

**Supplemental Table 4:** Association of *TNFRSF9* methylation and mRNA expression with overall survival with regard to tissue type. Cox proportional hazard analyses of overall survival and *TNFRSF9* methylation and mRNA expression in melanoma patients stratified according the tumor tissue type (all sites:  $N = 470$ , primary tumor:  $N = 103$ , regional lymph node metastases:  $N = 222$ , distant metastases:  $N = 68$ , regional cutaneous or subcutaneous tissue:  $N = 74$ , missing information:  $N = 3$ ). *TNFRSF9* mRNA expression was analyzed as log<sub>2</sub>-transformed variable. Significant features are shown in boldface. *P*-values refer to Wald test.

Analyte	CpG site no.	All Sites		Primary Tumors		Regional Lymph Nodes		Distant Metastases		Regional Cutaneous or Subcutaneous Tissues	
		Hazard Ratio [95% CI]	P-Value	Hazard Ratio [95% CI]	P-Value	Hazard Ratio [95% CI]	P-Value	Hazard Ratio [95% CI]	P-Value	Hazard Ratio [95% CI]	P-Value
mRNA	NA	<b>0.92 [0.87-0.97]</b>	<b>0.002</b>	1.07 [0.79-1.44]	0.68	<b>0.87 [0.80-0.94]</b>	<b>&lt;0.001</b>	0.92 [0.82-1.02]	0.11	1.00 [0.87-1.16]	0.98
cg16839093	1	0.20 [0.03-1.33]	0.096	39.4 [0-9.3x10 <sup>8</sup> ]	0.67	0.08 [0.00-1.59]	0.097	3.05 [0.11-83.7]	0.51	0.23 [0.01-10.6]	0.45
cg27305704	2	0.69 [0.31-1.53]	0.36	4.34 [0.11-172]	0.43	0.47 [0.14-1.63]	0.24	1.45 [0.33-6.41]	0.62	0.73 [0.13-4.00]	0.72
cg18859763	3	0.51 [0.15-1.76]	0.29	2.0x10 <sup>4</sup> [0-3.9x10 <sup>11</sup> ]	0.25	0.33 [0.04-2.52]	0.29	1.81 [0.19-17.3]	0.61	0.53 [0.05-5.82]	0.60
cg07836592	4	0.47 [0.15-1.53]	0.21	<b>7.4x10<sup>7</sup> [7.9-6.9x10<sup>14</sup>]</b>	<b>0.027</b>	0.36 [0.07-1.93]	0.23	2.96 [0.23-38.5]	0.41	0.46 [0.04-5.43]	0.54
cg23959705	5	0.59 [0.17-2.10]	0.42	4.86 [0.01-3.4 x10 <sup>3</sup> ]	0.64	0.32 [0.04-2.52]	0.28	2.20 [0.26-18.4]	0.47	0.57 [0.04-8.09]	0.67
cg06956444	6	<b>3.42 [1.28-9.14]</b>	<b>0.014</b>	6.10 [0.06-682]	0.45	2.98 [0.73-12.1]	0.13	1.93 [0.33-11.4]	0.47	10.1 [0.71-144]	0.089
cg14614416	7	<b>6.28 [2.06-19.2]</b>	<b>0.001</b>	1.6 x10 <sup>3</sup> [0.49-5.4 x10 <sup>6</sup> ]	0.074	<b>8.30 [1.71-40.3]</b>	<b>0.009</b>	8.32 [0.92-75.2]	0.059	0.43 [0.03-5.81]	0.52
cg18025409	8	1.80 [0.84-3.85]	0.13	6.18 [0.42-90.9]	0.18	1.41 [0.48-4.11]	0.53	<b>4.62 [1.05-20.4]</b>	<b>0.043</b>	1.03 [0.13-8.30]	0.98
cg14153654	9	<b>3.03 [1.01-9.07]</b>	<b>0.048</b>	13.8 [0.46-413]	0.13	1.65 [0.36-7.68]	0.52	<b>18.0 [1.68-192]</b>	<b>0.017</b>	1.65 [0.07-39.6]	0.76
cg08840010	10	<b>2.85 [1.23-6.63]</b>	<b>0.015</b>	13.8 [0.17-1.1x10 <sup>4</sup> ]	0.24	<b>3.78 [1.21-11.8]</b>	<b>0.022</b>	5.11 [0.71-36.7]	0.11	0.84 [0.10-7.26]	0.88
cg17123655	11	<b>3.89 [1.25-12.1]</b>	<b>0.019</b>	12.9 [0.02-8.1x10 <sup>4</sup> ]	0.44	4.61 [0.97-21.8]	0.054	<b>18.4 [1.17-292]</b>	<b>0.039</b>	0.22 [0.02-3.23]	0.27
cg16117781	12	<b>3.57 [1.65-7.76]</b>	<b>0.001</b>	3.80 [0.03-453]	0.58	<b>2.93 [1.05-8.14]</b>	<b>0.039</b>	<b>13.8 [1.75-109]</b>	<b>0.013</b>	1.64 [0.28-9.52]	0.58

NA: Not Applicable