Differential splicing: an effective way to expand molecular diversity of caseins and their ability to generate bioactive peptides

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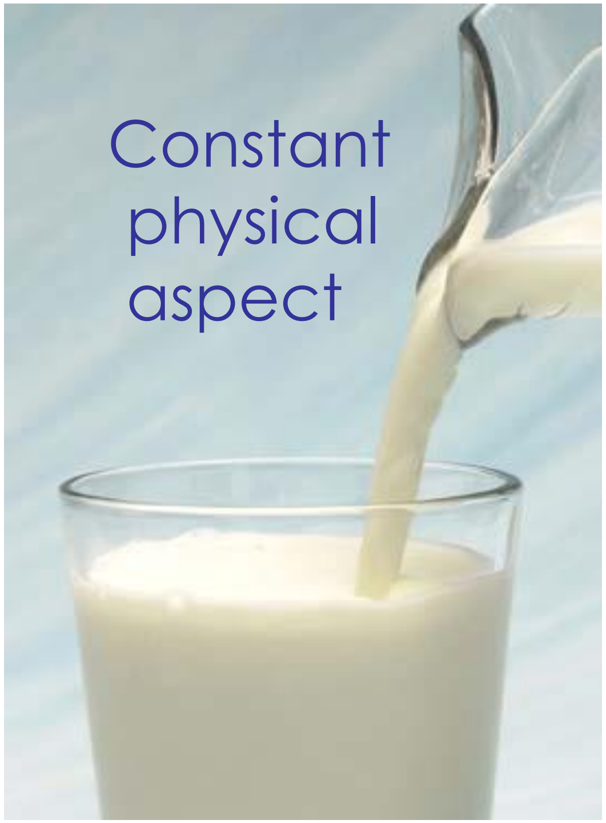
Symposium on Camel Milk - Montpellier, November 15 -16, 2021

Milk: a complete and complex food



Hide a large variability in composition between species

a paradox

"Designed" to fulfil **specific** requirements and provide optimal growth and development to mammalian **offsprings**



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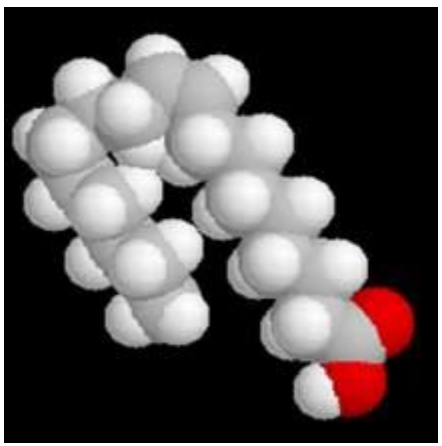
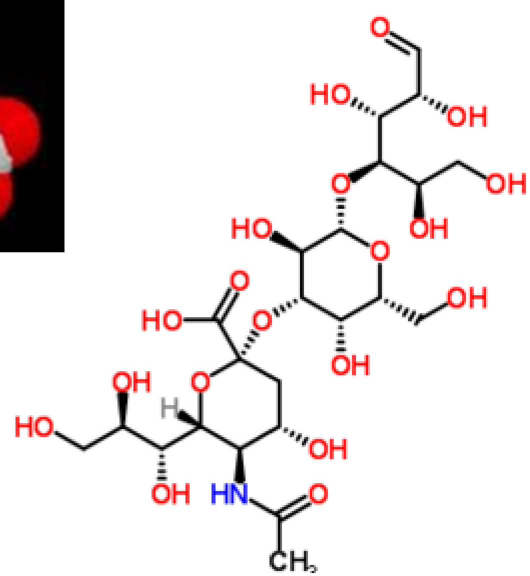
Milk is much more than a complete food

Milk is a source of bioactive components, including long chain fatty acids, complex oligosaccharides and proteins





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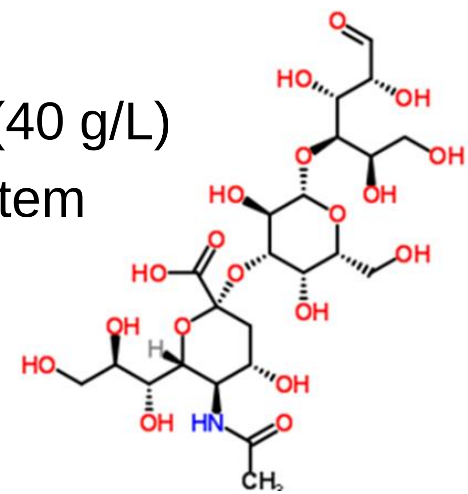
HMOs: the third most abundant solid component of human milk

- 10 g/L in mature milk after lactose (70 g/L) and lipids (40 g/L)
- Confer protection on the newborn whose immune system is functionnaly immature
- Prebiotics, promoting growth of beneficial bacteria,
- Protect against pathogenic infection
- Stimulate maturation of the immune system

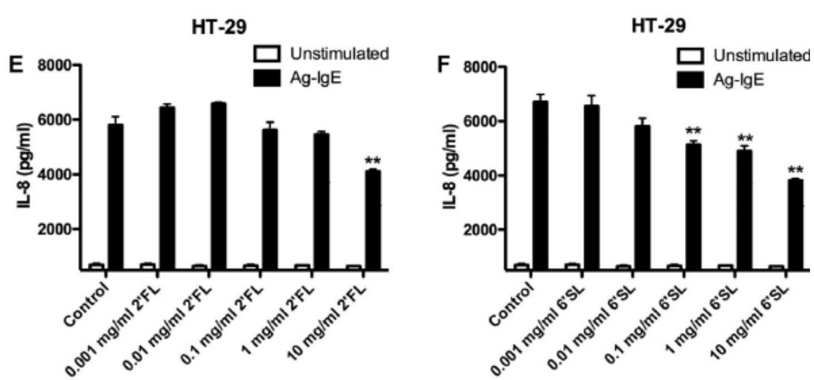


Fucosylated 40%
Sialylated 13%

Human Milk Oligosaccharides Attenuate Antigen–Antibody Complex Induced Chemokine Release from Human Intestinal Epithelial Cell Lines

Sehrish Zehra, Ibrahim Khambati, Megan Vierhout, M. Firoz Mian, Rachael Buck, and Paul Forsythe

Vol. 83, Nr. 2, 2018 • Journal of Food Science



Fucosylated Sialylated

Oligosacharrides in camel milk

J. Dairy Sci. 93:5572–5587
doi:10.3168/jds.2010-3151

Chemical characterization of the oligosaccharides in Bactrian camel (*Camelus bactrianus*) milk and colostrum

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J. Dairy Sci. 103:72–86
https://doi.org/10.3168/jds.2019-16710

Electrospray ionization mass spectrometry characterization of ubiquitous minor lipids and oligosaccharides in milk of the camel (*Camelus dromedarius*) and their inhibition of oxidative stress in human plasma

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Milk proteins: a source of biologically active peptides

β-casomorphins (BCMs), derived from β-casein, first identified in bovine milk

(Brantl & Teschemacher, 1979)

recently shown to occur naturally in breast milk (Enjapoori *et al.*, 2019)

Signal peptide

```
        10         20         30         40         50
MKVLILACLVALALA RELEE LNVPGEIVES LSSSEESITR INKKIEKFQS
        60         70         80         90        100
EEQQQTEDEL QDKIHPFAQT QSLVYPFPGP IHNSLPQNIP PLTQTPVVVP   BCM5-11
       110        120        130        140        150
PFLQPEVMGV SKVKEAMAPK HKEMPFPKYP VEPFTESQSL TLTDVENLHL
       160        170        180        190        200
PLPLLQSWMH QPHQPLPPTV MFPPQSVLSL SQSKVLPVPQ KAVPYPQRDM
       210        220
PIQAFLLYQE PVLGPVRGPF PIIV
```

