Supplementary Information

PKA plays a conserved role in regulating gene expression and metabolic adaptation by phosphorylating Rpd3/HDAC1

Wenjing Dai[1,3], Qi Yu[1,3], Rui Ma[1], Zhu Zheng[1], Lingling Hong[1], Yuqing Qi[1], Fei He[1], Min Wang[2], Feng Ge[2], Xilan Yu[1,*], Shanshan Li[1,*]

[1]State Key Laboratory of Biocatalysis and Enzyme Engineering, National & Local Joint Engineering Research Center of High-throughput Drug Screening Technology, College of Life Sciences, Hubei University, Wuhan, Hubei 430062, China

[2]Key Laboratory of Algal Biology, Institute of Hydrobiology, Chinese Academy of Sciences, Wuhan, Hubei 430072, China

[3]These authors contributed equally to this work

*Corresponding author

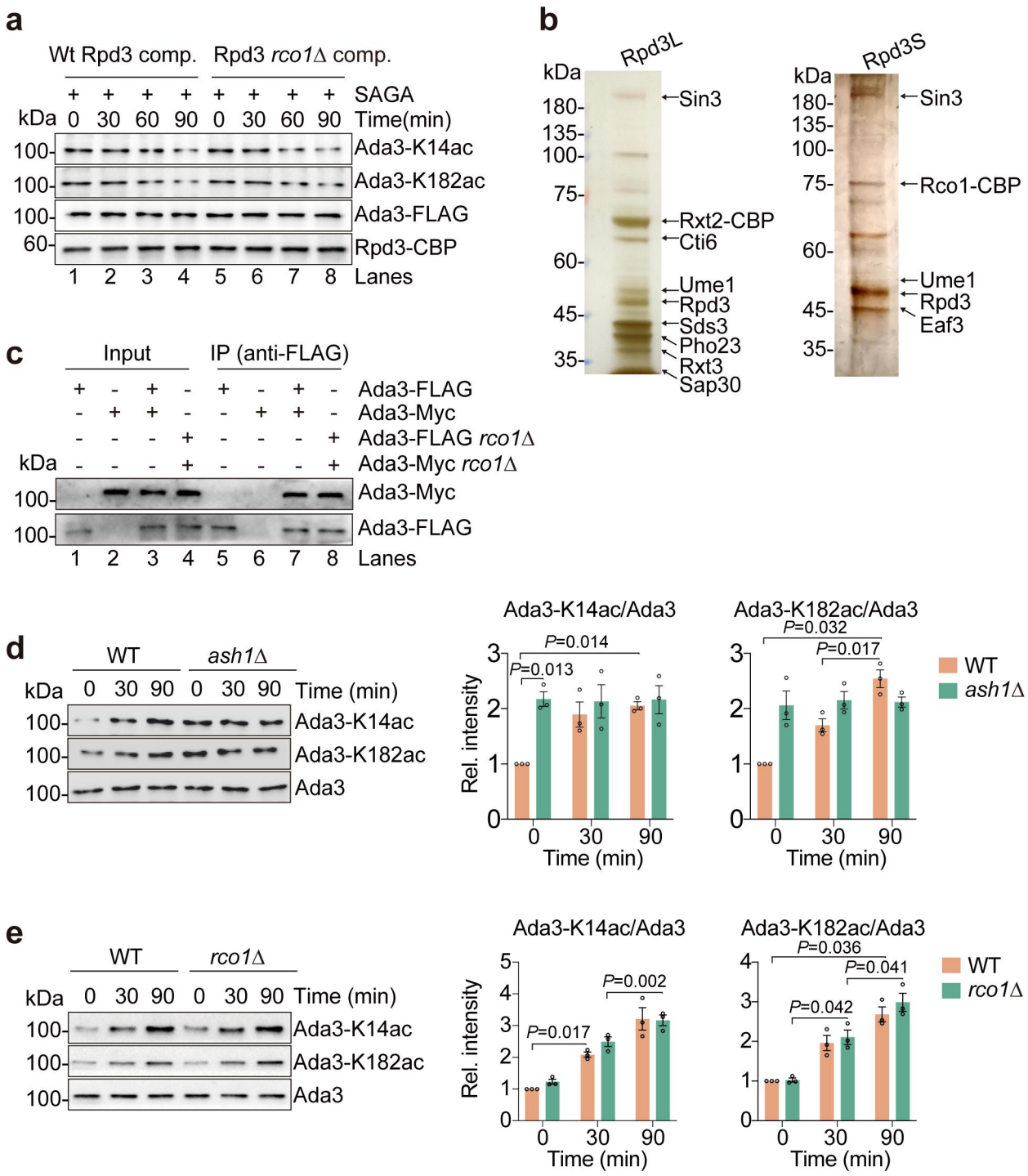
Shanshan Li, Email: shl@hubu.edu.cn.

Xilan Yu, Email: yuxilan@hubu.edu.cn

Supplementary Data：

1. **Supplementary Figures (S1-S12).**
2. **Spplemental Tables (S1-S3).**

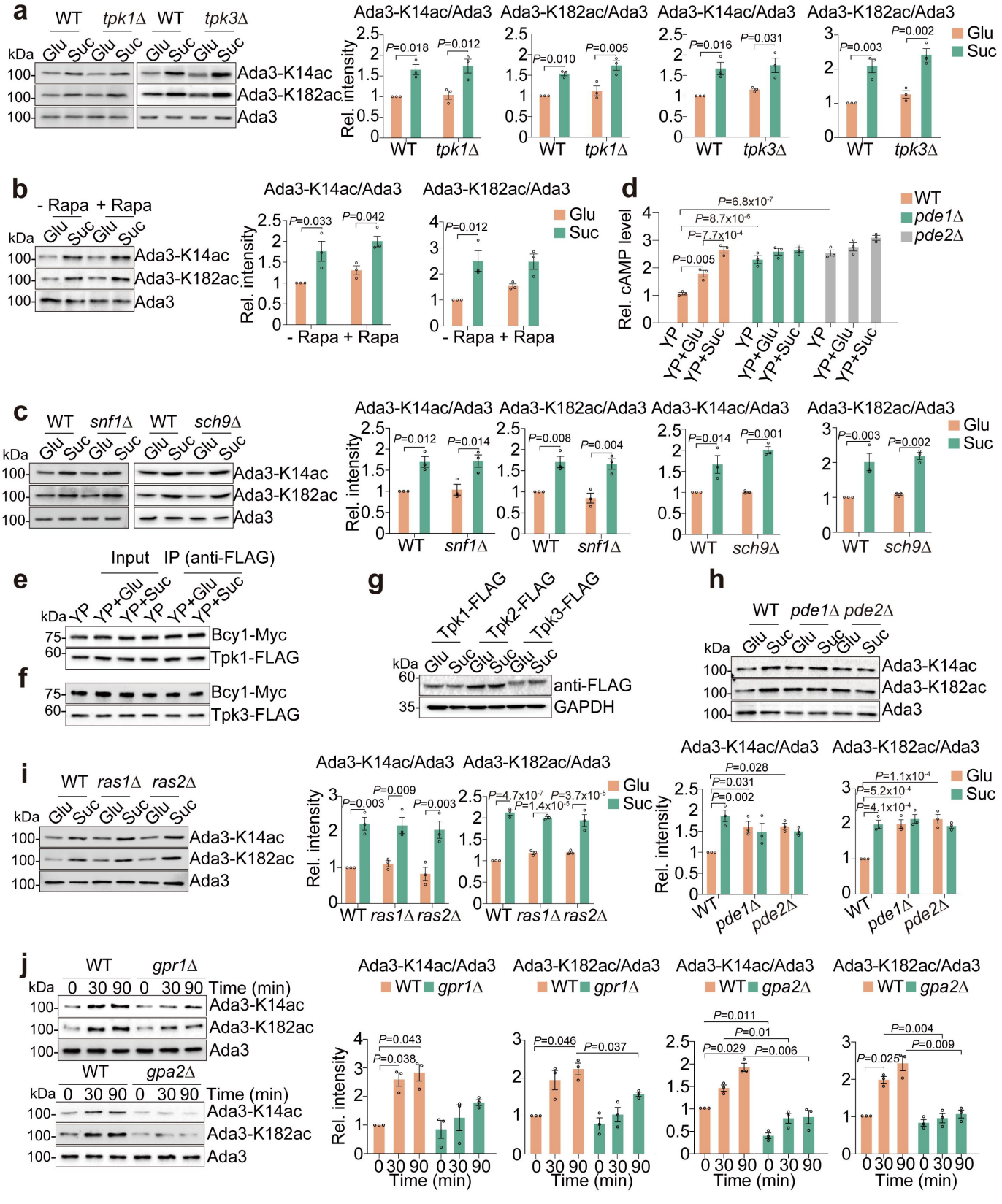
Supplementary Fig. 1



Supplementary Fig. 1 Rpd3L complex deacetylates Ada3.
(**a**) Analysis of Ada3 deacetylase activity of Rpd3 complex (Wt Rpd3 comp.) and Rpd3 *rco1*Δ complex (Rpd3 *rco1*Δ comp.) by in vitro deacetylase assay. Purified SAGA was used as the substrate. (**b**) Silver staining of purified Rpd3L complex and Rpd3S complex. Rpd3L complex and Rpd3S complex were purified from Rxt2-TAP and Rco1-TAP cells. Rxt2-TAP and Rco1-TAP contain both protein A and CBP tags. After purification, the protein A tag of Rxt2-TAP and Rco1-TAP was cleaved to produce Rxt2-CBP and Rco1-CBP. (**c**) Loss of Rpd3S specific subunit, Rco1 had no effect on SAGA dimerization. The diploid strain (Ada3-FLAG/Ada3-Myc) expressed Ada3-FLAG and Ada3-Myc. The diploid strain (Ada3-FLAG/Ada3-Myc *rco1*Δ/*rco1*Δ) expressed Ada3-FLAG and Ada3-Myc but with *RCO1* deleted. The haploid strain containing Ada3-Myc and the haploid strain containing Ada3-FLAG were used as controls. Ada3-FLAG was immunoprecipitated with anti-FLAG beads. (**d**) Analysis of Ada3 acetylation in WT and *ash1*Δ mutant when treated with YP + 2% sucrose for 0-90 min. The level of Ada3 acetylation was determined by immunoblots with anti-Ada3-K14ac antibody and anti-Ada3-K182ac antibody. (**e**) Analysis of Ada3 acetylation in WT and *rco1*Δ mutant when treated with YP + 2% sucrose for 0-90 min.

