

**Table S3.** Peptides sharing 100% of sequence homology with previously reported bioactive peptides identified in the low-molecular weight peptide fractions of un-digested and *in vitro* digested Ras cheese samples at different ripening time.

<i>Peptide sequence</i>	<i>Protein fragment</i>	<i>Bioactivity</i>	<i>Sample</i>
RELEEL	$\beta$ -casein (1-6)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
LNVPGEIVE	$\beta$ -casein (6-14)	ACE-inhibitor (IC <sub>50</sub> =300 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
NVPGEIVESL	$\beta$ -casein (7-16)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
VPGEIVE	$\beta$ -casein (8-14)	DPP-IV-inhibitor (IC <sub>50</sub> =225 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
S(pospho)S(pospho)S(pospho)EESITRIN	$\beta$ -casein (17-27)	Anti-microbial	R30
FQS(pospho)EEQQQTEDELQDK	$\beta$ -casein (33-48)	Promote calcium uptake	R30, R90, R180, DR30, DR90 and DR180
FQS(pospho)EEQQQTEDELQDKIHPF	$\beta$ -casein (33-52)	Promote calcium uptake	R30, R90, DR30, DR90 and DR180
DKIHP	$\beta$ -casein (47-51)	ACE-inhibitor (IC <sub>50</sub> =113 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
DKIHPF	$\beta$ -casein (47-52)	ACE-inhibitor (IC <sub>50</sub> =257 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
LVYFPFGPI	$\beta$ -casein (58-66)	ACE-inhibitor (IC <sub>50</sub> =180 $\mu$ mol/L)	R30, R90, DR30, DR90 and DR180
LVYFPFGPIP	$\beta$ -casein (58-67)	ACE-inhibitor (IC <sub>50</sub> =89 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
VYFPFGPIPN	$\beta$ -casein (59-68)	ACE-inhibitor (IC <sub>50</sub> =325 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
YFPF	$\beta$ -casein (60-63)	Opioid, anti-cancer	R30, R90, R180, DR30, DR90 and DR180
YFPFGPI	$\beta$ -casein (60-66)	ACE-inhibitor (IC <sub>50</sub> =500 $\mu$ mol/L), antioxidant, opioid, immunomodulator, anxiolytic, anti-cancer	R30, R180, DR30, DR90 and DR180
YFPFGPIP	$\beta$ -casein (60-67)	ACE-inhibitor (IC <sub>50</sub> =224 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
YFPFGPIPN	$\beta$ -casein (60-68)	ACE-inhibitor (IC <sub>50</sub> =15 $\mu$ mol/L), DPP-IV-inhibitor (IC <sub>50</sub> =670 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
PFP	$\beta$ -casein (61-63) $\alpha$ S1-casein (27-29)	ACE-inhibitor (IC <sub>50</sub> =144 $\mu$ mol/L)	R30, R90, R180 and DR180
PFPFGPIPN	$\beta$ -casein (61-68)	ACE-inhibitor	R30, R90, R180, DR30, DR90 and DR180