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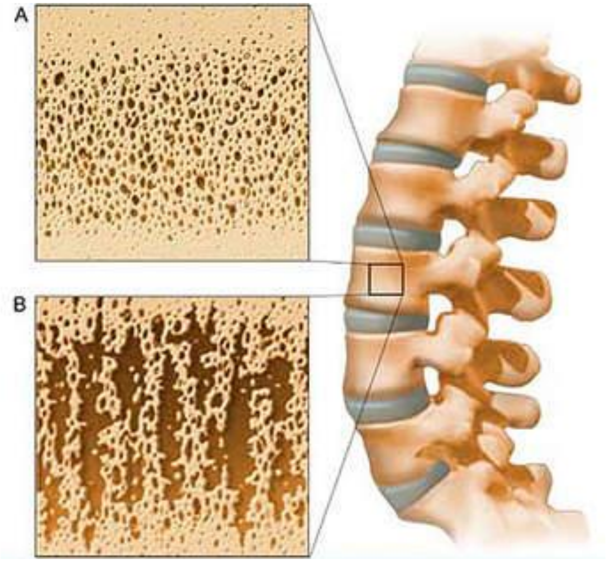
Therapeutic effects of milk-derived peptides in several health disorders

Hypertension
cardiovascular disease
obesity
osteoporosis
dental caries
gastrointestinal diseases
ageing, … and others



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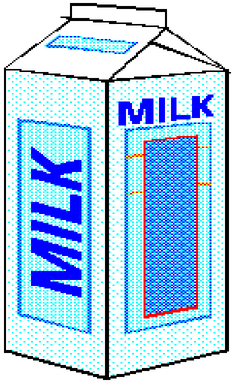
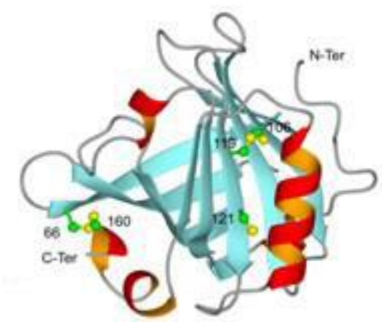
Milk proteins



Soluble fraction
(Whey proteins)



20%

β-lactoglobulin

α-lactalbumin

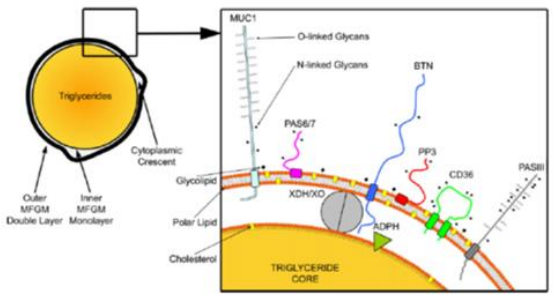
Lactoferrin, …

(Globular tertiary structure)

Milk Fat Globule Membrane

> 80 proteins (<1%)

(Butyrophilin, adipophilin, xanthine oxidase, FABP, lactadherin, ...)



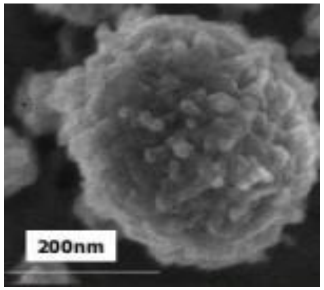
(Dewettinck *et al.*, 2008)

Colloidal fraction

80%

Caseins

(random coiled, organised in Micelles)



(Dalgleish *et al.*, 2004)

The bulk of the protein fraction in milk corresponds to the products of only 6 genes

Coding for: **4 caseins (αs1, αs2, β and κ)**
2 main whey proteins (β-lactoglobulin & α-lactalbumin)

95% of the protein fraction in cattle

Several tens or even hundreds of proteins in the remaining 5%

A fairly simple system, regarding the main milk proteins**,** but this milk proteome is much more complex with:

- **genetic variants**
- low-abundance gene products arising from **differential splicing**
- isoforms due to **post-translational modifications** such as **phosphorylation**, glycosylation and proteolytic processing.

up to 100 molecules, derived from the 6 major milk proteins

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Miranda *et al.*, 2020

Food Chemistry: X 5 (2020) 100080

Genetic variants of the main milk proteins

	CSN1S1 (αs1-casein)	CSN1S2 (αs2-casein)	CSN2 (β-casein)	CSN3 (κ-casein)	β-lactoglobulin	α-lactalbumin
	**9 variants** A to I	**4 variants** A to D	**12 variants** A^1, A^2, A^3, B to J	**15 variants** A, B, B2, C to E (F1,F2,G1, G2 and H to L)	**13 variants** A, B, B*, C, D and Dr, E to J and W	**4 variants** A to D
	**15 variants (+ 3 null alleles)**	**7 variants** (+1 null allele)	**6 variants** (+ 3 null alleles)	**17 variants**	**2 putative variants** (uncharacterized so far)	**2 Variants**
	**10 variants**	**8 variants**	**5 variants**	**3 variants**	**3 variants**	**2 variants**

from Martin *et al*. (2013),
Selvaggi *et al*. (2014a, 2014b)

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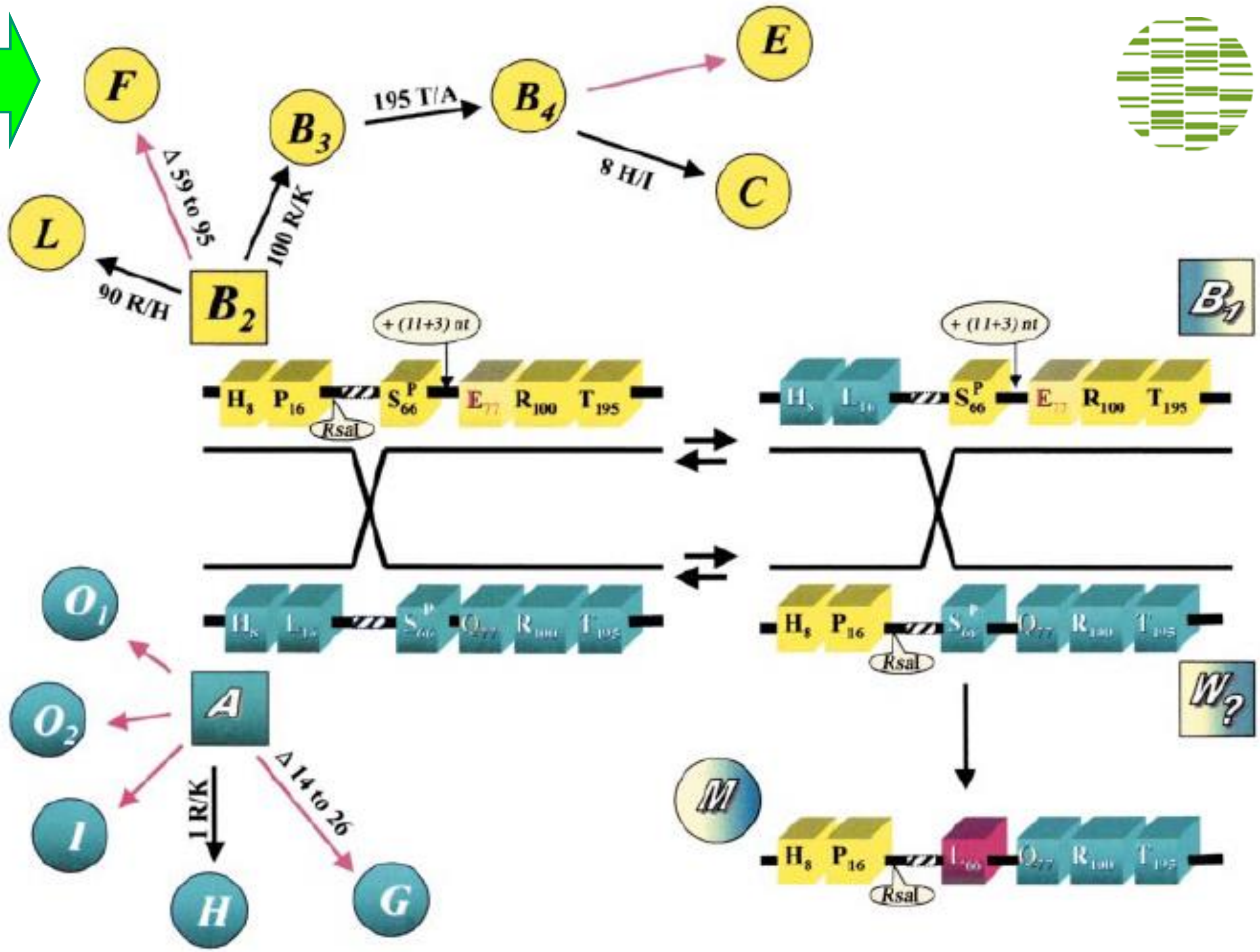
Genetic polymorphisms at the *CSN1S1* locus in the goat species

