

Supplementary Data

Evolution and Functional Trajectory of Sir1 in Gene Silencing

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Supplemental Figures

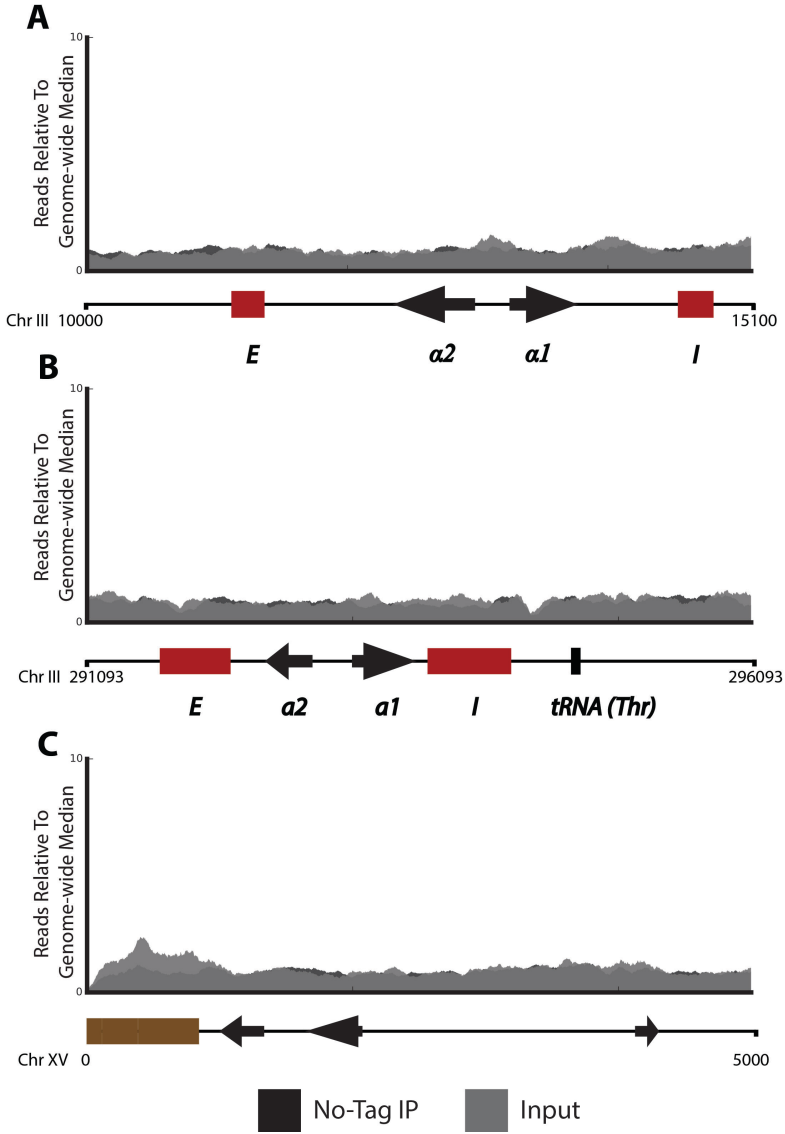


Figure S1. No tag IP and input enrichment in *S. cerevisiae*. No tag IP and input tracks shown for *S. cerevisiae* at *HMLα* (A), *HMRA* (B), and *TEL15L* (C). IP shown in black, input in gray, in terms of reads relative to genome-wide median.

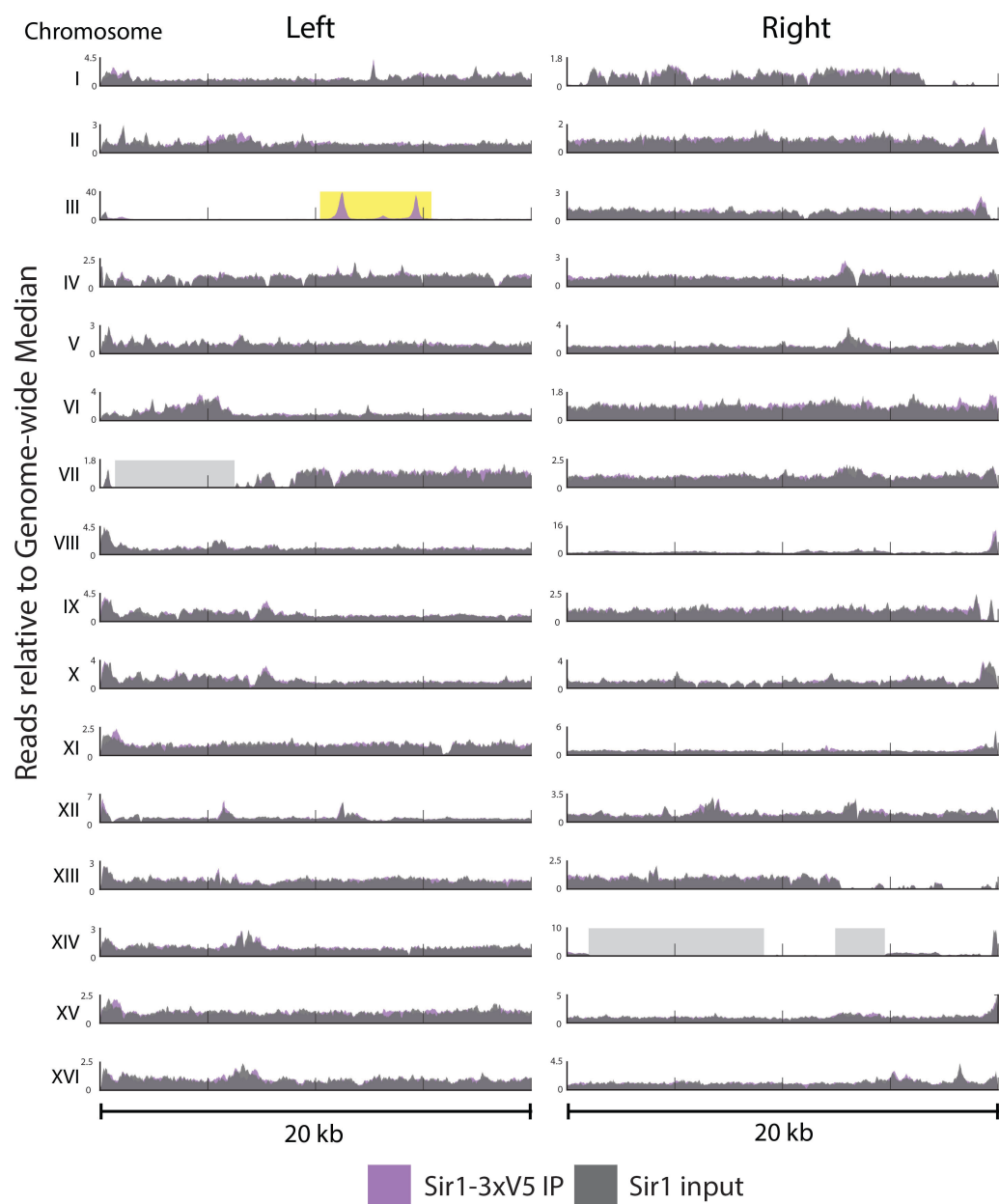


Figure S2. Lack of Sir1 enrichment at 31 out of 32 *S. cerevisiae* telomeres (W303 strain). Sir1 IP shown in purple, input shown in gray. Sir1 enrichment is seen at *HML α* on *TEL03L* (yellow box). 20kb inward from the left and right ends of each chromosome is shown. Regions deleted in the W303 strain relative to S288C are shown in gray.

