

Supplementary Figure and Table Legends

Supplementary Figure 1: Tumors that had histology subtype reassigned based on presence of clinically defining fusions. Left Clinical Histology contains the original histology subtype assignment while the right is the histology subtype following reassignment based on fusion and collapsing subtypes with < 5 samples to "Other".

Supplementary Figure 2: Gene level CNV in genes from the COSMIC Tier 1 gene list. Samples (columns) are clustered within their histologic subtype and genes (rows) are clustered within their broad category (when a gene has multiple roles in cancer as defined by COSMIC, they are clustered into "Multiple"). Included genes have mutations in more than 75% of a single histology subtype.

Supplementary Figure 3: Fusion-defined sarcoma subtypes including Ewing sarcoma (A), synovial sarcoma (B), desmoplastic small round cell tumor (C) and solitary fibrous tumor (D) predominantly cluster together by gene expressional profiling as highlighted on UMAP projection.

Supplementary Figure 4: Top differentially expressed genes among leiomyosarcomas, GISTs, myxoid liposarcomas, and dedifferentiated/well-differentiated liposarcomas. The corresponding genes are showed in a heatmap in Figure 3C. The figure shows normalized gene expression as the color gradient on an UMAP projection.

Supplementary Figure 5: A UMAP projection based on gene expression, showing sample assignment to the immune groups (A). Proportion of samples assigned to each immune group for each histology when considering only primary tumors (B) and only metastatic tumors (C).

Supplementary Figure 6: Kaplan-Meier curve showing the overall survival rate of patients with tumors assigned to each of the immune groups. The curves are separated according to primary tumor (A), metastatic tumors (B), and all samples except GISTs (C). P-values determined from the likelihood-ratio test.

Supplementary Figure 7: Samples colored according to their preservation (A, B) method and ORIEN origin site (C, D) projected on the UMAP calculated using uncorrected counts (A, C) or normalized batch-corrected counts (B, D).

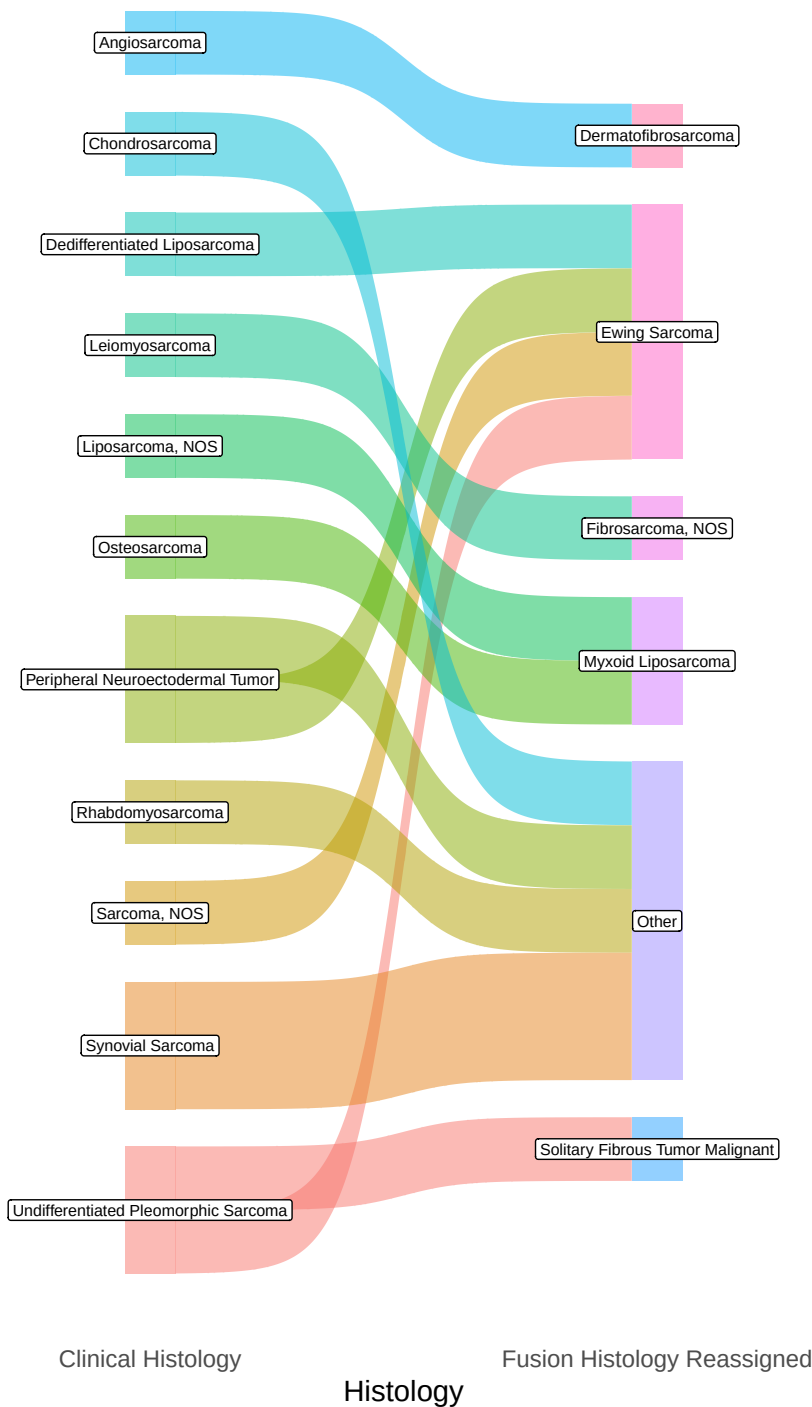
Supplementary Figure 8: Repeated RNA-sequencing analyses with removal of repeated measures in cases where >1 tumor was available for the same patient. For both GSEA (A) and survival by immune subgroup (B), the results closely mirror that of the corresponding primary study analyses. P-value determined from the likelihood-ratio test.

Supplementary Table 1: Histology level information at the patient (AVATAR) and tumor level included in WES analyses.

