

Supplementary materials

Table S1: Details of parent proteins from which peptides were derived. The last column indicate peptides from this parent protein were detected to have significant higher intensity in the AprX-hydrolysed samples than the blank UHT milk samples.

Protein IDs	Fasta headers	Peptide counts (all)	Mol. weight [kDa]	Sequence lengths	Higher in AprX
P02666	Beta-casein	738	25.107	224	✓
P02662	Alpha-S1-casein	576	24.529	214	✓
P02668	Kappa-casein	190	21.269	190	✓
P02754	Beta-lactoglobulin	216	19.883	178	✓
P02663	Alpha-S2-casein	279	26.018	222	✓
P80195	Glycosylation-dependent cell adhesion molecule 1	124	17.151	153	✓
Q0IIA4	Glycoprotein 2 (Zymogen granule membrane)	27	59.232	534	✓
P81265	Polymeric immunoglobulin receptor	65	82.434	757	✓
P31096	Osteopontin	51	30.904	278	✓
P80025	Lactoperoxidase	25	80.641	712	✓
P18892	Butyrophilin subfamily 1 member A1	35	59.276	526	✓
Q27960	Sodium-dependent phosphate transport protein 2B	21	75.825	693	✓
P80457	Xanthine dehydrogenase/oxidase	5	146.79	1332	
P17248	Tryptophan--tRNA ligase, cytoplasmic	2	53.811	476	
Q9TUM6	BOVIN Perilipin-2	24	49.368	450	✓
P00711	Alpha-lactalbumin	17	16.246	142	
P11151	Lipoprotein lipase	7	53.377	478	✓
Q5EA98	Microfibrillar-associated protein 1	1	51.977	439	
P01888	Beta-2-microglobulin	2	13.677	118	
Q05927	5-nucleotidase	2	62.965	574	✓
Q71SP7	Fatty acid synthase	5	274.55	2513	✓
P02769; P49065	Serum albumin	10	69.161	606;607; 607	
Q9MZ06	Fibroblast growth factor-binding protein 1	8	26.188	234	✓
Q1RMN8;A4IF10	Immunoglobulin light chain, lambda gene cluster	4	24.536	234;235	
A7E340	Mucin 15, cell surface associated	7	35.685	330	✓
P08037	Beta-1,4-galactosyltransferase 1	4	44.842	402	
Q9XS94	Major fibrous sheath protein	2	93.987	848	✓
Q5EA54	Solute carrier family 3 (Activators of dibasic and neutral amino acid transport), member 2	1	63.21	572	
P58073	Parathyroid hormone-related protein	5	20.408	177	✓
Q3ZCL0	Cysteine-rich secretory protein 2	3	27.453	244	
Q2UVX4	Complement C3	4	187.25	1661	✓
A6QQA8	Sulfhydryl oxidase	2	62.974	567	✓
Q76LV1;Q76LV2	Heat shock protein HSP 90-beta	3	83.252	724;733	✓
Q0P569	Nucleobindin-1	4	54.982	474	

Protein IDs	Fasta headers	Peptide counts (all)	Mol. weight [kDa]	Sequence lengths	Higher in AprX
Q4GZT4	ATP-binding cassette sub-family G member 2	1	72.724	655	✓
P61823	Ribonuclease pancreatic	1	16.461	150	
Q8WML4	Mucin-1	3	58.091	580	✓
P24627	Lactotransferrin	2	78.056	708	
P10790	Fatty acid-binding protein	1	14.779	133	
P62992;P63048;P0CG53;P0CH28	Ubiquitin-40S ribosomal protein S27a	2	17.965	156;128;305;690	
Q6QRN7	PP1201 protein	2	33.948	308	
P35541	Serum amyloid A protein	2	14.516	130	
P01035	Cystatin-C	1	16.265	148	
Q95122	Monocyte differentiation antigen CD14	1	39.666	373	
P38408	Guanine nucleotide-binding protein subunit alpha-14	1	41.498	355	
Q0VCX2	78 kDa glucose-regulated protein	1	72.399	655	
Q3T178	Vacuolar protein sorting-associated protein 28 homolog	1	25.484	221	

Table S2: Differing peptide sequences by LTI.

