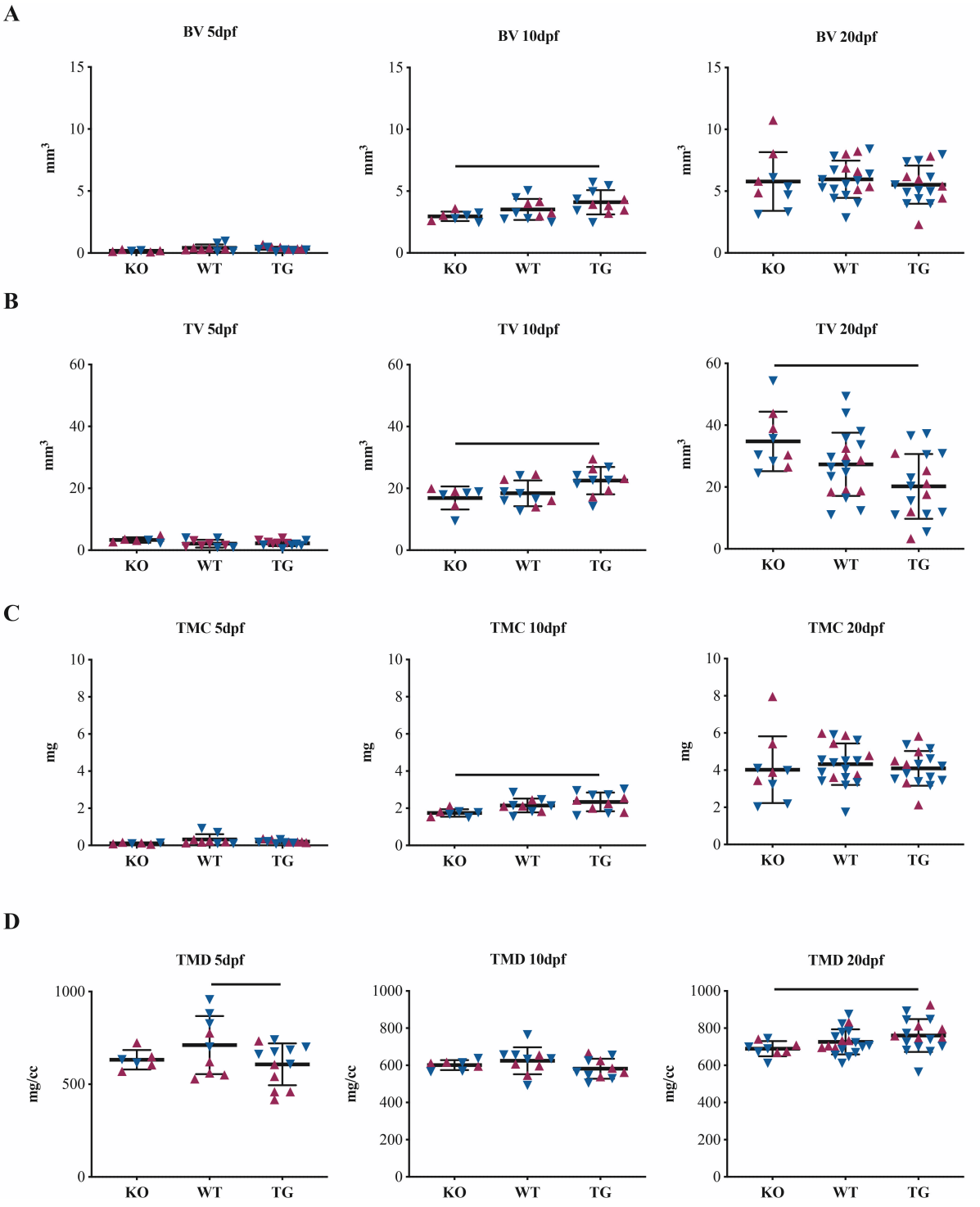
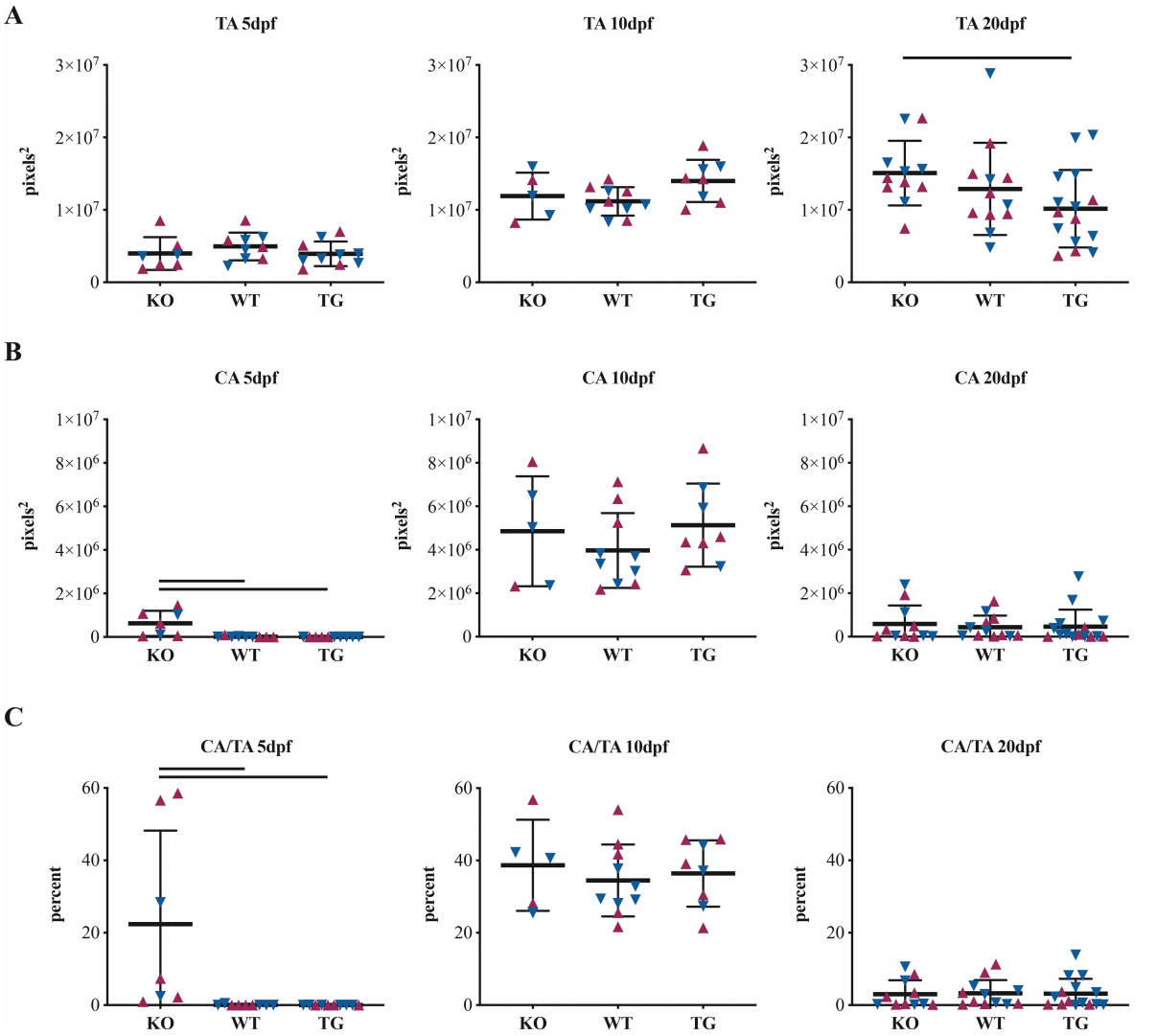
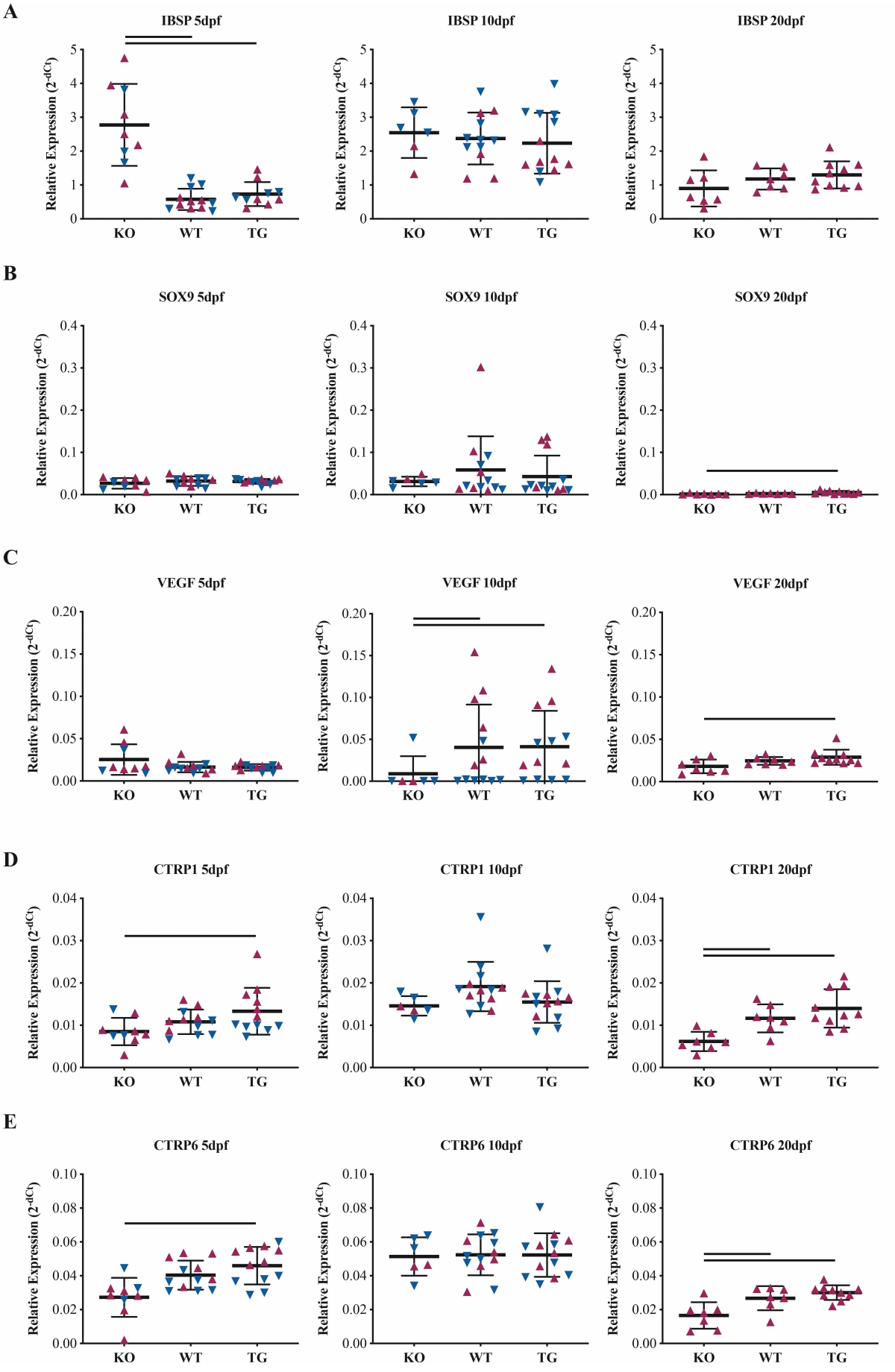


