Table SI. Yeast Strains

Strain	Genotype	Reference
LPY5	*(W303-1a) MATa ade2-1 can1-100 his3-11,15 leu2-3,112 trp1-1 ura3-1*	R. Rothstein
LPY11	*W303 MATa sir2Δ::HIS3*	
LPY3923	*W303 MATa sir2Δ::HIS3 hmr::TRP1*	
LPY4774	*W303 MATa esa1-414*	
LPY4908	*W303 MATa rDNA::ADE2-CAN1*	(21)
LPY4912	*W303 MATa esa1-414 rDNA::ADE2-CAN1*	(21)
LPY4916	*W303 MATa TELVR::URA3*	(21)
LPY5015	*W303 MATa sir2Δ::TRP1 rDNA::ADE2CAN1*	
LPY5034	*W303 MATa sir2Δ::HIS3 TELVR::URA3*	
LPY6496	*BY MATa his3Δ1 leu2Δ0 ura3Δ0*	
LPY6497	*BY MATa his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0*	
LPY11279	*W303 MATa esa1-414 sir2Δ::KanMX*	
LPY11509	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP1990*	
LPY12154	*W303 MATa rpd3Δ::KanMX*	(23)
LPY12156	*W303 MATa esa1-414 rpd3Δ::KanMX*	(23)
LPY13060	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP2146*	
LPY13062	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP1990*	
LPY13063	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP2146*	
LPY13064	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP2181*	
LPY13426	*BY MATa rpd3Δ::kanmx*	
LPY13472	*W303 MATa hda1Δ::KanMX*	(23)
LPY13478	*W303 MATa esa1-414 hda1Δ::KanMX*	(23)
LPY13583	*W303 MATa hos2::KanMX*	
LPY13585	*W303 MATa esa1-414 hos2::KanMX*	
LPY13654	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP1777*	(23)
LPY13656	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP2181*	(23)
LPY13706	*W303 MATa hos1Δ::KanMX*	
LPY13712	*W303 MATa esa1-414 hos1Δ::KanMX*	
LPY14161	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP1775*	(23)
LPY14162	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP2145*	(23)
LPY14163	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP1775*	
LPY14164	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP2145*	
LPY14577	*BY MATa hos2Δ::KanMX*	
LPY14757	*BY MATa lys2Δ0 esa1Δ::KanMX + pLP2354*	
LPY14761	*BY MATa esa1Δ::KanMX hos2Δ::KanMX + pLP2354*	
LPY14988	*W303 MATa esa1Δ::HIS3 + pLP796*	
LPY14989	*W303 MATa esa1Δ::HIS3 hos2Δ::kanmx + pLP796*	
LPY15851	*BY MATα snt1Δ::KanMX*	
LPY15853	*BY MATa met15Δ0 set3Δ::KanMX*	
LPY15857	*BY MATa lys2Δ0 met15Δ0 sif2Δ::KanMX*	
LPY15860	*BY MATa lys2Δ0 met15Δ0 hos4Δ::KanMX*	
LPY15862	*BY MATa lys2Δ0 sum1Δ::KanMX*	
LPY15863	*BY MATa lys2Δ0 esa1Δ::KanMX sif2Δ::KanMX + pLP2354*	
LPY15867	*BY MATα esa1Δ::KanMX snt1Δ::KanMX + pLP2354*	
LPY15869	*BY MATα esa1Δ::KanMX set3Δ::KanMX + pLP2354*	
LPY15906	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP1775*	
LPY15907	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP1775*	
LPY15909	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP1777*	
LPY15910	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP1777*	
LPY15911	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP2181*	
LPY15912	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP2145*	