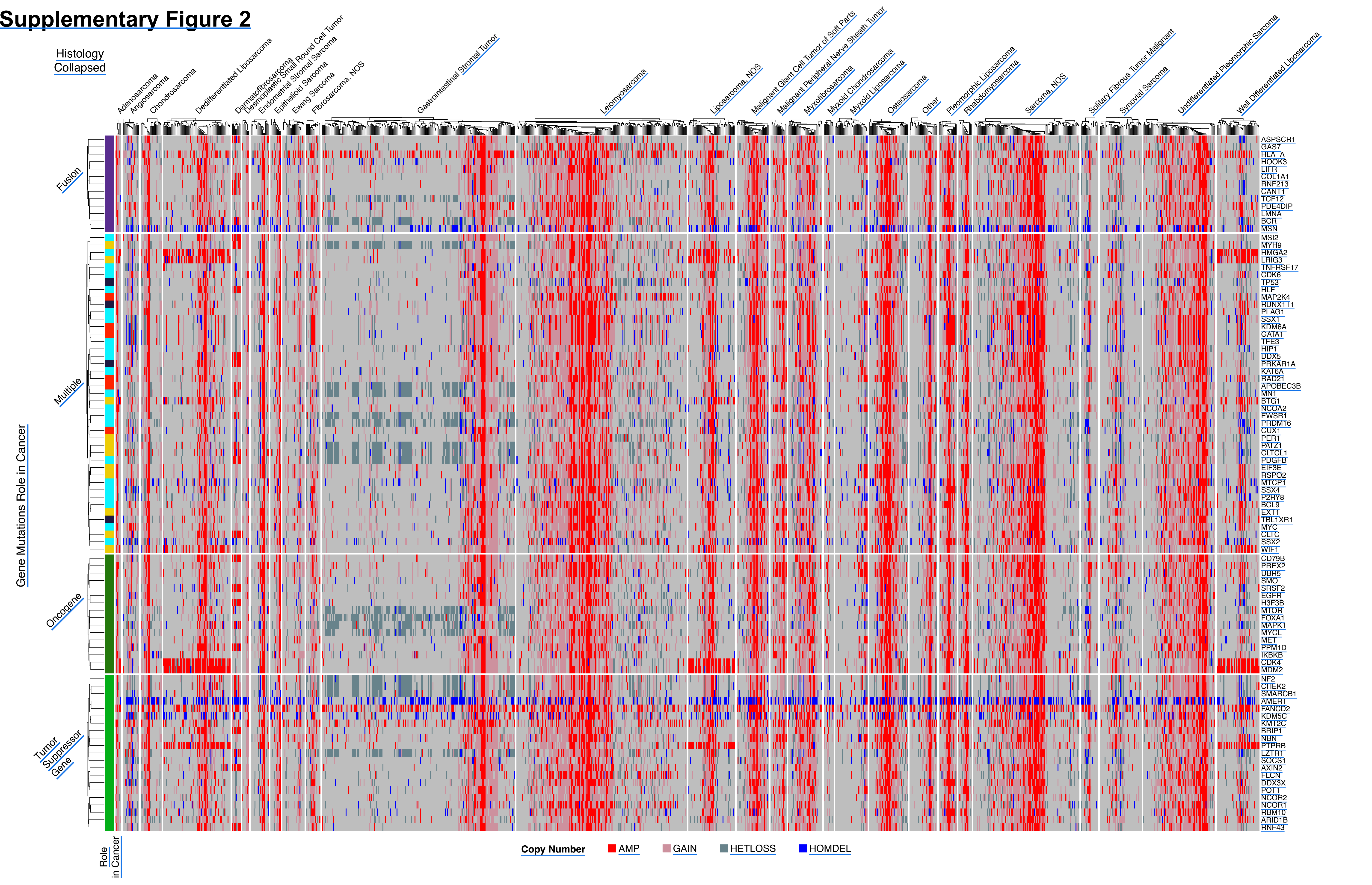
Supplementary Table 2: Histology level information at the patient (AVATAR) and tumor level included in RNAseq analyses.

Supplementary Table 3: Tumors reclassified as an alternate histology based on presence of a pathognomonic fusion.

Supplementary Figure 1: Sarcoma Histology Subtype Reassignment (based on fusions)

