

Deborah Fass, Ph.D. *Curriculum Vitae* September 2021

Date of birth: February 21, 1970

Citizenship: Israel/USA

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Education

Whitehead Institute, Cambridge, MA, USA	1997-1998
Post-doctoral training (Structural Biology)	
Advisor: James Berger	
Massachusetts Institute of Technology, Cambridge, MA, USA	1992-1997
Ph.D. (Structural Biology)	
Thesis title: "The Protein Structures Underlying Receptor Binding and Membrane Fusion of Ecotropic Murine Leukemia Viruses"	
Advisor: Peter Kim	
Harvard University, Cambridge, MA, USA	1987-1991
B.A. (Biochemistry)	
Thesis title: "hXBP-1 and ψ hXBP-1: Genomic Organization and Identification of <i>cis</i> -Regulatory Sequences from a Class II Major Histocompatibility Complex Transcription Activating Factor"	
Advisor: Jack Strominger	

Employment History

Department of Structural Biology, Weizmann Institute of Science, Rehovot, Israel	
Full Professor (department chair, 2017-present)	2013-present
Associate Professor	2006-2013
Senior Scientist	1998-2006
Department of Biochemistry, Harvard University, Cambridge, MA, USA	
Research Assistant	1991-1992

Teaching Experience

Feinberg Graduate School, Weizmann Institute	
Lecturer, Protein Structure and Function	1999-present
Massachusetts Institute of Technology	
Teaching Assistant, Graduate Biophysical Chemistry	1995
Teaching Assistant, Undergraduate Biochemistry	1993
Harvard University	
Teaching Assistant, Undergraduate Biochemistry	1992
Teaching Assistant, Undergraduate Organic Chemistry	1991

Prizes and Recognition

Elected to the European Molecular Biology Organization (EMBO)	2013
European Research Council (ERC) Consolidator Grant Award	2012
Israel Chemical Society Excellent Young Scientist Prize	2008
Krill Prize for Outstanding Research (under the auspices of the Wolf Foundation)	2005
Hestrin Prize (Israel Society for Biochemistry and Molecular Biology)	2005
Bergmann Memorial Research Award (Binational Science Foundation)	2002
Sir Charles Clore Prize	1998
Howard Hughes Graduate Studies Fellowship	1992
National Science Foundation Fellowship	1992
Phi Beta Kappa	1991
Bowdoin Prize for Essay in the Natural Sciences	1991

Patents

Douglas Lake, Benjamin Katchman, Deborah Fass.
“QSOX as an Anti-neoplastic Drug Target”
U.S. Patent Number: 8,946,186. February 3, 2015

Deborah Fass, Iris Grosman, Tal Ilani, Assaf Alon.
“Compositions for Inhibition of Quiescin Sulfhydryl Oxidase (QSOX1) and Uses of Same”
Publication number: 20150110786 (March 7, 2013)
Filed: April 23, 2015

David C. Chan, Deborah Fass, Min Lu, James M. Berger, and Peter S. Kim.
“Core Structure of gp41 from the HIV Envelope Glycoprotein”
U.S. Patent Number: 6,506,554. January 14, 2003

David C. Chan, Deborah Fass, Min Lu, James M. Berger, and Peter S. Kim.
“Core Structure of gp41 from the HIV Envelope Glycoprotein”
U.S. Patent Number: 6,150,088 November 21, 2000

Conference Organizing Committees

Functional Disulfide Bonds in Health and Disease	2021
Protein Society Annual Symposium	2018
Kavli Frontiers of Science U.S.-Israel Meeting	2015
Yale-Weizmann Encounter in the Biological, Physical, and Engineering Sciences	2014
Kavli Frontiers of Science U.S.-Israel Meeting	2013
Meeting of the Israel Chemical Society	2013
Ilanit (Federation of the Israeli Societies for Experimental Biology)	2011
Meeting of the Israel Chemical Society	2005
XIX Congress of the International Union of Crystallography	2002