LPY15913	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP2146*
LPY15914	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP1990*
LPY15915	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP1777*
LPY17505	*BY MATa esa1Δ::kanMX sum1Δ::KanMX + pLP2354*
LPY17911	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP2181*
LPY17912	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP2145*
LPY17913	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP2146*
LPY17914	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP1990*
LPY18067	*W303 MATa hos2Δ::KanMX hmr::TRP1*
LPY18070	*W303 MATa esa1-414 hos2Δ::KanMX TELVR::URA3*
LPY18071	*W303 MATa hos2Δ::KanMX TELVR::URA3*
LPY18073	*W303 MATa hos2Δ::KanMX rDNA::ADE2CAN1*
LPY18074	*W303 MATa esa1-414 hos2Δ::KanMX rDNA::ADE2CAN1*
LPY18266	*BY MATa esa1Δ::kanMX hst1Δ2::LEU2 + pLP2354*
LPY18268	*W303 MATa esa1-414 hmr::TRP1*
LPY18269	*W303 MATa esa1-414 hos2Δ::KanMX hmr::TRP1*
LPY18275	*BY MATa hst1Δ2::LEU2*
LPY19406	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP2232*
LPY19420	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP2209*
LPY19421	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP2209*
LPY19422	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP2209*
LPY19423	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP2209*
LPY19424	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP2232*
LPY19425	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP2232*
LPY19426	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP2232*
LPY21399	*W303 MATa hos2Δ::kanMX gcn5Δ::natR*
LPY21400	*W303 MATa esa1Δ::HIS3 + pLP863*
LPY21401	*W303 MATα esa1Δ::HIS3 hos2Δ::kanMX + pLP863*
LPY21426	*BY MATa hos2Δ::kanMX rpd3Δ::natR*
LPY21428	*BY MATa esa1Δ::kanMX hos2Δ::kanMX rpd3Δ::natR + pLP2354*
LPY21450	*BY MATa esa1Δ::kanMX rpd3Δ::natR + pLP2354*
LPY21468	*W303 MATa esa1Δ::HIS3 hos2Δ::kanMX gcn5Δ::natR + pLP863*
LPY21480	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH + pLP1779*
LPY21481	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 + pLP1779*
LPY21482	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH esa1-414 hos2Δ::KanMX + pLP1779*
LPY21483	*W303 MATa hht1-hhf1Δ::KanMX hht2-hhf2Δ::KanMX hta2-htb2Δ::HPH hos2Δ::KanMX + pLP1779*
LPY21494	*BY MATa cps40Δ::kanMX*
LPY21495	*BY MATa esa1Δ::kanMX cps40Δ::kanMX + pLP2354*
LPY21498	*BY MATa esa1Δ::kanMX cps25Δ::kanMX + pLP2354*
LPY21499	*BY MATa cps25Δ::kanMX*
LPY21503	*BY MATa esa1Δ::kanMX cps60Δ::kanMX + pLP2354*
LPY21520	*BY MATa cps60Δ::kanMX*
LPY21656	*BY MATa lys2Δ0 esa1Δ::kanMX hos2Δ::kanMX cps25Δ::kanMX + pLP2354*
LPY21651	*BY MATa lys2Δ0 esa1Δ::kanMX hos2Δ::kanMX cps40Δ::kanMX + pLP2354*

Unless otherwise noted, strains were constructed during the course of this study or are part of the standard lab collection.
All BY strains derive from the yeast deletion collection (Research Genetics).

Table S2. Plasmids

Plasmid	Description	Source/Reference
pJH33	*HTA1 HTB1 HHF2 HHT2 URA3 CEN*	(50)
pLP60	*pRS313, vector HIS3 CEN*	Sikorski and Hieter, 1989
pLP780	*esa1-L254P TRP1 CEN*	A. Clarke
pLP796	*ESA1 URA3 2μ*	A. Clarke
pLP863	*esa1-414 TRP1 CEN*	A. Clarke
pLP1358	*pRS415, vector LEU2 CEN*	
pLP1775	*HHF2 HHT2 TRP1 CEN*	S. L. Berger
pLP1777	*HHF2 hht2-K14A TRP1 CEN*	
pLP1779	*HHF2 hht2-K4A TRP1 CEN*	
pLP2181	*hhf2-K5A HHT2 TRP1 CEN*	(23)
pLP2145	*hhf2-K8A HHT2 TRP1 CEN*	(23)
pLP2146	*hhf2-K12A HHT2 TRP1 CEN*	(23)
pLP1990	*hhf2-K16A HHT2 TRP1 CEN*	(23)
pLP2209	*hhf2-K8A, K12A HHT2 TRP1 CEN*	
pLP2332	*hhf2-K5A, K12A HHT2 TRP1 CEN*	
pLP2354	*esa1-531 URA3 CEN*	(7)
pLP2374	*esa1-531 TRP1 CEN*	
pLP2567	*HOS2 HIS3 CEN*	
pLP2569	*hos2-H195A, H196A HIS3 CEN*	
pLP2856	*HOS2 HIS3 2μ*	
pLP2857	*hos2-H195S, H196A HIS3 2μ*	
pLP3020	*pSB1439, pRS415-set3-W140A-3xHA*	(40)

Unless otherwise noted, plasmids were constructed during the course of this study or are part of the standard lab collection.

