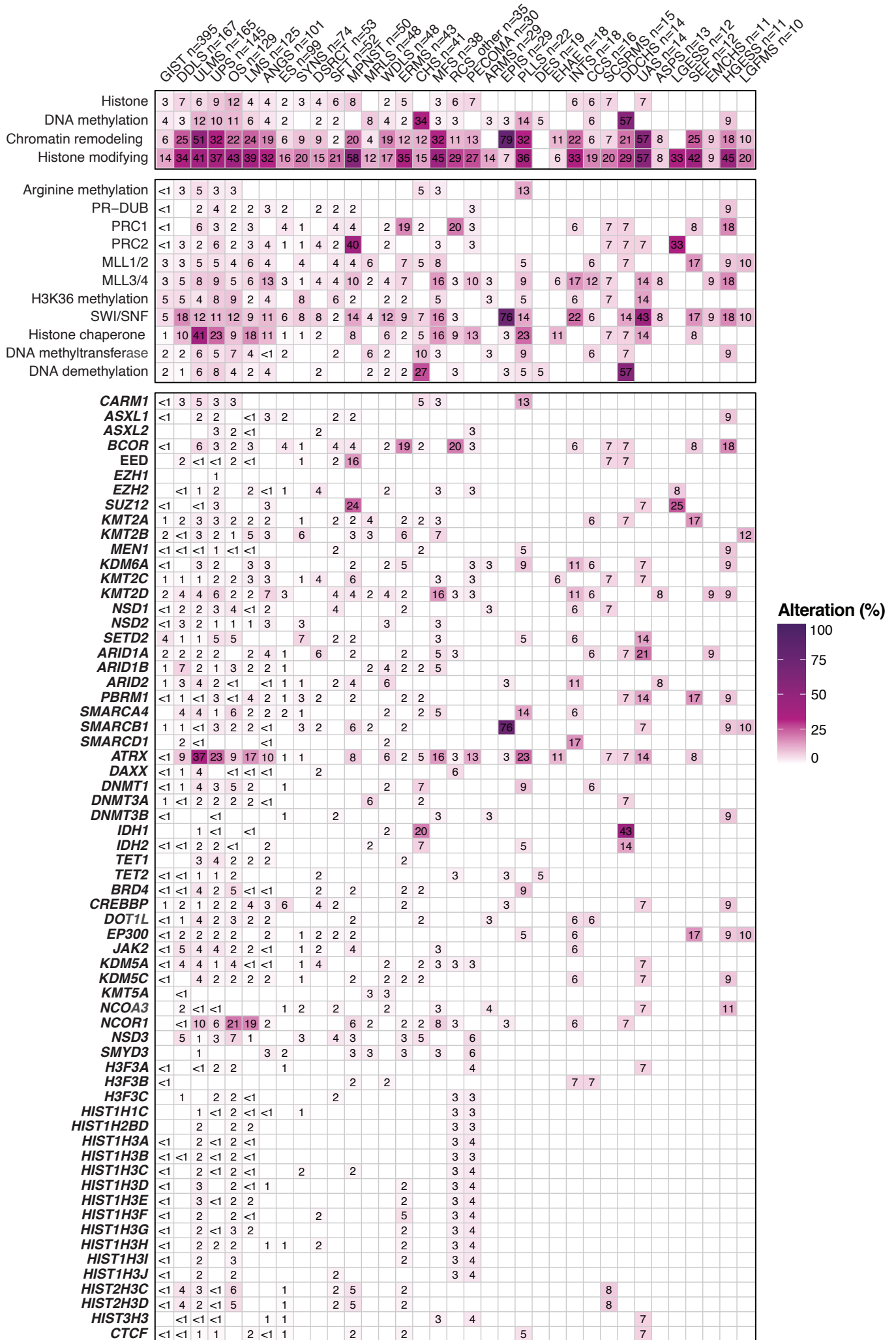
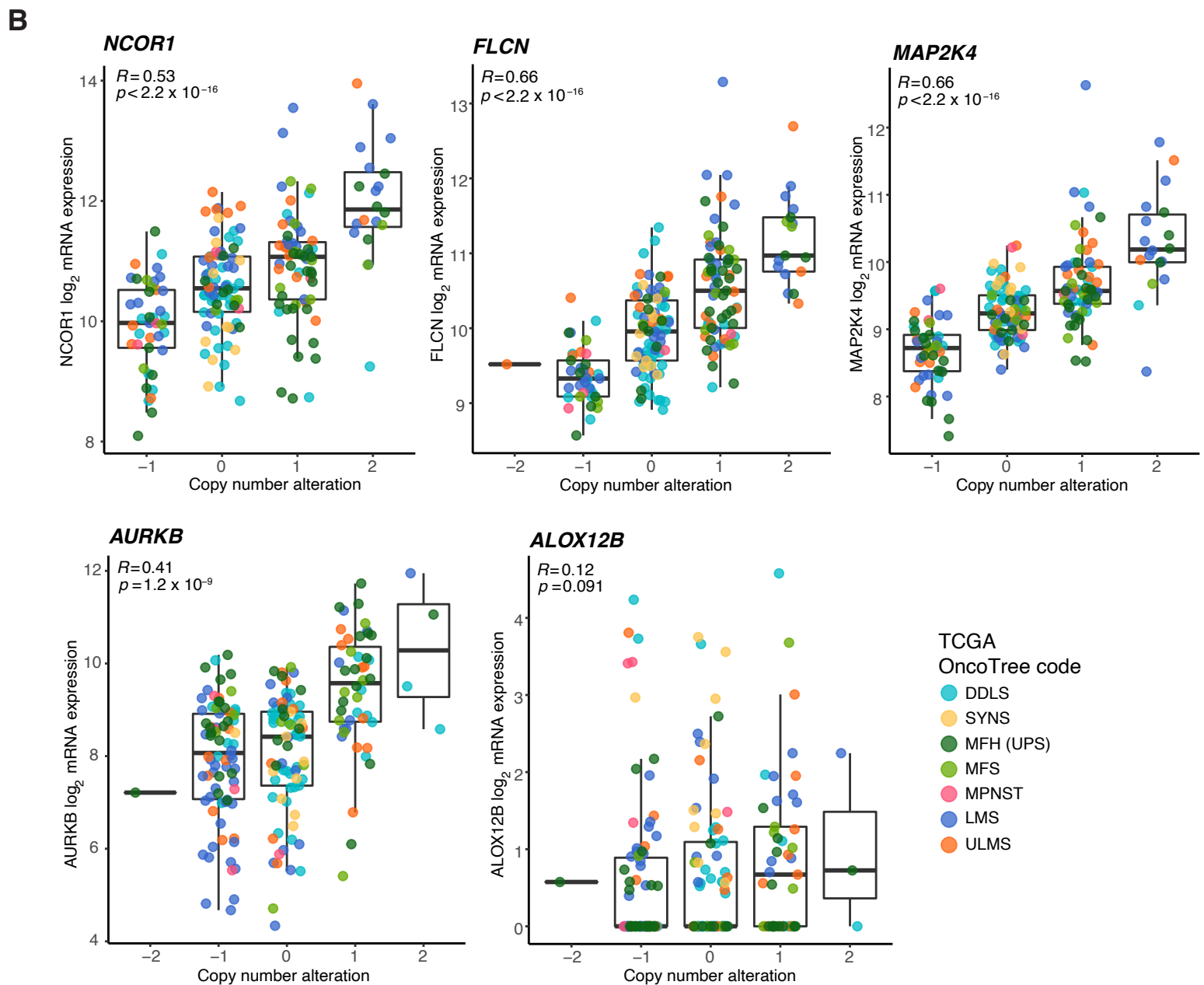
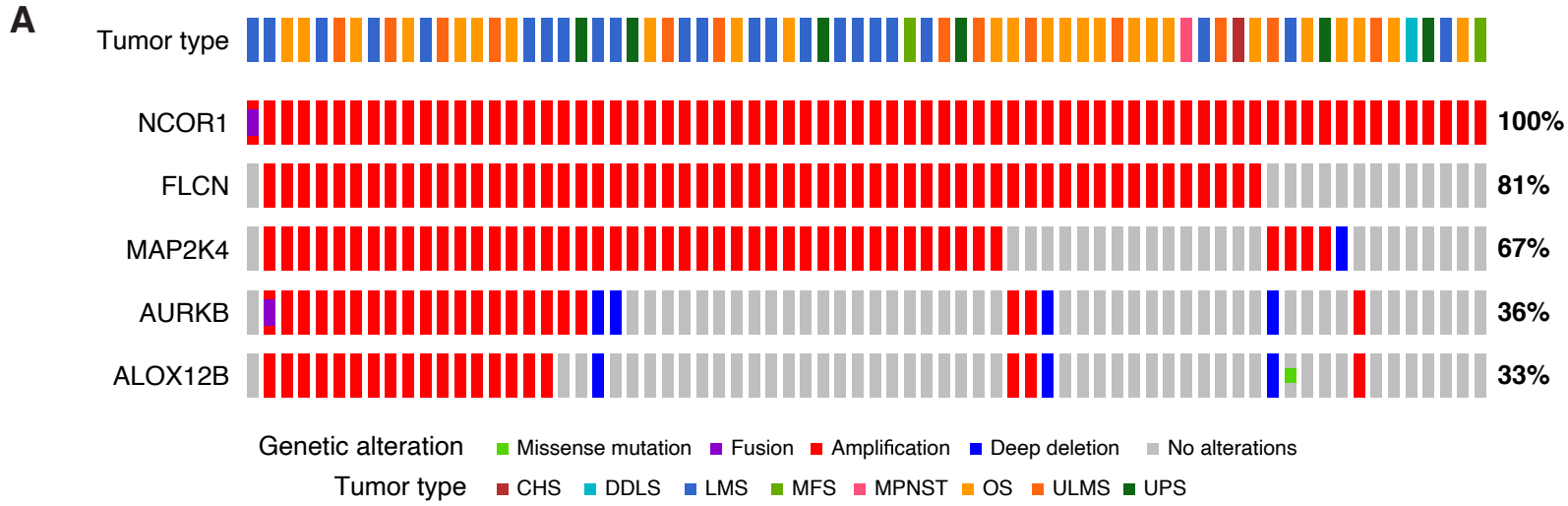


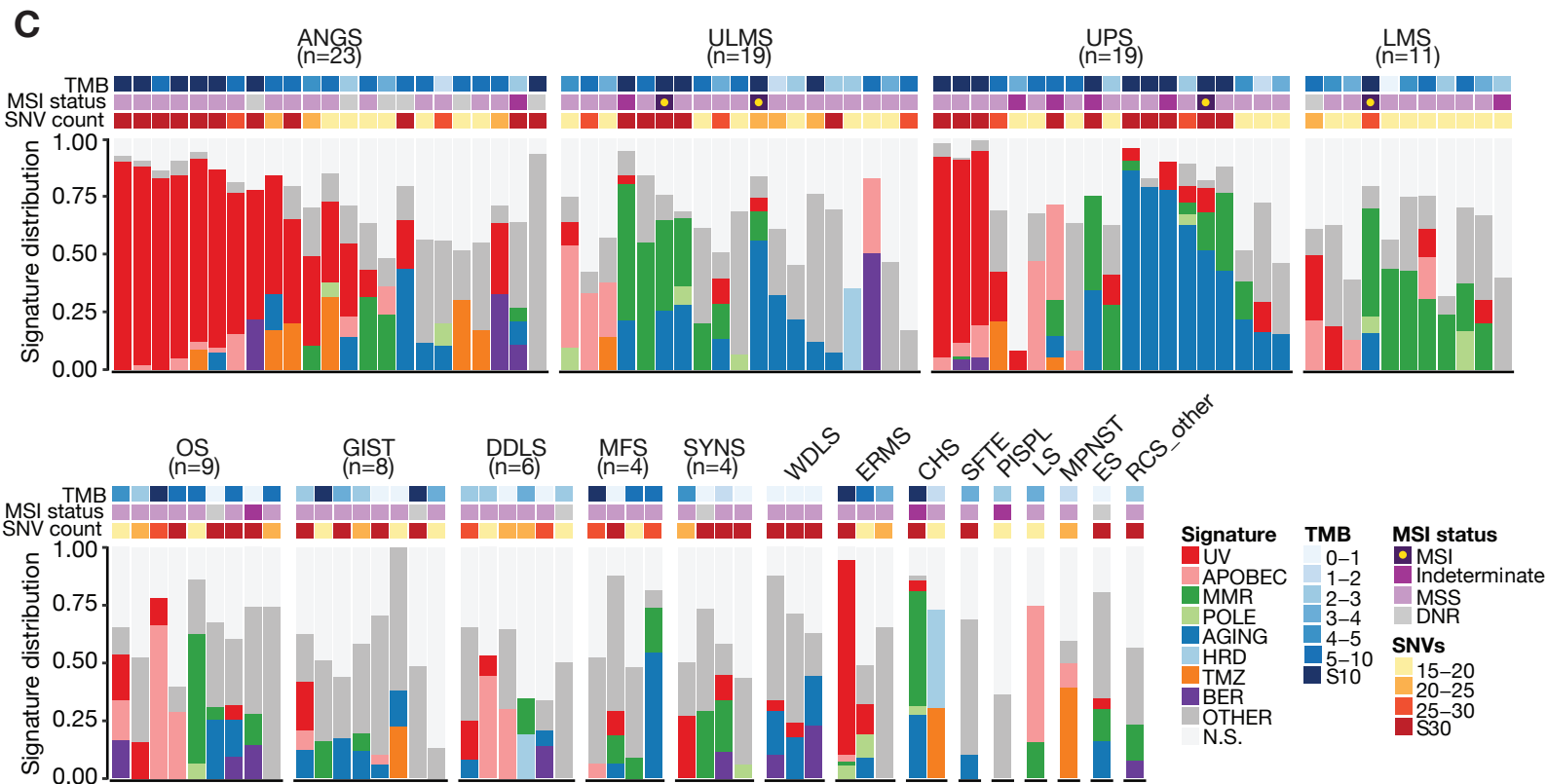
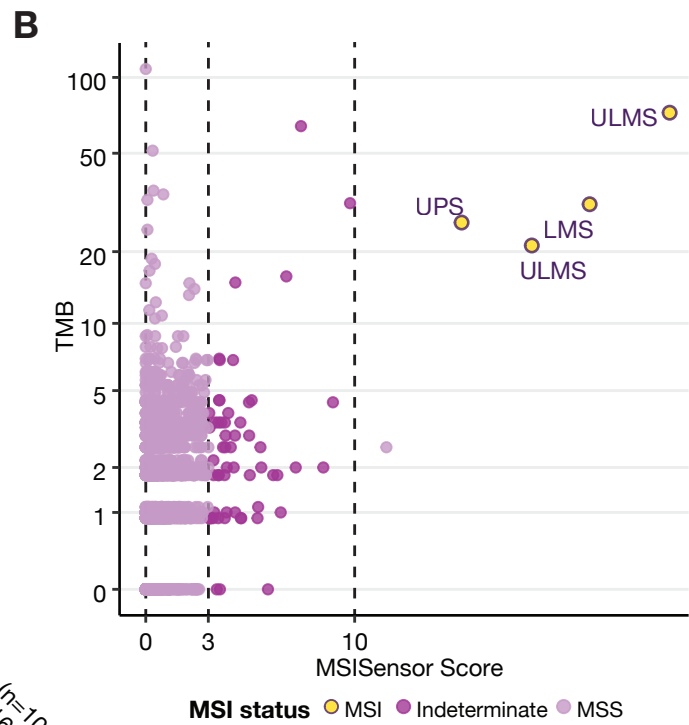
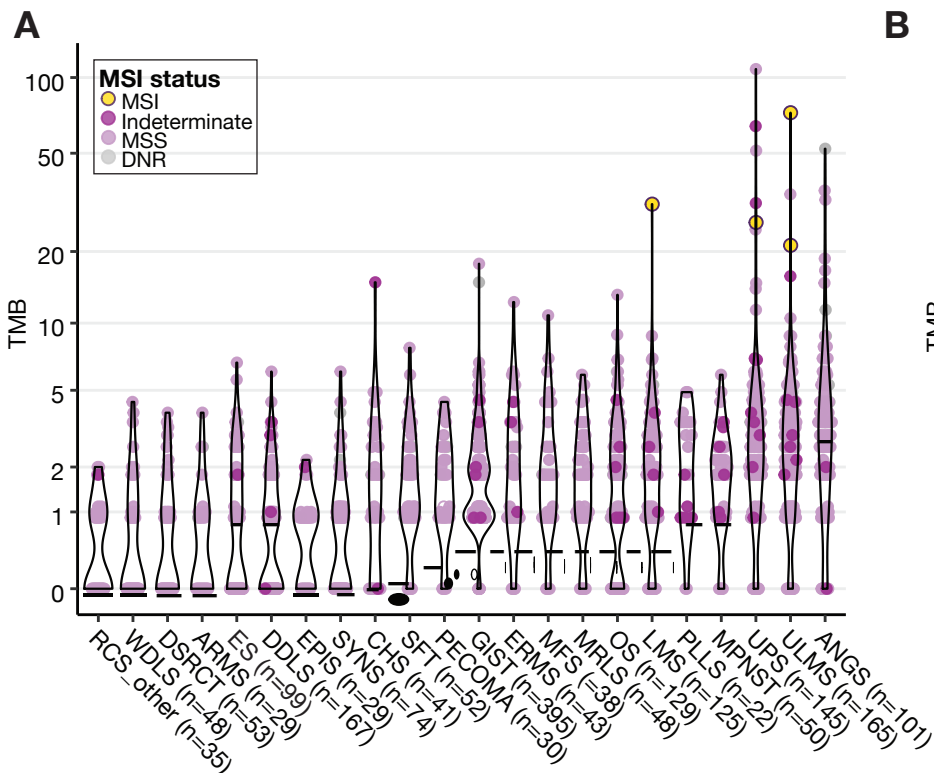
Supplementary Figure 1. Whole genome doubling (WGD) and survival probability. A, Frequency of WGD by subtype (green) compared to other