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
Peptides higher in SM+AprX	EELNVPGE	Beta-casein	-0.5843	<0.0001	L	E	E	I	19	26	8
	ESLSSEESITR	Beta-casein	-0.7138	0.0039	V	E	R	I	29	40	12
	SITRINKK	Beta-casein	-1.0485	0.0025	E	S	K	I	37	44	8
	ITRINKK	Beta-casein	-1.5296	0.0241	S	I	K	I	38	44	7
	INKKIEK	Beta-casein	-1.1594	0.0090	R	I	K	F	41	47	7
	IEKFQSEEQQTDELQDKI HPFAQTQS	Beta-casein	-2.1872	0.0001	K	I	S	L	45	72	28
	FQSEEQQTDELQDKIHFP	Beta-casein	-0.6608	0.0059	K	F	F	A	48	67	20
	FQSEEQQTDELQDKIHFP AQTQS	Beta-casein	-0.5741	0.0009	K	F	S	L	48	72	25
	SEEQQTEDELQD	Beta-casein	-0.6987	0.0054	Q	S	D	K	50	62	13
	TEDELQDKIHP	Beta-casein	-0.9307	<0.0001	Q	T	P	F	56	66	11
	KIHHPFAQTQS	Beta-casein	-0.9446	0.0068	D	K	S	L	63	72	10
	HPFAQTQS	Beta-casein	-1.6230	0.0030	I	H	S	L	65	72	8
	HPFAQTQ	Beta-casein	-1.2578	0.0009	I	H	Q	S	65	71	7
	TQTPVVVPPFLQPEVMGVS KVKEA	Beta-casein	-0.8663	0.0072	L	T	A	M	93	116	24
	QPEVMGVSKVKEA	Beta-casein	-0.8839	0.0044	L	Q	A	M	104	116	13
	VMGVSKVKE	Beta-casein	-1.2599	0.0046	E	V	E	A	107	115	9
	MGVSKVKEA	Beta-casein	-0.6874	0.0023	V	M	A	M	108	116	9
	GVSKVKE	Beta-casein	-1.4552	0.0032	M	G	E	A	109	115	7
	KEAMAPK	Beta-casein	-1.3473	0.0020	V	K	K	H	114	120	7
	EAMAPKH	Beta-casein	-1.4540	0.0106	K	E	H	K	115	121	7
	FTESQSLTL	Beta-casein	-0.9198	0.0120	P	F	L	T	134	142	9

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	WMHQPHQPLPPTVMFPPQS	Beta-casein	-1.0136	0.0016	S	W	S	V	158	176	19
	VMFPPQS	Beta-casein	-1.1825	0.0054	T	V	S	V	170	176	7
	SQSKVLPVP	Beta-casein	-0.7365	0.0027	L	S	P	Q	181	189	9
	KAVPYPQRD	Beta-casein	-1.3501	0.0116	Q	K	D	M	191	199	9
	KAVPYPQ	Beta-casein	-1.0703	0.0020	Q	K	Q	R	191	197	7
	KHQGLPQEV	Alpha-S1-casein	-1.6726	0.0011	I	K	L	N	22	31	10
	HQGLPQE	Alpha-S1-casein	-1.9143	0.0041	K	H	E	V	23	29	7
	FGKEKVNE	Alpha-S1-casein	-1.4346	0.0007	V	F	E	L	47	54	8
	VPSEYLGYLEQLL	Alpha-S1-casein	-0.5292	0.0031	D	V	L	R	101	114	14
	KKYKVPQ	Alpha-S1-casein	-1.9093	0.0027	L	K	Q	L	117	123	7
	LHSMKEG	Alpha-S1-casein	-1.0177	0.0109	R	L	G	I	135	141	7
	HSMKEGIHAQQKEPM	Alpha-S1-casein	-1.3291	0.0014	L	H	M	I	136	150	15
	IHAQQKEP	Alpha-S1-casein	-1.2844	0.0003	G	I	P	M	142	149	8
	HAQQKEPMIG	Alpha-S1-casein	-1.5918	<0.0001	I	H	G	V	143	152	10
	HAQQKEP	Alpha-S1-casein	-1.2237	0.0096	I	H	P	M	143	149	7
	AQQKEPM	Alpha-S1-casein	-1.5439	0.0010	H	A	M	I	144	150	7
	IGVNQEL	Alpha-S1-casein	-1.6067	0.0016	M	I	L	A	151	157	7
	PSFSDIPNPIGSENSEKTTMP	Alpha-S1-casein	-1.4067	0.0040	A	P	P	L	192	212	21
	PNPIGSENSEKTTMP	Alpha-S1-casein	-1.0467	0.0081	I	P	P	L	198	212	15
	ALNEINQ	Alpha-S2-casein	-0.6641	0.0062	K	A	Q	F	96	102	7
	KLTEEEKNR	Alpha-S2-casein	-1.1815	0.0023	T	K	R	L	167	175	9
	FLKKISQ	Alpha-S2-casein	-1.2629	0.0071	N	F	Q	R	178	184	7
	KISQRYQKF	Alpha-S2-casein	-1.7191	0.0010	K	K	F	A	181	189	9
	PQYLKTVYQHQ	Alpha-S2-casein	-0.7207	0.0061	L	P	Q	K	192	202	11

