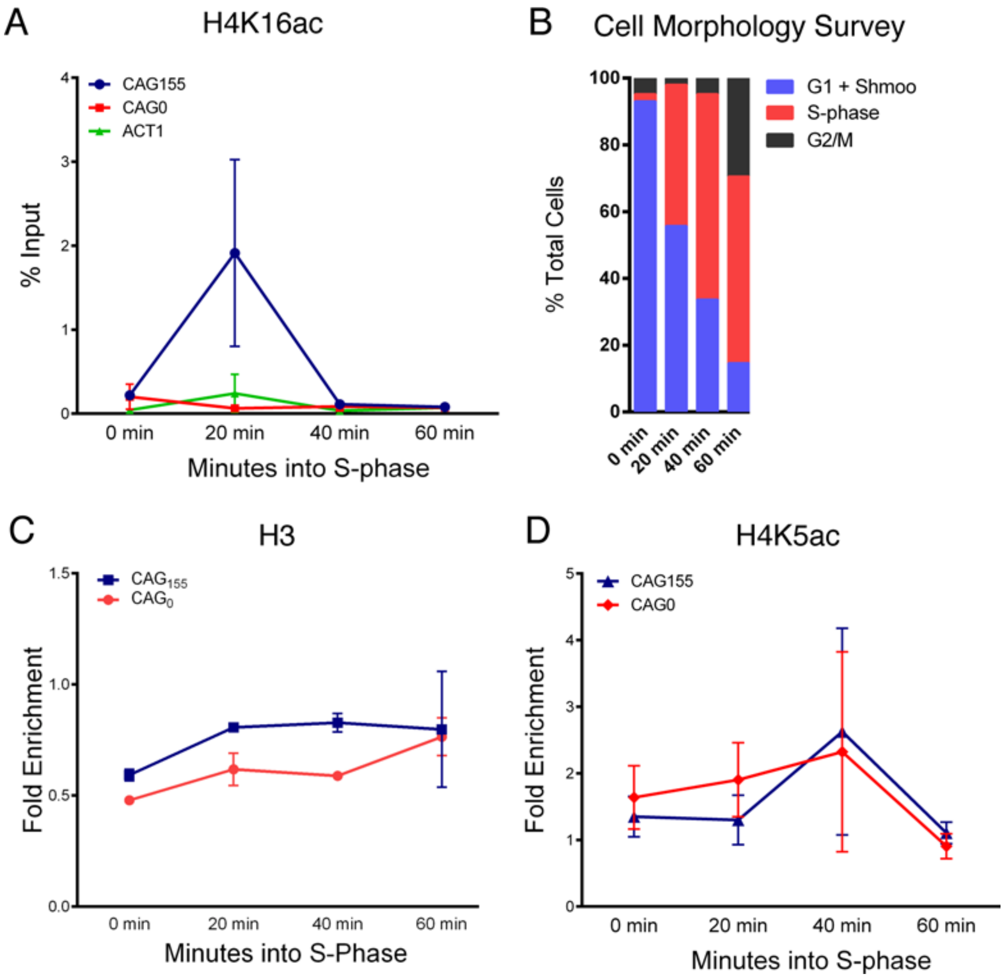

Figure S1. ChIP to detect acetyl-lysine residues at a $(CAG)_{155}$ repeat tract. Related to Figure 2. Cells were arrested in G1 with α-factor and time points taken after release into fresh media. qPCR used primers 0.4 and 0.6 kb upstream of the CAG repeat. (A) H4K16ac % Input ($2^{-\Delta Ct}$; no normalization) was measured at the CAG repeat (blue), a no-tract control (red), and at the ACT1 locus (green) as an internal control. (B) Cells used for ChIP were surveyed for cell cycle stage by morphology. Cells were arrested in G1 with α-factor and time points taken after release into fresh media. Cells were analyzed after crosslinking with formaldehyde and visualized under a light microscope. The bars represent the average of three CAG_{155} experiments. (C) Histone H3 levels were measured at the CAG repeat (blue) and a no-tract control (red); fold enrichment was calculated by normalization to an ACT1 control. (D) H4K5ac was measured at the CAG repeat (blue) and a no-tract control (red); fold enrichment was calculated by normalization to an ACT1 control. Data for A, C, D are represented as mean +/- SEM.