For Supplementary Fig. 1**d-e**, data represent means ± SE; n=3 biological independent experiments; Two-way ANOVA with Šídák's multiple comparisons tests were used for statistical analysis. For Supplementary Fig. 1**a-c**, data represent a typical example of at least two biological independent experiments.

Supplementary Fig. 2

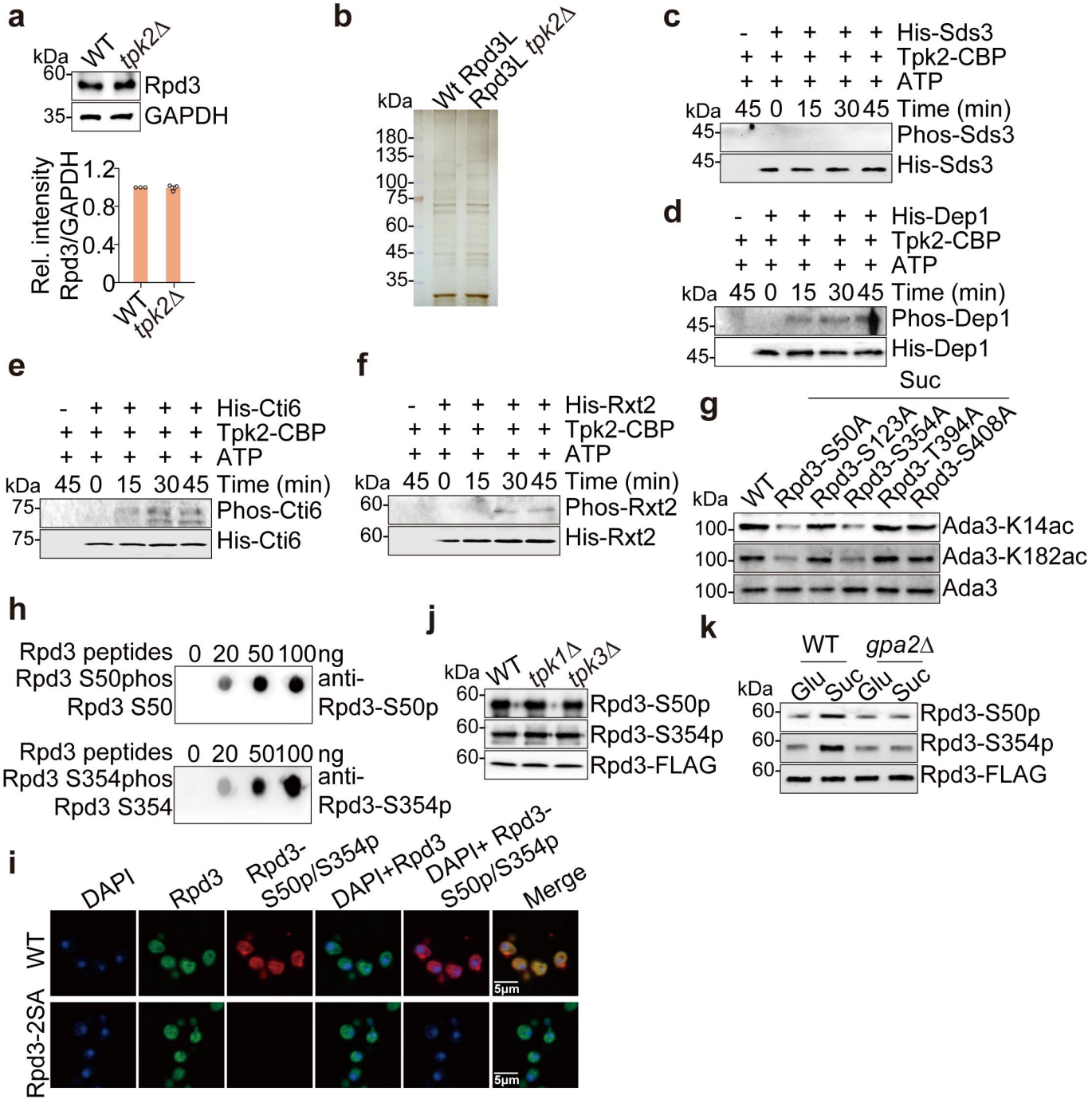


Supplementary Fig. 2 The Gpr1-Gpa2-Cyr1-Tpk2 pathway is required for sucrose to repress Rpd3L-mediated Ada3 deacetylation.

(**a**) Immunoblot analysis of Ada3 acetylation in WT, *tpk1*Δ and *tpk3*Δ mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. Tpk1 and Tpk3 are catalytic subunits of PKA. (**b**) Effect of rapamycin (Rapa) on Ada3 acetylation in yeast cells grown in YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) medium. Cells were treated with or without 1 μg/mL rapamycin (Rapa) for 1 h. (**c**) Immunoblot analysis of Ada3 acetylation in WT, *snf1*Δ and *sch9*Δ mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h, respectively. (**d**) Analysis of intracellular cAMP levels in WT, *pde1*Δ and *pde2*Δ mutants. Cells were first starved in YP medium for 1 h and then treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 10 min, respectively. (**e**) Co-IP analysis of the interaction between Tpk1 and Bcy1 in cells when treated with YP, YP + 2% glucose (YP + Glu) or YP + 2% sucrose (YP + Suc) for 0.5 h. Tpk1-FLAG was immunoprecipitated with anti-FLAG agarose beads. (**f**) Co-IP analysis of the interaction between Tpk3 and Bcy1 in cells when treated with YP, YP + 2% glucose (YP + Glu) or YP + 2% sucrose (YP + Suc) for 0.5 h. Tpk3-FLAG was immunoprecipitated with anti-FLAG beads. (**g**) Immunoblot analysis of Tpk1-FLAG, Tpk2-FLAG and Tpk3-FLAG in cells treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**h**) Immunoblot analysis of Ada3 acetylation in WT, *pde1*Δ and *pde2*Δ mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**i**) Immunoblot analysis of Ada3 acetylation in WT, *ras1*Δ and *ras2*Δ mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**j**) Analysis of Ada3 acetylation in WT, *gpr1*Δ and *gpa2*Δ mutants when treated with YP + 2% sucrose for 0-90 min.

For Supplementary Fig. 2**a-d**, **h-j**, data represent means ± SE; n=3 biological independent experiments; two-way ANOVA with Tukey's multiple comparisons tests (**a-d, h-i**) and Šídák's multiple comparisons tests (**j**) were used for statistical analysis. For Supplementary Fig. 2**e-g**, data represent a typical example of at least two biological independent experiments.

Supplementary Fig. 3

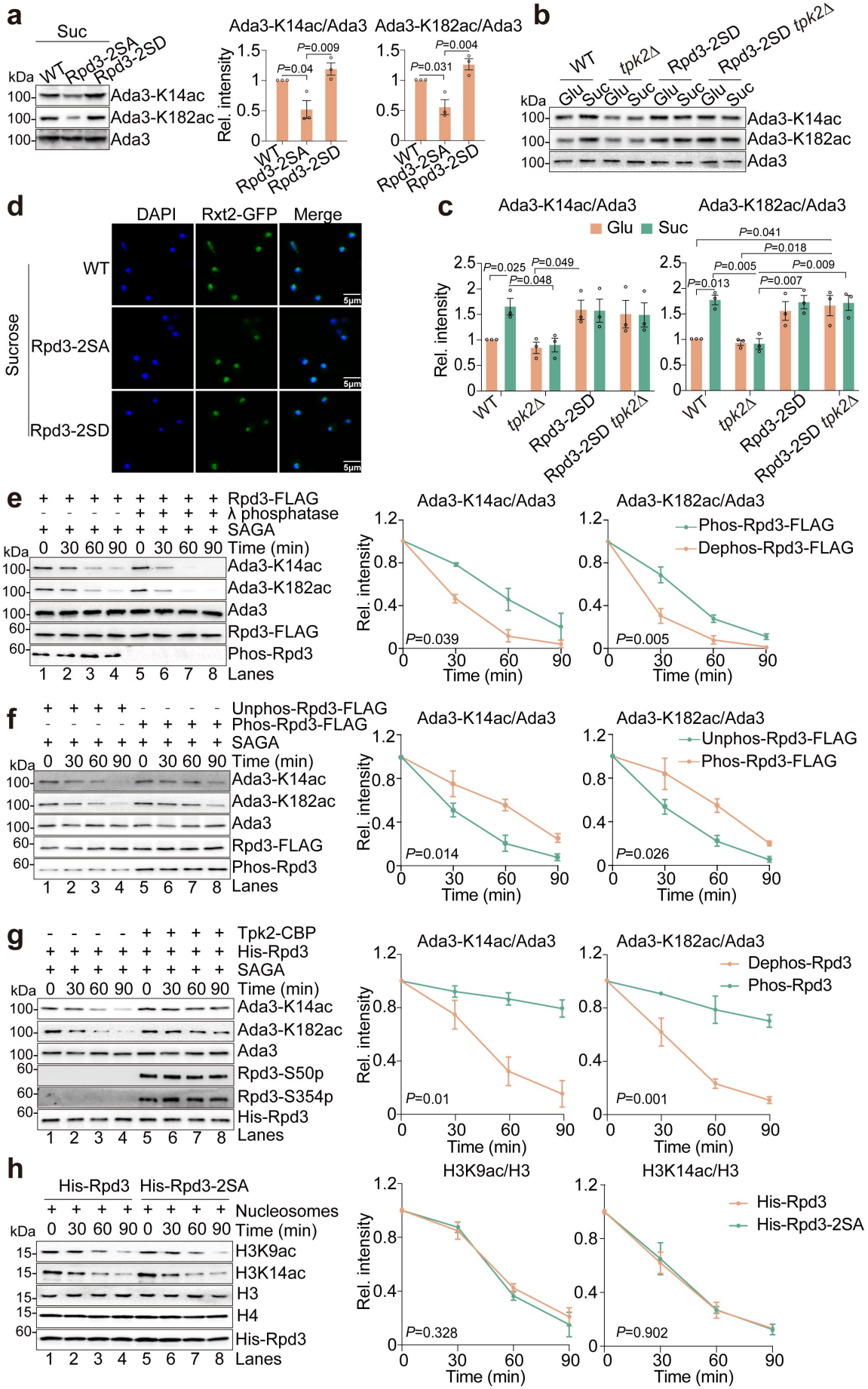


Supplementary Fig. 3 Tpk2 phosphorylates Rpd3 at S50 and S354 in response to sucrose treatment.

