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Deleting the 14-3-3 Protein Bmh1 Extends Life Span in *Saccharomyces cerevisiae* by Increasing Stress Response

Chen Wang, Craig Skinner, Erin Easlon and Su-Ju Lin

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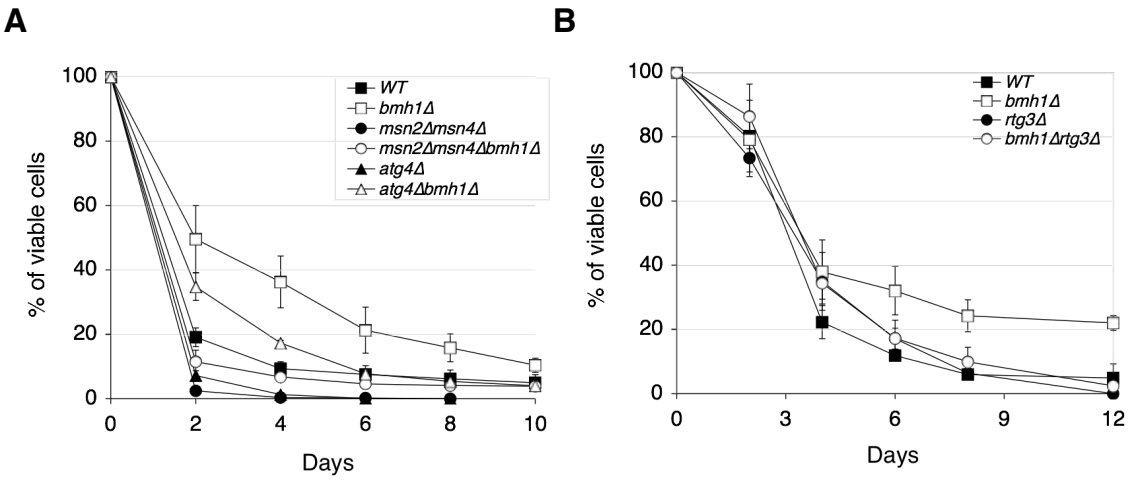

FIGURE S1.—Potential downstream factors required for *bmh1*Δ-induced chronological life span extension. (A) Msn2 and Msn4-mediated stress response and the autophagy pathway play important roles in *bmh1*Δ-induced life span extension. (B) A functional retrograde response is required for life span extension in the *bmh1*Δ mutant. WT: wild type control. One set of representative data is shown.

TABLE S1

List of genes encoding characterized and putative yeast kinases

No.	Standard Name	Position in KO collection	Annotation	Systematic Name
1	*CKA1*	129-B-5	Alpha' catalytic subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation	*YIL035C*
2	*CKA2*	106-D-2	Alpha' catalytic subunit of casein kinase 2, a Ser/Thr protein kinase with roles in cell growth and proliferation	*YOR061W|YOR29-12*
3	*YCK2*	127-E-2	Palmitoylated, plasma membrane-bound casein kinase I isoform	*YNL154C*
4	*ATG1*	148-D-7	Protein serine/threonine kinase, required for autophagy and for the cytoplasm-to-vacuole targeting (Cvt) pathway	*YGL180W|APG1|AUT3|CVT10*
5	*YCK1*	114-F-11	Palmitoylated, plasma membrane-bound casein kinase I isoform	*YHR135C|CKI2*
6	*CMK1*	129-H-4	Calmodulin-dependent protein kinase	*YFR014C*
7	*YGL059W*	126-G-1	Putative protein kinase of unknown cellular role	*YGL059W*
8	*ARK1*	140-G-6	Serine/threonine protein kinase involved in regulation of the cortical actin cytoskeleton	*YNL020C*
9	*SNF1*	149-D-6	AMP-activated serine/threonine protein kinase found in a complex containing Snf4p and members of the Sip1p/Sip2p/Gal83p family	*YDR477W|CAT1|GLC2|CCR1|HAF3|PAS14*
10	*HRR25*	inviable	Protein kinase involved in regulating diverse events including vesicular trafficking, DNA repair, and chromosome segregation; binds the CTD of RNA pol II; homolog of mammalian casein kinase 1delta (CK1delta)	*YPL204W*
11	*BCK1*	133-H-6	Mitogen-activated protein (MAP) kinase kinase kinase acting in the protein kinase C signaling pathway, which controls cell integrity	*YJL095W|SAP3|LAS3|SSP31|SLK1*
12	*GIN4*	147-F-1	Protein kinase involved in bud growth and assembly of the septin ring, proposed to have kinase-dependent and kinase-independent activities	*YDR507C|ERC47*
13	*HAL5*	143-D-10	Putative protein kinase	*YJL165C*
14	*HRK1*	144-H-9	Protein kinase implicated in activation of the plasma membrane H(+)-ATPase Pma1p in response to glucose metabolism	*YOR267C*
15	*HSL1*	117-B-8	Nim1p-related protein kinase that regulates the	*YKL101W|NIK1*

