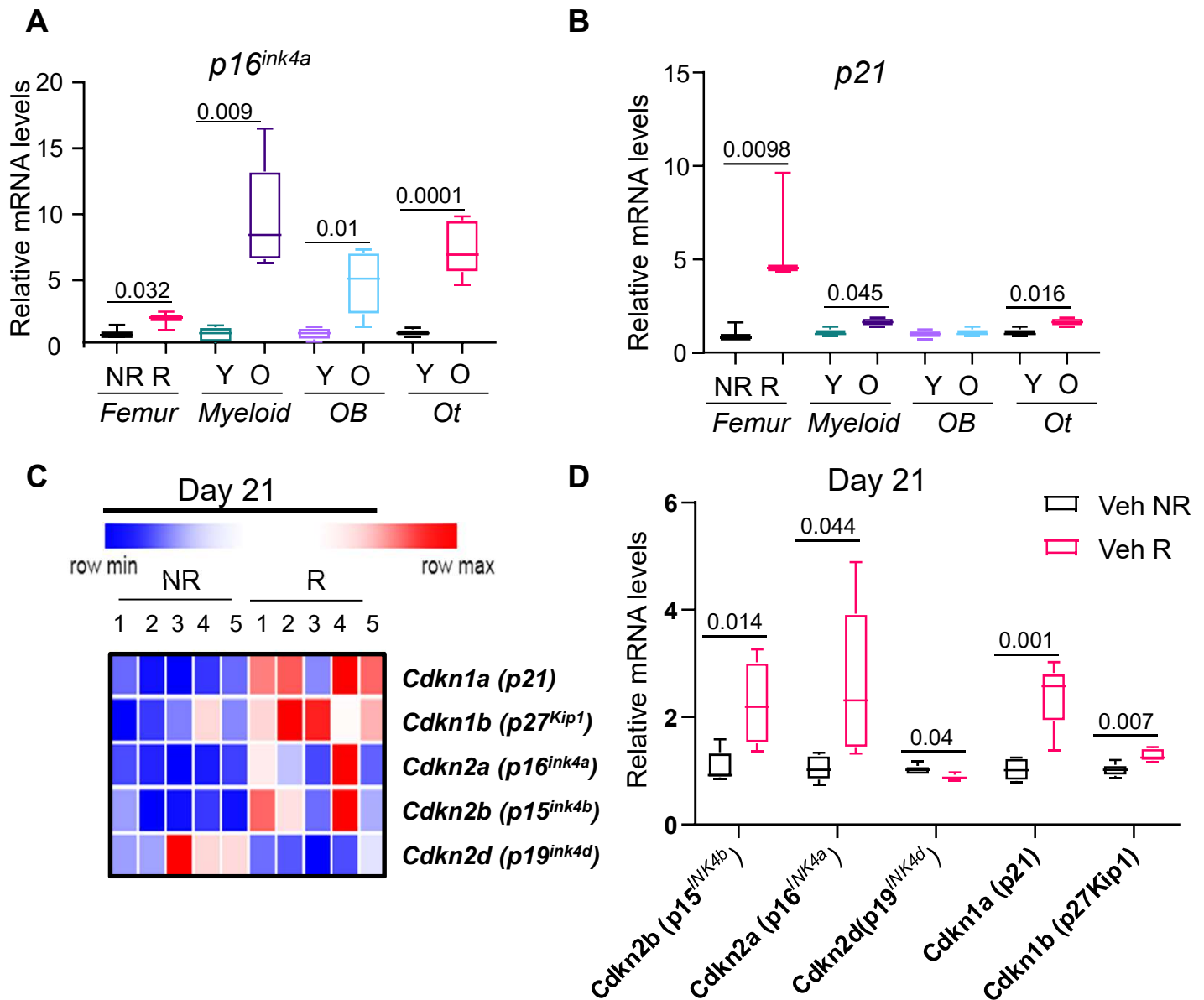
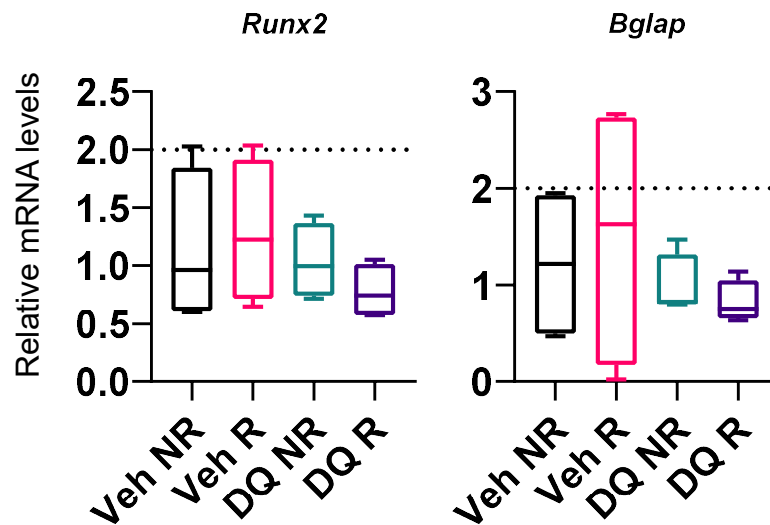


