

# Supplementary Material

## LC-MS based Cleavage Site Profiling of the Proteases ADAM10 and ADAM17 using Proteome-derived Peptide Libraries

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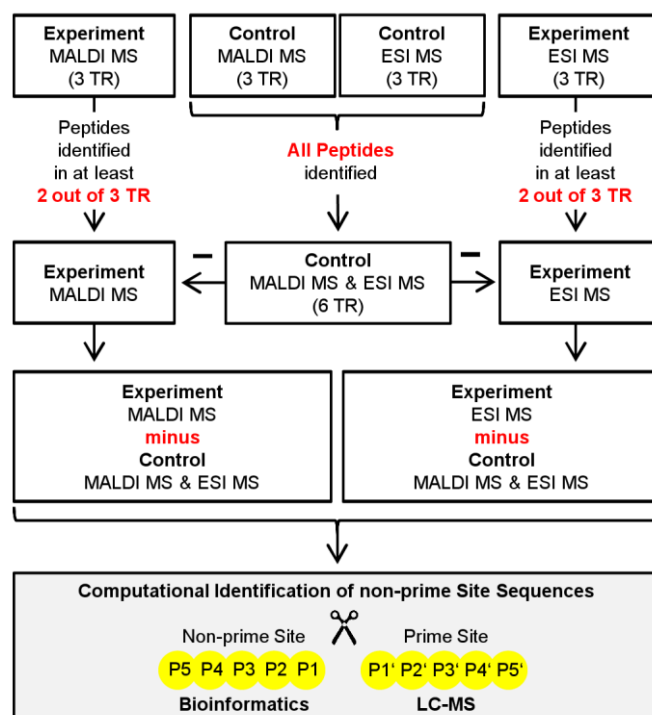
**Supplementary Table 1.** Purity of the murine enzyme preparations of ADAM10 and ADAM17. Proteins and the number of peptides and unique peptides identified in auto-proteolysis of ADAM10 (A) and ADAM17 (B) using Proteome Discoverer 1.4 (database: Swissprot containing 257,964 sequences; no enzyme specificity; for identification only proteins with at least two peptides per protein were considered).

**A) ADAM10**

Protein Description	Organism	Accession Number	# Peptides	# Unique Peptides
ADAM10 precursor	Mus musculus (Mouse)	O35598	32	21
	Homo sapiens (Human)	O14672	11	0
	Bos taurus (Bovine)	Q10741	6	0
	Rattus norvegicus (Rat)	Q10743	5	0
	Xenopus laevis (African clawed frog)	Q8JIY1	5	0
Alpha-2-HS-glycoprotein precursor	Bos taurus (Bovine)	P12763	6	6

**B) ADAM17**

Protein Description	Organism	Accession Number	# Peptides	# Unique Peptides
ADAM 17	Sus scrofa (Pig)	O77636	7	0
ADAM 17 precursor	Mus musculus (Mouse)	Q9Z0F8	41	12
	Rattus norvegicus (Rat)	Q9Z1K9	29	0
	Homo sapiens (Human)	P78536	12	0
Alpha-2-HS-glycoprotein precursor	Bos taurus (Bovine)	P12763	3	3
Major envelope glycoprotein precursor	Autographa californica nuclear polyhedrosis virus (AcMNPV)	P17501	4	4
Tubulin alpha chain	Plasmodium yoelii yoelii	P12543	2	0
	Plasmodium falciparum (isolate K1 / Thailand)	P14642	2	0
Tubulin alpha chain, testis-specific	Oncorhynchus mykiss (Rainbow trout)	P18288	2	0
Tubulin alpha-1 chain	Drosophila melanogaster (Fruit fly)	P06603	2	0
	Paracentrotus lividus (Common sea urchin)	P18258	2	0
Tubulin alpha-2 chain	Drosophila melanogaster (Fruit fly)	P06604	2	0
	Homo sapiens (Human)	Q13748	2	0
Tubulin alpha-2/alpha-4 chain	Patella vulgata (Common limpet)	P41383	2	0
Tubulin alpha-3 chain	Drosophila melanogaster (Fruit fly)	P06605	2	0



**Supplementary Figure 1.** Scheme of the handling of the peptides identified by MALDI MS or ESI MS in the three technical replicates (TR) of experiments and controls. For the experiments only peptides identified in at least two out of three TR were considered, whereas for the controls all peptides identified were considered. To identify cleavage events catalyzed by ADAM10 or ADAM17 peptides identified in the control (merged data from LC-MALDI MS and LC-ESI MS) were subtracted from either MALDI MS or ESI MS identified peptides in the experiment. The remaining peptides out of an experiment were combined and further analyzed.

**Supplementary Table 2.** Cleavage sites identified in the experiment „Lys-C peptide library + ADAM10“; number of cleavage sites: 69; x = ambiguous amino acid

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
AELGRLGYSVYEDAQYIGHAFK				S	N	A	E	L	G	R
AVIHGLK	A	F	I	A	N	A	V	I	H	G
CNWTPGAATIKPTVEDSK	G	T	V	L	P	C	N	W	T	P
DLLTRDEK	R	R	A	A	R	D	L	L	T	R
FNDSQRQATK	T	V	P	A	Y	F	N	D	S	Q
FSADANTK	I	I	A	D	A	F	S	A	D	A
FVNELPK	P	E	F	L	P	F	V	N	E	L
GLTATGKK	H	R	E	A	R	G	L	T	A	T
GMAFRVPTVDVSVVDLTVK				L	T	G	M	A	F	R
HMLDLSEETDEENISTCVK	P	L	F	S	S	H	M	L	D	L
HTAGRYANK	P	I	F	V	A	H	T	A	G	R
IADLSK				A	T	I	A	D	L	S
IALDTK	x	x	x	x	x	I	A	L	D	T
IATAIEK	x	x	x	x	R	I	A	T	A	I
IAYGLDK	P	T	A	A	A	I	A	Y	G	L
IIDDDVPTILQGAK	G	V	A	Q	R	I	I	D	D	D
ILTGDESSK	A	V	Q	A	A	I	L	T	G	D
IRADPAFKPTEK	S	A	H	E	A	I	R	A	D	P
LAALQIEDPSADELRK	A	L	S	D	A	L	A	A	L	Q
LAAQDVAAK	P	Y	A	A	M	L	A	A	Q	D
LAYGLEK	P	T	A	A	A	L	A	Y	G	L
LHGEGSGEK	G	A	L	M	A	L	H	G	E	G
LIFAGK	P	D	Q	Q	R	L	I	F	A	G
LIGDAK	T	x	x	E	R	L	I	G	D	A
LIGILENK	E	T	P	S	P	L	I	G	I	L
LILADSEIEISSEK	L	S	Y	A	A	L	I	L	A	D
LISDYADELAEALQPVIVNTPHLK	A	L	Q	A	R	L	I	S	D	Y
LLELTQKRMSK	D	L	L	W	L	L	L	E	L	T
LLGENIGMK	Y	E	C	S	F	L	L	G	E	N
LLLQGGNAAPSAADIK	Y	L	A	A	Y	L	L	L	V	Q
LMVGKDEEQVK	A	Q	A	E	A	L	M	V	G	K
LNPYAK	Q	V	L	L	R	L	N	P	Y	A
LPANLVDLNVPAK	P	V	Y	L	G	L	P	A	N	L
LPLQDVYK			P	L	R	L	P	L	Q	D
LQEFMIAPTGA	G	G	A	L	A	L	Q	E	F	M
LQQTAFDK	V	H	S	F	R	L	Q	Q	T	A
LTEVRAEDEAALAK	S	A	V	A	A	L	T	E	V	R
LTGIRDYVLNK	C	Q	Y	A	Y	L	T	G	I	R
LTGIRDYVLNKK	C	Q	Y	A	Y	L	T	G	I	R
LTVSEEVK	L	T	P	A	R	L	T	V	S	E
LVDDLRLPEFAGYSK	L	D	P	Q	Y	L	V	D	D	L
LVEQAK	D	A	P	Q	N	L	V	E	Q	A
LVIDRLLPYWQDVIAK	T	E	S	L	A	L	V	I	D	R
MIAPTGA	A	L	Q	E	F	M	I	A	P	T
NIQTAEALDLIVDAIK	G	G	V	A	P	N	I	Q	T	A
NSNLQDILAANAK	F	T	L	S	H	N	S	N	L	Q
QVLEVVDK	G	V	L	S	F	Q	V	L	E	V
RAAEENFNADDK	A	I	A	E	A	R	A	A	E	E
RVVDLIEYVAKA	Y	G	Y	S	A	R	V	V	D	L
RVVDLVEHVAKA	Y	G	Y	S	T	R	V	V	D	L
SHLGRPNGERNEK	Y	V	V	L	A	S	H	L	G	R
SLLPTFGAK	G	W	D	H	L	S	L	L	P	T
TGIRDYVLNK	Q	Y	A	Y	L	T	G	I	R	D
THTALVSYK	L	W	S	M	D	T	H	T	A	L
TSNGGAAYFAGK	P	I	I	L	Q	T	S	N	G	G
VFDAPQNLVEQAK	E	I	M	L	P	V	F	D	A	P
VHGEEDPTKK	Y	V	S	G	R	V	H	G	E	E
VLLSAPLSK	S	S	x	R	R	V	L	L	S	A