FPGPIP	$\beta$ -casein (62-68)	DPP-IV-inhibitor (IC <sub>50</sub> =260 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
PGPIP	$\beta$ -casein (63-68)	ACE-inhibitor, immunomodulator, anti-cancer, anti- inflammatory	R90, R180, DR30, DR90 and DR180
SLPQ	$\beta$ -casein (69-72)	ACE-inhibitor (IC <sub>50</sub> =330 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
SLPQNIPPL	$\beta$ -casein (69-77)	DPP-IV-inhibitor	R30, R90, R180, DR30, DR90 and DR180
NIPPLTQTPV	$\beta$ -casein (73-82)	ACE-inhibitor (IC <sub>50</sub> =173 $\mu$ mol/L)	R30, R90, DR30, DR90 and DR180
NIPPLTQTPVVPPFLQ	$\beta$ -casein (73-89)	ACE-inhibitor (IC <sub>50</sub> =450 $\mu$ mol/L)	DR30, DR90 and DR180
IPP	$\beta$ -casein (74-76) $\kappa$ -casein (108-110)	ACE-inhibitor (IC <sub>50</sub> =5 $\mu$ mol/L), DPP-IV- inhibitor (IC <sub>50</sub> =169 $\mu$ mol/L), antioxidant, anti-inflammatory	R30, R90, R180, DR30, DR90 and DR180
IPPLTQT	$\beta$ -casein (74-80)	DPP-IV-inhibitor (IC <sub>50</sub> =465 $\mu$ mol/L)	R90 and DR90
TQTPVVPPFLQPE	$\beta$ -casein (78-91)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
TPVVPPFLQP	$\beta$ -casein (80-90)	ACE-inhibitor (IC <sub>50</sub> =749 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
VVPP	$\beta$ -casein (83-86)	ACE-inhibitor (IC <sub>50</sub> =258 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
VPP	$\beta$ -casein (84-86)	ACE-inhibitor (IC <sub>50</sub> =8 $\mu$ mol/L), antioxidant, anti-inflammatory	R30, R90, R180, DR90 and DR180
EAMAPK	$\beta$ -casein (100-105)	Anti-microbial	R30, R90, R180, DR30, DR90 and DR180
HKEMPPFK	$\beta$ -casein (106-113)	Anti-microbial	R90, R180, DR30, DR90 and DR180
EMPPFK	$\beta$ -casein (108-113)	Anti-microbial	R30, R90, R180, DR30, DR90 and DR180
FPKYPVEPF	$\beta$ -casein (111-119)	Antioxidant	R30, R90, R180 and DR90
KYP	$\beta$ -casein (113-115)	ACE-inhibitor (IC <sub>50</sub> =364 $\mu$ mol/L)	R30, R90 and R180
YPVEPF	$\beta$ -casein (114-119)	DPP-IV-inhibitor (IC <sub>50</sub> =125 $\mu$ mol/L), antioxidant, anti- microbial, opioid	R30, R90, R180, DR30, DR90 and DR180
DVENLHLPLPL	$\beta$ -casein (129-139)	Anti-microbial	R30, DR30, DR90 and DR180
NLHLPLPLL	$\beta$ -casein (132-140)	ACE-inhibitor (IC <sub>50</sub> =15 $\mu$ mol/L)	R30, R90, DR90 and DR180
NLHLPLP	$\beta$ -casein (132-138)	ACE-inhibitor (IC <sub>50</sub> =51 $\mu$ mol/L)	R30, R90, DR30, DR90 and DR180
LHLPLPL	$\beta$ -casein (133-139)	ACE-inhibitor (IC <sub>50</sub> =425 $\mu$ mol/L)	R30, DR30, DR90 and DR180
LHLPLP	$\beta$ -casein (133-138)	ACE-inhibitor (IC <sub>50</sub> =3 $\mu$ mol/L)	R30, DR90 and DR180

