

Fungal Sirtuin E is a Global Transcription Regulator That Determines Transition Between Exponential Growth and Stationary Phases

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Supplementary Figure Legends

FIGURE S1. Sirtuins of *A. nidulans*.

A, Phylogenetic tree of sirtuins of *A. nidulans* and human. *B*, Structures of *A. nidulans* sirtuin isozymes. The conserved sirtuin core domains (black) and NLS (gray) are shown. *C*, Amino acid sequence alignment of the *A. nidulans* sirtuins isozymes.

FIGURE S2. Gene disruption of *A. nidulans sirE*.

Strategy for disruption of *sirE* gene (*left*) and Southern blot of total DNA of WT and SirEΔ strains digested with *XhoI* (*right*). Bars indicate positions and sizes of hybridization probes.

FIGURE S3. Activity for extracellular hydrolases in *A. nidulans* culture supernatant.

The *A. nidulans* A26 (WT) (●) and SirEΔ (■) were cultured in liquid GMM medium at 30°C, and hydrolase activities in the fungal culture supernatants were determined. The activities of β-cellobiase, β-xylosidase, α-glucosidase, β-glucosidase, β-galactosidase, and β-mannosidase were measured. Data are the mean ± the standard errors for three experiments. *, *P* < 0.05 versus WT.

FIGURE S4. Chromatin immunoprecipitation of the *pfkA*, *gpdA*, and *agsB* genes.

Chromatin immunoprecipitation analyses measured acetylation levels on the gene promoters of *pfkA*, *gpdA*, and *agsB* in *A. nidulans* A26 (WT) (black bars) and SirEΔ (white bars) cultured in GMM medium. Anti-H3K18ac antibody precipitated DNA and the relative amounts were presented to that precipitated by anti-histone H3 antibody. Negative controls without the acetyllysine antibodies were < 0.01. Left panels present levels of transcripts of the indicated genes. Data are means ± standard errors for three experiments. *, *P* < 0.05, and **, *P* < 0.07 versus WT.

Supplementary Table S1 Primers used in this study.

