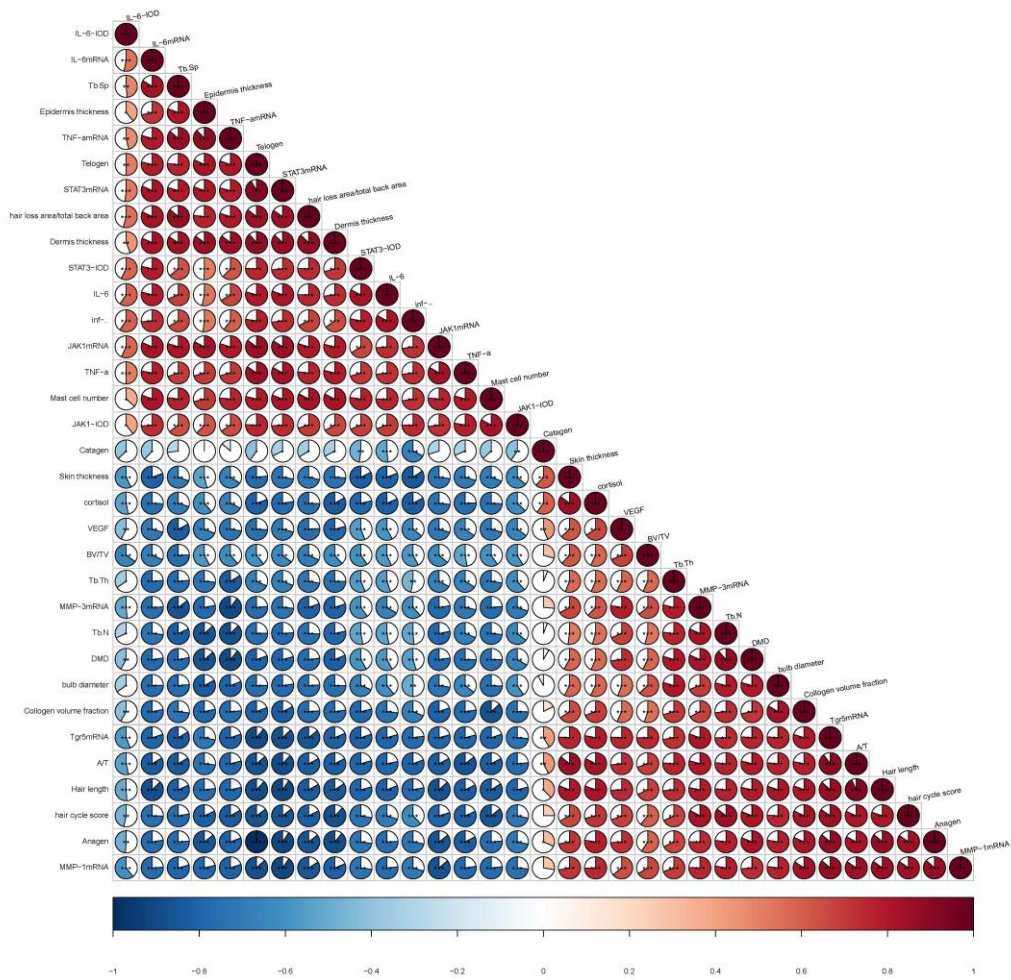
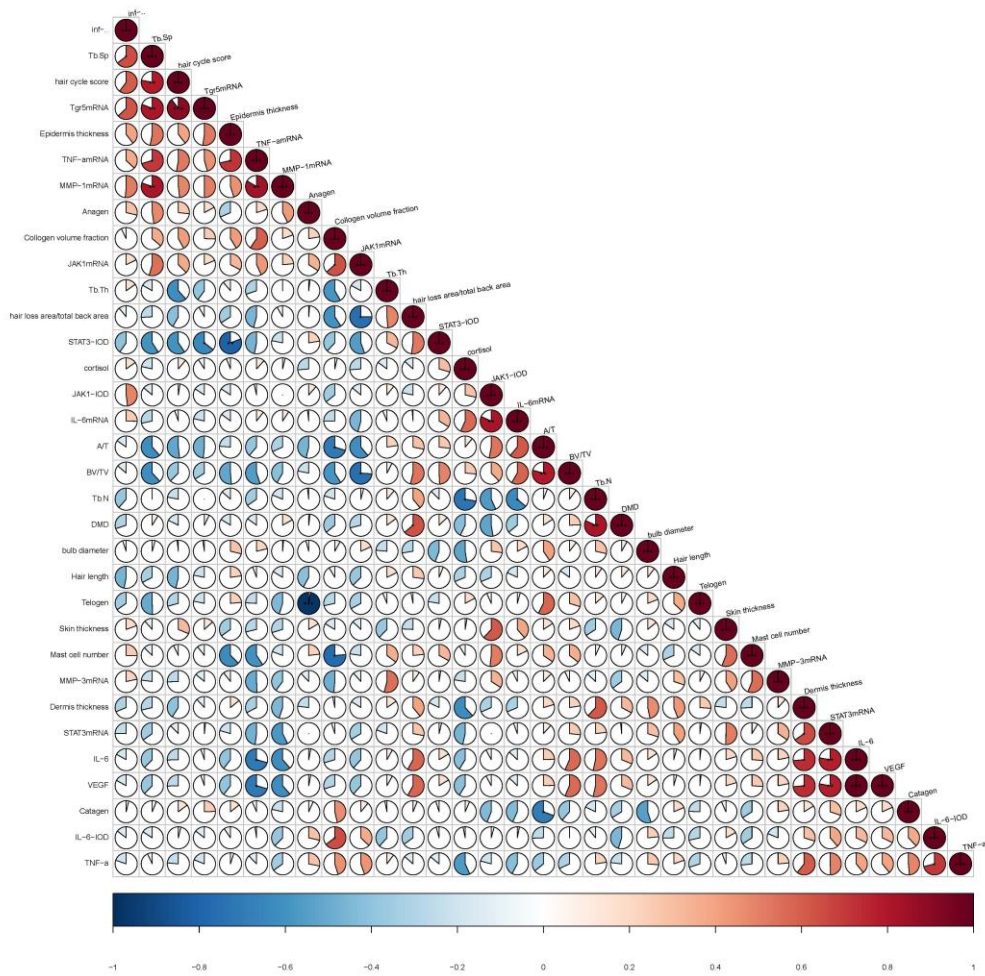