			morphogenesis and septin checkpoints	
16	*NPR1*	127-C-12	Protein kinase that stabilizes several plasma membrane amino acid transporters by antagonizing their ubiquitin-mediated degradation	*YNL183C*
17	*PKH2*	131-B-9	Serine/threonine protein kinase involved in sphingolipid-mediated signaling pathway that controls endocytosis	*YOL100W*
18	*PPZ2*	111-G-4	Serine/Threonine protein phosphatase Z	*YDR436W*
19	*PRR1*	117-C-5	Serine/threonine protein kinase that inhibits pheromone induced signalling downstream of MAPK, possibly at the level of the Ste12p transcription factor	*YKL116C*
20	*PSK1*	101-D-2	One of two (see also PSK2) PAS domain containing S/T protein kinases	*YAL017W|FUN31*
21	*PSK2*	107-G-2	One of two (see also PSK1) PAS domain containing S/T protein kinases	*YOL045W*
22	*YPL150W*	109-B-1	Putative protein of unknown function	*YPL150W*
23	*YNR047W*	141-D-9	Putative protein of unknown function	*YNR047W*
24	*YKL171W*	117-F-9	Putative protein of unknown function	*YKL171W*
25	*PXL1*	135-A-5	LIM domain-containing protein that localizes to sites of polarized growth, required for selection and/or maintenance of polarized growth sites, may modulate signaling by the GTPases Cdc42p and Rho1p; has similarity to metazoan paxillin	*YKR090W*
26	*AKL1*	140-D-12	Ser-Thr protein kinase, member (with Ark1p and Prk1p) of the Ark kinase family	*YBR059C*
27	*DIG1*	123-F-3	Regulatory protein of unknown function, constitutively-expressed, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription	*YPL049C*
28	*DIG2*	147-D-4	Regulatory protein of unknown function, pheromone-inducible, involved in the regulation of mating-specific genes and the invasive growth pathway, required for MAP-kinase imposed repression, inhibits pheromone-responsive transcription	*YDR480W*
29	*PRK1*	129-D-8	Protein serine/threonine kinase	*YIL095W|PAK1*
30	*KIN1*	110-G-12	Serine/threonine protein kinase involved in regulation of exocytosis	*YDR122W*
31	*KIN2*	102-F-11	Serine/threonine protein kinase involved in regulation of exocytosis	*YLR096W*

32	*KIN4*	119-D-3	Serine/threonine protein kinase that inhibits the mitotic exit network (MEN) when the spindle position checkpoint is activated	*YOR233W|KIN31|KIN3*
33	*KIN82*	124-G-6	Putative serine/threonine protein kinase, most similar to cyclic nucleotide-dependent protein kinase subfamily and the protein kinase C subfamily	*YCR091W*
34	*KKQ8*	117-F-8	Putative serine/threonine protein kinase with unknown cellular role	*YKL168C*
35	*KSP1*	114-D-1	Nonessential putative serine/threonine protein kinase of unknown cellular role	*YHR082C*
36	*SKM1*	131-C-10	Member of the PAK family of serine/threonine protein kinases with similarity to Ste20p and Cla4p	*YOL113W*
37	*CBK1*	inviable	Serine/threonine protein kinase that regulates cell morphogenesis pathways	*YNL161W*
38	*SMK1*	133-D-2	Middle sporulation-specific mitogen-activated protein kinase (MAPK) required for production of the outer spore wall layers	*YPR054W*
39	*RIM11*	144-E-9	Protein kinase required for signal transduction during entry into meiosis	*YMR139W|GSK3|MDS1*
40	*DUN1*	138-F-2	Cell-cycle checkpoint serine-threonine kinase required for DNA damage-induced transcription of certain target genes, phosphorylation of Rad55p and Sml1p, and transient G2/M arrest after DNA damage	*YDL101C*
41	*RIM15*	150-A-8 and 150-C-2	Glucose-repressible protein kinase involved in signal transduction during cell proliferation in response to nutrients, specifically the establishment of stationary phase	*YFL033C|TAK1*
42	*PBS2*	145-C-9	MAP kinase kinase that plays a pivotal role in the osmosensing signal-transduction pathway, activated under severe osmotic stress	*YJL128C|SSK4|SFS4|HOG4*
43	*TFG1*	inviable	TFIIF (Transcription Factor II) largest subunit	*YGR186W|RAP74|SSU71*
44	*PKH1*	147-E-1	Serine/threonine protein kinase involved in sphingolipid-mediated signaling pathway that controls endocytosis	*YDR490C*
45	*PKH3*	147-C-8	Protein kinase with similarity to mammalian phosphoinositide-dependent kinase 1 (PDK1) and yeast Pkh1p and Pkh2p, two redundant upstream activators of Pkc1p	*YDR466W*
46	*MCK1*	105-D-4	Protein serine/threonine/tyrosine (dual-specificity) kinase involved in control of chromosome segregation and in regulating entry into meiosis	*YNL307C|YPK1*

