



Figure S1. **EMSAs of additional CrebA binding sites.** For each SPCG, the enhancer region is presented with orange circles representing predicted CrebA binding sites. Green circles indicate gel shifts shown in Fig. 1. In each case, site 1 is to the left. Lanes are numbered from 1–10 or 1–11, and the key is listed at the bottom of the page. CrebA binds to each site and is competed away by unlabeled oligonucleotides that correspond to the same sequence, in a majority of examples. When the binding sequence is mutated (red) in the unlabeled oligos, they are no longer able to compete for CrebA binding.

Table S1. Clustering analysis of GO terms for CrebA target genes

Annotation cluster <sup>a</sup>	GO term	Fold enrichment	P-value
1 (15.12)	Cotranslational protein targeting to membrane	31	$3.1 \times 10^{-19}$
	Protein targeting to membrane	28	$3.0 \times 10^{-18}$
	Protein targeting to ER	30.5	$9.6 \times 10^{-18}$
	SRP-dependent cotranslational protein targeting to membrane	30.5	$9.6 \times 10^{-18}$
	Protein targeting	3.9	$3.1 \times 10^{-6}$
2 (10.63)	Endoplasmic reticulum membrane	11.5	$1.6 \times 10^{-11}$
	Nuclear envelope – endoplasmic reticulum network	11.2	$2.1 \times 10^{-11}$
	Endoplasmic reticulum part	9.7	$4.0 \times 10^{-11}$
3 (8.17)	Secretory pathway	4.4	$4.8 \times 10^{-9}$
	Secretion by cell	4.3	$5.2 \times 10^{-9}$
	Secretion	4.1	$1.2 \times 10^{-8}$
4 (6.35)	Protein localization	3	$3.5 \times 10^{-9}$
	Protein transport	3.1	$3.6 \times 10^{-8}$
	Establishment of protein localization	3	$4.7 \times 10^{-8}$
	Macromolecule localization	2.7	$6.9 \times 10^{-8}$
	Intracellular protein transport	3.2	$7.2 \times 10^{-8}$
	Cellular localization	2.1	$2.0 \times 10^{-5}$
	Intracellular transport	2.2	$3.9 \times 10^{-5}$
	Establishment of cellular localization	2.1	$7.4 \times 10^{-5}$
	Intracellular protein transport across a membrane	32.7	$5.8 \times 10^{-6}$
5 (4.23)	SRP-dependent cotranslational protein targeting to membrane, translocation	32.7	$5.8 \times 10^{-6}$
	Translocation	10.7	$5.9 \times 10^{-3}$
6 (3.78)	COPI coated vesicle membrane	25	$1.4 \times 10^{-6}$
	COPI vesicle coat	25	$1.4 \times 10^{-6}$
	COPI-coated vesicle	22.5	$2.8 \times 10^{-6}$
	Vesicle coat	8.3	$6.3 \times 10^{-4}$
	Coated vesicle membrane	8	$7.5 \times 10^{-4}$
	Cytoplasmic vesicle membrane	8	$7.5 \times 10^{-4}$
	Coated membrane	7.5	$1.0 \times 10^{-3}$
	Membrane coat	7.5	$1.0 \times 10^{-3}$
	Cytoplasmic vesicle part	6.4	$2.1 \times 10^{-3}$
	Vesicle membrane	5.9	$3.1 \times 10^{-3}$
7 (3.58)	Structural constituent of chitin-based cuticle	4.4	$8.4 \times 10^{-5}$
	Structural constituent of cuticle	3.7	$3.9 \times 10^{-4}$
	Insect cuticle protein	4.2	$5.6 \times 10^{-4}$
8 (3.14)	Golgi-associated vesicle	10.9	$9.9 \times 10^{-7}$
	Cytoplasmic membrane-bound vesicle	3.4	$2.3 \times 10^{-3}$
	Cytoplasmic vesicle	3.4	$2.5 \times 10^{-3}$
	Coated vesicle	3.7	$2.6 \times 10^{-3}$
	Membrane-bound vesicle	3.3	$3.0 \times 10^{-3}$
	Vesicle	3.3	$3.2 \times 10^{-3}$

<sup>a</sup>The enrichment score is shown in parentheses.