Selected Invited Lectures at International Meetings

Society for Redox Biology and Medicine, USA	2021
Cilia, Mucus and Mucociliary Interactions GRC, USA (cancelled)	2021
“The Molecular Fabric of Life” Royal Society and Israel Academy joint meeting	2020
15th International Workshop on Carcinoma-associated Mucins, UK	2019
Basement Membrane Workshop, American Society for Matrix Biology, USA	2019
ER and Redox Club Meeting, Germany	2019
Gordon Research Conference on Thiol-Based Redox Regulation, Spain	2018
FASEB Functional Disulfide Bonds in Health and Disease, USA	2018
Chemical Protein Synthesis Meeting, Israel	2017
ER and Redox Club Meeting, Germany	2017
Plenary lecture at the DFG Priority Program “Dynamics of Thiol-Based Redox Switches in Cellular Physiology,” Germany	2016
Five-year ceremony of the Buchman Institute, University of Frankfurt, Germany	2016
Lorne Conference on Protein Structure and Function, Australia	2015
Gordon Research Conference on Thiol-Based Redox Regulation, Spain	2014
Gordon Research Conference on Protein Processing and Secretion, USA	2014
Protein Society Meeting, USA	2013
Harvard Medical School Structural Biology Symposium	2011
Symposium on Protein Chemistry, Denmark	2011
EMBO Conference on Endoplasmic Reticulum Functions, Spain	2010

Current collaborators

Bernhard Radlwimmer, German Cancer Research Center (DKFZ), Heidelberg, Germany
David Chan, California Institute of Technology, Pasadena, CA, USA
Neil Bulleid, University of Glasgow, UK
Timothy Blackwell, Vanderbilt University Medical Center, Nashville, TN, USA
Christopher Evans, University of Colorado Denver School of Medicine, Aurora, CO, USA

Refereed original research articles

1. Javitt G, Kinzel A, Reznik N, Fass D (2021) Conformational switches and redox properties of the colon cancer-associated human lectin ZG16. *FEBS J.* in press.
2. Javitt G, Khmelnsky L, Albert L, Bigman LS, Elad N, Morgenstern D, Ilani T, Levy Y, Diskin R, Fass D. Assembly mechanism of mucin and von Willebrand factor polymers (2020) *Cell* **183**, 717-729.
3. Waugh B, Wolf SG, Fass D, Branlund E, Kam Z, Sedat JW, Elbaum M. Three-dimensional deconvolution processing for STEM cryotomography (2020) *Proc. Natl. Acad. Sci. USA* **117**, 27374-27380.
4. Javitt G, Cao Z, Resnick E, Gabizon R, Bulleid NJ, Fass D (2020) Structure and electron-transfer pathway of the human methionine sulfoxide reductase MsrB3. *Antioxid. Redox Signal.* **33**, 665-678.
5. Feldman T, Grossman-Haham I, Elkis Y, Vilela P, Moskovits N, Barshack I, Salame TM, Fass D, Ilani T (2020) Inhibition of fibroblast secreted QSOX1 perturbs extracellular matrix in the tumor microenvironment and decreases tumor growth and metastasis in murine cancer models. *Oncotarget* **11**, 386-398.