(**a**) Immunoblot analysis of Rpd3 in WT and *tpk2*Δ mutant. GAPDH was used as an endogenous loading control. (**b**) Silver staining of purified Wt Rpd3L and Rpd3L *tpk2*Δ. (**c**-**f**) In vitro kinase assay using purified Tpk2-CBP as the enzyme and purified recombinant His-Sds3 (**c**), His-Dep1 (**d**), His-Cti6 (**e**), or His-Rxt2 (**f**) as the substrates. The phosphorylation was detected using pan-phosphoserine/threonine (Phos-Ser/Tyr) antibody. (**g**) Immunoblot analysis of Ada3 acetylation in WT, Rpd3-S50A, Rpd3-S123A, Rpd3-S354A, Rpd3-T394A and Rpd3-S408A mutants when treated with YP + 2% sucrose (Suc) for 0.5 h. (**h**) Dot blot analysis of the specificity of anti-Rpd3-S50p and anti-Rpd3-S354p antibodies. The Rpd3 peptides containing phosphorylated (Rpd3 S50phos) or unphosphorylated S50 (Rpd3 S50), or S354 (Rpd3 S354phos, Rpd3 S354) were probed with anti-Rpd3-S50p and anti-Rpd3-S354p antibodies, respectively. Different dots represent different amounts of peptides used. (**i**) Analysis of the specificity of anti-Rpd3-S50p and anti-Rpd3-S354p antibodies in WT and Rpd3-2SA mutant treated with YP + 2% sucrose (Suc) for 0.5 h by immunofluorescence. (**j**) Analysis of Rpd3 phosphorylation in WT, *tpk1*Δ and *tpk3*Δ mutants. The phosphorylation of Rpd3 was determined by immunoblots with anti-Rpd3-S50p and anti-Rpd3-S354p antibodies. (**k**) Immunoblot analysis of Rpd3 phosphorylation in WT and *gpa2*Δ when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h.

For Supplementary Fig. 3**a**, data represent means ± SE; n=3 biological independent experiments; two tailed unpaired *t*-tests were used in statistical analysis. For Supplementary Fig. 3**c**-**k**, data represent a typical example of at least two biological independent experiments.

Supplementary Fig. 4

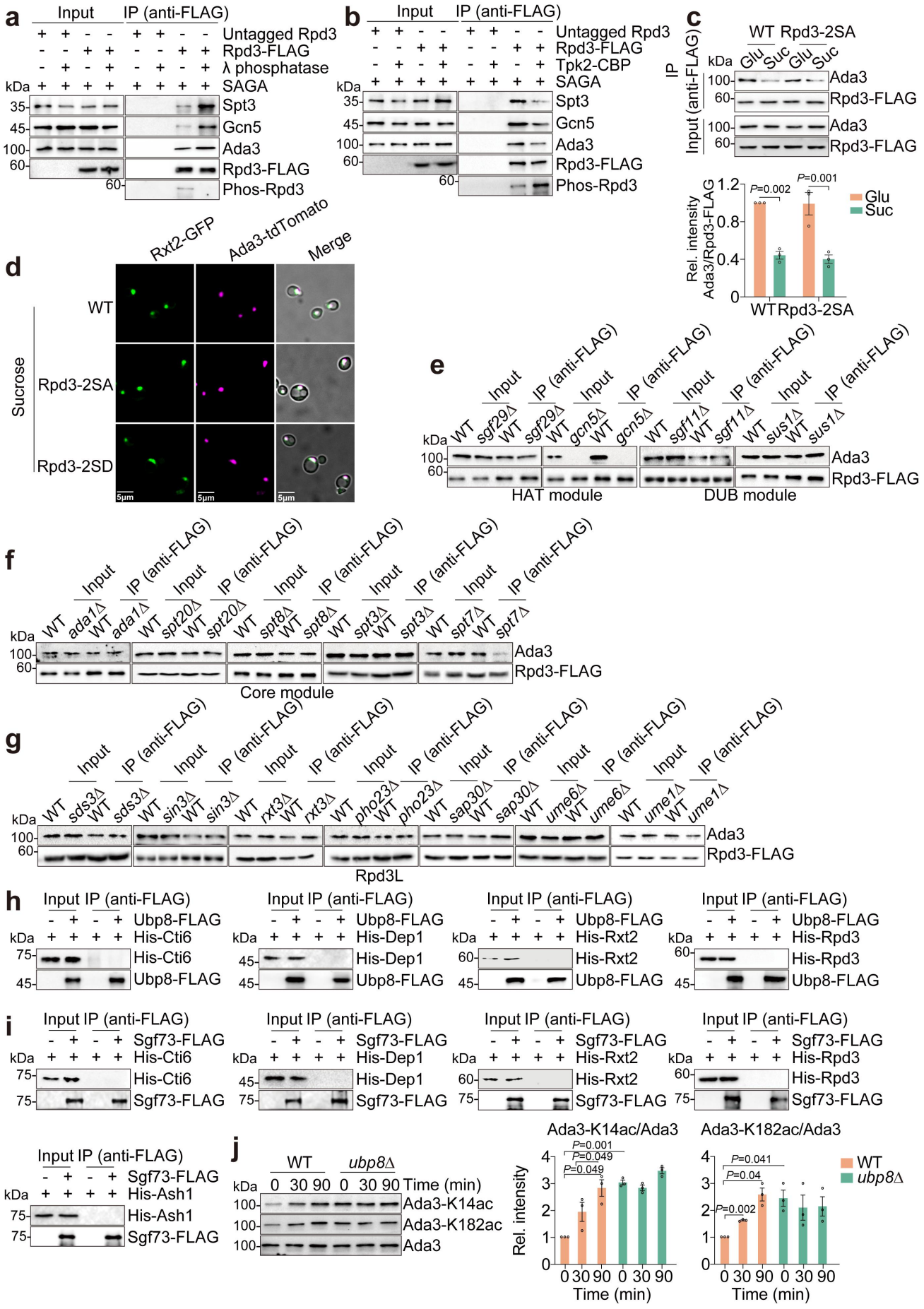


Supplementary Fig. 4 Tpk2-catalyzed phosphorylation of Rpd3 inhibits the deacetylase activity of Rpd3L.

(**a**) Immunoblot analysis of Ada3 acetylation in WT, Rpd3-2SA and Rpd3-2SD mutants when treated with YP + 2% sucrose (Suc) for 0.5 h. (**b**) Immunoblot analysis of Ada3 acetylation in WT, *tpk2*Δ, Rpd3-2SD and Rpd3-2SD *tpk2*Δ mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**c**) Quantitative analysis of the results presented in Supplementary Fig. 4b. (**d**) Fluorescence microscopy analysis of the effect of Rpd3-2SA and Rpd3-2SD mutations on the localization of Rpd3L (Rxt2-GFP) in yeast cells. Cells were treated with YP + 2% sucrose (YP + Suc) for 0.5 h. Nuclei were stained with DAPI (blue). Scale bar: 5 μm. (**e**) In vitro deacetylase assay showing dephosphorylation of Rpd3 by λ phosphatase enhanced its activity to deacetylate Ada3. Rpd3-FLAG was purified from yeast cells and treated with or without λ phosphatase, which was then used in deacetylase assay with purified SAGA as its substrate. (**f**) In vitro deacetylase assay showing Tpk2-catalyzed Rpd3 phosphorylation reduced its ability to deacetylate Ada3. Rpd3-FLAG was purified from yeast cells and then treated with or without Tpk2-CBP for 1 h, which was used in deacetylase assay with purified SAGA as its substrate. (**g**) In vitro deacetylase assay showing Tpk2-catalyzed His-Rpd3 phosphorylation reduced its ability to deacetylate Ada3. The recombinant His-Rpd3 was purified from *E. coli* and treated with or without Tpk2-CBP for 1 h, which were then used in deacetylase assay with purified SAGA as its substrate. (**h**) Analysis of the activity of His-Rpd3 and His-Rpd3-2SA to deacetylate nucleosomes using in vitro deacetylase assay. The recombinant His-Rpd3 and His-Rpd3-2SA were purified from *E. coli* and then used in deacetylase assay.

For Supplementary Fig. 4**a-c** and **e-h**, data represent means ± SE; n=3 biological independent experiments; one-way ANOVA with Tukey's multiple comparisons tests (**a**), two-way ANOVA with Tukey's multiple comparisons tests (**c**) and Šídák's multiple comparisons tests (**e-h**) were used for statistical analysis.