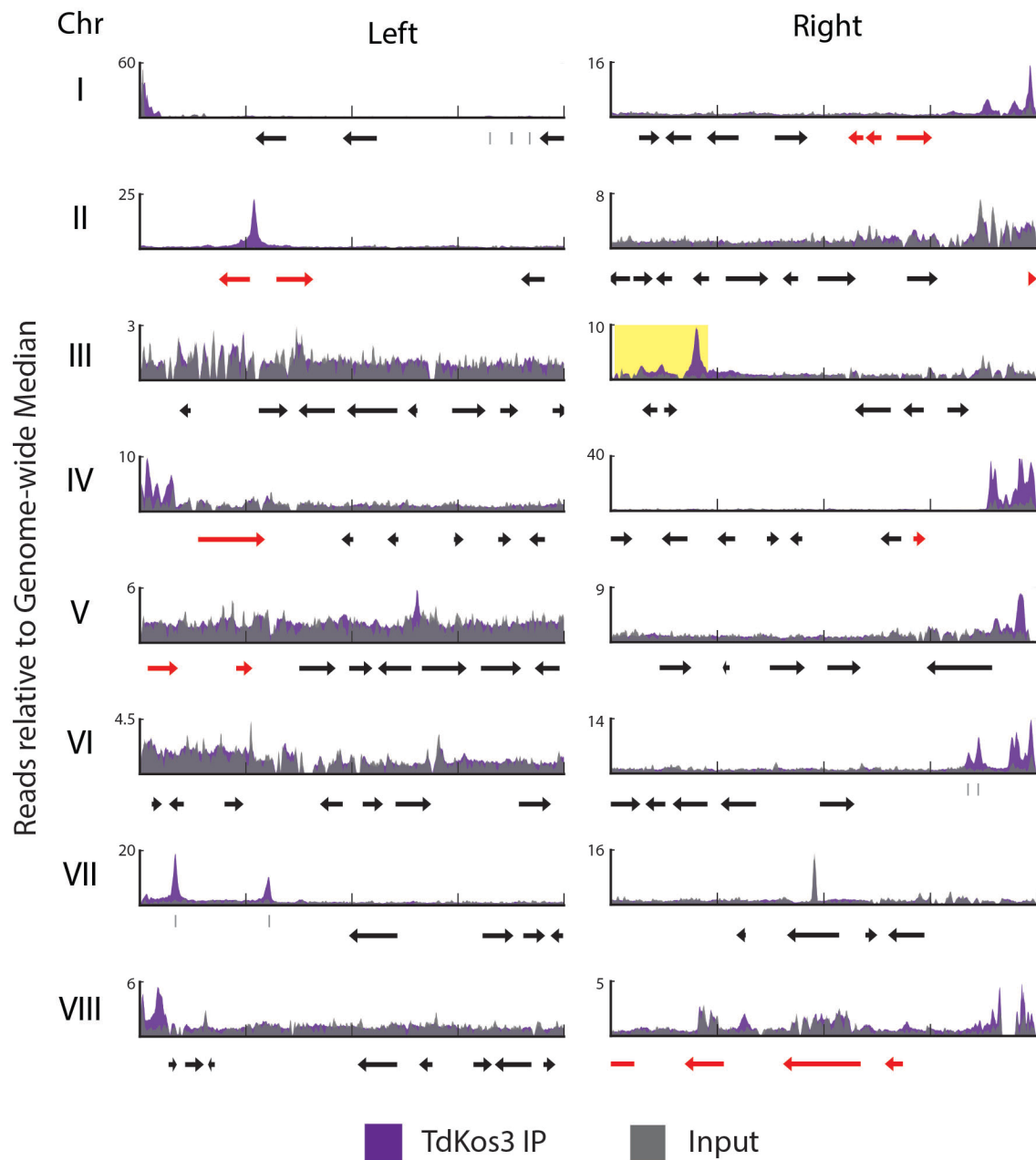


Figure S3. Enrichment of Kos3 (dark purple) at eleven telomeres in *T. delbrueckii*:

TEL01L, *TEL01R*, *TEL02L*, *TEL03R*, *TEL04L*, *TEL04R*, *TEL05R*, *TEL06R*,

TEL07L, *TEL08L*, and *TEL08R*. Open reading frames (ORFs) are depicted in black arrows

and tRNA genes are depicted in gray boxes. *HML* on *TEL03R* is boxed in yellow. Subtelomeric

genes that significantly increased in expression in all three *sir* mutants relative to wild type are shown as red arrows. Enrichment patterns for Td-Sir2 and Td-Sir4 were highly similar.

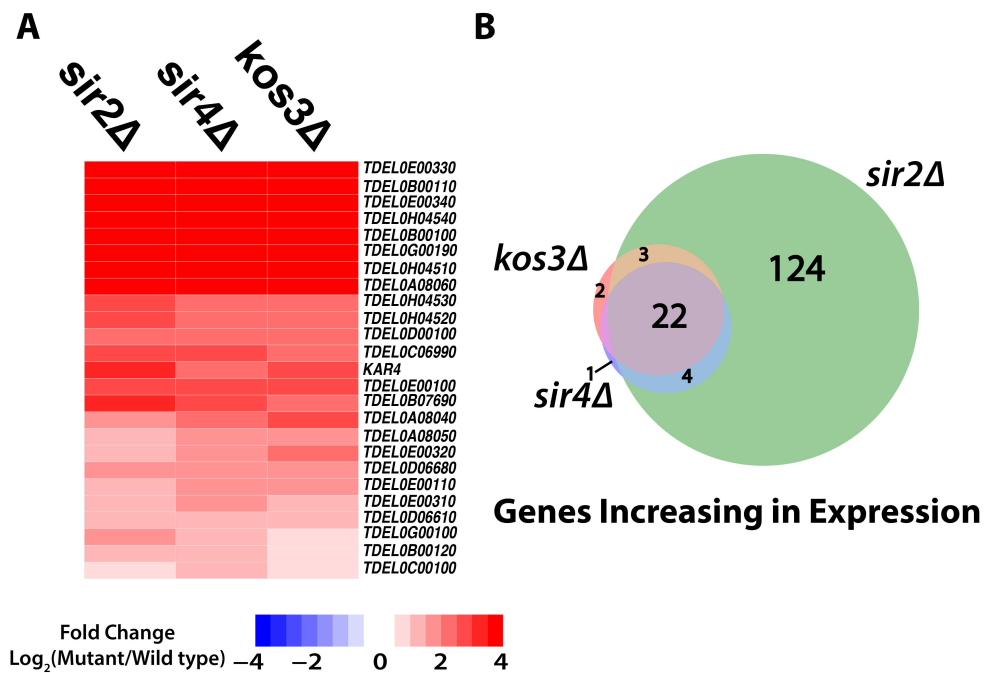


Figure S4. Summary of genes that significantly increased in expression in all three *sir* mutants in *T. delbrueckii* (*kos3Δ*, *sir2Δ*, and *sir4Δ*). (A) Heatmap of all genes that increased significantly relative to Wild type (red boxes) across all three mutants. (B) Venn diagram showing overlap of all genes that significantly increased in *kos3Δ*, *sir2Δ*, and *sir4Δ*. Genes whose expression increased in *kos3Δ* and *sir4Δ* were largely a subset of those whose expression increased in *sir2Δ*; suggesting that *SIR2* regulates many other genes in addition to the genes at telomeres, *HML* and the two copies of *HMR* in *T. delbrueckii*.

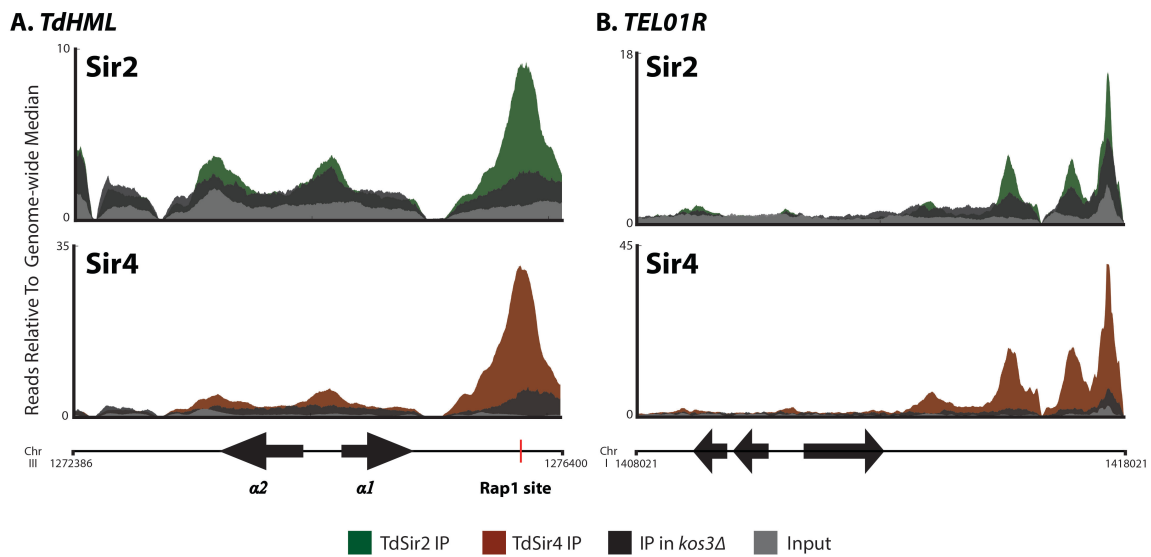


Figure S5. Sir2 and Sir4 had reduced enrichment at *HML* (A) and a representative telomere, *TEL01R* (B) in *kos3Δ* strains. Enrichment in *KOS3* wild-type strains for Sir2 and Sir4 shown in green and brown, respectively. Enrichment of Sir2 and Sir4 in the *kos3Δ* strain is shown in black. The signal from input chromatin is shown in gray. Genes are marked with black arrows; Rap1 site at *HML* is marked with red line.

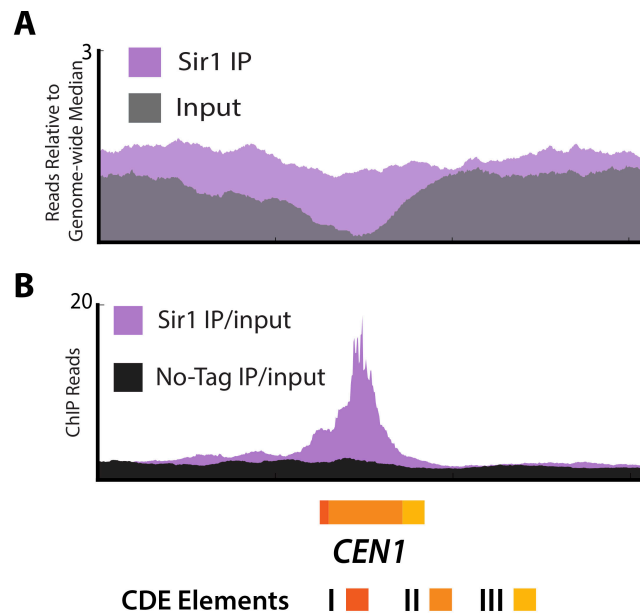


Figure S6. Under-enrichment of IP and input at *S. cerevisiae* centromeres. (A) Enrichment of Sir1 IP and input shown separately at *CEN1*. The input appears under-enriched. (B) Enrichment of Sir1 at *CEN1* viewed as IP over input. The No-tag negative control IP over input is shown in black.

