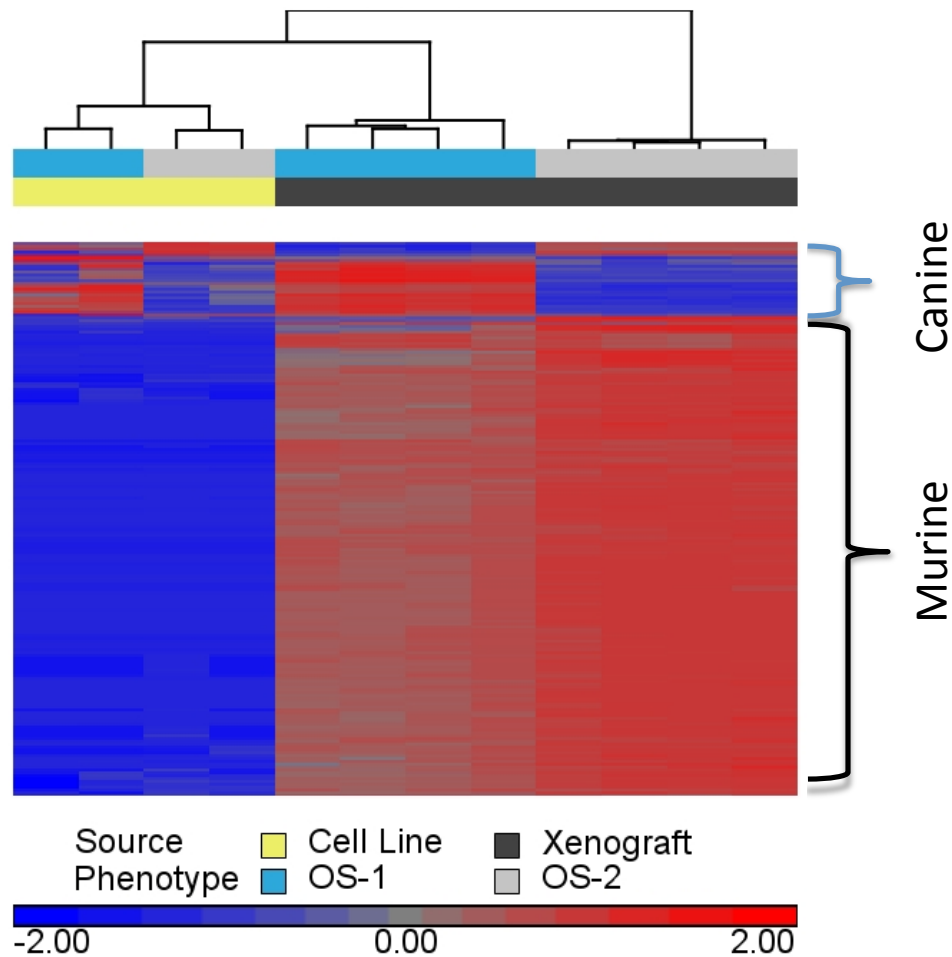


Supplementary Materials

**Fig.S1. Hierarchical clustering of tumor xenografts and parent cell lines with canine**

and murine genes. Log-transformed and mean-centered counts per million (CPM) values for 47,997 canine and murine genes in xenograft and parental cell line samples were filtered to remove genes that did not have a \log_2 CPM mean-centered value ≥ 3 in at least two samples. Expectantly, through this filtering step most of the canine genes were excluded while murine genes were included. Unsupervised hierarchical clustering with counts per million values for the remaining 13,968 canine and murine genes indicated that expression levels of murine genes in canine cell lines was absent in comparison to the tumor xenografts, suggesting that murine genes can be properly differentiated from the canine genes in xenografts.