HLPLP	$\beta$ -casein (134-138)	ACE-inhibitor (IC <sub>50</sub> =22 $\mu$ mol/L)	R30, R90, DR30, DR90 and DR180
LPLPLL	$\beta$ -casein (135-140)	ACE-inhibitor, DPP/IV-inhibitor (IC <sub>50</sub> =372 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
LPLPL	$\beta$ -casein (135-139)	DPP/IV-inhibitor (IC <sub>50</sub> =325 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
LPLP	$\beta$ -casein (135-138)	ACE-inhibitor (IC <sub>50</sub> =750 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
LQSW	$\beta$ -casein (140-143)	ACE-inhibitor (IC <sub>50</sub> =500 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
WMHQPHQPLPPT	$\beta$ -casein (143-154)	ACE-inhibitor, anti- inflammatory	DR30, DR90 and DR180
HQPHQPLPPT	$\beta$ -casein (145-154)	ACE-inhibitor	R30, R90, DR30, DR90 and DR180
SKVLPVPQ	$\beta$ -casein (168-175)	ACE-inhibitor (IC <sub>50</sub> =39 $\mu$ mol/L)	R90, DR30, DR90 and DR180
KVLPVPQ	$\beta$ -casein (169-175)	ACE-inhibitor (IC <sub>50</sub> =1000 $\mu$ mol/L), anti-inflammatory	R30, R90, R180, DR30, DR90 and DR180
VLPVPQK	$\beta$ -casein (169-175)	ACE-inhibitor (IC <sub>50</sub> =15 $\mu$ mol/L), antioxidant, anti- microbial	R30, R90, DR30, DR90 and DR180
LPVPQ	$\beta$ -casein (171-175)	DPP-IV-inhibitor (IC <sub>50</sub> =44 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
VPYPQR	$\beta$ -casein (178-183)	Antioxidant	R30, R90 and R180
VPYPQ	$\beta$ -casein (178-182)	DPP-IV-inhibitor (IC <sub>50</sub> =41 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
PYPQ	$\beta$ -casein (179-182)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
RDMPIQAF	$\beta$ -casein (183-190)	ACE-inhibitor (IC <sub>50</sub> =209 $\mu$ mol/L)	R30 and R90
LLY	$\beta$ -casein (191-193)	Antioxidant, immunomodulator, anti-inflammatory	R30, R90, DR30, DR90 and DR180
LYQEPVLGPVR	$\beta$ -casein (192-203)	ACE-inhibitor, anti- inflammatory	DR30, DR90 and DR180
YQEPVLGPVR	$\beta$ -casein (193-203)	ACE-inhibitor (IC <sub>50</sub> =3300 $\mu$ mol/L), antioxidant, immunomodulator, anti-inflammatory	R30, R90, R180, DR30, DR90 and DR180
YQEP	$\beta$ -casein (193-196)	ACE-inhibitor (IC <sub>50</sub> =317 $\mu$ mol/L), antioxidant	R30, R90 and R180
YQEPVLGPVRGPFPI	$\beta$ -casein (193-207)	Anti-microbial	R30, R90, R180, DR30, DR90 and DR180
YQEPVLGPVRGPFPIIV	$\beta$ -casein (193-209)	ACE-inhibitor (IC <sub>50</sub> =101 $\mu$ mol/L), anti-microbial, immunomodulator	R30, R90, R180, DR30, DR90 and DR180
QEPV	$\beta$ -casein (194-197)	Immunomodulator	R30, R180, DR30, DR90 and DR180

QEPVLGPVRGPFPIIV	$\beta$ -casein (194-209)	ACE-inhibitor (IC <sub>50</sub> =600 $\mu$ mol/L)	R30, R90, DR30, DR90 and DR180
EPVLGPVRGPFPP	$\beta$ -casein (195-206)	ACE-inhibitor (IC <sub>50</sub> =790 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
VLGPVRGPFPP	$\beta$ -casein (197-206)	ACE-inhibitor (IC <sub>50</sub> =137 $\mu$ mol/L)	R30, R90 and R180
VRGPFPIIV	$\beta$ -casein (201-209)	ACE-inhibitor (IC <sub>50</sub> =600 $\mu$ mol/L)	R30, R90, R180, DR90 and DR180
VRGPFPP	$\beta$ -casein (201-206)	ACE-inhibitor (IC <sub>50</sub> =592 $\mu$ mol/L)	R30, R90 and R180
RPK	$\alpha$ S1-casein (1-3)	ACE-inhibitor (IC <sub>50</sub> =92 $\mu$ mol/L), anti-cancer	DR30, DR90 and DR180
RPKHPI	$\alpha$ S1-casein (1-6)	ACE-inhibitor (IC <sub>50</sub> =40 $\mu$ mol/L)	R30, R90, R180, DR30 and DR90
RPKHPIK	$\alpha$ S1-casein (1-7)	Anti-microbial	R30 and R180
VLNENLLR	$\alpha$ S1-casein (15-22)	Anti-microbial	R30, R90 and R180
ENLLRF	$\alpha$ S1-casein (18-23)	ACE-inhibitor (IC <sub>50</sub> =82 $\mu$ mol/L),	R30, R90, R180, DR90 and DR180
LRFF	$\alpha$ S1-casein (21-24)	ACE-inhibitor (IC <sub>50</sub> =117 $\mu$ mol/L),	R30 and DR180
FVAPFPEVFG	$\alpha$ S1-casein (24-33)	ACE-inhibitor (IC <sub>50</sub> =650 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
APFPE	$\alpha$ S1-casein (26-30)	DPP-IV-inhibitor (IC <sub>50</sub> =49 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
PFPEVFGK	$\alpha$ S1-casein (27-34)	ACE-inhibitor (IC <sub>50</sub> =108 $\mu$ mol/L)	R30, R90 and R180
FPEVFGK	$\alpha$ S1-casein (28-34)	ACE-inhibitor (IC <sub>50</sub> =140 $\mu$ mol/L)	R30, R90 and R180
DIGS(pospho)ES(pospho)TEDQAMEDIK	$\alpha$ S1-casein (43-58)	Promote calcium uptake	R90, R180, DR30, DR90 and DR180
VPSERY	$\alpha$ S1-casein (86-91)	ACE-inhibitor (IC <sub>50</sub> =706 $\mu$ mol/L)	R30, R90 and R180
VPSERYL	$\alpha$ S1-casein (86-92)	ACE-inhibitor (IC <sub>50</sub> =250 $\mu$ mol/L)	R30, R90 and R180
RYLGY	$\alpha$ S1-casein (90-94)	ACE-inhibitor (IC <sub>50</sub> =3 $\mu$ mol/L), antioxidant	R30 and DR30
YLG	$\alpha$ S1-casein (91-93)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
YLGY	$\alpha$ S1-casein (91-94)	Antioxidant	R30, R90, R180, DR30 and DR180
YLGYLE	$\alpha$ S1-casein (91-96)	ACE-inhibitor (IC <sub>50</sub> =86 $\mu$ mol/L), antioxidant, opioid	R30, R90, R180, DR90 and DR180
YLGYLEQ	$\alpha$ S1-casein (91-97)	Anxiolytic	R30, R90 and R180
LGY	$\alpha$ S1-casein (92-94)	ACE-inhibitor (IC <sub>50</sub> =22 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
YLEQLLR	$\alpha$ S1-casein (94-100)	Anti-microbial	R30, R90, R180, DR30 and DR90
YKVPQL	$\alpha$ S1-casein (104-109)	ACE-inhibitor (IC <sub>50</sub> =22 $\mu$ mol/L)	R30, R90, R180, DR90 and DR180
LHSMK	$\alpha$ S1-casein (104-109)	Antioxidant	DR30, DR90 and DR180