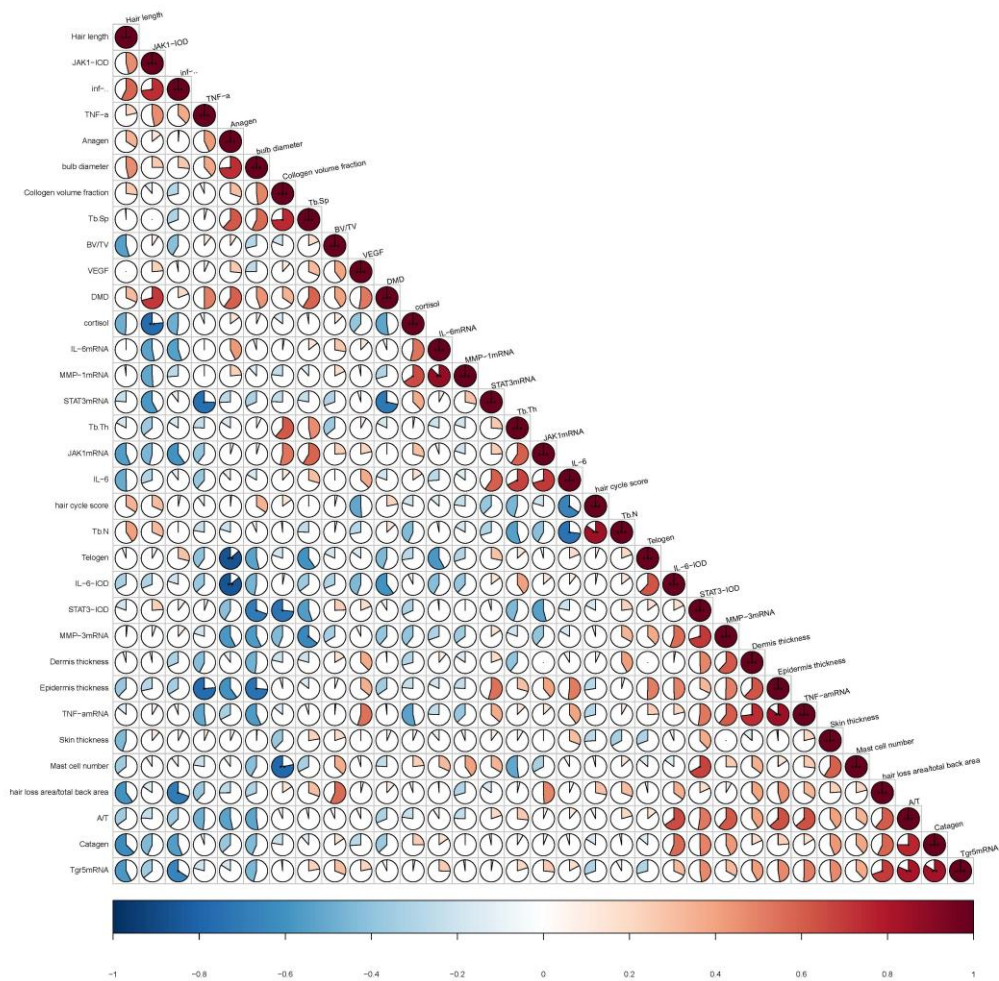
**Supplement Figure 1** Correlation of Tgr5 and AA, Osteoporosis in Tgr5<sup>-</sup> mice. **(A)** Lines show correlations based on Spearman’s rank analysis with  $p < 0.05$ , with line thickness proportional to the correlation strength. **(B)** Venn diagrams comparing unique and shared Correlations between WT group, WT+INT777 group, KO group, KO+INT777 group. **(C)** Principal coordinate analysis. **(D)** Primary “first neighbor” network of skin thickness. Data are expressed as the means  $\pm$  standard deviation. One-way ANOVA followed by Tukey’s multiple tests has been used.  $n=10$  per group. WT: wild type, KO: Knock Out. IOD: integrated Optical Density.



