

Patient		Age	Gender	Ethnicity	Histology	Genetics	[U- ¹³ C] glucose	Regimen	Metabolomics	Previous	
Number										Treatment	Chemotherapy
1	9	M	H	NBL	Non-MYCN AMP	Yes	1	No	No		
2	3	F	H	NBL	MYCN AMP	Yes	1	Yes	Yes	CP, CPP, D, EP, TT, VC	
3	2	F	C	NBL	Non-MYCN AMP	Yes	2	Yes	Yes	CP, CPP, D, EP, MTX, VC	
4	0.25	F	H	NBL	Non-MYCN AMP	Yes	2	Yes	Yes	CBP, CPP, D, EP	
5	5	F	C	NBL-G	Non-MYCN AMP	Yes	1	Yes	No		
6	2	M	C	NBL-G	Non-MYCN AMP	Yes	2	Yes	No		
7	3	F	C	NBL-G	Non-MYCN AMP	Yes	2	Yes	No		
8	13	F	H	S-LGF	FUS re-arrange	Yes	1	No	No		
9	11	F	C	S-OS	None	Yes	1	No	No		
10	1	M	H	S-CCS	None	Yes	2	Yes	Yes	CPP, EP, VC	
11	3	F	C	S-RMS	None	Yes	2	Yes	Yes	CPP, DM, VC	
12	19	F	H	S-OS	None	Yes	2	Yes	Yes	D, IF, O, MTX	
13	15	F	C	S-SS	SS18 (SYT) re-arrange	Yes	2	Yes	Yes	D, IF	
14	11	F	C	S-RMS	FOXO1 gene re-arrange	Yes	2	Yes	Yes	VC, CPP, AM	
15	5	F	H	S-RMS	FOXO1 gene re-arrange	Yes	2	Yes	No		
16	13	M	AA	O-D	None	Yes	1	Yes	Yes	Dx, MTX, V	
17	2	M	H	O-H	None	Yes	2	Yes	No		
18	2	M	H	O-H	None	Yes	2	Yes	Yes	CP	
19	10	F	H	O-HI	EWSR1-CREB1 fusion	Yes	2	Yes	No		
20	4	M	AA	O-P	None	Yes	2	No	Yes	CP, D	
21	5	M	AA	O-WT	Copy # gain 1q	Yes	2	Yes	No		
22	5	M	C	O-BP	None	Yes	2	Yes	No		
23	10	M	H	O-D	None	No	None	Yes	No		

Table S1: Patient demographics and tumor features (Related to Table 1). Gender: M = male, F = female. Ethnicity: H = Hispanic, C = Caucasian, AA = African American. Histology: NBL = neuroblastoma, NBL-G = ganglioneuroblastoma, S = sarcoma, O = others, S-LGF = low grade fibromyxoid, S-OS = osteosarcoma, S-CCS = clear cell sarcoma, S-RMS = rhabdomyosarcoma, S-SS = synovial sarcoma, O-D = desmoid, O-H = hepatoblastoma, O-HI = histiocytoma, O-P = pancreatoblastoma, O-WT = Wilms tumor, O-BP = benign urethral polyp. Genetics: AMP = Amplified. Chemotherapy: CP = cisplatin, CPP = cyclophosphamide, D = doxorubicin, EP = etoposide, TT = topotecan, VC = vincristine, MTX = methotrexate, CBP = carboplatin, DM = Dactinomycin, IF = Ifosfamide, O = Olaratumab, AM = Actinomycin, Dx = dexamethasone, V = Vinblastine. Patient 17 and 18 are the same child but represent tumors taken before and after 2 cycles of therapy with cisplatin. Patient 23 did not receive a glucose infusion.

