Making the most of the nourishment in bovine milk

John Newbold, SRUC

25 Nov 19

Leading the way in Agriculture and Rural Research, Education and Consulting

The nourishment in milk

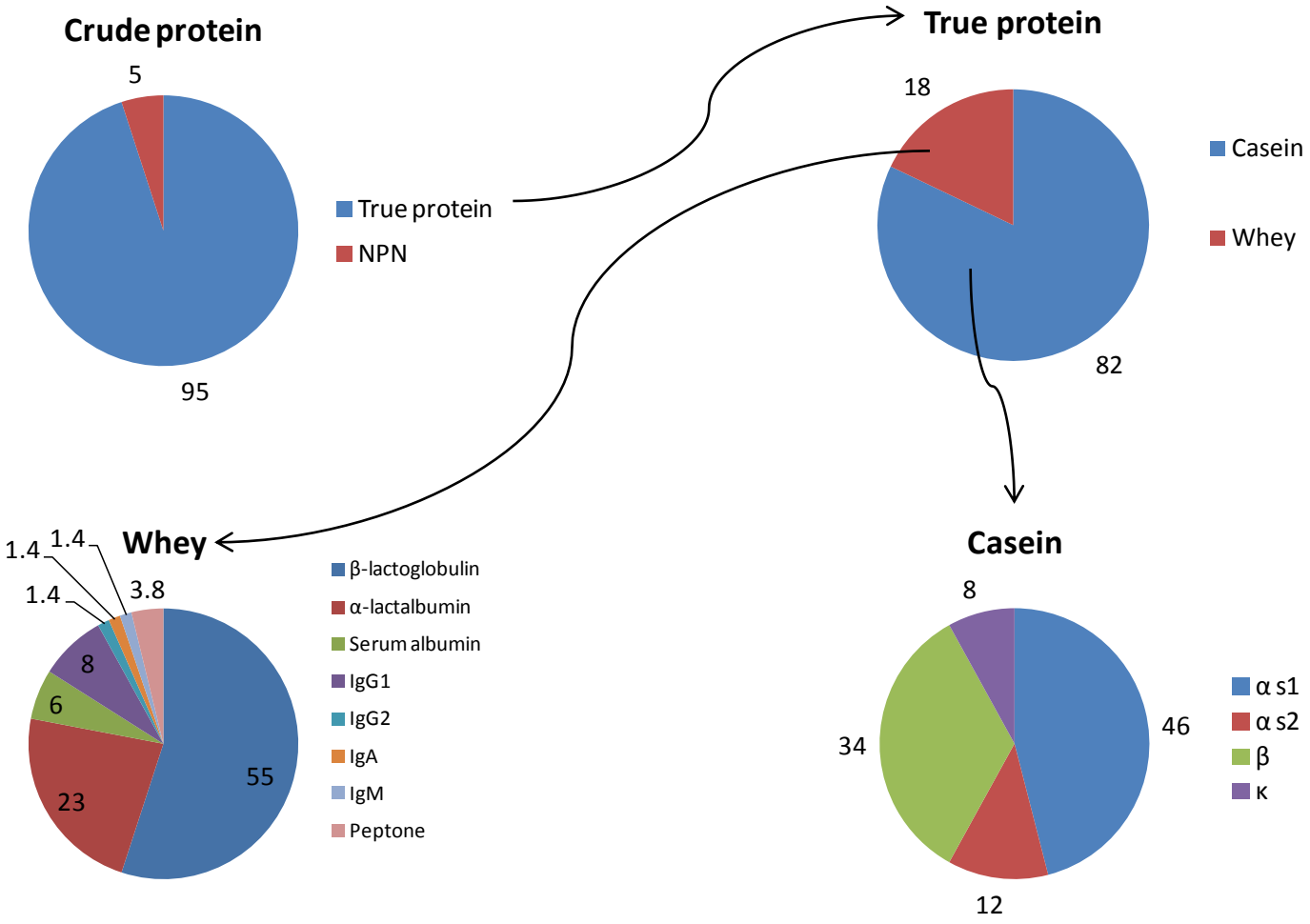
- ‘Nourishment’
  - Nutrition
  - Health
  - Food