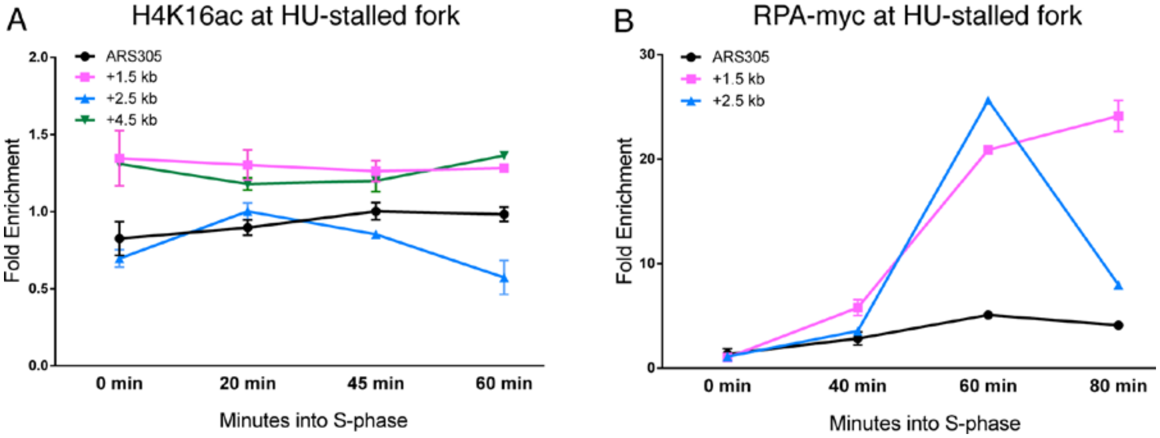

Figure S2 H4K16 acetylation at a stalled replication fork. Related to Figure 2. Cells were arrested in G1 with alpha factor and released into 0.2M HU and time points were taken as indicated. (A) H4K16ac ChIP was quantified by qPCR using primers at ARS305 and 1.5 kb, 2.5 kb, or 4.5 kb from the origin and fold enrichment over an ASI1 amplicon was used for normalization (Papamichos-Chronakis & Peterson, 2008). (B) A positive control shows enrichment for RPA 1.5 kb and 2.5 kb from the origin, indicating that the fork was efficiently stalled under these conditions. Fold enrichment over the ASI1 locus +/- SEM is shown.

