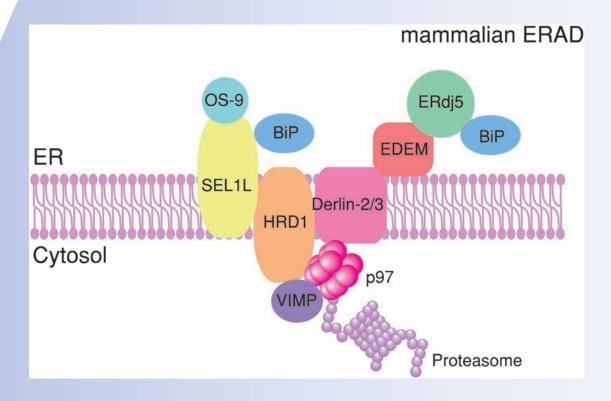


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**COVER:** Aberrant proteins produced in the ER are retrotranslocated from the ER into the cytosol and degraded by the ubiquitin-proteasome system by a process called ER-associated degradation (ERAD). In mammalian cells, the HRD1/SEL1L ERAD complex formed on the ER membrane interacts with the proteasome in the cytosol and facilitates clearance of misfolded proteins from the ER. Misfolded proteins are recognized by OS-9 through *N*-glycans, transferred to SEL1L and then retrotranslocated by the assistance of AAA<sup>+</sup> ATPase p97 from the ER to the cytosol. They are ubiquinated by the ubiquitin E3 ligase HRD1 and finally degraded by the proteasome. EDEM also recognizes *N*-glycans on terminally misfolded proteins and recruits them to Derlin-2/3 and p97. ERdj5, a disulfide reductase required for ERAD, interacts with EDEM and BiP and promotes dislocation of misfolded proteins into the cytosol by cleaving their incorrect disulfide bonds and preventing their aggregate formation. [See Hoseki *et al.*; p. 19].

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  - Messing, J. (1983) New M13 vectors for cloning in *Methods in Enzymology* (Wu, R., Grossman, L., and Moldave, K., eds.) Vol. 101, pp. 20–51, Academic Press, New York
- (3) For a book by one or more authors:
  - Sambrook, J., Fritsch, E.F., and Maniatis, T. (1989) Molecular Cloning. A Laboratory Manual pp. 1339–1341, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY

Text citations to references written by more than two authors should be styled for example as, Smith *et al.* In the reference list, however, the names of all authors (with initials) must be given. If an article has been accepted for publication by a journal but has not yet appeared in print, the reference should be styled as follows:

 Tanahashi, H. and Ito, T. (1994) Molecular characterization of a novel factor recognizing the interleukin-6 responsive element. J. Biochem. (in press)

The use of "in preparation" and "submitted for publication" is not allowed in the reference list.

Citation of the references written in a language which is usually unreadable for general readers and those published in a journal (or book) to which general reader could not easily access should be avoided.

### 6. Figure Legends

Figure legends and brief titles should be prepared for each figure. The figure legends should be provided after the reference list, with sufficient experimental detail to make the figure intelligible without reference to the text (unless the same material has been given with a previous figure, or in the Experimental Procedures section). The title should be provided along with the respective figure legend in bold script.

# 7. Nucleotide Sequence

New nucleotide data must be submitted and deposited in the DDBJ/EMBL/GenBank databases and an accession number obtained before the paper can be accepted for publication. Submission to any one of the three collaborating databanks is sufficient to ensure data entry in all. The accession number should be included in the manuscript e.g., as a footnote on the title page: "Note: Nucleotide sequence data reported are available in the DDBJ/EMBL/GenBank data-bases under the accession number(s)...". If requested, the database will withhold release of data until publication. The most convenient method for submitting sequence data is by World Wide Web:

DDBJ via SAKURA: http://sakura.ddbj.nig.ac.jp/ EMBL via WEBIN: http://www.ebi.ac.uk/embl/Submission/webin.html  $GenBank^{TM} \ via \ Banklt: \ http://www.ncbi.nlm.nih.gov/Banklt/$  or stand-alone submission tool

Sequin: http://www.ncbi.nlm.nih.gov/Sequin/

For special types of submissions (e.g., genomes, bulk submissions, etc.) additional submission protocols are available from the above sites.

