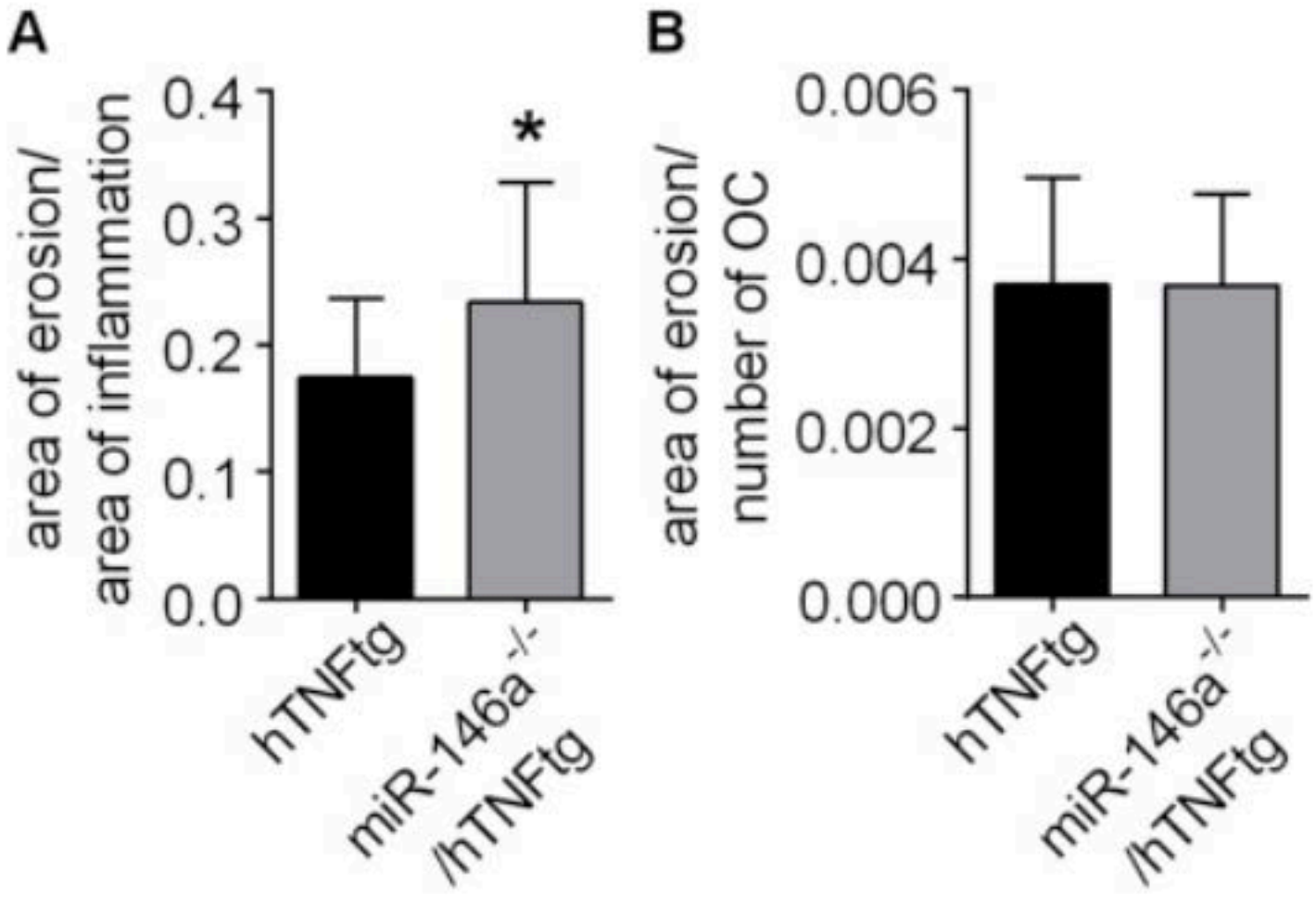
Appendix A. Supplementary data

The following is the supplementary data related to this article:



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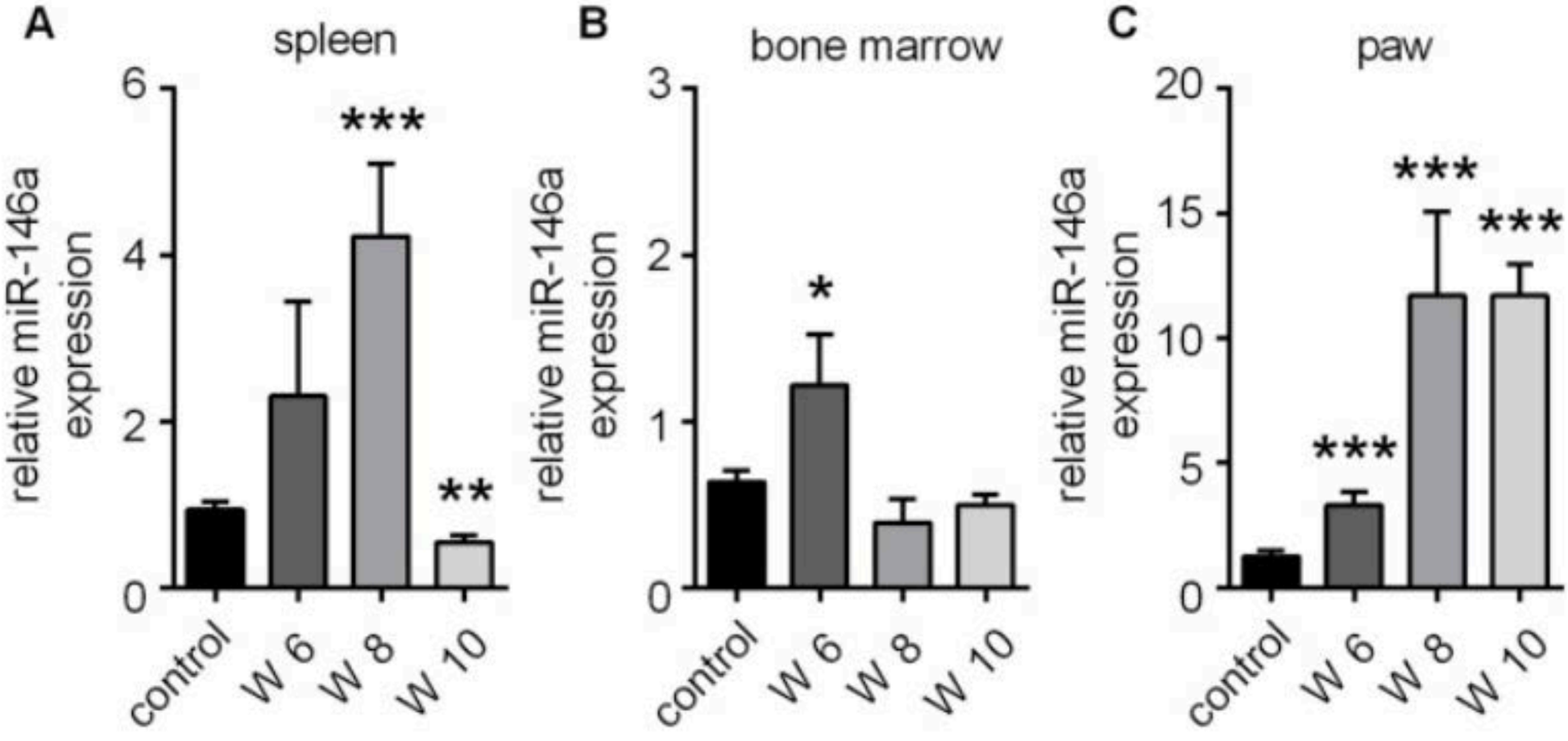
S1. Increased osteoclast numbers account for elevated bone erosion in miR-146a$^{-/-}$**/hTNFtg animals**. A, Histomorphometric analysis of the extent of area of erosion per area of inflammation and B, area of erosion per number of osteoclast; in the tarsal area of the hind paws of hTNFtg (n = 16) and miR-146a$^{-/-}$/hTNFtg (n = 15) mice. *p < 0,05 Results are shown as mean ± SEM.



