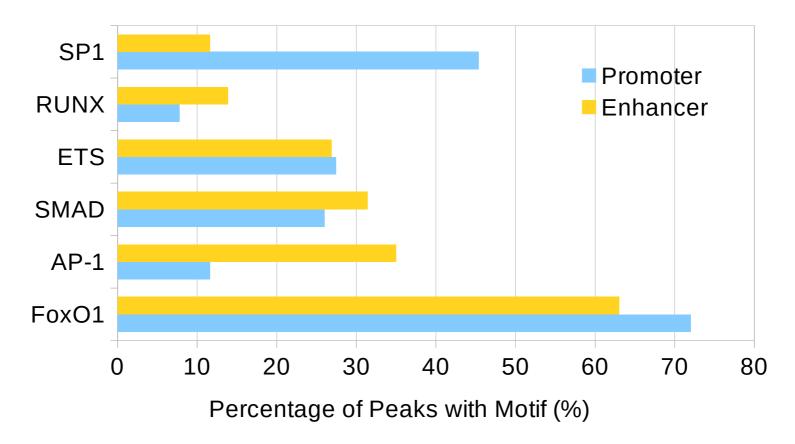


Suppl Figure S1. Heatmap of Pearson's correlation between FOXO1 ChIP-seq replicates from human primary chondrocytes.

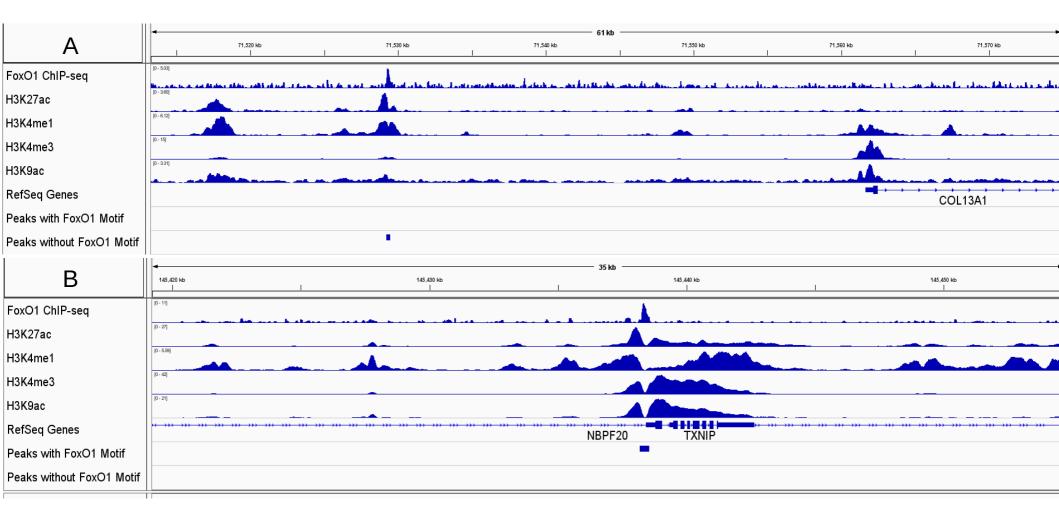
Rank Motif	P-value	log P-pvalue	% of Targets	% of Background	STD(Bg STD)	Best Match/Details
I ETGASTCASE	1e-230	-5.304e+02	36.04%	4.92%	51.3bp (64.9bp)	JunB(bZIP)/DendriticCells-Junb-ChIP-Seq(GSE36099)/Homer(0.989) <u>More Information</u> <u>Similar Motifs Found</u>
	1e-146	-3.378e+02	50.75%	17.15%	46.6bp (68.7bp)	PB0120.1_Foxj1_2/Jaspar(0.771) More Information Similar Motifs Found
3 TATTTACE	1e-41	-9.507e+01	15.95%	5.05%	47.2bp (58.9bp)	FOXD2/MA0847.1/Jaspar(0.838) More Information Similar Motifs Found
4 TGAEGEAA	1e-33	-7.661e+01	36.21%	20.58%	55.8bp (64.6bp)	CEBP:AP1(bZIP)/ThioMac-CEBPb-ChIP-Seq(GSE21512)/Homer(0.9 <u>More Information</u> <u>Similar Motifs Found</u>
5 ZACÊGGAA	1e-33	-7.631e+01	61.85%	43.95%	54.9bp (63.3bp)	MF0001.1_ETS_class/Jaspar(0.920) More Information Similar Motifs Found
6 ATTCTTGGCAAT	1e-22	-5.273e+01	12.25%	4.76%	54.2bp (63.4bp)	NFIC/MA0161.2/Jaspar(0.801) More Information Similar Motifs Found

Suppl Figure S2. de novo motif discovery at FOXO1 peaks without a canonical FOXO1 binding motif.

Fifty percent of the peaks without a canonical FOXO1 binding motif have a truncated FOXO1binding motif (motif 2).

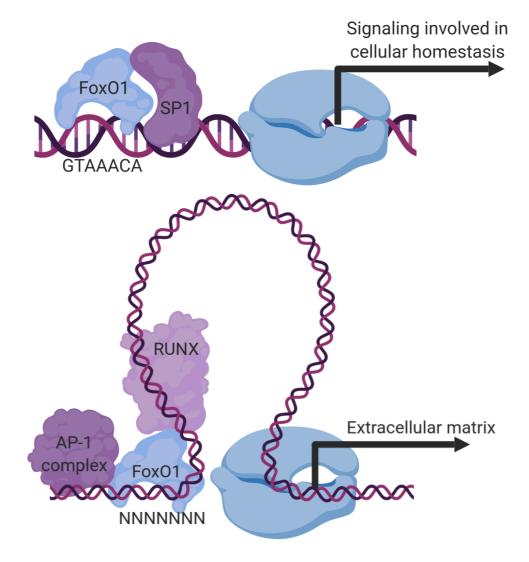


Suppl Figure S3. Distinct motif enrichment at FOXO1 occupied promoters and enhancers.



Suppl Figure S4. FOXO1 regulates distinct transcriptional programs at the promoter and enhancer levels.

- A) Chondrocyte-specific ACAN is regulated at the enhancer level with a combination of peaks with and without FOXO1 canonical binding motif.
- B) Ubiquitous TXNIP is regulated at the promoter level with a FOXO1 binding motif.



Suppl Figure S5. Schematic for distinct mechanisms by which FOXO1 regulates tissue specific and ubiquitous target genes.