Table S1. OS-1 and OS-2 Orthotopic Xenografts Show Differential Rate of Tumor Progression¹

Change in Volume (Affected tibia - Unaffected tibia)			<i>p-value</i>
Time	OS-1 n=16	OS-2 n=32	
Day 8 Median Mean (SD)	-8.03 -10.47 (18.6)	8.17 4.61 (18.8)	
Day 15 Median Mean (SD)	-15.94 -13.87 (16.4)	-1.02 0.86 (21.8)	
Day 22 Median Mean (SD)	1.45 0.83 (20.0)	9.36 9.9 (16.2)	
Day 29 Median Mean (SD)	1.54 3.73 (18.0)	42.25 38.27 (26.0)	p<0.001
Day 36 Median Mean (SD)	12.42 17.60 (33.7)	61.84 67.37 (38.8)	p<0.001
Day 43 Median Mean (SD)	39.62 35.31 (30.0)	75.89 86.46 (53.2)	p<0.01
Day 50 Median Mean (SD)	69.41 90.14 (85.7)	107.79 122.99 (65.74)	
Day 57 Median Mean (SD)	137.22 140.3 (109)	126.13 136.5 (78.6)	

¹Change in volume was calculated by subtracting the normal bone tissue volume of the contralateral unaffected (right) tibia from the volume of the affected (left) tibia. Statistically significant differences in tumor size were determined using multiple *t*-test and the Holm-Sidak method.

Table S2. List of differentially expressed murine genes in OS-2 relative to OS-1 xenografts. Fold change (FC), p values, and FDR-adjusted p values were calculated by pair-wise Exact Test comparisons in EdgeR (see Fig. 5 legend). Genes were annotated with the Ingenuity Knowledge Base of IPA.

[Click here to Download Table S2](#)

Table S3. Upstream regulators of differentially expressed murine genes in OS-2 relative to OS-1 xenograft tumors.¹

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	<i>p</i> -value of overlap
MTF1	transcription regulator	Activated	2.391	1.01E-08
CEBPA	transcription regulator	Activated	2.598	1.16E-08
ELK1	transcription regulator	Activated	2.000	1.39E-02
ARNT	transcription regulator	Activated	2.408	1.72E-03
XBP1	transcription regulator	Activated	2.155	1.88E-01
RELA	transcription regulator	Activated	2.372	2.30E-05
MDM2	transcription regulator	Activated	2.000	2.32E-02
KDM5A	transcription regulator	Activated	3.742	2.45E-07
NUPR1	transcription regulator	Activated	2.887	2.75E-01
IRF8	transcription regulator	Activated	2.223	2.86E-02
NFKB1	transcription regulator	Activated	2.201	3.94E-09
STAT4	transcription regulator	Activated	2.472	5.06E-06
CEBPD	transcription regulator	Activated	2.566	5.21E-06
CEBPB	transcription regulator	Activated	2.360	5.54E-10
FOXO1	transcription regulator	Activated	2.168	6.85E-04
HIF1A	transcription regulator	Activated	2.777	7.85E-13
RBPJ	transcription regulator	Inhibited	-2.942	1.23E-03
RB1	transcription regulator	Inhibited	-2.765	1.25E-04
MKL2	transcription regulator	Inhibited	-2.646	2.08E-04
MEF2C	transcription regulator	Inhibited	-3.138	2.54E-23
HAND2	transcription regulator	Inhibited	-2.975	2.84E-08
MYOCD	transcription regulator	Inhibited	-2.897	3.86E-08
FOXA2	transcription regulator	Inhibited	-2.578	3.88E-07
SPDEF	transcription regulator	Inhibited	-2.000	3.92E-02
MYOD1	transcription regulator	Inhibited	-3.878	5.83E-12
SIRT1	transcription regulator	Inhibited	-2.336	6.20E-08
CBX5	transcription regulator	Inhibited	-2.236	7.77E-02
PRDM1	transcription regulator	Inhibited	-2.015	8.43E-09
SRF	transcription regulator	Inhibited	-3.050	8.59E-12

¹Differentially expressed murine genes were determined by pair-wise Exact Test comparisons in EdgeR. IPA was used to determine upstream modulators of the 482 differentially expressed genes and their predicted activities. Predicted activity based on gene expression values in OS-2 xenografts relative to OS-1 xenografts. A Z-score >2 indicates activation, while a Z-score < -2 indicates inactivation.