Table S1 $(CAG)_{85}$ Stability Assay Data

		Expansions				Contractions			
Wildtype strains	Total reactions	#	%	Fold over wt	p-value to wt	#	%	Fold over wt	p-value to wt
Wildtype CFY801	299	4	1.3	--	--	33	11.0	--	--
H3/H4-wildtype CFY2501	156	3	1.9	1.4	1	27	17.3	1.6	1
ESA1-KAN wildtype CFY2048[a]	130	1	0.8	0.6	1	14	10.8	1.0	1
Single mutants									
esa1-1851[b]	125	10	8.0	6.0	5.0 x 10^{-3}	25	20.0	1.8	0.05
esa1-L357H[b]	104	2	1.9	1.4	0.65	17	16.4	1.5	0.17
yng2Δ	102	8	7.8	5.9	2.7 x 10^{-3}	14	13.7	1.2	0.48
hat1Δ	104	6	5.8	4.3	0.02	19	18.3	1.7	0.06
gcn5Δ	113	3	2.7	2.0	0.40	7	6.2	0.6	0.19
sas3Δ[c]	154	4	2.6	2.0	0.45	23	14.9	1.4	0.23
sas2Δ	179	3	1.7	1.3	1	17	9.5	0.9	0.65
sir2Δ	187	7	3.7	2.8	0.12	12	6.4	0.6	0.11
hst1Δ	105	1	1.0	0.7	1	10	9.5	0.9	0.65
hos2Δ	104	1	1.0	0.7	1	7	6.7	0.6	0.06
set3Δ	103	1	1.0	0.7	1	13	12.6	1.1	0.72
sum1Δ	104	0	0	0	0.58	10	9.6	0.9	0.85
rpd3Δ	218	2	0.9	0.7	1	12	5.5	0.5	0.03
HAT and HDAC double and triple mutants									
esa1-1851 sas2Δ[b]	104	6	5.8	4.3	0.02	21	20.2	1.8	0.03
hst1Δhos2Δ	101	5	5.0	3.7	4.9 x 10^{-2}	19	18.8	1.7	0.06
hst1Δsir2Δ	104	3	2.9	2.2	0.38	7	6.7	0.6	0.25
hos2Δrpd3Δ	174	4	2.3	1.7	0.47	13	7.5	0.7	0.26
hos2Δsir2Δ	102	9	8.8	6.6	9.3 x 10^{-4}	13	12.8	1.2	0.7
hst1Δhos2Δsir2Δ	205	19	9.3	6.9	9.9 x 10^{-4}	53	25.9	2.3	3.8 x 10^{-4}
Hda1 and Sae2 mutants									
hda1Δ	98	6	6.1	4.6	0.02	13	13.3	1.2	0.6
hda1Δhos2Δrpd3Δ	102	7	6.9	5.1	7.5 x 10^{-3}	11	10.8	1.0	1
sae2Δ	156	9	5.8	4.3	0.01	28	18.0	1.6	0.04
hda1Δsae2Δ	155	10	6.5	4.8	6.9 x 10^{-3}	37	23.9	2.2	5.4 x 10^{-4}
Histone mutants									
H4-K12R[d]	100	8	8.0	6.0	0.03	26	26.0	2.4	0.11
H4-K16R[d]	102	8	7.8	5.9	0.03	26	25.5	2.3	0.12
H4-K16Q[d]	204	11	5.4	4.0	0.11	40	19.6	1.8	0.68
H4-K5,8R[d]	104	5	4.8	3.6	0.27	17	16.3	1.5	0.86
H4-K5,8,12R[d]	102	10	9.8	7.3	7.1 x10^{-3}	21	20.6	1.9	0.52
H4-K5,8,12Q[d,e]	109	6	5.5	2.9	0.17	27	24.8	1.4	0.16
H4-K5,8,12,16R[d]	102	10	9.8	7.3	7.1 x 10^{-3}	29	28.4	2.6	0.04
H3/H4 WT rad5Δ[d]	96	6	6.3	4.7	0.09	25	26.0	2.7	0.11
H4-K12R rad5Δ[d]	153	2	1.3	1.0	1	40	26.1	2.4	0.07
H4-K16R rad5Δ[d]	151	3	2.0	1.5	1	15	9.9	0.9	0.07
H3-NΔ[d]	104	3	2.9	2.2	0.79	10	9.6	0.9	0.10