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
VMGVNEEK	T	A	P	M	F	V	M	G	V	N
VSLAASRAAAAEK	N	A	I	L	G	V	S	L	A	A
VSMAAARAAAAEK	N	A	I	L	G	V	S	M	A	A
VTLGPDGIEK	F	F	A	S	P	V	T	L	G	P
VVDLIEYVAKA	G	Y	S	A	R	V	V	D	L	I
WGSSNVDIAIDSTGVFK	P	A	N	L	P	W	G	S	S	N
YAALILADSEIEISSEK	E	S	A	L	S	Y	A	A	L	I
YAGEVSHDDK	S	T	H	G	R	Y	A	G	E	V
YISNPLNFGADIVVHSATK	T	F	L	S	P	Y	I	S	N	P
YKLDVDELGDVAQK	P	Q	A	D	F	Y	K	L	D	V
YQVTPDEEDEEEDEE	Y	R	L	A	F	Y	Q	V	T	P

**Supplementary Table 3.** Cleavage sites identified in the experiment „Glu-C peptide library + ADAM10“; number of cleavage sites: 149; x = ambiguous amino acid

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
AAGFLE		L	P	Q	R	A	A	G	F	L
AFPSAINQD	P	H	A	L	K	A	F	P	S	A
AIKKKDE	S	S	T	S	Y	A	I	K	K	K
AKAVGKVLPE	S	S	T	G	A	A	K	A	V	G
ATFPIAQPATDVE	V	L	S	A	A	A	T	F	P	I
AVFSAPIRPD	A	L	P	L	P	A	V	F	S	A
AVGKVLPE	T	G	A	A	K	A	V	G	K	V
AVQAAILTGDE	V	A	Y	G	A	A	V	Q	A	A
CLSALKNE	A	V	F	A	R	C	L	S	A	L
CNWTPGAATIKPTVE	G	T	V	L	P	C	N	W	T	P
FAGKGISNE	G	G	A	A	Y	F	A	G	K	G
FAGKQLE	Q	Q	R	L	I	F	A	G	K	Q
FDNINNE					F	F	D	N	I	N
FFDFFDNINNE	S	F	N	S	P	F	F	D	F	F
FGNCHGLYAGD	S	I	A	A	A	F	G	N	C	H
FILADAGLE	I	S	F	A	A	F	I	L	A	D
FITTVPCPWLD	N	G	S	Q	F	F	I	T	T	V
FKKTHGAPTDE	P	H	F	N	P	F	K	K	T	H
FKLIDVDGKPKIQVE	M	K	H	F	P	F	K	L	I	D
FKSTLEPVE	L	N	A	A	L	F	K	S	T	L
FKSTLEPVEQVLKD	L	N	A	A	L	F	K	S	T	L
FKTAGIQIVADDLTVTNPARIATAIE	A	W	S	H	F	F	K	T	A	G
FNSPFFD				M	S	F	N	S	P	F
FRVPTVDVSVVD	L	T	G	M	A	F	R	V	P	T
FSADANTKTVDKE					A	F	S	A	D	A
FVAIWKHGIVEE		G	T	T	P	F	V	A	I	W
FYDSPQQD	I	W	V	C	P	F	Y	D	S	P
GKITYLKGE				S	K	G	K	I	T	Y
GVLGYTE		G	x	x	K	G	V	L	G	Y
HDGKVKIGLDCASSE	I	K	A	A	G	H	D	G	K	V
HKGVNLPGTDVDLPALSE	G	K	I	C	S	H	K	G	V	N
HMLDLSEE	P	L	F	S	S	H	M	L	D	L
IAISQSDADSE	Y	K	F	Q	Y	I	A	I	S	Q
IAYGLDKKGKEE	P	T	A	A	A	I	A	Y	G	L
IFAGKQLE		Q	Q	R	L	I	F	A	G	K
IIKGWGE	L	K	P	L	A	I	I	K	G	W
IINVIGEPIDE		T	L	G	R	I	I	N	V	I
IKQAIASNV	A	N	P	A	A	I	K	Q	A	I
IKTGAPARSE	L	R	T	G	Q	I	K	T	G	A
ILADAGLE	S	F	A	A	F	I	L	A	D	A
ILGIIIE				L	K	I	L	G	I	I
ILQVFE	V	A	G	A	Q	I	L	Q	V	F
ILSQAPSELE	S	V	Q	S	K	I	L	S	Q	A
ILSQAPTELE	A	P	Q	A	K	I	L	S	Q	A
IMSPVGNPE					Y	I	M	S	P	V
INQDNYPNGGFTAE	A	F	P	S	A	I	N	Q	D	N
IVGIATTFD	A	A	G	C	K	I	V	G	I	A
IVVAKSGEL	A	T	K	A	R	I	V	V	A	K
IVWNGPPGVFE	A	K	A	K	T	I	V	W	N	G
KAFPSAINQD		P	H	A	L	K	A	F	P	S
KAFPSAINQDNYPNGGFTAE		P	H	A	L	K	A	F	P	S
KASGAFTGE	Q	N	A	Y	L	K	A	S	G	A
KIATYQE				G	x	K	I	A	T	Y
KKTHGAPTDE	H	F	N	P	F	K	K	T	H	G
LAADVPLEPE	A	S	T	S	K	L	A	A	D	V
LAKQAFDDAIAE		K	A	C	H	L	A	K	Q	A
LAKVIND	N	C	L	A	P	L	A	K	V	I
LAKVINDAFGIEE	N	C	L	A	P	L	A	K	V	I

