

Table 1S

	Protein	Location	Function	Animal and cellular models	Disease	References
folding	Calnexin (CNX)	ER membrane (Cell surface)	Chaperone assisting glycoprotein folding, Ca ²⁺ binding	<i>-/- mice:</i> Postnatal death and motor disorders <i>-/- cells:</i> Similar viability, proliferation rate, morphology and stress levels then wt cells No UPR induction	Alzheimer disease	Okazaki et al., 2000; Denzel et al., 2002; Molinari et al., 2004; Hoshino et al., 2007
	Calreticulin (CRT)	ER lumen Cytosol Nucleus	Chaperone assisting glycoprotein folding, Ca ²⁺ binding, Transcriptional regulation	<i>-/- mice:</i> Embryonic lethality at E14.5 due to defective embryonic cardiac development <i>-/- cells:</i> Similar viability, proliferation rate, morphology and stress levels then wt cells No upr induction	Cardiac hypertrophy Alzheimer Autoimmune disease	Mesaeli et al., 1999; Johnson et al., 2001; Erickson et al., 2005; Afshar et al., 2005; Eggleton and Llewellyn, 1999; Molinari et al., 2004; Kang et al., 2006
	ERdj1 ERdj2 ERdj3 ERdj4 ERdj5	ER lumen	BiP co-chaperones	<i>-/- cells (RNAi):</i> decreased degradation of SS linked glycoproteins (ERdj5)	Cancer (ERdj5)	Cunnea et al., 2003, 2007; Corazzari et al., 2007; Nagata (personal communications)
	ERp57	ER lumen	Oxidoreductase for SS bond catalysis in glycoproteins	<i>-/- mice:</i> lethal <i>-/- B cells:</i> defective in antigen presentation no UPR induction	Prion disease Alzheimer	Coppiari et al., 2002; Turano et al., 2002; Erickson et al., 2005; Hetz et al., 2005; Garbi et al., 2006; Solda et al., 2006
	ERp72	ER lumen	Oxidoreductase for SS bond catalysis	ND	ND	Satoh et al., 2005
	Ero1α	ER ERGIC	Oxidative protein folding, recharging of PDI	<i>Ero1 RNAi in C elegans:</i> shortened life span, UPR activation <i>Ero1-1 mutant yeast cells:</i> defective protein oxidation and PDI oxidation, increased sensitivity to DTT <i>Ero1 deleted yeast cells:</i> lethal	Cancer Hypoxia Diabetes	Frand and Kaiser, 1998, 1999; Pollard et al., 1998; Cuozzo and Kaiser, 1999; Chen et al., 2003; Harding et al., 2003; May et al., 2005; Qiang et al., 2007; Wang et al., 2007; Ceppi S. and Sitia R., unpublished results
	Glucosidase I	ER lumen	Glycoprotein quality control N-glycan processing	<i>-/- cells:</i> Lec23	Congenital disorder of glycosylation (CDG-II)	De Praeter et al., 2000; Volker et al., 2002
	Glucosidase II	ER lumen	Glycoprotein quality control N-glycan processing	<i>-/- cells:</i> Mouse lymphoma cell line Phar 2.7	Autosomal-dominant polycystic liver disease (ADPCLD)	Reynolds et al., 2000; Davila et al., 2004; Li et al., 2003; Drenth et al., 2004, 2005
	GRP78 (BiP)	ER lumen (Cell surface)	Chaperone Ca ²⁺ binding ER stress sensor UPR regulator Anti-apoptosis	<i>-/- mice:</i> embryonic lethality at E3.5 due to failure of embryo implantation <i>-/- cells:</i> non viable	Cancer Alzheimer Parkinson Prion disease Atherosclerosis	Kokame et al., 1996; Rao et al., 2002; Hetz et al., 2003; Reddy et al., 2003; Dong et al., 2005; Luo et al., 2006; Li and Lee, 2006; Fu and Lee, 2006
	GRP94	ER lumen (Cell surface)	Chaperone Ca ²⁺ binding Anti-apoptosis tumor immunity	<i>-/- mice:</i> Embryonic lethality	Cancer Prion disease Autoimmune disease	Reddy et al., 1999; Fu and Lee, 2006; Hetz et al., 2003; Parmiani et al., 2004; Liu et al., 2005; Fu and Lee, 2006
	PDI	ER lumen Cell surface Secreted	Oxidoreductase (catalysis of SS bond formation, isomerization, reduction), chaperone	<i>KO mouse model:</i> ND <i>PDI deleted yeast cells:</i> lethal	Alzheimer Parkinson	Scherens et al., 1991; Turano et al., 2002; Ellgaard and Ruddock, 2005; Uehara et al., 2006
	Sec62	ER membrane	Protein translocation in the ER (part of the Sec61 complex)	ND	Prostate cancer	Jung et al., 2006
	Sec63	ER membrane	Protein translocation in the ER (part of the Sec61 complex)	ND	Autosomal-dominant polycystic liver disease (ADPCLD) Hereditary nonpolyposis colorectal cancer-associated small-bowel cancer Cancer with frequent microsatellite instability	(Mori et al., 2002); (Davila et al., 2004); (Drenth et al., 2005); (Schulmann et al., 2005); (Waanders et al., 2006)
	Sil1	ER lumen	BiP nucleotide exchange factor	<i>Mutant "woozy mice":</i> Develop ataxia between 3 and 4 months of age, accompanied by Purkinje cells loss UPR induction in cerebellum before ataxia onset	Marinesco-Sjögren syndrome	Anttonen et al., 2005; Senderek et al., 2005; Zhao et al., 2005; Zoghbi, 2005
UGT1	ER lumen	Glycoprotein quality control Folding sensor	<i>-/- mice:</i> Variable phenotype, most mice embryonic lethal at E13, some mice surviving until birth <i>-/- MEF:</i> Prolonged association of folding-incompetent glycoproteins with calnexin	ND	Molinari et al., 2005; Solda et al., 2007	