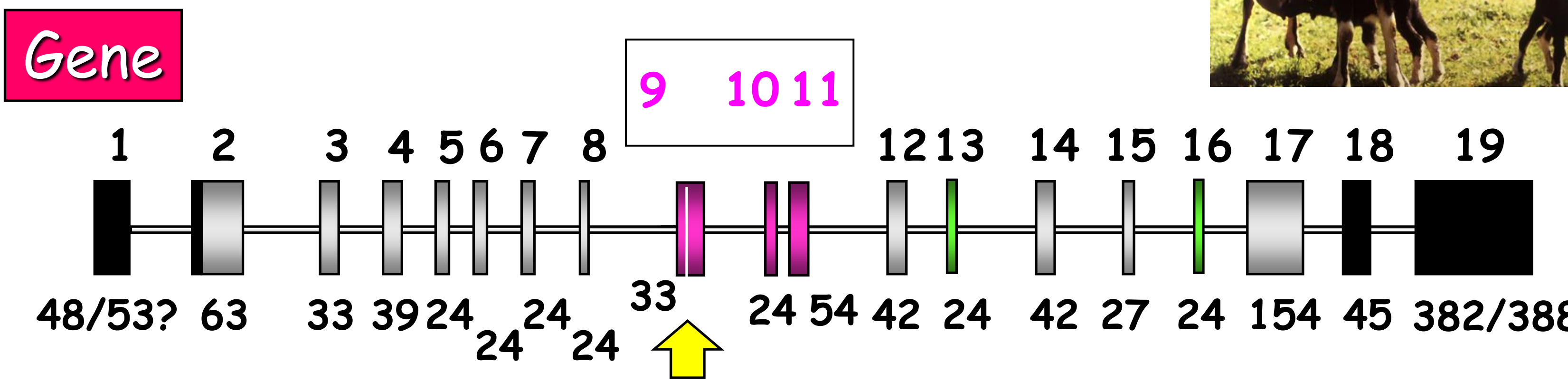


Bevilacqua *et al*., 2002

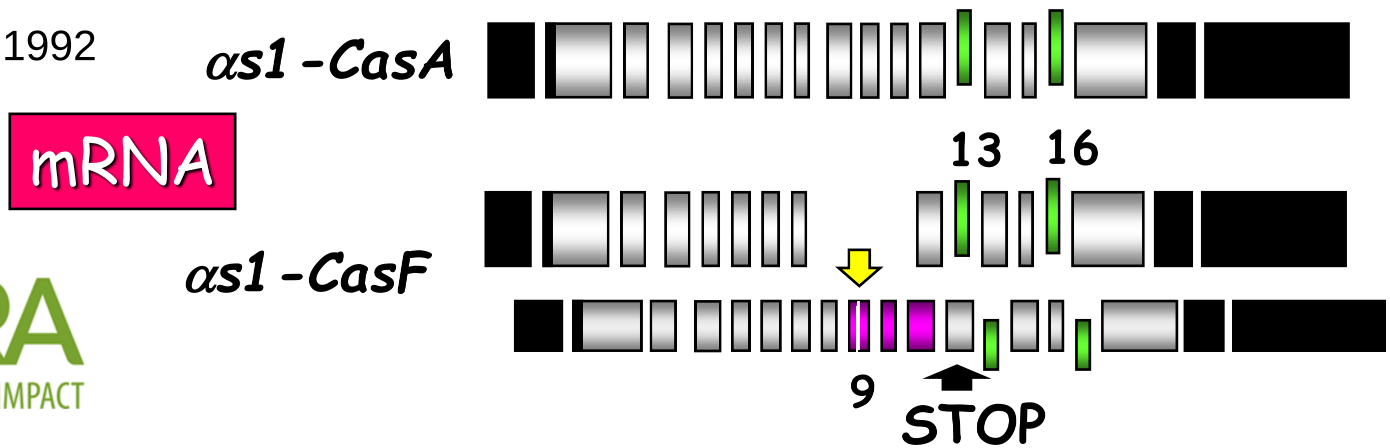
Allele F: A "frame shift" mutation

a multiplicity of transcripts (proteins)

a reduced expression



Leroux *et al.*, 1992



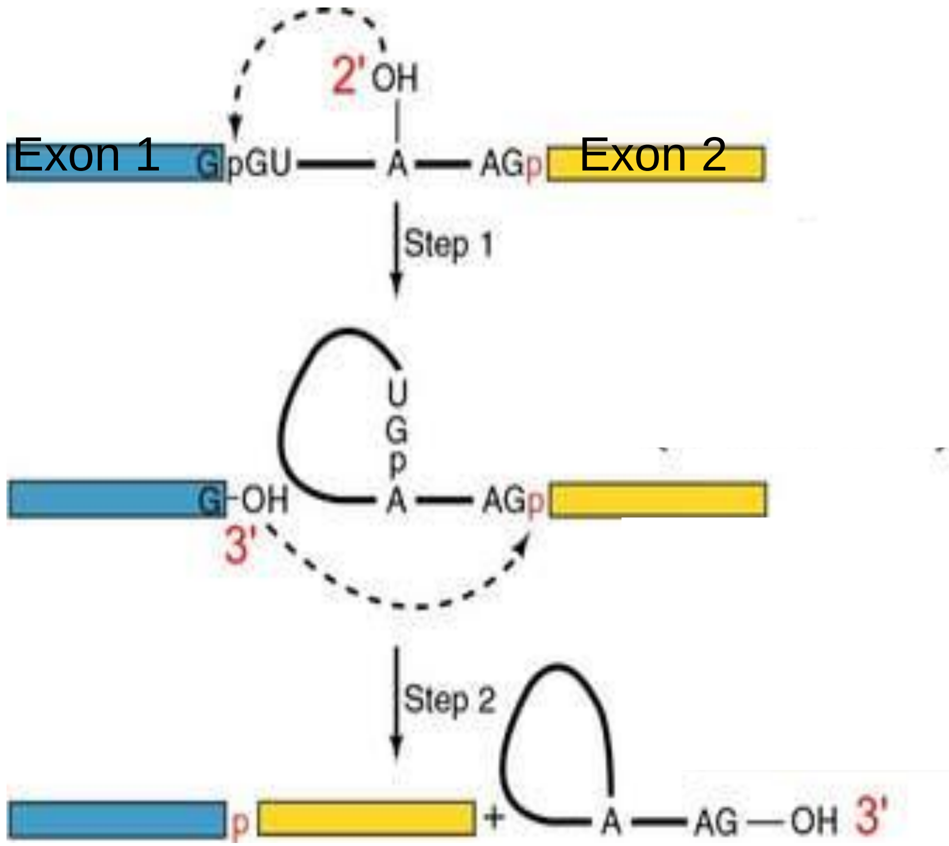
α_{s1}- ***CasF*** ⇨ 9 different transcripts as many different peptide chains

Occurrence of splicing variants due to cryptic splice site usage and exon skipping

Exon skipping (ES): loss of exon during the course of pre-mRNA maturation (assembly of exonic sequences and removal of introns)

Cryptic splice site usage (CSS): loss or gain of nucleotides (intron or exon sequences)

Quality control mechanisms



Events first reported in small ruminants: CSN1S in the goat species

Post-translational modifications contribute to increase molecular diversity

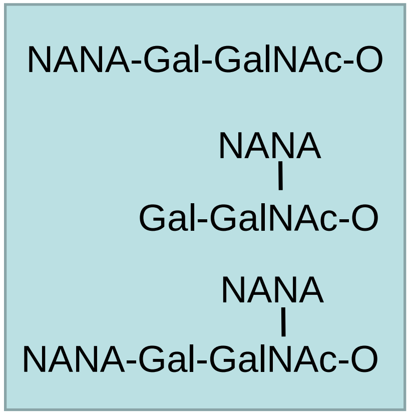
Glycosylation: κ-casein (O-glycosylation on up to 6 Thr residues)