AYFYPE	$\alpha$ S1-casein (143-148)	ACE-inhibitor (IC <sub>50</sub> =22 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
AYFYPEL	$\alpha$ S1-casein (143-149)	ACE-inhibitor (IC <sub>50</sub> =7 $\mu$ mol/L), antioxidant, opioid	R30, R180, DR30, DR90 and DR180
YFYPE	$\alpha$ S1-casein (144-148)	Opioid	R30, R90, R180, DR30, DR90 and DR180
YFYPEL	$\alpha$ S1-casein (144-149)	ACE-inhibitor (IC <sub>50</sub> =9 $\mu$ mol/L), antioxidant, opioid	DR30, DR90 and DR180
PEL	$\alpha$ S1-casein (147-149)	Antioxidant	R30, R90, R180, DR30, DR90 and DR180
DAYPSGAW	$\alpha$ S1-casein (157-164)	ACE-inhibitor (IC <sub>50</sub> =98 $\mu$ mol/L)	R90, R180, DR30, DR90 and DR180
GAW	$\alpha$ S1-casein (162-164)	ACE-inhibitor (IC <sub>50</sub> =240 $\mu$ mol/L)	DR30, DR90 and DR180
SDIPNPIGSENSEK	$\alpha$ S1-casein (147-149)	Anti-microbial	R30, R90, R180, DR30, DR90 and DR180
NMAINPSK	$\alpha$ S2-casein (25-32)	ACE-inhibitor (IC <sub>50</sub> =600 $\mu$ mol/L)	DR30, DR90 and DR180
KALNEINQF	$\alpha$ S2-casein (80-88)	Antioxidant	R30, R90, DR90 and DR180
YQKFPQY	$\alpha$ S2-casein (89-95)	ACE-inhibitor (IC <sub>50</sub> =98 $\mu$ mol/L), antioxidant	R30, R90 and R180
NPWDQ	$\alpha$ S2-casein (107-111)	Immunomodulator	R30, R90, R180, DR30, DR90 and DR180
VPITPT	$\alpha$ S2-casein (117-122)	DPP-IV-inhibitor (IC <sub>50</sub> =130 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
LKKISQ	$\alpha$ S2-casein (164-169)	Anti-microbial	R30
FALPQY	$\alpha$ S2-casein (174-179)	ACE-inhibitor (IC <sub>50</sub> =4 $\mu$ mol/L)	R30, R90 and R180
AMKPW	$\alpha$ S2-casein (189-193)	ACE-inhibitor (IC <sub>50</sub> =580 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
WIQP	$\alpha$ S2-casein (193-196)	ACE-inhibitor (IC <sub>50</sub> =14 $\mu$ mol/L), DPP-IV-inhibitor (IC <sub>50</sub> =237 $\mu$ mol/L)	R30, R90, R180, DR90 and DR180
TKVIP	$\alpha$ S2-casein (198-202)	ACE-inhibitor (IC <sub>50</sub> =400 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
TKVIPYVRYL	$\alpha$ S2-casein (193-207)	Anti-microbial	R30, R90 and R180
EKDERF	$\kappa$ -casein (12-17)	ACE-inhibitor (IC <sub>50</sub> =14 $\mu$ mol/L)	R30, R90 and R180
DERF	$\kappa$ -casein (14-17)	ACE-inhibitor (IC <sub>50</sub> =38 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
FFSDK	$\kappa$ -casein (17-21)	Anti-cancer, anti-microbial	R30, R90, DR30, DR90 and DR180
IAK	$\kappa$ -casein (22-24)	ACE-inhibitor (IC <sub>50</sub> =16 $\mu$ mol/L)	DR30, DR90 and DR180

