Supplementary Table I

Yeast strains used in this study

Name	Description	Source
BY4741	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0*	Dr. S. Michaelis
E3Δhrd1	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 hrd1Δ::KanR*	Open Biosystems
E3Δhrd3	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 hrd3Δ::KanR*	Open Biosystems
E3Δyos9	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 yos9Δ::KanR*	Open Biosystems
E3Δder1	*MAT***a** *his3Δ1 leu2Δ0 met15Δ0 ura3Δ0 der1Δ::KanR*	Open Biosystems
KNY140	*MAT***a** *ade2-1 ura3-1 his3-11,15 trp1-1 leu2-3,112 can1-100 pdr5Δ::HPH pep4Δ::LEU2*	(1)
KNY220	*MAT***a** *ade2-1 ura3-1 his3-11,15 trp1-1 leu2-3,112 can1-100 pdr5Δ::HPH pep4Δ::LEU2 HRD1-3FLAG- KAN^R*	(1)

Supplementary Table II

Plasmids used in this study

Name	Description	Source
pKN12-22	CPY*-3HA, *CEN/ARS*, *URA3* (CPY*: a soluble substrate due to the presence of a missense mutation in an otherwise vacuole-targeted protease)	(2)
pSM70	KHN-3HA, *CEN/ARS*, *URA3* (KHN: a heterologously expressed simian virus 5 hemagglutinin neuraminidase (HN) that is fused with the cleavable signal sequence from the yeast Kar2 (the ER luminal Hsp70))	(3)
pSM101	KWW-3HA, *CEN/ARS*, *URA3* (KWW: a chimeric protein comprising KHN luminal domain/Wsc1 transmembrane domain/Wsc1 cytosolic domain)	(4)
pKN66	Ste6*-3HA, *CEN/ARS*, *URA3* (Ste6*: a C-terminal truncated version of the a-factor transporter Ste6)	(5)
pKN515	3HA-Pca1, *CEN/ARS*, *URA3* (Pca1: a cadmium transporting P-type ATPase whose proteasome-dependent degradation is exclusively dependent on Doa10)	(6)
pKN541	3HA-Pdr5*, *CEN/ARS*, *URA3* (Pdr5*: a 12 transmembrane protein that harbors misfolded lesions near these domains)	This study
pKN562	6myc-Hmg2, *CEN/ARS*, *URA3* (Hmg2: the yeast HMG-CoA reductase isozyme)	This study
pJC104	4×UPRE (four copies of the unfolded protein response element)-*lacZ*, *2μ*, *URA3*	(7)

A plasmid encoding *3HA-PDR5** (pKN541) was constructed as follows. The PCR reaction was performed using a plasmid pKN44 (8), which encodes *1HA-PDR5**, as a template and using primers OKN2234 and OKN2235. The resulting linear fragment was transformed into Mach1 competent cell (Thermo Fisher Scientific). The circularized

plasmids were mini-prepped from the transformants and the DNA sequence was performed to verify that the single HA tag was replaced with triple HA tag.

A plasmid encoding 6myc-Hmg2 under the sequence of the *GPD* promoter (pKN562) was constructed as follows. The DNA fragment encoding the open reading frame of 6myc-Hmg2 was amplified by PCR from yeast strain expressing this protein (9) using primers OKN2273 and OKN2275. The resultant fragment was digested with *XbaI*/*XhoI* and inserted into the same sites of p416GPD (10).

Supplementary Table III

Oligonucleotide primers used in this study

Name	Sequence
OKN2234	CCTTATGATGTCCCAGATTACGCAGGTTCTTATCCTTACGATGTACCAGACTACGCCGGTCCCGAGGCCAAGCTTAACAATAACG
OKN2235	CCTGCGTAATCTGGGACATCATAAGGGTAACCAGCATAATCAGGAACGTCATAAGGGTATGAACCCATTTTTGTCTAAAGTCTTTCG
OKN2273	ATATCCTCGAGCACCATGTAAACTACAAGAG
OKN2275	GCTGCTCTAGAATGTCACTTCCCTTAAAAACGATAG

Supplementary Table IV

Antibodies used in this study

Antibody	Company	Identifier or reference
αHA	MEDICAL & BIOLOGICAL LABORATORIES	#M180-3
αPgk1	abcam	[22C5D8] (#ab113687)
αHrd1	In house	(1)
αCdc48	In house	(1)
αYos9	In house	(1)
αDer1	In house	(1)
αHrd3	Gift from Dr. Thomas Sommer and Dr. Ernst Jarosch (Max-Delbrück-Center for Molecular Medicine, Berlin, Germany)	
αSic1	Gift from Dr. Takumi Kamura (Nagoya University, Aichi, Japan)	
αClb2	Gift from Dr. Takumi Kamura (Nagoya University, Aichi, Japan)	
αmyc	Gift from Dr. Takumi Kamura (Nagoya University, Aichi, Japan)	

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