Supplemental material

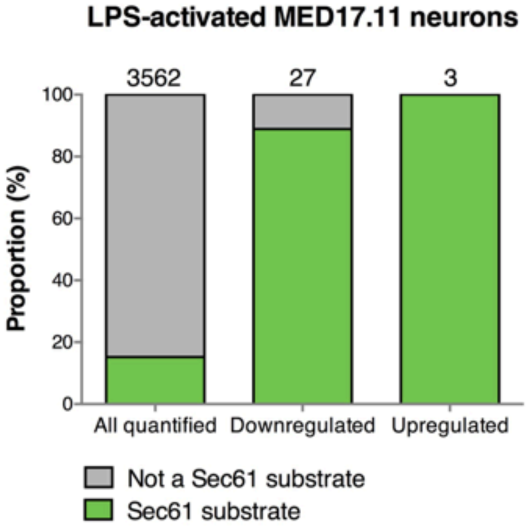

Figure S1: The proportion of Sec61 substrates in "all quantified" proteins is compared to that in "mycolactone-downregulated" or "mycolactone-upregulated" proteins, in MED17.11 cells exposed to mycolactone or not for 30 min, prior to activation with 10 nM LPS. The number of identified proteins in each subset is indicated on the top of each bar.

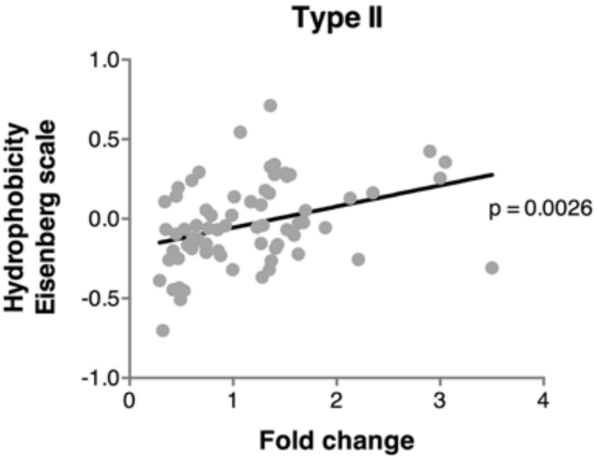

Figure S2: Average hydrophobicity of the 20-aminoacid long segments flanking the first N-terminal TMD, as a function of protein level variation (mycolactone/control relative LFQ intensity factor), in Type II TMPs of mycolactone-exposed MutuDCs. Linear regression line and p-value from Pearson's correlation test are shown.

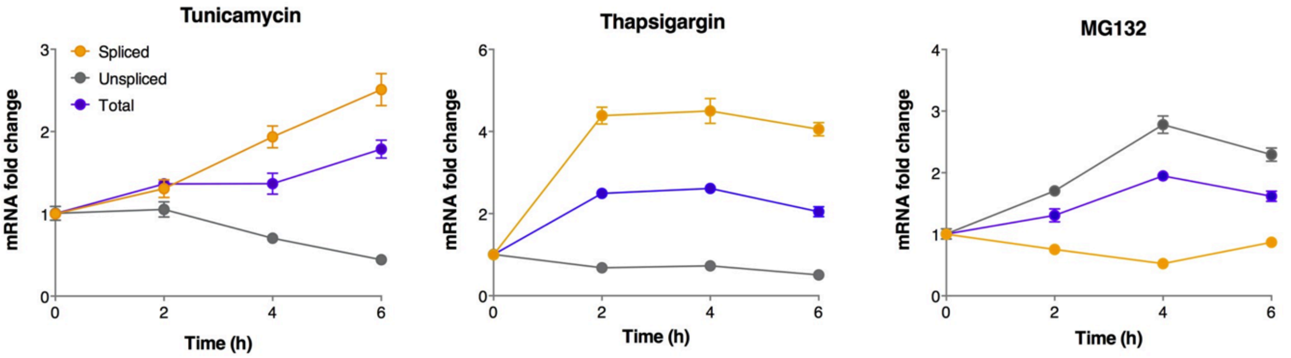

Figure S3: Differential effects of canonical ER stressors on Xbp-1 splicing. The kinetic effects of Tunicamycin (1µM), Thapsigargin (1µM) and MG132 (1 µM) on MutuDC expression of total, spliced and unspliced Xbp-1 are shown.