Supplementary Figure 1.



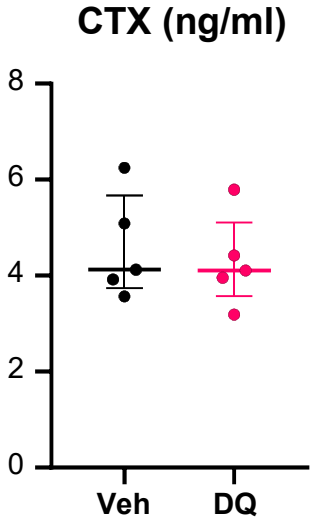
Supplementary Figure 1. (A) $p16^{ink4a}$ and (B) $p21$ mRNA levels in NR and R mouse femoral metaphyses, 14 days-post FRT, in comparison with expression levels in enriched cells from the myeloid lineage, osteoblasts (OB) and osteocytes (Ot), from 6-month old animals (Y) and 24 month old animals (O). Y-axis: fold change normalized against NR (for comparison between NR vs. R), and normalized against Y (for comparison between Y vs. O). (C) Heat map of CDKi genes determined by RT-qPCR from NR- and R-femurs (n=5 mice/group) collected 21 days post-FRT. (D) Gene expression of cell cycle inhibitors at 21 days post-FRT. See also ref (9) for information on enriched cells from Y and O animals. Statistical analysis was done using Graph-Pad Prism and p-value was calculated using a two-tailed paired t-test to compare the R- and NR-bones from the same animals, and using a two-sampled t-test for comparison of young and old bone cells.

Supplementary Figure 2.