primer	Nucleotide sequence	used to generate
<i>Cassette for gene disruption</i>		
SirE-5 F	5'-ATCAGTCCCAGGACAACAGG-3'	5'-region of <i>sirE</i>
SirE-5-argB R	5'-AAAACCGCGAAATAAAGCTTGGGATGACGCGAGAGTAGAG-3'	
SirE-3-argB F	5'-CGCAATGGCTGTAGGTCGACTAGATATGCCGTTGGCGTTT-3'	3'-region of <i>sirE</i>
SirE-3-R	5'-TCCATTACCTGCGACTAGC-3'	
argB-F	5'-AAGCTTATTTCCGCGTTTT-3'	<i>argB</i>
argB-R	5'-GTCGACCTACAGCCATTGCG-3'	
SirE-5-F2	5'-GAGCGACTGAGGCTAACAG-3'	disruptant cassette for <i>sirE</i>
SirE-3-R2	5'-CTGAATTCGAGGGTTCAG-3'	
<i>Plasmids for GFP-fused protein production</i>		
GAP F xba1	5'-GCTCTAGAAAAAGTCACACAACACAAGC-3'	<i>gdpA</i> promoter
GAP R	5'-CCATTGTGATGTCTGCTCAA-3'	
GAP SirE F	5'-TTGAGCAGACATCACAATGGATGGCACCTCGCAAAACCAA-3'	<i>sirE</i>
SirE linker R	5'-GGCACCGGCTCCAGCGCCTGCACCAGCTCCATCAAGCAACTTGCCCATTC-3'	
GAP SirA F	5'-CCGCTTGAGCAGACATCACAATGGACCTTGCTTCAGCGCC-3'	<i>sirA</i>
SirA linker R	5'-GGCACCGGCTCCAGCGCCTGCACCAGCTCCTCCGCTAACCTTGAATACAT-3'	
linker GFP F	5'-GGAGCTGGTGCAGGCGCTGGAGCCGGTGCCATGGTGTGAGCAAGGGCGAGGA-3'	<i>gfp</i>
GFP sac2 R	5'-GTGCCCGCGTTACTTGTACAGCTCGTCCA-3'	
GFP not1 R	5'-CGCGCGGGCGGCCGCTTACTTGTACAGCTCGTCCA-3'	
<i>Quantitative PCR</i>		
agsB RT F	5'-CTTATCTGGGTGGTGCCT TG-3'	<i>agsB</i>
agsB RT R	5'-CTGCACGTTACCTGGTA TG-3'	
agsA RT F	5'-GTATGAACCCAGACGGGAAG-3'	<i>agsA</i>
agsA RT R	5'-AGGGTGTTACAGGGAGGATG-3'	
fksA RT F	5'-GCGGGACCTTCAATTTACAC-3'	<i>fksA</i>
fksA RT R	5'-GCGAGAAGAGAGACCCAGAA-3'	
chsA RT F	5'-GGACGAAACCCACTTTACGA-3'	<i>chsA</i>
chsA RT R	5'-CTTTGCCCCATGTACGAGAC-3'	
chsB RT F	5'-CCCGAGGAGAAGGAAGAGAA-3'	<i>chsB</i>
chsB RT R	5'-ATGCAGACAGCGAGAAGACC-3'	
chsC RT F	5'-GTGGAGGTGCTTGTGGTGAG-3'	<i>chsC</i>
chsC RT R	5'-CCAGGATGTTGCTGAGCTTG-3'	
chiB RT F	5'-TACAGGAGATGACGCCGTAC-3'	<i>chiB</i>
chiB RT R	5'-GGTTACAGCTTGGACAGTG-3'	
engA RT F	5'-AGGGTGTTACAGGGAGGATG-3'	<i>engA</i>
engA RT R	5'-CTACATGGTGAGGCAGAGCA-3'	
nagA RT F	5'-TTCCCAACTTCAACCCATC-3'	<i>nagA</i>
nagA RT R	5'-GCGTCCCAATCTCCACATC-3'	
fluG RT F	5'-TACCTGCGGCTTTGAGATTG-3'	<i>fluG</i>
fluG RT R	5'-CCAGGAATGGTTGGTCACAG-3'	
flbA RT F	5'-GTCGCTGTTCCCTTCGTCTTC-3'	<i>flbA</i>
flbA RT R	5'-AAAACCTGGGTGTGGTTGTGG-3'	
brlA RT F	5'-CGAACTCCTGGTTCTGCT TC-3'	<i>brlA</i>
brlA RT R	5'-TTCCTGCCCTTCCATGCTAC-3'	
actA RT F	5'-GAAGTCTACGAACTGCCTGATG-3'	<i>actA</i>
actA RT R	5'-AAGAACGCTGGGCTGGAA-3'	
<i>ChIP assay</i>		
pfkA ChIP F	5'- TTGAGCAGTAATTCGTGTGTG -3'	<i>pfkA</i> promoter
pfkA ChIP R	5'- GAAGCAGTGACGAAAAGAGTGA -3'	
pkiA ChIP F	5'- TTGCTGGACGATTTATCAGG -3'	<i>pkiA</i> promoter
pkiA ChIP R	5'- TCGGTTGTTGCTTATCTGTTG -3'	
gpdA ChIP F	5'- TTGCTTCCGATCTGGTAAAAG -3'	<i>gpdA</i> promoter
gpdA ChIP R	5'- GGAGAGGCACGATATTGGA -3'	
agsB ChIP F	5'-CATCAACGACTCACCGACAC-3'	<i>agsB</i> promoter
agsB ChIP R	5'-CCGATAGACGAGACAAGACGA-3'	

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chiB ChIP F	5'- AGCGCTGAGTAAGCAACTTC -3'	<i>chiB</i> promoter
chiB ChIP R	5'- AACTGTACCTGAGACGCTGTG -3'	
pkiA ORF F	5'-GTAGACTTGCCCGCTCTTTC-3'	<i>pkiA</i> -ORF
pkiA ORF R	5'-CTCTTCACCCAACACCTCAC -3'	

Supplementary Table S1 (continued)

Sirtuin at transition of exponential to stationary growth

Supplementary Table S2 Summary of mRNA sequencing experiments.