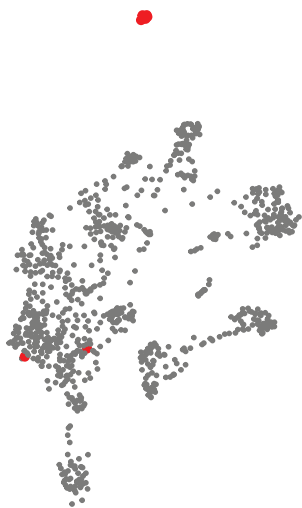


Supplementary Figure 2

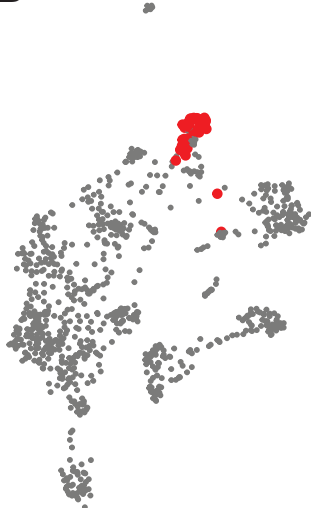


Supplementary Figure 3

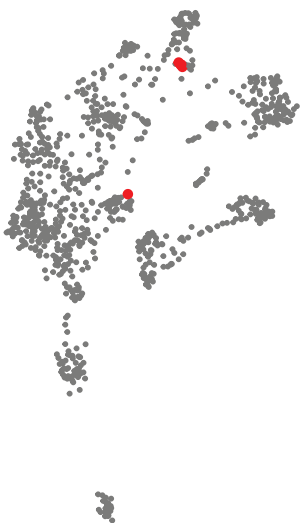
A Ewing Sarcoma



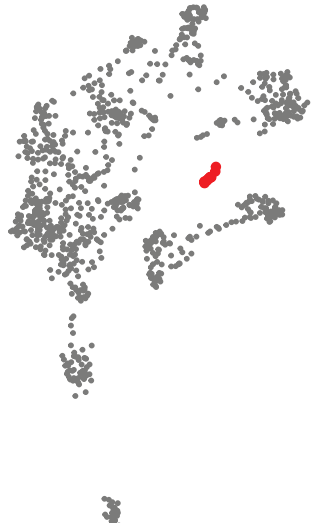
B Synovial Sarcoma



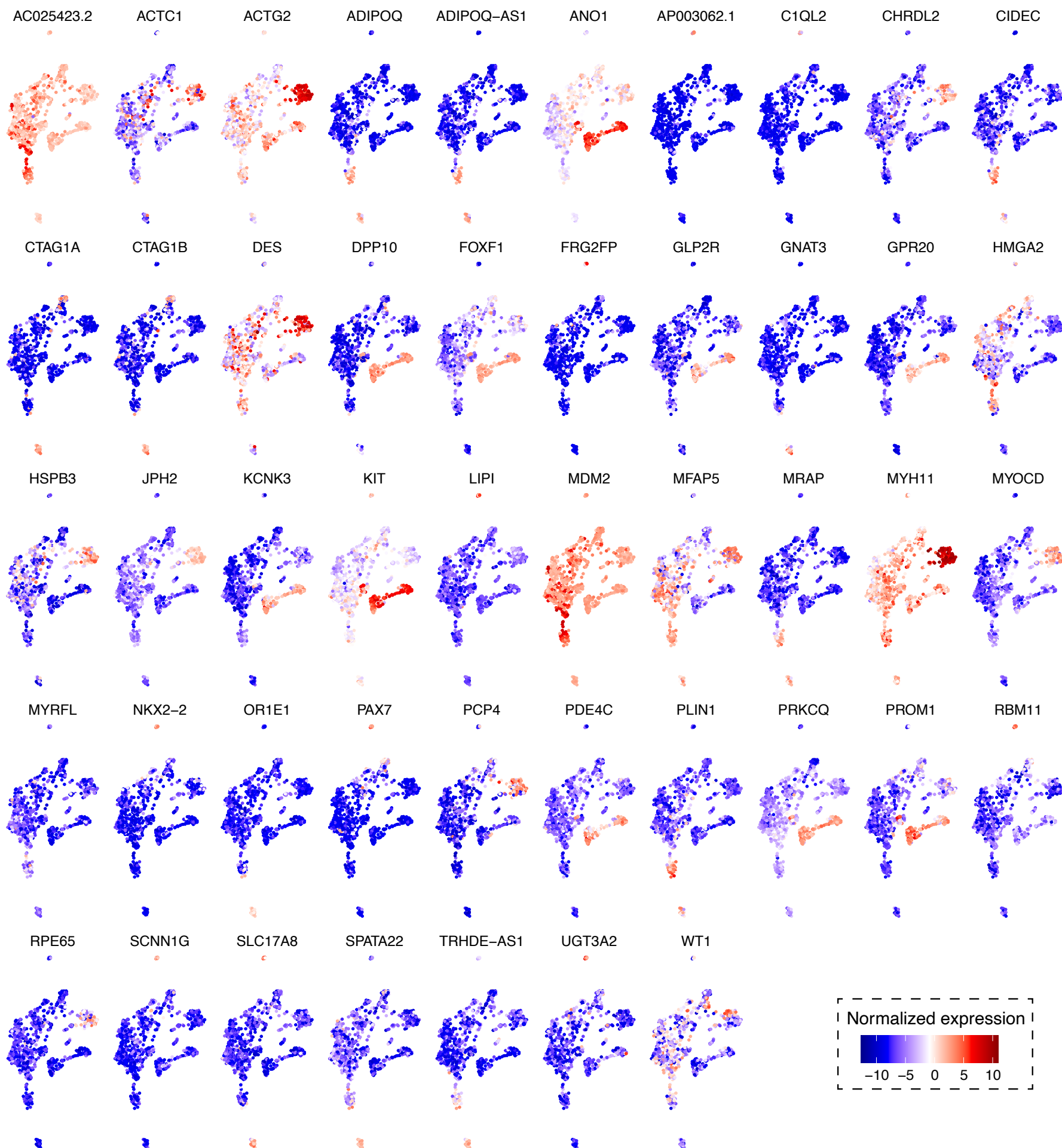