### **Database Contact Information**

DDBJ: Center for Information Biology and DNA Data Bank of Japan National Institute of Genetics, 1111 Yata, Mishima, Shizuoka 411-8540, JAPAN; telephone: +81 559 81 6853; fax: +81 559 81 6849; e-mail: ddbj@ddbj.nig.ac.jp; web URL: http://www.ddbj.nig.ac.jp/

EMBL: EMBL Nucleotide Sequence Submissions, European Bioinformatics Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge DB10 1SD U.K.; telephone: +44 1223 494499; fax: +44 1223 494472; e-mail: datasubs@ebi.ac.uk; web URL: http://www.ebi.ac.uk

GenBank: National Center for Biotechnology Information, National Library of Medicine, Bldg. 38A, Rm 8N-803, Bethesda, MD 20894, U.S.A.; telephone: +1 301 496 2475; fax: +1 301 480 9241; e-mail: info@ncbi.nlm.nih.gov; web URL: http://www.ncbi.nlm.nih.gov

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- Tables should be drawn on separate pages and numbered consecutively in Roman numerals. For aid in designing tables in acceptable style, refer to current issues of the Journal.
- Each table should have an explanatory title (in bold) and sufficient experimental detail, usually in a paragraph immediately following the title, to be intelligible without reference to the text (unless the procedure is given in the Experimental Procedures section, or under another table or figure).
- 3. Indicate units of measure clearly.
- 4. Footnotes to tables should be kept to a minimum and should be indicated by superscript lower cases, at the bottom of the table.
- 5. Table must be submitted as .DOC, .RTF, Excel or PowerPoint files.

### VI. PREPARATION OF ILLUSTRATIONS

- 1. Each figure (Scheme, Diagram) should be given on a separate file numbered with an Arabic numeral (Fig. 1, Fig. 2, *etc.*). Figures will be reduced to fit into the type area of the printed page (17.5 × 23.5 cm).
- Indicate the magnification of photomicrographs in the legend or include a bar indicating the scale in the figure.
- Flow diagrams and amino acid or nucleotide sequences should always be presented as direct photographic reproduction.
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- Figures must be submitted as .DOC, .EPS, .JPG, .PPT, .TIF, .PDF or .GIF.

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Supporting material that cannot be included, and which is not essential for inclusion in the full text of the manuscript, but would nevertheless benefit the reader can be published online. Authors are encouraged to take advantage of the opportunity to submit Supplementary data whenever appropriate; for example, when the amount of material is too great to warrant inclusion in the main body of the paper, or when the material is in a format that cannot be represented in print (i.e. video clips or animated graphics). All material to be considered as Supplementary data must be submitted at the same time as the main manuscript for peer review. Please indicate clearly the material intended as Supplementary data upon submission. Also ensure that the Supplementary data is referred to in the manuscript at an appropriate point in the text. Supplementary data should be submitted in a separate file(s), in its final form. Please note that Supplementary data will not be edited, so ensure that it is clearly and

succinctly presented, and that the style of terms conforms to the rest of the paper. Also ensure that the presentation will work on any internet browser