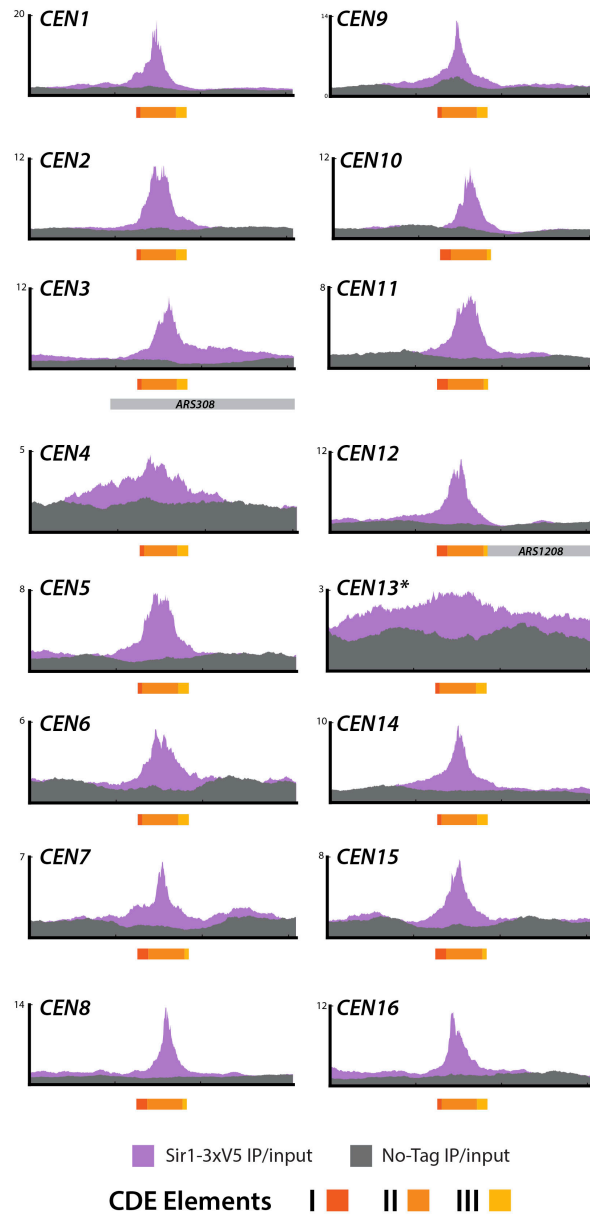


Figure S7. Sir1 enrichment at all 16 centromeres in *S. cerevisiae*. Enrichment is shown as IP over input. IP over input of the no-tag control is shown in gray. *The enrichment seen at *CEN13* is likely to be non-specific, as its enrichment was not greater than the IP over input of GFP-NLS, a protein expected to non-specifically bind in the genome. Centromere sequence elements, CDE I, CDE II, and CDE III are marked with red orange, orange, and yellow boxes, respectively.

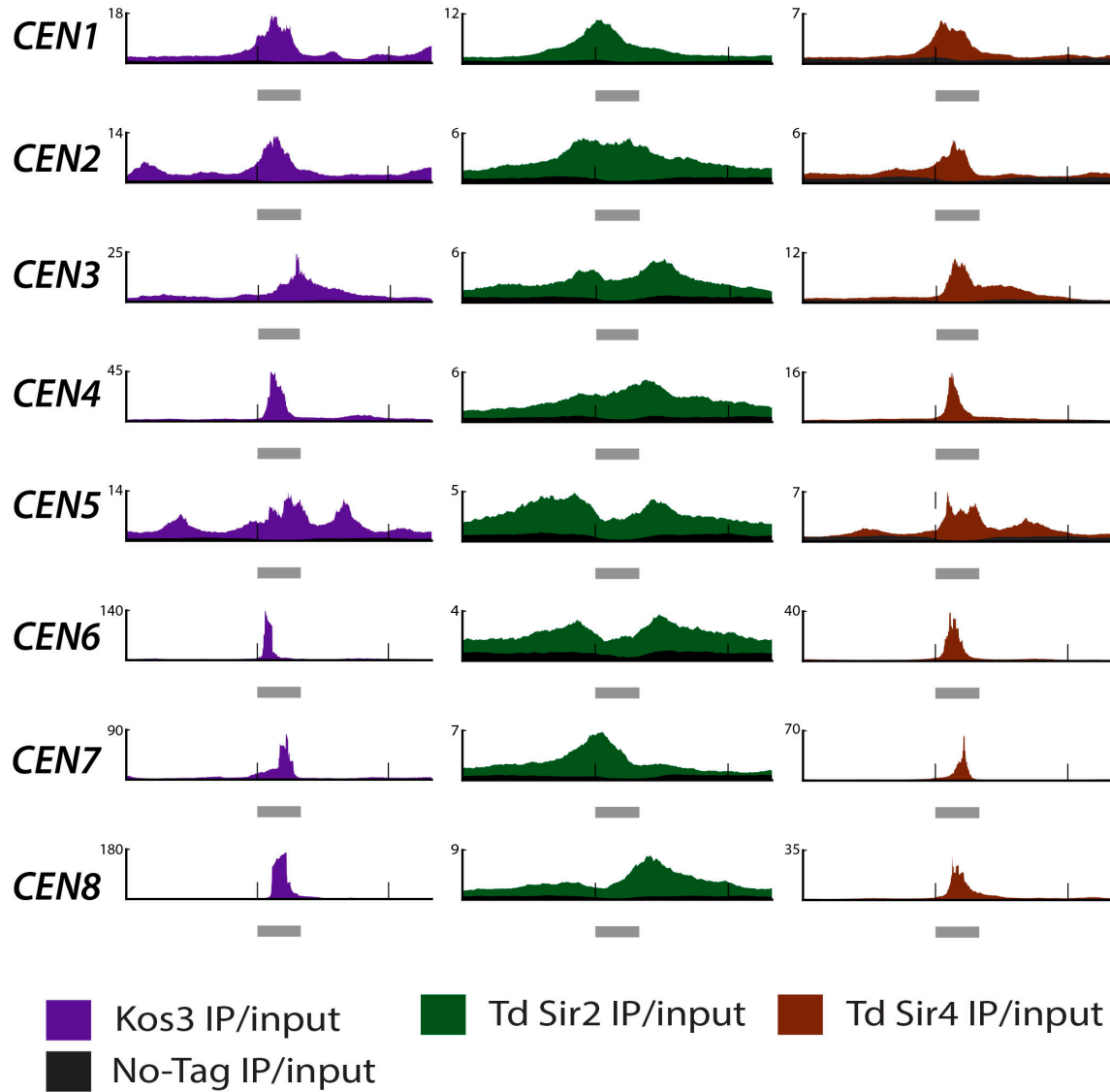


Figure S8. Enrichment of Kos3, Sir2, and Sir4 at all 8 *T. delbrueckii* centromeres. Enrichment is shown as IP/input (centromeres marked with gray boxes; tick marks represent 500 base pairs). Functionality of two centromeres, *CEN1* and *CEN3*, was confirmed experimentally.

Supplementary Tables

Table S1 Strains Used In This Study

*Unless otherwise indicated, strains were constructed for this study.