Experiment	Sample	Total reads	Total bases
1	WT	7,449,337	365,017,513
1	SirE Δ	7,445,910	364,849,590
2	WT	7,450,921	365,095,129
2	SirE Δ	7,448,668	364,984,732

Supplementary Table S3 Alignment statistics of reads aligned to the reference genome and the genes.

Sample	Total mapped reads (%)	Perfect match (%)	Mismatch (%)	Unique match (%)	Multi-position match (%)	Total unmapped reads (%)
Genome						
WT-1	91.76	85.08	6.68	91.32	0.44	8.24
SirEΔ-1	90	83.57	6.43	89.55	0.45	10
WT-2	89.89	79.39	10.5	89.35	0.54	10.11
SirEΔ-2	88.49	80.03	8.46	87.99	0.5	11.51
Gene						
WT-1	64.86	60.39	4.46	64.66	0.2	35.14
SirEΔ-1	68.58	64.13	4.45	68.34	0.24	31.42
WT-2	61.54	54.76	6.78	61.28	0.26	38.46
SirEΔ-2	62.14	56.5	5.64	61.9	0.24	37.86

Supplementary Table S6 Gene Ontology terms enriched in regulated genes in SirEΔ.Genes of log₂ ratio ≤ -3 or ≥3, Probability ≥ 0.8, and *P* < 0.01 were selected.

GO ID	GO term	Cluster frequency (%)	<i>P</i> value
<i>Down-regulated genes in SirEΔ (381 genes)</i>			
<i>Biological process</i>			
45460	sterigmatocystin metabolic process	4.0	2.38E-09
9404	toxin metabolic process	4.3	7.95E-09
45461	sterigmatocystin biosynthetic process	3.7	7.96E-09
1901376	organic heteropentacyclic compound metabolic process	4.3	3.53E-08
9403	toxin biosynthetic process	4.0	3.91E-08
19748	secondary metabolic process	9.1	8.62E-08
1901378	organic heteropentacyclic compound biosynthetic process	4.0	1.29E-07
44550	secondary metabolite biosynthetic process	7.2	1.03E-06
42438	melanin biosynthetic process	1.6	0.0006
44710	single-organism metabolic process	27.8	0.00077
6582	melanin metabolic process	1.6	0.00185
5975	carbohydrate metabolic process	9.9	0.00581
42243	asexual spore wall assembly	1.1	0.00975
<i>Molecular function</i>			
16705	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	5.1	0.00261
52689	carboxylic ester hydrolase activity	2.4	0.00773
20037	heme binding	4.5	0.00811
46906	tetrapyrrole binding	4.5	0.00811
<i>Cellular component</i>			
5576	extracellular region	8.3	5.70E-08
<i>Up-regulated genes in SirEΔ (300 genes)</i>			
<i>Biological process</i>			
44710	single-organism metabolic process	37.5	5.83E-13
44281	small molecule metabolic process	22.9	1.92E-11
44711	single-organism biosynthetic process	19.5	1.68E-10
44283	small molecule biosynthetic process	13.0	4.06E-10
46394	carboxylic acid biosynthetic process	8.2	5.06E-10
16053	organic acid biosynthetic process	10.2	2.17E-09
6082	organic acid metabolic process	15.4	7.48E-09
43436	oxoacid metabolic process	13.0	2.36E-08
55114	oxidation-reduction process	19.1	6.77E-08
19752	carboxylic acid metabolic process	12.3	1.54E-07
6633	fatty acid biosynthetic process	3.8	1.28E-05
72330	monocarboxylic acid biosynthetic process	4.1	3.08E-05
44699	single-organism process	42.3	0.00011
1901605	alpha-amino acid metabolic process	5.8	0.00026
1901607	alpha-amino acid biosynthetic process	4.1	0.00059
32787	monocarboxylic acid metabolic process	6.1	0.00232
33559	unsaturated fatty acid metabolic process	1.4	0.00393
6636	unsaturated fatty acid biosynthetic process	1.4	0.00393
6631	fatty acid metabolic process	4.1	0.00903

