

**Supplemental Table S13.**

The ratios of complementary mutation rates on the leading strand in regions belonging to the most extreme replication direction bin in MSS, MSI, MSS mutated pol epsilon, MSS mutated pol delta and bMMRD mutated pol epsilon and mutated pol delta cancers.

The values in brackets are 95% confidence intervals. n corresponds to number of samples used.

<b>Mutation</b>	<b>MSS (n=782)</b>	<b>MSI (n=159)</b>	<b>MSS mutated pol epsilon (n=27)</b>	<b>bMMRD mutated pol epsilon (n=5)</b>	<b>MSS mutated pol delta (n=1)</b>	<b>bMMRD mutated pol delta (n=2)</b>
A→G/T→C	1.03 (0.94-1.13)	1.92 (1.81-2.03)	0.95 (0.88-1.04)	1.20 (1.02-1.41)	2.39 (1.94-2.93)	1.98 (1.74-2.26)
C→T/G→A	0.89 (0.86-0.94)	1.22 (1.18-1.27)	1.93 (1.86-2.02)	2.01 (1.93-2.13)	1.08 (0.91-1.29)	1.09 (0.97-1.23)
A→T/T→A	1.10 (0.98-1.29)	0.73 (0.64-0.86)	0.62 (0.49-0.82)	0.89 (0.50-1.65)	0.44 (0.30-0.67)	0.63 (0.55-0.75)
T→G/A→C	0.87 (0.77-0.94)	0.72 (0.61-0.81)	2.27 (2.05-2.43)	1.84 (1.32-2.46)	0.54 (0.29-0.97)	0.66 (0.44-0.94)
C→A/G→T	0.92 (0.85-1.00)	0.72 (0.68-0.78)	2.14 (2.05-2.26)	1.97 (1.79-2.19)	0.51 (0.36-0.74)	0.48 (0.42-0.56)
C→G/G→C	0.86 (0.78-0.97)	0.98 (0.81-1.20)	0.74 (0.49-1.11)	0.69 (0.28-1.78)	0.43 (0.17-1.08)	0.63 (0.25-1.59)