MMKSFFLVVTILALTLPFLGA QEQNQEQPIRCEKDERFFSDKIAKYIPIQY

VLSRYPSYGLNYYQQKPVALINNQFLPYPYYAKPAAVRSPAQILQWQVLSNT

VPAKSCQAQPTTMARHPHPHLS**F-M**AIPPKKNQDKTEIPTINTIASGEPTST

PTTEAVESTVATLEDSPEVIESPPEINTVQVTSTAV



Phosphorylation: αs2-casein (theoretically up to16P on Ser/Thr residues)

MKFFIFTCLLAVALA KNTMEHVSSSEESIISQETYKQEKNMAINPSKENL

CSTFCKEVVRNANEEEYSIGSSSEESAEVATEEVKITVDDKHYQKALNEIN

QFYQKFPQYLQYLYQGPIVLNPWDQVKRNAVPITPTLNREQLSTSEENSKK

TVDMESTEVFTKKTKLTEEEKNRLNFLKKISQRYQKFALPQYLKTVYQHQK

AMKPWIQPKTKVIPYVRYL

LC-MS profiling of bovine milk proteins

An improved LC–MS method to profile molecular diversity and quantify the six main bovine milk proteins, including genetic and splicing variants as well as post-translationally modified isoforms

Guy Miranda[a,*], Leonardo Bianchi[a], Zuzana Krupova[a,1], Philippe Trossat[b], Patrice Martin[a,*]

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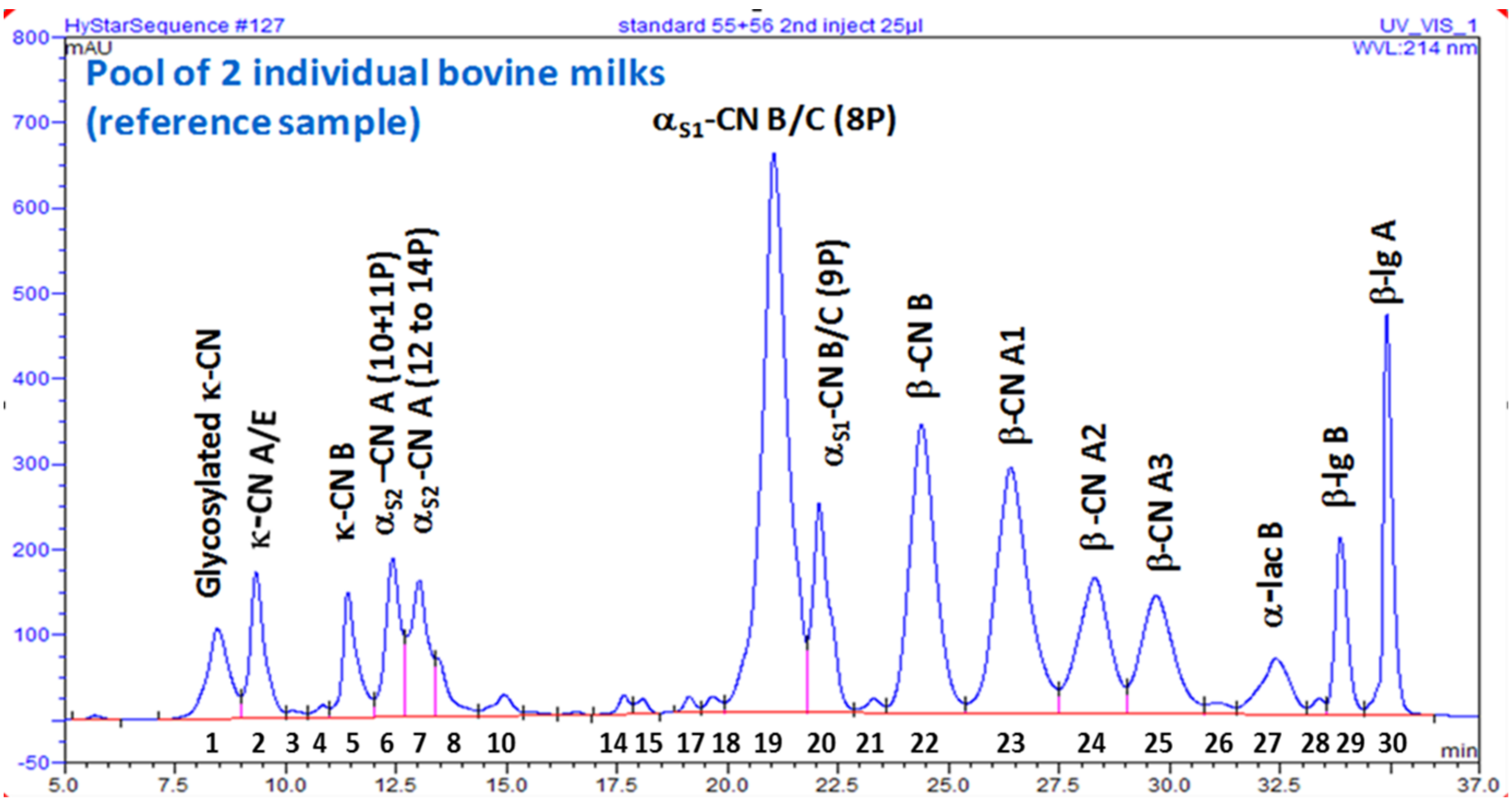
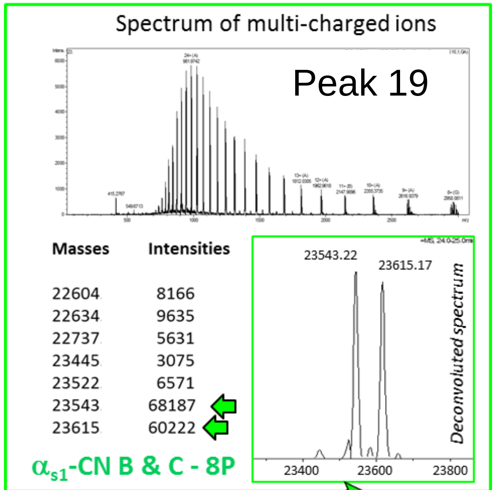
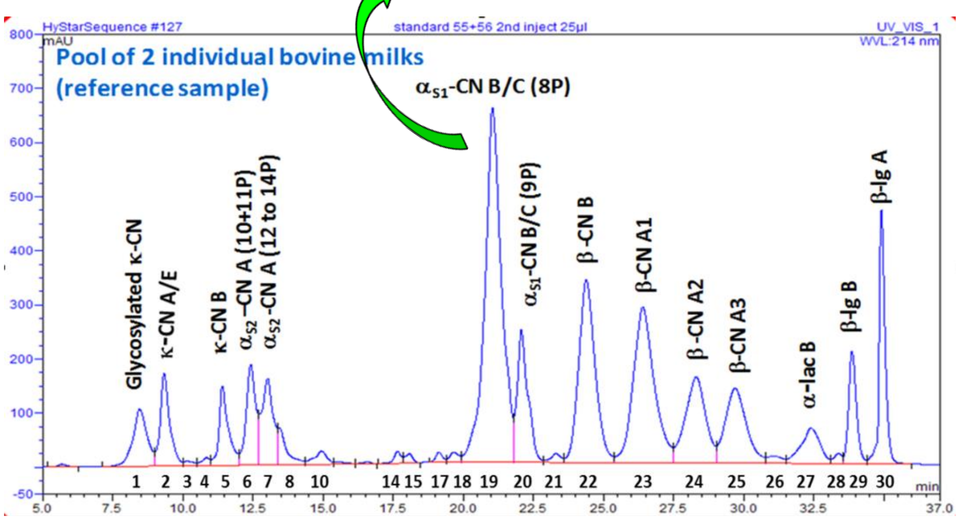
[b] ACTALIA, pôle expertise analytique, 39801 Poligny, France