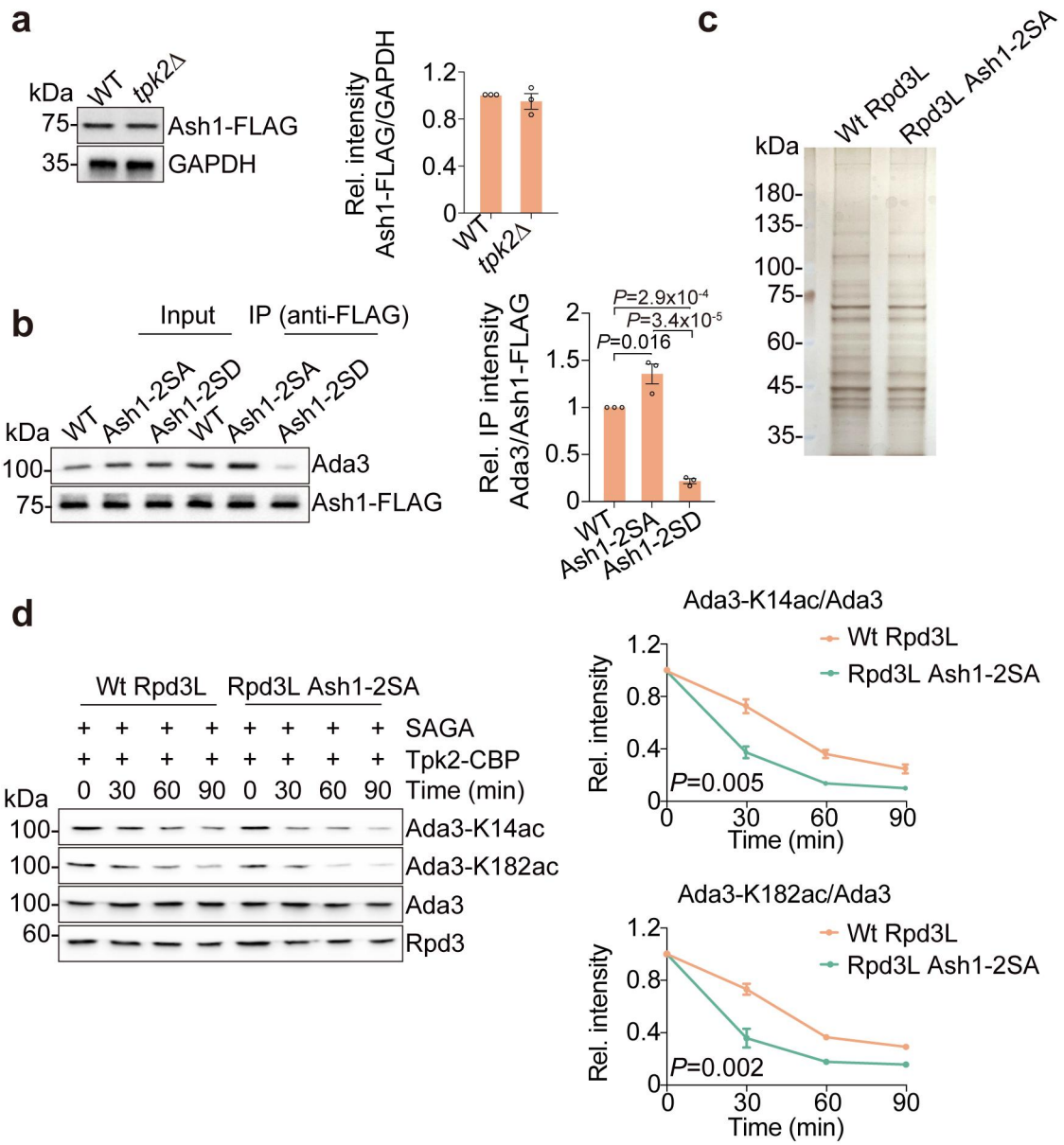
Supplementary Fig. 5



Supplementary Fig. 5 Ash1 and Ubp8 mediate the direct interaction between Rpd3L and SAGA. (**a**) Dephosphorylation of Rpd3 by λ phosphatase enhanced its interaction with SAGA. Rpd3-FLAG was purified from yeast cells, treated with λ phosphatase and then immobilized with anti-FLAG beads. The phosphorylated or dephosphorylated Rpd3-FLAG were incubated with purified SAGA and then subjected to immunoprecipitation. (**b**) Tpk2-catalyzed Rpd3 phosphorylation reduced its interaction with SAGA. Rpd3-FLAG was purified from yeast cells, phosphorylated with Tpk2-CBP and then immobilized with anti-FLAG beads. The treated Rpd3-FLAG was incubated with purified SAGA and then subjected to immunoprecipitation. (**c**) Sucrose treatment reduced the interaction between Rpd3 and Ada3 in both WT and Rpd3-2SA mutant. WT and Rpd3-2SA mutant were treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. Rpd3-FLAG was immunoprecipitated with anti-FLAG beads. (**d**) Fluorescence microscopy analysis of the effect of Rpd3-2SA and Rpd3-2SD mutations on the co-localization of Rpd3L (Rxt2-GFP) and SAGA (Ada3-tdTomato). Scale bar: 5 μm. (**e**) Analysis of the effect of SAGA HAT module (Sgf29, Gcn5) and DUB module (Sgf11, Sus1) on the interaction between Rpd3 and Ada3 by Co-IP. In *gcn5*Δ mutant, Ada3 protein level is low. (**f**) Analysis of the effect of SAGA core module (Ada1, Spt20, Spt8, Spt3, Spt7) on the interaction between Rpd3 and Ada3 by Co-IP. (**g**) Loss of Rpd3L subunits (Sds3, Sin3, Rxt3, Pho23, Sap30, Ume6, Ume1) had no effect on the interaction between Rpd3 and Ada3 as determined by Co-IP. (**h**) Purified recombinant Ubp8-FLAG had no interaction with purified recombinant His-Cti6, His-Dep1, His-Rxt2 and His-Rpd3 as determined by in vitro Co-IP. (**i**) Purified recombinant Sgf73-FLAG had no interaction with purified recombinant His-Cti6, His-Dep1, His-Rxt2, His-Rpd3 and His-Ash1 as determined by in vitro Co-IP. (**j**) Analysis of Ada3 acetylation in WT and *ubp8*Δ mutant when treated with YP + 2% sucrose for 0-90 min.

For Supplementary Fig. 5**c** and **j**, data represent means ± SE; n=3 biological independent experiments; two-way ANOVA with Tukey's multiple comparisons tests (**c**) and Šídák's multiple comparisons tests (**j**) were used for statistical analysis. For Supplementary Fig. 5**a**-**b** and **d**-**i**, data represent a typical example of at least two biological independent experiments.

Supplementary Fig. 6

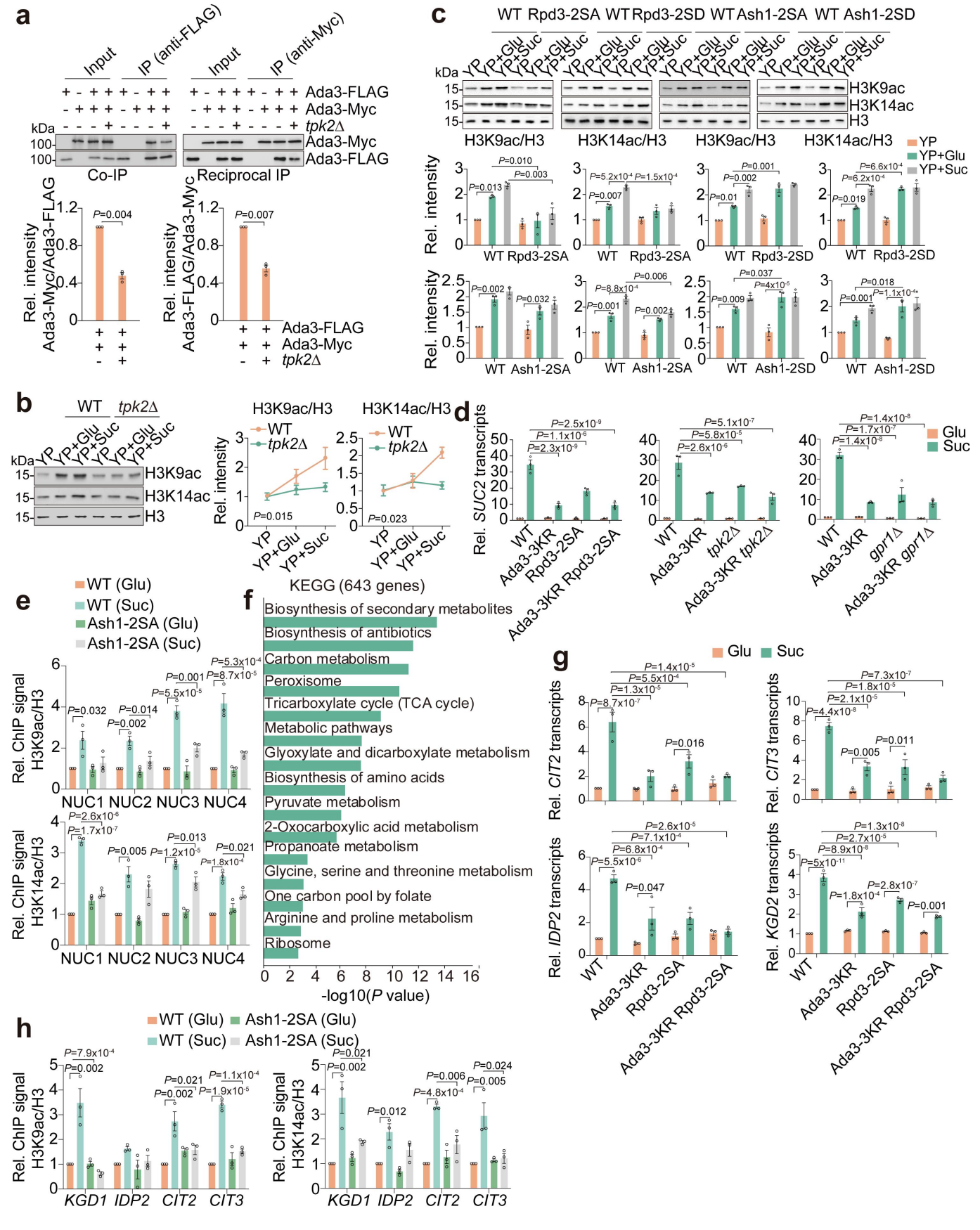


Supplementary Fig. 6 Tpk2 phosphorylates Ash1 to reduce the interaction between Rpd3L and SAGA.