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
LASKLGDKAASE	S	I	R	K	F	L	A	S	K	L
LIASKTFTTAE		T	T	L	F	L	I	A	S	K
LIDHIKVE	S	Y	A	K	Y	L	I	D	H	I
LIDVAVE	P	T	Y	A	K	L	I	D	V	A
LIDVDGKPQIQVE	H	F	P	F	K	L	I	D	V	D
LIFAGKQLE			Q	Q	R	L	I	F	A	G
LIGDAAKNQAALNPRNTVFD					R	L	I	G	D	A
LIGRNFNDPE			A	K	R	L	I	G	R	N
LIADSE		P	L	H	C	L	I	I	A	D
LILADSEIE	L	S	Y	A	A	L	I	L	A	D
LIYVPLPDE					Q	L	I	Y	V	P
LKAFPSAINQD			P	H	A	L	K	A	F	P
LKAFPSAINQDNYPNGGFTAE			P	H	A	L	K	A	F	P
LKASGFTGE	A	Q	N	A	Y	L	K	A	S	G
LKGALAKVPE	L	G	A	V	A	L	K	G	A	L
LKGDAGVSGVVKFE	Q	A	V	A	V	L	K	G	D	A
LLLQGGNAAPSAADIKAVVE	Y	L	A	A	Y	L	L	L	V	Q
LLPWFDGMLE	H	C	A	K	K	L	L	P	W	F
LLQTPIDMSLKPND	N	V	P	A	K	L	L	Q	T	P
LLRIEEE	A	K	L	N	Q	L	L	R	I	E
LLTDYLDRAE			Y	Q	A	L	L	T	D	Y
LNFSGEEIE	T	L	F	A	A	L	N	F	S	G
LNQLLRIEEE		R	L	A	K	L	N	Q	L	L
LPTFGAKDYE		H	L	S	L	L	P	T	F	G
LQVQIPATPTSLE	A	S	P	A	L	L	Q	V	Q	I
LSDPKQLE	I	R	Y	x	x	L	S	D	P	K
LSLQDYLNQQANNQFNKVPE	P	K	T	A	Q	L	S	L	Q	D
LTAATNAKQ	x	x	Q	A	x	L	T	A	A	T
LTGMAFRVPTVDVSVVD		L	Q	G	K	L	T	G	M	A
LTQDKSFND					K	L	T	Q	D	K
LVAPLKPLIE	C	S	T	A	G	L	V	A	P	L
LVDDLPE			P	Q	Y	L	V	D	D	L
LVDDVIYE				A	K	L	V	D	D	V
LVDIKKE	A	K	N	P	V	L	V	D	I	K
LVGGASLKPE				G	F	L	V	G	G	A
LVGGHE	P	x	K	L	P	L	V	G	G	H
LVQGGNAAPSAADIKAVVE	A	A	Y	L	L	L	V	Q	G	G
LVSWYDNE	P	K	F	V	K	L	V	S	W	Y
LYQAGGAPE	P	I	M	S	K	L	Y	Q	A	G
MIAPMIE	C	G	P	C	K	M	I	A	P	M
QLTSKLIPE	x	S	T	L	A	Q	L	T	S	K
QRFQPGTSNETPEE	Y	K	A	S	Q	Q	R	F	Q	P
RAGKVKSQTPKVE	H	G	S	L	A	R	A	G	K	V
RKTGVIVGE		Q	I	L	K	R	K	T	G	V
RQAVVNPE	G	I	P	A	K	R	Q	A	V	V
RTGQIKTGAPARSE	L	V	V	G	L	R	T	G	Q	I
RTKYDVAVDE	H	L	V	L	P	R	T	K	Y	D
RVDFKNPHDIE	Q	S	V	G	C	R	V	D	F	K
RVPTVDVSVVD	T	G	M	A	F	R	V	P	T	V
RYGASAGNVGDE	S	L	T	K	K	R	Y	G	A	S
SAADIKAVVE	G	N	A	A	P	S	A	A	D	I
SADANTKTVTDKE				A	F	S	A	D	A	N
SKLGDKAASE	R	K	F	L	A	S	K	L	G	D
SKNLVNDE					Y	S	K	N	L	V
SPSGATKARIVVAKSGEL			S	L	G	S	P	S	G	A
STQLLADIIE	A	S	S	V	Y	S	T	Q	L	L
SVGCRVDFKNPHDIE	L	G	T	A	Q	S	V	G	C	R
SVKDYPAAEE	P	I	L	A	P	S	V	K	D	Y
SVYDSRGNPTVE	K	V	Y	A	R	S	V	Y	D	S
TFGAKDYE	L	S	L	L	P	T	F	G	A	K
TGQIKTGAPARSE	V	V	G	L	R	T	G	Q	I	K

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
TSITRARFEE				F	Y	T	S	I	T	R
TSKLIPE	T	L	A	Q	L	T	S	K	L	I
TTVPCPWLD	S	Q	F	F	I	T	T	V	P	C
VAGKVQPE					K	V	A	G	K	V
VAPLKPLIE	S	T	A	G	L	V	A	P	L	K
VFDAPQNLVE		I	M	L	P	V	F	D	A	P
VFTDVE	W	G	T	I	L	V	F	T	D	V
VMGVNE	T	A	P	M	F	V	M	G	V	N
VQAAILTGDE	A	Y	G	A	A	V	Q	A	A	I
VSWYDNE	K	F	V	K	L	V	S	W	Y	D
VTIISAMGEE				L	M	V	T	I	I	S
VTYIQVE	G	H	Y	A	P	V	T	Y	I	Q
VVDLIE	G	Y	S	A	R	V	V	D	L	I
VVFKLYND	Q	P	I	G	R	V	V	F	K	L
VWAIGTGLAATPE					P	V	W	A	I	G
VYARSVYD	M	A	V	S	K	V	Y	A	R	S
WFDGMLE	K	K	L	L	P	W	F	D	G	M
WGSSNVDIAID	P	A	N	L	P	W	G	S	S	N
WGSSNVDIAIDSTGVFKE	P	A	N	L	P	W	G	S	S	N
WQGLDNGPE	G	I	P	A	G	W	Q	G	L	D
WTKGFDIPNIE	G	I	L	Q	R	W	T	K	G	F
WTKGFDIPNVE	G	I	L	Q	R	W	T	K	G	F
YIQVE	x	x	x	x	x	Y	I	Q	V	E
YISGQINE					P	Y	I	S	G	Q
YLIDHIKVE	A	S	Y	A	K	Y	L	I	D	H
YQAGGAPE	I	M	S	K	L	Y	Q	A	G	G
YQAGGAPGGAAGGAPGGFPGGAPPAPE	I	M	S	K	L	Y	Q	A	G	G
YTSITRARFEE					F	Y	T	S	I	T
YVGNRADTRE	x	I	x	G	S	Y	V	G	N	R
YVVDTSK	x	I	x	G	R	Y	V	V	D	T



**Supplementary Table 4.** Cleavage sites identified in the experiment „Lys-C peptide library + ADAM17“; number of cleavage sites: 197; x = ambiguous amino acid