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	KTVYQHQQK	Alpha-S2-casein	-1.6593	0.0008	L	K	K	A	196	203	8
	TVYQHQQKAM	Alpha-S2-casein	-1.1891	0.0046	K	T	M	K	197	205	9
	KAMKPWIQPK	Alpha-S2-casein	-1.2092	0.0003	Q	K	K	T	203	212	10
	KAMKPWIQPKT	Alpha-S2-casein	-0.8662	0.0109	Q	K	T	K	203	213	11
	PWIQPKTKVIP	Alpha-S2-casein	-0.5818	0.0027	K	P	P	Y	207	217	11
	KVIPYVR	Alpha-S2-casein	-1.0524	0.0059	T	K	R	Y	214	220	7
	VLSRYPS	Kappa-casein	-0.9401	0.0101	Y	V	S	Y	52	58	7
	VLSRYPSYG	Kappa-casein	-0.8316	0.0101	Y	V	G	L	52	60	9
	YGLNYYQQKP	Kappa-casein	-1.1033	0.0152	S	Y	P	V	59	68	10
	NYYQQKP	Kappa-casein	-0.6384	0.0011	L	N	P	V	62	68	7
	YYQQKPV	Kappa-casein	-1.6701	0.0016	N	Y	V	A	63	69	7
	YQQKPVAL	Kappa-casein	-0.9452	0.0068	Y	Y	L	I	64	71	8
	AVRSPAQ	Kappa-casein	-0.9103	0.0106	A	A	Q	I	87	93	7
	TMARHPPH	Kappa-casein	-1.9399	0.0005	T	T	H	L	115	123	9
	TMARHPPHLSF	Kappa-casein	-0.7175	0.0002	T	T	F	M	115	126	12
	VQVTSTA	Kappa-casein	-0.6943	0.0005	T	V	A	V	183	189	7
	AMAASDISLLDAQSAP	Beta-lactoglobulin	-1.5055	0.0006	L	A	P	L	39	54	16
	LDAQSAPLR	Beta-lactoglobulin	-0.6976	0.0020	L	L	R	V	48	56	9
	VEELKPTPEGDLEILL	Beta-lactoglobulin	-0.6786	0.0022	Y	V	L	Q	59	74	16
	LKPTPEGDLE	Beta-lactoglobulin	-0.7845	0.0051	E	L	E	I	62	71	10
	KKIIAEKT	Beta-lactoglobulin	-2.0448	0.0012	Q	K	T	K	85	92	8
	KIPAVFK	Beta-lactoglobulin	-1.9462	<0.0001	T	K	K	I	93	99	7
	VDDEALEK	Beta-lactoglobulin	-2.0315	0.0001	E	V	K	F	144	151	8

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	IRLSFNPT	Beta-lactoglobulin	-0.7458	<0.0001	H	I	T	Q	163	170	8
	NKPEDETH	Glycosylation-dependent cell adhesion molecule 1	-0.9185	0.0132	L	N	H	L	21	28	8
	LISKEQIVI	Glycosylation-dependent cell adhesion molecule 1	-0.4470	0.0010	D	L	I	R	62	70	9
	ISKEQIVIR	Glycosylation-dependent cell adhesion molecule 1	-0.7384	0.0051	L	I	R	S	63	71	9
	IVIRSSRQPQ	Glycosylation-dependent cell adhesion molecule 1	-2.1481	0.0003	Q	I	Q	S	68	77	10
	SSRQPQSQNPKLPL	Glycosylation-dependent cell adhesion molecule 1	-1.2167	0.0199	R	S	P	L	72	84	13
	SSRQPQSQNPKLPLS	Glycosylation-dependent cell adhesion molecule 1	-1.6997	0.0032	R	S	S	I	72	86	15
	SSRQPQSQNP	Glycosylation-dependent cell adhesion molecule 1	-1.5439	0.0028	R	S	P	K	72	81	10
	RQPQSQNPKLPL	Glycosylation-dependent cell adhesion molecule 1	-1.2258	0.0147	S	R	L	S	74	85	12
	KQSNSKY	Immunoglobulin light chain, lambda gene cluster	-1.1014	0.0041	S	K	Y	A	188	194	7
	QRPPKIQVY	Beta-2-microglobulin	-1.4791	<0.0001	I	Q	Y	S	22	30	9
	DGVAKLS	Complement C3	-0.9203	0.0081	D	D	S	I	402	408	7
	DRITGGKDFRDIES	Lipoprotein lipase	-0.8172	0.0005	A	D	S	K	29	42	14
	DELKRQEVS	Nucleobindin-1	-1.0866	0.0161	L	D	S	R	98	106	9
	KPDPSQKQT	Osteopontin	-0.9264	0.0027	L	K	T	F	45	53	9

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	SVAYGLKSRSKKF	Osteopontin	-0.8283	0.0102	D	S	F	R	155	167	13
	AAPAGAAIQS	Polymeric immunoglobulin receptor	-0.6642	0.0049	K	A	S	R	576	585	10
	AGEIQNKAL	Polymeric immunoglobulin receptor	-0.9442	0.0127	R	A	L	L	587	595	9
	GSSKALVSTLVPLA	Polymeric immunoglobulin receptor	-0.4460	0.0011	S	G	A	L	627	640	14
	DTHKSEIAHRF	Serum albumin	-1.6288	0.0001	R	D	F	K	24	34	11
	VKSVASLG	Xanthine dehydrogenase/oxidase	-1.5281	0.0141	Q	V	G	G	342	349	8
Peptides higher in SM+AprX+LTI	LEELNVPGEIVE	Beta-casein	0.5915	0.0014	E	L	E	S	18	29	12
	VMFPPQSVLS	Beta-casein	0.6033	0.0015	T	V	S	L	170	179	10
	VLSLSQSKVLPVPQ	Beta-casein	1.6872	0.0179	S	V	Q	K	177	190	14
	LSQSKVLPVPQKAVPYPQR DMPIQA	Beta-casein	0.6002	0.0003	S	L	A	F	180	204	25
	VPYPQRDMPIQA	Beta-casein	1.1906	0.0003	A	V	A	F	193	204	12
	RDMPIQAFL	Beta-casein	0.6851	0.0048	Q	R	L	Y	198	207	10
	RPKHPIKHQGLPQEVLENL	Alpha-S1-casein	1.9692	0.0104	A	R	L	L	16	35	20
	HQGLPQEVLENLL	Alpha-S1-casein	0.4842	0.0003	K	H	L	R	23	36	14
	VAPFPEVFGKEKVNEL	Alpha-S1-casein	0.8345	0.0045	F	V	L	S	40	55	16
	KVPQLEIVPNSAEERLHSMK EG	Alpha-S1-casein	2.0654	<0.0001	Y	K	G	I	120	141	22
	LEIVPNSAEERLHSMKEG	Alpha-S1-casein	1.1587	0.0006	Q	L	G	I	124	141	18
	EGIHAAQKQKPMIGVNQ	Alpha-S1-casein	0.9144	0.0102	K	E	Q	E	140	155	16
	IHAQKQKPMIGVNQELA	Alpha-S1-casein	1.8628	<0.0001	G	I	A	Y	142	158	17
	QGPIVLNPWDQVK	Alpha-S2-casein	1.2117	0.0010	Y	Q	K	R	116	128	13
	LINNQLFPYPYYA	Kappa-casein	1.2366	0.0002	A	L	A	K	71	83	13
	INNQLFPYPYYA	Kappa-casein	0.9053	0.0004	L	I	A	K	72	83	12

