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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-association 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⁺ 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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1. 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. Fe3+, SO42-.

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.

4. Isotopically Labeled Compounds—The symbol for an isotope is shown in square brackets directly before the name (word), as in [12C]urea, [2-13C]leucine, [12,13-methyl-1H]methionine. When more than one position in a substance is labeled with the same isotope and the positions are not indicated, the number of labeled atoms should be indicated as a right-hand subscript, as in [41C]glycolic acid. The symbol 0 indicates uniform, e.g. [13C]-glucose (where the 13C is uniformly distributed among all six positions). The isotopic prefix precedes that part of the name to which it refers, as in sodium [2H]formate, thiamine [2,3-2H]diphosphate. Terms such as 131I-labeled albumin should not be contracted to [131I]albumin. When isotopes of more than one element are introduced, their symbols should be arranged in alphabetical order: e.g. U, P. 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. 131I-, [1-14C, 2-3H, 15N]serine. The symbols 2H and 3H or D and T may be used for deuterium and tritium, respectively.

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. 14CO2, H218O, H3O. 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. 131I-labeled, 14C-sugar, 1,25-dihydroxy-32PO4- and [32P]-phosphate.

5. Spectrophotometric Data—Beer’s law may be stated as

\[ A = \log T = e \times c \times l \]

Where \( A \) is the absorbance; \( T \), the transmittance \((-\log E)\); \( e \), the molar absorption coefficient; \( c \), the concentration of the absorbing substances in moles per liter; and \( l \), the length of the optical path in centimeters. Under these conditions \( t \) has the dimensions liter \( \cdot \) mol \(-1\) \cdot cm\(-1\) or more briefly \( M \cdot cm\(-1\) \cdot mol\(^{-1}\). Do not use “O.D.” and “E.”

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TABLE II

(1) General

<table>
<thead>
<tr>
<th>Term</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosine 3',5'-cyclic monophosphate</td>
<td>cAMP</td>
</tr>
<tr>
<td>Adenosine 5'-mono-, di-, and triphosphates</td>
<td>cAMP</td>
</tr>
<tr>
<td>Adenosine triphosphatase</td>
<td>CD</td>
</tr>
<tr>
<td>Base pair(s)</td>
<td>bp</td>
</tr>
<tr>
<td>Bovine serum albumin</td>
<td>BSA</td>
</tr>
<tr>
<td>O-(Carboxymethyl)</td>
<td>CM</td>
</tr>
<tr>
<td>Circular dichroism</td>
<td>CD</td>
</tr>
<tr>
<td>Coenzyme A and its acyl derivatives</td>
<td>CoA</td>
</tr>
<tr>
<td>Complementary DNA</td>
<td>cDNA</td>
</tr>
<tr>
<td>Cyclic AMP</td>
<td>cAMP</td>
</tr>
<tr>
<td>Cyclic GMP</td>
<td>cGMP</td>
</tr>
<tr>
<td>Cytidine diphosphate choline, etc.</td>
<td>CDP-choline, etc.</td>
</tr>
<tr>
<td>Cytidine 5'-mono-, di-, and triphosphates</td>
<td>CMP, CDP, and CTP</td>
</tr>
<tr>
<td>Deoxyriboonuclease</td>
<td>DNase</td>
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<tr>
<td>Deoxyribonucleic acid</td>
<td>DNA</td>
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<td>O-(Diethylaminoethyl)</td>
<td>DEAE</td>
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<tr>
<td>Dithiothreitol</td>
<td>EPR</td>
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<tr>
<td>Electron paramagnetic resonance</td>
<td>EPR</td>
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<tr>
<td>Electron spin resonance</td>
<td>ESR</td>
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<tr>
<td>Ethylenediaminetetraacetic acid</td>
<td>EDTA</td>
</tr>
<tr>
<td>[Ethylenebis(oxyethylenenitrilo)]-tetraacetic acid</td>
<td>EGTA</td>
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(2) Amino acids

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<th>Term</th>
<th>Symbol</th>
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<td>cAMP, AMP, ADP, and ATP</td>
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<td>bp</td>
<td>bp</td>
</tr>
<tr>
<td>BSA</td>
<td>BSA</td>
</tr>
<tr>
<td>CMP, CDP, and CTP</td>
<td>CMP, CDP, and CTP</td>
</tr>
<tr>
<td>CoA (or CoASH)</td>
<td>CoA</td>
</tr>
<tr>
<td>and acyl-CoA</td>
<td>and acyl-CoA</td>
</tr>
<tr>
<td>cDNA</td>
<td>cDNA</td>
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<tr>
<td>cAMP</td>
<td>cAMP</td>
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<tr>
<td>cGMP</td>
<td>cGMP</td>
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<td>CDP-choline, etc.</td>
<td>CDP-choline, etc.</td>
</tr>
<tr>
<td>CMP, CDP, and CTP</td>
<td>CMP, CDP, and CTP</td>
</tr>
<tr>
<td>DNase</td>
<td>DNase</td>
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<td>EDTA</td>
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<tr>
<td>EGTA</td>
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</table>