The complexity of milk

Milk = carbohydrates + fat + protein + minerals

- Oligo-saccharides
  - Mono-saccharides
- Milk fat globule
  - Proteins
  - Phospholipids
  - Sphingolipids
  - Fatty acids
- Functional proteins
  - Amino acids

Milk protein



Farrell et al. (2004) J. Dairy Sci. 87:1641–1674

Supplementary Table 1 - Proteins from Bovine Milk

Symbol, identification number, name, localization and tentative physiological function are reported. Abbreviations: A, angiogen ; G, cell growth l tract maturatio ure; ST, signal t against gastroi

N.			Role/Function	Fraction
1.			I	W
2.			I, P	W
3.			U	W
4.				MF, W
5.				MF
6.				MF
7.				W
8.				MF, W
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37.				
38.				
39.				
40.	APOB*			
41.	APOC3			
42.	APOE			
43.	APOH			
44.	AQPEP			
45.	ARF1			
46.	ARF4			
47.	ARHGDIA			
48.	ARHGEF4			
49.	ARL15	Q3EA19		
50.	ATAD2*	Q6PL18		
51.	ATP13A3* (includes EG:79572)	Q9H7F0		

Supplementary Material (ESI) for Molecular BioSystems

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52.	ATP13A4*	Q8N1Q9	Cation transporting ATPase type 13A4	1, 10	PM	N, T	MF

Supplementary Material (ESI) for Molecular BioSystems

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116.	CIB1	Q17QE5	Calcium and integrin-binding protein 1	10	PM	G, I, Z	W

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176.	FABP3	P10790	Fatty acid binding protein 3, mammary-derived growth inhibitor	2, 3, 5, 6, 7, 8, 10, 11, 12, 13	C	G, L, N	MF, W

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231.	HBA	P01966	Hemoglobin alpha chain	4	C	A	MF
232.	HEBP1	Q148C9	Heme binding protein 1	10	C	L, N	W

Supplementary Material (ESI) for Molecular BioSystems

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290.	KIF22	A6QPL4	Kinesin-like protein KIF22	10	N	U	W

Supplementary Material (ESI) for Molecular BioSystems

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351.	NEK3	A4IFF6	NEK3 protein	10	U	D, G, ST	W
352.	NELL2	A6QR11	Protein kinase C-binding protein NEL-like 2	2	ES	D, G, V	W

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410.	PSMB1	Q2TBX6	Proteasome subunit beta type 1	2	C	P	W
411.	PTGD						
412.	PTHL1						
413.	PTX3						
414.	Q9XS9						
415.	QSOX						
416.	RAB1						
417.	RAB11						
418.	RAB11						
419.	RAB1						
420.	RAB1						
421.	RAB1						

Supplementary Material (ESI) for Molecular BioSystems

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475.	SERPINA3*	O9TTE1	Alpha-1-antichymotrypsin, serpin peptidase inhibitor, clade A	2, 5, 10, 12	ES	I, N, P, Z	MF, W