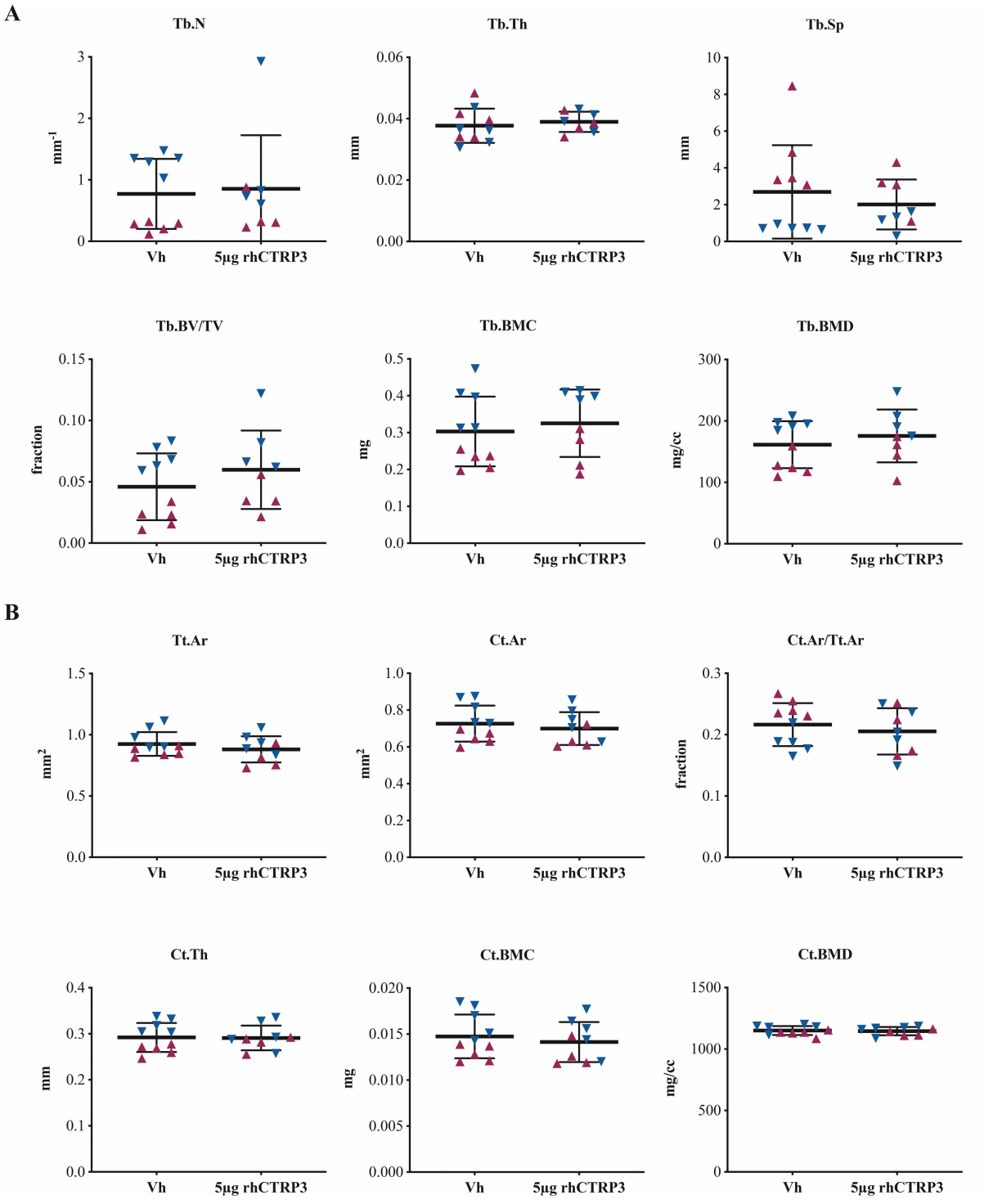
Supplementary Figure 1. *CTRP3 levels associate with callus remodeling (continued)*. Quantitative callus µCT data at 5, 10 and 20dpf for CTRP3 KO, WT and TG mice. Outputs include (A) callus bone volume (BV), (B) total callus volume (TV), (C) tissue mineral content (TMC) and (D) tissue mineral density (TMD). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



