

Table S1

Library Name	Protein Segment Identifier	Protein Sequence	Library Name	Protein Segment Identifier	Protein Sequence
AP 01	APP 1-18	MLPGLALLLLAAWTARAL	AP 33	APP 352-369	TTQEPLARDPVKLPPTAA
AP 02	APP 14-31	TARALEVPTDGNAGLLAE	AP 34	APP 365-382	PTTAASTPDAVDKYLETP
AP 03	APP 27-44 C38A	GLLAEPQIAMFAGRLNMH	AP 35	APP 378-395	YLETPGDENEHAHFQKAK
AP 04	APP 40-57	RLNMHMNVQNGKWDSDPS	AP 36	APP 391-408	FQKAKERLEAKHRERMSQ
AP 05	APP 53-70 C62A	DSDSPSGTKTAIDTKEGIL	AP 37	APP 404-421	ERMSQVMREWEEAERQAK
AP 06	APP 66-83 C73A	KEGILQYAEVYPELQIT	AP 38	APP 417-434	ERQAKNLPKADKKAVIQH
AP 07	APP 79-96	ELQITNVVEANQPVTIQN	AP 39	APP 430-447	AVIQHFQEKVESLEQEAA
AP 08	APP 92-109 CC98AA	VTIQNWAKRGRKQAKTHP	AP 40	APP 443-460	EQEAAANERQQLVETHMAR
AP 09	APP 105-122 CC105AA	AKTHPHFVIPYRALVGEF	AP 41	APP 456-473	THMARVEAMLNDRRRRAL
AP 10	APP 118-135 C133A	LVGEFVSDALLVPDKAKF	AP 42	APP 469-486	RRLALENYITALQAVPPR
AP 11	APP 131-148 CC133AA	DKAKFLHQERMDVAETHL	AP 43	APP 482-499	AVPPRPRHVFNMLKKYVR
AP 12	APP 144-161 CC144AA	AETHLHWHTVAKETASEK	AP 44	APP 495-512	KKYVRAEQKDRQHTLKHf
AP 13	APP 157-174 C174A	TASEKSTNLHDYGMLLPA	AP 45	APP 508-525	TLKHFEHVRMVDPKKAAQ
AP 14	APP 170-187 CCC174AAA	MLLPAGIDKFRGVEFVAA	AP 46	APP 521-538	KKAAQIRSQVMTHLRVIY
AP 15	APP 183-196 CC186AA	EFVAAPLAEESDNV	AP 47	APP 534-564	LRVIYERMNQSLSLLYNV
AP 16	APP 192-203	ESDNVDSADAE	AP 48	APP 547-564	LLYNVPAVAEEIQDEVDE
AP 17	APP 199-212	ADAEEDSDVWWGG	AP 49	APP 560-577	DEVDELLQKEQNYSDDL
AP 18	APP 208-223	VWVGADTDYADGSED	AP 50	APP 573-590	SDDVLANMISEPRISYGN
AP 19	APP 219-231	DGSEDKVVEVAEE	AP 51	APP 586-603	ISYGN DALMPSLTETKTT
AP 20	APP 228-238	VAEEEEVAEVE	AP 52	APP 599-616	ETKTTVELLPVNGEFLD
AP 21	APP 234-243	VAEVEEEEAAD	AP 53	APP 612-629	EFLSDDLQPHWSFGADSV
AP 22	APP 241-247	EADDDDED	AP 54	APP 625-642	GADSV PANTENEVEPVDA
AP 23	APP 245-251	DEDDDEDG	AP 55	APP 638-655	EPVDARPAADRGLTTRPG
AP 24	APP 249-256	EDGDEVEE	AP 56	APP 651-668	TTRPGSGLTNIKTEEISE
AP 25	APP 254-263	VEEEAEPEYE	AP 57	APP 664-681	EEISEVKMDAEFRHDSGY
AP 26	APP 261-278	PYEEATERTTSIATTTTT	AP 58	APP 677-694	HDSGYEVHHQKLVFFAED
AP 27	APP 274-291 C291A	TTTTTTTESVEEVREVA	AP 59	APP 690-707	FFAEDVGSNKGAIIGLMV
AP 28	APP 287-304 CC291AA BPTI	VREVASEQAETGPARAMI	AP 60	APP 703-720	IGLMVGGVVIATVIVITL
AP 29	APP 300-317 CC316AA	ARAMISRWFVDVTEGKAA	AP 61	APP 716-733	IVITLVMKKKKQYTSIHH
AP 30	APP 313-330 CC316AA	EGKAAPFFYGGAGGNRNN	AP 62	APP 729-746	TSIIHGVVEVDAAVTPEE
AP 31	APP 326-343 CC337AA	GNRNNFDTEEYAMAVAGS	AP 63	APP 742-759	VTPEERHLSKMQQNGYEN
AP 32	APP 339-356 C341A	AVAGSAMSQSLKTTQEP	AP 64	APP 755-770	NGYENPTYKFFEQMQN

Table S2

Cathepsins	Pre-activation:	Protease concentrations and pHs used for mass spectrometry:	Mass spectrometry time points:
CTSA	Trans-activated with CTSL following the manufacturer's recommendation. The irreversible cysteine protease inhibitor E-64 was then added for an additional 30 min at 37 °C to allow for inhibition of CTSL.	40 nM in pH 4.5 and 5.5	30min, 1h, 4h
CTSB	N/A	20 nM in pH 4.5 and 5.5	1h, 4h
CTSC	Trans-activated with CTSL following the manufacturer's recommendation. The irreversible cysteine protease inhibitor E-64 was then added for an additional 30 min at 37 °C to allow for inhibition of CTSL.	N/A	1h, 4h
CTSD	N/A	10 nM in pH 3.4 and 4.5	1h, 4h
CTSE	N/A	10 nM in pH 3.4 and 4.5	1h, 4h
CTSF	N/A	50 nM in pH 4.5 buffer	2h, 6h
CTSG	N/A	2 nM in pH 4.5, 5.5 and 7.5	30 min, 1h, 4h
CSTH	Trans-activated with thermolysin following the manufacturer's recommendation. Phosphoramidon was then added to these preparations for an additional 30 min at 37 °C to allow for inhibition of thermolysin	N/A	1h, 4h
CTSK	N/A	1 nM at pH 4.5	15min, 2h
CTSL	N/A	8.0 nM at pH 4.5 and 5.5	1h, 4h
CTSO	N/A	25 nM at pH 5.5	1h, 4h
CTSS	N/A	10 nM at pH 4.5 and 5.5	1h, 4h
CTSV	N/A	20 nM at pH 3.4 and 4.5	1h, 4h
CTSX	Preincubated with dithiothreitol (DTT) following the manufacturer's recommendation.	50 nM at pH 3.4 and 4.5	1h, 4h
AEP	N/A	20 nM at pH 4.5 and 5.5	1h, 4h

Table S3

	APP		
WT APP: 598-696	{D-ARG}{D-ARG}{LYS(MCA)}LVFFA E DVG{LYS(DNP)}		
E693G	{D-ARG}{D-ARG}{LYS(MCA)}LVFFA G DVG{LYS(DNP)}		
E693Q	{D-ARG}{D-ARG}{LYS(MCA)}LVFFA Q DVG{LYS(DNP)}		
	Tau Peptide		
WT Tau: 274-282	{D-ARG}{D-ARG}{LYS(MCA)}KVQIINKKL{LYS(DNP)}		