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
AAAGAAAVANQGKK	L	D	P	E	A	A	A	A	G	A
AAGFLLEK	D	L	P	Q	R	A	A	G	F	L
AARPTRPDK	N	V	I	H	R	A	A	R	P	T
AELGRLGYSVYEDAQYIGHAFK				S	N	A	E	L	G	R
AFAAEEIDPKK	A	T	L	G	A	A	F	A	A	E
AFGNCHGLYAGDIALRPEILAEHQK	F	S	I	A	A	A	F	G	N	C
AFKPTEK	I	R	A	D	P	A	F	K	P	T
AFRVPTVDVSVVDLTVK		L	T	G	M	A	F	R	V	P
AFRVQVGDIVTVGQCRPISK	V	H	V	S	P	A	F	R	V	Q
AGAAAVANQGKK	P	E	A	A	A	A	G	A	A	A
AGITVYK	A	P	I	L	C	A	G	I	T	V
AIAYGLDK	E	P	T	A	A	A	I	A	Y	G
AIAYGLGAGK	E	P	T	A	A	A	I	A	Y	G
AIRGFLSDLPDFEK	T	M	V	R	R	A	I	R	G	F
AIRPAGQATQK	S	E	I	Q	S	A	I	R	P	A
AQSHNPIENK	D	F	I	L	A	A	Q	S	H	N
ARAAAAEK	V	S	M	A	A	A	R	A	A	A
ARAGELLK	G	Q	Q	E	A	A	R	A	G	E
ARTPANAAPASTPLK	P	V	A	V	P	A	R	T	P	A
AVAAVFEQK	T	V	A	A	S	A	V	A	A	V
AVFSAPIRPDIVHTVFTSVNK	A	L	P	L	P	A	V	F	S	A
CNWTPGAATIKPTVEDSK	G	T	V	L	P	C	N	W	T	P
FLAILGGAK	N	P	T	R	P	F	L	A	I	L
FRSTLDPVEK	L	C	A	D	L	F	R	S	T	L
FRVPTVDVSVVDLTVK	L	T	G	M	A	F	R	V	P	T
FSADANTK	I	I	A	D	A	F	S	A	D	A
FTFVCPTEIIAFSEAAK	F	I	P	L	A	F	T	F	V	C
IACRFDELLEK	C	H	T	A	H	I	A	C	R	F
IADLSK				A	T	I	A	D	L	S
IALDTK	x	x	x	x	x	I	A	L	D	T
IATAIEK	x	x	x	x	R	I	A	T	A	I
IAYGLDK	P	T	A	A	A	I	A	Y	G	L
IFNLQVPTK	Y	E	T	L	P	I	F	N	L	Q
IGSEVYHNLK	A	E	A	x	R	I	G	S	E	V
IIADAFSADANTK	L	P	V	D	F	I	I	A	D	A
IIEIAK	L	A	M	D	E	I	I	E	I	A
IIGALK		N	N	E	L	I	I	G	A	L
IINEPTAAAIAYGLDK	x	N	V	L	R	I	I	N	E	P
ILCAGITVYK	A	x	V	A	P	I	L	C	A	G
ILTGDESSK	A	V	Q	A	A	I	L	T	G	D
IQLSPK	D	A	x	A	G	I	Q	L	S	P
IRADPAFKPTEK	S	A	H	E	A	I	R	A	D	P
IRAGIIIAK	E	V	A	G	A	I	R	A	G	I
IRRGNVCGDAK					E	I	R	R	G	N
IRTANDVLTIREVLGEQ GK	V	F	A	S	F	I	R	T	A	N
ISSMVLGK	F	T	P	E	Q	I	S	S	M	V
IYAALPTIK	T	S	N	Q	R	I	V	A	A	L
IVAHVDHGK	x	R	N	x	x	I	V	A	H	V
IVALRK	S	T	I	F	L	I	V	A	L	R
IVGLDK	P	D	E	E	N	I	V	G	L	D
IVSNDELSK	G	Q	S	L	S	I	V	S	N	D
IWADIFAK	V	P	V	E	N	I	W	A	D	I
LAALQIEDPSADELRK	A	L	S	D	A	L	A	A	L	Q
LAAQDVAAK	P	Y	A	A	M	L	A	A	Q	D
LAYGLEK	P	T	A	A	A	L	A	Y	G	L
LCADLFRSTLDPVEK	A	R	F	E	E	L	C	A	D	L
LEAARDSK	T	A	V	A	A	L	E	A	A	R
LGGFAITK	L	E	P	R	F	L	G	G	F	A

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
LHGEESGEEK	G	A	L	M	A	L	H	G	E	G
LIFAGK	P	D	Q	Q	R	L	I	F	A	G
LIGDAAK	T	x	x	E	R	L	I	G	D	A
LIGILENK	E	T	P	S	P	L	I	G	I	L
LILADSEIEISSEK	L	S	Y	A	A	L	I	L	A	D
LINQIVPQLEK	A	P	V	D	A	L	I	N	Q	I
LIQVEIK	E	R	Q	L	Q	L	I	Q	V	E
LISIVNAVNPVIAK	V	A	S	E	T	L	I	S	I	V
LISLDGTANK	A	V	D	D	F	L	I	S	L	D
LISNASDALDK	I	F	L	R	E	L	I	S	N	A
LIVDAIK	E	E	A	L	D	L	I	V	D	A
LLELTQKRMSK	D	L	L	W	L	L	L	E	L	T
LLSDFNTGSFSYSYK	L	S	x	G	A	L	L	S	D	F
LLSSLEGK	A	R	I	N	E	L	L	S	S	L
LMALHGEESGEEK	F	D	V	G	A	L	M	A	L	H
LMVGKDEEQVK	A	Q	A	E	A	L	M	V	G	K
LNAAGNTPDATK	A	A	Y	L	L	L	N	A	A	G
LNAVLEEVK	V	V	E	R	Q	L	N	A	V	L
LNISGEFFRNK	V	R	A	E	x	L	N	I	S	G
LNPHYAK	Q	V	L	L	R	L	N	P	Y	A
LPANLVDLNVPK	P	V	Y	L	G	L	P	A	N	L
LPLQDVYK			P	L	R	L	P	L	Q	D
LQQTAFDK	V	H	S	F	R	L	Q	Q	T	A
LQSGIGNIANAVIEGLAQAQFK	E	N	L	L	P	L	Q	S	G	I
LQVQIPATPTSLETAK	A	S	P	A	L	L	Q	V	Q	I
LRGLFIIDPK	x	E	G	x	A	L	R	G	L	F
LRVHIEEGSRK	I	L	L	E	N	L	R	Y	H	I
LSKPEVK	V	Y	V	G	T	L	S	K	P	E
LSRSNGVLNVNDQTSDLVK	V	S	A	L	D	L	S	R	S	N
LSTNETEVAK		H	F	A	A	L	S	T	N	E
LTEVRAEDEAALAK	S	A	V	A	A	L	T	E	V	R
LTGIRDYVLNK	C	Q	Y	A	Y	L	T	G	I	R
LTGIRDYVLNKK	C	Q	Y	A	Y	L	T	G	I	R
LTISPALLDK	A	G	V	D	Y	L	T	I	S	P
LTRRADVK		Q	F	L	E	L	T	R	R	A
LTVSEEVK	L	T	P	A	R	L	T	V	S	E
LVAEAQLSNITREK	A	E	A	E	S	L	V	A	E	A
LVAGIERYPK	P	F	G	H	A	L	V	A	G	I
LVAIEEEFDIEIPDK	D	T	V	E	L	L	V	A	I	E
LVAPLKPLIEK	C	S	T	A	G	L	V	A	P	L
LVDDLRFEPAGYSK	L	D	P	Q	Y	L	V	D	D	L
LVDLNVPK	G	L	P	A	N	L	V	D	L	N
LVGGASLKPEFVDIINSRN	D	V	D	G	F	L	V	G	G	A
LVIDNGSGMCK	S	E	V	A	A	L	V	I	D	N
LVIDRLLPYWQDVIAK	T	E	S	L	A	L	V	I	D	R
LVLELNEK	G	E	L	L	R	L	V	L	L	E
LVQGGNAAPSAADIK	A	A	Y	L	L	L	V	Q	G	G
LVSNELEQLSSEALEAARICANK	P	L	C	V	H	L	V	S	N	E
LYAGDIALRPEILAEHQK	G	N	C	H	G	L	Y	A	G	D
MIAPTGA	A	L	Q	E	F	M	I	A	P	T
NIHVRK	I	F	P	L	Q	N	I	H	V	R
NIQTAAEALDLIVDAIK	G	G	V	A	P	N	I	Q	T	A
QGVGVILCIGETLEEK		F	A	L	G	Q	G	V	G	V
SHLGRPNGERNEK	Y	V	V	L	A	S	H	L	G	R
SHNPIENK	I	L	A	A	Q	S	H	N	P	I
SLKPNDASEK	T	P	I	D	M	S	L	K	P	N
SSGVGVTPLLAMLEEQVK	P	L	V	L	L	S	S	G	V	G
STRVVDLVEHVAKA	N	E	Y	G	Y	S	T	R	V	V
SVSLVK	T	Y	L	D	Y	S	V	S	L	V
TFSFPASQNK	I	P	L	G	F	T	F	S	F	P
TFSYPASQNK	L	P	L	G	F	T	F	S	Y	P