6. Warszawski S, Borenstein Katz A, Lipsh R, Khmelnsky L, Ben Nissan G, Javitt G, Dym O, Unger T, Knop O, Albeck S, Diskin R, Fass D, Sharon M, Fleishman SJ (2019) Optimizing antibody affinity and stability by the automated design of the variable light-heavy chain interfaces. *PLoS Comput. Biol.* **15**, e1007207.
7. Javitt G, Calvo MLG, Albert L, Reznik N, Ilani T, Diskin R, Fass D (2019) Intestinal gel-forming mucins polymerize by disulfide-mediated dimerization of D3 domains. *J. Mol. Biol.* **431**, 3740-3752.
8. Javitt G, Grossman-Haham I, Alon A, Resnick E, Mutsafi Y, Ilani T, Fass D (2019) *cis*-Proline mutants of quiescin sulfhydryl oxidase 1 with altered redox properties undermine extracellular matrix integrity and cell adhesion in fibroblast cultures. *Protein Sci.* **28**, 228-238.
9. Lansky Z, Mutsafi Y, Houben L, Ilani T, Armony G, Wolf SG, Fass D (2019) 3D mapping of native extracellular matrix reveals cellular responses to the microenvironment. *J. Structural Biology: X* **1**, 100002.
10. Szekely O, Armony G, Olsen GL, Bigman LS, Levy Y, Fass D, Frydman L (2018) Identification and rationalization of kinetic folding intermediates for a low-density lipoprotein receptor ligand-binding module. *Biochem.* **57**, 4776-4787.
11. Horowitz B, Javitt G, Ilani T, Gat Y, Morgenstern D, Bard FA, Fass D (2018) Quiescin sulfhydryl oxidase 1 (QSOX1) glycosite mutation perturbs secretion but not Golgi localization. *Glycobiol.* **28**, 580-591.
12. Wolf SG, Mutsafi Y, Dadosh T, Ilani T, Lansky Z, Horowitz B, Rubin S, Elbaum M, Fass D (2017) 3D visualization of mitochondrial solid-phase calcium stores in whole cells. *Elife* **6**, e29929.
13. Armony G, Jacob E, Moran T, Levin Y, Mehlman T, Levy Y, and Fass, D (2016) Cross-linking reveals laminin coiled-coil architecture. *Proc. Natl. Acad. Sci. USA* **113**, 13384-13389.
14. Zhang L, Cheng Q, Zhang L, Wang Y, Merrill GF, Ilani T, Fass D, Arnér ESJ, Zhang J (2016) Serum thioredoxin reductase is highly increased in mice with hepatocellular carcinoma and its activity is restrained by several mechanisms. *Free Radic. Biol. Med.* **99**, 426-435.
15. Grossman I, Ilani T, Fleishman SJ, Fass D (2016) Overcoming a species-specificity barrier in development of an inhibitory antibody targeting a modulator of tumor stroma. *Protein Eng. Des. Sel.* **29**, 135-147.
16. Grossman I, Aviram HY, Armony G, Horovitz A, Hofmann H, Haran G, Fass (2015) Single-molecule spectroscopy exposes hidden states in an enzymatic electron relay. *Nature Comm.* **6**, 8624.
17. Moran T, Gat Y, Fass D (2015) Laminin L4 domain structure resembles adhesion modules in ephrin receptor and other transmembrane glycoproteins. *FEBS J.* **282**, 2746-2757.