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<i>Molecular function</i>			
16491	oxidoreductase activity	23.8	1.49E-09
48037	cofactor binding	10.5	3.67E-05
16705	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	6.1	0.00037
15113	nitrite transmembrane transporter activity	1.0	0.00402
15513	nitrite uptake transmembrane transporter activity	1.0	0.00402
<i>Cellular component</i>			
5886	plasma membrane	7.5	0.00329
45277	respiratory chain complex IV	1.4	0.00696
5751	mitochondrial respiratory chain complex IV	1.4	0.00696
71944	cell periphery	9.5	0.00897

Supplementary Table S6 (continued)

Supplementary Table S9 Up-regulated genes in the stationary growth phase SirEA.

Gene ID	Name	Putative products	SirEΔ/WT*	24/48 h†	Carbon starvation‡
			<i>log₂R</i>	<i>log₂R</i>	<i>log₂R</i>
<i>Glycolytic metabolisms</i>					
AN2286§	<i>alcC</i>	Alcohol dehydrogenase III	8.19	6.06	-1.62
AN4888§	<i>pdhA</i>	Pyruvate decarboxylase	6.03	6.26	-4.69
AN3223	<i>pfkA</i>	6-Phosphofructokinase	3.78	3.09	0.2
AN8041	<i>gpdA</i>	Glyceraldehyde-3-phosphate dehydrogenase	2.94	0.86	-3.05
AN5210§	<i>pkiA</i>	Pyruvate kinase	2.88	2.38	-1.14
AN5746§	<i>acuN</i>	Phosphopyruvate hydratase	2.36	1.23	-1.95
AN1246§	<i>pgkA</i>	Phosphoglycerate kinase	2.2	2.44	-2.84
AN4591		Phosphopentomutase	1.4	-0.63	-0.81
AN6900§	<i>tpiA</i>	Triose-phosphate isomerase	1.38	1.64	-1.3
<i>TCA cycle metabolisms</i>					
AN5447§		Glutamate decarboxylase	5.79	6.1	-4.12
AN4376§	<i>gdhA</i>	NADP-linked glutamate dehydrogenase	5.24	4.17	-1.34
AN2436§		ATP citrate synthase	3.08	1.4	-1.99
AN2435§	<i>aclB</i>	ATP citrate synthase	2.86	1.64	-1.69
AN8275§	<i>aclA</i>	Mitochondrial citrate synthase	2.37	2.18	-3.54
AN6717	<i>citA</i>	Mitochondrial malate dehydrogenase	1.82	2.23	-0.16
AN5790§	<i>mdhA</i>	Isocitrate dehydrogenase (NAD ⁺)	1.6	1.69	-1.11
AN1003		Isocitrate dehydrogenase (NAD ⁺)	1.53	2.23	-0.82
<i>Pentose phosphate pathway</i>					
AN3954§		Phosphogluconate dehydrogenase	2.66	1.53	-2.23
AN0240	<i>pppA</i>	Transaldolase	2.42	1.39	-0.65
AN0688		Transketolase	1.98	1.96	0.61
AN2981§	<i>gsdA</i>	Glucose 6-phosphate 1-dehydrogenase	1.58	1.86	-2.37
<i>Nitrate assimilation</i>					
AN1006§	<i>niaD</i>	Nitrate reductase (NADPH)	9.34	10.56	-4.21
AN1007§	<i>niiA</i>	Nitrite reductase	8.41	5.92	-4.33
AN1008§	<i>crnA</i>	Nitrate transporter	7.33	7.49	-2.09
AN0399	<i>nrtB</i>	High-affinity nitrate transporter	6.59	6.41	0.06
<i>Cell wall synthesis</i>					
AN3307§	<i>agsB</i>	α-1,3-Glucan synthase	7.82	5.36	-4.35
AN4367	<i>chsF</i>	Chitin synthase III	5.21	0.96	-3.09
AN4515	<i>crhB</i>	Transglycosidase	2.9	2.18	-0.61
AN6697	<i>sunA</i>	SUN-family protein	2.88	0.52	-1.21
AN0726	<i>sunB</i>	SUN-family protein	2.78	1.54	3.15
AN7511§	<i>gelE</i>	β-1,3-Transglycosidase	2.45	5.51	-3.74
AN10709	<i>gfaA</i>	Glutamine fructose-6-phosphate transaminase	1.46	-0.01	0.96

Determined using *DNA microarrays, †mRNA sequencing and ‡according to Szilágyi *et al.* §Overlap among genes up-regulated by SirE, stationary-phase and carbon starvation. ID, identity.