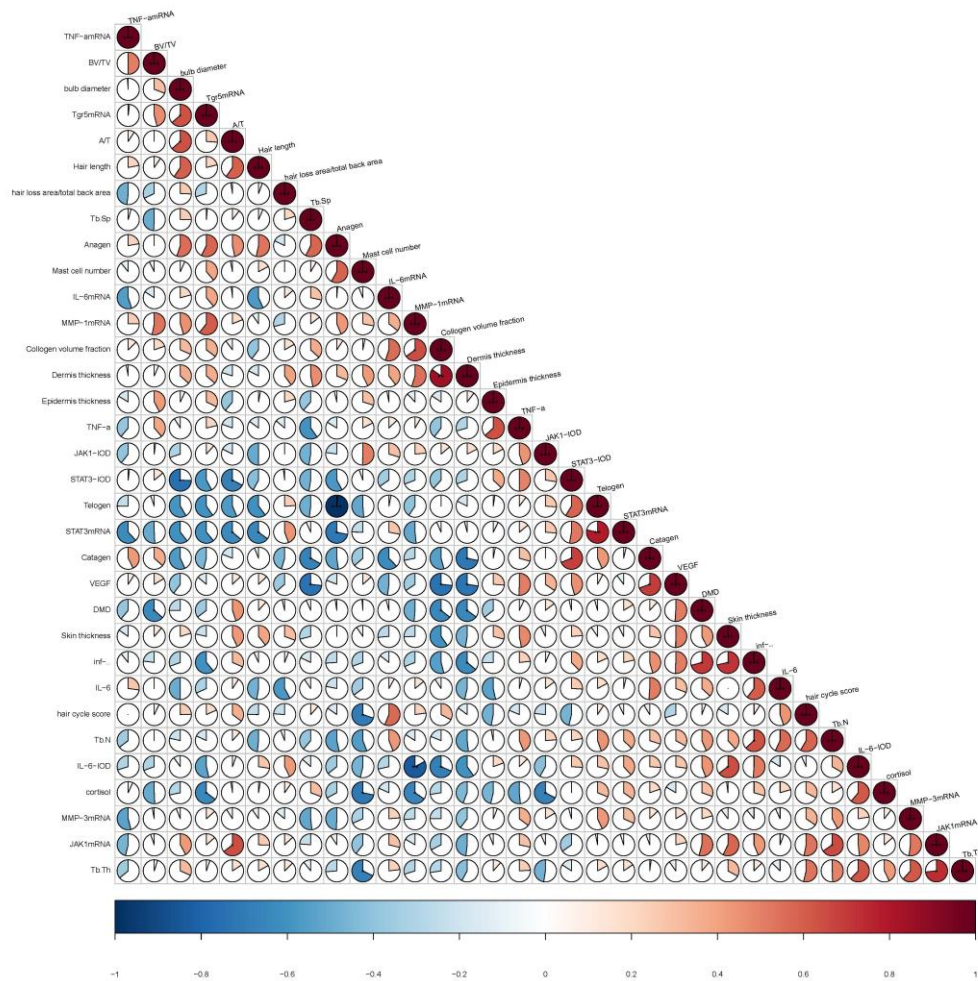
**Supplement Figure 2** The detailed correlation networks of All groups.\*  $P < 0.05$ , \*\* $P < 0.01$ . IL-6, Interleukin-6. IOD, integrated optical density. TNF- $\alpha$ , tumor necrosis factor- $\alpha$ . STAT3, Signal transducer, and activator of transcription 3. VEGF, vascular endothelial growth factor. IFN- $\gamma$ , interferon- $\gamma$ . Tgr5: G-protein-coupled bile acid receptor-5. JAK1, Janus kinase1. MMP-1: matrix metalloproteinase-1. MMP-3: matrix metalloproteinase-3.