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
TRAEVSDVGNAILDGADCVMLSGETAK	Y	N	P	R	P	T	R	A	E	V
TSAGQPNLLLSASRDK	V	T	S	L	A	T	S	A	G	Q
TSNGGAAYFAGK	P	I	I	L	Q	T	S	N	G	G
TTNCLAPLAK	S	N	A	S	C	T	T	N	C	L
TTQNPDELWEFIADSLK	P	D	A	M	R	T	T	Q	N	P
TTVLAAAK	P	N	A	L	A	T	T	V	L	A
TYQRFVGHK	V	A	T	G	E	T	Y	Q	R	F
VAATLGPK	T	L	A	E	A	V	A	A	T	L
VAAVFEQK	V	A	A	S	A	V	A	A	V	F
VAFTPEERLIGDAAK	V	T	P	S	F	V	A	F	T	P
VAIPVGK	C	P	A	L	G	V	A	I	P	V
VATTGEWDK	Y	E	T	H	R	V	A	T	T	G
VAVPVDILDHDNNYELK	G	F	P	R	S	V	A	V	P	V
VFDAPQNLVEQAK	E	I	M	L	P	V	F	D	A	P
VFGLNNIQAEELVEFSSGVK	D	G	I	A	R	V	F	G	L	N
VFGLPGDFNLSLLDK	V	N	x	N	T	V	F	G	L	P
VFSMFGGK	P	P	S	S	A	V	F	S	M	F
VFTGIPGK	F	A	V	A	E	V	F	T	G	I
VFTNEPLTEIK	G	N	V	G	F	V	F	T	N	E
VFTPQDGRGAEGELGAASK	V	E	L	F	E	V	F	T	P	Q
VGAEVDEARINELLSSLECK	A	V	V	E	S	V	G	A	E	V
VGFDLPQRAAGFLEK	A	H	S	S	M	V	G	F	D	L
VGKDEEQVK	A	E	A	L	M	V	G	K	D	E
VGNPEGPEKPNK	Y	I	M	S	P	V	G	N	P	E
VGNPEGPEKPNKK	Y	I	M	S	P	V	G	N	P	E
VGSLTFDENYNLLDTSGVAK	V	L	P	R	A	V	G	S	L	T
VHGEEDPTKK	Y	V	S	G	R	V	H	G	E	E
VHLVSNELEQLSSEALEAARICANK	E	F	P	L	C	V	H	L	V	S
VIAAAFVK	N	N	V	N	N	V	I	A	A	A
VIAALSEK	G	A	G	A	A	V	I	A	A	L
VIAHVDHGK	V	R	N	M	S	V	I	A	H	V
VIGGPQGDAGLTGRK	P	S	G	R	F	V	I	G	G	P
VIQLLDSLPK	E	I	P	E	H	V	I	Q	L	L
VITFPVPIDADGIIPEK	A	E	A	Q	G	V	I	T	F	P
VLAGEAEK	A	E	V	E	A	V	L	A	G	V
VLGDVIK	V	T	A	A	G	V	L	G	D	V
VLGRAIFTESVK	T	T	S	A	T	V	L	G	R	A
VLVASAK	S	Y	V	E	P	V	L	V	A	S
VMGVNEEK	T	A	P	M	F	V	M	G	V	N
VNTGMEPGK	I	W	V	R	A	V	N	T	G	M
VQAAHIPQGTDLAQVAPILCAGITVYK	A	T	A	D	A	V	Q	A	A	H
VQAAITGDESSK	A	Y	G	A	A	V	Q	A	A	I
VQGAILTGQSTSDETK	A	Y	G	A	A	V	Q	G	A	I
VQGGEEVNAEELK	E	L	V	A	R	V	Q	G	G	E
VQGGNAAPSAADIK	A	Y	L	L	L	V	Q	G	G	N
VQQAQTEIK	P	I	P	E	E	V	Q	Q	A	Q
VQSLIPKPLESVK	P	T	S	F	P	V	Q	S	L	I
VQVGDIVTVGQCRPIK	S	P	A	F	R	V	Q	V	G	D
VQVRQPIFVAHTAGRYANK	S	L	V	D	Y	V	Q	V	R	Q
VRANGTTVLVGMPAGAK	A	S	T	R	Y	V	R	A	N	G
VRAPEQFDEVVAAIGNK	L	H	V	D	F	V	R	A	P	E
VRDLSEASVYPEYALPK	V	E	A	A	A	V	R	D	L	S
VRSGEWK	E	F	S	E	Q	V	R	S	G	E
VRVVPNEK	D	W	V	S	Q	V	R	V	V	P
VSGRVHGEEDPTK	D	A	V	E	Y	V	S	G	R	V
VSGRVHGEEDPTKK	D	A	V	E	Y	V	S	G	R	V
VSVSVLVDRK	P	T	Y	R	Y	V	S	V	S	V
VTLGPDGIEK	F	F	A	S	P	V	T	L	G	P
VTRMPEHQK	S	L	T	D	Y	V	T	R	M	P
VVDLIEYVAKA	G	Y	S	A	R	V	V	D	L	I
VVGIYNGK	E	M	I	G	S	V	V	G	I	Y