LC-MS profiling of bovine milk proteins





Peak number	Retention Time	Main masses Observed	Identification	Therotical masses	Area	Relative Area	Others	Protein family	Relative concentration
	min	Da		Da	mAU*min	%			%
1	8.46	20901.6615 20931.8947 21850.3951	κ-CN B 1P 2OG κ-CN A 1P 2OG κ-CN E 1P 3OG	20901.098 20933.054 21850.869	60.187	2.97		Glycosylated κ-CN	2,97
2	9.34	19007.3305 19037.2153	κ-CN E 1P κ-CN A 1P	19007.345 19037.371	66.752	3.30		κ-CN	3.30
3	10.15		n.a.		3.133	0.15	0.15		
4	10.84		n.a.		4.843	0.24	0.24		
5	11.41	19005.3940	κ-CN B 1P	19005.416	56.887	2.81		κ-CN	2.81
6	12.42	25148.4917 25228.5579	αs2-CN A 10 & 11P	25148.348 25228.328	74.018	3.66		αs2-CN	8,43
7	13.02	25308.4656	αs2-CN A 12P	25308.308	77.015	3.81			
8	13.43	25388.2338 25468.6767	αs2-CN A 13 & 14P	25388.288 25468.268	19.390	0.96			
9	13.89		n.a.		5.193	0.26	0.26		
10	14.95	12096.3734 12177.1687	PP5 f(1-105) A2/A3 4P PP5 A2/A3 5P	12097.294 12177.274	14.213	0.70		β-CN	0.70
11	15.58		n.a.		3.396	0,.17	0.17		
12	16.60		n.a.		3.0344	0.15	0.15		
13	17.38		n.a.		1.450	0.07	0.07		
14	17.66	21997.0835 22068.8598	αs1-CN C 8P Δe4 αs1-CN B 8P Δe4	21996.831 22068.910	7.395	0.37		αs1-CN	0.75
15	18.07	14031.9655 14105.6761	f (80-199) αs1-CN C 1P f (80-199) αs1-CN B 1P	14035.772 14107.836	7.746	0.38			
16	18.64		n.a.		1.598	0.08	0.08		
17	19.14	22426.9941 22601.9471	αs1-CN B 8P Δe8 ΔQ59 & Q78 αs1-CN B 7P Δe8	22427.422 22603.703	8.347	0.41		αs1-CN	0.41
18	19.66		n.a.		9.622	0.48	0.48		
19	21.04	23542.3689 23614.8144	αs1-CN C 8P αs1-CN B 8P	23542.648 23614.712	462.326	22.84		αs1-CN	28.48
20	22.07	23624.2794 23695.6948	αs1-CN C 9P αs1-CN B 9P	23622.628 23694.692	114.171	5.64			
21	23.29		n.a.		9.975	0.49	0.49		
22	24.39	24092.5726	β-CN B 5P	24092.319	237.283	11.72		β-CN	37.91
23	26.40	24023.4698	β-CN A1 5P	24023.209	257.687	12.73			
24	28.31	23983.5160	β-CN A2 5P	23983.185	138.520	6.84			
25	29.69	23974.1909	β-CN A3 5P	23974.174	124.969	6.17			
26	31.09	11558.4804	γ3 f (108-209) β-CN 0P	11558.612	9.201	0.45			
27	32.40	14185.8586	α-lactalbumin B	14186.064	53.580	2.64		α-LA	2,65
28	33.37	18605.2732	lactosyl-β-lactoglobulin B	18605.320	6.831	0.34		β-LG	9,49
29	33.86	18281.1176	β-lactoglobulin B	18281.208	68.804	3.40			
30	34.91	18367.2233 18691.6191	β-lactoglobulin A lactosyl-β-lactoglobulin A	18367.298 18691.300	116.472	5.75			
Total					2024.040	100.00	2.10		97,90

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Miranda *et al.*, 2013

92,9% of the protein fraction identified

LC-MS profiling of Camel milk proteins

Combining different proteomic approaches to resolve complexity of the milk protein fraction of dromedary, Bactrian camels and hybrids, from different regions of Kazakhstan

Alma Ryskaliyeva[1]*, CeÂline Henry[2], Guy Miranda[1], Bernard Faye[3], Gaukhar Konuspayeva[4], Patrice Martin[1]

1 INRA, UMR GABI, AgroParisTech, UniversiteÂ Paris-Saclay, Jouy-en-Josas, France, **2** INRA, MICALIS Institute, Plateforme d'Analyse ProteÂomique Paris Sud-Ouest (PAPPSO), UniversiteÂ Paris-Saclay, Jouy-en-Josas, France, **3** CIRAD, UMR SELMET, France, **4** Al-Farabi Kazakh State National University, Biology department, Almaty, Kazakhstan

PLOS ONE

2018

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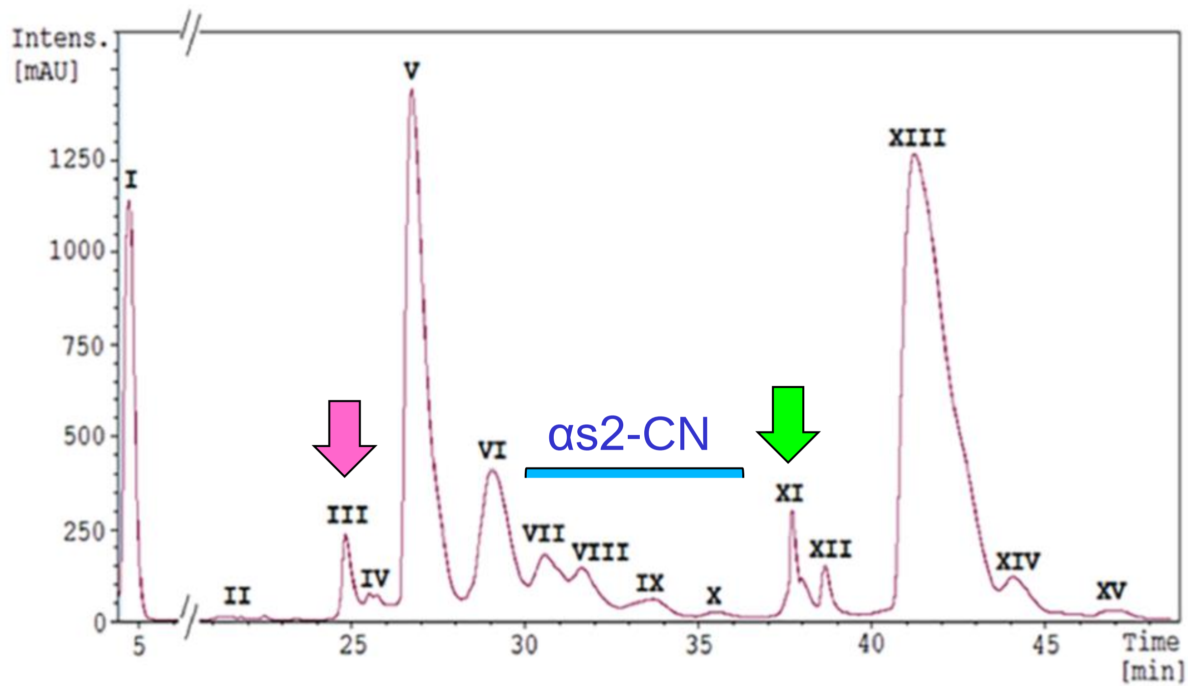
peak I: κ-CN
peak III: WAP
peaks IV & V: αs1-CN
peak VI: α-LAC,
peak VII: αs2-CN
peaks VIII, IX, & X: αs2-CN
peak XI: PGRP
peak XII: CSA/LPO
peaks XIII & XIV: β-CN
peak XV: γ2-CN.