(**a**) Immunoblot analysis of Ash1 expression in WT and *tpk2Δ* mutant. The endogenous expressed Ash1 was tagged with FLAG. (**b**) Analysis of the interaction between Ash1 and Ada3 in WT, Ash1-2SA, and Ash1-2SD mutants by Co-IP. (**c**) Silver staining of purified Wt Rpd3L and Rpd3L Ash1-2SA. (**d**) Analysis of the effect of Tpk2-catalyzed Ash1 phosphorylation on Ada3 deacetylase activity of Rpd3L. The purified Wt Rpd3L and Rpd3L Ash1-2SA were phosphorylated by Tpk2-CBP and then used for in vitro deacetylase assay using purified SAGA as the substrate.

For Supplementary Fig. 6**a**, **b** and **d**, data represent means ± SE; n=3 biological independent experiments; two tailed unpaired *t*-tests (**a**); one-way ANOVA with Tukey's multiple comparisons tests (**b**) and two-way ANOVA with Šídák's multiple comparisons tests (**d**) were used for statical analysis.

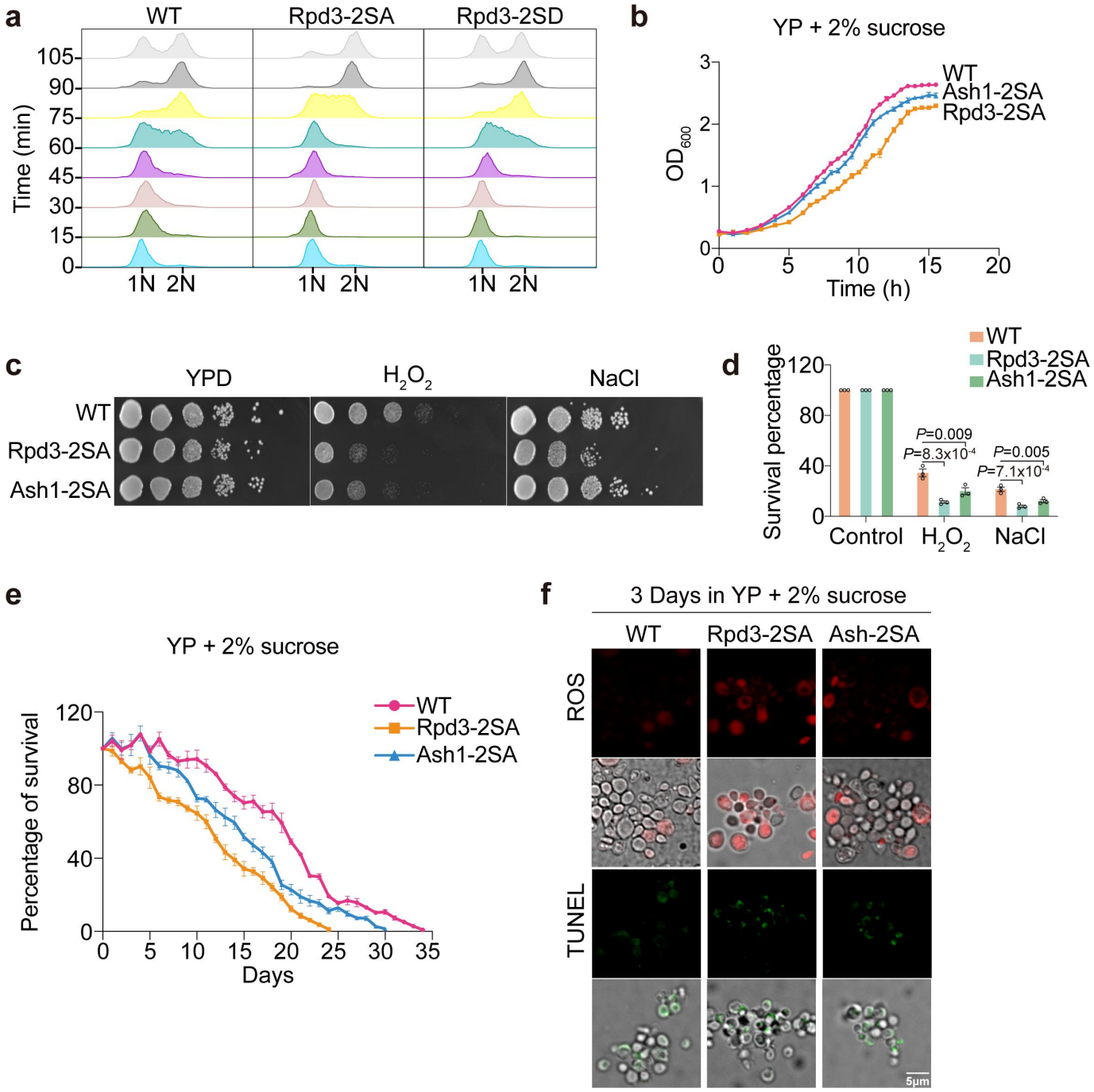
Supplementary Fig. 7



Supplementary Fig. 7 Tpk2-catalyzed Rpd3L phosphorylation promotes SAGA dimerization, histone acetylation and metabolic gene transcription.
(**a**) Loss of Tpk2 reduced the interaction between Ada3-FLAG-containing SAGA and Ada3-Myc-containing SAGA as determined by Co-IP and reciprocal IP. (**b**) Immunoblot analysis of H3K9ac and H3K14ac in WT and *tpk2*Δ mutant when treated with YP, YP + 2% glucose (YP + Glu) or YP + 2% sucrose (YP + Suc) for 0.5 h. (**c**) Analysis of H3K9ac and H3K14ac in WT, Rpd3-2SA, Rpd3-2SD, Ash1-2SA, and Ash1-2SD mutants when treated with YP, YP + 2% glucose (YP + Glu) or YP + 2% sucrose (YP + Suc) for 0.5 h. (**d**) RT-qPCR analysis of *SUC2* transcription in WT, Ada3-3KR, Rpd3-2SA, Ada3-3KR Rpd3-2SA, *tpk2*Δ, Ada3-3KR *tpk2*Δ, *gpr1*Δ, and Ada3-3KR *gpr1*Δ mutants. Cells were treated with YP + 2% glucose (YP+Glu) or YP + 2% sucrose (YP+Suc) for 0.5 h. (**e**) ChIP-qPCR analysis of H3K9ac/H3 and H3K14ac/H3 at *SUC2* promoter regions (NUC1, NUC2, NUC3, NUC4) in WT and Ash1-2SA mutant when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**f**) KEGG analysis of 643 genes that were induced by sucrose, activated by Ada3 acetylation and Rpd3 phosphorylation. One-side hypergeometric test was used to calculate *P* values. (**g**) RT-qPCR analysis of *CIT2*, *CIT3*, *IDP2* and *KGD2* transcription in WT, Ada3-3KR, Rpd3-2SA and Ada3-3KR Rpd3-2SA mutants when treated with YP + 2% glucose (Glu) or YP + 2% sucrose (Suc) for 0.5 h. (**h**) ChIP-qPCR analysis of H3K9ac/H3 and H3K14ac/H3 at indicated TCA cycle genes in WT and Ash1-2SA mutants when treated with YP + 2% glucose (YP + Glu) or YP + 2% sucrose (YP + Suc) for 0.5 h. *CIT2*, citrate synthase 2; *CIT3*, citrate synthase 3; *IDP2*, isocitrate dehydrogenase ($NADP^+$); *KGD2*, dihydrolipoyl transsuccinylase; *KGD1*, alpha-ketoglutarate dehydrogenase.

For Supplementary Fig. 7**a-e, g-h**, data represent means ± SE; n=3 biological independent experiments; two tailed unpaired *t*-tests (**a**); two-way ANOVA with Tukey's multiple comparisons tests (**b-e**, **g-h**) were used for statistical analysis.