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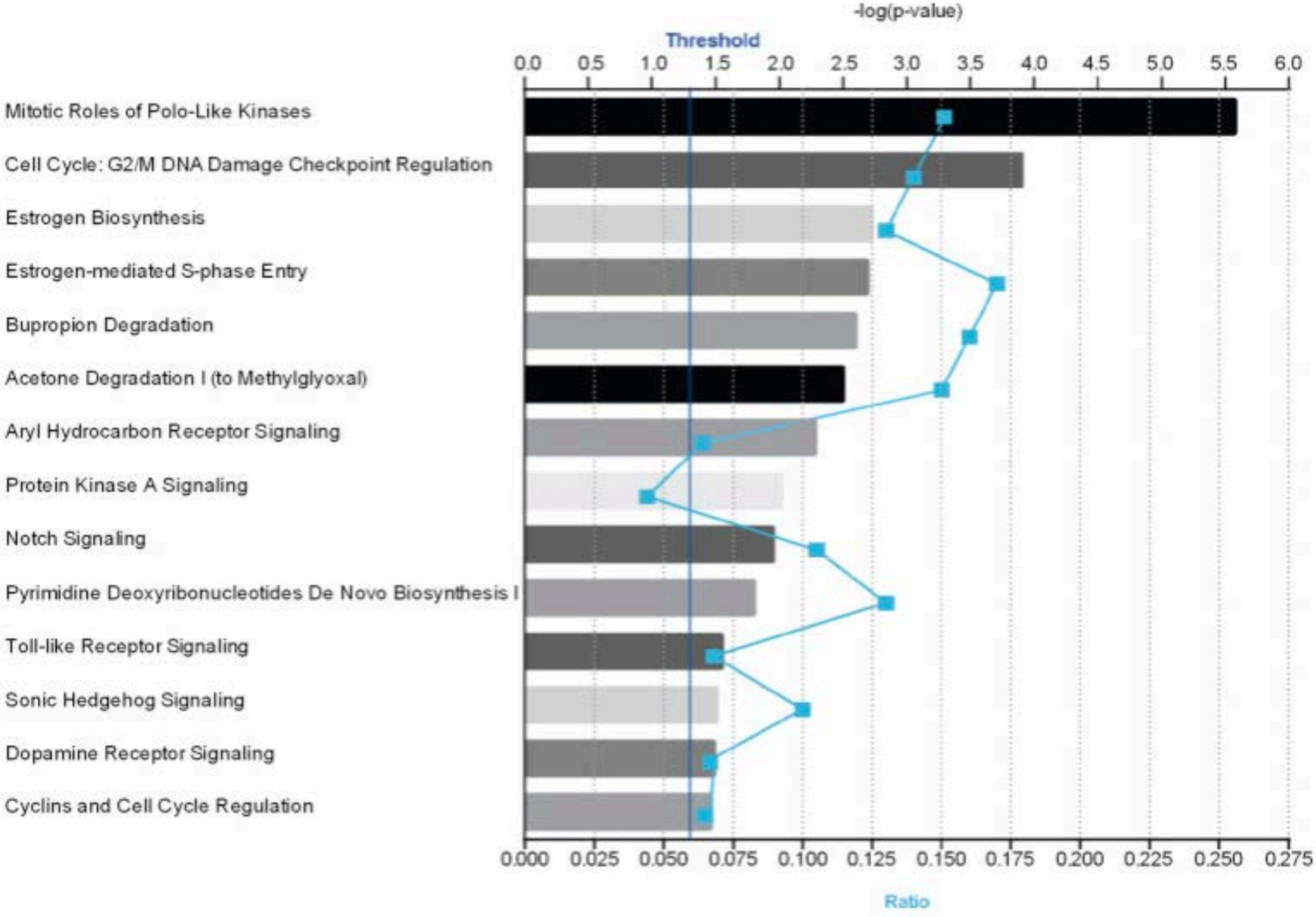
S2. **Variable expression of miR-146a in lymphoid organs and locally in arthritic paws of hTNFtg animals**. A-C, Quantitative real time PCR analysis of miR-146a expression in spleen- (A), bone marrow- (B) and paw cells (C). Cells were isolated at the indicated age (weeks) of hTNFtg mice (n = 4). *p < 0,05, **p < 0,01, ***p < 0,001 as indicated or versus the control. Results are shown as mean ± SEM.