Table S2. Clustering analysis of GO terms for genes regulated by Creb3L1 T in HeLa cells

Annotation cluster <sup>a</sup>	GO term	Fold enrichment	P-value
1 (9.25)	Golgi vesicle transport	6.9	$2.9 \times 10^{-14}$
	Secretory pathway	3.7	$3.0 \times 10^{-9}$
	Secretion by cell	3.3	$1.4 \times 10^{-8}$
	Secretion	2.8	$8.1 \times 10^{-8}$
2 (5.2)	Intracellular transport	2.1	$1.1 \times 10^{-6}$
	Cellular localization	1.8	$1.1 \times 10^{-5}$
	Establishment of cellular localization	1.8	$2.1 \times 10^{-5}$
3 (4.95)	Response to virus	5.3	$3.7 \times 10^{-8}$
	Response to other organism	2.9	$6.0 \times 10^{-5}$
	Multi-organism process	2.2	$6.4 \times 10^{-4}$
4 (4.94)	Protein transport	2.1	$2.9 \times 10^{-6}$
	Establishment of protein localization	2	$3.6 \times 10^{-6}$
	Protein localization	1.9	$1.8 \times 10^{-5}$
	Macromolecule localization	1.8	$8.8 \times 10^{-5}$
5 (4.24)	PIRSF001733:rfp transforming protein	5.9	$1.2 \times 10^{-5}$
	SPla/Ryanodine receptor SPRY	4.7	$1.7 \times 10^{-5}$
	B302, (SPRY)-like	4.6	$2.2 \times 10^{-5}$
	Butyrophilin-like	5.2	$4.2 \times 10^{-5}$
	Domain:B30.2/SPRY	5.5	$6.7 \times 10^{-5}$
	SPRY	4	$9.7 \times 10^{-5}$
	SPRY-associated	5.6	$1.7 \times 10^{-4}$
	PRY	4.7	$5.7 \times 10^{-4}$
	Localization	1.4	$8.3 \times 10^{-6}$
6 (4.2)	Establishment of localization	1.4	$1.5 \times 10^{-4}$
	Transport	1.4	$1.9 \times 10^{-4}$
7 (3.29)	Positive regulation of cellular metabolic process	2.1	$2.2 \times 10^{-4}$
	Positive regulation of metabolic process	2	$3.1 \times 10^{-4}$
	Positive regulation of transcription	2.2	$8.4 \times 10^{-4}$
	Positive regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolic process	2.1	$1.2 \times 10^{-3}$
	Endoplasmic reticulum part	2	$1.3 \times 10^{-4}$
8 (3.27)	Nuclear envelope-endoplasmic reticulum network	1.9	$9.1 \times 10^{-4}$
	Endoplasmic reticulum membrane	1.9	$1.4 \times 10^{-3}$
9 (3.1)	Regulation of I-kappaB kinase/NF-kappaB cascade	3.7	$2.0 \times 10^{-4}$
	Positive regulation of I-kappaB kinase/NF-kappaB cascade	3.7	$3.8 \times 10^{-4}$
	I-kappaB kinase/NF-kappaB cascade	3	$8.2 \times 10^{-4}$
	Positive regulation of signal transduction	2.5	$6.2 \times 10^{-3}$
10 (3.03)	Vesicle coat	5.3	$9.2 \times 10^{-5}$
	Coated vesicle membrane	4.9	$1.6 \times 10^{-4}$
	Golgi-associated vesicle	4.6	$2.8 \times 10^{-4}$
	Membrane coat	4.3	$5.0 \times 10^{-4}$
	Coated membrane	4.3	$5.0 \times 10^{-4}$
	Cytoplasmic vesicle membrane	2.8	$5.7 \times 10^{-3}$
	Cytoplasmic vesicle part	2.7	$8.1 \times 10^{-3}$
	Vesicle membrane	2.5	$1.2 \times 10^{-2}$

<sup>a</sup>The enrichment score is shown in parentheses.

**Table S3 lists genes regulated by CrebA and associated human orthologues, and is available as a PDF file. Table S4 lists genes up-regulated by Creb3L1 T expression in HeLa cells, and is available as an Excel file.**