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- Refer in the text to simple chemical compounds by their formulae when these can be printed in simple horizontal lines of type. Do not use structural formulae in the running text.
- 2. Ionic charge should be shown as a superscript following the chemical symbol, e.g.  ${\rm Fe^{3+},\ SO_4^{2-}}$ .
- 3. Prepare large structural formulae and long mathematical equations in a form suitable for direct photographic reproduction and include them as a Diagram at the end of the paper.
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For simple molecules, the labeling is indicated by writing the chemical formulae with the prefix superscripts attached to the correct atomic symbols in the formulae: *e.g.* <sup>14</sup>CO<sub>2</sub>, H<sub>2</sub><sup>18</sup>O, <sup>2</sup>H<sub>2</sub>O. Square brackets should not be used for them, or when the isotopic symbol is attached to a word that is not a specific chemical name, abbreviation or symbol: *e.g.* <sup>131</sup>I-labeled, <sup>14</sup>C-sugar, <sup>14</sup>C-steroids, <sup>32</sup>PO<sub>4</sub><sup>3-</sup>, but [<sup>32</sup>P]-phosphate.

5. **Spectrophotometric Data**—Beer's law may be stated as  $A = -\log T = \varepsilon lc$ 

Where A is the absorbance; T, the transmittance  $(-I/I_0)$ ;  $\varepsilon$ , the molar absorption coefficient;  $\varepsilon$ , the concentration of the absorbing substances in moles per liter; and I, the length of the optical path in centimeters. Under these conditions  $\varepsilon$  has the dimensions liter  $\cdot$  mol<sup>-1</sup>  $\cdot$  cm<sup>-1</sup> or more briefly  $M^{-1} \cdot$  cm<sup>-1</sup> (not cm<sup>-</sup>  $\cdot$  mol<sup>-1</sup>). Do not use "O.D." and "E."

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- 1. Abbreviations with specific meanings may be used for convenience for complex chemical substances, particularly in equations, tables, or figures. Avoid using abbreviations in titles and summaries except the standard ones listed in Table II of Section X-8.
- 2. Use abbreviations and symbols sparingly in the text. In chemical equations, which traditionally depend upon symbols, an abbreviation or symbol may be used for a term that appears in full in the neighboring text. Trivial names are usually sufficiently short not to require abbreviations.
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- 4. For spelling of chemical names consult current issues of the Journal. For chemical terms follow essentially the usages and rules recommended by International Scientific Union, especially Nomenclature Committee of IUBMB (NC-IUBMB, IUBMB: International Union of Biochemistry and Molecular Biology) and IUPAC-IUBMB Joint Commission on Biochemical Nomenclature (JCBN, IUPAC: International Union of Pure and Applied Chemistry): see the recommendations in Biochemical Nomenclature and Related Documents (1978), available from The Biochemical Society, 7 Warwick Court, London WC1R 5DP, U.K. and in Biochemical Nomenclature and Related Documents. A Compendium, 2nd edn (Liébecq, C., ed.), Portland Press Ltd, London (1992). (see Eur. J. Biochem. 213, 1-3 (1993)).

Refer also to http://www.chem.qmw.ac.uk/iupac/jcbn/

5. Enzymes—Where one or more enzymes figure prominently in a manuscript, authors should use the recommended (trivial) name or systematic name given by Nomenclature Committee of IUBMB and IUPAC-IUBMB Commission on Biochemical Nomenclature: see Enzvme Nomenclature, Recommendations (1992), Academic Press, Inc.,

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see also Eur. J. Biochem. 213, 1-3 (1993).
-Supplement Eur. J. Biochem. 223, 1-5 (1994).
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- -Supplement 2 Eur. J. Biochem. 232, 1-6 (1995). -Supplement 3 Eur. J. Biochem. 237, 1–5 (1996).
- -Supplement 4 Eur. J. Biochem. **250**, 1–6 (1997).

When an enzyme is the main subject of a paper, its source, trivial name, systematic name (or the reaction that it catalyzes) and code number (preceded by "EC") should be included.