Name	Species	Genotype	Source*
JRY10152	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 SIR1-3xV5-KanMX</i>	
JRY9316	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52</i>	Teytelman et al. 2013
JRY9319	<i>S. cerevisiae</i>	<i>matΔ::HygMX lys2 his3-11 leu2-3,112 trp1-1 ura3-52 can1-100 SIR2-13xMyc::KanMX</i>	“
JRY10153	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir1Δ::KanMX</i>	
JRY10154	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir1Δ::KanMX</i>	
JRY10155	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir1Δ::KanMX</i>	
JRY9720	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir2Δ::KanMX</i>	Ellahi et al. 2015
JRY9721	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir2Δ::KanMX</i>	“
JRY9722	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir2Δ::KanMX</i>	“
JRY9723	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir3Δ::KanMX</i>	“
JRY9724	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir3Δ::KanMX</i>	“
JRY9725	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir3Δ::KanMX</i>	“
JRY9726	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir4Δ::KanMX</i>	“
JRY9727	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir4Δ::KanMX</i>	“
JRY9728	<i>S. cerevisiae</i>	<i>matΔ::HygMX can1-100 his3-11 leu2-3,112 lys2- trp1-1 ura3-52 sir4Δ::KanMX</i>	“
JRY10156	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1</i>	
JRY10157	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 kos3Δ::KanMX</i>	
JRY10158	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 sir2Δ::KanMX</i>	
JRY10159	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 sir4Δ::KanMX</i>	
JRY10160	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 KOS3-3xV5-NatMX</i>	
JRY10161	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 SIR2-3xV5-NatMX</i>	
JRY10162	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 SIR4-3xV5-NatMX</i>	
JRY10163	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 ago1Δ::NatMX</i>	

JRY10164	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 dcr1Δ::NatMX</i>	
JRY10165	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 ago1Δ::NatMX dcr1Δ::KanMX</i>	
JRY10166	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3</i>	
JRY10167	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 kos3Δ::NatMX [pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3]</i>	
JRY10168	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 sir2Δ::NatMX [pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3]</i>	
JRY10169	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3] sir4Δ::NatMX</i>	
JRY10170	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3]</i>	
JRY10173	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3_regionEΔ]</i>	
JRY10174	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmlα2Δ::K. lactis URA3_rap1-site-mutant]</i>	
JRY10175	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3]</i>	
JRY10176	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 kos3Δ::NatMX [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3]</i>	
JRY10177	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 sir2Δ::NatMX [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3]</i>	
JRY10178	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 sir4Δ::NatMX [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3]</i>	
JRY10179	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3_regionCΔ]</i>	
JRY10180	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3_regionAΔ]</i>	
JRY10181	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3_regionBΔ]</i>	
JRY10182	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3_rap1-siteΔ]</i>	
JRY10183	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 [pRS41H-TdCEN3-hmra1Δ::K. lactis URA3_rap1-site-mutant]</i>	
JRY10184	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 kos3Δ::KanMX SIR2-3xV5-NatMX</i>	
JRY10185	<i>T. delbrueckii</i>	<i>MATα ura3Δ0 trp3-1 kos3Δ::KanMX SIR4-3xV5-NatMX</i>	
JRY10207	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) RAP1-3xV5-NAT</i>	
JRY10208	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) [pRS41H-TdCEN3]</i>	
JRY10209	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) sir2Δ::NAT [pRS41H-TdCEN3]</i>	
JRY10210	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) sir2Δ::NAT [pRS41H-TdCEN3]</i>	
JRY10211	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) kos3Δ::kan [pRS41H-TdCEN3-Td-KOS3]</i>	
JRY10212	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) kos3Δ::kan [pRS41H-TdCEN3-Td-KOS3]</i>	
JRY10213	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466A) kos3Δ::Kan sir2Δ::Nat [pRS41H-</i>	

		<i>TdCEN3-Td-KOS3</i>	
JRY10214	<i>T. delbrueckii</i>	<i>MAT@ uraΔ trp3(G466.A) kos3Δ::Kan sir2Δ::Nat [pRS41H-TdCEN3-Td-KOS3]</i>	

Table S2 Genes Increasing and Decreasing in Expression in *sir1Δ*

Shown below is the list of genes that statistically significantly increased or decreased in expression by 2-fold or greater in the *sir1Δ* mutant relative to Wild type. Expression is shown in units of Fragments per Kilobase per Million reads (FPKM).

Gene	Systematic Name	Wild type FPKM	<i>sir1Δ</i>	Log ₂ Fold-Change
<i>HMR1</i>	<i>YCR097W</i>	0.02	21.62	Inf
<i>HMLALPHA1</i>	<i>YCL066W</i>	0	2.14	Inf
<i>YCL065W</i>	<i>YCL065W</i>	0	3.37015	Inf
<i>HMLALPHA2</i>	<i>YCL067C</i>	0.02	11.17	Inf
<i>FUS1</i>	<i>YCL027W</i>	2.80	13.0	2.17
<i>HMX1</i>	<i>YLR205C</i>	6.71	28.62	2.16
<i>YDR426C</i>	<i>YDR426C</i>	3.95	12.82	2.02
<i>AGA1</i>	<i>YNR044W</i>	18.81	75.23	2.01
<i>AGA2</i>	<i>YGL032C</i>	87.78	300.10	1.76
<i>GPM2</i>	<i>YDL021W</i>	6.54	17.01	1.39
<i>TMA10</i>	<i>YLR327C</i>	48.23	99.15	1.28
<i>KAR4</i>	<i>YCL055W</i>	12.85	30.56	1.27
<i>CYC7</i>	<i>YEL039C</i>	11.21	25.88	1.22
<i>BAR1</i>	<i>YIL015W</i>	44.74	101.48	1.19
<i>SPO11</i>	<i>YHL022C</i>	0.99	2.81	1.19
<i>SCM4</i>	<i>YGR049W</i>	51.79	110.81	1.16
<i>YNL155W</i>	<i>YNL155W</i>	22.01	47.49	1.07
<i>STR3</i>	<i>YGL184C</i>	11.73	24.72	1.07
<i>GPG1</i>	<i>YGL121C</i>	22.92	46.69	1.02
<i>YLR413W</i>	<i>YLR413W</i>	389.82	194.19	-1.00
<i>PHO5</i>	<i>YBR093C</i>	915.81	453.48	-1.00
<i>PHO89</i>	<i>YBR296C</i>	73.89	36.65	-1.10
<i>ZRT1</i>	<i>YGL255W</i>	389.91	184.98	-1.10
<i>TOS6</i>	<i>YNL300W</i>	340.12	172.12	-1.10
<i>PHO12</i>	<i>YHR215W</i>	400.97	151.36	-1.34
<i>PHO11</i>	<i>YAR071W</i>	244.35	81.25	-1.66

Table S3 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii kos3Δ* Mutant

Shown below are the two-fold or greater statistically significant expression changes that occurred in the *kos3Δ* mutant relative to Wild type.

Gene Name	Description/S.cerevisiae ortholog	Wild Type Read Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0E00330	<i>silenced copy of a1 gene at T. delbrueckii HMR-2 locus</i>	0	23.34	inf
TDEL0B00100	N/A	23.54	5151.5	7.77
TDEL0G00190	<i>silenced copy of a1 gene at T. delbrueckii HMR-1 locus</i>	0.3	41.67	7.12
TDEL0H04540	N/A	20.37	1855.18	6.51
TDEL0B00110	N/A	31.5	2304.93	6.19
TDEL0E00340	<i>silenced copy of a2 gene at T. delbrueckii HMR-2 locus</i>	0.56	33.59	5.91
TDEL0H04510	N/A	34.31	650.35	4.24
TDEL0A08060	N/A	19.43	329.58	4.08
TDEL0C06910	<i>Anc_1.12 YCL055W KAR4</i>	14.82	103.18	2.8
TDEL0E00100	N/A	66.67	389.42	2.55
TDEL0A08040	N/A	46.49	269.21	2.53
TDEL0B07690	N/A	240.6	1216.89	2.34
TDEL0H04530	N/A	358.29	1763.19	2.3
TDEL0H04520	N/A	99.47	464.31	2.22
TDEL0D00100	N/A	33.22	151.71	2.19
TDEL0C06990	<i>additional copy of DIC1 in X region of T. delbrueckii HML locus</i>	3.66	15.83	2.11
TDEL0E00320	N/A	44.16	178.34	2.01
TDEL0E00110	<i>Possible pseudogene</i>	52.84	202.37	1.94
TDEL0A08050	N/A	15.63	59.74	1.93
TDEL0D06680	N/A	31.31	110.8	1.82
TDEL0E00270	N/A	110.71	305.47	1.46
TDEL0E00310	N/A	166.41	432.48	1.38
TDEL0E05490	<i>Anc_6.240 YGL138C YGL138C</i>	9.42	24.41	1.37
TDEL0D06610	N/A	266.07	644.94	1.28
TDEL0A08020	N/A	197.16	429.64	1.12
TDEL0A07280	<i>Anc_6.313 YCR045C RRT12</i>	94.62	205.37	1.12
TDEL0A07990	<i>Anc_1.194 YKR066C CCP1</i>	424.18	876.8	1.05
TDEL0E00350	<i>KOS3</i>	187.66	2.46	-6.25

Table S4 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii sir2Δ* mutant

Shown below are statistically significant expression changes that occurred in the *sir2Δ* mutant relative to Wild type. GO term analysis revealed some genes that function in meiosis (*) and carbohydrate metabolism (**). Genes that specifically increased in only in the *sir2Δ* mutant and were located near a statistically significant Td-Sir2 peak are marked(‡).

