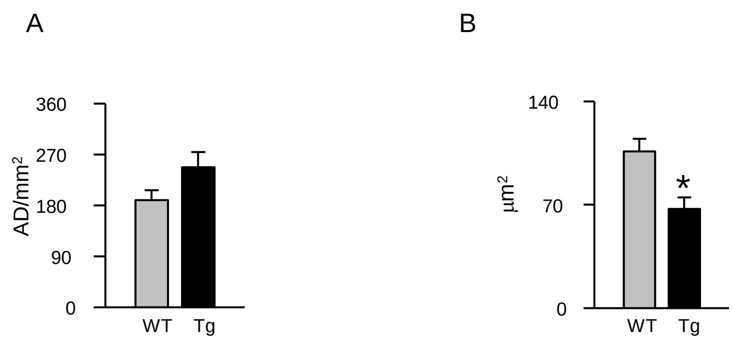


**Supplemental Figure 1. Adipocytes in proximal tibia.** A. Number of adipocytes. B. Average area of single adipocyte. * $p < 0.05$

**Supplemental Table 1.** Primers used for determination of gene expression in real-time q-PCR.

| Gene | Forward (5'→3') | Reverse (5'→3') |
|---|---|---|
| 18S | TTCGAACGTCTGCCCTATCAA | ATGGTAGGCACGGCGACTA |
| FoxC2 | CACCGGCTGGGGATTGAG | ATAGAGAGGCGGCGTGGAT |
| Prdm16 | CCTAACTTTCCCCACTCCCTTA | GCTCAGCCTTGACCAGCAA |
| B3AR | GGCACAGGAATGCCACTCCAAT | AGGAGGGGAAGGTAGAAGGAGAC |
| UCP1 | GCAACTTGGAGGAAGAGATACTGAA | TGTAAATAAAGTCAACGGAGCTGTTC |
| Dio2 | AAATGACCCCTTTGGTTTCC | TTCCCCATTATCCTTTCC |
| IRS1 | CCAGCCTGGCTATTTAGCTG | CCCAACTCAACTCCACCACT |
| Socs3 | CCTTTGACAAGCGGACTCTC | GGTTATTTCTTTGGCCAGCA |
| CyclinD1 | CCAGAGGCGGATGAGAACAA | GGCACAGAGGGCCACAAA |
| Dlx5 | TGACAGGAGTGTTTGACAGAAGAGT | CGGGAACGGAGCTTGGA |
| Osteocalcin | CGGCCCTGAGTCTGACAAA | GCCGGAGTCTGTTCACTACCTT |
| SOST | CCTCCTCCTGAGAACAACCA | ACATCTTTGGCGTCATAGGG |
| Dmp1 | TGTCATTCTCCTTGTGTTCCTTTG | AGAGCTTTCAGATTCAGTATTGTGGTAT |
| RANKL | CCTGAGGCCCAGCCATTT | CTTGGCCCAGCCTCGAT |
| IGFBP2 | CTGTGACAAGCATGGCCGGT | AGCTCCCTGGATGGGCTTCCC |
| Wnt10b | AATGAAGGTGAGCCTCGCC | TGAAAGAGAGCAGCCCTCACA |
| IGF1 | AATTTGGCCTCCTTAAGAGCAA | ATGCCACAGATGGAGTCAGGT |
| Adiponectin | GGCCGTTCTCTTCACCTACG | TGGAGGAGCACAGAGCCAG |
| BMP4 | TCAAGGGAGTGGAGATTGGG | GCCATCATGGCCAAAAGTG |
| Angiopoietin2 | GCATGACCTAATGGAGACCGT | GATAGCAACCGAGCTCTTGGAG |