C Desmoplastic Small Round Cell Tumor



D Solitary Fibrous Tumor Malignant

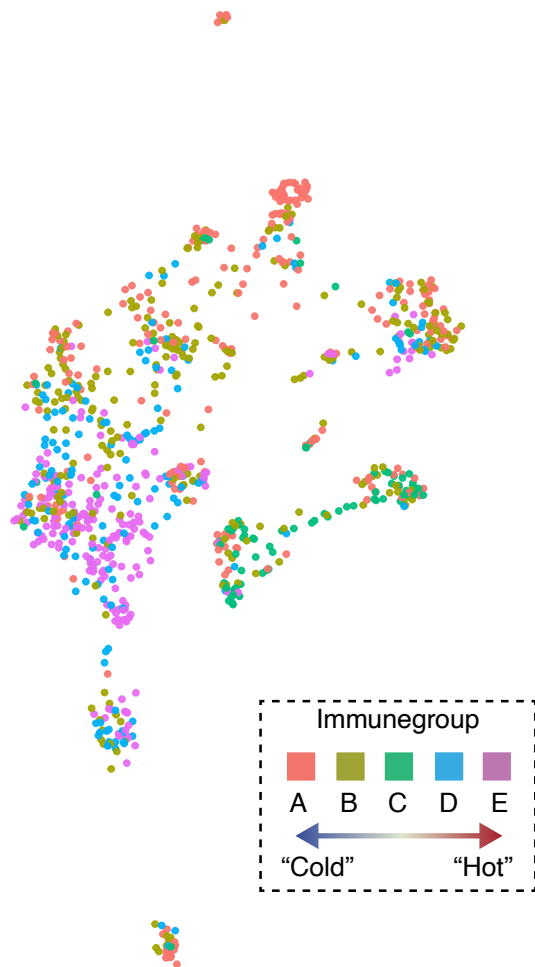


Supplementary Figure 4

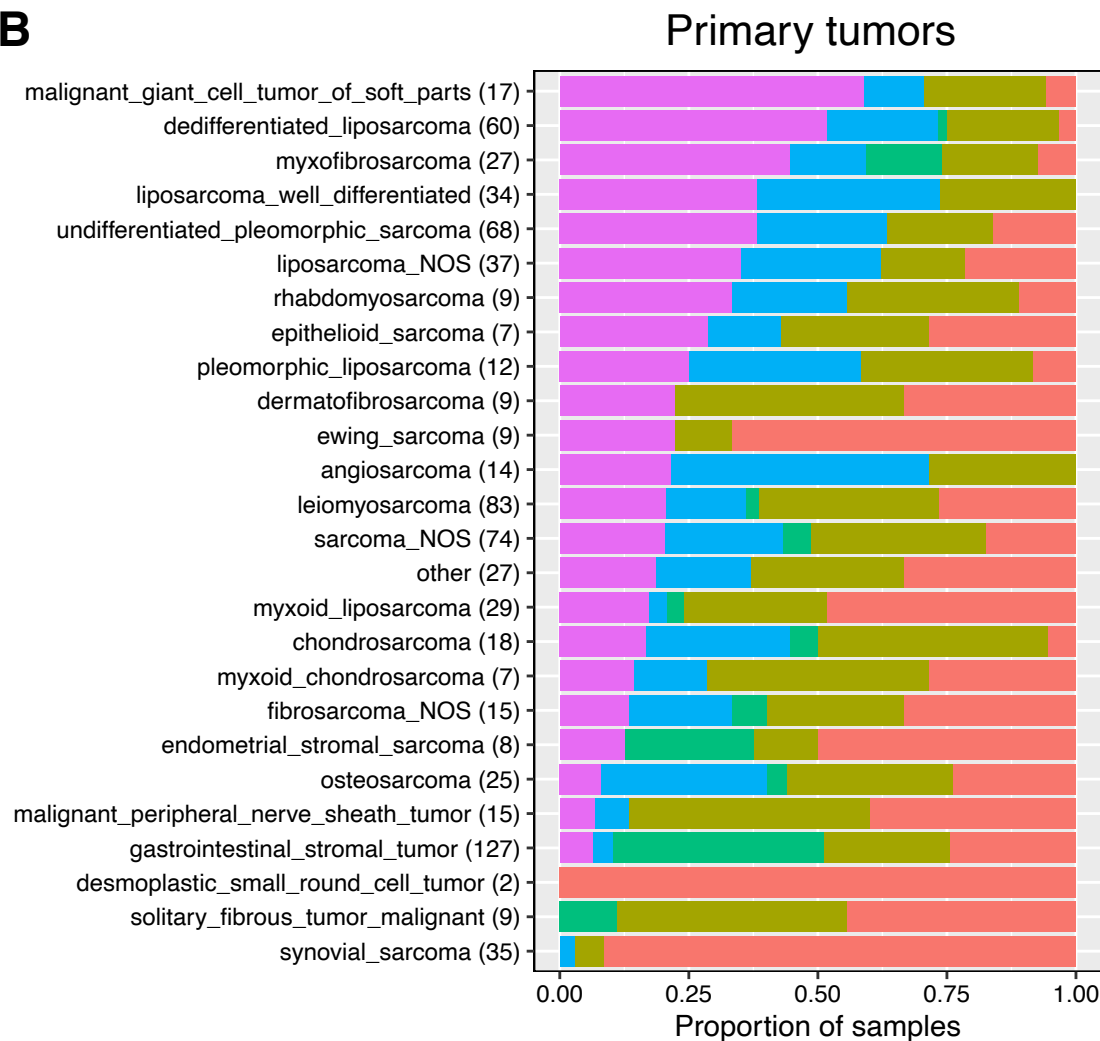


Supplementary Figure 5

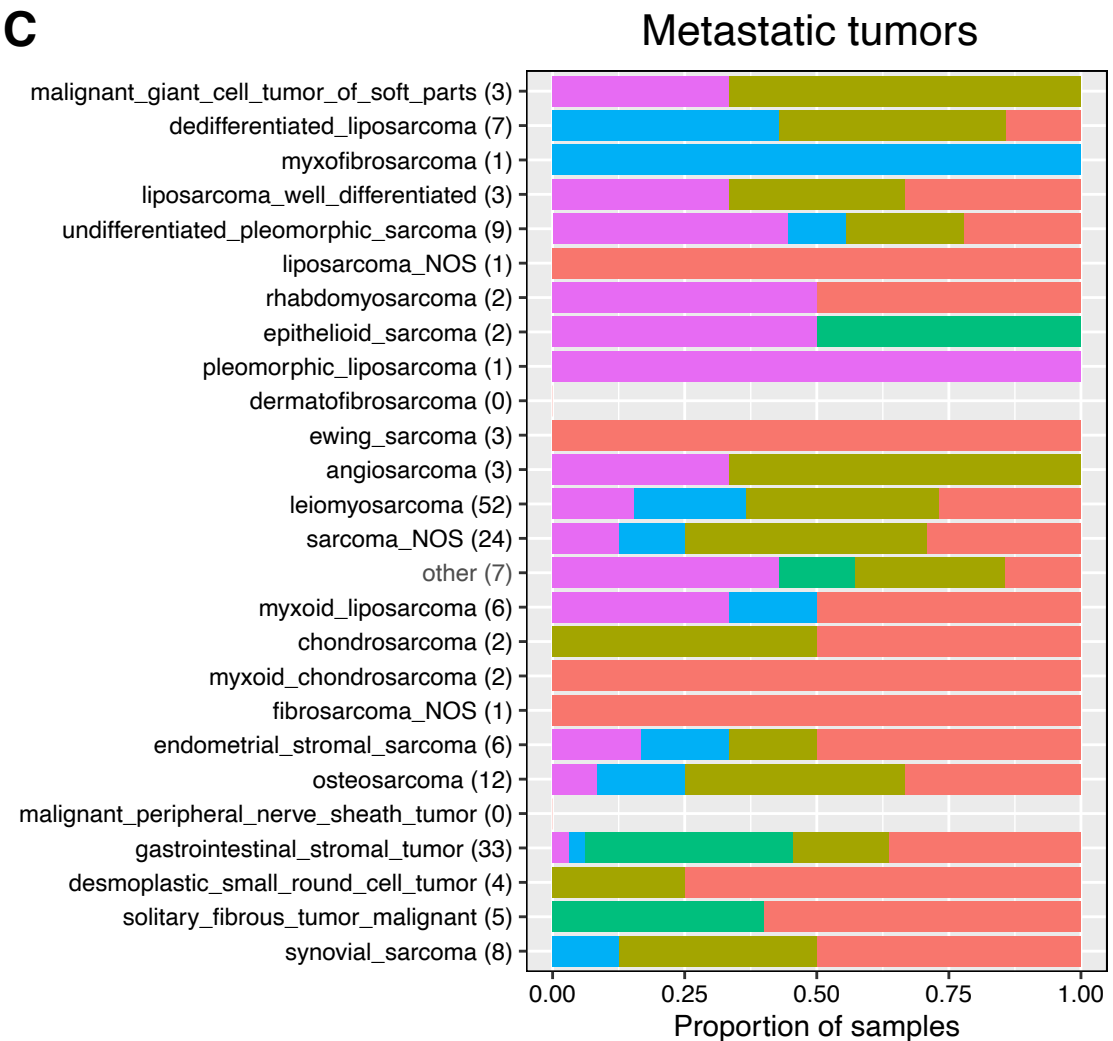
A Immunegroup (UMAP)