IPIQY	$\kappa$ -casein (26-30)	DPP-IV-inhibitor (IC <sub>50</sub> =35 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
YVL	$\kappa$ -casein (30-32)	Antioxidant, anti- microbial	R30, R90, R180, DR30, DR90 and DR180
YGL	$\kappa$ -casein (38-40)	ACE-inhibitor (IC <sub>50</sub> =409 $\mu$ mol/L)	R30, R90, R180, DR30 and DR180
INNQFLPYPY	$\kappa$ -casein (51-60)	DPP-IV-inhibitor (IC <sub>50</sub> =40 $\mu$ mol/L)	R30, DR30, DR90 and DR180
LPYPY	$\kappa$ -casein (56-60)	ACE-inhibitor (IC <sub>50</sub> =29 $\mu$ mol/L), DPP-IV-inhibitor (IC <sub>50</sub> =108 $\mu$ mol/L)	R30, R90, R180, DR30, DR90 and DR180
IIAEK	$\beta$ -lactoglobulin (71- 75)	ACE-inhibitor (IC <sub>50</sub> =64 $\mu$ mol/L)	DR30, DR90 and DR180
IAEK	$\beta$ -lactoglobulin (72- 75)	ACE-inhibitor (IC <sub>50</sub> =26 $\mu$ mol/L)	DR30, DR90 and DR180
VLDTDYK	$\beta$ -lactoglobulin (94- 100)	ACE-inhibitor (IC <sub>50</sub> =946 $\mu$ mol/L)	DR90 and DR180
YLL	$\beta$ -lactoglobulin (78- 80)	ACE-inhibitor (IC <sub>50</sub> =519 $\mu$ mol/L), antioxidant	R30, R90, R180, DR30, DR90 and DR180
TPEVDDEALEK	$\beta$ -lactoglobulin (125- 135)	DPP-IV-inhibitor (IC <sub>50</sub> =320 $\mu$ mol/L), anti-microbial	DR30, DR90 and DR180
ALPM	$\beta$ -lactoglobulin (142- 145)	ACE-inhibitor (IC <sub>50</sub> =928 $\mu$ mol/L)	DR30, DR90 and DR180
ALPMH	$\beta$ -lactoglobulin (142- 146)	ACE-inhibitor (IC <sub>50</sub> =521 $\mu$ mol/L)	DR30, DR90 and DR180

Peptide bioactivities and IC<sub>50</sub> values were obtained from the Milk Bioactive Peptides Database.

Abbreviations are: R30: Ras cheese at 30 days of ripening; R90: Ras cheese at 90 days of ripening; R180: Ras cheese at 180 days of ripening; DR30: digested Ras cheese at 30 days of ripening; DR90: digested Ras cheese at 90 days of ripening; DR180: digested Ras cheese at 180 days of ripening; ACE: angiotensin-converting enzyme; DPP-IV: dipeptidyl peptidase IV; PEP: prolyl-endopeptidase.