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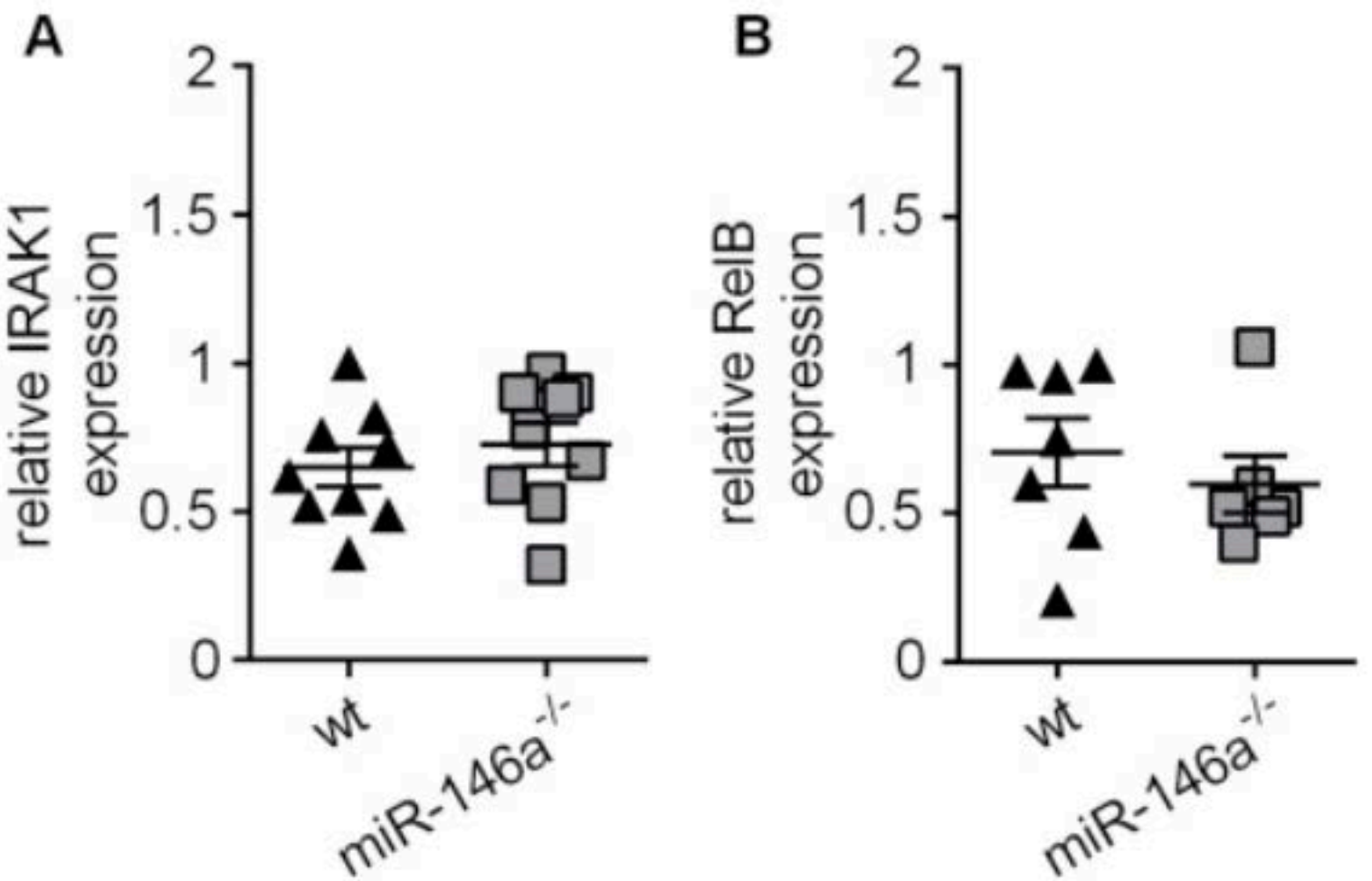
S3. MiR-146a deficient fibroblasts show increased expression of genes involved in proliferation and pyrimidine synthesis. A, Pathways affected by loss of miR-146a in synovial fibroblasts as detected by ingenuity pathway analysis (IPA).