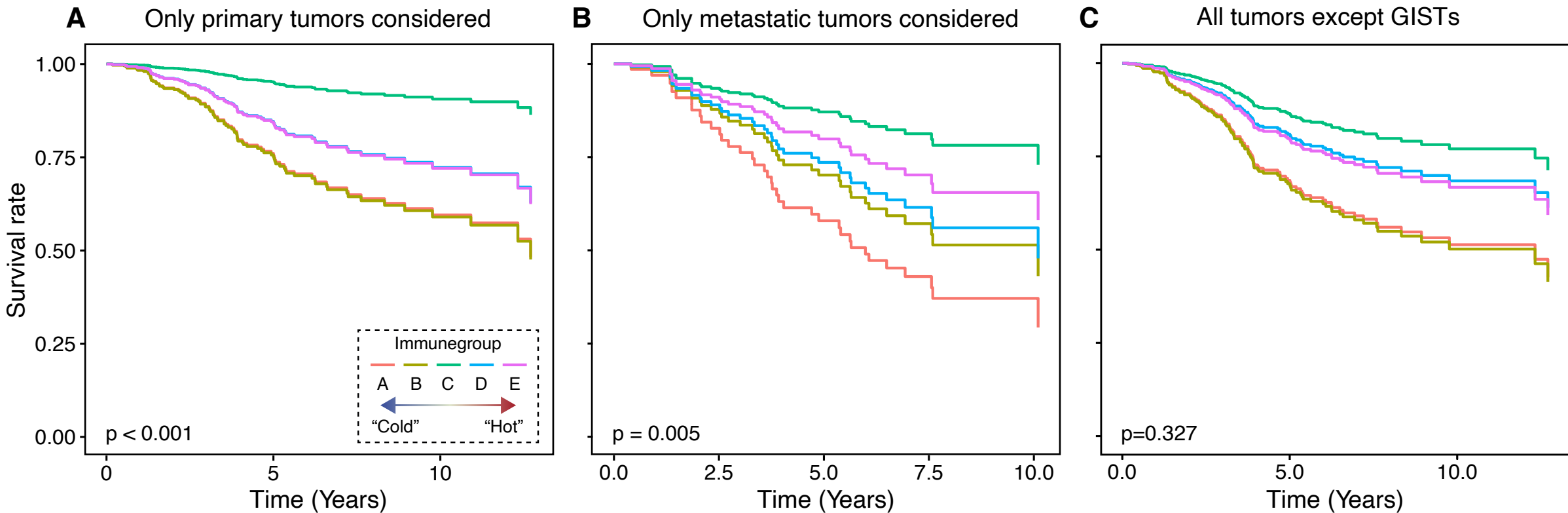
B



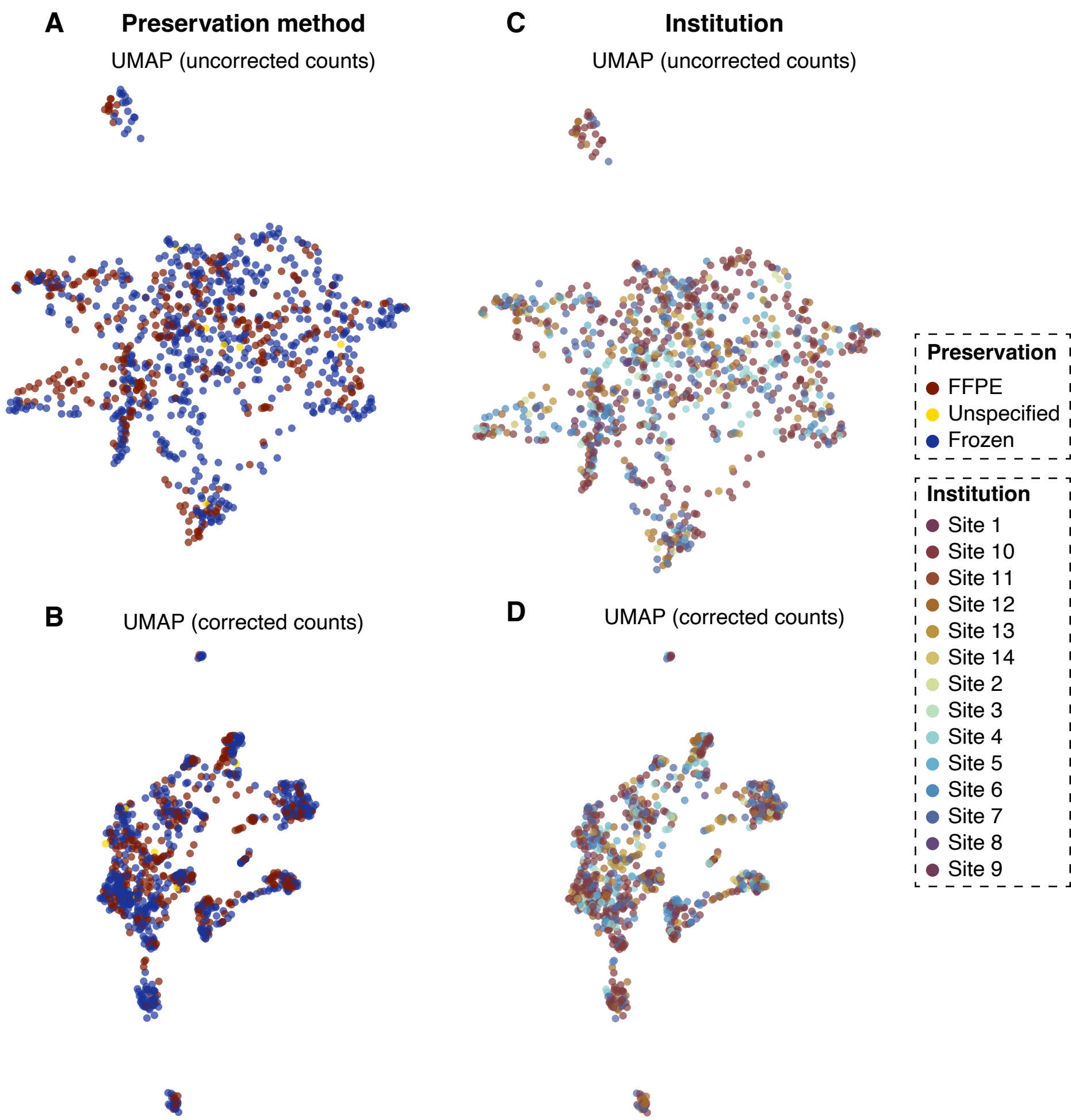
C