Table S3. Oligonucleotides

Oligo	Name	Sequence	Source/Reference
oLP798	ACT1-F	GGTGGTTCTATCTTGGCTTC	J.M. WIlson
oLP799	ACT1-R	GGTGGTTCTATCTTGGCTTC	J.M. Wilson
oLP1495	HOS2-H195A-H196A-F	GATATCGACTTAGCTGCCGGCGATGGTGTCCAG	
oLP1496	HOS2-H195A-H196A-R	CTGGACACCATCGCCGGCAGCTAAGTCGATATCG	
oLP1504	RNR3-F	TTATTCAACGCTGGTACGCC	
oLP1505	RNR3-R	GAAGTACCGTTGGTACCAGC	
oLP1506	HUG1-F	CATGGACCAAGGCCTTAACC	
oLP1507	HUG1-R	TGATGTTGGCAGAAGGAACG	
oLP2003	GRE2-F	GCCTTCCAAAAGAGGGAAAC	
oLP2004	GRE2-R	GGGTAGCACCAGAACCTG	
oLP2011	ERG5-F	AGGTTCCATCGCAGGTCC	
oLP2012	ERG5-R	CCGGATGCCCACTTAGCC	

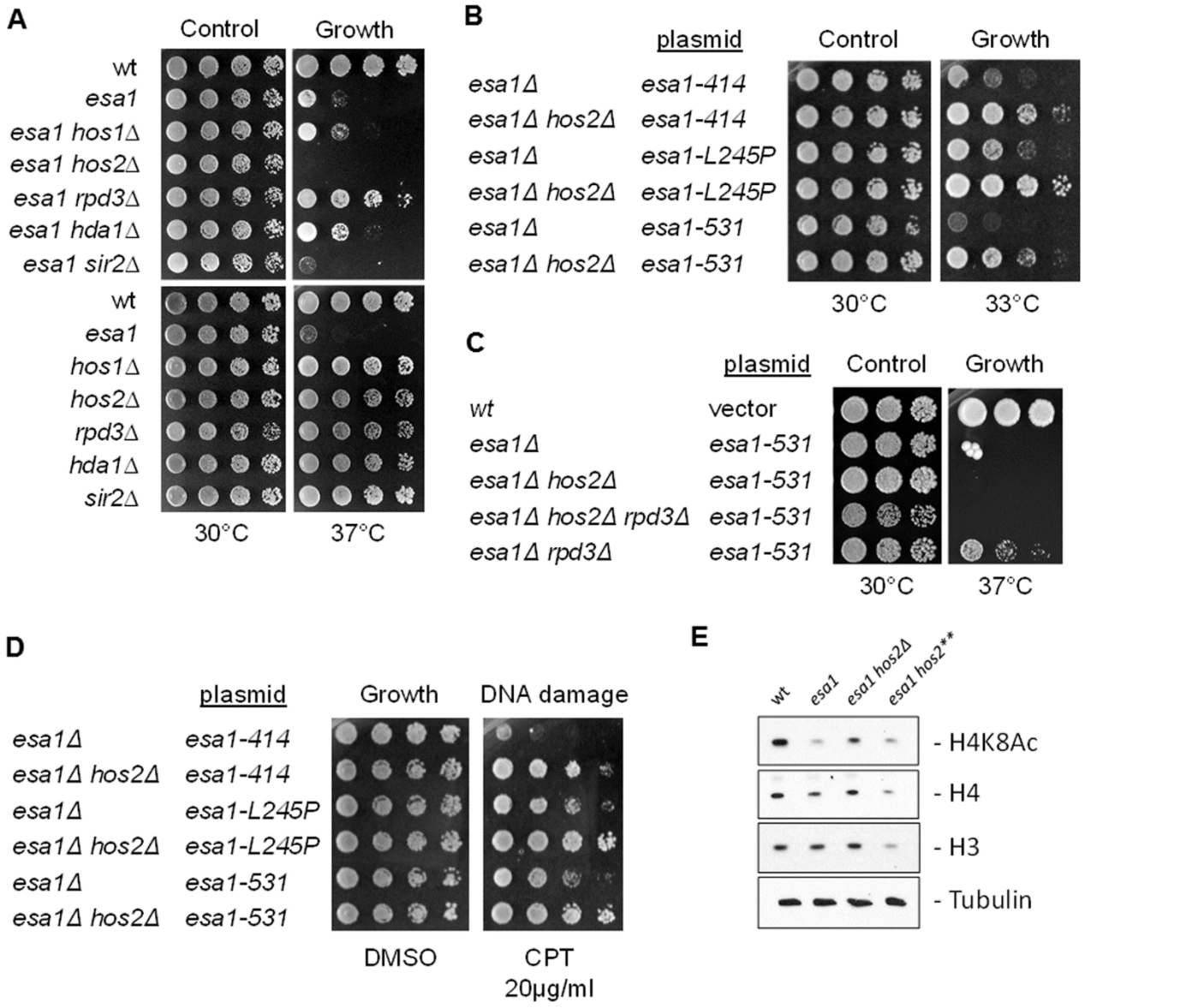

FIG S1 Deletion of *HOS2* was a poor suppressor of the temperature sensitivity, and a good suppressor of the DNA damage sensitivity of *esa1*. (A) Deletion of *HOS2* exacerbated the temperature sensitivity of *esa1* integrated alleles at 37°C. Strains in Fig. 1A grown at 30 and 37°C. Deletion of *RPD3* was previously shown to suppress temperature sensitivity of *esa1* (23). Note that although *hos2Δ* suppressed the DNA damage sensitivity of *esa1*, it aggravated the growth defect at high temperatures. The exacerbated temperature sensitivity of the *esa1Δ hos2Δ* strain was in contrast to the synthetic rescue identified in a global survey of interactions among HATs and HDACs (7). We pursued the discrepancy by analyzing high temperature growth of strains similar to the one used by Lin *et al*., which were *esa1Δ* strains expressing *esa1* alleles from a plasmid. (B) The *HOS2* deletion suppressed the temperature sensitivity of three different plasmid-borne *esa1* alleles at 33°C, whereas the high temperature