18. Biran S, Gat Y, Fass D (2014) The Eps1p protein disulfide isomerase conserves classic thioredoxin superfamily amino acid motifs but not their functional geometries. *PLoS One* **9**, e113431.
19. Gat Y, Vardi-Kilshtain A, Grossman I, Major DT, Fass D (2014) Enzyme structure captures four cysteines aligned for disulfide relay. *Protein Sci.* **23**, 1102-1112.
20. Grossman I, Alon A, Ilani T, Fass D (2013) An inhibitory antibody blocks the first step in the dithiol/disulfide relay mechanism of the enzyme QSOX1. *J. Mol. Biol.* **425**, 4366-4378.
21. Ilani T, Alon A, Grossman I, Horowitz B, Kartvelishvily E, Cohen SR, Fass D (2013) A secreted disulfide catalyst controls extracellular matrix composition and function. *Science* **341**, 74-76.
22. Limor-Waisberg K, Ben-Dor S, Fass D (2013) Diversification of quiescin sulfhydryl oxidase in a preserved framework for redox relay. *BMC Evol. Biol.* **13**, 70.
23. Hakim M, Ezerina D, Alon A, Vonshak O, Fass D (2012) Exploring ORFan domains in giant viruses: structure of mimivirus sulfhydryl oxidase R596. *PLoS One* **7**, e50649.
24. Limor-Waisberg K, Alon A, Mehlman T, Fass D (2012) Phylogenetics and enzymology of plant quiescin sulfhydryl oxidase. *FEBS Lett.* **586**, 4119-4125.
25. Alon A, Grossman I, Kodali V, DiMaio F, Mehlman T, Haran G, Baker D, Thorpe C, Fass D (2012) The dynamic disulphide relay of quiescin sulfhydryl oxidase. *Nature* **488**, 414-418.
26. Hakim M, Mandelbaum A, Fass D (2011) Structure of a baculovirus sulfhydryl oxidase, a highly divergent member of the Erv flavoenzyme family. *J. Virol.* **85**, 9406-9413.
27. DiMaio F, Terwilliger TC, Read RJ, Wlodawer A, Oberdorfer G, Wagner U, Valkov E, Alon A, Fass D, Axelrod HL, Das D, Vorobiev SM, Iwai H, Pokkuluri PR, Baker D (2011) Improved molecular replacement by density- and energy-guided protein structure optimization. *Nature* **473**, 540-543.
28. Heldman N, Vonshak O, Sevier CS, Vitu E, Mehlman T, Fass D (2010) Steps in reductive activation of the disulfide-generating enzyme Ero1p. *Protein Sci.* **19**, 1863-1876.
29. Kogan K, Spear ED, Kaiser CA, Fass D (2010) Structural conservation of components in the amino acid sensing branch of the TOR pathway in yeast and mammals. *J. Mol. Biol.* **402**, 388-398.
30. Blais JD, Chin KT, Zito E, Zhang Y, Heldman N, Harding HP, Fass D, Thorpe C, Ron D (2010) A small molecule inhibitor of endoplasmic reticulum oxidation 1 (ERO1) with selectively reversible thiol reactivity. *J. Biol. Chem.* **285**, 20993-21003.
31. Vitu E, Kim S, Sevier CS, Lutzky O, Heldman N, Bentzur M, Unger T, Yona M, Kaiser CA, Fass D (2010) Oxidative activity of yeast Ero1p on protein disulfide isomerase and related oxidoreductases of the endoplasmic reticulum. *J. Biol. Chem.* **285**, 18155-18165.
32. Alon A, Heckler EJ, Thorpe C, Fass D (2010) QSOX contains a pseudo-dimer of functional and degenerate sulfhydryl oxidase domains. *FEBS Lett.* **584**, 1521-1525.
33. Hakim M, Fass D (2009) Dimer interface migration in a viral sulfhydryl oxidase. *J. Mol. Biol.* **391**, 758-768.
34. Farver O, Vitu E, Wherland S, Fass D, Pecht I (2009) Electron transfer reactivity of the *Arabidopsis thaliana* sulfhydryl oxidase AtErv1. *J. Biol. Chem.* **284**, 2098-2105.
35. Vitu E, Gross E, Greenblatt HM, Sevier CS, Kaiser CA, Fass D (2008) Yeast Mpd1p reveals the structural diversity of the protein disulfide isomerase family. *J. Mol. Biol.* **384**, 631-640.
36. Bar M, Celik Y, Fass D, Braslavsky I (2008) Interactions of β -helical antifreeze protein mutants with ice. *Cryst. Growth Des.* **8**, 2954-2963.
37. Portnaya I, Ben-Shoshan E, Cogan U, Khaflin R, Fass D, Ramon O, Danino D (2008) Self-assembly of bovine beta-casein below the isoelectric pH. *J. Agric. Food Chem.* **56**, 2192-2198.
38. Heckler EJ, Alon A, Fass D, Thorpe C (2008) Human quiescin-sulfhydryl oxidase, QSOX1: probing internal redox steps by mutagenesis. *Biochem.* **47**, 4955-4963.
39. Bar M, Scherf T, Fass D (2008) Two-dimensional surface display of functional groups on a β -helical antifreeze protein scaffold. *Protein Eng. Des. Sel.* **21**, 107-114.
40. Magidovich E, Orr I, Fass D, Abdu U, Yifrach O (2007) Intrinsic disorder in the C-terminal domain of the shaker voltage-activated K⁺ channel modulates its interaction with scaffold proteins. *Proc. Natl. Acad. Sci. USA* **104**, 13022-13027.
41. Ben-Shem A, Fass D, Bibi E (2007) Structural basis for intramembrane proteolysis by rhomboid serine proteases. *Proc. Natl. Acad. Sci. USA* **104**, 462-466.