FIGURE S1

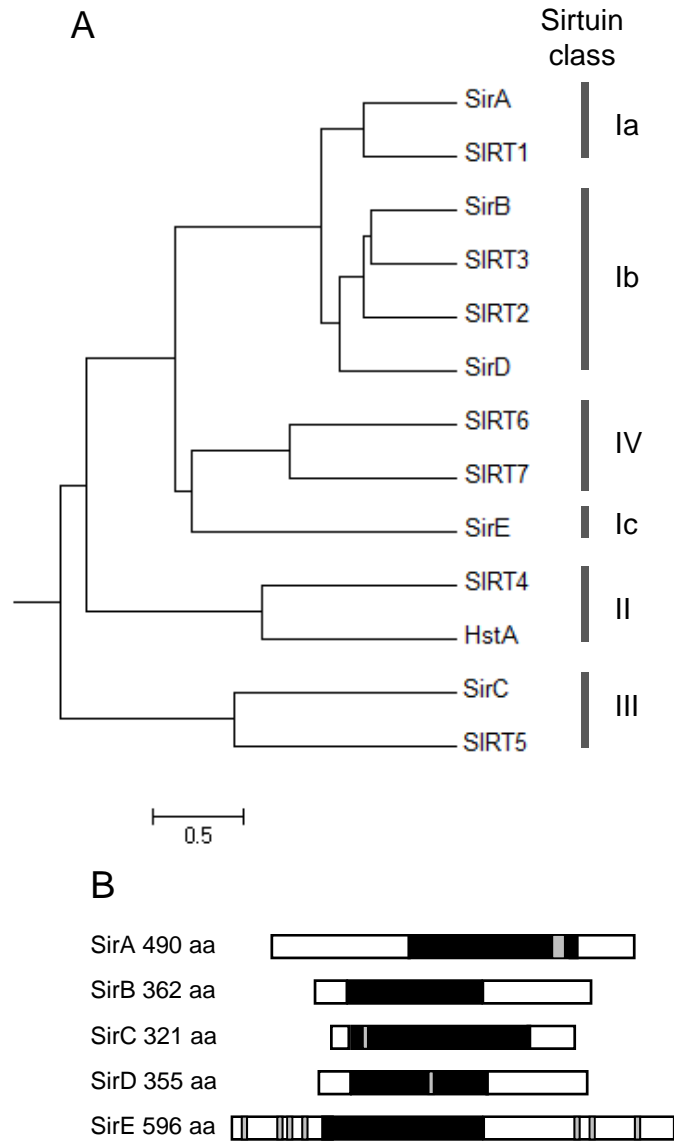


FIGURE S1

Sirtuin at transition of exponential to stationary growth

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1      10      20      30      40      50      60      70      80
ScSir2p MTIPHMKYAVSKTSENKVSNTVSPQTQDKDAIRKQPDDIINNDEPSHKKIKVAQPDLSRENTTDDPLGHTKAALGEVASME
SirA     .....MDLASAPRGESFP LKAP.....LVEIEAAEVERSLPQENAAPEEKGSNSQSEYESDS
SirB     .....
SirC     .....
SirD     .....
SirE     .....MAPRKTTPATKPAKPTPASTATTS
HstA     .....