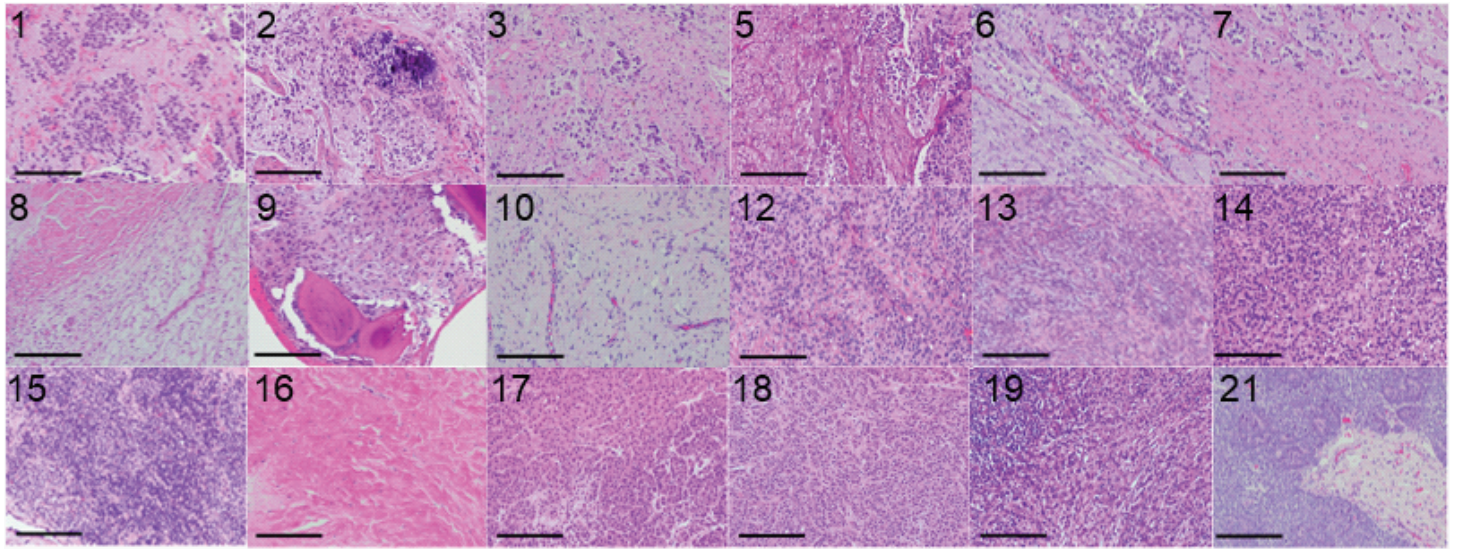


Figure S1: Tumor histology (Related to Figure 3). Original magnification x200, with scale bar corresponding to 200 microns. Patient samples 1-7 are neuroblastomas, 8-14 are sarcomas, and 15-21 are a variety of other tumor types as described in Supplemental Table 1. Patient 16's histology is a paucicellular bland spindle cell lesion with a collagenous background, consistent with a desmoid tumor. All other tumors demonstrate classic features of their tumor types. No post-surgical pathological confirmation was available for tumors from patients 4, 11, 20, 22, and 23.