degradation	Derlin1 Derlin2 Derlin3	ER membrane	ERAD (translocon?)	ND	Alzheimer CFTR	Sun et al., 2006; Huttunen et al., 2007
	EDEM1 EDEM2 EDEM3	ER lumen (and membrane)	ERAD (recognition and targeting misfolded glycosylated proteins to the translocon)	ND	ND	Molinari et al., 2003; Olivari and Molinari, 2007
	HERP	ER membrane	ERAD (ubiquitin-like protein)	ND	Alzheimer	Kokame et al., 2000; Sai et al., 2002
	HRD1	ER membrane	(ERAD) E3 ubiquitin ligase	<u>Over-expressing mice:</u> Spontaneous arthropathy <u>+/- mice:</u> resistant to collagen-induced arthritis	Parkinson Rheumatoid arthritis Diabetes	Bordallo et al., 1998; Amano et al., 2003; Allen et al., 2004; Yamasaki et al., 2005; Omura et al., 2006
	SEL1	ER membrane	(ERAD) Capturing ERAD substrates	ND	Cancer	Biunno et al., 2000, 2006; Mueller et al., 2006
transport	ERGIC-53 (LMAN 1)	ERGIC	Glycoprotein transport from ER to the Golgi	<u>RNAi cells:</u> Lower IgM polymerization MCFD2 secretion	F5F8D	Nichols et al., 1998; Neerman-Arbez et al., 1999; Nyfeler et al., 2006; Mattioli et al., 2006; Anelli et al., 2007; Neerman-Arbez et al., 1999; Nichols et al., 1998; Nyfeler et al., 2006
	ERp44	ERGIC-cisGolgi	Thiol-mediated retention Quality control of oligomeric proteins IP3R regulation	<u>RNAi cells:</u> Lower thiol mediated retention Increased IP3 induced Calcium release No UPR induction	ND	Anelli et al., 2002, 2003, 2007; Higo et al., 2005
Stress sensing and signalling	ATF6	ER membrane Golgi	ER stress sensor	<u>-/- cells:</u> suboptimal ER protein processing after ER stress Prolonged UPR activation <u>-/- mice:</u> Increased toxicity of UPR inducing treatments	Hereditary Hemochromatosis Type II Diabetes	Yoshida et al., 1998; Thameem et al., 2006; Lawless et al., 2007; Meex et al., 2007; Wu et al., 2007
	eIF2α	Cytosolic	Transcriptional control	<u>eIF2α</u> <u>S51A/S51A mice:</u> embryonic lethal for B cell deficiency and defective glycogen storage and gluconeogenesis <u>S51/S51A mice:</u> In high fat diet: obese and ER stress, glucose intolerant <u>S51A knockin MEFs:</u> higher apoptotic sensitivity to hypoxia	Diabetes Tumor progression	Brewer and Diehl, 2000; Scheuner et al., 2001, 2005; Bi et al., 2005
	IRE1α	ER	ER stress sensor, Endonuclease (with broad substrate specificity)	<u>-/- mice:</u> Embryonic lethal <u>-/- haematopoietic cells:</u> can differentiate to proB cells but not to Pre B cells <u>-/- MEFs:</u> No EDEM1 induction after UPR induction (TM)	Parkinson Alzheimer Hyperhomocysteine mia	Urano et al., 2000; Katayama et al., 2001; Zhang et al., 2001, 2005; Ryu et al., 2002; Hollien and Weissman, 2006; Wu et al., 2007
	P58IPK	ER membrane	Negative regulator of eIF2 α (UPR induced)	<u>-/- mice:</u> development of diabetes with increased β cell death	Diabetes (mouse)	Tan et al., 1998; Melville et al., 2000; Yan et al., 2002; van Huizen et al., 2003; Ladiges et al., 2005
	PERK	ER membrane	ER stress sensor	<u>-/- mice:</u> Type II Diabetes Bone abnormalities Small body size <u>-/- cells:</u> More prone to apoptosis under ER stress Accumulation of endogenous peroxides Lower survival after hypoxia Lower capacity to induce tumors <u>Pek1 deleted C.elegans:</u> Shortened life span, accumulation of endogenous peroxides	Wollcott Rallison Syndrome Type II diabetes Parkinson Alzheimer Tumor progression	Bi et al., 2005; Delepine et al., 2000; Harding et al., 2001; Harding et al., 2000; Harding et al., 2003; Koumenis et al., 2002; Hoozemans et al., 2005, 2007; Koumenis and Wouters, 2006; Unterberger et al., 2006
	XBP1	Cytosolic Nuclear	UPR effector (transcription factor in the form sXbp1)	<u>-/- mice:</u> embryonic lethal <u>+/- mice:</u> insulin resistance and type II diabetes on high fat diet <u>-/- lymphocytes:</u> cannot differentiate to plasma cells <u>-/- MEF:</u> more sensitive to hypoxia (= more apoptosis) <u>-/- cells:</u> Cannot form tumors in mice	Multiple myeloma	Wen et al., 1999; Ozcan et al., 2004; Reimold et al., 2000; Reimold et al., 2001; Romero-Ramirez et al., 2004; Carrasco et al., 2007

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