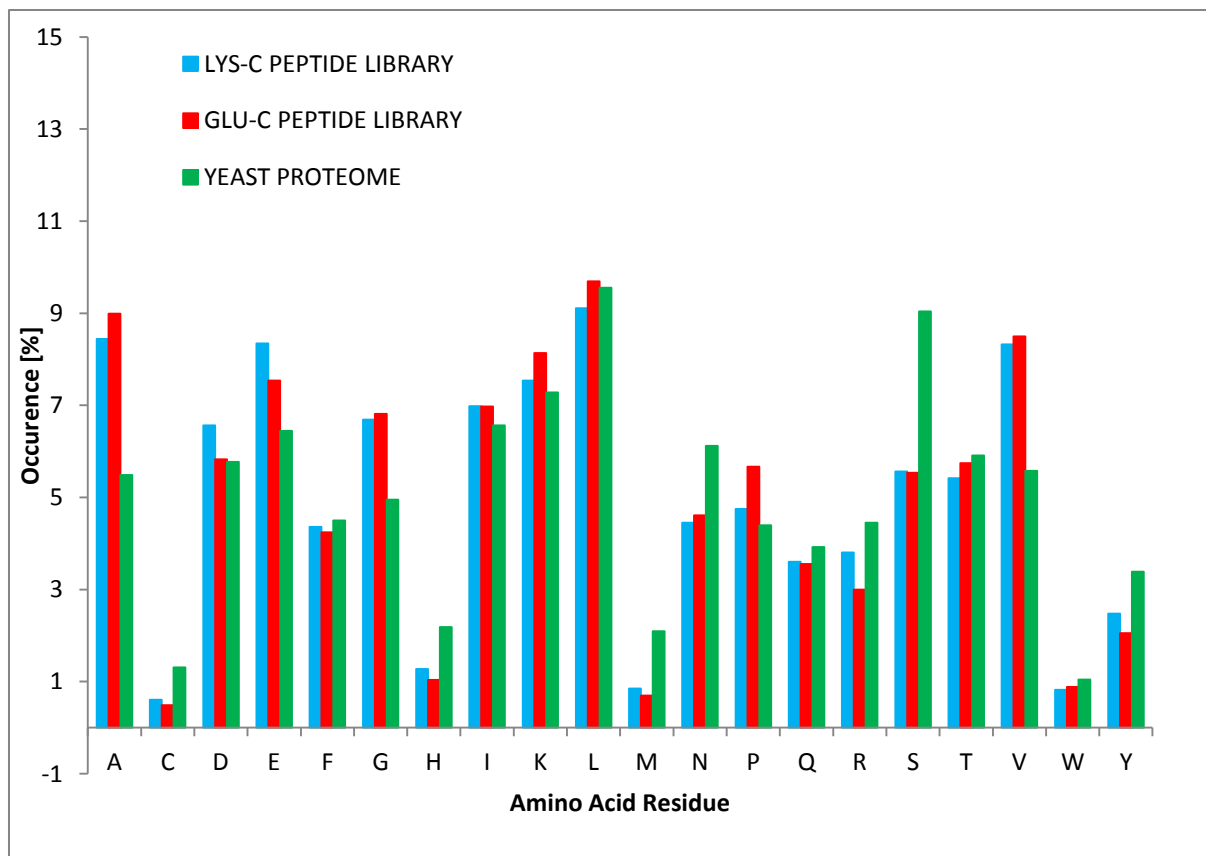
Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
VVGLRTGQIK	F	I	A	D	L	V	V	G	L	R
VVGLVNTK	N	E	A	F	S	V	V	G	L	V
VVGVNHTK	S	A	P	M	F	V	V	G	V	N
VVGVPSSSQAK	V	G	V	L	H	V	V	G	V	P
VVHLEK	I	H	F	E	P	V	V	H	L	E
VVNPEHLDIVAQK	P	L	I	V	P	V	V	N	P	E
VVQVAVEVK	F	S	V	S	P	V	V	Q	V	A
VVRAPTVK	D	L	L	R	P	V	V	R	A	P
VVSSDFLGDSNSSIFDAAAGIQLSPK	Y	T	E	D	A	V	V	S	S	D
VYDSRGNPTVEVELTTEK	V	Y	A	R	S	V	Y	D	S	R
VYLGLPANLVDLNPAK	x	T	Q	R	P	V	Y	L	G	L
VYNVYK			P	E	Q	V	Y	N	V	Y
VYQGERVNCK	T	V	Q	F	P	V	Y	Q	G	E
VYSTQLLADIISEASK	E	Q	A	S	S	V	Y	S	T	Q
VYVGTLSPKEVK	P	R	Y	G	G	V	Y	V	G	T
WQGLDNGPESRK	G	I	P	A	G	W	Q	G	L	D
WTNIPRK	Y	S	L	L	A	W	T	N	I	P

**Supplementary Table 5.** Cleavage sites identified in the experiment „Glu-C peptide library + ADAM17“; number of cleavage sites: 168; x = ambiguous amino acid

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
AAGFLL		L	P	Q	R	A	A	G	F	L
AFGNCHGLYAGD	F	S	I	A	A	A	F	G	N	C
AFPSAINQD	P	H	A	L	K	A	F	P	S	A
AFRVPTVDVSVVD	K	L	T	G	M	A	F	R	V	P
AIANFLEPQALE	A	P	V	G	A	A	I	A	N	F
AIAYGLDKKGKEE		P	T	A	A	A	I	A	Y	G
AKAVGKVLPE	S	S	T	G	A	A	K	A	V	G
AKGLQTVVVEE	V	L	V	A	S	A	K	G	L	Q
ARSVYDSRGNPTVE	V	S	K	V	Y	A	R	S	V	Y
ARTPANAAVPASTPLKQE	P	V	A	V	P	A	R	T	P	A
ATFPIAQPATDVE	V	L	S	A	A	A	T	F	P	I
AVFSAPIRPD	A	L	P	L	P	A	V	F	S	A
AVGKVLPE	T	G	A	A	K	A	V	G	K	V
AVQAAILTGD	V	A	Y	G	A	A	V	Q	A	A
FAGKQLE	Q	Q	R	L	I	F	A	G	K	Q
FILADAGLE	I	S	F	A	A	F	I	L	A	D
FKSTLEPVEQVLKD	L	N	A	A	L	F	K	S	T	L
FLASKLGDKAASE	A	S	I	R	K	F	L	A	S	K
FNSPFFD				M	S	F	N	S	P	F
FNSPFFDFFD				M	S	F	N	S	P	F
GVLGYTE		G	x	x	K	G	V	L	G	Y
IACRFDE	C	H	T	A	H	I	A	C	R	F
IAYGLDKKGKEE	P	T	A	A	A	I	A	Y	G	L
IFAGKQLE		Q	Q	R	L	I	F	A	G	K
IGTVPVGRVE	Y	K	I	G	G	I	G	T	V	P
IIKGWGE	L	K	P	L	A	I	I	K	G	W
IKAAGHDGKVKIGLDCASSE					A	I	K	A	A	G
IKQAIAANA	A	N	P	A	A	I	K	Q	A	I
IKQAIASNV	A	N	P	A	A	I	K	Q	A	I
IKTGAPARSE	L	R	T	G	Q	I	K	T	G	A
ILADAGLE	S	F	A	A	F	I	L	A	D	A
ILGIIE				L	K	I	L	G	I	I
ILSQAPTELE	A	P	Q	A	K	I	L	S	Q	A
IMALLDEGE	V	K	A	L	G	I	M	A	L	L
IQIVADDLTVTNPARIATAIE	F	K	T	A	G	I	Q	I	V	A
IQTANIALE	K	L	S	R	A	I	Q	T	A	N
IVKFSPNEQNKHIGE				L	A	I	V	K	F	S
KAFPSAINQD		P	H	A	L	K	A	F	P	S
KAFPSAINQDNYPNGGFTAE		P	H	A	L	K	A	F	P	S
KASGFTGE	Q	N	A	Y	L	K	A	S	G	A
KGNGWGKPGDE	x	x	G	x	G	K	G	N	W	G
KIATYQE				G	x	K	I	A	T	Y
KLNQLLRIEEE			R	L	A	K	L	N	Q	L
KLPLVGGHE	W	P	L	P	x	K	L	P	L	V
KRGSKSKIE	L	S	S	K	L	K	R	G	S	K
LAKQAFDDAIAE		K	A	C	H	L	A	K	Q	A
LAKVIND	N	C	L	A	P	L	A	K	V	I
LAKVINDAFGIEE	N	C	L	A	P	L	A	K	V	I
LASKLGDKAASE	S	I	R	K	F	L	A	S	K	L
LIFAGKQLE			Q	Q	R	L	I	F	A	G
LIGRNFNDPE			A	K	R	L	I	G	R	N
LIADSE		P	L	H	C	L	I	I	A	D
LISLGLNIDE	S	R	I	N	R	L	I	S	L	G
LKAFPSAINQD			P	H	A	L	K	A	F	P
LKAFPSAINQDNYPNGGFTAE			P	H	A	L	K	A	F	P
LKASGFTGE	A	Q	N	A	Y	L	K	A	S	G
LKGALAKVPE	L	G	A	V	A	L	K	G	A	L
LKNTISE	S	I	A	Y	S	L	K	N	T	I