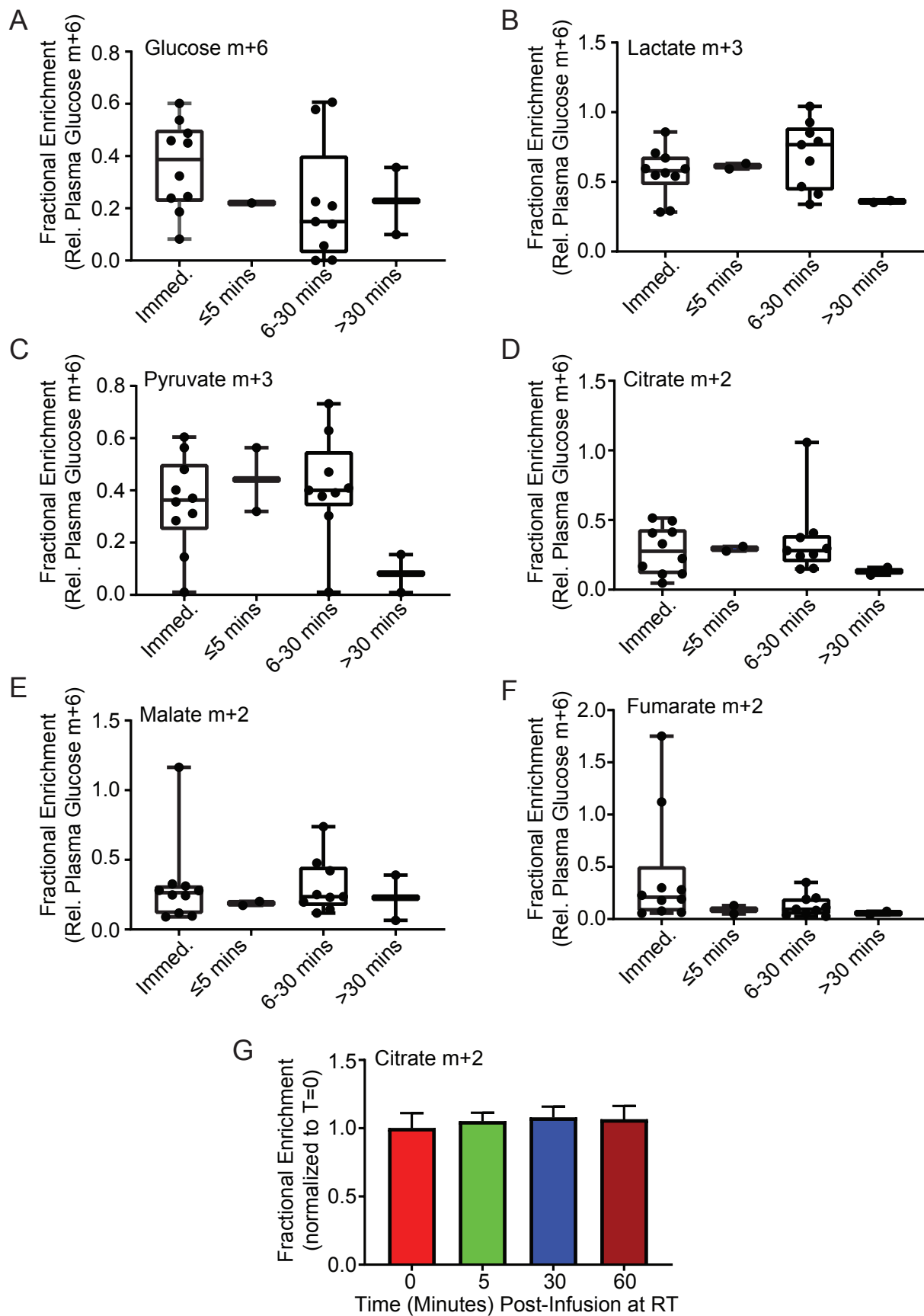


Figure S2: ^{13}C -labeling features in metabolites from central carbon pathways are maintained for a significant period of time after surgical resection (Related to Figure 3). (A-F) Fractional enrichment of the labeled metabolites, grouped according to the time between removal of the sample from the patient and freezing in liquid nitrogen. Fractional enrichments are normalized to glucose m+6 enrichment in the plasma at the time of surgical resection. G) Mice ($n=3$) bearing SK-N-AS xenografts were infused with $[\text{U-}^{13}\text{C}]$ glucose for 3 hours, then the tumor was resected and samples were frozen immediately (time 0) or kept at room temperature and then frozen at the indicated time points. The citrate m+2 fraction in each sample was normalized to citrate m+2 at time zero. Abbreviations: Immed., immediately. RT, room temperature.