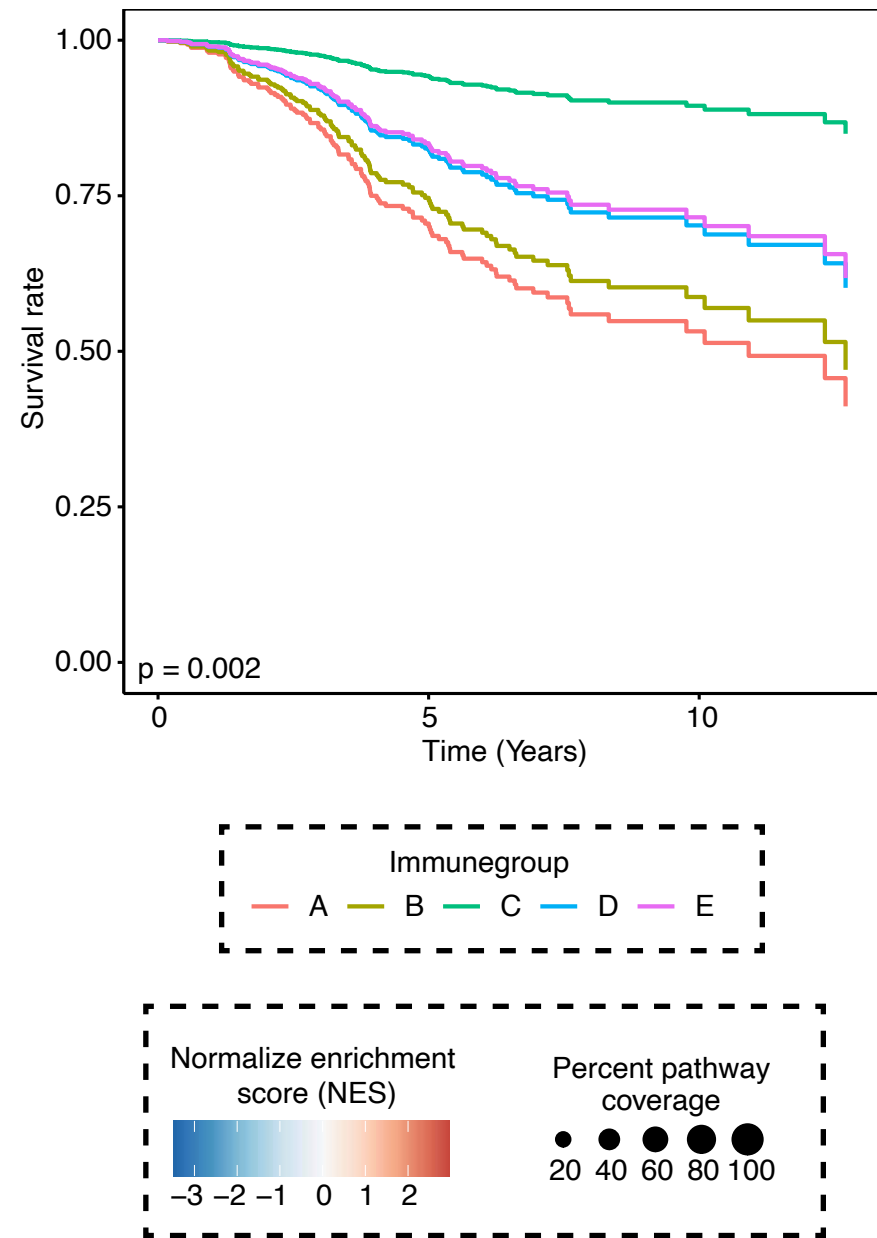
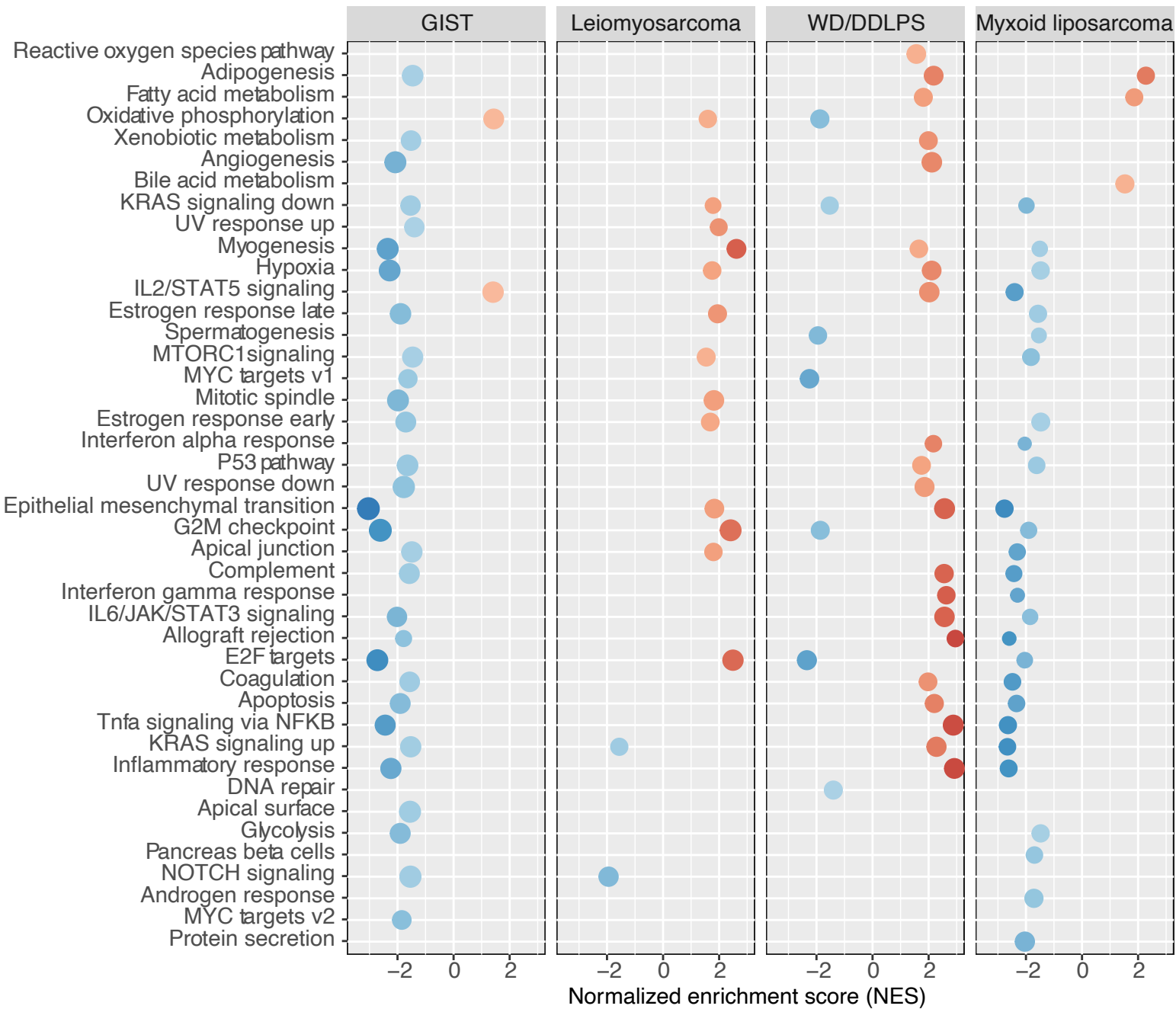
Supplementary Figure 6