Tdel Gene Name	Description/S.cerevisiae ortholog	Wild type Read Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0E00330	<i>silenced copy of a1 gene at T. delbrueckii HMR-2 locus</i>	0	30.34	inf

TDEL0B00100	N/A	28.56	5030.33	7.46
TDEL0H04540	N/A	24.73	3376.62	7.09
TDEL0G00190	<i>silenced copy of a1 gene at T. delbrueckii HMR-1 locus</i>	0.36	42.41	6.88
TDEL0B00110	N/A	38.16	2754.24	6.17
TDEL0E05490	<i>Anc_6.240 YGL138C</i> YGL138C	11.42	579.83	5.67
TDEL0D03040	N/A	6.42	275.89	5.43
TDEL0E00340	<i>silenced copy of a2 gene at T. delbrueckii HMR-2 locus</i>	0.67	27.74	5.36
TDEL0H03220 [‡]	N/A	21.89	573.92	4.71
TDEL0C02460 [‡]	<i>Anc_7.301 YDL186W</i> YDL186W	6.76	159.44	4.56
TDEL0H04510	N/A	41.63	830.98	4.32
TDEL0A03570* [‡]	<i>Anc_5.493 YDR402C DIT2</i>	66.44	1280.49	4.27
TDEL0A05800* [‡]	<i>Anc_8.634 YPL130W</i> SPO19 YOR214C YOR214C	326.1	4960.5	3.93
TDEL0A08060	N/A	23.54	355.85	3.92
TDEL0D02390	N/A	7.06	105.6	3.9
TDEL0G02080 [‡]	<i>Anc_1.169 YJL170C ASG7</i>	11.47	124.36	3.44
TDEL0B07690	N/A	291.82	3152.53	3.43
TDEL0C06230 [‡]	<i>Anc_1.78</i>	21.03	196.88	3.23
TDEL0G00740 [‡]	<i>Anc_5.50 YGR260W</i> TNA1	760.16	6641.08	3.13
TDEL0A03580* [‡]	<i>Anc_5.494 YDR403W</i> DIT1*	305.27	2584.58	3.08
TDEL0C06910	<i>Anc_1.12 YCL055W KAR4</i>	18	145.73	3.02
TDEL0A00420 [‡]	<i>Anc_3.23 YNL318C</i> HXT14	63.73	494.54	2.96
TDEL0G01600 [‡]	<i>Anc_6.185 YGL089C</i> MF(ALPHA)2 YPL187W MF(ALPHA)1	39.76	297.07	2.9
TDEL0D02770* [‡]	<i>Anc_4.174 YLR343W</i> GAS2	45.12	315.62	2.81
TDEL0A06450*	<i>Anc_8.700 YOR255W</i> OSW1	35.61	247.62	2.8
TDEL0B03880	N/A	62.55	431.69	2.79
TDEL0E00100	<i>probable pseudogene</i>	80.85	540.34	2.74
TDEL0A00530*	<i>Anc_3.34 YOL132W</i> GAS4	85.16	547.68	2.69
TDEL0H04530	N/A	434.83	2760.86	2.67
TDEL0C06990	<i>additional copy of DIC1 in X region of T. delbrueckii HML locus</i>	4.44	27.27	2.62
TDEL0H04520	N/A	120.74	717.27	2.57
TDEL0D02810* [‡]	<i>Anc_4.171 YLR341W</i> SPO77	69.47	405.68	2.55
TDEL0D04700	<i>Anc_3.152 YOL067C</i> RTG1	110.74	633.36	2.52
TDEL0A05130* [‡]	<i>Anc_8.570 YBR180W</i> DTR1	62.24	352.79	2.5
TDEL0D00830	<i>Anc_4.335</i>	109.78	619.08	2.5
TDEL0A04250	YBR298C MAL31	368.48	2063.52	2.49

TDEL0G03030	<i>Anc_2.371 YPL033C SRL4</i>	52.91	295.22	2.48
TDEL0E01490**	<i>Anc_4.223 YDL049C KNH1</i>	99.52	518.7	2.38
TDEL0G00780*‡	<i>Anc_5.54 YHR184W SSP1</i>	176.73	918.42	2.38
TDEL0D00100	<i>N/A</i>	40.36	209.06	2.37
TDEL0B03420*‡	<i>Anc_8.768 YOR298W MUM3</i>	60.68	306.94	2.34
TDEL0E00260	<i>N/A</i>	2566.61	12859.78	2.32
TDEL0H03650	<i>N/A</i>	97.84	483.86	2.31
TDEL0C06770*‡	<i>Anc_1.25 YCL048W SPS22 YDR522C SPS2</i>	121.68	595.33	2.29
TDEL0B07410‡	<i>N/A</i>	37.16	178.54	2.26
TDEL0H03270‡	<i>N/A</i>	422.23	1923.48	2.19
TDEL0B01080*‡	<i>Anc_8.790 YOR313C SPS4</i>	75.47	330.11	2.13
TDEL0C01450	<i>Anc_7.402 YER106W MAM1</i>	85.7	374.03	2.13
TDEL0H02150‡	<i>Anc_7.229 YER053C-A YER053C-A</i>	278.61	1212.99	2.12
TDEL0A07280	<i>Anc_6.313 YCR045C RRT12</i>	114.78	495.69	2.11
TDEL0A02610*	<i>Anc_2.485 YKL096W CWPI*</i>	418.19	1720.12	2.04
TDEL0D01720‡	<i>N/A</i>	148.46	589.36	1.99
TDEL0A06900	<i>Anc_6.277 YMR189W GCV2</i>	5122.21	20210.34	1.98
TDEL0H00530	<i>N/A</i>	491.32	1927.45	1.97
TDEL0H02590‡	<i>Anc_7.188 YFR032C RRT5</i>	59.24	229.4	1.95
TDEL0D06570‡	<i>N/A</i>	984.99	3787.33	1.94
TDEL0G02530‡	<i>Anc_2.323 YDL114W YDL114W</i>	76.26	289.63	1.93
TDEL0A08040	<i>N/A</i>	56.36	211.62	1.91
TDEL0C00760*	<i>Anc_8.50 YLR054C OSW2</i>	222.35	818.13	1.88
TDEL0D03790	<i>Anc_3.246 YDR019C GCV1</i>	1394.09	5092.1	1.87
TDEL0F00170	<i>N/A</i>	514.16	1840.41	1.84
TDEL0D04720‡	<i>Anc_3.150 YDL043C PRP11</i>	169.35	603.95	1.83
TDEL0B06100‡	<i>Anc_1.396 YLR174W IDP2 YNL009W IDP3</i>	1408.31	5002.87	1.83
TDEL0A05020	<i>Anc_5.636 YDR270W CCC2</i>	651.52	2274.87	1.8
TDEL0A07980	<i>N/A</i>	278.86	972.97	1.8
TDEL0A02410‡	<i>Anc_2.465 YMR096W SNZ1</i>	1800.5	6156.83	1.77
TDEL0A02420	<i>Anc_2.466 YMR095C SNO1</i>	383.86	1300.79	1.76
TDEL0C00160	<i>N/A</i>	38.7	121.52	1.65
TDEL0B01290	<i>Anc_8.508 YBR157C ICS2</i>	16.04	50.17	1.64
TDEL0G04960	<i>no start codon apparent</i>	2339.73	7093.07	1.6
TDEL0D02340‡	<i>N/A</i>	316.47	953.87	1.59
TDEL0B06220‡	<i>Anc_1.385</i>	127.12	380.25	1.58
TDEL0G00100	<i>N/A</i>	401.9	1199.81	1.58
TDEL0E01760	<i>Anc_4.197 YLR359W</i>	4490.51	13391.34	1.58

	<i>ADE13</i>			
TDEL0D05600 [‡]	<i>Anc_3.492 YGR130C</i> YGR130C	2352.85	6992.01	1.57
TDEL0D06680	N/A	38.03	112.78	1.57
TDEL0D05330 [‡]	N/A	104.35	308.51	1.56
TDEL0E02790 [‡]	<i>Anc_5.348 YDR317W</i> HIM1	64.76	191.21	1.56
TDEL0E04950	<i>Anc_5.134 YGR204W</i> ADE3	3636.91	10599.18	1.54
TDEL0A00960* [‡]	<i>Anc_2.55 YDL222C</i> FMP45 YNL194C YNL194C	1683.93	4875.4	1.53
TDEL0A02500 [‡]	<i>Anc_2.474 YMR087W</i> YMR087W	201.34	579.65	1.53
TDEL0G00760* [‡]	<i>Anc_5.52 YHR185C PFS1</i>	196	563.98	1.52
TDEL0D05160 [‡]	<i>Anc_3.108 YBR149W</i> ARA1	1852.55	5329.9	1.52
TDEL0C05600 [‡]	<i>Anc_3.424 YGR088W</i> CTT1	6793.72	19384.26	1.51
TDEL0H04480 [‡]	N/A	7320.05	20813.2	1.51
TDEL0G01610 [‡]	<i>Anc_6.184 YPL186C UIP4</i>	136.95	389.23	1.51
TDEL0B06310** [‡]	<i>Anc_1.375 YFR015C</i> GSY1 YLR258W GSY2	1267.26	3569.67	1.49
TDEL0H03660	N/A	37.04	102.96	1.47
TDEL0A08050	N/A	18.95	51.66	1.45
TDEL0C01830 [‡]	N/A	1567.76	4262.27	1.44
TDEL0B05440	N/A	45.96	124.44	1.44
TDEL0C00840	<i>Anc_8.58 YFL017C GNA1</i>	340.96	906.62	1.41
TDEL0C04590* [‡]	<i>Anc_2.242 YNL065W</i> AQR1 YIL120W QDR1	1794.04	4734.42	1.4
TDEL0C00630	<i>Anc_8.38 YLR058C SHM2</i>	8025.37	20980.43	1.39
TDEL0C00170	<i>Anc_2.89 YNL165W</i> YNL165W	43.18	112.8	1.39
TDEL0C02500 [‡]	<i>Anc_1.489 YEL046C</i> GLY1	3378.27	8801.43	1.38
TDEL0E00310	N/A	202	522.53	1.37
TDEL0A00140	N/A	109.36	282.47	1.37
TDEL0E00350	N/A	227.73	587.63	1.37
TDEL0G00210	N/A	449.42	1158.59	1.37
TDEL0E00850 [‡]	<i>Anc_4.285 YKL187C</i> YKL187C YLR413W YLR413W	2873.13	7339.53	1.35
TDEL0B05780 [‡]	N/A	102.69	260.58	1.34
TDEL0D05040 [‡]	<i>Anc_3.119 YOL084W</i> PHM7	5727.35	14415.9	1.33
TDEL0E00320	N/A	53.58	133.94	1.32
TDEL0A05760 [‡]	<i>Anc_8.630 YPL128C TBF1</i>	139.06	346.38	1.32
TDEL0H00120	N/A	90.65	222.93	1.3
TDEL0D05750 [‡]	<i>Anc_3.507</i>	495.87	1215.55	1.29
TDEL0C00210 [‡]	N/A	641.94	1543.38	1.27
TDEL0D03430 [‡]	<i>Anc_3.281 YBR066C</i> NRG2 YDR043C NRG1	300.95	717.87	1.25
TDEL0C04620 [‡]	<i>Anc_2.245 YNL063W</i>	416.43	983	1.24