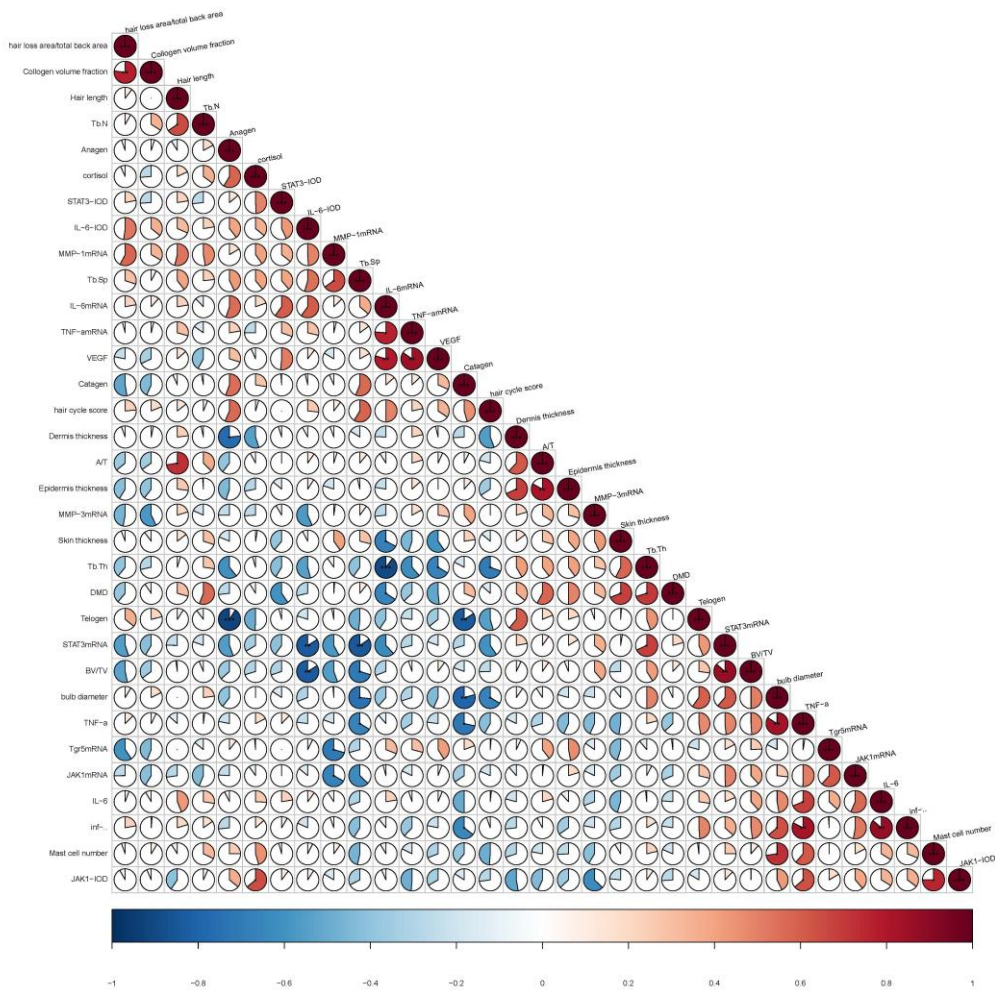
**Supplement Figure 3** The detailed correlation networks of the WT group. n=10 per group. \*  $P < 0.05$ , \*\*  $P < 0.01$ . IL-6, Interleukin-6. IOD, integrated optical density. TNF- $\alpha$ , tumor necrosis factor- $\alpha$ . STAT3, Signal transducer, and activator of transcription 3. VEGF, vascular endothelial growth factor. INF- $\gamma$ , interferon- $\gamma$ . Tgfr5: G-protein-coupled bile acid receptor-5. JAK1, Janus kinase1. MMP-1: matrix metalloproteinase-1. MMP-3: matrix metalloproteinase-3.