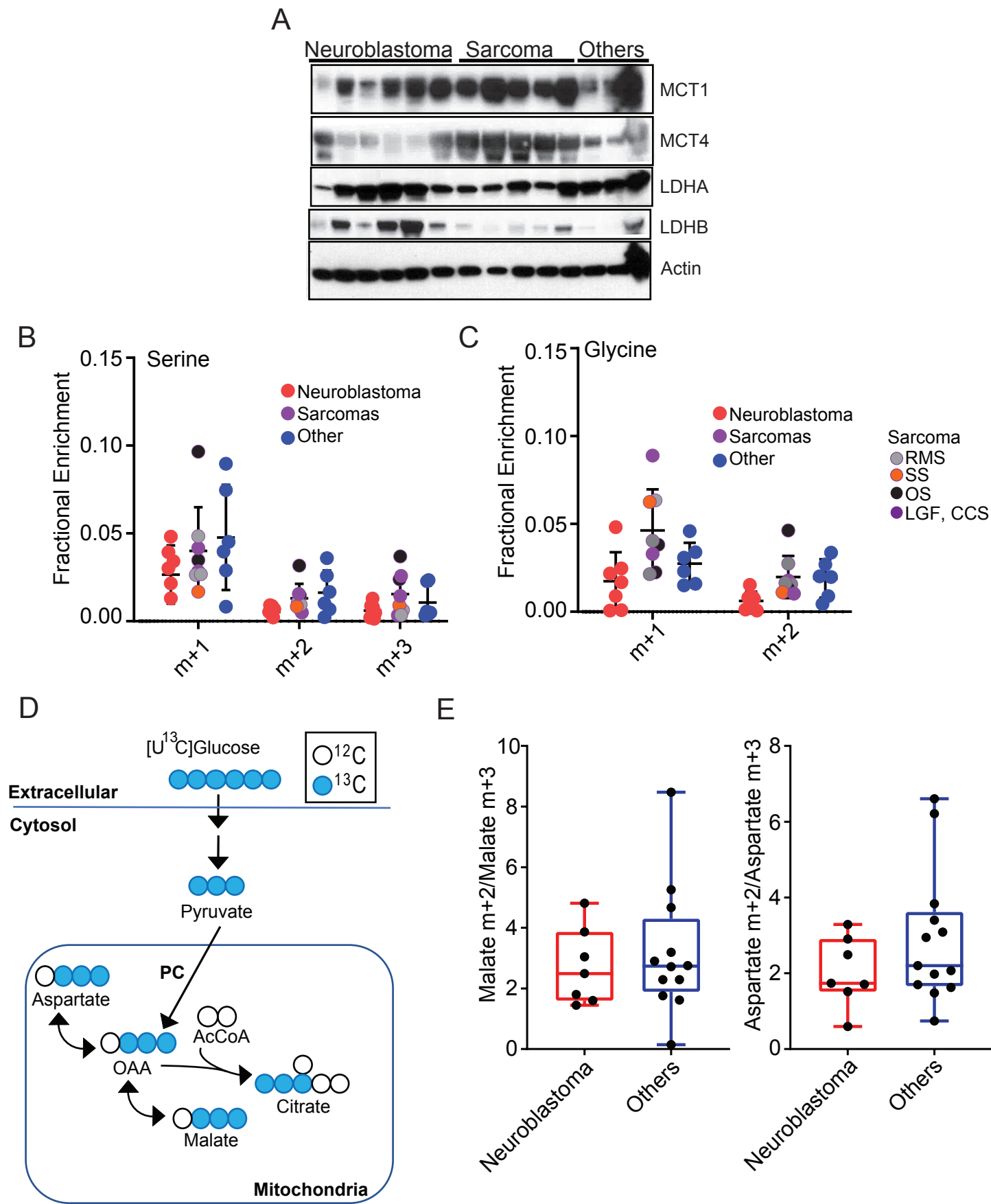


Figure S3: Additional metabolic features in [U-¹³C]glucose-infused tumors (Related to Figures 2,3).

(A) Expression of transporters and enzymes relevant to lactate metabolism in pediatric tumors. (B) Fractional enrichment of serine extracted from all pediatric tumors in the cohort. (C) Fractional enrichment of glycine extracted from all pediatric tumors in the cohort. (D) Expected labeling downstream of PC activity in tumors infused with [U-¹³C] glucose, resulting in m+3 labeling in malate and aspartate. Labeling from PDH, which results in m+2 labeling in malate and aspartate, is demonstrated in Figure 2A. (E) Ratios of m+2 vs. m+3 labeling in both malate and aspartate exceeded 1.0, consistent with predominant entry of ¹³C into the TCA cycle via PDH.