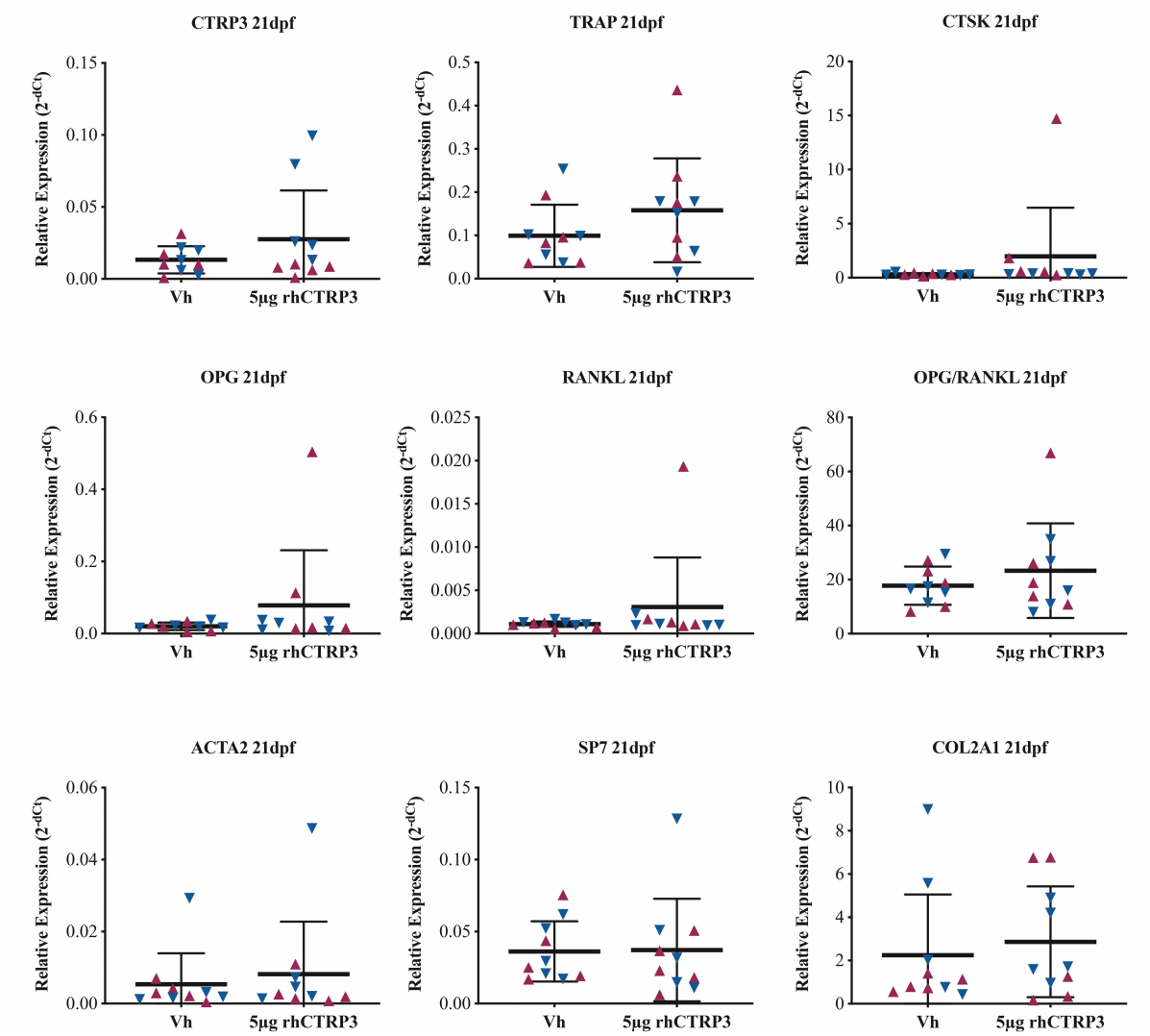
Supplementary Figure 2. *CTRP3 regulates callus cartilage formation and resorption (continued)*. Safranin-O histomorphometry from CTRP3 KO, WT and TG mice at 5, 10 and 20dpf. Outputs include (A) total area (TA), (B) callus area (CA) and cartilage area fraction (CA/TA). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice.