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	FLPYPYA	Kappa-casein	1.2008	0.0050	Q	F	A	K	76	83	8
	QILWQVL	Kappa-casein	0.7815	0.0053	A	Q	L	S	93	100	8
	ILWQVL	Kappa-casein	0.6821	0.0071	Q	I	L	S	94	100	7
	RHPHPLSF	Kappa-casein	0.8695	0.0034	A	R	F	M	118	126	9
	VEELKPTPEGDLEIL	Beta-lactoglobulin	0.4452	0.0001	Y	V	L	L	59	73	15
	ILNKPEDETHLEAQPTDASA QFI	Glycosylation-dependent cell adhesion molecule 1	2.1153	0.0006	A	I	I	R	19	41	23
	LNKPEDETHLEAQPTDASA QFIRNLQ	Glycosylation-dependent cell adhesion molecule 1	1.5057	0.0150	I	L	Q	I	20	45	26
	KPEDETHLEAQPTDASAQF	Glycosylation-dependent cell adhesion molecule 1	0.8986	0.0059	N	K	F	I	22	40	19
	VGVHPPLQGSSHGAAAIGQP SGELRL	Beta-1,4-galactosyltransferase 1	1.6472	0.0010	L	V	L	R	54	79	26
	KAFLDSRTRL	Lactoperoxidase	1.5394	0.0011	N	K	L	K	47	56	10
Peptides higher in FM+AprX	EKFQSEEQQTEDELQDKIH P	Beta-casein	-1.3218	0.0003	I	E	P	F	46	66	21
	LQPEVMGVS	Beta-casein	-0.4501	0.0028	F	L	S	K	103	111	9
	VSKVKEAMAPK	Beta-casein	-0.8267	0.0032	G	V	K	H	110	120	11
	AMAPKHKEMPFP	Beta-casein	-0.6816	0.0027	E	A	P	K	116	127	12
	APKHKEMPFP	Beta-casein	-1.0089	<0.0001	M	A	P	K	118	127	10
	TESQSLT	Beta-casein	-1.0848	0.0005	F	T	T	L	135	141	7
	HQPHQPLPPT	Beta-casein	-1.0521	<0.0001	M	H	T	V	160	169	10
	VLPVPQKAVPYPQRDMPIQ A	Beta-casein	-0.6612	0.0004	K	V	A	F	185	204	20
	AVPYPQRDMPIQA	Beta-casein	-0.7613	0.0107	K	A	A	F	192	204	13
	KHIQKEDVP SER	Alpha-S1-casein	-1.4111	0.0007	Q	K	R	Y	94	105	12

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	HIQKEDVPSE	Alpha-S1-casein	-0.5579	0.0039	K	H	R	Y	95	105	11
	IQKEDVPSE	Alpha-S1-casein	-0.6132	0.0005	H	I	Y	L	96	106	11
	KEDVPSE	Alpha-S1-casein	-1.4112	0.0090	Q	K	E	R	98	104	7
	LGYLEQLLR	Alpha-S1-casein	-0.3543	0.0005	Y	L	R	L	107	115	9
	NSEKTTMP	Alpha-S1-casein	-0.8696	0.0004	E	N	P	L	205	212	8
	ITVDDKH	Alpha-S2-casein	-0.7826	0.0094	K	I	H	Y	86	92	7
	TVDDKHY	Alpha-S2-casein	-0.7824	0.0037	I	T	Y	Q	87	93	7
	LTEEEKNRL	Alpha-S2-casein	-0.5805	0.0033	K	L	L	N	168	176	9
	VYQHQKAM	Alpha-S2-casein	-1.0697	0.0060	T	V	M	K	198	205	8
	KAMKPWIQP	Alpha-S2-casein	-0.4065	0.0014	Q	K	P	K	203	211	9
	AMKPWIQPKTK	Alpha-S2-casein	-1.4551	0.0002	K	A	K	V	204	214	11
	TKVIPYVR	Alpha-S2-casein	-0.6573	0.0054	K	T	R	Y	213	220	8
	VLSRYPSYGLNYYQKPVA	Kappa-casein	-1.0824	0.0196	Y	V	A	L	52	70	19
	YYQQKPVAL	Kappa-casein	-0.3850	0.0001	N	Y	L	I	63	71	9
	TMARHPPH	Kappa-casein	-1.6366	0.0121	T	T	H	L	115	123	9
	TMARHPPHLS	Kappa-casein	-0.8927	0.0029	T	T	S	F	115	125	11
	TPEVDDEALEKFDKAL	Beta-lactoglobulin	-0.6142	0.0009	R	T	L	K	141	156	16
	IVIRSSRQPQ	Glycosylation-dependent cell adhesion molecule 1	-1.7614	0.0009	Q	I	Q	S	68	77	10
	LPLSILKE	Glycosylation-dependent cell adhesion molecule 1	-0.4394	0.0013	K	L	E	K	83	90	8
	AHVQVL	Lactotransferrin	-0.8082	0.0017	A	A	L	L	624	630	7
	AGEIQNKA	Polymeric immunoglobulin receptor	-1.3216	0.0004	R	A	A	L	587	594	8
	DTHKSEIAHRF	Serum albumin	-0.8169	0.0158	R	D	F	K	24	34	11