90      100     110     120     130     140     150     160
ScSir2p LKPTNDMDPLAVSAASVVSMSNDVLPKPTPKGPIIISKNPSNGIFYGPSFTKRESLNARMFLKYYGAHKFLDITYLPEDLN
SirA     DALDDEWETQSLYEDAIQMIRDDQLRDGTIPG.....ACTLEEAIEFRKRLHEVGAQVFEETIARDT.
SirB     .....
SirC     .....
SirD     .....
SirE     SCSPSPKSFPIPMVDDFSFSDSELSDAQSLIEP.....
HstA     .....

170     180     190     200     210     220     230     240
ScSir2p SLYIIYLIKLLGFVVKDQALIGTINSIVHINSQERVQDLGSAISVTNVEDPLAKKQTVRLIKDLQRAINVLCTRRLRLSN
SirA     .....VTAKKLCTAFG.....ILPPSFLEGAPDEAYHPLLAIAISREFARRQKLPQ
SirB     .....MGNESSTLVDEKTPPSVLE
SirC     .....MV
SirD     .....MSSLRAHQKKNPTPTQOCN
SirE     .....EGFSLLSPDESSGGRSQDELPPARKKRRVAGPKERRTQHLDLTPRLGFSD
HstA     .....MISEVFGALPVIILSAKHVYCYCSMTAPAIRIPFTGPLPPP IIVPASASSVSGAIDAFNLFL

250     260     270     280     290     300     310
ScSir2p FFTIDHFIQKHTA...RKILVLTGAGVSTSLGTFDFRS.SEGFYSKIKHLGLDDPQDVFNYNIFMHDPSVFYNTANMV
SirA     YNSVDDAVKLLKES...KNIIVLTGAGISTSLGTFDFRSKDTGLYSKLENLGLNDPQEVFDIRIFREDPGIFYSLAKDI
SirB     ARTVEAVAKYVKEKPV...RRVVMVGCAGISTAACDFDFRSPDTGIYANLVHLDLPDPEAVFDISFFRONPKPFYALAREL
SirC     SNDIKSFQEYLLKGS...KRIMALLGAGISTASSGLTFFRG.AGGLRWSYDATELATPEAFEAN...PDLVWQFYSYRRH
SirD     QTTLDSICKDIQTGKI...TRIVALVGCAGISTSSGLADDFRTPDTGLYAKLEPLQLPYPEALFHISYFKHTPEPFYALARGR
SirE     YGDQEPQLNLLVNTIRNHKKIVVIAGAGISTSAGTFDFRS.DDGLFKTLQKKHNLKASGKLMFDDAAVYQDEALTAQSFQEM
HstA     TAPPSPYLRLGVDVGRN...SQTVLLTGAGISTVASGLDYRGE.ENGTYVTKNKYR...PIYFHEFATRHESEKRYWALRSFIG

320     330     340     350     360     370
ScSir2p LP.....PEKITYSPLHSFTKMLQMKGKLLRNYTONIDNLESYAG.....ISTDKLVQCHGSFATATCVTCHWN
SirA     LP.....TEKKFSPTHGFIIRLLQDKGKLLTNYTONIDNLEANAG.....VFPENIVQCHGSFATATCVKCOYK
SirB     AP.....GOYRPTLAHSFVKLLYDKGKLLKHFTONIDCLEANAG.....VPGDMIIEAHGSFATQRCIECKTA
SirC     MA.....LKAKPNKAHYALAEARRKREFITLSONVDGLSQORAN.....HPPEQLHLLHGNLFTVCKCTSFYCK
SirD     HP.....WNTKPGVGHAFALALLKKGVLGFVFTONIDGLELDAG.....VSRERVMNLLHGDWSDQHCICRCS
SirE     VRSLSEEAEEKSPTAFHMLARLGS DNRLRLYTONIDGLETSMPLATQIPLNVKAPWPRTIQHGSLEKMCQKCRHM
HstA     WPGGL...LKAKPNSTHWAIRDLGKGYVSSVITONVDSFHSIA.....HPEIPSIIEHGYLRSVVCLSCRNQ