Table S4. Upstream regulators of upregulated murine genes in OS-2.¹

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	<i>p</i> -value of overlap
TGFB1	growth factor	Activated	3.566	1.26E-27
IL1B	cytokine	Activated	4.930	9.70E-25
TNF	cytokine	Activated	5.048	8.53E-23
IL6	cytokine	Activated	4.559	9.03E-22
OSM	cytokine	Activated	3.974	1.76E-19
IL1A	cytokine	Activated	4.571	2.36E-19
IFNG	cytokine	Activated	3.995	5.25E-19
STAT3	transcription regulator	Activated	2.037	4.47E-18
IL17A	cytokine	Activated	4.457	9.76E-18
EGF	growth factor	Activated	4.154	1.28E-17
IL13	cytokine		1.939	1.17E-15
JUN	transcription regulator	Activated	3.486	1.26E-15
NFKBIA	transcription regulator		1.049	3.57E-15
IL4	cytokine		1.418	4.38E-15
IL1	group	Activated	4.111	5.52E-15
HIF1A	transcription regulator	Activated	3.672	6.04E-15
FOS	transcription regulator	Activated	2.013	9.40E-15
IKBKB	kinase	Activated	4.465	1.87E-14
PDGF BB	complex	Activated	4.590	1.95E-14
S100A8	other		0.058	2.41E-14
TREM1	transmembrane receptor	Activated	2.123	2.47E-14
IL17RA	transmembrane receptor	Activated	2.209	7.80E-14
S100A9	other		1.189	1.11E-13
Cg	complex	Activated	2.426	1.31E-13
Tgf beta	group		1.086	3.75E-13
EGFR	kinase	Activated	2.610	6.01E-13
TMEM173	other	Activated	2.611	6.30E-13
NFkB (complex)	complex	Activated	4.286	9.89E-13
TGFBR2	kinase		0.966	1.21E-12

¹Differentially expressed genes were determined by pair-wise Exact Test comparisons in EdgeR (see Fig. 5). IPA was used to determine upstream modulators of the 240-upregulated murine genes in OS-2 xenografts. Predicted activity based on gene expression values in OS-2 xenografts. A Z-score > 2 indicates activation, while a Z-score < -2 indicates inactivation.

Table S5. Upstream regulators of downregulated murine genes in OS-2 relative to OS-1 xenograft tumors.¹

Upstream Regulator	Molecule Type	Predicted Activation State	Activation z-score	<i>p</i> -value of overlap
MEF2C	transcription regulator	Inhibited	-3.503	1.15E-24
MYOD1	transcription regulator	Inhibited	-4.158	2.16E-15
SMTNL1	other	Activated	3.162	7.55E-14
MYOCD	transcription regulator	Inhibited	-3.138	5.36E-09
PTCH1	transmembrane receptor		1.914	5.96E-09
GATA4	transcription regulator	Inhibited	-2.048	6.24E-09
DMD	other		-1.982	1.61E-08
INSR	kinase		-1.009	1.70E-08
HAND2	transcription regulator	Inhibited	-2.804	2.40E-08
NOS2	enzyme	Activated	2.030	3.84E-08
TRPS1	transcription regulator		-1.732	7.29E-08
SRF	transcription regulator	Inhibited	-3.323	9.39E-08
FGF8	growth factor		-1.066	2.30E-07
TBX5	transcription regulator	Inhibited	-2.795	2.65E-07

¹Differentially expressed genes were determined by pair-wise Exact Test comparisons in EdgeR (see Fig. 5). IPA was used to determine upstream modulators of the 242 downregulated murine genes in OS-2 xenografts. Predicted activity based on gene expression values in OS-2 xenografts. A Z-score > 2 indicates activation, while a Z-score < -2 indicates inactivation.