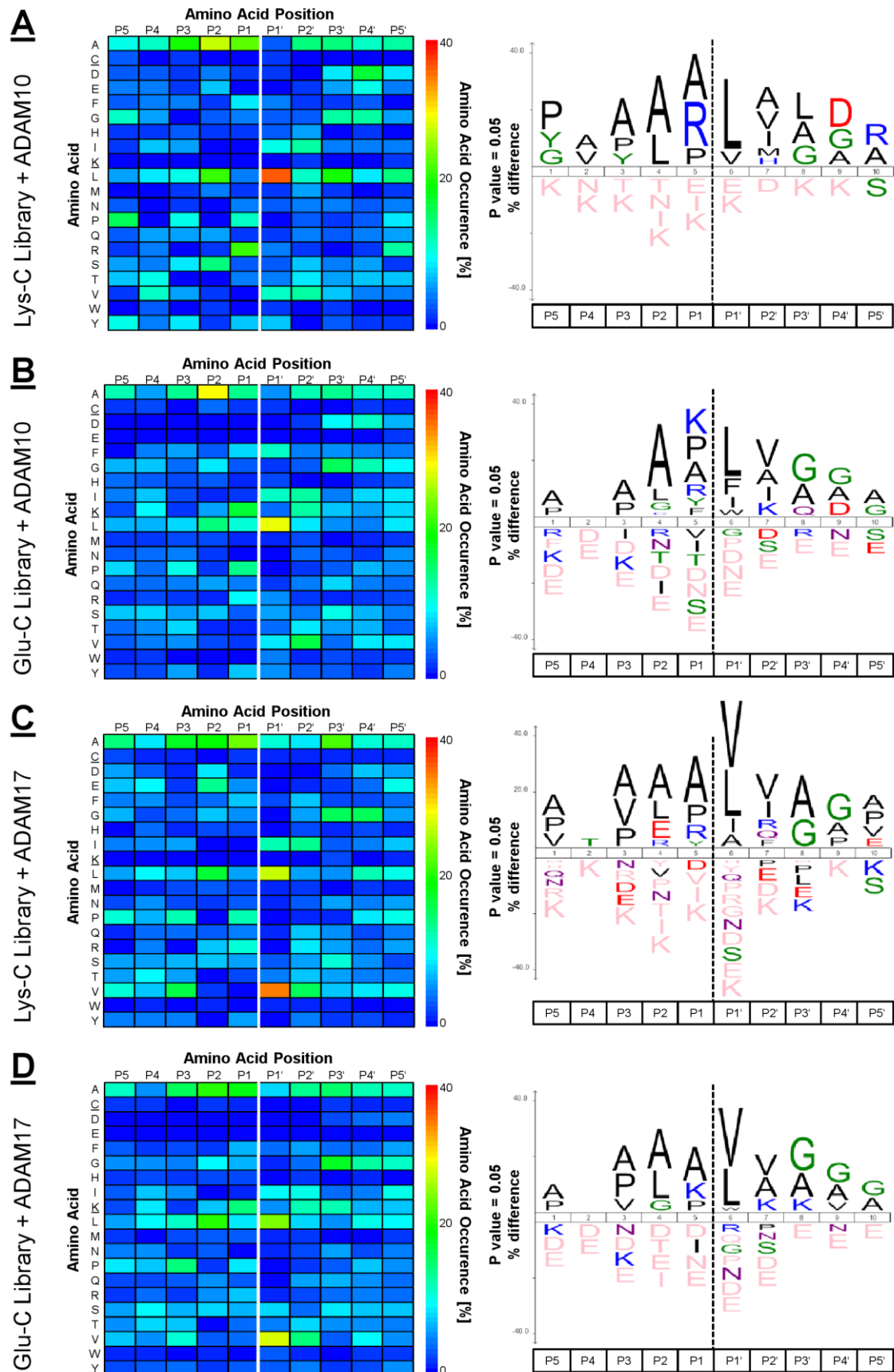
Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
LKTKGGNAGTKAYN	S	T	T	S	S	L	K	T	K	G
LLAGIGQITPE	T	T	T	G	L	L	L	A	G	I
LLPWFDGMLE	H	C	A	K	K	L	L	P	W	F
LLQTPIDMSLKPND	N	V	P	A	K	L	L	Q	T	P
LNQLINVQIAID			I	K	K	L	N	I	Q	L
LNQLLRIEEE		R	L	A	K	L	N	Q	L	L
LPLVGGHE	P	L	P	x	K	L	P	L	V	G
LPTFGAKDYE		H	L	S	L	L	P	T	F	G
LQSGIGNIANAVIE		N	L	L	P	L	Q	S	G	I
LQVQIPATPTSLE	A	S	P	A	L	L	Q	V	Q	I
LSKKGSLE	A	F	V	K	F	L	S	K	K	G
LSLQDYLNQANNQFNKVPE	P	K	T	A	Q	L	S	L	Q	D
LTAATNAKQ	x	x	Q	A	x	L	T	A	A	T
LTATQKTVD	T	T	V	H	S	L	T	A	T	Q
LTGKTITLE	I	F	V	K	T	L	T	G	K	T
LTKKRYGASAGNVGDE	H	N	L	K	S	L	T	K	K	R
LTNAANVPVE		K	L	L	T	L	T	N	A	A
LTVPKLKPQKD	N	G	V	L	T	L	T	V	P	K
LVAPLKPLIE	C	S	T	A	G	L	V	A	P	L
LVDDLPE			P	Q	Y	L	V	D	D	L
LVDIKKE	A	K	N	P	V	L	V	D	I	K
LVGGASLKPE				G	F	L	V	G	G	A
LVGKNHDE	S	S	V	F	Q	L	V	G	K	N
LVKDAKNPVILAD		T	I	L	A	L	V	K	D	A
LVQGGNAAPSAADIKAVVE	A	A	Y	L	L	L	V	Q	G	G
LVSWDNE	P	K	F	V	K	L	V	S	W	Y
LYQAGGAPE	P	I	M	S	K	L	Y	Q	A	G
LYQAGGAPGGAAGGAPGGFPGGAPPAPPE	P	I	M	S	K	L	Y	Q	A	G
MIAPMIE	C	G	P	C	K	M	I	A	P	M
NIQVWRPADGNE	F	R	S	L	P	N	I	Q	V	W
RVPTVDVSVVD	T	G	M	A	F	R	V	P	T	V
SAGAAAPAGVAGGVAGGEAGEAE	L	L	V	N	F	S	A	G	A	A
SAKSIVPLMD	S	T	L	L	K	S	A	K	S	I
SGATKARIVVAKSGEL	S	L	G	S	P	S	G	A	T	K
SHLGRPNGE	Y	V	V	L	A	S	H	L	G	R
SHLGRPNGERNE	Y	V	V	L	A	S	H	L	G	R
SKLGDKAASE	R	K	F	L	A	S	K	L	G	D
SLGLSPSEAE	A	T	V	M	R	S	L	G	L	S
SRQLKSNDSQE	F	L	A	L	M	S	R	Q	L	K
SSGVGVTPLLAMLE	P	L	V	L	L	S	S	G	V	G
SSNVDAIDSTGVFKE	N	L	P	W	G	S	S	N	V	D
SVGCRVDFKNPHDIE	L	G	T	A	Q	S	V	G	C	R
SVKDYRPAEE	P	I	L	A	P	S	V	K	D	Y
SVYDSRGNPTVE	K	V	Y	A	R	S	V	Y	D	S
SYKTKNIVE	G	S	F	S	Y	S	Y	K	T	K
TFGAKDYE	L	S	L	L	P	T	F	G	A	K
TFYPASQNKINE	L	P	L	G	F	T	F	S	Y	P
TGQIKTGAPARSE	V	V	G	L	R	T	G	Q	I	K
TIKYVLE	V	A	A	L	P	T	I	K	Y	V
TKKRYGASAGNVGDE	N	L	K	S	L	T	K	K	R	Y
TSKLIPE	T	L	A	Q	L	T	S	K	L	I
TVKAYLPVNE	G	T	P	L	F	T	V	K	A	Y
VAAPARAGAVAPE	I	V	S	N	R	V	A	A	P	A
VAAVFE	V	A	A	S	A	V	A	A	V	F
VAGKVQPE					K	V	A	G	K	V
VAPLKPLIE	S	T	A	G	L	V	A	P	L	K
VARNRGIDIVVNE	N	S	V	L	A	V	A	R	N	R
VAVQLKRQPAQPRE	A	K	A	Q	G	V	A	V	Q	L
VFDAPQNLVE		I	M	L	P	V	F	D	A	P
VFGLNNIQAEE		G	I	A	R	V	F	G	L	N
VFGLPGDFNLSLLDKIYE	V	N	V	N	T	V	F	G	L	P

