Table S1. Summary of experiments with megamers

Locus, ssODN orientation (megamer concentration)	ssODN bridges or Step 2[a]	Plates with *dpy-10* edits/injected worms	Positives[b]/worms screened (%)	Partial insertions	Cas9 (ng/µl)
GFP::*sftb-1*, sense (20 ng/ul)	Bridges	10/28	0/175 (65 pools, 2-3 worms/pool)	3	1500
GFP::*sftb-1*, sense (20 ng/ul)	Bridges	22/25	0/150 (42 pools, 2-3 worms/pool)	3	1500
GFP::*sftb-1*, antisense (20 ng/ul)	Bridges	3/15	0/31 (14 pools, 2-3 worms/pool)	2	1500
GFP::*ubh-4*, antisense (20 ng/ul)	Bridges	7/15	0/250 (40 pools, 2-3 worms/pool)	0	1500
gtbp-1::GFP, sense (41 ng/ul)	Step 2	23/37	0/200 (40 pools, 2-3 worms/pool)	0	1500
pgl-1::GFP, sense (41 ng/ul)	Step 2	14/20	0/460 (100 pools, 4-6 worms/pool)	0	1500
prpf-4::GFP, sense (41 ng/ul)	Step 2	3/20	0/219 (100 pools, 2-3 worms/pool)	1	1500
prpf-4::mCherry, antisense (210 ng/ul)	Step 2	8/34	0/41	1	250

[a] The insertion of GFP with megamers was attempted either by its direct incorporation at the locus with the use of ssODN bridges at a concentration of 42 ng/µl, or used as a repair template in Step 2 of Nested CRISPR where the GFP 1-3 or mCherry 1-3 fragment was previously inserted, subsequently serving the purpose of homology arms. [b] Based on PCR genotyping (amplicons of the correct size are considered positives) and visual screening of jackpot plates. For experiments using bridges, the distance of the insertion from the DSB is 5 bases upstream (in both *sftb-1* and *ubh-4*) whereas for experiments using megamers as repair templates in Step 2 of Nested CRISPR, the insertions are designed to be integrated exactly at the DSB. We utilized both sense and antisense ssODNs. However, ssODN polarity has marginal effects on editing efficiency in proximal edits (<10 bp), and a specific polarity is only favored in distal edits (Paix *et al.* 2017).