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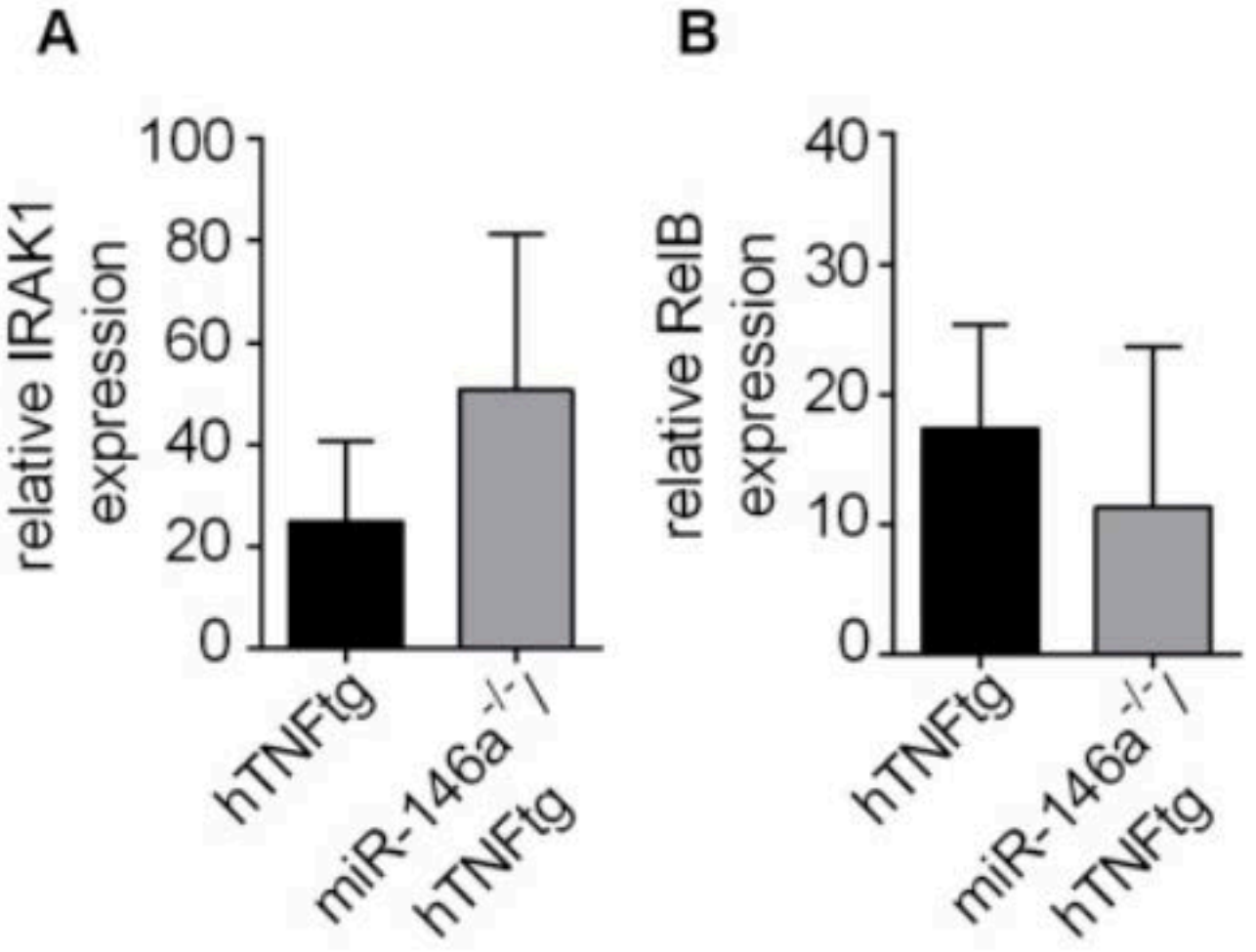
S4. **MiR-146a target gene expression in synovial fibroblasts**. A, Expression level of IRAK1 in synovial fibroblasts from wt (n = 9) and miR-146a$^{-/-}$ (n = 9) animals. B, Expression level of RelB in synovial fibroblasts from wt (n = 7) and miR-146a$^{-/-}$ (n = 6) animals were analyzed using quantitative real time PCR. Results are shown as mean ± SEM.