A
IBSP 5dpf
IBSP 10dpf
IBSP 20dpf
B
SOX9 5dpf
SOX9 10dpf
SOX9 20dpf
C
VEGF 5dpf
VEGF 10dpf
VEGF 20dpf
D
CTRP1 5dpf
CTRP1 10dpf
CTRP1 20dpf
E
CTRP6 5dpf
CTRP6 10dpf
CTRP6 20dpf
Relative Expression (2-dCt)
KO
WT
TG

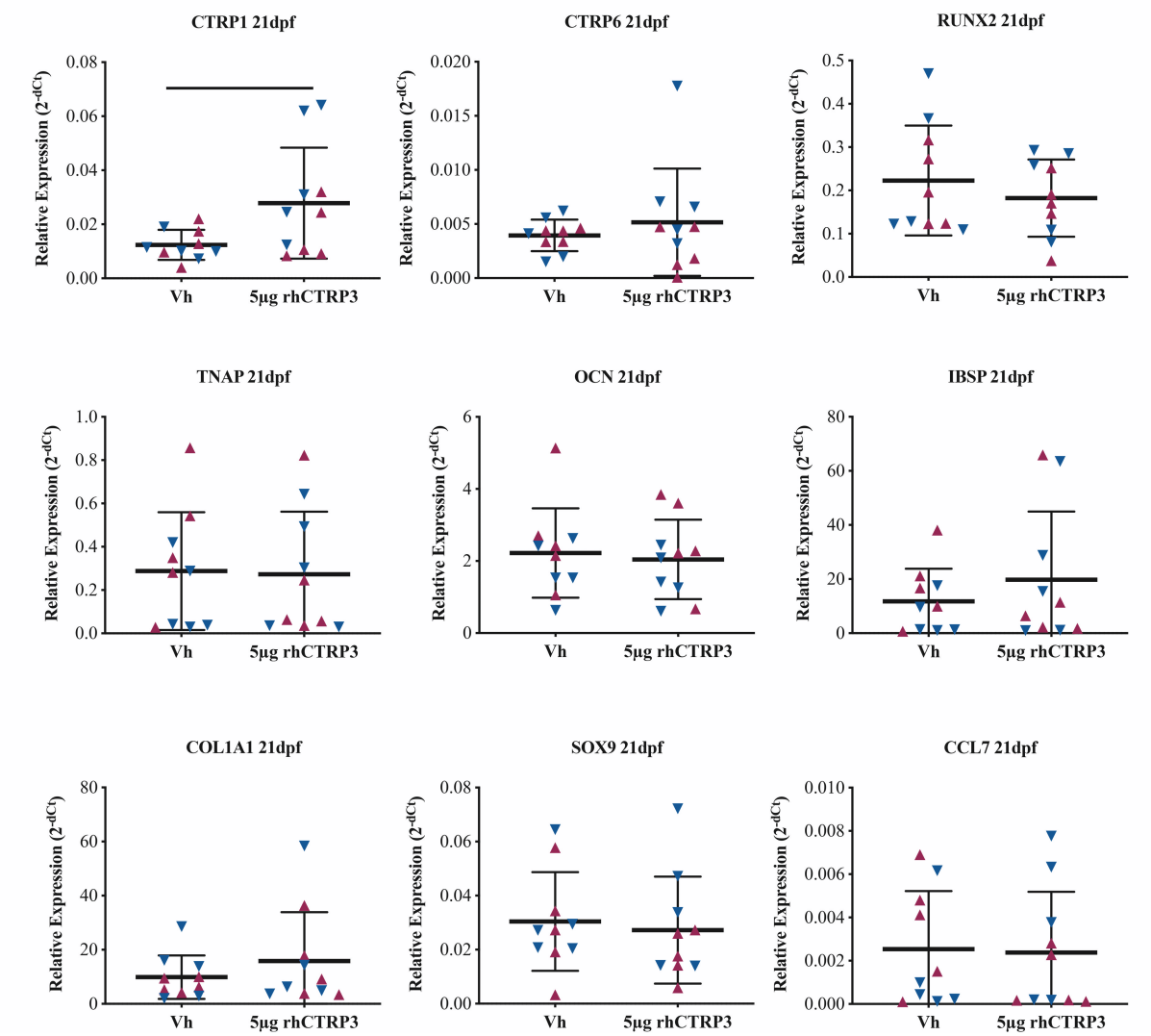
Supplementary Figure 3. *CTRP3 alters gene expression profiles during healing (continued)*. Whole-callus mRNA expression of (A) bone sialoprotein (IBSP), (B) SRY-box transcription factor 9 (SOX9), (C) vascular endothelial growth factor (VEGF), (D) CTRP1 and (E) CTRP6 vary based on CTRP3 genotype. Relative expression is presented at 2^{-dCt} with ACTB as a housekeeping gene. Statistics were run on dCt values. Consistent y-axis scales are used over time to more easily convey changes in relative abundance, but this results in compression of some timepoints. Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



