

Supplementary Data for

**The efficacy of DNA mismatch repair enzyme immunohistochemistry as a screening test  
for hypermutated gliomas**

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Tumor #	Sex	Age	Location	Diagnosis	Histotype	WHO grade	IDH1	MGMT	Primary vs recurrent	Pre vs post-TMZ	TMZ dose	TMZ cycles pre-recurrence	CCNU pre-recurrence?	Bev pre-recurrence?	Radiation pre-recurrence?	Hypermutated?
1	F	56	R Parietal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	14	N	N	Y	Y
2	F	56	R Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200mg/m2	12	N	N	Y	Y
3	M	53	L Frontal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	Incomplete data	Incomplete data	N	N	Y	Y
4	M	63	R Parietal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	Incomplete data	10	N	Y	Y	Y
5	M	42	L Temporal	GBM	Astrocytic	IV	Mutant	Unmethylated	Recurrent	Post	Incomplete data	Incomplete data	N	N	Y	Y
6	F	65	L Occipital	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	18	Y	N	Y	Y
7	F	43	L Frontal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	150 mg/m2	Non-cyclic	N	N	N	Y
8	M	32	R Frontal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	200 mg/m2	6	N	N	Y	Y
9	M	58	R Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	Incomplete data	Incomplete data	N	Y	Y	Y
10	F	68	L Occipital	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	75 mg/m2	Non-cyclic	N	N	Y	N
11	M	39	L Temporal	GBM	Astrocytic	IV	Mutant	Unmethylated	Recurrent	Post	Incomplete data	Incomplete data	N	N	Y	N
12	M	34	L Temporal	A Astro	Astrocytic	III	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
13	M	40	L Fronto-temporal	A Oligo	Oligodendroglial	III	Mutant	Methylated	Recurrent	Pre	N/A	N/A	N	N	Y	N
14	M	40	L Parietal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	200 mg/m2	6	N	N	Y	N
15	M	19	L Frontal	Oligo	Oligodendroglial	II	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
16	F	24	R Frontal	D Astro	Astrocytic	II	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
17	F	69	R Parietal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
18	F	73	R Parietal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
19	F	65	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	Incomplete data	6	N	Y	Y	N
20	F	48	R Parieto-temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
21	M	45	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	150 mg/m2	7	N	N	Y	N
22	M	47	L Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	12	N	N	Y	N
23	F	73	R Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
24	M	32	L Frontal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
25	F	49	R Frontal	GBM	Astrocytic	IV	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
26	M	48	R Frontal	A Oligo	Oligodendroglial	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
27	M	76	R Parietal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
28	M	24	L Temporal	A Astro	Astrocytic	III	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
29	F	67	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
30	M	69	L Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
31	F	28	L insular	D Astro	Astrocytic	II	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
32	M	26	L Frontal	A Astro	Astrocytic	III	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N

33	F	74	L Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
34	F	25	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Pre	N/A	N/A	N	N	N	N
35	F	21	R Frontal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
36	M	50	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
37	M	68	R Temporal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	Incomplete data	2	N	N	Y	N
38	M	85	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	Incomplete data	3	N	N	Y	N
39	F	53	R Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
40	M	43	R Temporal	GBM	Astrocytic	IV	Mutant	Unmethylated	Recurrent	Pre	N/A	N/A	Y	N	Y	N
41	M	48	R Temporal	D Astro	Astrocytic	II	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
42	F	74	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
43	M	63	R Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	Incomplete data	5 (8 week cycles)	Y	Y	Y	N
44	M	28	R Temporal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
45	M	44	R Fronto-temporal	GBM	Astrocytic	IV	Mutant	Methylated	Recurrent	Post	150 mg/m2	6	N	N	Y	N
46	M	48	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
47	F	26	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
48	F	68	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
49	F	82	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
50	F	31	L Parietal	PXA	Astrocytic	II	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
51	F	48	Corpus callosum	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	14	N	N	Y	N
52	F	48	L Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	150 mg/m2	3	N	N	Y	N
53	M	68	R Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
54	F	32	R Frontal	A Astro	Astrocytic	III	Mutant	Methylated	Recurrent	Post	150 mg/m2	6	N	N	Y	N
55	F	36	R Parietal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
56	F	56	L Frontal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
57	F	21	R Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
58	M	33	3rd Ventricle	Ganglioglioma	Glioneuronal	I	Wild type	N/A	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
59	F	47	L Temporal	A Astro	Astrocytic	III	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
60	F	29	R Parietal	A Astro	Astrocytic	III	Mutant	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
61	F	48	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
62	F	76	R Fronto-parietal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
63	M	74	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
64	F	48	L Frontal	GBM	Astrocytic	IV	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
65	F	37	R Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
66	F	35	L Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	150 mg/m2	12	N	N	Y	N