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- 7. Abbreviations of Units of Measurement and Physical and Chemical Quantities—These abbreviations listed in Table I may be used without definition.

ohm

TA	BLE I						
(1) Prefixes to the names of units							
	tera	$10^{12}$	T		milli	$10^{-3}$	m
	giga	$10^{9}$	G		micro	$10^{-6}$	μ
	mega	$10^{6}$	M		nano	$10^{-9}$	n
	kilo	$0^{3}$	k		pico	$10^{-12}$	p
	Deci	$10^{-1}$		(not d)	femto	$10^{-15}$	f
	centi	$10^{-2}$	c <sup>1)</sup>	2)	atto	$10^{-18}$	a
	Units of			n <sup>2)</sup>			
	molar (1	,	-		M	2	
	millimol				$mM \text{ (not } 10^{-3} \text{ M)}$		
		,		les/liter)		$\mu$ M (or $10^{-6}$ M)	
	nanomo	,		, ,		$nM (or \times 10^{-9} M)$	
	picomol			liter)	pM (or	$r \times 10^{-12}$	<sup>2</sup> M)
	Units of	Lengt	h				
	meter				m		
	centimet				cm		
	millimet			>	mm		
	microme		ot micr	on)	μm (not μ) nm (not μ)		
	nanome		nm)		Å	π)	
	Angstro Units of			Juma	A		
				nume	cm <sup>2</sup>		
square centimeter cubic centimeter			cm <sup>3</sup>				
liter			l (in tables only)				
milliliter			ml				
microliter			$\mu$ l (not $\lambda$ )				
	Units of				per (mor	, ,,	
. ,	gram				g (kg,	mg, μg	[not γ], ng, pg)
	dalton <sup>3)</sup>				Da	0,10	. 717 67 167
(6)	Units of	Time					
	hour		h	year	yr		
	minute		min	month	mo		
	second		S	week	wk		
				day	d		
(7)	Units of	of Radi	oactivi	ty			
becquerel			Bq (=	l dps or	60 dpm)		
counts per minute			cpm				
curie(s)			,	$3.7 \times 10^{10}$	<sup>o</sup> Bq)		
disintegrations per minute			dpm				

(8) Other Units

mole mol (mmol, µmol, nmol, pmol) degree Celsius  $^{\circ}C$ degree absolute (kelvin) K ioule J kilojoule kJ calorie ca1 kilocalorie kcal parts per billion ppb parts per million ppm cycles per second (hertz) Hz (not cps) equivalent eq ampere A (mA)

Ω

	volt	V
	gauss	G
	pascal	Pa
	revolutions per minute	rpm
	Svedberg unit of sedimentation	S
	coefficient $(10^{-13} \mathrm{s})$	
(9)	Physical and Chemical Quantities	
	absorbance	A
	equilibrium constant	K
	rate constant	k
	maximum velocity	$V_{ m max}$
	Michaelis constant	$K_{ m m}$
	equilibrium dissociation constant	$K_{\rm d}$
	isoelectric point	pI
	molecular weight <sup>3)</sup>	$M_{ m r}$
	retardation factor	$R_f$
	acceleration of gravity	g
	specific rotation	$[\alpha]^{\mathrm{t}}_{\lambda}$
	partial specific volume	$\bar{\nu}$
	diffusion constant	D
	sedimentation coefficient	S
	density	ρ
	sedimentation coefficient	$s_{20,\mathrm{w}}^0$
	in water at 20°C,	
	extraporated to zero	
	concentration	
	Gibbs energy change	$\Delta G$
	entropy change	$\Delta S$
	enthalpy change	$\Delta H$
	melting temperature	$T_{ m m}$
10)	Other Terms	
	logarithm	log
	logarithm (natural)	ln
	standard deviation of a series	SD
	standard error of mean of series	SE

1) to be avoided where possible (except for cm).
2) Terms such as milligram percent (mg%) should not be used. Weight

concentrations should be given as g/ml, g/100 ml, etc.

3) Molecular weight is dimensionless. Only molecular mass is expressed by daltons.

8. Accepted Abbreviations and Symbols—Authors may use, without definition, the abbreviations given in Table II and the symbols and abbreviations for amino acid or nucleotide residues in polymers or sequences. Define other abbreviations in a single footnote on the title page.