**Supplemental Table 2.** mCT analysis of bone derived from 2 and 5 mo old $FoxC2_{AD}^{+/Tg}$ and WT mice.

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 mo | | 5 mo | | 2 mo | | 5 mo | |
| | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ |
| | N = 7 | N = 8 | N = 8 | N = 8 | N = 5 | N = 5 | N = 8 | N = 10 |
| *Proximal Tibia* | | | | | | | | |
| TV ($mm^3$) | 2.341 (0.449) | 2.928$^{A}$ (0.339) | 2.353 (0.312) | 2.804 (0.280) | 3.176 (0.193) | 3.784 (0.185) | 2.943 (0.384) | 3.540 (0.400) |
| BV ($mm^3$) | 0.068 (0.022) | 0.141$^{A}$ (0.035) | 0.064 (0.018) | 0.128$^{A,B}$ (0.034) | 0.096 (0.034) | 0.161$^{A}$ (0.015) | 0.157 (0.017) | 0.309$^{A,B,C}$ (0.090) |
| BV/TV (%) | 2.84 (0.537) | 4.83$^{A}$ (1.029) | 2.71 (0.615) | 4.62$^{A,B}$ (1.453) | 2.98 (0.953) | 4.24$^{A}$ (0.354) | 5.58$^{B}$ (1.187) | 8.63$^{A,B,C}$ (1.528) |
| Conn.D | 125.8 | 412.8$^{A}$ | 89.9 | 159.9$^{C}$ | 93.3 | 353.6$^{A}$ | 356.2$^{B}$ | 621.1$^{B}$ |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| (1/mm$^3$) | (69.4) | (176.0) | (38.1) | (65.1) | (78.6) | (63.0) | (89.0) | (218.6) |
| SMI | 3.443 | 3.132 | 3.124 | 2.387$^{A,B,C}$ | 3.640 | 3.578 | 2.364$^{B}$ | 2.068$^{B,C}$ |
| | (0.250) | (0.268) | (0.283) | (0.222) | (0.205) | (0.091) | (0.215) | (0.100) |
| Tb.N (1/mm) | 2.854 | 3.338$^{A}$ | 2.272$^{B}$ | 1.914$^{A,B,C}$ | 4.047 | 4.396 | 3.825 | 4.385$^{A}$ |
| | (0.294) | (0.368) | (0.448) | (0.362) | (0.200) | (0.334) | (0.394) | (0.170) |
| Tb.Th (mm) | 0.023 | 0.024 | 0.032$^{B}$ | 0.038$^{A,B,C}$ | 0.021 | 0.021 | 0.029$^{B}$ | 0.03$^{B,C}$ |
| | (0.003) | (0.003) | (0.002) | (0.004) | (0.002) | (0.001) | (0.002) | (0.000) |
| Tb.Sp (mm) | 0.358 | 0.309$^{A}$ | 0.473$^{B}$ | 0.555$^{A,B,C}$ | 0.256 | 0.232 | 0.267 | 0.233$^{A}$ |
| | (0.036) | (0.036) | (0.123) | (0.090) | (0.018) | (0.019) | (0.029) | (0.010) |
| *Cortical bone in tibia metaphysis* | | | | | | | | |
| CtAr (mm$^2$) | 0.186 | 0.198 | 0.195 | 0.207 | 0.196 | 0.187 | 0.258$^{B}$ | 0.262$^{B,C}$ |
| | (0.017) | (0.026) | (0.081) | (0.085) | (0.021) | (0.014) | (0.022) | (0.030) |
| CtTh (mm) | 0.166 | 0.165 | 0.189 | 0.183 | 0.162 | 0.155 | 0.197$^{B}$ | 0.192$^{B,C}$ |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | (0.011) | (0.019) | (0.019) | (0.017) | (0.008) | (0.003) | (0.011) | (0.014) |
| MdAr ($mm^2$) | 0.156 | 0.174 | 0.138 | 0.214[A] | 0.180 | 0.188 | 0.195 | 0.213 |
| | (0.014) | (0.013) | (0.053) | (0.050) | (0.023) | (0.016) | (0.005) | (0.030) |
| *Vertebral body (L4 lumbar vertebra)* | | | | | | | | |
| TV ($mm^3$) | 1.442 | 1.840 | 2.436[B] | 2.986[B,C] | 1.937 | 2.138 | 2.558[B] | 2.847[B,C] |
| | (0.567) | (0.493) | (0.480) | (0.579) | (0.030) | (0.153) | (0.136) | (0.283) |
| BV ($mm^3$) | 0.024 | 0.060[A] | 0.153[B] | 0.234[B,C] | 0.042 | 0.066[A] | 0.164[B] | 0.216[B,C] |
| | (0.010) | (0.015) | (0.056) | (0.073) | (0.009) | (0.007) | (0.027) | (0.013) |
| BV/TV (%) | 1.70 | 3.45[A] | 6.16[B] | 7.75[B,C] | 2.18 | 3.09[A] | 6.47[B] | 7.65[B,C] |
| | (0.21) | (1.14) | (1.41) | (1.52) | (0.961) | (0.952) | (1.42) | (1.99) |
| Tb.N (1/mm) | 2.840 | 4.019[A] | 2.850 | 3.394[A,B] | 3.963 | 4.920[A] | 4.443[B] | 5.102[A,B] |
| | (0.365) | (0.462) | (0.407) | (0.287) | (0.303) | (0.272) | (0.265) | (0.141) |
| Tb.Th (mm) | 0.025 | 0.027 | 0.036[B] | 0.035[B,C] | 0.023 | 0.023 | 0.030[B] | 0.029[B,C] |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | (0.005) | (0.003) | (0.003) | (0.002) | (0.001) | (0.001) | (0.002) | (0.001) |
| Tb.Sp (mm) | 0.358<br>(0.046) | 0.252[A]<br>(0.026) | 0.361<br>(0.048) | 0.301[A,B,C]<br>(0.026) | 0.253<br>(0.018) | 0.203[A]<br>(0.011) | 0.227<br>(0.014) | 0.196[A,B]<br>(0.006) |