		Expansions				Contractions			
	Total reactions	#	%	Fold over wt	p-value to wt	#	%	Fold over wt	p-value to wt
H2A-NΔ[f]	93	2	2.2	1.6	1	25	26.9	2.4	0.03
htz1Δ	103	2	1.9	1.5	0.65	24	23.3	2.1	3.1 x 10^{-3}
HATs and HDACs and repair mutants									
lif1Δ	96	4	4.2	3.1	0.10	16	16.7	1.5	0.16
lif1Δ esa1-1851	102	9	8.8	6.6	9.3 x 10^{-4}	20	19.6	1.8	0.04
lif1Δhst1Δhos2Δsir2Δ	104	11	10.6	7.9	1.2 x 10^{-4}	15	14.4	1.3	0.38
rad52Δ	199	4	2	1.5	1	45	22.6	2.1	6.4 x 10^{-4}
rad52Δ esa1-1851[b]	92	1	1.1	0.8	1	4	4.4	0.4	0.07
rad52Δhat1Δ	92	0	0	0	0.58	16	17.4	1.6	0.15
rad52Δhst1Δhos2Δ	156	3	1.9	1.4	0.7	17	10.9	1.0	1
rad52Δhst1Δhos2Δsir2Δ	205	8	3.9	2.9	0.08	21	10.2	0.9	0.88
rad5Δ	170	7	4.1	3.1	0.11	31	18.2	1.7	0.04
rad5Δ esa1-1851	204	4	2.0	1.5	0.72	31	15.2	1.4	0.18
rad5Δhst1Δhos2Δsir2Δ	229	9	3.9	2.9	0.09	39	17.0	1.5	0.05
rad57Δ	146	7	4.8	3.6	0.05	24	16.4	1.5	0.13
rad57Δ esa1-1851	167	7	4.2	3.1	0.06	20	12.0	1.1	0.76
rad57Δhst1Δhos2Δsir2Δ	205	8	3.9	2.9	0.07	30	14.6	1.3	0.27
Chromatin remodeling									
rsc1Δ	100	6	6.0	4.5	0.02	9	9.0	0.8	0.71
rsc1Δ esa1-1851	163	17	10.4	7.8	1.5 x 10^{-5}	31	19.0	1.7	0.02
rsc1Δrad5Δ	148	4	2.7	2.0	0.45	22	14.9	1.4	0.28
rsc2Δ	104	5	4.8	3.6	0.05	22	21.2	1.9	0.01
rsc2Δ esa1-1851	179	15	8.4	6.3	3.2 x 10^{-4}	24	13.4	1.2	0.47
rsc2Δhst1Δhos2Δsir2Δ	199	11	5.5	4.1	0.01	28	14.1	1.3	0.33
rsc2Δrad5Δ	151	4	2.6	2.0	0.45	25	16.6	1.5	0.10
bdf1Δ	202	8	4.0	3.0	0.04	53	26.2	2.4	1.9 x 10^{-5}
bdf1Δ esa1-1851	103	7	6.8	5.1	7.9 x 10^{-3}	12	11.6	1.1	0.86
bdf1Δhst1Δhos2Δsir2Δ	99	7	7.1	5.3	6.6 x 10^{-3}	14	14.1	1.3	0.47
snf2Δ	96	1	1.5	1.1	1	10	10.4	0.9	1
snf2Δ esa1-1851	104	9	8.7	6.5	1.0 x 10^{-4}	18	17.3	1.6	0.12
snf2Δhst1Δhos2Δsir2Δ	103	10	9.7	7.3	3.2 x 10^{-4}	18	17.5	1.6	0.12
swr1Δ	93	2	2.2	1.6	0.63	15	16.3	1.5	0.21

All instability values statistically analyzed by Fisher's exact test, *$p < 0.05$, **$p < 0.01$.

[a] Instability was measured in a wildtype strain in which the KANMX6 cassette was integrated 150 bp 5' to the ESA1 stop codon to evaluate if integration of KANMX6 induced instability. These results indicate that KANMX6 downstream of ESA1 does not increase repeat instability. Therefore, instability in the *esa1* mutant allele strains can be attributed to the mutant allele.

[b] Compared to ESA1-wildtype (CFY2048).

[c] Data provided by M Koch.

[d] Compared to H3/H4 wildtype plasmid system, endogenous H3 and H4 copies deleted (CFY2051).

[e] H4K5,8,12Q plasmid provided by L Pillus (Torres-Machorro & Pillus, 2014).

[f] Compared to H2A/H2B wildtype plasmid system, endogenous H2A and H2B copies deleted (unpublished).