growth defect was exacerbated by *hos2Δ* in the chromosomally integrated *esa1-414* allele at 37°C (Fig. S1A). Serial dilutions of *esa1Δ* (LPY14988) and *esa1Δ hos2Δ* (LPY14989) strains carrying one of three different *esa1* mutant alleles on *TRP1* centromeric plasmids were assayed on YPD for growth at permissive (30°C) and non-permissive (33°C) temperature after selecting against the covering *URA3* plasmid by growth on 5-FOA. The three different alleles tested were *esa1-414* (pLP863), *esa1-L254P* (pLP780), and *esa1-*

531 (pLP2374). Plating on selective media was not necessary as strains were unable to live without covering *esa1* alleles. (C) Deletion of *HOS2* could not suppress the temperature sensitivity of the plasmid-borne allele *esa1-531* at 37°C. As observed for the *esa1-414* allele, the control *RPD3* deletion suppressed *esa1-531'*s defect at 37°C. (D) The differential suppression of the temperature sensitivity of *esa1* integrated and plasmid-borne alleles observed in Fig. S1A-B was not found for the suppression of the DNA damage sensitivity phenotype, as the *HOS2* deletion equally suppressed both types of alleles (see also Fig. 1A), confirming *hos2Δ* as a general suppressor of *esa1* DNA damage sensitivity. Strains were plated on DMSO and CPT plates and grown at 30°C. (E) *esa1 hos2Δ* strains transformed with vector or with catalytic *hos2*** mutant have increased H4K8 acetylation levels relative to *esa1* single mutants. Whole cell lysates of strains in Fig. 1B were probed with the indicated antibodies. Note that the *esa1 hos2Δ* strain expressing *hos2*** had low histone H3 and H4 levels.