cancers (all available samples) (gray). **B-C**, Overall survival based on WGD status within metastatic and primary tumor cohorts in **B**, all sarcoma subtypes; **C**, MFS.



Supplementary Figure 3. All epigenetic pathway alterations, including variants of unknown significance (VUS). Frequency of somatic alterations in epigenetic pathway genes in each subtype with ≥ 10 samples. Top , aggregate number of alterations in each gene family and biochemical process.



Supplementary Figure 4. Amplification and expression of 17p12-p11.2 genes NCOR1, FLCN, MAP2K4, AURKB, and ALOX12B. **A**, Oncoprint demonstrating the frequency of co-amplification of other genes at cytoband 17p12-p11.2 in the MSK-IMPACT panel in cases where NCOR1 is amplified. **B**, Correlation of gene expression in the sarcoma TCGA dataset with CNV. Box boundaries indicate 25th and 75th percentiles, interior lines indicate medians, and whiskers indicate 1.5 times the interquartile range. P values calculated by Spearman's rank correlation.



Supplementary Figure 5. Tumor mutation burden (TMB), microsatellite instability (MSI) status, and mutational signatures. A, Distribution of TMB (mutations/Mb) by subtype with sample-level MSI status. **B**, MSISensor score versus TMB for the cohort with sample-level MSI status. **C**, Mutational signature profile of each evaluable sample. Each bar represents the signature distribution of an individual sample, grouped by subtype. TMB, MSI status, and single nucleotide polymorphism (SNV) count are shown above.