	<i>MTQ1</i>			
TDEL0B04150**‡	<i>Anc_8.195 YDR074W</i> TPS2	2150.3	5060.38	1.23
TDEL0B02500	<i>Anc_5.673 YKR080W</i> MTD1	2761.04	6492.77	1.23
TDEL0D06610	<i>possible pseudogene; N added at two sites to avoid frameshifts</i>	322.84	758.48	1.23
TDEL0E00110	<i>possible pseudogene; N added to avoid frameshift</i>	64.14	149.43	1.22
TDEL0E00270	N/A	134.39	312.28	1.22
TDEL0F01320	<i>Anc_2.177 YNL101W</i> AVT4	1132.4	2618.17	1.21
TDEL0D05430	<i>Anc_3.81 YNL280C</i> ERG24	1549.78	3578.89	1.21
TDEL0E03600‡	<i>Anc_5.266 YHR022C</i> YHR022C	839.36	1936.88	1.21
TDEL0F03380	N/A	54.95	126.65	1.2
TDEL0D00650‡	N/A	389.91	880.46	1.18
TDEL0C01310‡	N/A	2145.74	4806.19	1.16
TDEL0G01510	<i>Anc_6.195 YGL082W</i> YGL082W YPL191C YPL191C	407.25	908.44	1.16
TDEL0A07230	<i>Anc_6.309</i> YMR206W/YNR014W	518.47	1152.23	1.15
TDEL0B00120	N/A	169.29	374.84	1.15
TDEL0H01710	<i>Anc_7.273 YER081W</i> SER3 YIL074C SER33	6936.33	15341.48	1.15
TDEL0B00960‡	<i>Anc_8.801 YMR250W</i> GAD1	953.92	2108.67	1.14
TDEL0B05680**	<i>Anc_1.435 YEL011W</i> GLC3	809.34	1762.59	1.12
TDEL0C00140	N/A	85.09	184.53	1.12
TDEL0D02250	<i>Anc_1.357 YFR023W</i> PES4 YHR015W MIP6	308.62	668.74	1.12
TDEL0G01710	<i>Anc_4.20 YHL028W</i> WSC4	695.11	1506.14	1.12
TDEL0D02460	<i>Anc_5.455 YOR128C</i> ADE2	2232	4829.7	1.11
TDEL0E00280	N/A	376.24	806.8	1.1
TDEL0B03240	<i>Anc_8.525 YPL061W</i> ALD6	994.1	2127.76	1.1
TDEL0C02550‡	<i>Anc_1.484 YEL041W</i> YEF1 YJR049C UTR1	690.63	1476.64	1.1
TDEL0H04260	<i>Anc_7.25 YAL044C</i> GCV3	2743.83	5814.64	1.08
TDEL0C05340‡	<i>Anc_3.397 YBR132C</i> AGP2	596.01	1262.57	1.08
TDEL0C05240**‡	<i>Anc_3.386 YBR126C</i> TPS1	2205.2	4663.53	1.08
TDEL0C00450‡	<i>Anc_8.22 YFL040W</i> YFL040W	80.29	169.32	1.08
TDEL0A02400‡	<i>Anc_2.464 YKL109W</i> HAP4	1447.85	3053.05	1.08
TDEL0G00200	<i>silenced copy of a2 gene at T. delbrueckii HMR-1 locus</i>	80.13	168.35	1.07
TDEL0E03690**‡	<i>Anc_5.257 YKL152C</i>	53511.14	111819.2	1.06

	<i>GPM1</i>			
TDEL0C00130	N/A	718.82	1499.25	1.06
TDEL0D03730*†	<i>Anc_3.252 YBR045C GIP1</i>	180.07	372.7	1.05
TDEL0D03300‡	<i>Anc_3.296</i>	3786.42	7762.59	1.04
TDEL0A00130	N/A	312.57	639.12	1.03
TDEL0H02310	<i>Anc_7.215 YER047C SAP1</i>	463.53	947.02	1.03
TDEL0E00210**	<i>Anc_2.445 YKL127W PGM1 YMR105C PGM2</i>	7533.93	15266.2	1.02
TDEL0G03220*†	<i>Anc_2.391 YDL079C MRK1 YMR139W RIM11</i>	1715.92	3476.54	1.02
TDEL0C03290	<i>Anc_7.465 YJR094C IME1</i>	31.65	64.13	1.02
TDEL0B00340	<i>Anc_8.865 YML091C RPM2</i>	2336.03	4731.25	1.02
TDEL0B00830	<i>Anc_8.814 YMR262W YMR262W</i>	412.6	834.55	1.02
TDEL0A02430	<i>Anc_2.467 YMR094W CTF13</i>	103.45	208.01	1.01
TDEL0D01220‡	<i>Anc_1.255 YJL106W IME2</i>	86.48	173.31	1
TDEL0D04710	<i>Anc_3.151 YDL042C SIR2 YOL068C HST1</i>	1073.99	9.22	-6.86
TDEL0D06630	<i>YFR055W IRC7</i>	1735.47	356.24	-2.28
TDEL0F02930	<i>Anc_4.59 YGR161C RTS3</i>	3158.93	941.4	-1.75
TDEL0H00860	<i>YGR286C BIO2</i>	526.47	185.53	-1.5
TDEL0F04600	<i>Anc_8.336 YDR155C CPR1</i>	10592.71	3790.99	-1.48
TDEL0G03300	N/A	869.19	319.86	-1.44
TDEL0B04040	<i>Anc_6.150 YBR238C YBR238C YGL107C RMD9</i>	5774.79	2164.77	-1.42
TDEL0C02270	<i>Anc_7.319 YLR214W FRE1</i>	8103.25	3287.34	-1.3
TDEL0H02760	<i>Anc_7.169</i>	136.54	58.79	-1.22
TDEL0C01030	N/A	2182.98	941.75	-1.21
TDEL0E03870	<i>Anc_5.239 YJL034W KAR2</i>	6060.81	2660.19	-1.19
TDEL0E02290	<i>Anc_5.395 YDR343C HXT6 YHR094C HXT1</i>	2305.49	1013	-1.19
TDEL0F05620	<i>YKL216W URA1</i>	2366.8	1054.72	-1.17
TDEL0B04210	<i>Anc_8.189 YDR070C FMP16</i>	681.14	311.42	-1.13
TDEL0F01940	<i>Anc_6.244 YMR173W DDR48</i>	3659.39	1681.12	-1.12
TDEL0B02690	<i>Anc_5.654 YKR071C DRE2</i>	921.33	425.21	-1.12
TDEL0B01220	<i>Anc_8.516 YBR162W-A YSY6</i>	532.41	253.33	-1.07
TDEL0G04350	<i>Anc_6.34 YMR002W MIC17</i>	792.64	378.4	-1.07
TDEL0H01600	N/A	1848.38	892.09	-1.05
TDEL0F00720	<i>Anc_2.84 YHR144C DCD1</i>	262.29	129.14	-1.02
TDEL0A01990	<i>Anc_4.186 YGR041W BUD9 YLR353W BUD8</i>	394.24	195.73	-1.01
TDEL0B00270	<i>Anc_8.858 YML123C</i>	7365.58	3679.29	-1

	PHO84			
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Table S5 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii sir4Δ* Mutant

Shown below are the two-fold or greater statistically significant expression changes that occurred in the *sir4Δ* mutant relative to Wild type.

