Vogt et al., http://www.jem.org/cgi/content/full/jem.20071987/DC1

SUPPLEMENTAL DISCUSSION

N-glycosylation and quality control of proteins undergoing trafficking in the secretory pathway

In the secretory pathway of mammalian cells, glycosidases play a key role in trimming and editing the peptide-linked oligosaccharide, the folding of newly formed glycoproteins, and quality control for nascent proteins in the ER (Fig. 2 B) (1–9). Glucosidases I and II in the ER remove glucose residues from the common oligosaccharide of the nascent polypeptides. This step occurs early in the N-glycosylation maturation process, before other enzymes further trim and edit the glycan moieties on glycoproteins. Moreover, by producing monoglucosylated oligosaccharides, these two enzymes also contribute to the proper folding and subsequent trafficking of glycoproteins in the ER, facilitating concomitant quality control by calnexin-calreticulin. The N-glycans are then processed by ER-mannosidases (such as ER–mannosidase I), which are also involved in glycoprotein folding, quality control, and trafficking. ER-mannosidases may be involved in the proteasomal or nonproteasomal proteolysis of misfolded glycoproteins. Finally, Golgi-endomannosidases provide an alternative pathway for glycan editing, facilitating quality control by calnexin-calreticulin for glycoproteins. During this step, the proteasomal proteolysis of misfolded glycoproteins is promoted. The editing of glycoproteins continues in the Golgi apparatus, with enzymes such as Golgi–mannosidases I and II. A more comprehensive description of the N-glycosylation and quality control processes along the secretory pathway is available from the references (1–9).

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Table S1. Chemical compounds used and their known targets, as reported in published studies

C	Compound	Abbr.	Glu-I	Glu-II	ERM-I	ERM-II	M9M	GM-I	GnT-I	GM-II	Ref.
■	N-(7-oxa-9,9,9-trifluorononyl)deoxynojirimycin	**NF-DNJ**	■								1[a]
	Australine	**Aust**	■	■							2
	N-dodecyldeoxynojirimycin	**ND-DNJ**	■								1, 3
	(2S,5S)-bishydroxymethyl-(3R,4R)-bishydroxypyrrolidine	**DMDP**	■								2, 4
	Miglitol	**Mgt**		■							5
	Bromoconduritol (mixture of isomers)	**Brcd**		■							4, 6
■	Castanospermine	**Cst**	■	■	■	■	■	■		■	2, 6–8
■	N-butyldeoxynojirimycin	**NB-DNJ**	■	■							2, 9
■	Deoxynojirimycin	**DNJ**	■	■							2, 6, 9
■	Nojirimycin-1-sulfonic acid	**NJ-1-S**	■	■							2
■	N-methyldeoxynojirimycin	**NM-DNJ**	■	■							2, 4, 9
■	N-(n-nonyl)deoxynojirimycin	**NN-DNJ**	■	■							1
■	Kifunensine	**Kif**	■	■	■		■	■		■	2, 7, 8, 10
■	1,4-dideoxy-1,4-imino-D-mannitol	**DIM**			■	■		■		■	2, 4, 7
	Deoxymannojirimycin	**DMJ**	■	■	■	■	■	■		■	2, 4, 6–8
	Swainsonine	**Swn**	■	■		■		■		■	2, 4, 7
	Mannostatin A, hydrochloride	**Mst**	■	■	■	■	■	■	■	■	2, 11
	N-(n-butyl)deoxygalactonojirimycin	**NB-DGJ**	■	■	■	■	■	■	■	■	9
	N-(n-nonyl)deoxygalactonojirimycin	**NN-DGJ**	■	■							12
■	N-butyldeoxymannojirimycin	**NB-DMJ**									9
■	D-mannojirimycin	**DM**									[b]
■	5-epi-isofagomine	**5-fgm**									[c]
■	2,5-dideoxy-2,5-imino-D-mannitol	**2-5-DM**									[d]
	1-deoxy-L-idonojirimycin	**1-Dli**									[e]
	Conduritol B	**CdrB**									13, 14
	2-acetamido-1,2-dideoxynojirimycin	**2A-DNJ**									1, 15
	(+)-Valienamine	**Vali**									[f]
	Voglibose	**Vglb**									16

Chemical compounds complementing the 382–387 mutation are indicated in black (column C). The full name and abbreviation of each chemical compound are indicated. Glu-I, Glu-II, ERM-1, ERM-2, M9M, GM-I, GnT-I, and GM-II are enzymes known to be associated with maturation by N-glycosylation. The effects on these enzymes of the chemical compounds tested are indicated in color (red, inhibition; gray, no effect; white, undescribed effects on N-glycosylation enzymes).

[a]An inhibitor of glucosidase I (Toronto Research Chemicals Inc.).

[b]A potent inhibitor of α-mannosidase (Toronto Research Chemicals Inc.).

[c]A selective and very strong inhibitor of beta-glucosidase (Toronto Research Chemicals Inc.).

[d]A glucosidase inhibitor (Toronto Research Chemicals Inc.).

[e]An inhibitor of yeast α-glucosidase (Toronto Research Chemicals Inc.).

[f]A glucosidase inhibitor (Toronto Research Chemicals Inc.).

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