67	M	62	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
68	M	62	Corpus callosum	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
69	F	35	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	150 mg/m2	9	N	N	Y	N
70	M	71	R Frontal	GBM	Astrocytic	IV	Wild type	N/A	Recurrent	Post	Incomplete data	3	Y	Y	Y	N
71	F	48	R Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
72	F	41	L Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	4	N	N	Y	N
73	M	56	R Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
74	M	74	L Occipital	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
75	M	22	L Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
76	F	55	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	200 mg/m2	6	Y	N	Y	N
77	F	41	L Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
78	M	31	Brainstem	Ganglioglioma	Glioneuronal	I	Wild type	N/A	Recurrent	Pre	N/A	N/A	N	N	N	N
79	F	25	L Temporal	Pilocytic Astro	Astrocytic	I	Wild type	N/A	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
80	F	30	L Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Recurrent	Pre	N/A	N/A	N	N	N	N
81	F	31	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
82	F	74	L Occipital	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
83	M	50	R Frontal	GBM	Astrocytic	IV	Wild type	N/A	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
84	M	63	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	Incomplete data	2	N	N	Y	N
85	M	56	L Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
86	M	68	L Temporal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	21	N	N	Y	N
87	M	63	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
88	F	26	L Frontal	A Astro	Astrocytic	III	Mutant	Methylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
89	F	58	R Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
90	M	45	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
91	F	76	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Recurrent	Post	200 mg/m2	6	N	N	N	N
92	F	53	L Frontal	Oligo	Oligodendroglial	II	Mutant	Methylated	Recurrent	Post	75 mg/m2	5	Y	N	N	N
93	F	56	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
94	F	42	L Parietal	A Astro	Astrocytic	III	Mutant	Methylated	Recurrent	Post	Incomplete data	Incomplete data	N	N	Y	N
95	F	59	L Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
96	F	53	L Parietal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
97	M	41	R Temporal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
98	M	54	L Frontal	GBM	Astrocytic	IV	Wild type	Methylated	Recurrent	Post	200 mg/m2	3	N	N	Y	N
99	F	30	L Temporal	Ganglioglioma	Glioneuronal	I	Wild type	N/A	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N
100	M	66	L Frontal	GBM	Astrocytic	IV	Wild type	Unmethylated	Primary	Pre	N/A	N/A	N/A	N/A	N/A	N

**Supplementary Table 1:** Detailed clinical and pathologic data for the full cohort of 100 gliomas. Tumors 1-9 are hypermutated and are also shown in **Table 1** of the main manuscript. The following tumors are from the same patients: 1 and 2; 5, 11, and 12; 7 and 94. Pre-TMZ gliomas were designated as N/A in the TMZ dose and duration columns. Records on temozolomide dosage and cycles were incomplete for many post-TMZ patients, because they had been treated at outside institutions prior to re-resection at Northwestern. “D Astro”=diffuse astrocytoma; “A Astro”=anaplastic astrocytoma; “A Oligo”=anaplastic oligodendroglioma; N/A=not available or not applicable.

	hypermutant	age	male	astrocytic	WHO grade	IDH1 mutant	MGMT methylated	recurrent	post-TMZ
hypermutant	1								
age	0.03	1							
male	0.11	0.037	1						
astrocytic	0.10	0.31	0.0047	1					
WHO grade	0.19	0.61*	0.099	0.59*	1				
IDH1 mutant	0.17	-0.56*	0.074	-0.43*	-0.61*	1			
MGMT methylated	0.25*	-0.22*	0.0056	-0.27*	-0.30*	0.40*	1		
recurrent	0.39*	-0.0083	0.098	0.029	0.24*	0.10	0.29*	1	
post-TMZ	0.43*	0.082	0.092	0.15	0.29*	0.032	0.29*	0.91*	1

**Supplementary Table 2: Correlation matrix.** N=93 tumors (cases without *MGMT* data were excluded, as well as hypermutated tumor #2 since it came from the same patient as tumor #1, see **Figure 2** and **Supplementary Table 1**). Each value represents Spearman  $\rho$  (rho) correlation coefficients, with 1=perfect direct correlation, 0=no correlation, and -1=perfect inverse correlation. \* $P$ <0.05. TMZ=temozolomide.