# TABLE II

TABLE II		Tris(hydroxyme
(1) General		Ultraviolet
Adenosine 3':5'-cyclic monophosphate	cAMP	Uridine diphos
Adenosine 5'-mono-, di, and triphosphates <sup>1)</sup>	AMP, ADP, and ATP	Uridine 5'-mon
Adenosine triphosphatase	ATPase	(2) Amino ac
Base pair(s)	bp	Alanine
Bovine serum albumin	BSA	Arginine
O-(Carboxymethyl)	CM-	Asparagine
Circular dichroism	CD	Aspartic acid
Coenzyme A and its acyl derivatives	CoA (or CoASH)	Aspartic acid of
	and acyl-CoA	Cysteine
Complementary DNA	cDNA	Glutamic acid
Cyclic AMP	cAMP	Glutamine
Cyclic GMP	cGMP	Glutamic acid
Cytidine diphosphate choline, etc.	CDP-choline, etc.	Glycine
Cytidine 5'-mono-, di-, and triphosphates	CMP, CDP, and CTP	Histidine
Deoxyribonuclease	DNase	Isoleucine
Deoxyribonucleic acid	DNA	Leucine
O-(Diethylaminoethyl)	DEAE-	Lysine
Dithiothreitol	DTT	Methionine
Electron paramagnetic resonance	EPR	Phenylalanine
Electron spin resonance	ESR	Proline
Ethylenediaminetetraacetic acid	EDTA	Serine
[Ethylenebis(oxyethlenenitrilo)]-tetraacetic	EGTA	Threonine
acid		Tryptophan

Flavin-adenine dinucleotide and its fully	FAD and FADH <sub>2</sub>
reduced form	
Flavin mononucleotide and its fully reduced	FMN and FMNH <sub>2</sub>
form	ET
Fourier transform Gas chromatography-mass spectrometry	FT GC MS
Gas liquid chromatography	GC-MS GLC
Glutathione and its oxidized form	GSH and GSSG
Guanosine 3':5'-cyclic monophosphate	cGMP
Guanosine 5'-mono-, di-, and triphosphates	GMP, GDP, and
	GTP
Guanosine triphosphatase	GTPase
Hemoglobin	Hb
Heterogenous nuclear RNA High performance (pressure) liquid	hnRNA HPLC
chromatography	III LC
4-(2-Hydroxyethyl)-1-piperazineethane-	HEPES
sulfonic acid	
Immunoglobulin	Ig (IgG, IgM, etc.)
Infrared	IR
Inorganic orthophosphate	P <sub>i</sub>
Inorganic pyrophosphate Inosine 5'-mono-, di-, and triphosphates	PP <sub>i</sub> IMP, IDP, and ITP
Kilobases	kb
Kilobase pairs	kbp
Lethal dose, 50%	$\mathrm{LD}_{50}$
Messenger RNA	mRNA
Nicotinamide adenine dinucleotide and	NAD <sup>+</sup> and NADH <sup>2)</sup>
its reduced form	NIADD± 1
Nicotinamide adenine dinucleotide phosphate and its reduced form	NADP <sup>+</sup> and NADPH <sup>2)</sup>
Nuclear magnetic resonance	NMR
Nuclear RNA	nRNA
Optical rotatory dispersion	ORD
Phosphoric acid residue	P- or -P
Pseudouridine and pseudouridine	$\psi$ and $\psi$ MP
mono-nucleotide	DACE
Polyacrylamide gel electrophoresis Poly(adenylic acid), polyadenylate <sup>3)</sup>	PAGE Poly(A) <sup>3)</sup>
Polymerase chain reaction	PCR
Restriction fragment length polymorphism	RFLP
Ribonuclease	RNase
Ribonucleic acid	RNA
Ribosomal RNA	rRNA
Ribosylthymine 5'-mono-, di-, and	TMP, TDP, and
triphosphates Sodium dodecyl sulfate	TTP SDS
Thin layer chromatography	TLC
Thymidine (2'-deoxyribosylthymine)	dTMP, dTDP,
5'-mono-, di-, and triphosphates	and dTTP <sup>4)</sup>
Transfer RNA	tRNA
Tris(hydroxymethyl)aminomethane	Tris
Ultraviolet	UV
Uridine diphosphate glucose, <i>etc</i> . Uridine 5'-mono-, di-, and triphosphates	UDP-glucose, <i>etc</i> . UMP, UDP, and UTP
(2) Amino acids	OMI, ODI, and OTI
Alanine	Ala (A)
Arginine	Arg (R)
Asparagine	A (3.T)
Aspartic acid	Asn (N)
Aspartic acid or asparagine	Asp (D)
	Asp (D) Asx (B)
Cysteine	Asp (D) Asx (B) Cys (C)
Cysteine Glutamic acid	Asp (D) Asx (B) Cys (C) Glu (E)
Cysteine Glutamic acid Glutamine	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q)
Cysteine Glutamic acid	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q)
Cysteine Glutamic acid Glutamine Glutamic acid or glutamine Glycine Histidine	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q) Glx (Z) Gly (G) His (H)
Cysteine Glutamic acid Glutamine Glutamic acid or glutamine Glycine Histidine Isoleucine	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q) Glx (Z) Gly (G) His (H) Ile (I)
Cysteine Glutamic acid Glutamine Glutamic acid or glutamine Glycine Histidine Isoleucine Leucine	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q) Glx (Z) Gly (G) His (H) Ile (I) Leu (L)
Cysteine Glutamic acid Glutamine Glutamic acid or glutamine Glycine Histidine Isoleucine	Asp (D) Asx (B) Cys (C) Glu (E) Gln (Q) Glx (Z) Gly (G) His (H) Ile (I)