(3) Amino acids

<table>
<thead>
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<th>Term</th>
<th>Symbol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adenosine diphosphate glucose, etc.</td>
<td>UDP-glucose, etc.</td>
</tr>
<tr>
<td>Adenosine 5'-mono-, di-, and triphosphates</td>
<td>UDP-glucose, etc.</td>
</tr>
<tr>
<td>Alamine</td>
<td>Ala (A)</td>
</tr>
<tr>
<td>Arginine</td>
<td>Arg (R)</td>
</tr>
<tr>
<td>Asparagine</td>
<td>Asp (D)</td>
</tr>
<tr>
<td>Aspartic acid</td>
<td>Asx (B)</td>
</tr>
<tr>
<td>Cysteine</td>
<td>Cys (C)</td>
</tr>
<tr>
<td>Gluetic acid</td>
<td>Glu (E)</td>
</tr>
<tr>
<td>Glutamine</td>
<td>Gln (Q)</td>
</tr>
<tr>
<td>Glutamic acid or glutamin</td>
<td>Glx (Z)</td>
</tr>
<tr>
<td>Glycin</td>
<td>Gly (G)</td>
</tr>
<tr>
<td>Histidine</td>
<td>His (H)</td>
</tr>
<tr>
<td>Isoleucine</td>
<td>Ile (I)</td>
</tr>
<tr>
<td>Lysine</td>
<td>Lys (K)</td>
</tr>
<tr>
<td>Methionine</td>
<td>Met (M)</td>
</tr>
<tr>
<td>Phenylalanine</td>
<td>Phe (F)</td>
</tr>
<tr>
<td>Proline</td>
<td>Pro (P)</td>
</tr>
<tr>
<td>Serine</td>
<td>Ser (S)</td>
</tr>
<tr>
<td>Threonine</td>
<td>Thr (T)</td>
</tr>
<tr>
<td>Tryptophan</td>
<td>Trp (W)</td>
</tr>
</tbody>
</table>


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 sl  
6-thioinosine 'a nucleoside' Nuc or N  
Pseudouridine  
'p or Q'  
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.

2) NAD(P)+ and NAD(P)H indicate either NAD+ or NADP+ and either NADH or NADPH, respectively.

3) Similarly abbreviate oligo- and polynucleotides composed of repeating sequences or of unknown sequence of given purine or pyrimidine bases, e.g. oligothymidylic acid, oligo(dT); alternating copolymer of A and U, poly(A-U); random copolymer of A and U, poly(A,U).

4) The d prefix may be used to represent the corresponding deoxyribonucleoside phosphates, e.g. dADP.

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10. The cytochromes should be designated by a small italicized letter, e.g. cytochrome a, b, c, etc.

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(vi) If the files have not been uploaded to your satisfaction, go back to the file upload screen where you can remove the files you do not want, and repeat the upload process.

6. When you are satisfied with the uploaded manuscript proof, click on ‘Save and Continue’ which will take you to the ‘Review & Submit’ screen. The system will check that you have completed all the mandatory fields and that you have viewed your manuscript proof. It will also present you with a summary of all the information you have provided and give you a final chance to edit it. When you have finished reviewing this information press ‘Submit’.

7. After the manuscript has been submitted you will see a confirmation screen and receive an email confirmation stating that your manuscript has been successfully submitted. This will also give the assigned manuscript number, which is used in all correspondence. If you do not receive this, your manuscript will not have been successfully submitted to the journal and the paper cannot progress to peer review. If this is the case your manuscript will still be sitting in the ‘Unsubmitted Manuscripts’ section of your ‘Author Center’ awaiting your attention.

8. If you return to your ‘Author Center’ you will notice that your newly submitted manuscript can be found in the ‘Submitted Manuscripts’ area. Among the information listed there, the ‘Status’ section provides information on the status of your manuscript as it moves through the review process.

SUBMITTING A REVISED MANUSCRIPT

1. Please supply your revised paper through the online submission website using your User ID and Password to log-on—remember that these are both case-sensitive. Log on to the online submission website and, in the ‘Author Center’, click on ‘Manuscripts with Decisions’ under ‘My Manuscripts’. You will then see a list of all manuscripts you have submitted where the editors have been able to make a decision.

2. Find the manuscript you wish to revise and click on the link 'create a revision' in the ‘Actions’ column. This will initiate a revised-submission process that prompts you to respond to the points made by the Editors and/or reviewers. Continue to follow the 7-step submission process, providing information when prompted.

Please note: All the files from your previous submission will have been retained by the system. So, when you reach the ‘File Upload’ screen (Step #6), you will need to delete any files that are no longer needed or need replacing with revised versions.

Getting help
If you experience any problems during the online submission process, please consult the Author’s User Guide which provides more detailed submission instructions, and ‘movie tutorials’ explaining how to submit your paper. Alternatively, please contact the Journal's Editorial Office who will be pleased to assist you.