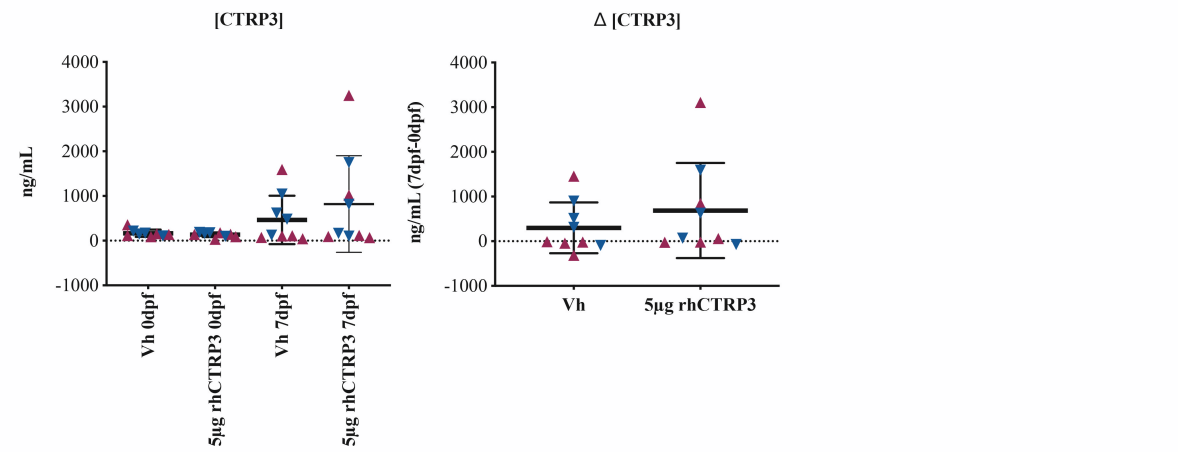
Supplementary Figure 4. *Single injection of rhCTRP3 protein does not alter tibia structure/function (I)*. µCT analysis of (A) trabecular and (B) cortical bone of the tibiae of mice at 21dpf, following treatment with Vh or 5µg rhCTRP3 at time of fracture. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



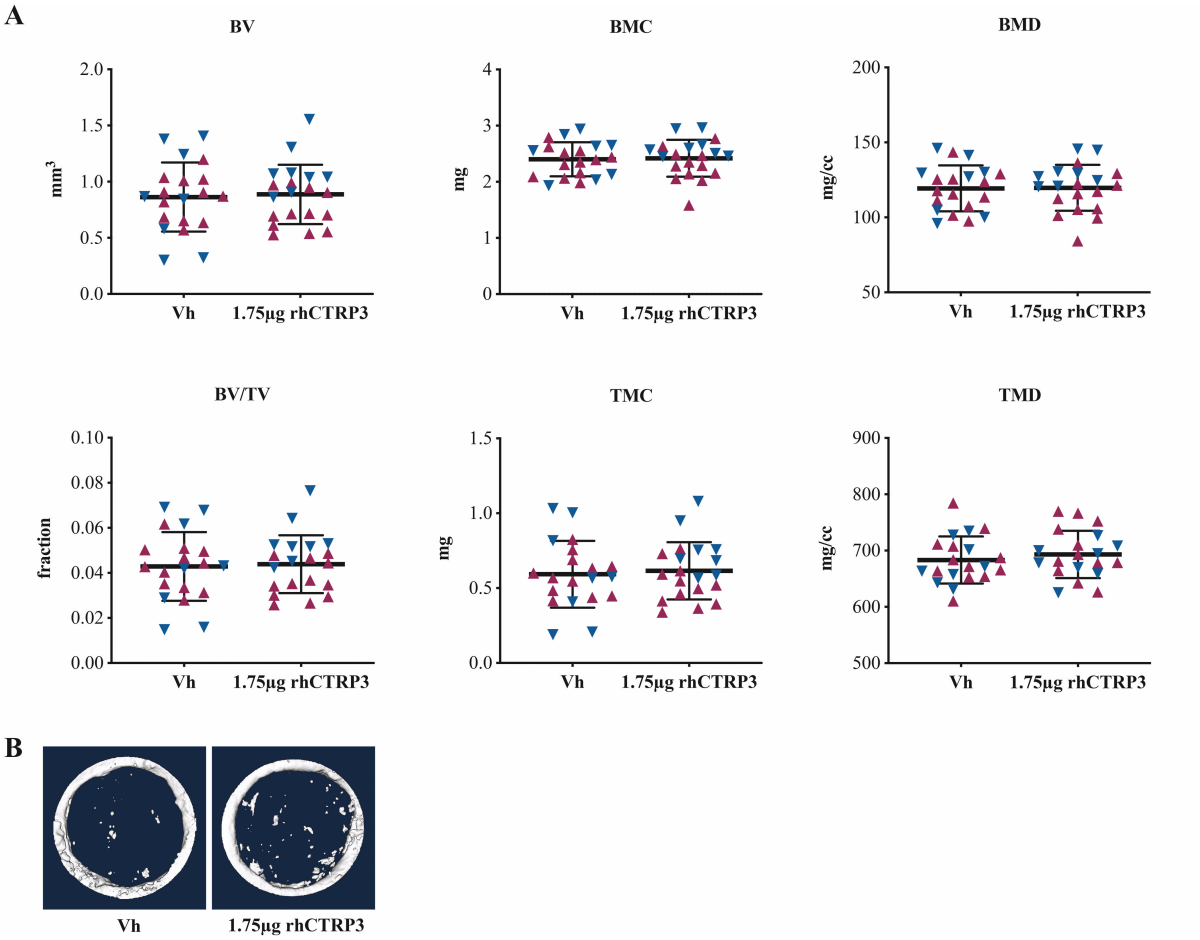
Supplementary Figure 5. *Single injection of rhCTRP3 protein does not alter tibia structure/function (II)*. Whole-callus gene expression analysis did not identify differentially expressed osteochondral genes. Relative expression is presented at 2^{-dCt} with ACTB as a housekeeping gene. Statistics were run on dCt values. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