Peak	Ret.Time, min	Observed M_r, Da	TheoreticalM_r, Da	Protein description	UniProt/ NCBI GenBank Accession number	Intensity
I	4.50	21,157	21,158	κ-CN A, 1P, (GaN-Ga-SA2)x3*, pyro-E		1,361
		21,184	**21,182**	**κ-CN B, 0P, (GaN-Ga)x3 + (GaN-Ga-SA2)x2**, pyro-E**		**5,810**
II	18.61	18,210	18,210	κ-CN B, 0P ?	L0P304	161
		18,236	18,235	κ-CN A, 0P, pyro-E	P79139	72
III	24.32	12,564	12,564	WAP, 0P	P09837	1,756
		12,644	12,644	WAP, 1P		1,575
IV	24.97	23,878	23,878	α_{s1}-CN A—short isoform (Δex 16 and Δex 13'), 4P		242
V	26.23	24,547	24,547	α_{s1}-CN C -short isoform (Δex 16), 5P, splice variant (ΔQ83)		4,885
		24,627	**24,627**	**α_{s1}-CN C—short isoform (Δex 16), 6P, splice variant (ΔQ83**		**21,606**
		24,707	24,707	α_{s1}-CN C—short isoform (Δex 16), 7P, splice variant (ΔQ83)		6,990
		24,675	24,675	α_{s1}-CN C—short isoform (Δex 16), 5P		9,441
		24,755	**24,755**	**α_{s1}-CN C—short isoform (Δex 16), 6P**	**K7DXB9**	**47,392**
		24,835	24,835	α_{s1}-CN C—short isoform (Δex 16), 7P		7,046
		24,689	24,689	α_{s1}-CN A—short isoform (Δex 16), 5P		9,748
		24,768	**24,769**	**α_{s1}-CN A—short isoform (Δex 16), 6P**	**O97943-2**	**50,634**
		24,849	24,849	α_{s1}-CN A—short isoform (Δex 16), 7P		6,909
VI	28.53	**14,430**	**14,430**	**α-LAC**	**P00710**	**17,797**
		22,939	n/a	Uncharacterized protein 1 (UP1)	n/a***	2,701
		23,020	n/a	UP1+80Da	n/a	2,489
		23,099	n/a	UP1+160Da	n/a	1,079
		25,646	25,645	α_{s1}-CN C, 6P, splice variant (ΔQ83)		3,501
		25,693	25,693	α_{S1}-CN C, 5P		564
		25,773	**25,773**	**α_{s1}-CN C, 6P**		**7,880**
		25,787	**25,787**	**α_{s1}-CN A, 6P**	**O97943-1**	**3,472**
VII	30.05	21,825	21,826	α_{s2}-CN, 7P		552
		21,906	**21,906**	**α_{s2}-CN, 8P**	**O9794**	**5,242**
		21,984	21,986	α_{s2}-CN, 9P		403
		23,178	n/a	UP1+240Da	n/a	1,256
VIII	31.11	21,986	21,986	α_{s2}-CN, 9P	O97944	356
		22,066	**22,066**	**α_{s2}-CN, 10P**		**4,790**
IX	33.18	22,066	22,066	α_{s2}-CN, 10P		148
		22,145	**22,146**	**α_{s2}-CN, 11P**		**1,964**
X	35.05	22,226	22,226	α_{s2}-CN, 12P		894
		23,046	n/a	Uncharacterized protein 2 (UP2)	n/a	231
X	37.16	**19,143**	**19,143**	**PGRP**	**Q9GK12**	**7,207**
		23,206	n/a	UP2+160Da	n/a	1,592
		23,286	n/a	UP2+240Da	n/a	735
XII	38.09	66,481	66,477	CSA ?	XP_010981066.1	1,096
			66,491	LPO ?	Q9GJW6	
		66,512	n/a	CSA ? LPO?		2,663
		67,342	n/a	CSA ? LPO?		1,010
XIII	40.67	24,746	24,745	β-CN A, 3P, splice variant (ΔQ29)		2,073
		24,793	24,792	β-CN A, 2P		5,469
		24,825	24,825	β-CN A, 4P, splice variant (ΔQ29)		9,586
		24,873	24,872	β-CN A, 3P		10,177
		24,953	**24,953**	**β-CN A, 4P**	**A0A077SL35**	**84,494**
		24,842	24,842	β-CN B, 4P, splice variant (ΔQ29)		10,029
		24,891	24,890	β-CN B, 3P		10,365
		24,970	**24,971**	**β-CN B, 4P**	**Q9TVD0**	**87,973**
XIV	43.71	23,878	23,878	β-CN A-short isoform (Δ946 Da), 4P, splice variant (ΔQ29)		707
		23,963	23,958	β-CN A-short isoform (Δ946 Da), 5P, splice variant (ΔQ29)		244
		23,929	23,926	β-CN A-short isoform (Δ946 Da), 3P		438
		24,006	**24,006**	**β-CN A-short isoform (Δ946 Da), 4P**		**9,026**

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Mass Sprectrometry Analysis

Molecular masses obtained after deconvolution of multi-charged ions spectra

αS2-caseins

Peak	Ret.Time, min	Observed M_r, Da	TheoreticalM_r, Da	Protein description	UniProt/ NCBI GenBank Accession number	Intensity
		22,939	n/a	Uncharacterized protein 1 (UP1)	n/a***	2,701
		23,020	n/a	UP1+80Da	n/a	2,489
		23,099	n/a	UP1+160Da	n/a	1,079
		25,646	25,645	α_{s1}-CN C, 6P, splice variant (ΔQ83)		3,501
		25,693	25,693	α_{S1}-CN C, 5P		564
		25,773	**25,773**	**α_{s1}-CN C, 6P**		**7,880**
		25,787	**25,787**	**α_{s1}-CN A, 6P**	**O97943-1**	**3,472**
VII	30.05	21,825	21,826	α_{s2}-CN, 7P		552
		21,906	**21,906**	**α_{s2}-CN, 8P**	**O9794**	**5,242**
		21,984	21,986	α_{s2}-CN, 9P		403
		23,178	n/a	UP1+240Da	n/a	1,256
VIII	31.11	21,986	21,986	α_{s2}-CN, 9P	O97944	356
		22,066	**22,066**	**α_{s2}-CN, 10P**		**4,790**
IX	33.18	22,066	22,066	α_{s2}-CN, 10P		148
		22,145	**22,146**	**α_{s2}-CN, 11P**		**1,964**
X	35.05	22,226	22,226	α_{s2}-CN, 12P		894
		23,046	n/a	Uncharacterized protein 2 (UP2)	n/a	231
X	37.16	**19,143**	**19,143**	**PGRP**	**Q9GK12**	**7,207**
		23,206	n/a	UP2+160Da	n/a	1,592
		23,286	n/a	UP2+240Da	n/a	735