47	*CLA4*	105-D-11	Cdc42p activated signal transducing kinase of the PAK (p21-activated kinase) family, involved in septin ring assembly and cytokinesis	*YNL298W|ERC10*
48	*IME2*	133-H-1	Serine/threonine protein kinase involved in activation of meiosis, associates with Ime1p and mediates its stability, activates Ndt80p	*YJL106W|SME1*
49	*YMR291W*	105-A-2	Putative kinase of unknown function	*YMR291W*
50	*SAT4*	115-F-2	Ser/Thr protein kinase involved in salt tolerance	*YCR008W|HAL4*
51	*YDL025C*	146-E-2	Putative protein kinase, potentially phosphorylated by Cdc28p	*YDL025C*
52	*SWE1*	119-G-12	Protein kinase that regulates the G2/M transition by inhibition of Cdc28p kinase activity	*YJL187C|WEE1*
53	*PRR2*	136-F-12	Serine/threonine protein kinase that inhibits pheromone induced signalling downstream of MAPK, possibly at the level of the Ste12p transcription factor	*YDL214C*
54	*SKY1*	104-E-1	SR protein kinase (SRPK) involved in regulating proteins involved in mRNA metabolism and cation homeostasis	*YMR216C*
55	*ISR1*	124-A-9	Predicted protein kinase, overexpression causes sensitivity to staurosporine, which is a potent inhibitor of protein kinase C	*YPR106W*
56	*STE11*	149-G-7	Signal transducing MEK kinase involved in pheromone response and pseudohyphal/invasive growth pathways where it phosphorylates Ste7p, and the high osmolarity response pathway, via phosphorylation of Pbs2p	*YLR362W*
57	*DBF2*	143-C-1	Ser/Thr kinase involved in transcription and stress response	*YGR092W*
58	*CAK1*	inviable	Cyclin-dependent kinase-activating kinase required for passage through the cell cycle, phosphorylates and activates Cdc28p	*YFL029C|CIV1*
59	*TOS3*	148-D-6	Protein kinase, related to and functionally redundant with Elm1p and Sak1p for the phosphorylation and activation of Snf1p	*YGL179C*
60	*MPS1*	inviable	Dual-specificity kinase required for spindle pole body (SPB) duplication and spindle checkpoint function	*YDL028C|RPK1*
61	*MKK1*	119-D-2	Mitogen-activated kinase kinase involved in protein kinase C signaling pathway that controls cell integrity	*YOR231W|SSP32*
62	*IKS1*	134-B-3	Putative serine/threonine kinase	*YJL057C*
63	*MKK2*	109-B-7	Mitogen-activated kinase kinase involved in protein kinase C signaling pathway that controls cell integrity	*YPL140C|LPI6|SSP33*