Supplementary Fig. 8

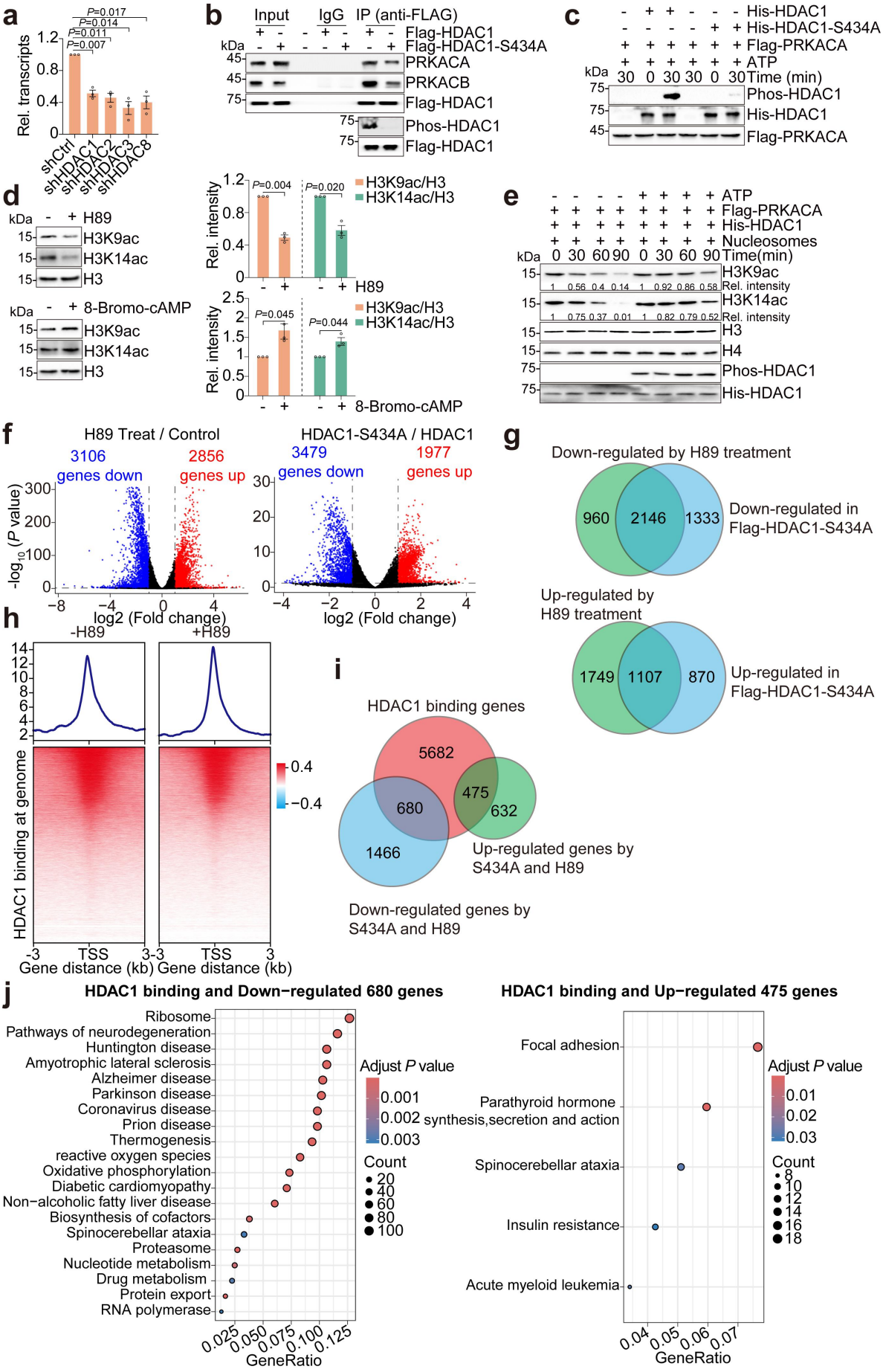


Supplementary Fig. 8 Tpk2-catalyzed Rpd3L phosphorylation promotes cell cycle progression and cell survival under stress conditions.

(**a**) Analysis of cell cycle profiling of WT, Rpd3-2SA and Rpd3-2SD when treated with YP + 2% sucrose by flow cytometry. 1N represents one cell contains a set of chromosomes (BY4741 is haploid cell). 2N represents two copies of each chromosome. (**b**) Growth curves of WT, Rpd3-2SA, and Ash1-2SA mutants in YP + 2% sucrose. (**c-d**) WT, Rpd3-2SA and Ash1-2SA mutants were treated with 0.1% H_2O_2 or 5 M NaCl for 2 h. Cells were split into 2 aliquots. One aliquot of cells was spotted on YPD plates (**c**). The other aliquot of cells was used to calculate the survival percentage by counting the number of colonies formed on YPD (**d**). (**e**) Chronological lifespan of WT, Rpd3-2SA, and Ash1-2SA mutants in YP + 2% sucrose. (**f**) Analysis of ROS accumulation and DNA fragmentation in WT, Rpd3-2SA, and Ash1-2SA mutants after 3 days in YP + 2% sucrose medium as determined by DHE and TUNEL. Scale bars, 5 μm.

For Supplementary Fig. 8**b**, **d** and **e**, data represent means ± SE; n=3 biological independent experiments; one-way ANOVA with Dunnett's multiple comparisons tests (**d**) were used for statistical analysis. For Supplementary Fig. 8**a**, **c** and **f**, data represent a typical example of at least two biological independent experiments.

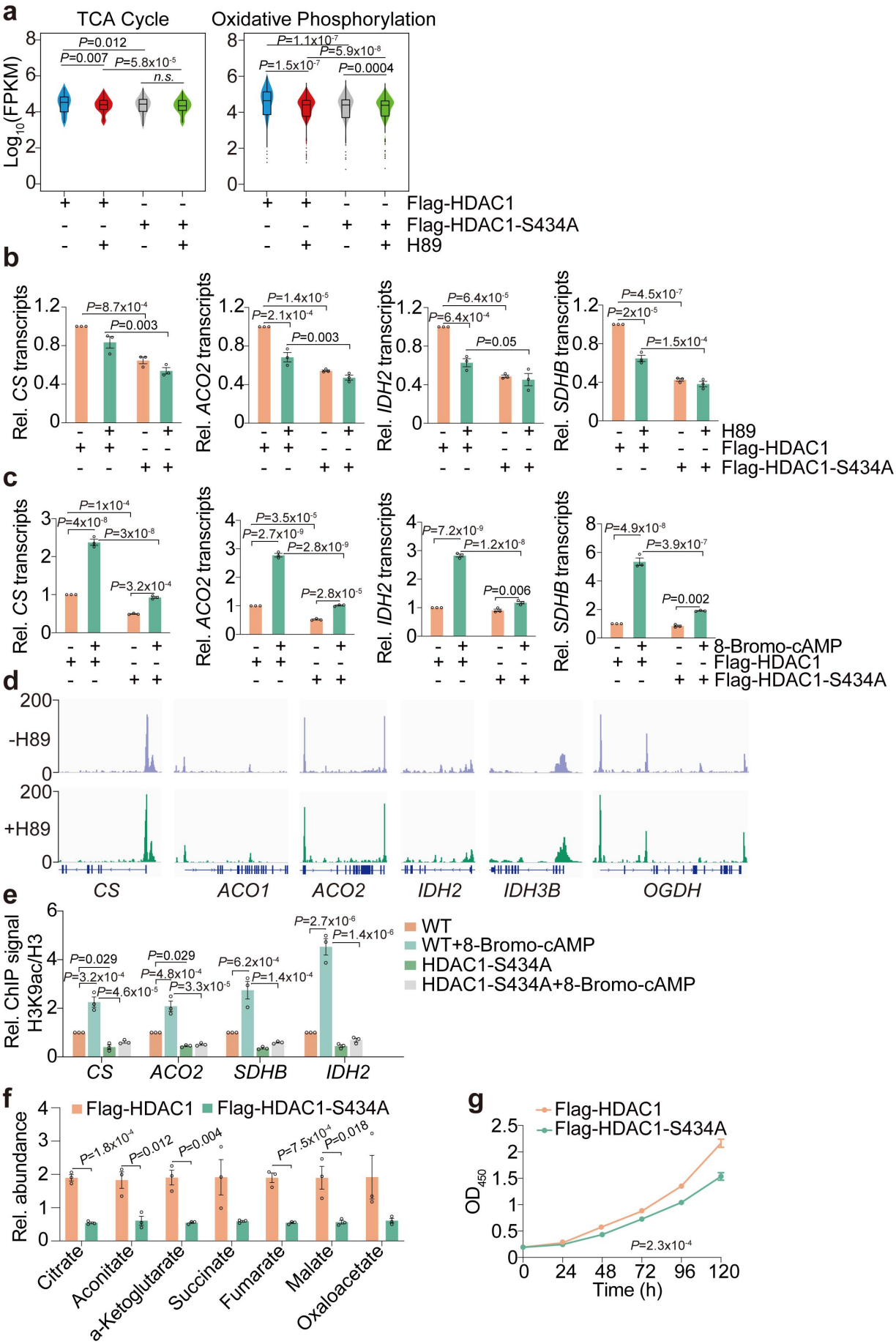
Supplementary Fig. 9



Supplementary Fig. 9 PKA phosphorylates HDAC1 to repress its deacetylase activity.
(**a**) RT-qPCR analysis of knockdown efficiency of HDAC1, HDAC2, HDAC3 and HDAC8 in shHDAC1, shHDAC2, shHDAC3 and shHDAC8 HepG2 cells, respectively. (**b**) Mutation of HDAC1-S434A reduced the interaction between HDAC1 with PKA (PRKACA, PRKACB) as determined by Co-IP. Flag-HDAC1 was immunoprecipitated from HepG2 cells ectopically expressing Flag-HDAC1 and Flag-HDAC1-S434A by anti-FLAG beads. (**c**) In vitro kinase assay showing that purified Flag-PRKACA phosphorylated His-HDAC1 but not His-HDAC1-S434A. The recombinant His-HDAC1 and His-HDAC1-S434A were expressed and purified from *E. coli*. (**d**) Immunoblot analysis of H3K9ac and H3K14ac in HepG2 cells when treated with H89 or 8-Bromo-cAMP) for 12 h. (**e**) PRKACA-mediated phosphorylation of His-HDAC1 reduced its activity to deacetylate nucleosomes as determined by in vitro deacetylase assay. (**f**) Volcano plots for differentially expressed genes by H89 treatment and HDAC1-S434A. Differential expression levels of aligned sequences were calculated using significant thresholds set at fold change over two and adjusted P value < 0.05. (**g**) Venn diagrams showing genes differentially co-regulated by H89 and HDAC1-S434A. (**h**) Heatmap showing the genome-wide occupancy of HDAC1 in HepG2 cells treated with or without H89. (**i**) Venn diagrams showing the overlap between co-regulated genes from RNA-seq data and HDAC1 binding genes from CUT & Tag data. (**j**) KEGG analysis of HDAC1 binding and co-regulated genes in Supplementary Fig. 9i.

For Supplementary Fig. 9**a** and **d**, data represent means ± SE; n=3 biological independent experiments; two tailed unpaired *t*-tests were used.