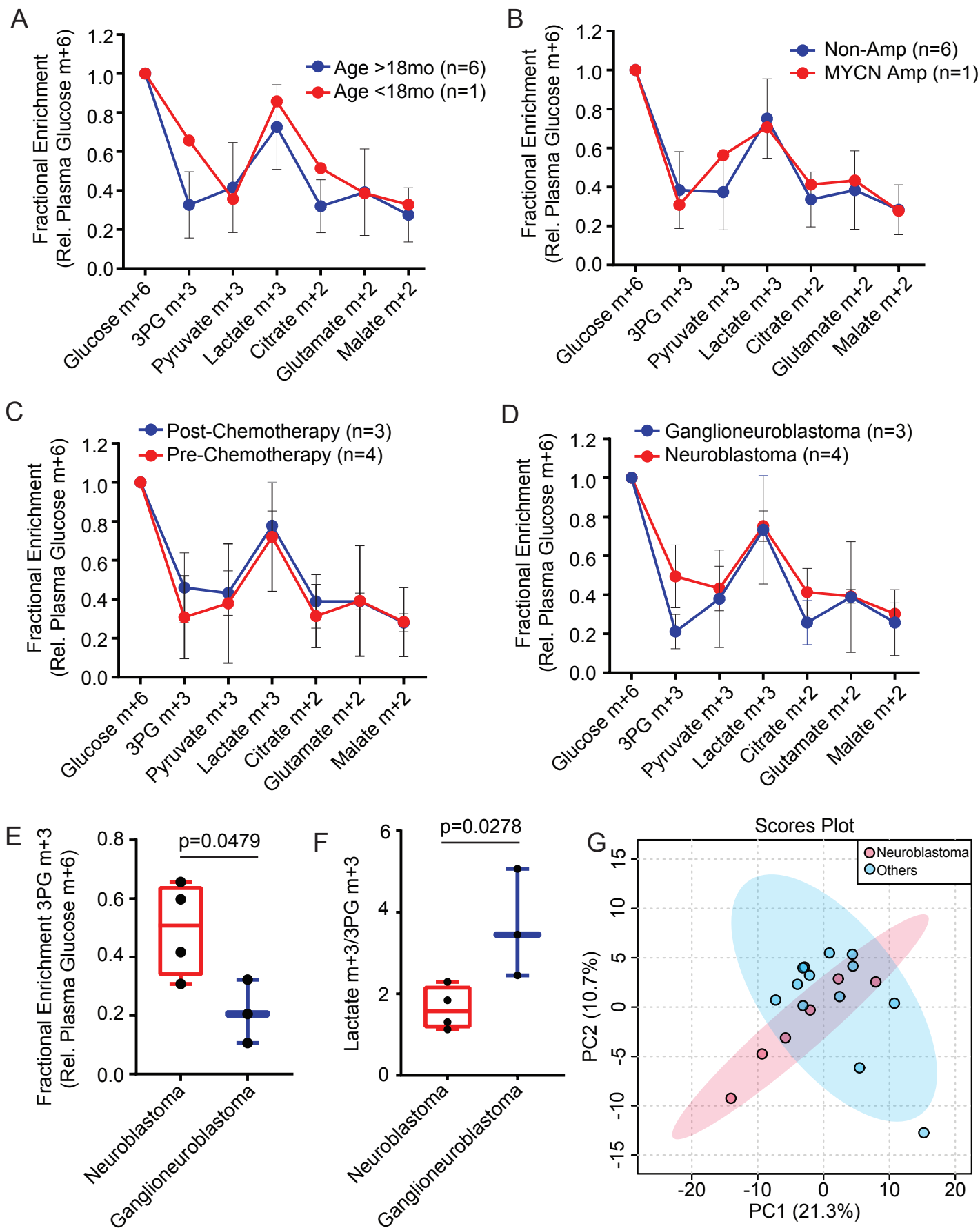


Figure S4: Labeling and metabolomic properties of human neuroblastomas (Related to Figures 3,4).

Fractional enrichment of metabolites relative to plasma glucose in neuroblastomas, compared by age (A), MYCN status (B), treatment status (C) and histological subtype (D). Comparison of labeling features between neuroblastomas and ganglioneuroblastomas are shown in (E) and (F). Principal component analysis of metabolomic features in neuroblastomas and other tumor types (G).