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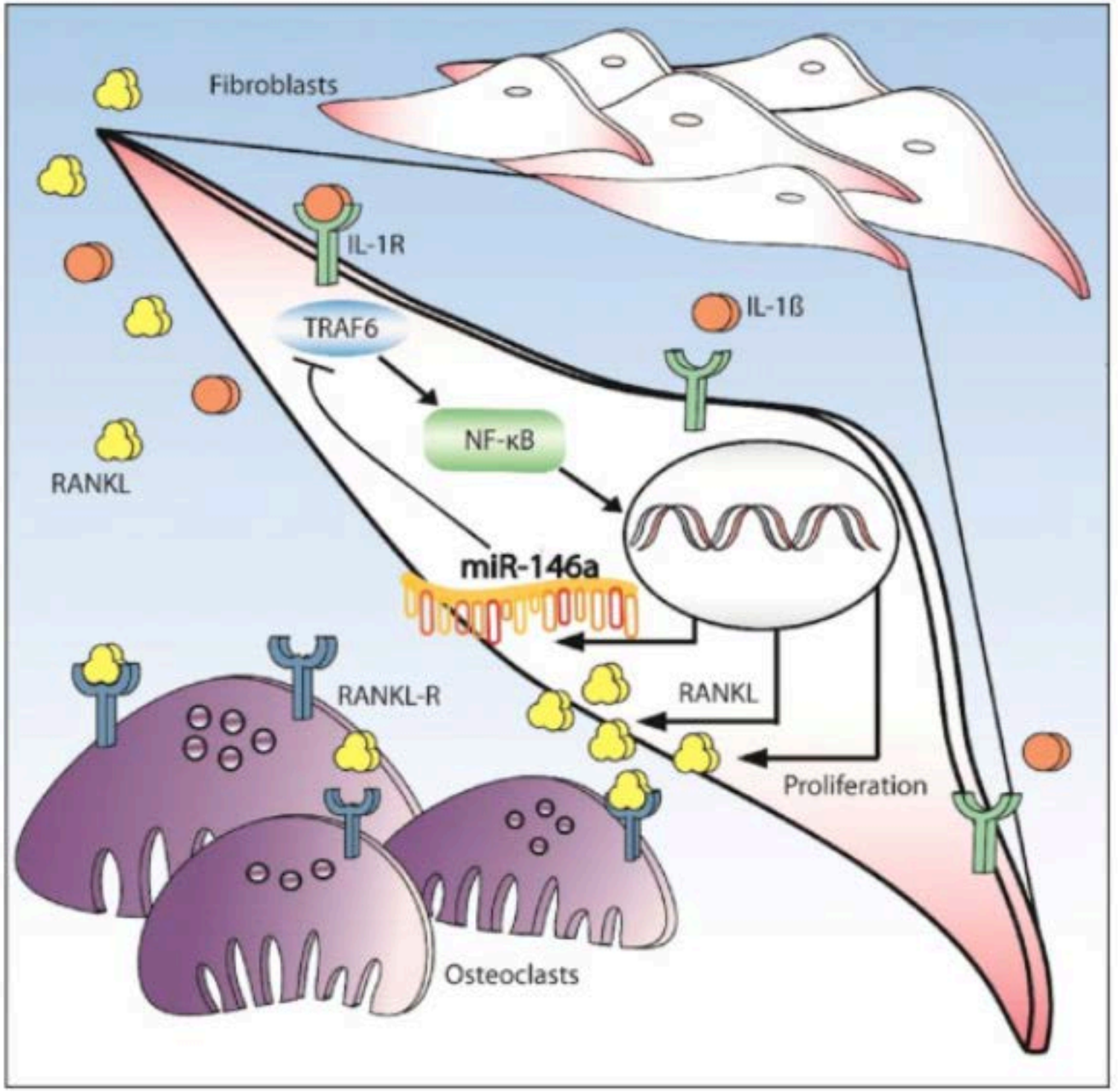
S5. **MiR-146a target gene expression in hind paws of hTNFtg and miR-146a$^{-/-}$/hTNFtg mice.** A, Expression level of IRAK1 in hind paws from hTNFtg (n = 5) and miR-146a$^{-/-}$/hTNFtg (n = 5) animals. B, Expression level of RelB in hind paws from hTNFtg (n = 8) and miR-146a$^{-/-}$/hTNFtg (n = 4) animals were analyzed using quantitative real time PCR. Results are shown as mean ± SEM.



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S6. **Schematically illustration of miR-146a regulatory function in synovial fibroblasts**. MiR-146a acts as a negative regulator of proliferation and RANKL production in synovial fibroblasts, through controlling the target TRAF6 in the NF-κB signaling pathway.

Gene	Sequence
TRAF6	5'-AAAGCGAGAGATTCTTTCCCTG-'3
	5'-ACTGGGGACAATTCACTAGAGC-'3
IRAK1	5'-GACCAAGTATTTGAAAGACCTG-'3
	5'-GTAGTGCCTCCCTGGGTACA-'3
RelB	5'-GCTGGGAATTGACCCCTACA-'3
	5'-CATGTCGACCTCCTGATGGTT-'3
OPG	5'-TACCTGGAGATCGAATTCTGCTT-'3
	5'-CCATCTGGACATTTTTTGCAAA-'3
RANKL	5'-TCGTGGAACATTAGCATGGA-'3
	5'-CCTCTCCCAATCTGGTTCAA-'3
GAPDH	5'-TGGCATTGTGGAAGGGCTCATGAC-'3
	5'-ATGCCAGTGAGCTTGCCGTTCAGC -'3

Supplementary Table 1. Primers used for real time PCR.