Identified Peptides	P5	P4	P3	P2	P1	P1'	P2'	P3'	P4'	P5'
VFKLYND	P	I	G	R	V	V	F	K	L	Y
VGCRVDFKNPHDIE	G	T	A	Q	S	V	G	C	R	V
VGSLTFDE	V	L	P	R	A	V	G	S	L	T
VIGLTN	R	P	A	C	G	V	I	G	L	T
VIGSFKDWE	T	Y	V	K	K	V	I	G	S	F
VINDAFGIEE	A	P	L	A	K	V	I	N	D	A
VINNIPWDITPE	P	P	Y	R	A	V	I	N	N	I
VINVSAQRD	K	L	P	L	S	V	I	N	V	S
VKLPLVGGHE		W	P	L	P	V	K	L	P	L
VKLWSYDNE	L	S	P	K	F	V	K	L	V	S
VKNQQLEDE	I	K	S	L	T	V	K	N	Q	Q
VKRGGYGKGNWKGPGDE		S	P	N	H	V	K	R	G	G
VKSQTPKVE	A	R	A	G	K	V	K	S	Q	T
VLGKMKE	Q	I	S	S	M	V	L	G	K	M
VLGRAIFTE	T	T	S	A	T	V	L	G	R	A
VLKGDAGVSGVVKFE	V	Q	A	V	A	V	L	K	G	D
VLSALE		K	V	S	S	V	L	S	A	L
VMGVNE	T	A	P	M	F	V	M	G	V	N
VMGVNEE	T	A	P	M	F	V	M	G	V	N
VQAAILTGDE	A	Y	G	A	A	V	Q	A	A	I
VQGAILTGQSTSDE	A	Y	G	A	A	V	Q	G	A	I
VQGGNAAPSAADIKAVVE	A	Y	L	L	L	V	Q	G	G	N
VQIPATPTSLE	P	A	L	L	Q	V	Q	I	P	A
VQSLIPKPLE	P	T	S	F	P	V	Q	S	L	I
VSTGGGASLE		K	I	S	H	V	S	T	G	G
VTIISAMGEE				L	M	V	T	I	I	S
VTKHFISE		T	L	Q	A	V	T	K	H	F
VTKYSSSTQA		G	T	R	A	V	T	K	Y	S
VTYIQVE	G	H	Y	A	P	V	T	Y	I	Q
VVFKLYND	Q	P	I	G	R	V	V	F	K	L
VVGASVVVKNWGAETDE	G	N	A	R	K	V	V	G	A	S
VVRSGLDASGVASLLATTE			P	F	K	V	V	R	S	G
VVTFAPAGVTTE	I	K	P	G	M	V	V	T	F	A
VVGKDTLLTNKHVVD	F	I	A	S	G	V	V	V	G	K
VWAIGTGLAATPE					P	V	W	A	I	G
VYARSVYD	M	A	V	S	K	V	Y	A	R	S
VYARSVYDSRGNPTVE	M	A	V	S	K	V	Y	A	R	S
VYDSRGNPTVE	V	x	A	R	x	V	Y	D	S	R
VYVGTLSKPE	P	R	Y	G	G	V	Y	V	G	T
WAIGTGLAATPE				P	V	W	A	I	G	T
WQGLDNGPE	G	I	P	A	G	W	Q	G	L	D
WTKGFDIPNIE	G	I	L	Q	R	W	T	K	G	F
WTKGFDIPNVE	G	I	L	Q	R	W	T	K	G	F
WTNIPRKE	Y	S	L	L	A	W	T	N	I	P
YAALILADSE		S	A	L	S	Y	A	A	L	I
YARSVYD	A	V	S	K	V	Y	A	R	S	V
YARSVYDSRGNPTVE	A	V	S	K	V	Y	A	R	S	V
YKASQQRFPQGTNETPEE			Q	L	Y	Y	K	A	S	Q
YVGTLSKPE	R	Y	G	G	V	Y	V	G	T	L



**Supplementary Figure 2.** Amino acid distribution of the yeast proteome and the Lys-C and Glu-C peptide libraries (data from control experiments; Proteome Discoverer 1.4; enzyme specificity: Lys-C or Glu-C; fixed modifications: carbamidomethylation on cysteines, dimethylation on lysines and N-termini).





Supplementary Figure 3 (legend overleaf)

**Supplementary Figure 3.** Heat map and iceLogo for (A) ADAM10 including 69 cleavage sites identified in the Lys-C library. (B) ADAM10 including 149 cleavage sites identified in the Glu-C library. (C) ADAM17 including 197 cleavage sites identified in the Lys-C library. (D) ADAM17 including 168 cleavage sites identified in the Glu-C library. C = Carbamidomethylated cysteine; K = Dimethylated lysine; The cleavage site between P1 and P1' is marked with a white line in the heat map and with a dashed black line in the iceLogo.