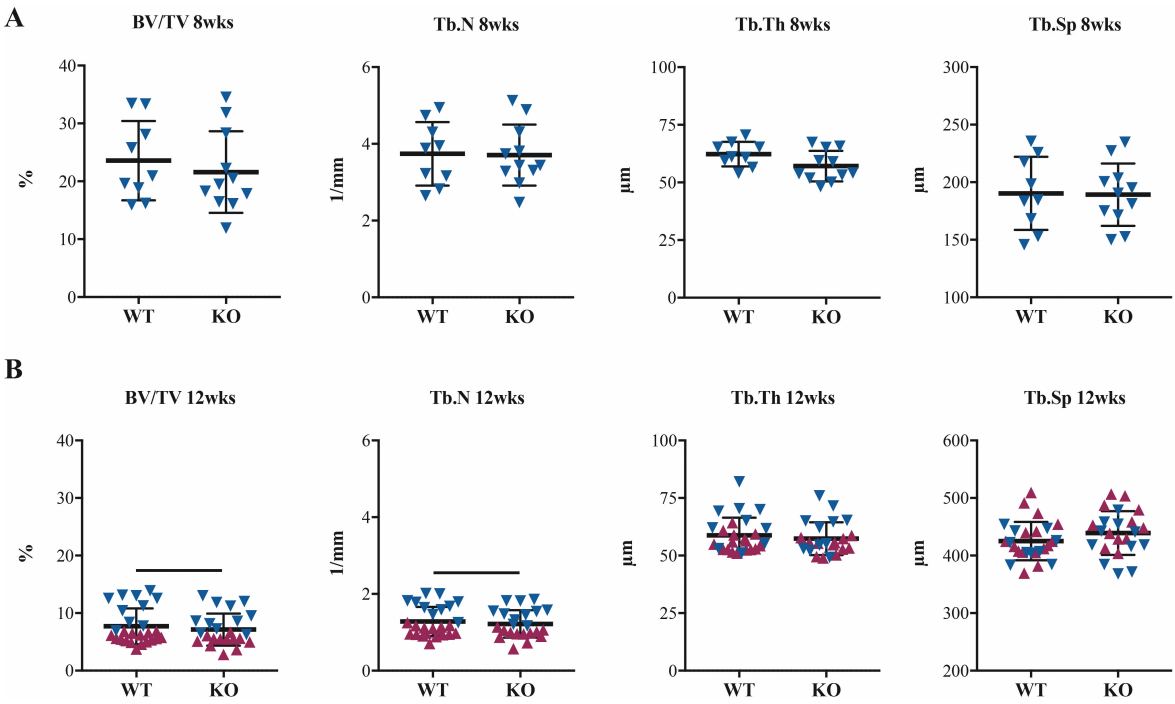
Supplementary Figure 6. *Single injection of rhCTRP3 protein does not alter tibia structure/function (III)*. Whole-callus gene expression analysis revealed upregulation of CTRP3 in response to rhCTRP3 treatment. Relative expression is presented at 2^{-dCt} with ACTB as a housekeeping gene. Statistics were run on dCt values. Solid lines represent $p<0.05$ by treatment. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



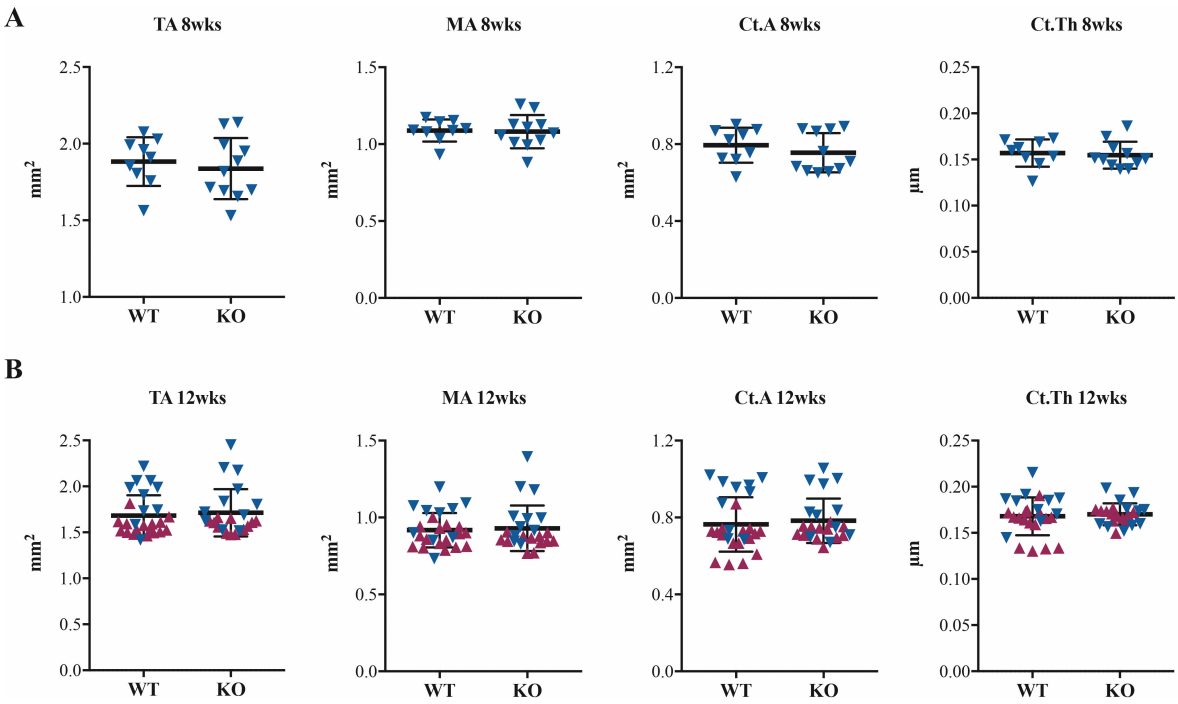
Supplementary Figure 7. *Assessment of CTRP3 protein in longitudinally collected serum samples*. Mean levels of circulating CTRP3 increase at 7dpf, but inter-subject variation precluded statistical significance. Graphs portray raw concentrations ([CTRP3]) at 0dpf and 7dpf as well as change in concentrations (Δ[CTRP3]) at 7dpf, following treatment with Vh or rhCTRP. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



