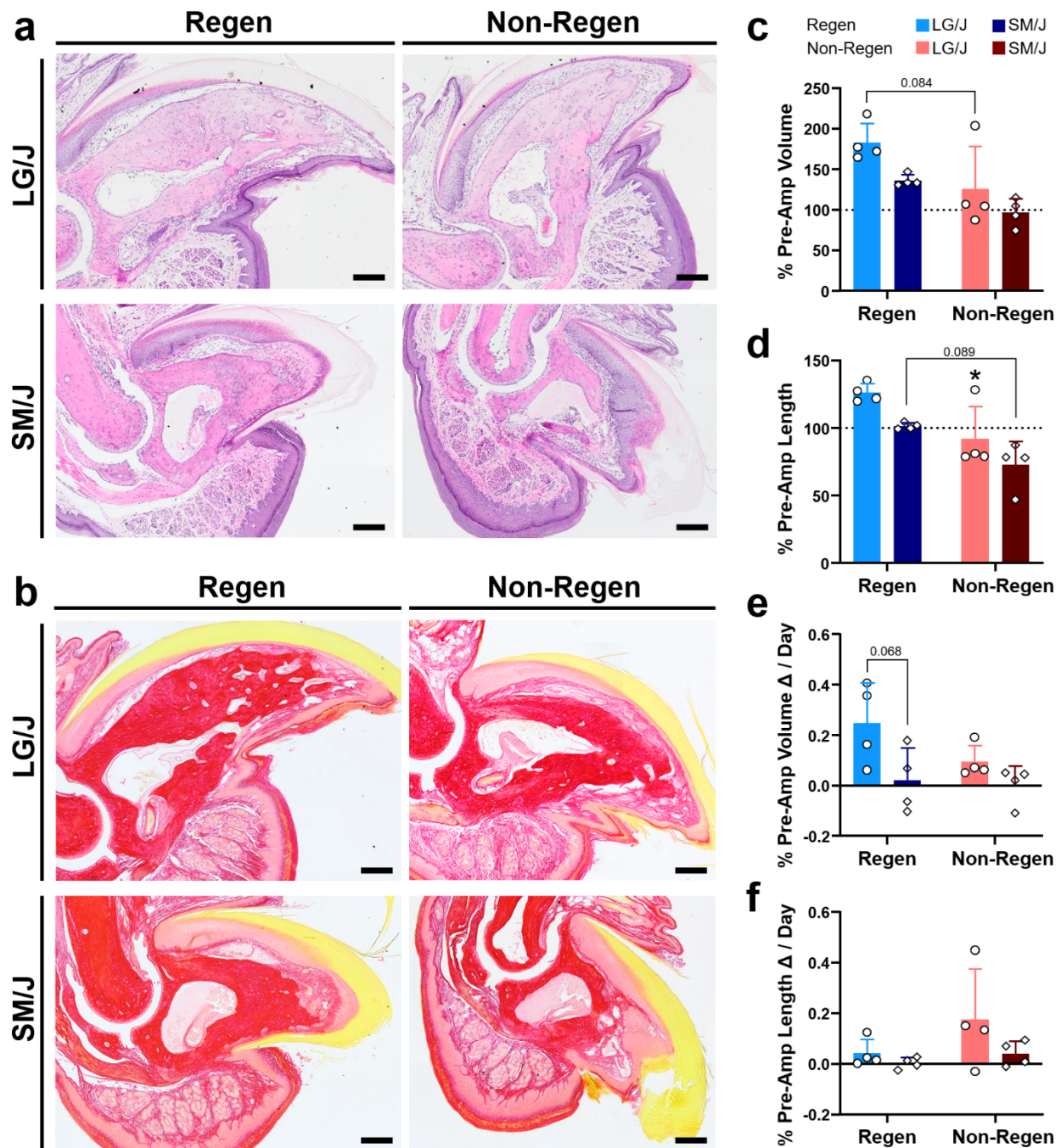
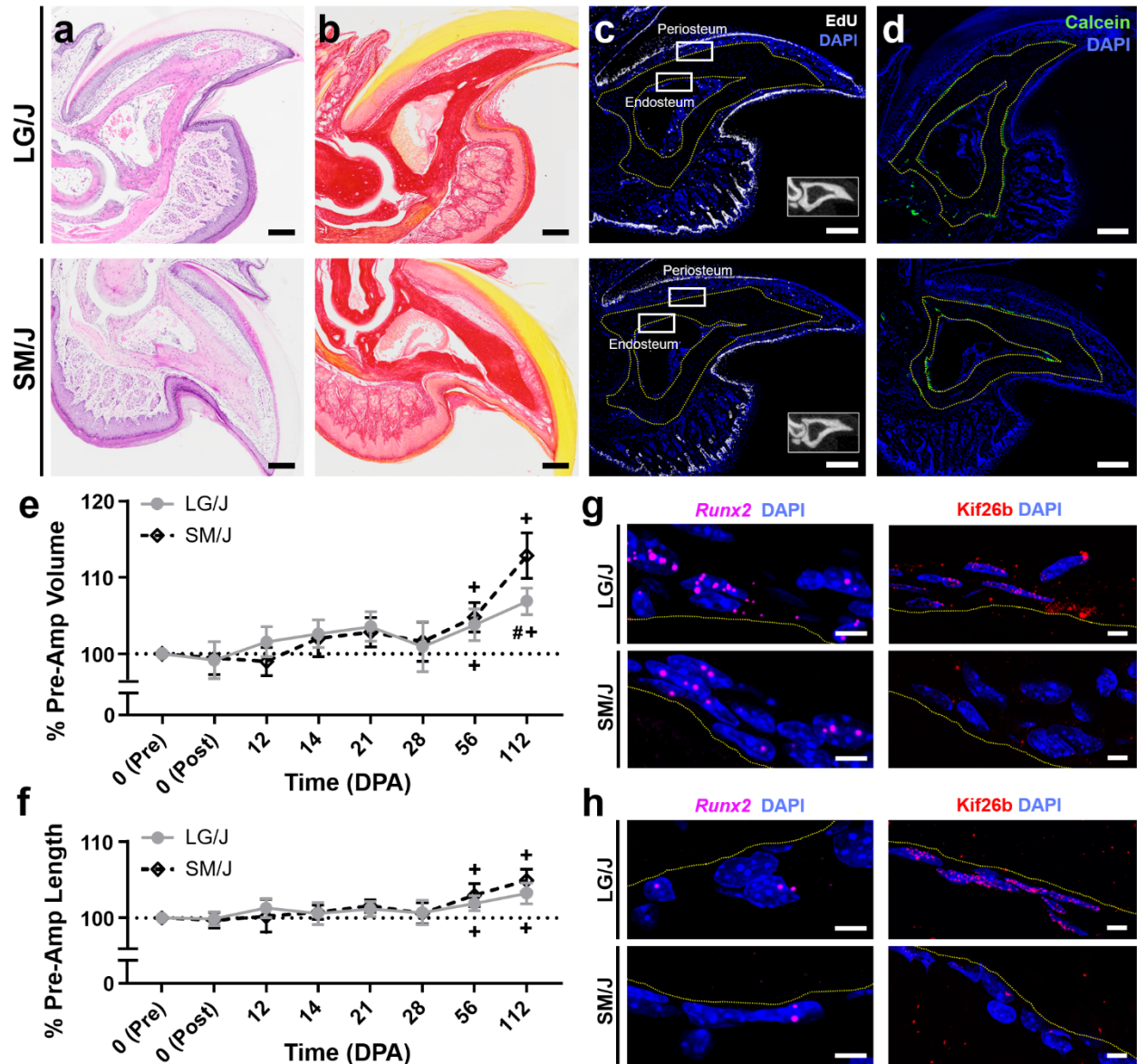


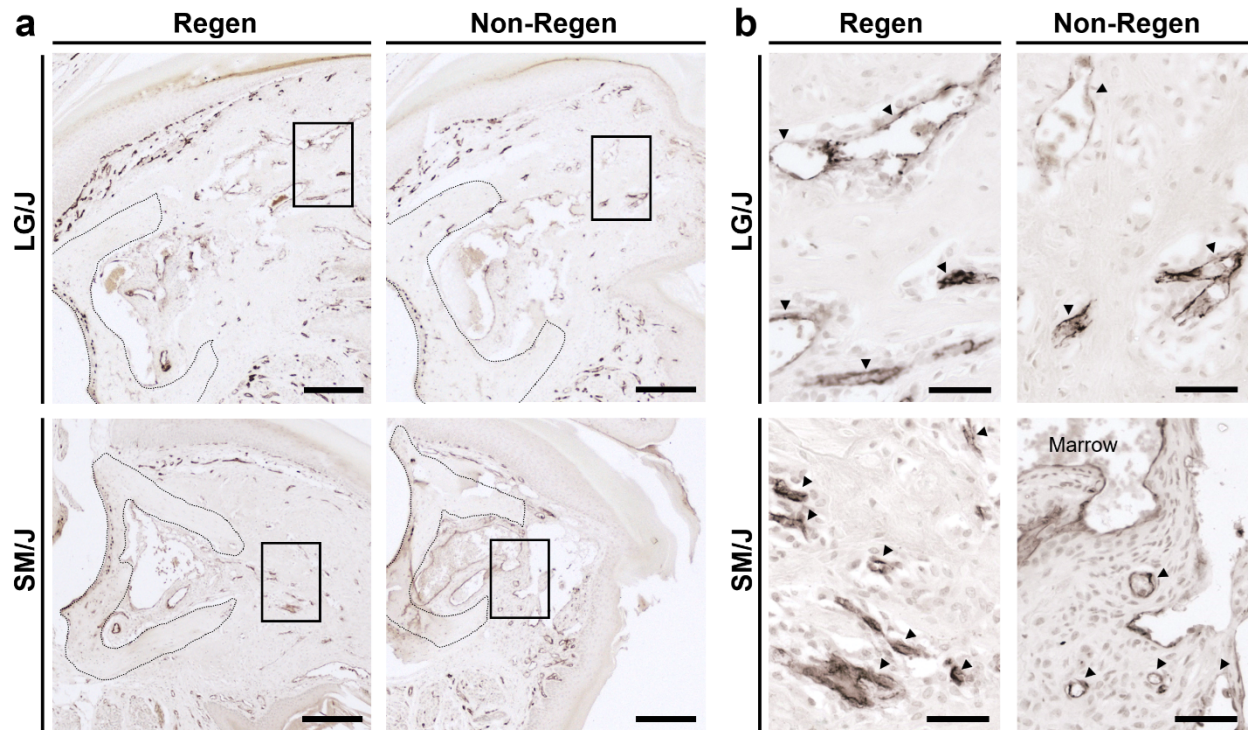
## Supplementary Information



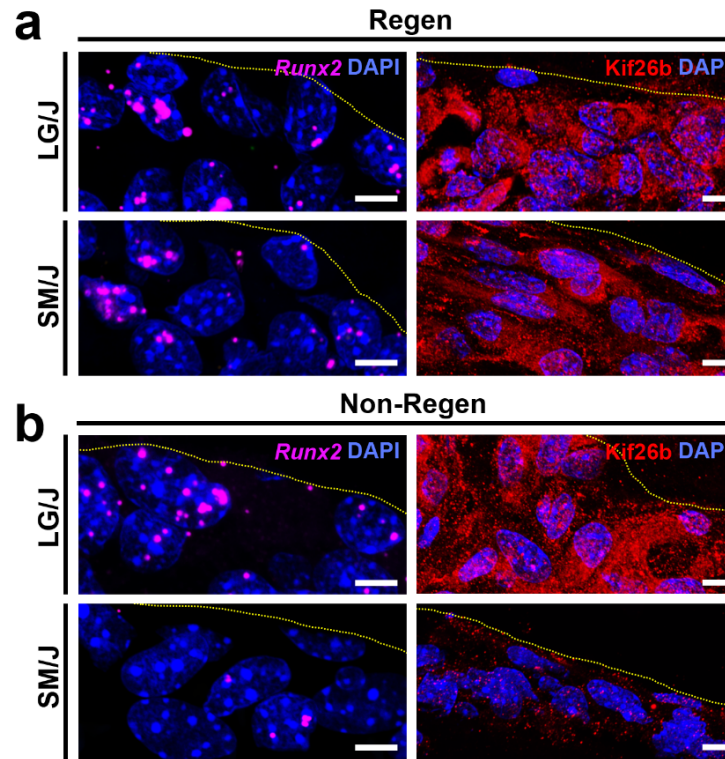
**Supplementary Figure 1. LG/J mice exhibit enhanced restoration of bone morphology at homeostasis compared to SM/J mice.** (a) H&E and (b) Picrosirius Red staining of Regen and Non-Regen digits of LG/J and SM/J mice at 112 DPA. Scale=0.2 mm. (c) % P3 volume and (d) length at 112 DPA for Regen and Non-Regen digits of LG/J and SM/J mice (n=4 digits/strain/group from 2 mice/strain, mean ± SD). Dotted line shows pre-amputated state. \*p<0.05 