Values in parentheses correspond to ± SD. [A] $p < 0.05$ *vs*. age-matched WT control; [B] $p < 0.05$ *vs*. 2 mo old WT; [C] $p < 0.05$ 2 mo vs 5 mo old $FoxC2_{AD}^{+/Tg}$

**Supplemental Table 3.** MicroCT-based determination of moment of inertia

| | Females | | | | Males | | | |
|---|---|---|---|---|---|---|---|---|
| | 2 mo | | 5 mo | | 2 mo | | 5 mo | |
| | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ | WT | $FoxC2_{AD}^{+/Tg}$ |
| | N = 5 | N = 5 | N = 5 | N = 5 | N = 5 | N = 5 | N = 5 | N = 5 |
| pMOI | 0.091 | 0.101 | 0.188 | 0.238[A] | 0.117 | 0.112 | 0.185 | 0.201 |
| ($mm^4$) | (0.020) | (0.018) | (0.021) | (0.026) | (0.026) | (0.019) | (0.023) | (0.048) |
| Imin/Cmin | 0.077 | 0.084 | 0.130 | 0.140 | 0.091 | 0.088 | 0.119 | 0.128 |
| ($mm^3$) | (0.009) | (0.009) | (0.011) | (0.015) | (0.014) | (0.008) | (0.009) | (0.021) |
| Imax/Cmax | 0.087 | 0.094 | 0.151 | 0.181[A] | 0.104 | 0.104 | 0.154 | 0.160 |
| ($mm^3$) | (0.019) | (0.015) | (0.013) | (0.010) | (0.021) | (0.016) | (0.014) | (0.030) |

pMOI (polar moment of inertia) indicates torsional strength along the bone; Imin/Cmin indicates bending strength across the bone along the minimal centroid-edge distance; Imax/Cmax indicates bending strength across the bone along the maximal centroid-edge distance. Values in parentheses correspond to ± SD. [A] $p < 0.05$ *vs.* age-matched WT control.