## **Supplementary Material**

## A Histone Deacetylase-Dependent Screen in Yeast

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Table S1. Deacetylase activity of immunoprecipitated Rpd3-LexA-FLAG fusions\*

Column	Sample	Trial1	Trial2	Trial3	Mean	S.E
1	No protein	17	4	31	17	8
2	Rpd3	100	100	100	100	-
3	Rpd3+TSA	7	16	7	10	3
4	Rpd3H150/151A	18	16	9	14	3
5	Rpd3H150/151A +TSA	18	14	13	15	2

\*percentage activity compared to wild type (WT) Rpd3-LexA-FLAG (100%) observed with three independent trials is shown with standard error (S.E). Data is shown as a histogram in Figure 3 of the manuscript.

Table S2. Data from the quantitative ONPG screen\*

Column #	Sample contents	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Mean	S.E
1	LACZ reporter alone	3.5	2.9	3.4	6.5	5.9	4.4	0.7
2	LACZ reporter + TSA	2.9	2.8	4.6	4.8	6.2	4.3	0.7
3	WT Rpd3	1.0	1.0	1.0	1.0	1.0	1.0	-
4	WT Rpd3 + TSA	1.4	1.5	2.2	1.6	1.4	1.6	0.1
5	Rpd3 mutant	2.3	2.0	2.9	3.3	4.2	3.0	0.4
6	Rpd3 mutant + TSA	2.2	2.5	3.2	4.8	5.2	3.6	0.6

\*mean fold change compared to wild type (WT) Rpd3-LexA-FLAG (1.00- column 3) observed with three independent trials is shown with standard error (S.E). Data is shown as a histogram in Figure 4 of the manuscript.

Table S3. Dose dependent inhibition of Rpd3-LexA-FLAG by TSA\*

Column #	TSA	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Mean	S.E
1	0 μΜ	1.0	1.0	1.0	1.0	ND	1.0	-
2	1 µM	1.2	1.2	1.2	1.3	ND	1.2	0.03
3	10 μM	1.1	1.6	1.7	1.6	ND	1.5	0.1
4	18 μM	1.8	1.4	1.5	1.8	ND	1.6	0.1
5	100 μM	1.4	1.5	2.2	1.4	1.6	1.6	0.1

\*mean fold change compared to wild type Rpd3-LexA-FLAG in the absence of TSA (1.00- column 1) observed with at least four independent trials is shown with standard error (S.E). ND = Not determined. Data is shown as a histogram in Figure 5 of the manuscript.

Table S4. TSA sensitivity of Rpd3-LexA-FLAG as a function of zymolyase concentration

Column #	Zymolyase U /mL	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Mean	S.E
1	0	1.5	1.7	2.0	1.7	ND	1.7	0.1
2	1	1.8	2.0	1.7	ND	ND	1.8	0.09
3	13	2.2	2.2	3.3	ND	ND	2.6	0.4
4	20	2.2	3.5	3.7	2.1	2.1	2.7	0.4
5	50	3.6	3.2	3.8	ND	ND	3.5	0.2

\*mean fold change compared to wild type Rpd3-LexA-FLAG in the absence of TSA (1.00- data not shown) observed with at least three independent trials is shown with standard error (S.E). ND = Not determined. Data is shown as a histogram in Figure 6 of the manuscript.

Table S5 Data from the quantitative ONPG screen in the presence of zymolyase\*

Column #	Sample	Trial	Trial	Trial	Trial	Trial	Mean	S.E
		1	2	3	4	5		
1	LacZ reporter	5.6	5.4	6.4	ND	ND	5.8	0.3
2	LacZ reporter + TSA	4.7	6.0	5.8	ND	ND	5.5	0.4
3	WT Rpd3	1.0	1.0	1.0	ND	ND	1.0	-
4	WT Rpd3 + TSA	2.2	3.5	3.7	2.1	2.1	2.7	0.4
5	Rpd3 mutant	4.5	4.9	3.7	3.2	ND	4.1	0.4
6	Rpd3 mutant + TSA	4.4	4.2	4.2	4.7	ND	4.4	0.1

\*mean fold change compared to wild type (WT) Rpd3-LexA-FLAG in the absence of TSA (1.00- column 3) observed with at least three independent trials is shown with standard error (S.E). ND = Not determined. Data is shown as a histogram in Figure 7 of the manuscript.

Table S6 Data from the screen with Apicidin and SAHA\*

Column #	Sample	Trial 1	Trial 2	Trial 3	Trial 4	Mean	S.E
1	zymolyase	1.0	1.0	1.0	1.0	1.0	ı
2	apicidin	1.0	1.1	1.0	ND	1.0	0.03
3	zymolyase + apicidin	1.3	1.4	1.4	ND	1.4	0.03
4	SAHA	0.92	0.88	0.91	ND	0.90	0.01
5	Zymolyase + SAHA	1.6	1.4	1.3	1.3	1.4	0.07

\*mean fold change compared to wild type Rpd3-LexA-FLAG in the absence of inhibitor (1.00- column 1) observed with at least three independent trials is shown with standard error (S.E). ND = Not determined. Data is shown as a histogram in Figure 8 of the manuscript.