Table S2 (CAG)$_{85}$ Fragility Assay Data

Strain	Wildtype	*esa1-1851*	esa1-1851 CAG$_{155}$	*hat1Δ*	*hst1Δhos2Δ*
Mean Rate (x 10^{-6})[a]	**17.11**	**15.55**	**13.43**	**9.59***	**7.27***
SEM	2.45	2.26	2.25	1.23	2.08
No. replicates	(13)	(6)	(4)	(6)	(6)

	H3/H4 WT	*H4-K12R*	*H4-K16R*
Mean Rate (x 10^{-6})[a]	**34.67**	**38.3**	**22.4**
SEM	4.47	2.57	1.97
No. replicates	(3)	(3)	(3)

*$p<0.05$ to wt, Student's t-test

[a] Mean rate of Leu$^+$FOA^R mutants (x 10^{-6})

Table S3 Sister Chromatid Recombination Assay Data

Strain	Wildtype	*rad57Δ*	*rad5Δ*	*esa1-1851*	*yng2Δ*	*hst1Δhos2Δsir2Δ*	*rsc1Δ*	*rsc2Δ*	*bdf1Δ*
Mean Rate[a] (x 10^{-5})	**7.48**	**0.10****	**0.70***	**1.66****	**1.62****	**10.31**	**3.37***	**2.97***	**1.74***
SEM	1.06	0.02	0.16	0.21	0.53	1.60	0.37	0.73	0.71
No. replicates	(5)	(3)	(3)	(5)	(3)	(6)	(3)	(3)	(3)

Strain	Wildtype HU	Wildtype MMS	*esa1-1851* + MMS	*rsc1Δ* + MMS	*rsc2Δ* + MMS	*rad5Δ* + MMS	*bdf1Δ* + MMS
Mean Rate[a] (x 10^{-5})	**6.32**	**15.59****	**0.27****	**13.77****	**3.47**	**4.23**	**5.83**
SEM	1.72	1.40	0.05	1.85	0.21	0.50	1.15
No. replicates	(3)	(3)	(3)	(3)	(3)	(3)	(3)

Strain	H3/H4 WT	H4-K12R	H4K16R
Mean Rate[b] (x 10^{-5})	**11.47**	**3.89**	**2.24***
SEM	0.10	2.38	0.57
No. replicates	(4)	(3)	(3)

*$p<0.05$ to wt, **$p<0.01$ to wt, Student's t-test

[a] SCR Mean rate of Trp$^+$Ade$^+$ recombinants (x 10^{-5})

[b] SCR Mean rate of Ura$^+$Ade$^+$ recombinants (x 10^{-5})

Supplemental Experimental Procedures

Yeast strains and plasmids. Plasmids containing H4K12R, H4K16R, and H4K16Q were made by cloning a SpeI/SalI fragment from pQQ18H4K12R, pQQ18H4K16R, and pQQ18H4K16Q plasmids (Blackwell et al., 2007) into pRS314 digested by SpeI/SalI. Plasmids were introduced into *HHT2ΔHHF2Δ* BY4705, CAG85 cells under Trp selection and correct point mutations were confirmed by sequencing. *HHT1* and *HHF2* were then deleted. The H4K5,8R, H4K5,8,12R, H4K5,8,12,16R (Dion et al, 2005), and H3-NΔ (Mann and Grunstein, 1992) *MET15*-marked plasmids were obtained from OJ Rando, JS Thompson, and M Grunstein. Yeast mutants were obtained by plasmid shuffle into CFY2051, using FAA counter selection to select for loss of the *TRP1*-marked plasmid containing wild-type copies of the H3/H4 genes. Trp$^-$ cells were verified to be Met$^+$ indicating gain of the point mutant plasmid. The H4K5,8,12Q plasmid contains a *TRP1* marker (Torres-Machorro and Pillus, 2014); this strain was obtained by plasmid shuffle with the H3K5,8,12R mutant strain (plasmid contains *MET15*), selecting for Trp$^+$ and verifying Met$^-$. The H2A-NΔ plasmid, pJH161 (H2A-Δ5-21; marked with *HIS3*), was obtained from the Winston lab (Hirschhorn et al., 1995) and shuffled into the FY406 strain which has both wild-type copies of H2A and H2B deleted, then selecting for loss of the *URA3*-marked plasmid containing the wild-type H2A/H2B genes. YAC CF1, $(CAG)_{85}$ was then introduced by a kar cross and CAG repeat tract length was confirmed by PCR.

Supplemental References

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