Supplemental Table S2 Evaluation of the independence of constrained reference bases and possible motifs

Example three-way contingency table to evaluate the effect of constrained reference base-disrupting mutations ("Independent Pos") on nearby ones ("Combination Pos")

		Num. of mutations disrupting Combination Pos reference allele	Num. of reference alleles - Num. of Combination Pos mutations
Table 1: Independent Pos mutation = Yes	pLI < 0.9	a1	b1
	pLI > 0.9	c1	d1
Table 2: Independent Pos mutation = No	pLI < 0.9	a2	b2
	pLI > 0.9	c2	d2

Results of the Breslow-Day test studying whether the presence of an independent position mutation affects odds ratios of nearby combination position mutations. Rows where such effect is significant (Breslow-Day p-value < 0.05) are highlighted in light blue.

Independent Pos	Combination Pos	Breslowday.pvalue	Odds.inde.mut	Odds.inde.wt
D+6	D+5, D+4, D+3	0.213	1.41	1.69
D+5	D+6, D+4, D+3	0.001	0.91	1.47
D+4	D+6, D+5, D+3	0.418	1.53	1.72
D+3	D+6, D+5, D+4	0.046	1.41	1.85
D+6	D+5, D+4, D+3, D-1	0.905	1.54	1.58
D+5	D+6, D+4, D+3, D-1	0.021	0.99	1.45
D+4	D+6, D+5, D+3, D-1	0.905	1.53	1.56
D+3	D+6, D+5, D+4, D-1	0.232	1.37	1.67
D-1	D+6, D+5, D+4, D+3	0.004	0.95	1.43
D+6	D+5	0.461	2.09	2.30
D+6	D+4	0.806	1.55	1.49
D+6	D+3	0.080	1.12	1.44
D+6	D-1	0.722	2.19	2.29
D+5	D+4	0.005	1.04	1.46
D+5	D+3	0.022	1.12	1.42
D+5	D-1	0.069	1.97	2.32
D+4	D+3	0.200	1.17	1.37
D+4	D-1	0.271	2.06	2.35
D+3	D-1	0.120	2.25	2.67