380     390     400     410     420     430     440
ScSir2p LPGE.RIFNKIRNLELPLCPYCYKRRRE..YFPEGYNKVGVAASQ.....GSMSEPPYILNSYGLKPDITFFGEA
SirA     VAGD.EIYDDIKKGLIPECAQCRKRIAEDSQKPGQKRRKNSTSAHKDRSKSGEDSSDGEDYEIPTPGVMKPDITFFGED
SirB     YPDD.LMKEAIAKGEVPCN.....KNIPEPRPFTDDKSGEK
SirC     YVRE.NDFTDPIVPAALAI.....QANCEGIVKPAIVMFGES
SirD     YPAD.RMRKALITGEVPEPCV.....GQRSHGIGKMRPRIVLYNEH
SirE     STFDRVMFDRPDAPCEPECVLTNQFRMET.....ALDTONPEEQRRRGLKLNPDG
HstA     FPRS.EFQKSLERLNP SWAEFLARMVDIG.....ALDTONPEEQRRRGLKLNPDG

450     460     470     480     490     500     510
ScSir2p L..P[N]KF.HKSIRE DILECDLLTICIGTSLK[V]APVSE[IVN].MVP SHVP...QVLINRD...P[V]KHAE.FDLSL[GL]YCD[DD]
SirA     L..PDEFGRLLHDDRDKVDLVIVIGTSLK[V]APVAV[VP]G.VLPPHIP...QIYISRT...PVAHTN.FDIDL[GL]GDCDV
SirB     L..PSAFFDN.RTLPET.ADLCTVMGTSLS[V]QPFASLPS.FVADGVP...RVLINRERVGG[GL]SRP.DDVLILDDCDN
SirC     A..SESLASALKQQKPENEEEAELDISARIPLNFVSR.DALPRCP...ECKEGLLRPGVVMFGESLPVQTLDLVDN
SirD     L..PEGFDSREEEMLST.ADLLLVIGTSLK[V]APCSE[IPR].RLPSHVP...RVLVNRELVGNITGIRE.SDVCL[GL]GDCDA
SirE     NPDEA[IT]SVMNADIRSRPDALIVVGTSLK[V]IPGVRRLVKS[L]CSVIRSRNGV[TM]WINNEPPSGKEFEDCFDLLV[GL]GDCDE
HstA     D..VELPEAPYSTFRYPCSTCLEKPPRLADGTPARMEVERKDGAWL...TSEAGILKPAVIMFGENIEPPV[GL]LAEE

520     530     540     550     560
ScSir2p IAAMVAQKCGWTIPK.K.WNDLKNKNFKCQEKDKGVYVVTSD EHPKTL.....
SirA     VVSELRRRAGWELKHEM.I SPDEKVDVTPVFGYGRHVFVSG.....
SirB     GVRKLARALGWEDELER.LWEEANPNQK...SREEELATPRTREERLENEISRL.....TAEIDKTLKISDAY
SirC     WMNEGRLDMLVIGTSRVVWPAAGYAEQARAKGARVAVVNDPNDMGKGTFS.....KDWFFQG.....
SirD     WLRVARHLGWDEELES.VWKDTLVRKEKSSRDKGWDDKAESPTLEECIVRA.....AEQMKVRMVGSEGH
SirE     VAR.LAQKLRWDDSKPIFDEQCSADV ERVKNEQGPLSVVITTPKKEKVAQTGMLTPSSSYDGDVENASTTTLSNPASK
HstA     AIDDAERLLVLGTSLAT..YSAWRLVERAYKRGMPGIINIGGVRNESVLLKE.....ADKGSDFLARYTRC

ScSir2p .....
SirA     .....
SirB     QKRVRERLEGEPLSSPESNGTGLAHVFP HLARR.....
SirC     .....DAGVIVPEILKSVTGEV.....
SirD     RR...MLEG.....HLGEKMAEIMAKRGQ.....
SirE     GRKLTEILKASKKDAPKTESAGVKKPAPRKRTKKEPVKNAKITTF SKVTKAQKVTPEEKSVKLEEHKAMHPLPPGAARTN
HstA     S.....LHSDAILPSVASQLPSLSR.....

ScSir2p .....
SirA     .....
SirB     .....
SirC     .....
SirD     .....
SirE     APMLPGLAKDDSKSTPSGKRGQLETISPDRIPKGMGKLLD
HstA     .....