αS2-caseins

αS2-caseins

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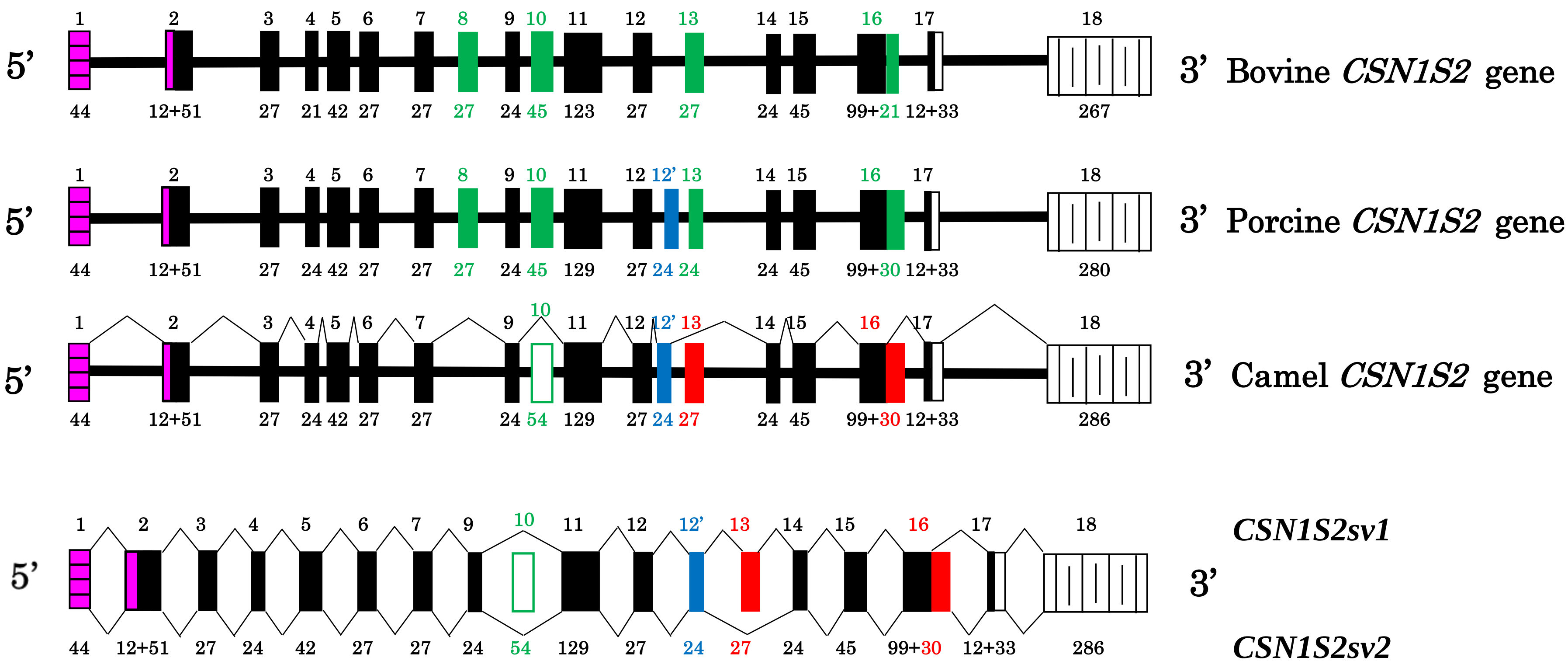
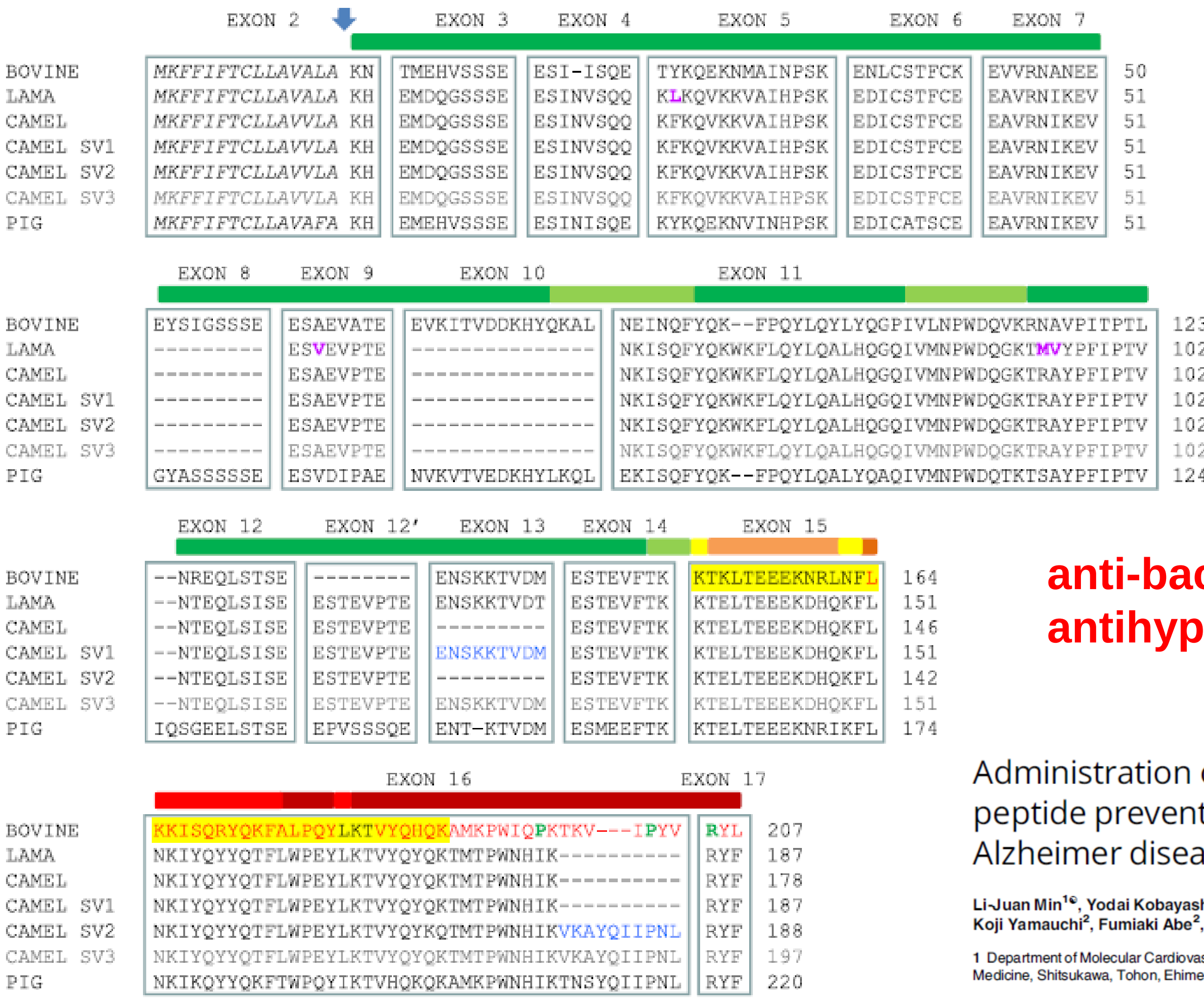
CSN1S2 in camels



Splicing isoforms impacts the C-terminal sequence of camel α_{s2}-casein



Ryskaliyeva *et al.*, 2019

anti-bacterial and antihypertensive activities

PLOS | ONE

Administration of bovine casein-derived peptide prevents cognitive decline in Alzheimer disease model mice

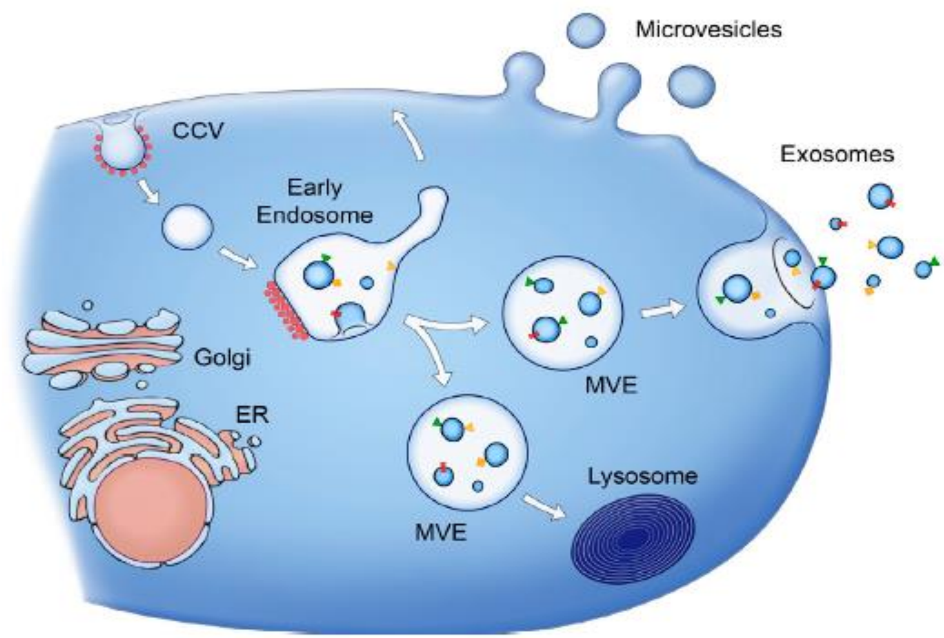
Li-Juan Min[1©], Yodai Kobayashi[2©], Masaki Mogi[1*], Kana Tsukuda[1], Akio Yamada[2], Koji Yamauchi[2], Fumiaki Abe[2], Jun Iwanami[1], Jin-Zhong Xiao[2], Masatsugu Horiuchi[1]

1 Department of Molecular Cardiovascular Biology and Pharmacology, Ehime University, Graduate School of Medicine, Shitsukawa, Tohon, Ehime, Japan, 2 Morinaga Milk Industry Co., Ltd., Zama, Kanagawa, Japan

PLOS ONE | DOI:10.1371/journal.pone.0171515 February 3, 2017

Beside its unique nutritional content breast milk also contains extracellular vesicles and live cells from the mother

Extracellular vesicles
30 and 100 nm



Multi Vesicular Bodies released into the extracellular medium by fusion with the cell plasma membrane

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CAMEL MILK-DERIVED EVs: a SOURCE of MILK PROTEINS SO FAR UNEXPLORED

Milk-derived Exosomes and microRNA

The Journal of Immunology

This information is current as of September 23, 2019.