Phe (F) Pro (P)

Ser (S)

Thr (T)

Trp (W)

Tyrosine	Tyr (Y)
Valine	Val (V)
(3) Nucleic acids	
Adenosine	A
Bromouridine	BrUrd or B
Cytidine	C
Dihydrouridine	D or hU
Guanosine	G
Inosine	I
6-Mercaptopurine ribonucleoside	M or sI
(6-thioinosine)	
'a nucleoside'	Nuc or N
Pseudouridine	$\psi$ or $Q^a$
'a purine nucleoside'	R
'a pyrimidine nucleoside'	Y
Thiouridine	S or sU
Thymidine (2'-deoxyribosylthymine)	dT
Uridine	U
Xanthosine	X
Phosphoric residue	-P or p

- 1) The various isomers of adenosine monophosphate may be written 2'-AMP, 3'-AMP, or 5'-AMP (in case of possible ambiguity). A similar procedure may be applied to other nucleoside or deoxyribonucleoside monophosphates.
- <sup>2)</sup> NAD(P)<sup>+</sup> and NAD(P)H indicate either NAD<sup>+</sup> or NADP<sup>+</sup> and either NADH or NADPH, respectively.
- <sup>3)</sup> Similarly abbreviate oligo- and polynucleotides composed of repeating sequences or of unknown sequence of given purine or pyrimidine bases, *e.g.* oligothymidylate, oligo(dT); alternating copolymer of A and U, poly(A-U); random copolymer of A and U, poly(A,U).
- <sup>4)</sup> The d prefix may be used to represent the corresponding deoxyribonucleoside phosphates, *e.g.* dADP.
- 9. Names of Animals, Plants, and Microorganisms—The scientific names are Latin binomials and should be given in full in the title and summary and on first mention in the text (e.g. Escherichia coli). Subsequently, the generic name may be contracted (usually to the first letter), e.g., E. coli. The strain of laboratory animals and if possible the source should be stated.
- 10. The cytochromes should be designated by a small italicized letter, *e.g.* cytochrome *a, b*<sub>2</sub>, *c*<sub>1</sub>, *etc*.

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