42. Sevier CS, Qu H, Heldman N, Gross E, Fass D, Kaiser CA (2007) Modulation of cellular disulfide-bond formation and the ER redox environment by feedback regulation of Ero1. *Cell* **129**, 333-344.
43. Vitu E, Bentzur M, Lisowsky T, Kaiser CA, Fass D (2006) Gain of function of an ERV/ALR sulfhydryl oxidase by molecular engineering of the shuttle disulfide. *J. Mol. Biol.* **362**, 89-101.
44. Frenkiel-Krispin D, Wolf SG, Albeck S, Unger T, Peleg Y, Jacobovitch J, Michael Y, Daube S, Sharon M, Robinson CV, Svergun DI, Fass D, Tzfira T, Elbaum M (2007) Plant transformation by *Agrobacterium tumefaciens*: modulation of single-stranded DNA-VirE2 complex assembly by VirE1. *J. Biol. Chem.* **282**, 3458-3464.
45. Sirkis R, Gerst JE, Fass D (2006) Ddi1, a eukaryotic protein with the retroviral protease fold. *J. Mol. Biol.* **364**, 376-387.
46. Gross E, Sevier CS, Heldman N, Vitu E, Bentzur M, Kaiser CA, Thorpe C, Fass D (2006) Generating disulfides enzymatically: reaction products and electron acceptors of the endoplasmic reticulum thiol oxidase Ero1p. *Proc. Natl. Acad. Sci. USA* **103**, 299-304.
47. Bar M, Bar-Ziv R, Scherf T, Fass D (2006) Efficient production of a folded and functional, highly disulfide-bonded beta-helix antifreeze protein in bacteria. *Protein Expr. Purif.* **48**, 243-252.
48. Sevier CS, Kadokura H, Tam VC, Beckwith J, Fass D, Kaiser CA (2005) The prokaryotic enzyme DsbB may share key structural features with eukaryotic disulfide bond forming oxidoreductases. *Protein Sci.* **14**, 1630-1642.
49. Förster F, Medalia O, Zauberman N, Baumeister W, Fass D (2005) Retrovirus envelope protein complex structure *in situ* studied by cryo-electron tomography. *Proc. Natl. Acad. Sci. USA* **102**, 4729-4734.
50. Gross E, Kastner DB, Kaiser CA, Fass D (2004) Structure of Ero1p, source of disulfide bonds for oxidative protein folding in the cell. *Cell* **117**, 601-610.
51. Barnett AL, Wensel DL, Li W, Fass D, Cunningham J M (2003) Structure and mechanism of a co-receptor for infection by a pathogenic feline retrovirus. *J. Virol.* **77**, 2717-2729.
52. Gross E, Sevier CS, Vala A, Kaiser CA, Fass D (2002) New FAD-binding fold and intersubunit disulfide shuttle in the thiol oxidase Erv2p. *Nat. Struct. Biol.* **9**, 61-67.
53. Paz Y, Elazar Z, Fass D (2000) Structure of GATE-16, membrane transport modulator and mammalian ortholog of autophagocytosis factor Aut7p. *J. Biol. Chem.* **275**, 25445-25550.
54. Babor SM, Fass D (1999) Crystal structure of the Sec18p N-terminal domain. *Proc. Natl. Acad. Sci. USA* **96**, 14759-14764.
55. Fass D, Bogden CE, Berger JM (1999) Crystal structure of the N-terminal domain of the DnaB hexameric helicase. *Structure* **7**, 691-698.
56. Fass D, Bogden CE, Berger J (1999) Quaternary Changes in topoisomerase II may direct orthogonal movement of two DNA strands. *Nat. Struct. Biol.* **6**, 322-326.
57. Bogden CE, Fass D, Bergman N, Nichols MD, Berger JM (1999) Structural basis for terminator recognition by the Rho transcription termination factor. *Mol. Cell* **3**, 487-493.
58. Berger JM, Fass D, Wang JC, Harrison SC (1998) Structural similarities between topoisomerases that cleave one or both DNA strands. *Proc. Natl. Acad. Sci. USA* **95**, 7876-7881.
59. Fass D, Davey RA, Hamson CA, Kim PS, Cunningham JM, Berger JM (1997) Structure of a murine leukemia virus receptor-binding glycoprotein at 2.0 Å resolution. *Science* **277**, 1662-1666.
60. Fass D, Blacklow S, Kim PS, Berger JM (1997) Molecular basis of familial hypercholesterolemia from structure of LDL receptor module. *Nature* **388**, 691-693.
61. Chan DC, Fass D, Berger JM, Kim PS (1997) Core structure of gp41 from the HIV envelope glycoprotein. *Cell* **89**, 263-273.
62. Fass D, Harrison SC, Kim PS (1996) Retrovirus envelope domain at 1.7 Å resolution. *Nat. Struct. Biol.* **3**, 465-469.
63. Fass D, Kim PS (1995) Dissection of a retrovirus envelope protein reveals structural similarity to influenza hemagglutinin. *Curr. Biol.* **5**, 1377-1383.
64. Ellenberger T, Fass D, Arnaud M, Harrison SC (1994) Crystal structure of transcription factor E47 E-box recognition by a basic region helix-loop-helix dimer. *Genes Dev.* **8**, 970-980.