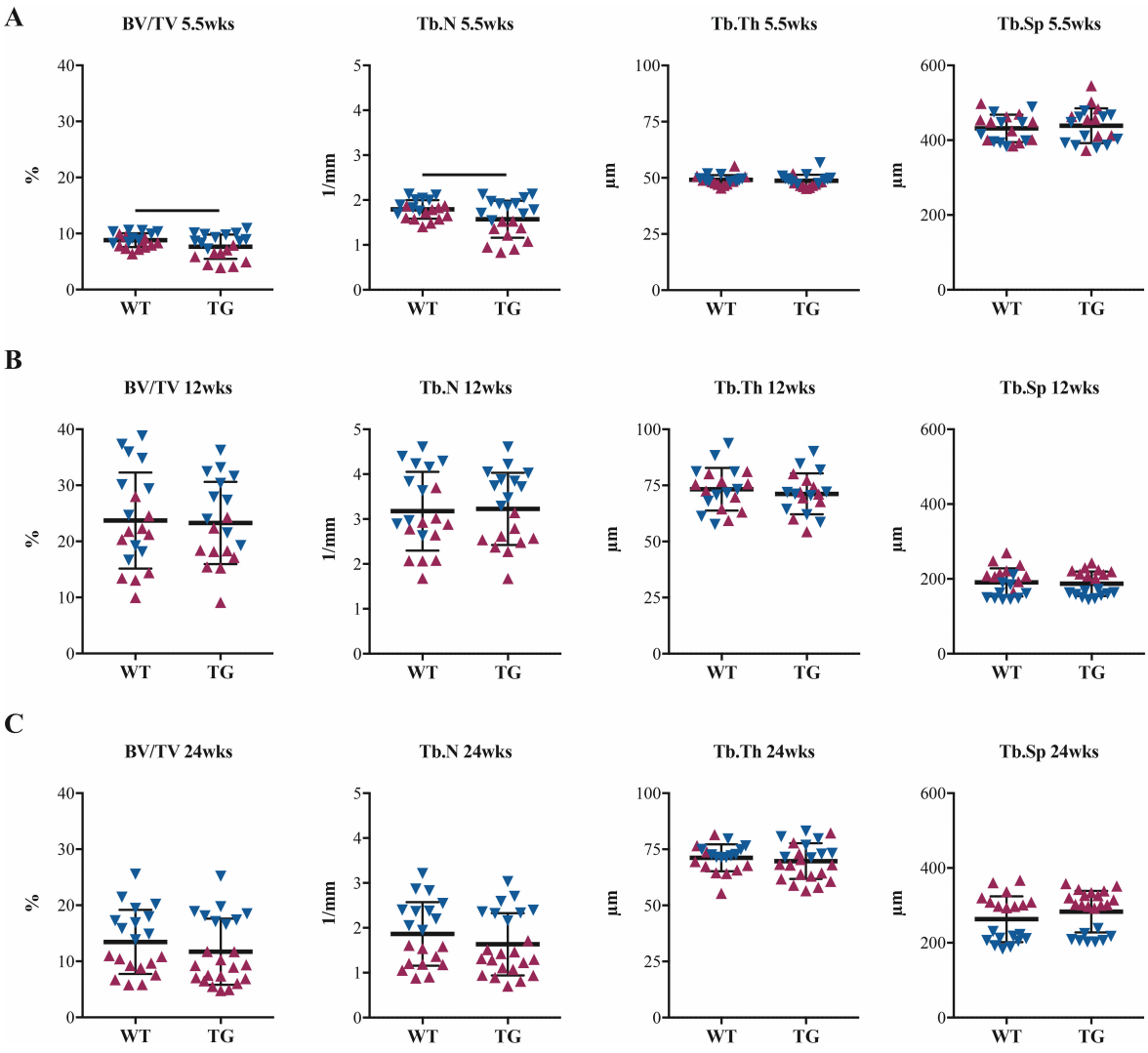
Supplementary Figure 8. *Local delivery of rhCTRP3 protein does not promote intramembranous regeneration*. µCT (A) quantitation and (B) isosurface renderings at 43dpd in mice that received either Vh or 5µg rhCTRP3 protein delivered to calvarial defects. Outputs include total volume (TV), bone volume (BV), bone volume fraction (BV/TV), bone mineral content (BMC), bone mineral density (BMD), tissue mineral content (TMC) and tissue mineral density (TMD). Maroon up-arrows represent female mice and navy down-arrows represent male mice.



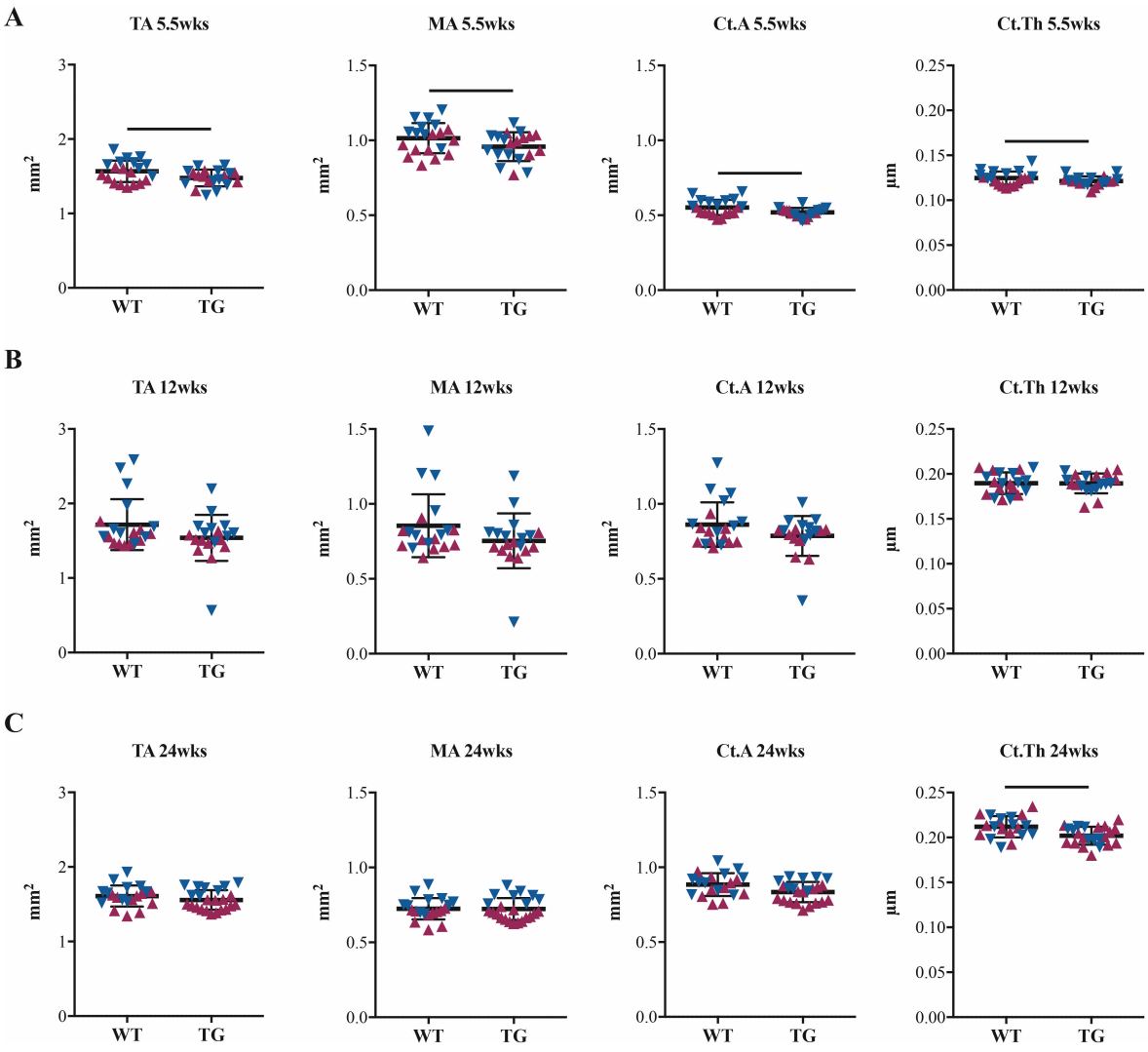
Supplementary Figure 9. *Genetic modification of CTRP3 induces a minor adult bone phenotype (I)*. µCT analysis of trabecular bone at (A) 8wks and (B) 12wks of age in KO mice versus WT littermates. Outputs include bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th) and trabecular spacing (Tb.Sp). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