vs. Regen. (e) Rate of change in % P3 volume and (f) length for Homeostasis (56–112 DPA) (n=4 digits/strain/group from 2 mice/strain, mean ± SD).



**Supplementary Figure 2. Uninjured digits exhibit minimal growth at early time points.** (a) H&E, (b) Picrosirius Red, (c) EdU with microCT inset, and (d) Calcein staining of uninjured hindlimb digits of LG/J (top) and SM/J (bottom) mice, with nuclei counterstained with DAPI (blue). Dotted line shows the terminal phalanx (P3) bone. Boxes in (c) indicate corresponding regions shown in (g) and (h). Scale=0.2 mm. (e) % P3 volume and (f) length over time for uninjured digits of LG/J and SM/J mice (n=4–16 digits/strain/time/group from 2–8 mice/strain/time, mean  $\pm$  SD). Dotted line shows pre-amputated state. #= $p < 0.05$  vs. SM/J. += $p < 0.05$  vs. 0 DPA (Post). RNA FISH targeting *Runx2* (magenta) and immunostaining for Kif26b (red) in the (g) periosteum and (h) endosteum of uninjured LG/J and SM/J digits. Nuclei are counterstained with DAPI (blue). Dotted line indicates bone border. Scale=5  $\mu$ m.



**Supplementary Figure 3. Neovasculature in the blastema is aligned in the direction of bone outgrowth.** (a) Immunostaining for CD31 reveals endothelial cells at 21 DPA within Regen and Non-Regen digits of LG/J and SM/J mice. Boxes indicate corresponding regions shown in (b). Dotted line shows the amputated bone stump. Scale=0.2 mm. (b) Magnified regions in the blastema, with arrowheads indicating regions of angiogenesis. Scale=50  $\mu$ m.



**Supplementary Figure 4. Expression of *Runx2* and *Kif26b* in the endosteum is associated with bone regeneration.** RNA FISH targeting *Runx2* (magenta) and immunostaining for *Kif26b* (red) at 14 DPA in the endosteum of (a) Regen and (b) Non-Regen digits of LG/J and SM/J mice. Nuclei are counterstained with DAPI (blue). Bone is above the dotted line. Scale=5  $\mu$ m.