Supplementary Figure 7



Supplementary Figure 8



Supplementary Table 1: Histology level information at the patient (AVATAR) and tumor level included in WES analyses.

Histology Subtype	Avatars	Tumors	Tumor Location		Preservation Method			Unknown	Follow-Up Mean (SD)
			Primary	Metastatic	Formalin-Fixer	Fresh Frozen	Other		
Adenosarcoma	6	6	5	1	4	2	0	0	3.8 (1.85)
Angiosarcoma	15	17	12	5	12	5	0	0	2.64 (2.09)
Chondrosarcoma	19	22	19	3	10	12	0	0	2.39 (1.78)
Dedifferentiated Liposarcoma	66	71	61	10	21	50	0	0	4.08 (2.85)
Dermatofibrosarcoma	9	9	9	0	5	4	0	0	1.83 (0.85)
Desmoplastic Small Round Cell Tumor	7	7	1	6	4	3	0	0	3.3 (2.63)
Endometrial Stromal Sarcoma	18	19	12	7	10	8	1	0	4.89 (2.97)
Epithelioid Sarcoma	11	11	9	2	8	3	0	0	3.08 (2.01)
Ewing Sarcoma	22	23	15	8	15	8	0	0	2.77 (1.83)
Fibrosarcoma, NOS	15	15	14	1	6	9	0	0	3.06 (2.59)
Gastrointestinal Stromal Tumor	198	204	164	40	110	94	0	0	4.57 (3.05)
Leiomyosarcoma	163	180	113	67	81	97	2	0	4.39 (3.24)
Liposarcoma, NOS	48	49	45	4	20	29	0	0	4.04 (3.3)
Malignant Giant Cell Tumor of Soft Parts	33	34	29	5	25	9	0	0	3.72 (3.06)
Malignant Peripheral Nerve Sheath Tumor	17	17	17	0	10	7	0	0	3.75 (3.95)
Myxofibrosarcoma	35	36	32	4	19	17	0	0	3.52 (1.99)
Myxoid Chondrosarcoma	10	10	8	2	3	7	0	0	5.13 (4.6)
Myxoid Liposarcoma	29	34	29	5	16	18	0	0	4.64 (3.51)
Osteosarcoma	40	41	28	13	19	22	0	0	4.4 (4)
Other ¹	29	29	23	6	17	12	0	0	3.89 (2.74)
Pleomorphic Liposarcoma	19	19	15	4	9	9	0	1	3.04 (2.35)
Rhabdomyosarcoma	14	14	10	4	8	6	0	0	2.41 (2.34)
Sarcoma, NOS	106	112	86	26	61	49	2	0	4.03 (3.39)
Solitary Fibrous Tumor Malignant	18	18	13	5	8	10	0	0	2.99 (1.98)
Synovial Sarcoma	42	44	39	5	25	19	0	0	4.75 (3.1)
Undifferentiated Pleomorphic Sarcoma	74	76	66	10	25	51	0	0	3.09 (2.55)
Well Differentiated Liposarcoma	43	45	40	5	17	28	0	0	4.6 (3.09)

¹Includes Adamantinoma of Long Bones (n = 1), Alveolar Rhabdomyosarcoma (n = 1), Alveolar Soft Part Sarcoma (n = 2), Chordoma (n = 3), Clear Cell Chondrosarcoma (n = 3), Clear Cell Sarcoma (n = 3), Dedifferentiated Chondrosarcoma (n = 1), Epithelioid Hemangioendothelioma (n = 2), Inflammatory Myofibroblastic Tumor (n = 1), Intimal Sarcoma (n = 1), Kaposi Sarcoma (n = 1), Malignant Rhabdoid Tumor (n = 1), Myoepithelial Carcinoma (n = 1), Peripheral Neuroectodermal Tumor (n = 4), Pleomorphic Rhabdomyosarcoma (n = 2), Round Cell Sarcoma (n = 2).