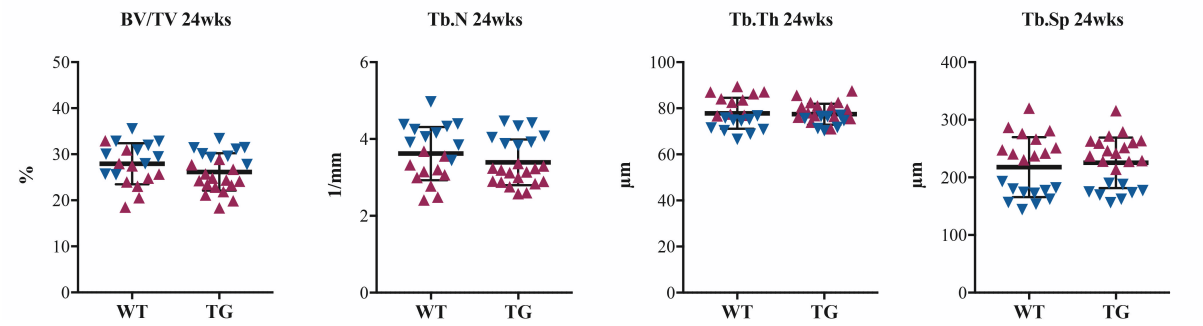
Supplementary Figure 10. *Genetic modification of CTRP3 induces a minor adult bone phenotype (II)*. µCT analysis of cortical bone at (A) 8wks and (B) 12wks of age in KO mice versus WT littermates. Outputs include total area (TA), marrow area (MA), cortical area (Ct.A) and cortical thickness (Ct.Th). Maroon up-arrows represent female mice and navy down-arrows represent male mice.



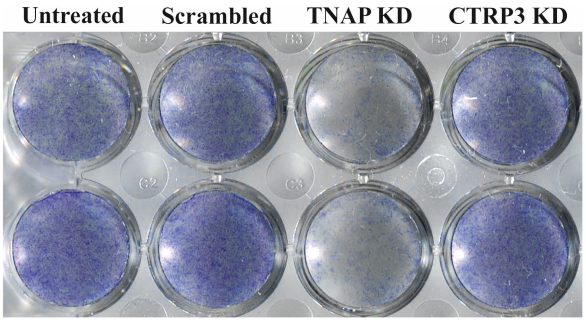
Supplementary Figure 11. *Genetic modification of CTRP3 induces a minor adult bone phenotype (III)*. µCT analysis of trabecular bone at (A) 5.5wks, (B) 12wks and (C) 24wks of age in TG mice versus WT littermates. Outputs include bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th) and trabecular spacing (Tb.Sp). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



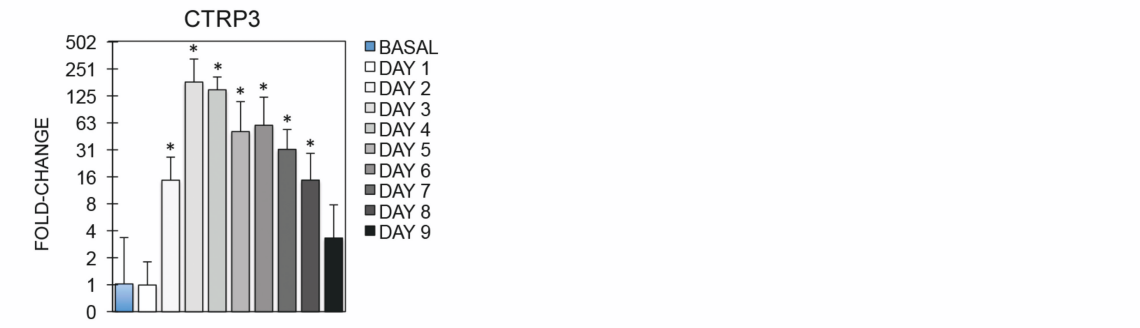
Supplementary Figure 12. *Genetic modification of CTRP3 induces a minor adult bone phenotype (IV)*. µCT analysis of cortical bone at (A) 5.5wks, (B) 12wks and (C) 24wks of age in TG mice versus WT littermates. Outputs include total area (TA), marrow area (MA), cortical area (Ct.A) and cortical thickness (Ct.Th). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



Supplementary Figure 13. *Genetic modification of CTRP3 induces a minor adult bone phenotype (IV)*. µCT analysis of vertebral trabecular bone at 24wks of age in TG mice versus WT littermates. Outputs include bone volume fraction (BV/TV), trabecular number (Tb.N), trabecular thickness (Tb.Th) and trabecular spacing (Tb.Sp). Solid lines represent $p<0.05$ by genotype. Maroon up-arrows represent female mice and navy down-arrows represent male mice. Maroon up-arrows represent female mice and navy down-arrows represent male mice.



Supplementary Figure 14. *siRNA knockdown of CTRP3 does not alter early osteoblast differentiation in vitro*. Human primary MSCs treated with siRNA against CTRP3 did not experienced altered alkaline phosphatase staining 4 days into an osteogenesis assay. The untreated and scrambled groups represent negative controls, and siRNA against the alkaline phosphatase gene (TNAP) represents a positive control.



Supplementary Figure 15. *CTRP3 gene expression in a mouse femoral marrow ablation model*. cDNA stocks were revisited from a recent study [22]. CTRP3 expression at each timepoint (n=6-12) is compared to basal bone using the 2^{-ddCt} method relative to ACTB. Statistical significance is symbolized with * for $p<0.05$.