64	*IPL1*	inviable	Aurora kinase involved in regulating kinetochore-microtubule attachments	*YPL209C|PAC15*
65	*YKL161C*	117-F-2	Protein kinase implicated in the Slt2p mitogen-activated (MAP) kinase signaling pathway	*YKL161C|MLP1*
66	*SGV1*	inviable	Cyclin (Bur2p)-dependent protein kinase that functions in transcriptional regulation	*YPR161C|BUR11*
67	*KIN28*	inviable	Serine/threonine protein kinase, subunit of the transcription factor TFIIH	*YDL108W*
68	*ELM1*	116-G-3	Serine/threonine protein kinase that regulates cellular morphogenesis, septin behavior, and cytokinesis	*YKL048C|LDB9*
69	*BUD32*	171-D-4	Protein kinase proposed to be involved in bud-site selection, telomere uncapping and elongation, and transcription	*YGR262C|LDB14*
70	*FUS3*	125-F-7	Mitogen-activated serine/threonine protein kinase involved in mating	*YBL016W|DAC2*
71	*RIO1*	inviable	Essential serine kinase involved in cell cycle progression and processing of the 20S pre-rRNA into mature 18S rRNA	*YOR119C|RRP10*
72	*CDC5*	inviable	Polo-like kinase with similarity to Xenopus Plx1 and S. pombe Plo1p	*YMR001C|PKX2|MSD2*
73	*RIO2*	inviable	Essential serine kinase involved in the processing of the 20S pre-rRNA into mature 18S rRNA	*YNL207W*
74	*STE20*	121-E-10	Signal transducing kinase of the PAK (p21-activated kinase) family, involved in pheromone response and pseudohyphal/invasive growth pathways, activated by Cdc42p	*YHL007C*
75	*SPS1*	147-G-3	Putative protein serine/threonine kinase expressed at the end of meiosis and localized to the prospore membrane, required for correct localization of enzymes involved in spore wall synthesis	*YDR523C*
76	*SSN3*	123-F-8	Cyclin-dependent protein kinase, component of RNA polymerase II holoenzyme	*YPL042C|SRB10|UME5|RYE5|CDK8|GIG2|NUT7*
77	*CDC7*	inviable	DDK (Dbf4-dependent kinase) catalytic subunit required for firing origins and replication fork progression in mitosis through phosphorylation of Mcm2-7p complexes and Cdc45p	*YDL017W|SAS1|LSD6*
78	*YCK3*	148-F-4	Palmitoylated, vacuolar membrane-localized casein kinase I isoform	*YER123W|CKI3*
79	*KIN3*	101-E-6	Nonessential protein kinase with unknown cellular role	*YAR018C|FUN52|NPK1*
80	*MEC1*	inviable	Genome integrity checkpoint protein and PI kinase superfamily member	*YBR136W|ESR1|SAD3*

81	*CMK2*	132-C-5	Calmodulin-dependent protein kinase	*YOL016C*
82	*YPK1*	117-D-1	Serine/threonine protein kinase required for receptor-mediated endocytosis	*YKL126W|SLI2*
83	*YPK2*	145-D-12	Protein kinase with similarityto serine/threonine protein kinase Ypk1p	*YMR104C|YKR2*
84	*KSS1*	143-B-7	Mitogen-activated protein kinase (MAPK) involved in signal transduction pathways that control filamentous growth and pheromone response	*YGR040W*
85	*SCH9*	175-F-9	Protein kinase involved in transcriptional activation of osmostress-responsive genes	*YHR205W|KOM1*
86	*KIC1*	inviable	Protein kinase of the PAK/Ste20 kinase family, required for cell integrity possibly through regulating 1,6-beta-glucan levels in the wall	*YHR102W|NRK1*
87	*VPS15*	171-C-10	Myristoylated serine/threonine protein kinase involved in vacuolar protein sorting	*YBR097W|GRD8|VAC4|VPL19*
88	*CDC15*	inviable	Protein kinase of the Mitotic Exit Network that is localized to the spindle pole bodies at late anaphase	*YAR019C|LYT1*
89	*HRR25*	inviable	Protein kinase involved in regulating diverse events including vesicular trafficking, DNA repair, and chromosome segregation	*YPL204W*
90	*YGK3*	131-D-9	Protein kinase related to mammalian glycogen synthase kinases of the GSK-3 family	*YOL128C*
91	*DBF20*	124-A-11	Ser/Thr kinase involved in late nuclear division, one of the mitotic exit network (MEN) proteins	*YPR111W*
92	*YBR028C*	140-B-9	Putative protein kinase, possible substrate of cAMP-dependent protein kinase (PKA)	*YBR028C*
93	*SSK22*	144-B-6	MAP kinase kinase kinase of the HOG1 mitogen-activated signaling pathway	*YCR073C*
94	*SKS1*	123-G-8	Putative serine/threonine protein kinase	*YPL026C|SHA3*
95	*TEL1*	126-C-5	Protein kinase primarily involved in telomere length regulation	*YBL088C*
96	*MEK1*	107-B-4	Meiosis-specific serine/threonine protein kinase, functions in meiotic checkpoint, promotes recombination between homologous chromosomes by suppressing double strand break repair between sister chromatids	*YOR351C|MRE4*
97	*SLT2*	114-A-8	Serine/threonine MAP kinase involved in regulating the maintenance of cell wall integrity and progression through the cell cycle	*YHR030C|SLK2|BYC2|MPK1*
98	*CHK1*	137-D-4	Serine/threonine kinase and DNA damage checkpoint effector, mediates cell cycle arrest via phosphorylation	*YBR274W*