Supplementary Table 1. Patient characteristics by subtype.

SAMPLES	AGE			SEX		SAMPLE TYPE	
	Count	Mean \pm SD	Range	Male	Female	Metastatic	Primary
TOTAL	2138	49.3 \pm 20.0	0–90	1040	1098	790	1348
GIST	395	58.5 \pm 14.2	11–90	213	182	123	272
DDL5	167	62.1 \pm 11.7	29–90	115	52	58	109
ULMS	165	57.2 \pm 10.3	30–83	0	165	91	74
UPS	145	55.6 \pm 18.1	3–87	74	71	52	93
OS	129	26.1 \pm 16.6	8–78	79	50	52	77
LMS	125	57.8 \pm 14.6	7–83	49	76	71	54
ANGS	101	58.6 \pm 16.7	15–89	41	60	24	77
ES	99	26.9 \pm 16.1	2–79	60	39	28	71
SYNS	74	40.7 \pm 16.0	7–85	36	38	24	50
DSRCT	53	23.4 \pm 9.4	8–48	48	5	24	29
SFT	52	60.2 \pm 11.0	39–80	25	27	22	30
MPNST	50	43.7 \pm 20.2	11–89	30	20	12	38
MRLS	48	44.7 \pm 13.4	13–67	29	19	16	32
WDLS	48	57.8 \pm 9.9	34–74	27	21	25	23
ERMS	43	15.5 \pm 16.8	1–70	20	23	7	36
CHS	41	47.9 \pm 15.4	16–76	26	15	16	25
MFS	38	64.5 \pm 12.6	31–80	21	17	13	25
RCS_other	35	27.8 \pm 18.0	0–70	14	21	3	32
PECOMA	30	55.9 \pm 15.0	14–76	7	23	15	15
ARMS	29	23.5 \pm 16.4	1–67	16	13	13	16
EPIS	29	38.5 \pm 15.2	16–67	14	15	9	20
PLLS	22	53.0 \pm 18.9	12–87	10	12	8	14

Supplementary Table 3. Biochemical function/complex assignments for epigenetic pathway genes.

DNA methylation		Histone modifying		Chromatin remodeling/histone chaperone		Histone	Other
Gene	Group classification	Gene	Group classification	Gene	Group classification	Gene	CTCF
DNMT1	DNA methyltransferase	ASXL1	PR-DUB	ARID1A	SWI/SNF	H3F3A	
DNMT3A	DNA methyltransferase	ASXL2	PR-DUB	ARID1B	SWI/SNF	H3F3B	
DNMT3B	DNA methyltransferase	BCOR	PRC1	ARID2	SWI/SNF	H3F3C	
IDH1	DNA demethylation	BRD4		ATRX	Histone chaperone	HIST1H1C	
IDH2	DNA demethylation	CARM1	Arginine methylation	DAXX	Histone chaperone	HIST1H2BD	
TET1	DNA demethylation	CREBBP		PBRM1	SWI/SNF	HIST1H3A	
TET2	DNA demethylation	DOT1L		SMARCA4	SWI/SNF	HIST1H3B	
		EED	PRC2	SMARCB1	SWI/SNF	HIST1H3C	
		EP300		SMARCD1	SWI/SNF	HIST1H3D	
		EZH1	PRC2			HIST1H3E	
		EZH2	PRC2			HIST1H3F	
		JAK2				HIST1H3G	
		KDM5A				HIST1H3H	
		KDM5C				HIST1H3I	
		KDM6A	MLL3/4			HIST1H3J	
		KMT2A	MLL1/2			HIST2H3C	
		KMT2B	MLL1/2			HIST2H3D	
		KMT2C	MLL3/4			HIST3H3	
		KMT2D	MLL3/4				
		KMT5A					
		MEN1	MLL1/2				
		NCOA3					
		NCOR1					
		NSD1	H3K36 methylation				
		NSD2	H3K36 methylation				
		NSD3					
		SETD2	H3K36 methylation				
		SMYD3					
		SUZ12	PRC2				