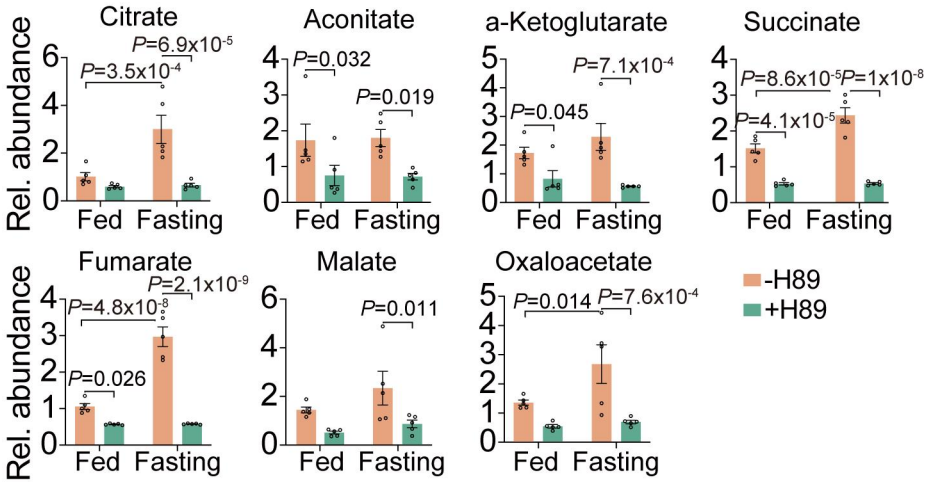
Supplementary Fig. 10



Supplementary Fig. 10 PKA phosphorylates HDAC1 to regulate the transcription of genes in TCA cycle.

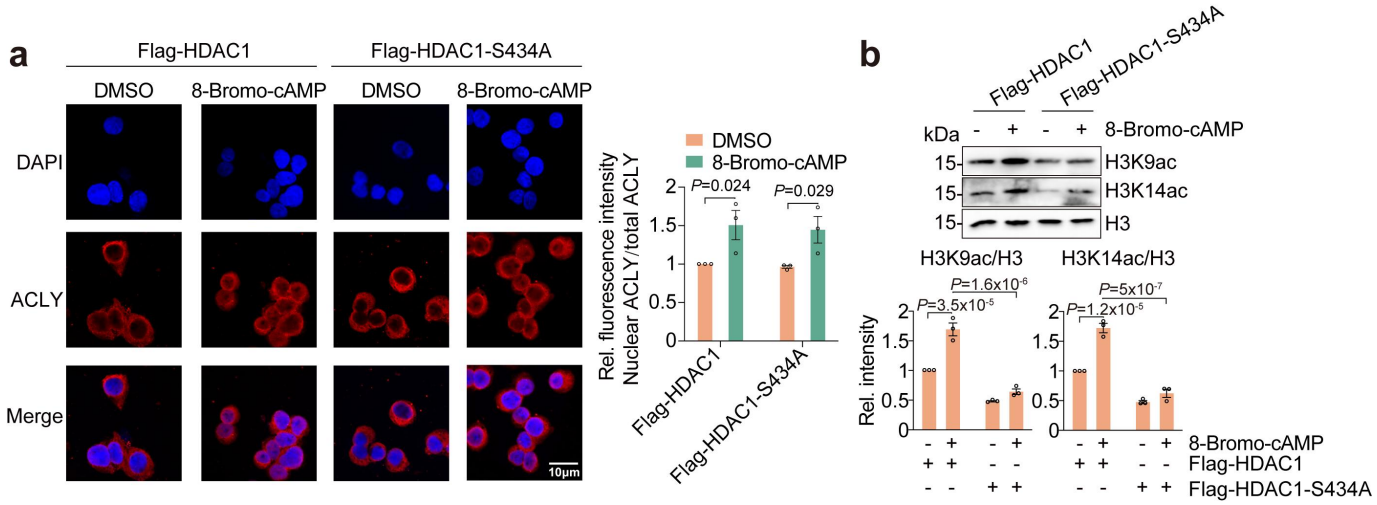
(**a**) Violin diagram showing the transcription of genes involved in the TCA cycle and oxidative phosphorylation pathways in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A when treated with H89. Two-sided Wilcoxon test in R (package ggpval) was used for statistical analysis. (**b-c**) RT-qPCR analysis of indicated TCA cycle gene transcription in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A when treated with H89 (**b**) or 8-Bromo-cAMP (**c**). (**d**) CUT & Tag tracks showing HDAC1 binding at indicated TCA cycle genes. (**e**) ChIP-qPCR analysis of H3K9ac occupancy at indicated TCA cycle gene promoters in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A when treated with or without 8-Bromo-cAMP. (**f**) Analysis of intracellular TCA cycle metabolites in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A. (**g**) Ectopic expression of HDAC1-S434A in shHDAC1 HepG2 cells reduced cell growth as determined by CCK-8 assay. *ACO1*, aconitase 1; *ACO2*, aconitase 2; *CS*, citrate synthase; *IDH2*, isocitrate dehydrogenase ($NADP^+$) 2; *IDH3B*, isocitrate dehydrogenase (NAD^+) 3 non-catalytic subunit beta; *OGDH*, oxoglutarate dehydrogenase; *SDHB*, succinate dehydrogenase complex iron sulfur subunit B.

For Supplementary Fig. 10**b-c**, **e-g**, data represent means ± SE; n=3 biological independent experiments; two-way ANOVA with Tukey's multiple comparisons tests (**b**, **c**, **e**) and Šídák's multiple comparisons tests (**g**); two tailed unpaired t-tests (**f**) were used for statistical analysis .



Supplementary Fig. 11 Analysis of TCA cycle metabolites in the liver of mice under fed and fasting conditions. Mice were injected with or without 5 mg/kg H89 followed by fed *ad libitum* or fasting for 12 h (5 mice per group). Data represent means ± SE; n=5 biological independent experiments; two-way ANOVA with Tukey's multiple comparisons tests were used.

Supplementary Fig. 12



Supplementary Fig. 12 PKA regulates histone acetylation primarily by repressing HDAC1. (**a**) Immunofluorescence analysis of ACLY localization in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A when treated with or without 8-Bromo-cAMP. Scale bar: 10 μm. (**b**) Immunoblot analysis of H3K9ac and H3K14ac in shHDAC1 HepG2 cells that ectopically expressed Flag-HDAC1 and Flag-HDAC1-S434A cells treated with or without 8-Bromo-cAMP.

For Supplementary Fig. 12**a-b**, data represent means ± SE; n=3 biological independent experiments; two-way ANOVA with Tukey's multiple comparisons tests were used for statistical analysis.

Supplementary Table 1. List of strains used in this study

Name	Parental Strain	Genotype	Source
WT	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0*	Open Biosystems
WT Ada3-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::KAN*	In this study
Ada3-3KR-FLAG *gpr1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3KR-3xFLAG::KAN gpr1Δ::LEU*	In this study
Ada3-3KR-FLAG *rpd3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3KR-3xFLAG::KAN rpd3Δ::LEU*	In this study
Ada3-3KR-FLAG Rpd3-S50A/S354A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3KR-3xFLAG::KAN RPD3-S50A/S354A-3xFLAG::URA3*	In this study
Ada3-3KR-FLAG *tpk2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3KR-3xFLAG::KAN tpk2Δ::LEU*	In this study
Ada3-FLAG *ash1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 ash1Δ::KAN*	In this study
Ada3-FLAG Ash1-S149A/S388A	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 ASH1-S149A/S388A::HIS*	In this study
Ada3-FLAG *cti6*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 cti6Δ::KAN*	In this study
Ada3-FLAG *dep1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 dep1Δ::KAN*	In this study
Ada3-FLAG *gpa2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::KAN gpa2Δ::LEU*	In this study
Ada3-FLAG *gpr1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::KAN gpr1Δ::LEU*	In this study
Ada3-FLAG *rco1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 rco1Δ::KAN*	In this study
Ada3-FLAG *rpd3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 rpd3Δ::LEU*	In this study
Ada3-FLAG Rpd3-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::KAN RPD3-13xMyc::HIS*	In this study
Ada3-FLAG Rpd3-S50A/S354A	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50A/S354A::URA3 ADA3-3xFLAG::KAN*	In this study

Ada3-FLAG *sap30*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 sap30Δ::KAN*	In this study
Ada3-FLAG *sds3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 sds3Δ::KAN*	In this study
Ada3-FLAG *sin3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 sin3Δ::KAN*	In this study
Ada3-FLAG *snt2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 snt2Δ::KAN*	In this study
Ada3-FLAG *spt20*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 spt20Δ::KAN*	In this study
Ada3-FLAG *spt3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 spt3Δ::KAN*	In this study
Ada3-FLAG *spt7*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 spt7Δ::KAN*	In this study
Ada3-FLAG *spt8*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 spt8Δ::KAN*	In this study
Ada3-FLAG *sus1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 sus1Δ::KAN*	In this study
Ada3-FLAG *tpk1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 tpk1Δ::KAN*	In this study
Ada3-FLAG *tpk2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 tpk2Δ::KAN*	In this study
Ada3-FLAG *tpk3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 tpk3Δ::KAN*	In this study
Ada3-FLAG *ubp8*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 ubp8Δ::KAN*	In this study
Ada3-FLAG *ume1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 ume1Δ::KAN*	In this study
Ada3-FLAG *ume6*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ADA3-3xFLAG::URA3 ume6Δ::KAN*	In this study
Ada3-Myc	BY4742	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0 ADA3-13xMyc::HIS3*	In this study
Ada3-Myc *ash1*Δ	BY4742	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0 ADA3-13xMyc::HIS3 ash1Δ::LEU*	In this study
Ada3-Myc *rco1*Δ	BY4742	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0 ADA3-13xMyc::HIS3 rco1Δ::LEU*	In this study
Ada3-Myc Rpd3-S50A/S354A	BY4742	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0 ADA3-13xMyc::HIS3 RPD3-S50A/S354A::URA3*	In this study
Ada3-Myc *tpk2*Δ	BY4742	*MATα his3Δ1 leu2Δ0 lys2Δ0 ura3Δ0 ADA3-13xMyc::HIS3 tpk2Δ::LEU*	In this study
Ash1-S149A/S388A-FLAG Rpd3-S50A/S354A	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-S149A/S388A-3xFLAG::HIS3 RPD3-S50A/S354A::URA3*	In this study