Table S1. MED17.11 proteins modulated by mycolactone. Excel file with three tabs: [Differentially expressed tab]: List of all proteins found differential expressed in response to mycolactone in both non-activated and LPS activated conditions. [All quantified tab] List all the proteins that were quantified in the analysis. Proteins in each category are shown with Uniprot accession number, FDR, variation extent of mycolactone/control, gene name and an indication of whether the protein is a Sec61 substrate inferred according to www.uniprot.org. Upregulated: significantly upregulated by mycolactone (FDR≤0.1, log2 mycolactone/control ratio>0.5). Downregulated: significantly downregulated by mycolactone (FDR≤0.1, log2 mycolactone/control ratio<-0.5). [Statistics tab] Statistics on Sec61 substrates in each category, as shown in Figures 1 and 2.

Table S2: qPCR primers used in this study

Genebank	Name	Primer-Forward	Primer-Reverse
NM_009078	Rpl-19	TACTGCCAATGCTCGG	AACACATTCCCTTTGACC
NM_022331.1	Herpud1	ACTCCTCGCTGAGCAGATTT	CTCTGTCTGAACGGAAACCA
NM_024439	Vimp/Selenos	GCAGGAAGATCTAAATGCCC	CATGCTGTCCCACATTTCAA
NM_010442.2	Hmox1 (Heme oxygenase 1)	AGGTACACATCCAAGCCGAGA	CATCACCAGCTTAAAGCCTTCT
NM_009735	Beta2 microglobulin	TTCTGGTGCTTGTCTCACTGA	CAGTATGTTCGGCTTCCCATTC
NM_001161413	SLC3a2 /CD98hc	TGATGAATGCACCCTTGTACTTG	TCCCCAGTGAAAGTGGA
NM_001271730	Spliced Xbp1	CTGAGTCCGAATCAGGTGCAG	GTCCATGGGAAGATGTTCTGG
NM_001271730	Unspliced Xbp1	CAGCACTCAGACTATGTGCA	GTCCATGGGAAGATGTTCTGG
NM_001271730	Total Xbp1	TGGCCGGGTCTGCTGAGTCCG	GTCCATGGGAAGATGTTCTGG
NM_001290183	Chop	CCACCACACCTGAAAGCAGAA	AGGTGAAAGGCAGGGACTCA
NM_001163434	Bip	TTCAGCCAATTATCAGCAAACTCT	TTTTCTGATGTATCCTCTTCACCAGT

Table S3: Comparison of mycolactone-modulated proteins across datasets. All human proteins found in the Jurkat cell dataset were mapped to their mouse orthologs when available. Human genes for which no mouse ortholog was found were not included. The numbers in the table correspond to the number of genes that were found upregulated/downregulated/not modulated in multiple datasets; the percentages represent the proportion of these genes to the total above. Note that the total numbers of detected genes are slightly lower than the numbers of detected proteins presented in other figures, due to missing or redundant protein to gene mapping.

		Total	MutuDCs			MED17.11 neurons		
			Not modulated	**Upregulated**	**Downregulated**	**Not modulated**	**Upregulated**	**Downregulated**
Total			2806	169	206	3473	8	45
Jurkat T cells	**Not modulated**	2002	1018 (36.3%)	51 (30.2%)	51 (24.8%)	1137 (32.7%)	1 (12.7%)	3 (6.5%)
	Upregulated	1	0 (0%)	1 (0.6%)	0 (0%)	1 (0.03%)	0 (0%)	0 (0%)
	Downregulated	29	6 (0.2%)	0 (0%)	9 (4.4%)	10 (0.3%)	0 (0%)	3 (6.5%)
MutuDCs	**Not modulated**	2806				2094 (60.3%)	2 (25%)	4 (8.7%)
	Upregulated	169				123 (3.5%)	1 (12.5%)	0 (0%)
	Downregulated	206				131 (3.8%)	0 (0%)	9 (19.6%)

Table S4. Detailed information on MED17.11 neuron peptide and protein identifications