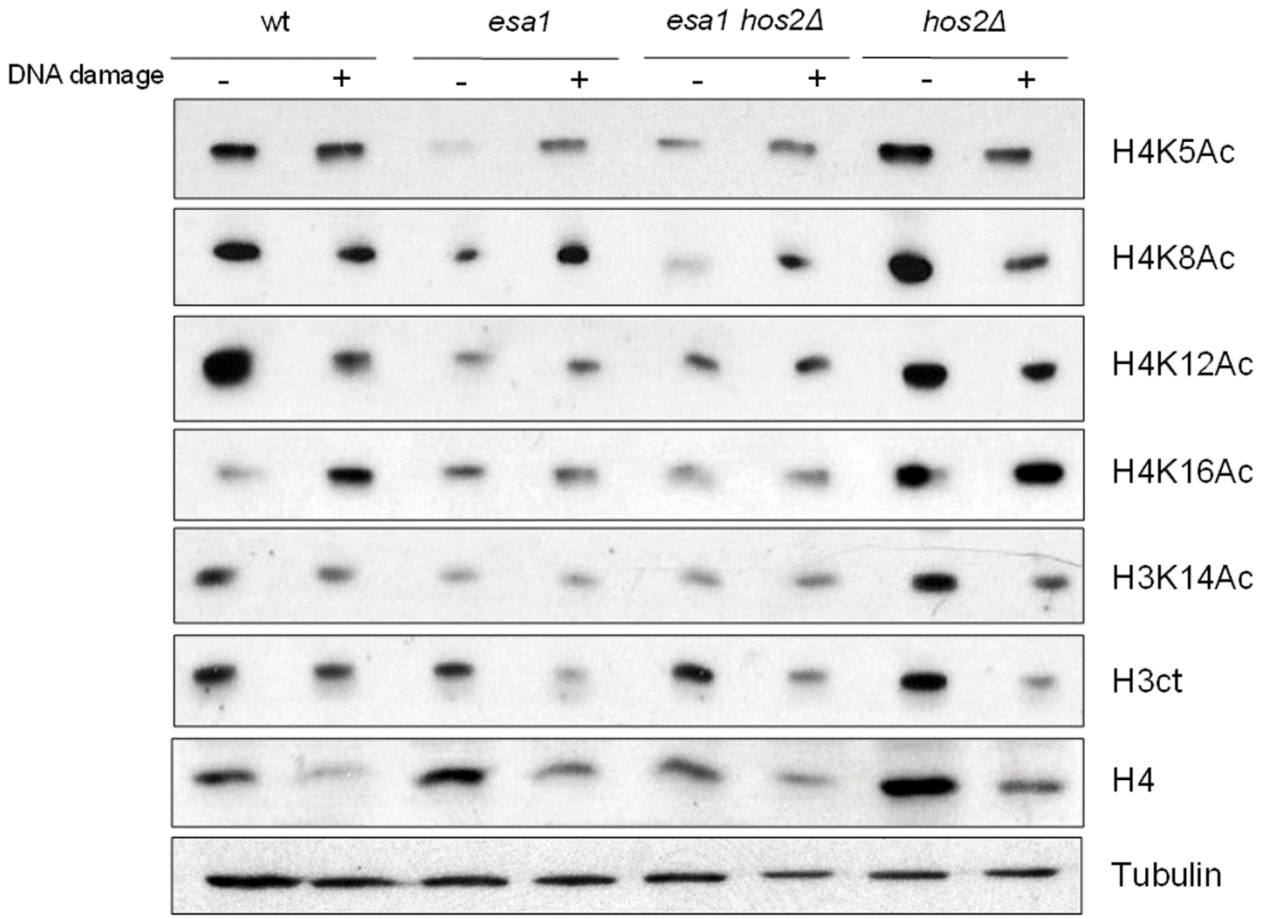

FIG S2 Deletion of *HOS2* improved low histone H4K5 acetylation of *esa1* independently of DNA damage. Lysates from strains in Fig. 2D, treated with HU to induce DSBs, were probed with the specified antisera. The total histone levels (H3 and H4) were reduced when cells were treated with HU, a result of diminished transcription of histone genes (72). DNA damage was induced with HU. The *esa1* strains are also sensitive to HU and it was preferable to CPT because of its enhanced aqueous solubility. The experiment was also performed in *esa1-414* strains with similar results.

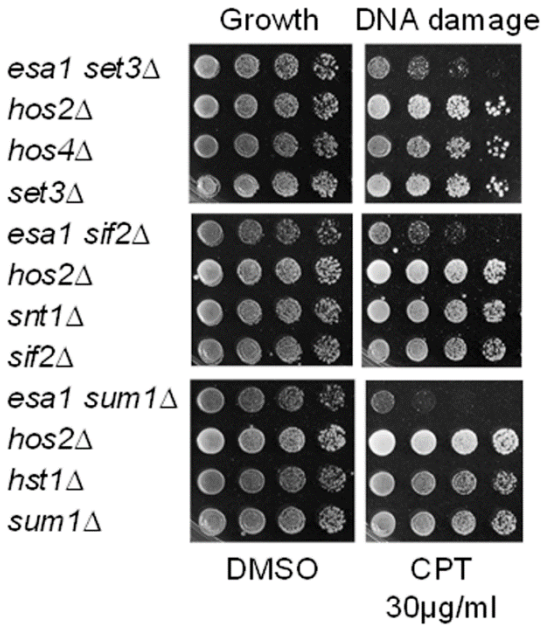

FIG S3 Deletions of single subunits of Set3C were not sensitive to DNA damage. Strains tested included *hos2Δ* (LPY14577), *hos4Δ* (LPY15860), *set3Δ* (LPY15853), *snt1Δ* (LPY15851), *sif2Δ* (LPY15857), *hst1Δ2* (LPY18277) and *sum1Δ* (LPY15862).