Ash1-S149A/S388A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-S149A/S388A-3xFLAG::HIS3*	In this study
Ash1-S149A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-S149A-3xFLAG::HIS3*	In this study
Ash1-S149D/S388D-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-S149D/S388D-3xFLAG::HIS3*	In this study
Rco1-TAP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RCO1-TAP::URA3*	In this study
*rpd3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 rpd3Δ::LEU*	In this study
Rpd3-FLAG *ada1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 ada1Δ::KANA*	In this study
Rpd3-FLAG *ash1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 ash1Δ::KAN*	In this study
Rpd3-FLAG *cti6*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 cti6Δ::KAN*	In this study
Rpd3-FLAG *dep1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 dep1Δ::KAN*	In this study
Rpd3-FLAG *gcn5*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 gcn5Δ::KANA*	In this study
Rpd3-FLAG *pho23*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 pho23Δ::KAN*	In this study
Rpd3-FLAG *rxt2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 rxt2Δ::KAN*	In this study
Rpd3-FLAG *rxt3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 rxt3Δ::KAN*	In this study
Rpd3-FLAG *sap30*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sap30Δ::KAN*	In this study
Rpd3-FLAG *sds3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sds3Δ::KAN*	In this study
Rpd3-FLAG sgf11Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sgf11Δ::KANA*	In this study
Rpd3-FLAG *sgf29*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sgf29Δ::KANA*	In this study
Rpd3-FLAG sgf73Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sgf73Δ::KANA*	In this study
Rpd3-FLAG *sin3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sin3Δ::KAN*	In this study
Rpd3-FLAG *spt20*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 spt20Δ::KANA*	In this study
Rpd3-FLAG *spt3*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 spt3Δ::KANA*	In this study
Rpd3-FLAG *spt7*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 spt7Δ::KANA*	In this study

Rpd3-FLAG *spt8*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 spt8Δ::KANA*	In this study
Rpd3-FLAG *sus1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 sus1Δ::KANA*	In this study
Rpd3-FLAG *tpk2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 tpk2Δ::LEU*	In this study
Rpd3-FLAG Tpk2-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 TPK2-13xMyc::HIS3*	In this study
Rpd3-FLAG *ubp8*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 ubp8Δ::KANA*	In this study
Rpd3-FLAG *ume1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 ume1Δ::KAN*	In this study
Rpd3-FLAG *ume6*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 ume6Δ::KAN*	In this study
Rpd3-S123A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S123A-3xFLAG::URA3*	In this study
Rpd3-S354A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S354A-3xFLAG::URA3*	In this study
Rpd3-S408A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S408A-3xFLAG::URA3*	In this study
Rpd3-S50A/S354A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50A/S354A-3xFLAG::URA3*	In this study
Rpd3-S50A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50A-3xFLAG::URA3*	In this study
Rpd3-T394A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-T394A-3xFLAG::URA3*	In this study
Rpd3-TAP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-TAP::HIS3*	Open Biosystems
Rpd3-TAP *ash1*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-TAP::HIS3 ash1Δ::LEU*	In this study
Rxt2-TAP Ash1-S149A/S388A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RXT2-TAP::URA3 ASH1-S149A/S388A-3xFLAG::HIS3*	In this study
Rxt2-TAP *tpk2*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RXT2-TAP::HIS3 tpk2Δ::LEU*	In this study
Spt7-TAP Ash1-S149A/S388A-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-S149A/S388A-3xFLAG::HIS3 SPT7-TAP::URA3*	In this study
Spt7-TAP *ubp8*Δ	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 SPT7-TAP::HIS3 ubp8Δ::LEU*	In this study
Tpk1-FLAG Bcy1-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK1-3xFLAG::KAN BCY1-13xMyc::HIS3*	In this study

Tpk2-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK2-3xFLAG::KAN*	In this study
Tpk2-FLAG Bcy1-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK2-3xFLAG::KAN BCY1-13xMyc::HIS3*	In this study
Tpk2-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK2-13xMyc::HIS3*	In this study
Tpk2-TAP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK2-TAP::HIS3*	In this study
Tpk3-FLAG Bcy1-Myc	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 TPK3-3xFLAG::KAN BCY1-13xMyc::HIS3*	In this study
WT Ash1-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 ASH1-3xFLAG::HIS3*	In this study
WT Rpd3-FLAG	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3*	In this study
Rpd3-S50A/S354A-FLAG Ada3-tdTomato	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50A/S354A-3xFLAG::URA3 Ada3-tdTomato::HIS3*	In this study
Rpd3-S50A/S354A-FLAG Ada3-tdTomato Rxt2-GFP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50A/S354A-3xFLAG::URA3 Ada3-tdTomato::HIS3 Rxt2-GFP::LEU*	In this study
Rpd3-S50D/S354D-FLAG Ada3-tdTomato	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50D/S354D-3xFLAG::URA3 Ada3-tdTomato::HIS3*	In this study
Rpd3-S50D/S354D-FLAG Ada3-tdTomato Rxt2-GFP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-S50D/S354D-3xFLAG::URA3 Ada3-tdTomato::HIS3 Rxt2-GFP::KANA*	In this study
Rpd3-FLAG Ada3-tdTomato	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 Ada3-tdTomato::HIS3*	In this study
Rpd3-FLAG Ada3-tdTomato Rxt2-GFP	BY4741	*MATa his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 RPD3-3xFLAG::URA3 Ada3-tdTomato::HIS3 Rxt2-GFP::LEU*	In this study

Supplementary Table 2. List of shRNA used in this study	
Gene name	**Sequence**
Primers for shRNA	

shHDAC1	GGAAATCTATCGCCCTCAC
shHDAC2	GCTACTACTACGACGGTGA
shHDAC3	CAAGAGTCTTAATGCCTTC
shHDAC8	GTCCCGAGTATGTCAGTAT
shPRKACA#1	GACAACTCAAACTTATACA
shPRKACA#2	GGGTCAACGATATCAAGAA
shPRKACB#1	GCAGCTCAGATAGTGCTAA
shPRKACB#2	GGAGTGCTAATCTATGAAA

Supplementary Table 3. List of oligonucleotides used in this study

Gene name	**Sequence**
Primers for qPCR	
NUC1-F	TTGTGAGCAAATTACCAGTCGG
NUC1-R	GCCCTCATAATGGATCGAGTTC
NUC2-F	CGCATTTTTATTACTCTGAA
NUC2-R	CTGGACGTGGGGTCGATTAA
NUC3-F	GTGATGTCTAAGACTTTTAAGG
NUC3-R	ACTATAGAGCCCTTAGGCAACA
NUC4-F	GGAAGAAAGATTTGACGAC
NUC4-R	AGCACAAGAACAAGAGAATG
SUC2-ORF-F	TGGGCTTCAAACTGGGAGTACAGT
SUC2-ORF-R	AAACGAGACCAGGGACCAGCATTA
ACTIN-F	CTGTCGAGAGATTTCTCTTTTACC
ACTIN-R	GCCCCTATTTATTCCAATAATATCG
RT-yCIT2-F	CGGTATTCGTTTCAGAGGTCG
RT-yCIT2-R	GCTTCTGGTAGTGGTTGTGAG
RT-yCIT3-F	GTGACCCGTATCTCAGCTATTC
RT-yCIT3-R	CTTGTTCTCGTGCAATGCTG
RT-yIDP2-F	TCTTGCCCTATCTTGACGTTG
RT-yIDP2-R	CTCATCGGGTGTAATAGTCGC
RT-yKGD2-F	CCAGTAGCCTCTAACTCTTTCAC
RT-yKGD2-R	GGCAATCCTCAATCTCATACGG
CHIP-yIDP2-F	CACTCTTGACTTGTCGACTACAG
CHIP-yIDP2-R	TCATCGCCGTCCATTTCC
CHIP-yKGD1-F	ATCCTTTGGCTTATTCTCTGGG
CHIP-yKGD1-R	AAACGGTCGAAGCTAACTGG
CHIP-yCIT3-F	CCTAAGAAAAGAGATGCTGTGAAG

CHIP-yCIT3-R	GACTGATTACCTCTCATCCCAC
CHIP-yCIT2-F	GCTTCCCCTTCTTGGAACTTA
CHIP-yCIT2-R	CTGCCGGAATAGTGCAAATTG
RT-hACO2-F	CAATCGTCACCTCCTACAACAGG
RT-hACO2-R	GTCTCTGGGTTGAACTTGAGGG
RT-hCS-F	CACAGGGTATCAGCCGAACCAA
RT-hCS-R	CCAATACCGCTGCCTTCTCTGT
RT-hSDHB-F	GCTCCCCGTATCAAGAAATTTGCC
RT-hSDHB-R	CCAATACCATGGGGCCACATTTAT
RT-hIDH2-F	CCCACCTCGCAAGAGCAG
RT-hIDH2-R	TCAGTCTGGTCACGGTTTGG
CHIP-hACO2-F	GTCTGTTCGTTGCACGTGAG
CHIP-hACO2-R	GCGCCTTTAAAGCCTTTGGG
CHIP-hCS-F	TTCCATACCGGACCAATGGC
CHIP-hCS-R	AAAGAGTAGACGAACCGGCG
CHIP-hSDHB-F	CCTCTCAGACTCCTCCCCTT
CHIP-hSDHB-R	GTACGAGCAACCAAGTGGGA
CHIP-hIDH2-F	AGGGAAGCAAGAGTTCGCTC
CHIP-hIDH2-R	TCTCCAGGATGCCCCATGTA
RT-mCS-F	GGAAGGCTAAGAACCCTTGG
RT-mCS-R	TCATCTCCGTCATGCCATAGT
RT-mACO2-F	AAGGATCACTTGGTGCCTGA
RT-mACO2-R	GAAGGGCCCATTGATGTGT
RT-mSDHD-F	CTACGTTCATGGGGACACCC
RT-mSDHD-R	TCAGAGCTTCCACAGCATGG