Exosomes with Immune Modulatory Features Are Present in Human Breast Milk

Charlotte Admyre, Sara M. Johansson, Khaleda Rahman Qazi, Jan-Jonas Filén, Riitta Lahesmaa, Mikael Norman, Etienne P. A. Neve, Annika Scheynius and Susanne Gabrielsson

J Immunol 2007; 179:1969-1978; ;

Isolation of bovine milk-derived microvesicles carrying mRNAs and microRNAs

Taketoshi Hata [a], Kosuke Murakami [b], Hajime Nakatani [b], Yasunari Yamamoto [c], Tsukasa Matsuda [b], Naohito Aoki [a,*]

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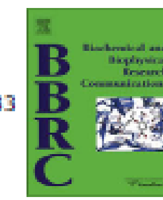
[b] Department of Applied Molecular Biosciences, Graduate School of Bioagricultural Sciences, Nagoya University, Nagoya 464-8601, Japan
[c] Mie Prefecture Livestock Research Institute, Ureshino, Matsusaka, Mie 515-2324, Japan

Biochemical and Biophysical Research Communications 396 (2010) 528–533



MicroRNAs: Milk's epigenetic regulators

Bodo C. Melnik, MD, Associate Professor, Dermatologist [a,*], Gerd Schmitz, MD, Professor, Specialist for Laboratory and Transfusion Medicine [b]

[a] Department of Dermatology, Environmental Medicine, and Health Theory, University of Osnabrück, Germany
[b] Institute for Clinical Chemistry and Laboratory Medicine, University Hospital Regensburg, Regensburg, Germany

Best Practice & Research Clinical Endocrinology & Metabolism 31 (2017) 427–442

INRA SCIENCE & IMPACT

Human Milk MicroRNAs/Exosomes: Composition and Biological Effects

Bo Lönnerdal

Donovan SM, German JB, Lönnerdal B, Lucas A (eds): Human Milk: Composition, Clinical Benefits and Future Opportunities. Nestlé Nutr Inst Workshop Ser, vol 90, pp 83–92, (DOI: 10.1159/000490297)
Nestlé Nutrition Institute, Switzerland/S. Karger AG., Basel, © 2019

Extracellular vesicles in camel milk

Comprehensive proteomic analysis of camel milk-derived extracellular vesicles

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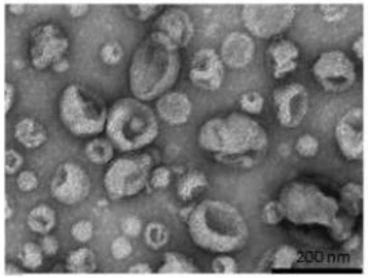
[3]INRA, MICALIS Institute, Plateforme d'Analyse Protéomique
Paris Sud-Ouest, Université Paris-Saclay, France
[4]CIRAD, UMR SELMET, France
[5]RPE Co Antigen Ltd., Kazakhstan



International Journal of Biology and Chemistry 12, № 2, 93 (2019)

Contents lists available at ScienceDirect
Biomedicine & Pharmacotherapy
Biomedicine & Pharmacotherapy 143 (2021) 112220
ELSEVIER

Therapeutic potential of camel milk exosomes against HepaRG cells with potent apoptotic, anti-inflammatory, and anti-angiogenesis effects for colostrum exosomes

Azza M. El-kattawy [a], Ola Algezawy [a], Mohammad Y. Alfaifi [b], Enas A. Noseer [c], Yousef M. Hawsawi [d,e], Othman R. Alzahrani [f,g], Abdulrahman Algarni [h], Khaled A. Kahilo [a], Mohammed A. El-Magd [i,*,1]

[a] Department of Biochemistry, Faculty of Veterinary Medicine, Kafrelsheikh University, P.O. Box 33516, Kafrelsheikh, Egypt
[b] Biology Department, Faculty of Science, King Khalid University, Abha 9004, Saudi Arabia
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[e] College of Medicine, Al-Faisal University, P.O. Box 50927, Riyadh 11533, Saudi Arabia
[f] Genome and Biotechnology Unit, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia
[g] Department of Biology, Faculty of Sciences, University of Tabuk, Tabuk, Saudi Arabia
[h] Department of Biomedical Science, the Northern Border University, P.O.Box 1321, Arar, Saudi Arabia
[i] Department of Anatomy, Faculty of Veterinary Medicine, Kafrelsheikh University, P.O. Box 33516, Kafrelsheikh, Egypt

Therapeutic Effect of Camel Milk and Its Exosomes on MCF7 Cells In Vitro and In Vivo

2018

Integrative Cancer Therapies

Abdelnaser A. Badawy, PhD[1,2], Mohammed A. El-Magd, PhD[3], and Sana A. AlSadrah, PhD[4]

[1]Department of Biochemistry, Faculty of Medicin, Northern Border University, Arar, Saudi Arabia
[2]Department of Medical Biochemistry, Faculty of Medicine, Mansoura University, Mansoura, Egypt
[3]Department of Anatomy, Faculty of Veterinary Medicine, Kafrelsheikh University, Kafrelsheikh, Egypt
[4]Department of Preventive Medicine, Governmental Hospital Khobar, Health Centers in Khobar, Ministry of Health, Saudi Arabia

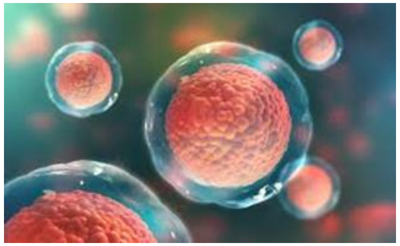
Breast milk stem cells transfer to offspring

SCIENTIFIC REPORTS

SCIENTIFIC REPORTS | (2018) 8:14289 | DOI:10.1038/s41598-018-32715-5

Transfer and Integration of Breast Milk Stem Cells to the Brain of Suckling Pups

Mehmet Şerif Aydın[1], Esra Nur Yiğit[1], Emre Vatandaşlar[1], Ender Erdoğan[2] & Gürkan Öztürk[1,3]



Milk SC reach the brain where they turn into functioning cells

Accepted: 28 November 2017

DOI: 10.1111/pai.12841

REVIEW ARTICLE

WILEY

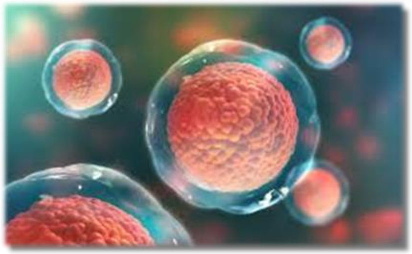
INRA SCIENCE & IMPACT

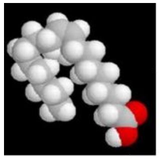
Breastmilk cell trafficking induces microchimerism-mediated immune system maturation in the infant

Jean-Pierre Molès[1] | Edouard Tuaillon[1,2] | Chipepo Kankasa[3] | Anne-Sophie Bedin[1] | Nicolas Nagot[1,2] | Arnaud Marchant[4] | Joann M. McDermid[5] | Philippe Van de Perre[1,2]

Breast-milk: the postnatal maternal blood through which
a multitude of active soluble and cellular factors are delivered to the offspring

Conclusions





Milk has to be considered as a sophisticated nutrient but also as a **communication system delivering** a multitude of active soluble and cellular factors orchestrating early development of the offspring

Differential splicing is an effective way to **increase** molecular diversity and possibly **the repertoire of bioactive peptides** encrypted in milk proteins

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Cabridge (genomics)

PAPPSO (proteomics)

EXCILONE

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cirad