC^{low}), Granulocytes ($Mac1^{+}SSC^{high}$), B cells ($CD19^{+}CD3^{-}Mac1^{-}$), T cells ($CD3^{+}CD19^{-}Mac1^{-}$), GMPs ($Lin^{-}Kit^{+}Sca1^{-}CD34^{+}Fc\gamma R^{+}$) and HSCs ($Lin^{-}Kit^{+}Sca1^{+}CD150^{+}CD48^{-}$).



Supplementary Figure 7. Hematopoietic iPSC colonies. (A) Brightfield and GFP fluorescence images of nascent iPSC colonies forming from granulocytes and HSCs cultured in the presence of doxycycline for 10 days. Note that Oct4-GFP fluorescence is patchy and that GFP^- cells with ESC morphology can be identified (highlighted by arrows), indicated incomplete reprogramming at this timepoint. (B) Images of the samel colonies after 6 additional days of culture in the absence of doxycycline. GFP^- cells are absent and GFP fluorescence has become homogenous.