Tdel Gene Name	Description/S.cerevisiae ortholog	Wild type Read Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0E00330	<i>silenced copy of a1 gene at T. delbrueckii HMR-2 locus</i>	0	32.67	inf
TDEL0B00100	N/A	31.67	8351.03	8.04
TDEL0G00190	<i>silenced copy of a1 gene at T. delbrueckii HMR-1 locus</i>	0.4	63.04	7.3
TDEL0H04540	N/A	27.41	1842.8	6.07
TDEL0B00110	N/A	42.34	2713.53	6
TDEL0E00340	<i>silenced copy of a2 gene at T. delbrueckii HMR-2 locus</i>	0.75	38.91	5.7
TDEL0H04510	N/A	46.16	745.75	4.01
TDEL0A08060	N/A	26.12	401.23	3.94
TDEL0B07690	N/A	323.59	2190.76	2.76
TDEL0C06990	<i>additional copy of DIC1 in X region of T. delbrueckii HML locus</i>	4.92	29.95	2.61
TDEL0E00100	<i>probable pseudogene; NNN added at 2 sites to avoid internal stop codons</i>	89.67	518.29	2.53
TDEL0C06910	<i>Anc_1.12 YCL055W KAR4</i>	19.95	101.29	2.34
TDEL0D00100	N/A	44.73	214.92	2.26
TDEL0H04530	N/A	482.14	2313.94	2.26
TDEL0H04520	N/A	133.86	606.11	2.18
TDEL0A08040	N/A	62.52	273.11	2.13
TDEL0A08050	N/A	21.02	75.4	1.84
TDEL0E00320	N/A	59.4	204.09	1.78
TDEL0D06680	N/A	42.15	144.07	1.77
TDEL0E00310	N/A	223.93	716.54	1.68
TDEL0E00110	<i>possible pseudogene; N added to avoid frameshift</i>	71.11	213.67	1.59
TDEL0G00100	N/A	445.66	1243.04	1.48
TDEL0E00350	N/A	252.49	659.05	1.38
TDEL0D06610	<i>possible pseudogene; N added at two sites to avoid frameshifts</i>	357.97	842.67	1.24
TDEL0B00120	N/A	187.69	426.62	1.18
TDEL0E00260	N/A	2845.36	6178.25	1.12
TDEL0C00100	N/A	58.85	120.26	1.03
TDEL0B01940	<i>Anc_8.442 YDR227W SIR4</i>	775.97	1.07	-9.5

Table S6 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii ago1Δ* Mutant

Tdel Gene Name	Description/S.cerevisiae ortholog	Wild type Read Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0E05620	<i>Anc_4.53_YLR303W_MET17</i>	1282.81	2605.93	1.02
TDEL0D03430	<i>Anc_3.281_YBR066C_NRG2_YDR043C_NRG1</i>	313.05	686.07	1.13
TDEL0C00130	<i>None</i>	747.86	1511.21	1.01
TDEL0A00960	<i>Anc_2.55_YDL222C_FMP45_YNL194C_YNL194C</i>	1753.09	3807.72	1.12
TDEL0G04020	<i>Anc_6.70_YLR273C_PIG1_YOR178C_GAC1</i>	782.76	1570.67	1
TDEL0H04480	<i>None</i>	7605.79	16321.03	1.1
TDEL0D00760	<i>AGO1</i>	4105.13	18.85	-7.77
TDEL0D00160	<i>None</i>	2316.09	1132.09	-1.03
TDEL0H00100	<i>None</i>	180.65	89.78	-1.01
TDEL0B00270	<i>Anc_8.858_YML123C_PHO84</i>	7680.71	3103.39	-1.31
TDEL0F05620	<i>YKL216W_UR1</i>	2471.09	1104.82	-1.16
TDEL0E03110	<i>Anc_5.316_YDR299W_BFR2</i>	848.82	367.55	-1.21
TDEL0E00130	<i>Anc_3.217_YBR018C_GAL7</i>	5447.66	1847.84	-1.56
TDEL0B06990	<i>Anc_2.606_YKL067W_YNK1</i>	1149.35	551.91	-1.06
TDEL0A08040	<i>None</i>	58.8	27.88	-1.08

Table S7 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii dcr1*Δ Mutant

Tdel Gene Name	Description/S.cerevisiae ortholog	Wild type Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0E05620	<i>YLR303W (MET17)</i>	1282.81	2919.77	1.19
TDEL0B07040	<i>YKL068W-A</i>	115.16	253.29	1.14
TDEL0D03430	<i>Anc_3.281_YBR066C_NRG2_YDR043C_NRG1</i>	313.05	640.28	1.03
TDEL0D03620	<i>Anc_3.263_YBR054W_YRO2_YDR033W_MRH1</i>	1143.57	2645.5	1.21
TDEL0B00490	<i>TdDCR1</i>	527.95	0.49	-10.09
TDEL0D00150	<i>None</i>	2483.46	1224.75	-1.02
TDEL0D00160	<i>None</i>	2316.09	1156.62	-1
TDEL0B00270	<i>Anc_8.858_YML123C_PHO84</i>	7680.71	3726.61	-1.04
TDEL0E00130	<i>Anc_3.217_YBR018C_GAL7</i>	5447.66	1831.02	-1.57

Table S8 Genes Increasing and Decreasing in Expression Relative to Wild Type in *T. delbrueckii ago1*Δ*dcr1*Δ Mutant

A total of 15 genes increased in expression, while 36 genes decreased in expression (excluding *AGO1* and *DCR1* themselves, which were deleted). Statistically significant associated GO terms are starred: *oxidation-reduction process and **small molecule metabolism.

Tdel Gene Name	Description/S.cerevisiae ortholog	Wild type Counts	Mutant Counts	Log ₂ Fold-Change
TDEL0D05180	<i>Anc_3.106_YOL091W_SPO21_YBR148W_YSW1</i>	315.93	818.69	1.37
TDEL0H02150	<i>Anc_7.229_YER053C-A_YER053C-A</i>	290.62	638.93	1.14

TDEL0E05620**	<i>Anc_4.53_YLR303W_MET17</i>	1282.81	3371.21	1.39
TDEL0A02860**,**	<i>Anc_2.510_YKL001C_MET14</i>	500.72	1049.28	1.07
TDEL0B07040	<i>Anc_2.611_YKL068W-A_YKL068W-A</i>	115.16	293.26	1.35
TDEL0C02250	<i>Anc_7.321_YLR213C_CRR1</i>	393.95	872.25	1.15
TDEL0H00530	<i>None</i>	511.71	1924.72	1.91
TDEL0A03070**	<i>Anc_2.533_YMR070W_MOT3</i>	531.53	1184.55	1.16
TDEL0D02810	<i>Anc_4.171_YLR341W_SPO77</i>	72.41	165.49	1.19
TDEL0G04810	<i>Anc_5.225_YJR004C_possible_pseudogene;_NNN_added_to_avoid_internal_stop_codon_SAG1</i>	2856.36	8065.96	1.5
TDEL0H02590	<i>Anc_7.188_YFR032C_RRT5</i>	61.8	177.97	1.53
TDEL0B03030**	<i>Anc_8.543_YPL075W_GCR1</i>	3043.67	6173.95	1.02
TDEL0H03220	<i>None</i>	22.84	50.38	1.14
TDEL0E01150	<i>Anc_4.255_YLR394W_CST9</i>	151.86	386.56	1.35
TDEL0F02030	<i>Anc_3.314_YBL029W_YBL029W</i>	1882.73	5733.91	1.61
TDEL0D00760	<i>DCR1</i>	4105.13	15.95	-8.01
TDEL0B00490	<i>AGO1</i>	527.95	0.93	-9.15
TDEL0F04930	<i>Anc_8.369_YDR171W_HSP42</i>	2110.06	942.43	-1.16
TDEL0C06700**	<i>Anc_1.33_YCL040W_GLK1_YDR516C_EMI2</i>	5278.83	2026.37	-1.38
TDEL0C03660	<i>Anc_1.187_YJL160C_YJL160C_YKL164C_PIR1</i>	9328.27	4467.78	-1.06
TDEL0C03310	<i>Anc_7.467_YJR095W_SFC1</i>	760.01	293.07	-1.37
TDEL0A07760**	<i>Anc_6.361_YNR041C_COQ2</i>	1513.9	745.09	-1.02
TDEL0B06100**,**	<i>Anc_1.396_YLR174W_IDP2_YNL009W_IDP3</i>	1468.89	674.28	-1.12
TDEL0A08000	<i>None</i>	1015.03	494.25	-1.04
TDEL0C03550	<i>Anc_7.492_YBL049W_MOH1</i>	189.09	89.77	-1.07
TDEL0H04450**,**	<i>Anc_7.6_YOR374W_ALD4</i>	2790.18	883.98	-1.66
TDEL0H04500	<i>None</i>	505.82	239.16	-1.08
TDEL0C05240	<i>Anc_3.386_YBR126C_TPS1</i>	2297.85	1130.33	-1.02
TDEL0A00300	<i>Anc_3.11_YNL327W_EGT2</i>	1436.95	705.1	-1.03
TDEL0B02120**	<i>Anc_5.708_YKR097W_PCK1</i>	142.3	57.36	-1.31
TDEL0G04910	<i>None</i>	2657.68	1038.52	-1.36
TDEL0H04490	<i>None</i>	417.79	192.3	-1.12
TDEL0B00960**	<i>Anc_8.801_YMR250W_GAD1</i>	993.32	465.26	-1.09
TDEL0G01820**	<i>Anc_4.9_YHL032C_GUT1</i>	1450.81	509.11	-1.51
TDEL0H01960*	<i>Anc_7.248_YER067W_RGI1_YIL057C_RGI2</i>	615.46	183.96	-1.74
TDEL0H03410	<i>Anc_7.110_YHL021C_AIM17</i>	1713.68	693.58	-1.3
TDEL0G04760	<i>None</i>	9784.29	3968.18	-1.3
TDEL0H04480	<i>None</i>	7605.79	2054.54	-1.89
TDEL0B06230**	<i>Anc_1.384_YLR251W_SYM1</i>	115.5	55.21	-1.06
TDEL0A00950	<i>None</i>	4708.18	2187.3	-1.11
TDEL0D05820**,**	<i>Anc_3.514_YGL205W_POX1</i>	697.91	305.94	-1.19
TDEL0C02900	<i>None</i>	2157.25	708.44	-1.61
TDEL0F00170	<i>None</i>	535.08	221.04	-1.28
TDEL0B06310*	<i>Anc_1.375_YFR015C_GSY1_YLR258W_GSY2</i>	1318.21	570.62	-1.21
TDEL0D04470**	<i>Anc_3.176_YAR035W_YAT1</i>	631.43	159.06	-1.99
TDEL0B00110	<i>None</i>	39.85	19.29	-1.05
TDEL0C00160	<i>None</i>	40.29	19.48	-1.05
TDEL0D03060	<i>Anc_4.146_YGR008C_STF2_YLR327C_TMA10</i>	2032.38	733.81	-1.47
TDEL0E00130**	<i>Anc_3.217_YBR018C_GAL7</i>	5447.66	2480.8	-1.13
TDEL0A06070	<i>Anc_8.661_YPL147W_PXA1</i>	431.99	206.53	-1.06
TDEL0E00180	<i>None</i>	11043.2	4472.84	-1.3
TDEL0B05680*	<i>Anc_1.435_YEL011W_GLC3</i>	841.87	411.07	-1.03
TDEL0B06280	<i>Anc_1.378_YLR257W_YLR257W</i>	426.12	195.76	-1.12