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	KLPTQKT	Xanthine dehydrogenase/oxidase	-1.7934	<0.0001	A	K	T	E	318	324	7
Peptides higher in FM+AprX+LTI	RELEELNVPGEIVESLS	Beta-casein	0.5408	0.0069	A	R	S	S	16	32	17
	IEKFQSEEQQQTEDELQDKI HPF	Beta-casein	0.6972	0.0014	K	I	F	A	45	67	23
	ELQDKIHP	Beta-casein	1.5036	0.0046	D	E	P	F	59	66	8
	KIHPFAQTQS	Beta-casein	0.6829	0.0006	D	K	S	L	63	72	10
	HPFAQTQ	Beta-casein	1.2820	0.0006	I	H	Q	S	65	71	7
	SLPQNIPPLTQTPVVPPFLQ PEVMG	Beta-casein	2.1611	0.0024	N	S	G	V	84	109	26
	QPEVMGVSKVKEA	Beta-casein	0.7390	0.0020	L	Q	A	M	104	116	13
	VMGVSKVKE	Beta-casein	1.3490	0.0026	E	V	E	A	107	115	9
	MGVSKVKEA	Beta-casein	1.0357	0.0125	V	M	A	M	108	116	9
	SKVKEAM	Beta-casein	0.8323	0.0061	V	S	M	A	111	117	7
	KYPVEPFOTES	Beta-casein	0.7219	0.0076	P	K	S	Q	128	137	10
	QSWMHQPH	Beta-casein	1.7925	0.0002	L	Q	H	Q	156	163	8
	RDMP IQA	Beta-casein	0.6770	0.0014	Q	R	A	F	198	204	7
	RPKHPIK	Alpha-S1-casein	2.0576	0.0012	A	R	K	H	16	22	7
	RPKHPIKHQG	Alpha-S1-casein	2.0585	<0.0001	A	R	G	L	16	25	10
	HPIKHQGLPQE	Alpha-S1-casein	1.2809	<0.0001	K	H	E	V	19	29	11
	HQGLPQEVLENENLLRF	Alpha-S1-casein	0.5776	0.0052	K	H	F	F	23	38	16
	HQGLPQEVLENENLL	Alpha-S1-casein	0.6000	0.0014	K	H	L	R	23	36	14
	FVAPFPEVFGKEKVNEL	Alpha-S1-casein	0.6913	0.0024	F	F	L	S	39	55	17
	PEVFGKEKVNEL	Alpha-S1-casein	0.7808	0.0050	F	P	L	S	44	55	12
	FGKEKVNE	Alpha-S1-casein	0.8642	0.0043	V	F	E	L	47	54	8
	FGKEKVNEL	Alpha-S1-casein	1.1872	0.0007	V	F	L	S	47	55	9

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	HIQKEDVPS	Alpha-S1-casein	1.2070	0.0029	K	H	S	E	95	103	9
	HIQKEDVPSE	Alpha-S1-casein	1.8426	<0.0001	K	H	E	R	95	104	10
	IQKEDVPSE	Alpha-S1-casein	1.5730	0.0004	H	I	R	Y	96	105	10
	ERYLGYLEQ	Alpha-S1-casein	0.3803	0.0003	S	E	Q	L	104	112	9
	SAEERLHSM	Alpha-S1-casein	1.3892	<0.0001	N	S	M	K	130	138	9
	LHSMKEGIHAQQKEPM	Alpha-S1-casein	0.9538	0.0023	R	L	M	I	135	150	16
	LHSMKEGIHAQQ	Alpha-S1-casein	1.5561	0.0003	R	L	Q	K	135	146	12
	HSMKEGIHAQQKEPM	Alpha-S1-casein	1.3995	0.0005	L	H	M	I	136	150	15
	SMKEGIHAQQKEPM	Alpha-S1-casein	1.5232	0.0018	H	S	M	I	137	150	14
	MKEGIHAQQKEPMIGVNQE LAY	Alpha-S1-casein	1.1235	0.0080	S	M	Y	F	138	159	22
	KEGIHAQQKEP	Alpha-S1-casein	0.6405	0.0010	M	K	P	M	139	149	11
	IHAQQKEP	Alpha-S1-casein	1.7443	<0.0001	G	I	P	M	142	149	8
	HAQQKEP	Alpha-S1-casein	0.8158	0.0069	I	H	P	M	143	149	7
	PIGSENSEKTTMPLW	Alpha-S1-casein	0.6979	0.0105	N	P	W	-	200	214	15
	SENSEKTTMPLW	Alpha-S1-casein	0.4700	0.0004	G	S	W	-	203	214	12
	IISQETYKQEK	Alpha-S2-casein	0.7924	0.0156	S	I	K	N	29	39	11
	NREQLSTSEENS	Alpha-S2-casein	0.5119	0.0061	L	N	S	K	139	150	12
	TKLTEEEKNRL	Alpha-S2-casein	1.7827	<0.0001	K	T	L	N	166	176	11
	KISQRYQKF	Alpha-S2-casein	0.8682	0.0132	K	K	F	A	181	189	9
	YLKTVYQHQ	Alpha-S2-casein	1.7842	<0.0001	Q	Y	Q	K	194	202	9
	LKTVYQHQ	Alpha-S2-casein	1.4345	0.0008	Y	L	Q	K	195	202	8
	TVYQHQKAM	Alpha-S2-casein	1.0371	0.0190	K	T	M	K	197	205	9
	KAMKPWIQPKT	Alpha-S2-casein	1.2896	0.0089	Q	K	T	K	203	213	11

