

**Table S13:** Ranking of dimethylated (naturally unmodified) N-termini reduced in the TAILS experiment comparing wild-type and *Ctsb*<sup>-/-</sup> skin.

Non Prime Site	Prime Site	Fold change (log <sub>2</sub> ) of ASAPRatio (replicate 1)	Fold change (log <sub>2</sub> ) of ASAPRatio (replicate 2)	Ranking (max. 6 points / min. -6 points)	Uniprot ID	Protein Name
YGGGGGGYG	GGSGYGGGGGGYGGGEGYSISPNSYR	-5.64	-6.64	4	E9QNN1_MOUSE	ATP-dependent RNA helicase A
FEHRLGEAAR	SLGNAGNEIGR	-4.06	-1.06	4	DMKN_MOUSE	Dermokine;
IIRKVVQRVD	SSGAIDTQQHEEVELR	-1.84	-1.32	4	ANK1_MOUSE	Ankyrin-1;
DFHRCEKAMT	AKGGDVSCEWYR	-1.29	-2.25	3	CX6B1_MOUSE	Cytochrome c oxidase subunit 6B1;
HSKINFRDKR	SALQSIWASQTTDGKLEVTKDVER	-2.40	-3.18	2	SERPH_MOUSE	Serpin H1;
SCLVLAARHA	SASSTNLKDVLSNLPKEQAR	-2.56	-1.40	2	CISY_MOUSE	Citrate synthase, mitochondrial;
NIDIRSAFKR	SGEGQEDAGELDFSGLLKR	-6.64	-2.32	2	D3YU50_MOUSE	RIKEN cDNA 8030451F13, isoform CRA_c
AITARRQHKL	SVMLQIAATELEKEESR	-1.32	-1.40	2	TNNI2_MOUSE	Troponin I, fast skeletal muscle;
KIREGEVEVL	KATEMVEVGPEDVEGAER	-0.84	-1.64	2	PTRF_MOUSE	Polymerase I and transcript release factor;
ASGPENFQVG	SMPPAQQTSGQMHR	-0.84	-4.32	2	TLN1_MOUSE	Talin-1;
SVTREDSGQY	AAYISNAVGAAYSSAR	-6.64	-4.64	1	OBSCN_MOUSE	Obscurin;
KNVREATESF	ASDPILYRPVAVALDTKGPEIR	-1.18	-1.09	1	KPYM_MOUSE	Pyruvate kinase isozymes M1/M2;
WTGYFGKVLV	ASTSYLPSQVTEMFNQGR	-2.94	-3.84	1	WIPI2_MOUSE	WD repeat domain phosphoinositide-interacting protein 2;
LASLLSGQA	EVEDASEEAPLR	-0.76	-1.64	1	SRCA_MOUSE	Sarcalumenin;
LSKDITANTW	AVTVDPCCSTNAKR	-6.64	-2.74	1	PPR3A_MOUSE	Protein phosphatase 1 regulatory subunit 3A;
AIPNLRENYG	ELADCCTKQEPER	-3.84	-2.74	1	ALBU_MOUSE	Serum albumin;
PSNQVIMLTF	GKFDVDPDYCR	-1.47	-6.64	1	PCOC1_MOUSE	Procollagen C-endopeptidase enhancer 1;
TQCEKIVQKY	GYTHLSTGDLR	-1.84	-1.15	1	KAD1_MOUSE	Adenylate kinase isoenzyme 1;
ILLWLYGADG	NIVMTQSPKSMMSVGER	-1.06	-1.56	1	KV5A2_MOUSE	Ig kappa chain V-V region MOPC 21;
M	SATHHKTSLPQGV	-6.64	-3.32	1	LEG7_MOUSE	Galectin-7;
GMLPEKDCRY	ALYDASFETKESR	-1.25	-0.92	0	DEST_MOUSE	Dextrin;
PREIFKQKER	AMSTTSVTSSQPGKLR	-1.18	-2.12	0	DBNL_MOUSE	Drebrin-like protein;
CDIDIRKDL	ANNVMMSGTTMYPGIADR	-2.84	-3.84	0	ACTS_MOUSE	Actin, alpha skeletal muscle;
PKLPGRVAFG	EDIDLPEFDAR	-5.64	-5.64	0	CATB_MOUSE	Cathepsin B;
D	IQMTQTSSLSASLGDR	-3.84	-1.29	0	KV5AF_MOUSE	Ig kappa chain V-V region HP 91A3;
MYTPIQ	SGSPFPASVQDPLHIWR	-2.64	-1.52	0	CAPG_MOUSE	Macrophage-capping protein;
AMKANTMSNY	SLLPASLLDHR	-1.22	-1.64	0	ST2B1_MOUSE	Sulfotransferase family cytosolic 2B member 1;
IFVKAVLVGT	DDEATILADNKCMCTR	-0.84	-2.94	-1	IGJ_MOUSE	Immunoglobulin J chain;
PTKETGWASF	SEFTSSLTKESLR	-0.86	-3.18	-1	PP6R3_MOUSE	Serine/threonine-protein phosphatase 6 regulatory subunit 3;
WTHEVFSSRS	SEVVLSDGDEDEYQR	-0.81	-1.52	-1	E9Q616_MOUSE	Ahnak
SGLLLTQG	EEAQEIDCNDEAVFQAVDASLKKLNAR	-1.84	-3.18	-1	Q6S9I3_MOUSE	HMW kininogen-II
APPWKDSKFF	KDAPDGPTVVLTVDGR	-6.64	-6.64	-1	FA12_MOUSE	Coagulation factor XII;
EDVQETDSQ	KDQSPASHEIATNLGDFAIPLYR	-5.64	-1.79	-1	A1AT2_MOUSE	Alpha-1-antitrypsin 1-2;
MVHL	TDAEKSAVSCLVAKVNPDEVGGEALGR	-6.64	-5.06	-1	HBB2_MOUSE	Hemoglobin subunit beta-2;
SLLGSVQGY	MEQASKTVQDALSSVQESDIAVVAR	-1.00	-2.84	-2	APOC3_MOUSE	Apolipoprotein C-III;
IENHEGVRFF	DEILEASDGIMVAR	-1.18	-1.03	-2	KPYM_MOUSE	Pyruvate kinase isozymes M1/M2;
PSSGAATTV	SEKPGKAAEVGDDFLGDFVVGER	-2.74	-2.06	-2	CLIP2_MOUSE	CAP-Gly domain-containing linker protein 2;