Supplementary Table 2: Histology level information at the patient (AVATAR) and tumor level included in RNAseq analyses.

Histology Subtype	Avatars	Samples	Tumor Location		Preservation Method			Unknown	Follow-Up Mean (SD)
			Primary	Metastatic	Formalin-Fixer	Fresh Frozen	Other		
Angiosarcoma	16	17	14	3	10	7	0	--	3.31 (2.4)
Chondrosarcoma	19	20	18	2	11	9	0	--	2.8 (2.29)
Dedifferentiated Liposarcoma	61	67	60	7	17	50	0	--	4.08 (2.95)
Dermatofibrosarcoma	9	9	9	0	5	4	0	--	2.5 (2.22)
Desmoplastic Small Round Cell Tumor	6	6	2	4	1	5	0	--	3.5 (3.3)
Endometrial Stromal Sarcoma	13	14	8	6	4	9	1	--	4.37 (2.98)
Epithelioid Sarcoma	9	9	7	2	6	3	0	--	3.08 (2.01)
Ewing Sarcoma	12	12	9	3	4	8	0	--	3.2 (2)
Fibrosarcoma, NOS	14	16	15	1	6	10	0	--	3.07 (2.55)
Gastrointestinal Stromal Tumor	156	160	127	33	69	91	0	--	4.64 (3.1)
Leiomyosarcoma	123	135	83	52	38	95	2	--	4.75 (3.46)
Liposarcoma, NOS	38	38	37	1	8	29	1	--	4.11 (3.42)
Malignant Giant Cell Tumor of Soft Parts	20	20	17	3	11	9	0	--	3.94 (3.37)
Malignant Peripheral Nerve Sheath Tumor	15	15	15	0	7	8	0	--	5.01 (4.68)
Myxofibrosarcoma	28	28	27	1	11	17	0	--	3.57 (2.56)
Myxoid Chondrosarcoma	9	9	7	2	3	6	0	--	6.74 (5.68)
Myxoid Liposarcoma	29	35	29	6	12	23	0	--	4.18 (3.22)
Osteosarcoma	35	37	25	12	17	19	1	--	3.63 (2.39)
Other ¹	34	34	27	7	20	14	0	--	3.93 (2.62)
Pleomorphic Liposarcoma	13	13	12	1	2	11	0	--	4.28 (3.28)
Rhabdomyosarcoma	10	11	9	2	5	6	0	--	1.48 (1.14)
Sarcoma, NOS	93	98	74	24	41	56	1	--	4.3 (3.48)
Solitary Fibrous Tumor Malignant	14	14	9	5	2	12	0	--	3.41 (2.06)
Synovial Sarcoma	39	43	35	8	23	20	0	--	5.21 (3.37)
Undifferentiated Pleomorphic Sarcoma	72	77	68	9	17	60	0	--	3.03 (2.78)
Well Differentiated Liposarcoma	36	37	34	3	10	27	0	--	4.92 (3.2)

¹Includes Adamantinoma of Long Bones (n = 1), Adenosarcoma (n = 4), Alveolar Rhabdomyosarcoma (n = 2), Alveolar Soft Part Sarcoma (n = 4), Chordoma (n = 2), Clear Cell Chondrosarcoma (n = 3), Clear Cell Sarcoma (n = 2), Dedifferentiated Chondrosarcoma (n = 2), Epithelioid Hemangioendothelioma (n = 2), Inflammatory Myofibroblastic Tumor (n = 2), Kaposi Sarcoma (n = 1), Malignant Rhabdoid Tumor (n = 1), Mesenchymal Chondrosarcoma (n = 1), Peripheral Neuroectodermal Tumor (n = 4), Pleomorphic Rhabdomyosarcoma (n = 1), Round Cell Sarcoma (n = 2).

Supplementary Table 3: Tumors reclassified as an alternate histology based on presenece of a pathognomonic fusion.

Original Diagnosis	orien_avatar_key	FusionName	LeftBreakpoint	RightBreakpoint	Primary/Meta:	Revised Histology
Sarcoma	MABKO2FPI0	EWSR1--FLI1	22:29287134	11:128805366	Primary	Ewing Sarcoma
Osteosarcoma	HPFMSDAR8A	DDIT3--FUS	12:57520417	16:31184940	Primary	Myxoid Liposarcoma
Dedifferentiated Liposarcoma	SFZ81NTJFI	EWSR1--ERG	22:29296368	21:38563558	Primary	Ewing Sarcoma
Undifferentiated Pleomorphic Sarcoma	1OYM4S02HP	NAB2--STAT6	12:57092968	12:57108299	Primary	Solitary Fibrous Tumor Malignant
Chondrosarcoma	Z3O2PHWDOY	EWSR1--NFATC2	22:29287134	20:51516955	Primary	Round Cell Sarcoma
Rhabdomyosarcoma	5TXEXLTG1E	PAX3--FOXO1	2:222220140	13:40560860	Metastatic	Alveolar Rhabdomyosarcoma
Peripheral Neuroectodermal Tumor	RBT46B6XU2	EWSR1--FLI1	22:29287134	11:128805366	Metastatic	Ewing Sarcoma
Liposarcoma	Z7WUCP2ZME	DDIT3--FUS	12:57520417	16:31184940	Primary	Myxoid Liposarcoma
Synovial Sarcoma	FJPHVTTTBV	BCOR--CCNB3	X:40052113	X:50308505	Primary	Round Cell Sarcoma
Angiosarcoma	6CKNLNEDPO	COL1A1--PDGFB	17:50196314	22:39235874	Primary	Dermatofibrosarcoma
Peripheral Neuroectodermal Tumor	C2YGLQCDI1	EWSR1--ATF1	22:29288786	12:50809456	Metastatic	Clear Cell Sarcoma
Undifferentiated Pleomorphic Sarcoma	DFE4YFTTHH	EWSR1--ERG	22:29287134	21:38392444	Primary	Ewing Sarcoma
Leiomyosarcoma	MRHRBIV7N0	COL1A1--PDGFB	17:50195232	22:39235874	Metastatic	Fibrosarcoma, NOS
Synovial Sarcoma	XAPRXLMI7E	EWSR1--CREB1	22:29287134	2:207575272	Primary	Clear Cell Sarcoma