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	YYQQKPV	Kappa-casein	0.9148	0.0013	N	Y	V	A	63	69	7
	LINNQLPYPYYA	Kappa-casein	0.7645	0.0036	A	L	A	K	71	83	13
	RHPHPHLS	Kappa-casein	1.9511	0.0056	A	R	S	F	118	125	8
	KKNQDKTEIPTINT	Kappa-casein	0.4838	0.0007	P	K	T	I	132	145	14
	KKNQDKTEIPT	Kappa-casein	1.7450	<0.0001	P	K	T	I	132	142	11
	IASGEPTSTPTTE	Kappa-casein	0.9918	0.0038	T	I	E	A	146	158	13
	IIAEKTKIP	Beta-lactoglobulin	1.4816	0.0006	K	I	P	A	87	95	9
	NENKVLV	Beta-lactoglobulin	1.6553	0.0003	L	N	V	L	104	110	7
	LKALPMH	Beta-lactoglobulin	1.1575	0.0069	A	L	H	I	156	162	7
	KPEDETHLEAQPTDASAQFIRN	Glycosylation-dependent cell adhesion molecule 1	0.6926	<0.0001	N	K	N	L	22	43	22
	KPEDETHLEAQPTDASAQF	Glycosylation-dependent cell adhesion molecule 1	0.6462	<0.0001	N	K	F	I	22	40	19
	KPEDETHLEAQPTDASAQ	Glycosylation-dependent cell adhesion molecule 1	1.9871	<0.0001	N	K	Q	F	22	39	18
	LISKEQIVI	Glycosylation-dependent cell adhesion molecule 1	0.5336	0.0068	D	L	I	R	62	70	9
	ISKEQIVIRSS	Glycosylation-dependent cell adhesion molecule 1	1.0395	0.0010	L	I	S	R	63	73	11
	SSRQPQSQNP	Glycosylation-dependent cell adhesion molecule 1	0.7048	0.0027	R	S	K	L	72	82	11
	RQPQSQNP	Glycosylation-dependent cell adhesion molecule 1	0.7420	0.0004	S	R	P	K	74	81	8
	RQPQSQNPKLPL	Glycosylation-dependent cell adhesion molecule 1	0.5531	0.0002	S	R	L	S	74	85	12
	RQPQSQNP	Glycosylation-dependent cell adhesion molecule 1	0.8064	0.0009	S	R	K	L	74	82	9
	RQPQSQNPKL	Glycosylation-dependent cell adhesion molecule 1	1.8172	0.0001	S	R	P	L	74	84	11
	IVQNNDSTEY	Alpha-lactalbumin	1.1108	0.0076	A	I	G	L	60	70	11

	Sequence	Protein group	Log 10 fold change	p-value	Amino acid before	First amino acid	Last amino acid	Amino acid after	Start position	End position	Length
	VSREGQEQEGEEMAEYRG	Butyrophilin subfamily 1 member A1	0.6974	0.0030	F	V	G	R	76	93	18
	KNVQTEIVNKHND	Cysteine-rich secretory protein 2	1.1886	0.0008	L	K	D	L	35	47	13
	KLDELKRQEVs	Nucleobindin-1	0.9952	0.0061	T	K	S	R	96	106	11
	DELKRQEVs	Nucleobindin-1	0.7373	0.0028	L	D	S	R	98	106	9
	HELDSASSEVN	Osteopontin	1.4522	0.0002	S	H	N	-	268	278	11
	KPDPSQKQT	Osteopontin	0.7022	0.0081	L	K	T	F	45	53	9
	GAAIQSRAGEIQN	Polymeric immunoglobulin receptor	0.4862	0.0026	A	G	N	K	580	592	13
	AAGGPGAPADPGRPTGYSG SSKA	Polymeric immunoglobulin receptor	0.5806	0.0074	D	A	A	L	609	631	23
	KDLGEEHF	Serum albumin	0.5609	0.0014	F	K	F	K	35	42	8
	KVPQVSTPT	Serum albumin	1.3455	0.0022	R	K	T	L	436	444	9