**Supplement Figure 4** The detailed correlation networks of WT+INT777 group. \*  $P < 0.05$ , \*\*  $P < 0.01$ . IL-6, Interleukin-6. IOD integrated optical density. TNF- $\alpha$ , tumor necrosis factor- $\alpha$ . STAT3, Signal transducer, and activator of transcription 3. VEGF, vascular endothelial growth factor. INF- $\gamma$ , interferon- $\gamma$ . Tgr5: G-protein-coupled bile acid receptor-5. JAK1, Janus kinase1. MMP-1: matrix metalloproteinase-1. MMP-3: matrix metalloproteinase-3.



**Supplement Figure 5** The detailed correlation networks of the KO group. \*  $P < 0.05$ , \*\*  $P < 0.01$ . IL-6, Interleukin-6. IOD integrated optical density. TNF- $\alpha$ , tumor necrosis factor- $\alpha$ . STAT3, Signal transducer, and activator of transcription 3. VEGF, vascular endothelial growth factor. INF- $\gamma$ , interferon- $\gamma$ . Tgr5: G-protein-coupled bile acid receptor-5. JAK1, Janus kinase1. MMP-1: matrix metalloproteinase-1. MMP-3: matrix metalloproteinase-3.



**Supplement Figure 6** The detailed correlation networks of the KO+INT777 group. \*  $P < 0.05$ , \*\*  $P < 0.01$ . IL-6, Interleukin-6. IOD integrated optical density. TNF- $\alpha$ , tumor necrosis factor- $\alpha$ . STAT3, Signal transducer, and activator of transcription 3. VEGF, vascular endothelial growth factor. INF- $\gamma$ , interferon- $\gamma$ . Tgr5: G-protein-coupled bile acid receptor-5. JAK1, Janus kinase1. MMP-1: matrix metalloproteinase-1. MMP-3: matrix metalloproteinase-3.

Supplement Table 1: Primer Sequences used for RT-qPCR

	Forward primer sequences	Reverse primer sequences
GAPDH	5'-AACTTTGGCATTGTGGAAGG-3'	5'ACACATTGGGGGTAGGAACA-3'
JAK1	5'- - TGCACCGACTTTGACAACATT-3'	5'TGAGGTGGTTCATGAGGTCTC-3'
STAT3	5'-TGGGCATCAATCCTGTGGTAT -3'	5'- - TAGTTCACACCAGGCCCTAAG-3'
MMP-1	5'CAGAGATGAAGTCCGGTTTTTC-3'	5'-GGGGTATCCGTGTAGCACAT-3'
TNF-a	5'- AGGCTGCCCCGACTACGT-3'	5'- GACTTTCTCCTGGTATGAGATAG CAA-3'
IL-6	5'-GGCGGATCGGATGTTGTGAT-3'	5'-GGACCCCAGACAATCGGTTG-3'
MMP-3	5'-GTCCTCCACAGACTTGTCCC-3'	5'-AGGACATCAGGGGATGCTGT-3'
TGR5	5'-CCCAACUUCUCCUCCUCUTT-3'	3'-AGAGGAAGGAGAAGUUGGGTT-5'

Supplement Table 2: the Tgr5 mRNA level in the rescue experiment

	WT group	KO group
Left tibia	1.156±0.098	0.141±0.051**
Tail	1.026±0.105	0.122±0.032*
Skin	1.119±0.163	0.195±0.072**

\* Compare with WT group, \*  $P < 0.05$ , \*\*  $P < 0.01$