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FIGURE S2

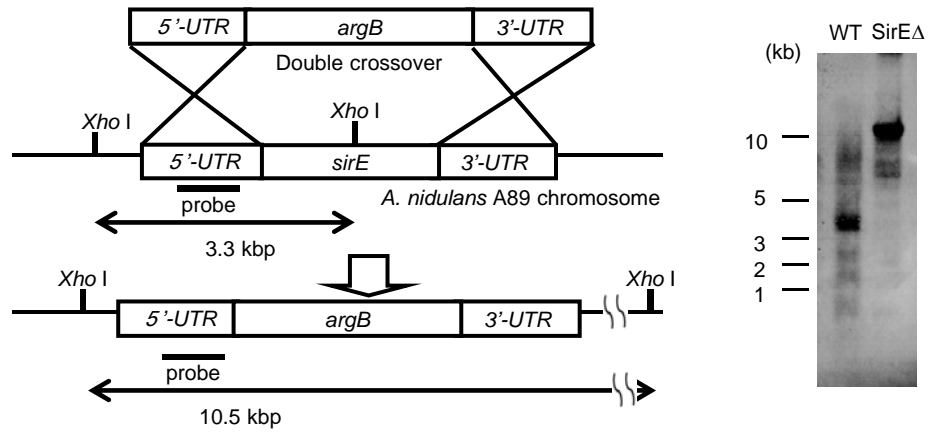


FIGURE S3

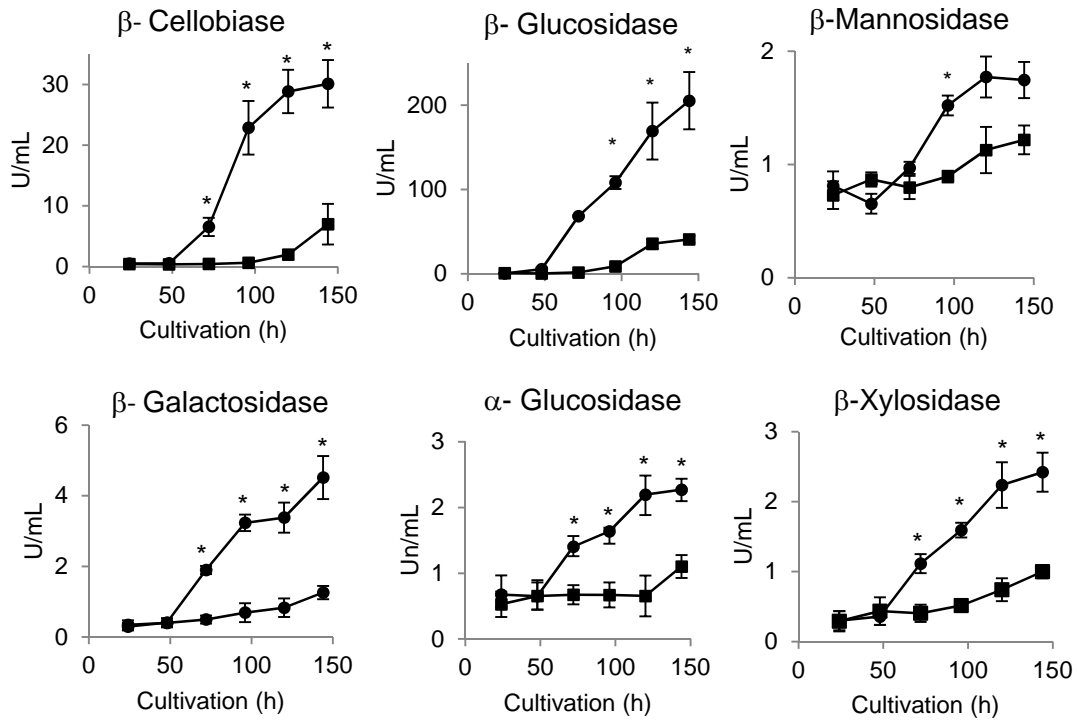


FIGURE S4