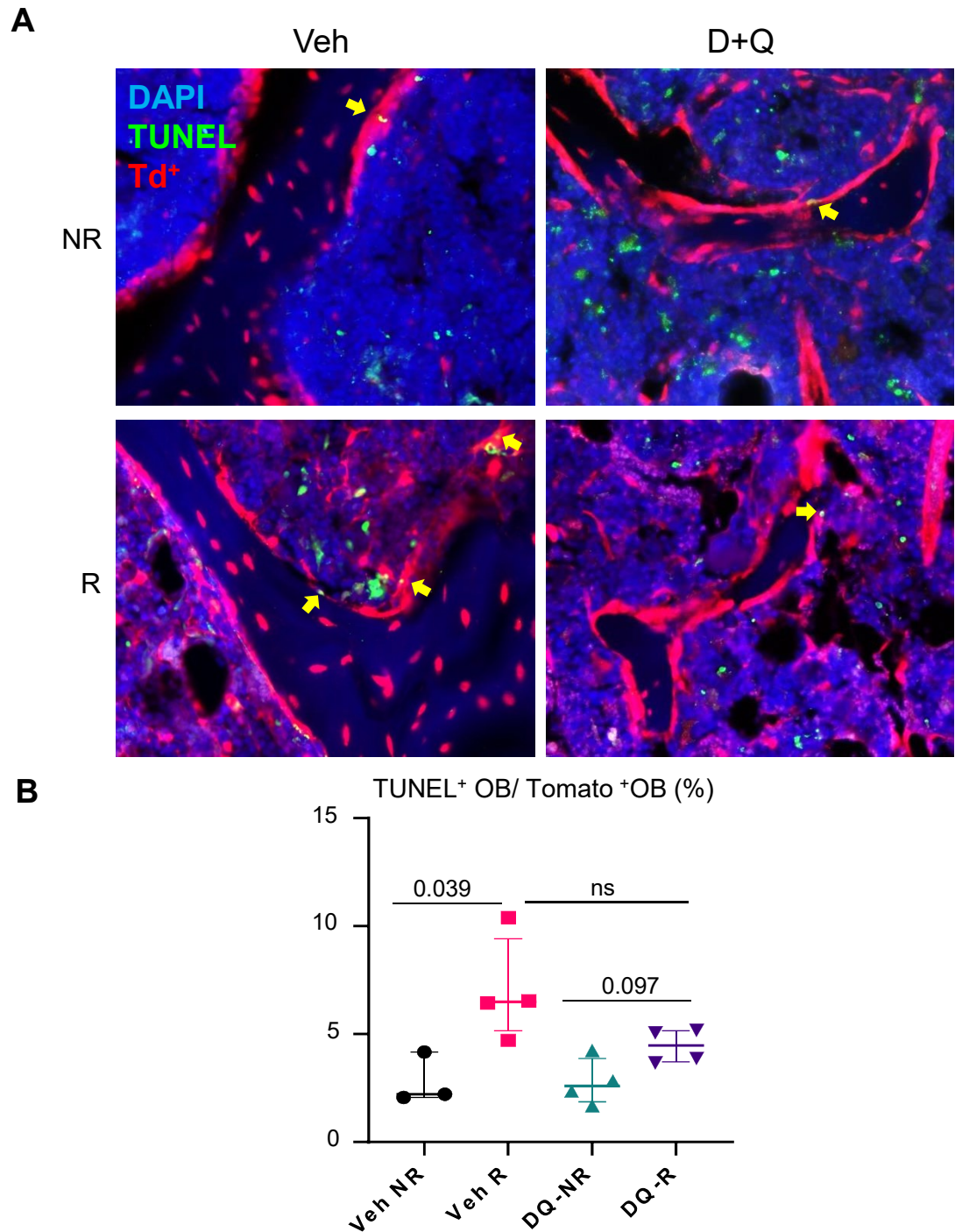
Supplementary figure 2. D+Q does not affect gene expression of bone marker genes, *Runx2* and *Bglap* (Osteocalcin) . 4-month old C57BL/6 male mice received radiation (24Gy) in a 5 mm region of the right femoral metaphysis, accompanied with intermittent treatments on day 0 and 14, with either vehicle (n=4 mice) or D+Q (5mg/kg D and 50mg/kg Q , n=4 mice), and bones were collected on day 42 post-FRT and processed for mRNA analysis. Relative mRNA expression of *Runx2* (left panel) and *Bglap* (Osteocalcin) (right panel) are presented. No significant changes were observed in any of the groups.

Supplementary Figure 3.



Supplementary Figure 3. Serum C-terminal telopeptide of type I collagen (CTX) measured at 6-weeks post FRT.

Supplementary Figure 4.



Supplementary Figure 4. D+Q does not affect radiation induced osteoblast apoptosis. 4-month old Col2-Cre-Td+Tomato male mice received radiation (24Gy) in a 5 mm region of the right femoral metaphysis, accompanied with intermittent treatments on day 0 and 14, with either vehicle (n=4 mice) or D+Q (n=4 mice), and bones were collected on day 42 post-FRT and processed for frozen sectioning.

(A) Representative TUNEL stained bone sections are shown from each group. Sections clearly show the red fluorescent osteoblasts confirming the expression of the tomato reporter. Yellow arrows indicate TUNEL⁺ osteoblasts. (B) Quantification of TUNEL⁺ osteoblast on bone surface normalized against total Tomato⁺ osteoblasts on the bone surface. Results are expressed median with interquartile range. Statistical analyses were done using Graph-Pad Prism and p-values were calculated using a two-way ANOVA ($\alpha=0.05$) with a Tukey post-hoc analysis.