65. Ponath PD, Fass D, Liou HC, Glimcher LH, Strominger JL (1993) The regulatory gene, hXBP-1, and its target, HLA-DRA, utilize both common and distinct regulatory elements and protein complexes. *J. Biol. Chem.* **268**, 17074-17082.
66. Gupta S, Fass D, Shimizu M, Vayuvegula B (1989) Potentiation of immunosuppressive effects of cyclosporin A by 1 α ,25-dihydroxyvitamin D₃. *Cell. Immunol.* **121**, 290-297.

Reviews and analyses

1. Fass D, Thorpe C (2018) Chemistry and enzymology of disulfide cross-linking in proteins. *Chem. Rev.* **118**, 1169-1198.
2. Kryshtafovych A, Moulton J, Baslé A, Burgin A, Craig TK, Edwards RA, Fass D, Hartmann MD, Korycinski M, Lewis RJ, Lorimer D, Lupas AN, Newman J, Peat TS, Piepenbrink KH, Prahlad J, van Raaij MJ, Rohwer F, Segall AM, Seguritan V, Sundberg EJ, Singh AK, Wilson MA, Schwede T (2016) Some of the most interesting CASP11 targets through the eyes of their authors. *Proteins* **84**, Suppl. 1, 34-50.
3. Kryshtafovych A, Moulton J, Bales P, Bazan JF, Biasini M, Burgin A, Chen C, Cochran FV, Craig TK, Das R, Fass D, Garcia-Doval C, Herzberg O, Lorimer D, Luecke H, Ma X, Nelson DC, van Raaij MJ, Rohwer F, Segall A, Seguritan V, Zeth K, Schwede (2014) Challenging the state of the art in protein structure prediction: highlights of experimental target structures for the 10th Critical Assessment of Techniques for Protein Structure Prediction Experiment CASP10. *Proteins* **82**, Suppl. 2, 26-42.
4. Alon A, Fass D (2012) Catalysis of disulfide bond formation by the Quiescin sulfhydryl oxidases. eLS Wiley Online Library. DOI: 10.1002/9780470015902.a0024168.
5. Fass D (2012) Disulfide bonding in protein biophysics. *Ann. Rev. Biophys.* **41**, 63-79.
6. Hakim M, Fass D (2010) Cytosolic disulfide bond formation in cells infected with large nucleocytoplasmic DNA viruses. *Antiox. Redox Signal.* **13**, 1261-1271.
7. Erez E, Fass D, Bibi E (2009) How intramembrane proteases bury hydrolytic reactions in the membrane. *Nature* **459**, 371-378.
8. Fass D (2008) The Ero family of sulfhydryl oxidases. *Biochim. Biophys. Acta* **1783**, 371-378.
9. Fass D (2003) Conformational changes in enveloped virus surface proteins during cell entry. *Adv. Prot. Chem.* **64**, 325-362.

Book chapters

1. Fass D, Ilani T. "Disulfide Bond Formation Downstream of the Endoplasmic Reticulum," in *Oxidative Folding of Proteins: Principles, Biological Regulation and Design*. M. J. Feige, editor, RSC Publishing, 2018, pp. 267-284.
2. Fass D, Sevier CS. "The Ero1 Sulfhydryl Oxidase and the Oxidizing Potential of the Endoplasmic Reticulum," in *Oxidative Folding of Peptides and Proteins*. J. Buchner and L. Moroder, editors, RSC Publishing, 2009, pp. 105-120.

Commentaries and editorials

1. Fass D, Semenov SN (2021) An overlooked protein crosslink. *Nature* **593**, 343-344.
2. Fass D (2019) Going for the Golgi: small PDI protein helps ATF6 perform better under stress. *EMBO J.* **38**, e102743.
3. Fass D, Rittinger K (2014) Multi-protein assemblies in signaling. *Curr. Opin. Struct. Biol.* **29**, vi-viii.
4. Ilani T, Fass D (2013) Now at the Met: fine art of reversible sulfoxidation. *Mol. Cell* **51**, 281-282.
5. Fass D (2010) Hunting for alternative disulfide bond formation pathways: endoplasmic reticulum janitor turns professor and teaches a lesson. *Mol. Cell* **40**, 685-686.