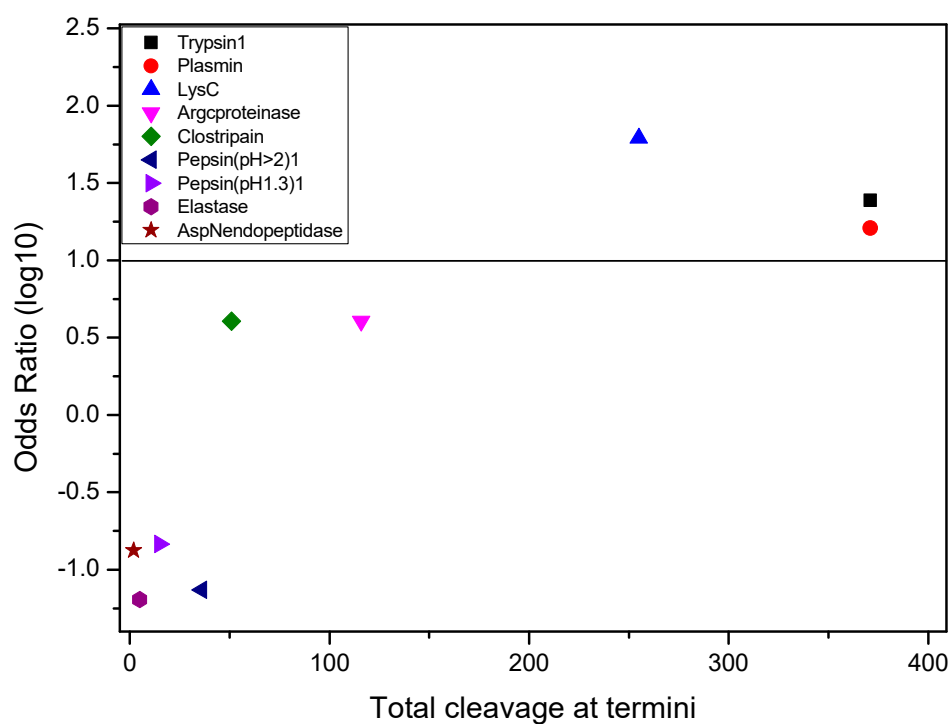
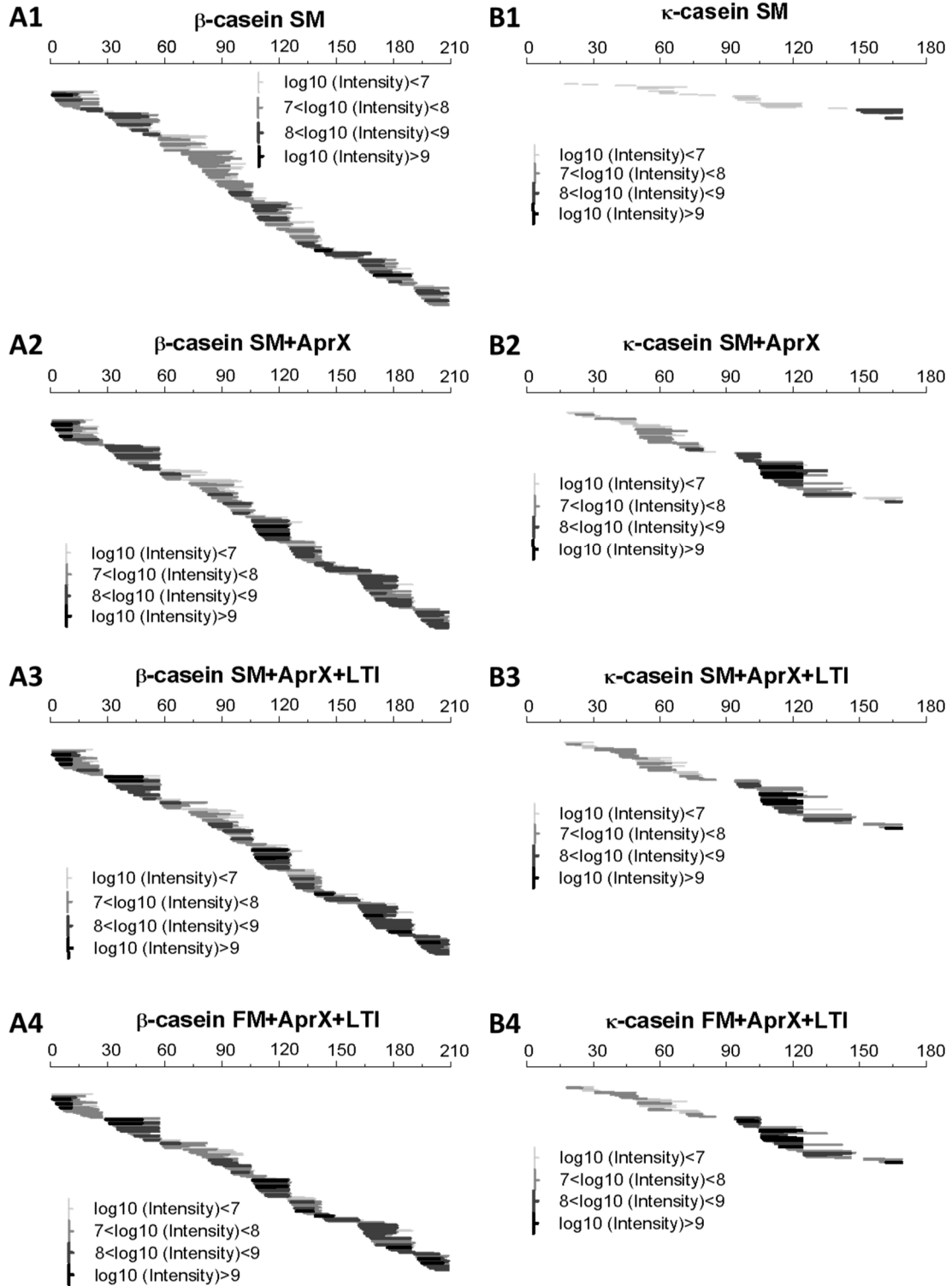