Table S9 Genes Increasing In Expression in *T. delbrueckii* *sir* Mutants

Listed below are twenty-two subtelomeric genes and silent mating type loci genes that were de-repressed in all three *T. delbrueckii* *sir* mutants. Many subtelomeric genes on the same telomeric arm are adjacent to each other (for example, *TDEL0B00100* and *TDEL0B00110*). For those genes that have *S. cerevisiae* orthologs, the *S. cerevisiae* systematic name and three-letter name is provided.

T. delbrueckii Gene	<i>S. cerevisiae</i> ortholog	Wild type FPKM	<i>kos3Δ</i> FPKM	<i>sir2Δ</i> FPKM	<i>sir4Δ</i> FPKM	Description
<i>TDEL0E00330</i>	a1 gene at T. delbrueckii Chr V HMR	0.67	40.95	44.37	53.57	Silent mating type locus
<i>TDEL0E00340</i>	a2 gene at Chr V HMR	4.91	30.53	28.16	29.11	Silent mating type locus
<i>TDEL0G00190</i>	a1 gene at T. delbrueckii Chr VII HMR	0.67	39.07	43.35	52.26	Silent mating type locus
<i>TDEL0E00310</i>	N/A	14.29	37.15	37.41	48.66	Adjacent to silent mating type locus
<i>TDEL0E00320</i>	N/A	8.39	33.06	20.1	28.03	Adjacent to silent mating type locus
<i>TDEL0A08040</i>	N/A	10.44	61.2	37.98	46.64	Subtelomeric (<i>TEL01R</i>)
<i>TDEL0A08050</i>	N/A	3.05	10.85	6.85	8.77	Subtelomeric (<i>TEL01R</i>)
<i>TDEL0A08060</i>	N/A	1.49	26.46	21.86	24.12	Subtelomeric (<i>TEL01R</i>)
<i>TDEL0B00100</i>	N/A	2.28	503.74	402.2	608.34	Subtelomeric (<i>TEL02L</i>)
<i>TDEL0B00110</i>	N/A	2.77	192.53	190.95	168.79	Subtelomeric (<i>TEL02L</i>)
<i>TDEL0B07690</i>	N/A	101.14	503.52	1056.35	683.41	Subtelomeric (<i>TEL02R</i>)
<i>TDEL0C06910</i>	<i>YCL055W (KAR4)</i>	1.85	14.01	16.53	10.11	Subtelomeric (<i>TEL03R</i>)
<i>TDEL0C06990</i>	<i>DIC1</i> copy in X-region of <i>HML</i>	77.04	166.36	131.33	171.66	Subtelomeric (<i>TEL03R</i>)
<i>TDEL0D00100</i>	N/A	26.89	46.74	59.84	48.29	Subtelomeric (<i>TEL04L</i>)
<i>TDEL0D06610</i>	N/A	25.19	60.31	54.86	57.05	Subtelomeric (<i>TEL04R</i>)
<i>TDEL0D06680</i>	N/A	5.78	22.74	17.81	18.5	Subtelomeric (<i>TEL04R</i>)
<i>TDEL0E00100</i>	N/A	5.86	33.8	40.74	34.04	Subtelomeric (<i>TEL05L</i>)
<i>TDEL0E00110</i>	N/A	9.01	32.16	21.11	28.72	Subtelomeric (<i>TEL05L</i>)
<i>TDEL0H04510</i>	N/A	2.62	51.31	53.12	43.62	Subtelomeric

						(TEL08R)
TDEL0H04520	N/A	32.92	80.85	121.08	83.02	Subtelomeric (TEL08R)
TDEL0H04530	N/A	26.32	96.68	123.82	96.46	Subtelomeric (TEL08R)
TDEL0H04540	N/A	3.31	284.53	430.43	211.64	Subtelomeric (TEL08R)

Table S10 ChIP-Seq Reads Per Data Set

Strain	Alias	Sample	Total_Reads	Reads_Mapped	Genome-wide_Median
JRY10152	scSir1_IP	IP	38416222	20135820	132
JRY10152	scSir1_in	input	24223214	13916174	91
JRY9316	scNoTag_IP	IP	41359126	33887088	211
JRY9316	scNoTag_in	input	30951676	22488089	143
JRY10160	kos3_IP	IP	30692204	28180256	208
JRY10160	kos3_in	input	37857090	23046669	83
JRY10161	tdSir2_IP	IP	64772046	61078532	283
JRY10161	tdSir2_in	input	33789380	26576719	253
JRY10162	tdSir4_IP	IP	34959374	26516814	198
JRY10162	tdSir4_in	input	49459360	35696614	267
JRY10156	td_NoTag_IP	IP	34902818	30961776	271
JRY10156	td_NoTag_in	input	53648772	46344215	431
JRY10185	td_sir4_kos3Δ_IP	IP	33347158	23556275	39
JRY10184	td_sir2_kos3Δ_IP	IP	42035285	31642374	152
JRY10184	td_sir2_kos3Δ_in	input	42467510	8631392	30

Table S11 RNA-Seq Reads Per Data Set

Strain	Alias	Total Reads	Reads Mapped	% Reads Mapped	% Mapped Non-Uniquely
JRY9316	wildTypeA	15747860	14480231	92	6.9
JRY9316	wildTypeB	20204590	18636063	92.2	6.8
JRY9316	wildTypeC	19988764	18323263	91.7	9
JRY10153	sir1_A	16667732	15105456	90.6	7.1
JRY10154	sir1_B	21854922	20320743	93	6.9
JRY10155	sir1_C	25010370	23014267	92	7.1
JRY10156	td_Wildtype_A	15286600	14186364	92.8	2.2
JRY10156	td_Wildtype_B	19561586	17479536	89.4	3.8
JRY10156	td_Wildtype_C	15787518	14440572	91.5	2.7
JRY10157	kos3_A	18855860	16598907	88	2.4
JRY10157	kos3_B	12373772	10960974	88.6	2.4
JRY10157	kos3_C	9463160	8657370	91.5	2.1

JRY10158	td_sir2_A	22461150	19501160	86.8	1.9
JRY10158	td_sir2_B	34093000	30790506	90.3	2.7
JRY10158	td_sir2_C	17313930	15385654	88.9	2.3
JRY10159	td_sir4_A	34504902	31345497	90.8	2.3
JRY10159	td_sir4_B	19359522	17642827	91.1	2.7
JRY10159	td_sir4_C	22980378	20541732	89.4	2.3
JRY10163	td_ago1_A	20246704	18125537	89.5	1.8
JRY10163	td_ago1_B	17229086	15783662	91.6	2.3
JRY10163	td_ago1_C	25218810	22352227	88.6	1.8
JRY10164	td_dcr1_A	26475104	24049831	90.8	2.9
JRY10164	td_dcr1_B	26475104	24049831	90.8	2.9
JRY10164	td_dcr1_C	18018972	15589654	86.5	2.5
JRY10165	ago1dcr1_A	17995398	15313261	85.1	2
JRY10165	ago1dcr1_B	24626138	23131252	93.9	2.4
JRY10165	ago1dcr1_C	17013842	16058396	94.4	3.3