

Table S3 Estimation of false-negative rates for mutation-detection algorithms**A. False-negative rate of GATK mutation detection**

Deletion size (bp)	Overall (n)	False-negative frequency:	
		Within repetitive regions (n)	Outside repetitive regions (n)
1	32% (1000)	41% (311)	28% (689)
2	32% (1000)	37% (325)	30% (675)
3	28% (1000)	36% (291)	25% (709)
5	34% (1000)	42% (328)	30% (672)
10	35% (500)	45% (147)	31% (353)
20	100% (500)	100% (148)	100% (352)
50	100% (250)	100% (72)	100% (178)

B. False-negative rate of split-read mutation detection

Deletion size (bp)	Overall (n)	False-negative frequency:	
		Within repetitive regions (n)	Outside repetitive regions (n)
1	36% (1000)	65% (311)	23% (689)
2	35% (1000)	68% (325)	20% (675)
3	34% (1000)	66% (291)	21% (709)
5	35% (1000)	62% (328)	22% (672)
10	31% (500)	63% (147)	18% (353)
20	35% (500)	68% (148)	22% (352)
50	38% (250)	69% (72)	25% (178)

The whole-genome sequencing output from the *dpy-11(sy740)* and *dpy-11(sy745)* strains were tested for the detection of deletions against versions of the *C. elegans* reference genome sequence into which small insertions had been made, of known position and sequence, using the same mutation-detection methods used to seek off-target effects of CRISPR-Cas-mediated mutagenesis. The frequencies at which each method failed to detect these insertions as being apparent homozygous deletions in the genome of the sequenced strain is shown for each analysis method. In each case, the results are further broken down between insertion sites within regions noted using RepeatMasker (www.RepeatMasker.org) as being highly repetitive, and insertion sites not determined to be within highly repetitive regions.