			of Pds1p	
99	*HOG1*	102-G-10	Mitogen-activated protein kinase involved in osmoregulation via three independent osmosensors	*YLR113W|SSK3*
100	*KNS1*	101-G-7	Nonessential putative protein kinase of unknown cellular role	*YLL019C|L124*
101	*SSK2*	141-C-8	MAP kinase kinase kinase of the HOG1 mitogen-activated signaling pathway	*YNR031C*
102	*ALK1*	126-D-11	Protein kinase	*YGL021W*
103	*ALK2*	125-F-1	Protein kinase	*YBL009W*
104	*MRK1*	146-H-9	Glycogen synthase kinase 3 (GSK-3) homolog	*YDL079C*
105	*GCN2*	128-E-5	Protein kinase, phosphorylates the alpha-subunit of translation initiation factor eIF2 (Sui2p) in response to starvation	*YDR283C|AAS1*
106	*YPL141C*	109-B-6	Putative protein kinase	*YPL141C*
107	*SAK1*	148-F-7	Upstream serine/threonine kinase for the SNF1 complex	*YER129W|PAK1*
108	*RCK1*	148-C-1	Protein kinase involved in the response to oxidative stress	*YGL158W*
109	*PKC1*	inviable	Protein serine/threonine kinase essential for cell wall remodeling during growth	*YBL105C|HPO2|STT1|CLY15*
110	*RCK2*	121-H-5	Protein kinase involved in the response to oxidative and osmotic stress	*YLR248W|CMK3|CLK1*
111	*BUB1*	134-F-4	Protein kinase that forms a complex with Mad1p and Bub3p that is crucial in the checkpoint mechanism required to prevent cell cycle progression into anaphase in the presence of spindle damage, associates with centromere DNA via Skp1p	*YGR188C*
112	*YPL236C*	108-D-7	Putative protein kinase that exhibits Akr1p-dependent palmitoylation	*YPL236C*
113	*FMP48*	117-H-12	Putative protein of unknown function	*YGR052W*
114	*PHO85*	123-G-5	Cyclin-dependent kinase, with ten cyclin partners	*YPL031C|LDB15*
115	*PTK1*	127-E-6	Putative serine/threonine protein kinase that regulates spermine uptake	*YKL198C|STK1|KKT8|YKL199C|YKT9|POT1*
116	*CDC28*	inviable	Catalytic subunit of the main cell cycle cyclin-dependent kinase (CDK)	*YBR160W|SRM5|HSL5|CDK1*
117	*PTK2*	138-E-6	Putative serine/threonine protein kinase involved in regulation of ion transport across plasma membrane	*YJR059W|STK2*
118	*VHS1*	128-B-8	Cytoplasmic serine/threonine protein kinase	*YDR247W*
119	*TPK1*	120-A-3	cAMP-dependent protein kinase catalytic subunit	*YJL164C|PKA1|SRA3*
120	*RAD53*	inviable	Protein kinase, required for cell-cycle arrest in response to DNA damage	*YPL153C|LSD1|MEC2|SPK1*

121	*TPK2*	108-F-4	cAMP-dependent protein kinase catalytic subunit	*YPL203W|YKR1|PKA2|PKA3*
122	*TPK3*	117-F-6	cAMP-dependent protein kinase catalytic subunit	*YKL166C*
123	*STE7*	139-A-8	Signal transducing MAP kinase kinase involved in pheromone response, where it phosphorylates Fus3p, and in the pseudohyphal/invasive growth pathway, through phosphorylation of Kss1p	*YDL159W*
124	*YAK1*	143-D-4	Serine-threonine protein kinase that is part of a glucose-sensing system involved in growth control in response to glucose availability	*YJL141C*
125	*CTK1*	143-E-10	Catalytic (alpha) subunit of C-terminal domain kinase I (CTDK-I), which phosphorylates the C-terminal repeated domain of the RNA polymerase II large subunit (Rpo21p) to affect both transcription and pre-mRNA 3' end processing	*YKL139W*
126	*KCC4*	115-C-3	Protein kinase of the bud neck involved in the septin checkpoint, associates with septin proteins, negatively regulates Swe1p by phosphorylation, shows structural homology to bud neck kinases Gin4p and Hsl1p	*YCL024W*
127	*TOR1*	149-C-4	PIK-related protein kinase and rapamycin target	*YJR066W|DRR1*
128	*TOR2*	inviable	PIK-related protein kinase and rapamycin target	*YKL203C|DRR2*
129	*IRE1*	114-C-10	Serine-threonine kinase and endoribonuclease	*YHR079C|ERN1*