Figure. S1. Scatter plot of the total sites cleaved by an enzyme, at termini (x-axis) and log odds ratio (y-axis). Enzymes that are the most likely to be active in milk are those with a combined high number of total cleavages and a high odds ratio, represented by the top most right corner. For the enzymes that do not have expression in milk, data indicate the presence of other enzymes with similar activity.



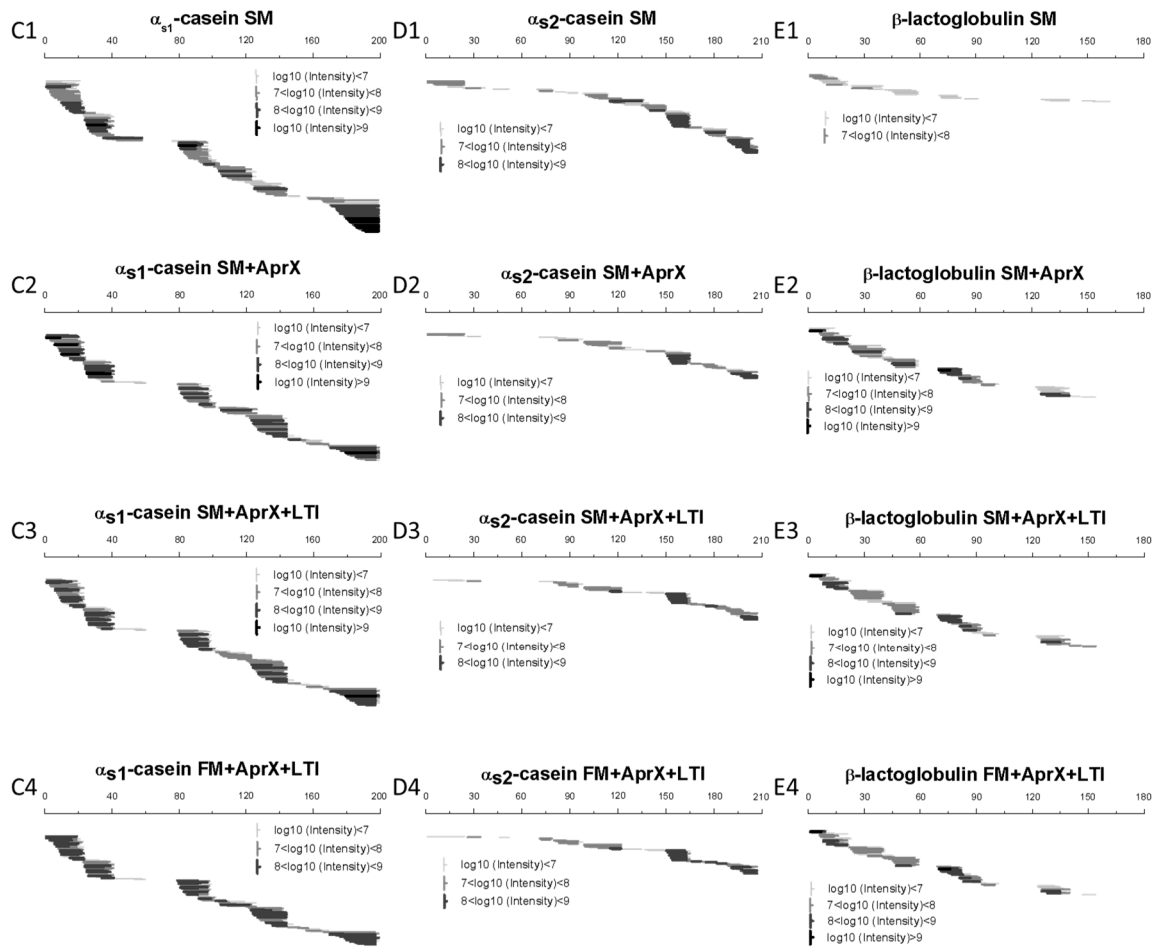


Figure. S2. Peptidomic profile from β -casein (A), κ -casein (B), α_{s1} -casein (C), α_{s2} -casein (D) and β -lactoglobulin (E) in SM, SM+AprX, SM+AprX+LTI and FM+AprX+LTI, respectively, analyzed by a nano-LC/LTQ and Orbitrap. MS/MS. Peptides with different intensity were distinguished by color and width. The intensity showed in the figure were the average value of triplicates.