Supplementary Material (ESI) for Molecular BioSystems

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532.	TPP1	Q0V8B6	Tripeptidyl peptidase I	2	C	P	
533.	TPT1	Q5E984	Translationally-controlled tumor protein	6	C	L, N, S	
534.	TRIM11	A0JN74	Tripartite motif-containing protein 11	10	C	O	
535.	TRIM68*	Q6AZZ1	E3 ubiquitin-protein ligase TRIM68, tripartite motif-containing protein 68	1	C	O	
536.	TRIP12	Q0P5M6	TRIP12 protein	10	C	P	
537.	TRY	P00760	Cationic trypsin, alpha trypsin 1	2	ES	P	
538.	TSHB	P01223	Thyroid stimulating hormone subunit beta	15	ES	D, G, ST	
539.	TTN	Q8WZ42	Titin, connectin	10	C	L, S, ST	
540.	TTR	O46375	Transthyretin	2, 5, 8, 10, 12	ES	G, N, T, V	
541.	TTYH1	Q2KJ98	Protein tweety homolog 1	4	PM	T	
542.	TUBA3C	Q13748	Tubulin alpha 3C/D chain, tubulin alpha 2 chain	4	C	S	
543.	TUBB2C	Q3MHM5	Tubulin beta 2C chain	3	C	S	
544.	TULP1	O00294	Tubby-related protein 1	10	C	V	
545.	UBB	P62990	Ubiquitin B, ribosomal protein S27a	4, 10	C	P	
546.	UBL3*	O95164	Ubiquitin-like protein 3, membrane-anchored ubiquitin-fold protein	1	ES	P	
547.	UGP2	Q07130	UDP-glucose-1-phosphate uridylyltransferase, UDP-glucose pyrophosphorylase	2	C	N, O	
548.	UMOD	P48733	Uromodulin	1	ES	I, L, N	
549.	VAMP2	P63026	Vesicle-associated membrane protein 2, synaptobrevin 2, cellubrevin	1	PM	L, N	
550.	VAMP8	Q3T0Y8	Vesicle-associated membrane protein 8, endobrevin	1, 10	PM	L, N	
551.	VAT1*	Q99536	Synaptic vesicle membrane protein VAT-1 homolog, vesicle amine transport protein 1 homolog	1, 4, 10	PM	L, N	
552.	VCP	Q3ZBT1	Transitional endoplasmic reticulum ATPase, TER ATPase	6	C	L, N	
553.	VDAC1	P45879	Voltage-dependent anion-selective channel protein 1	3	C	T, V	
554.	VIM	P48616	Vimentin	3	C	L, S	

REVIEW www.rsc.org/molecularbiosystems | Molecular BioSystems

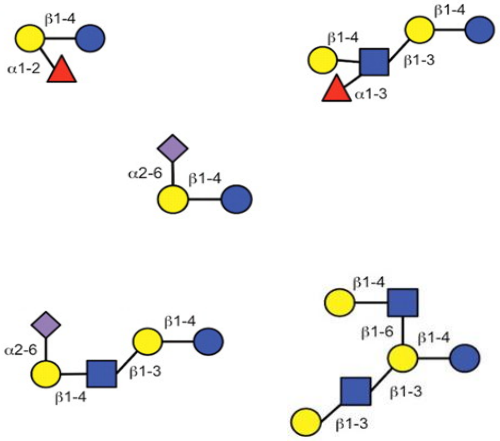
The bovine milk proteome: cherishing, nourishing and fostering molecular complexity. An interactomics and functional overview†‡

Angelo D'Alessandro,[a] Lello Zolla*[a] and Andrea Scaloni*[b]

Milk oligosaccharides

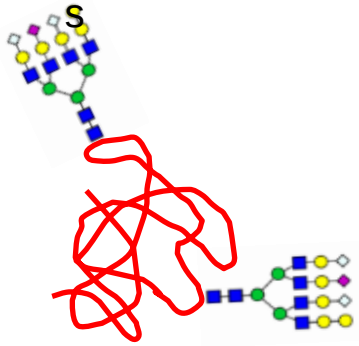
- Macromolecules comprising:
  - glucose, galactose, fucose, N-acetylneuraminic acid (sialic acid), N-acetyl-glucosamine, N-glycolylneuraminic acid

Free glycans (oligosaccharides)

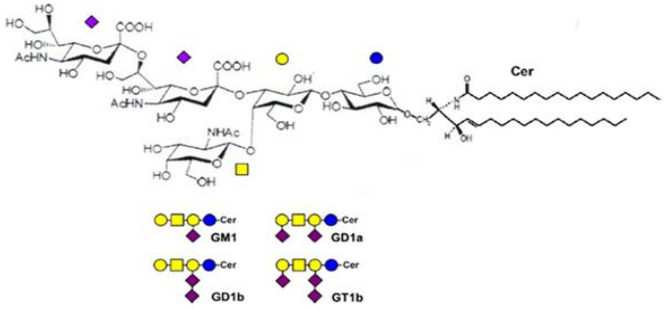


Conjugated glycans

Glycoprotein

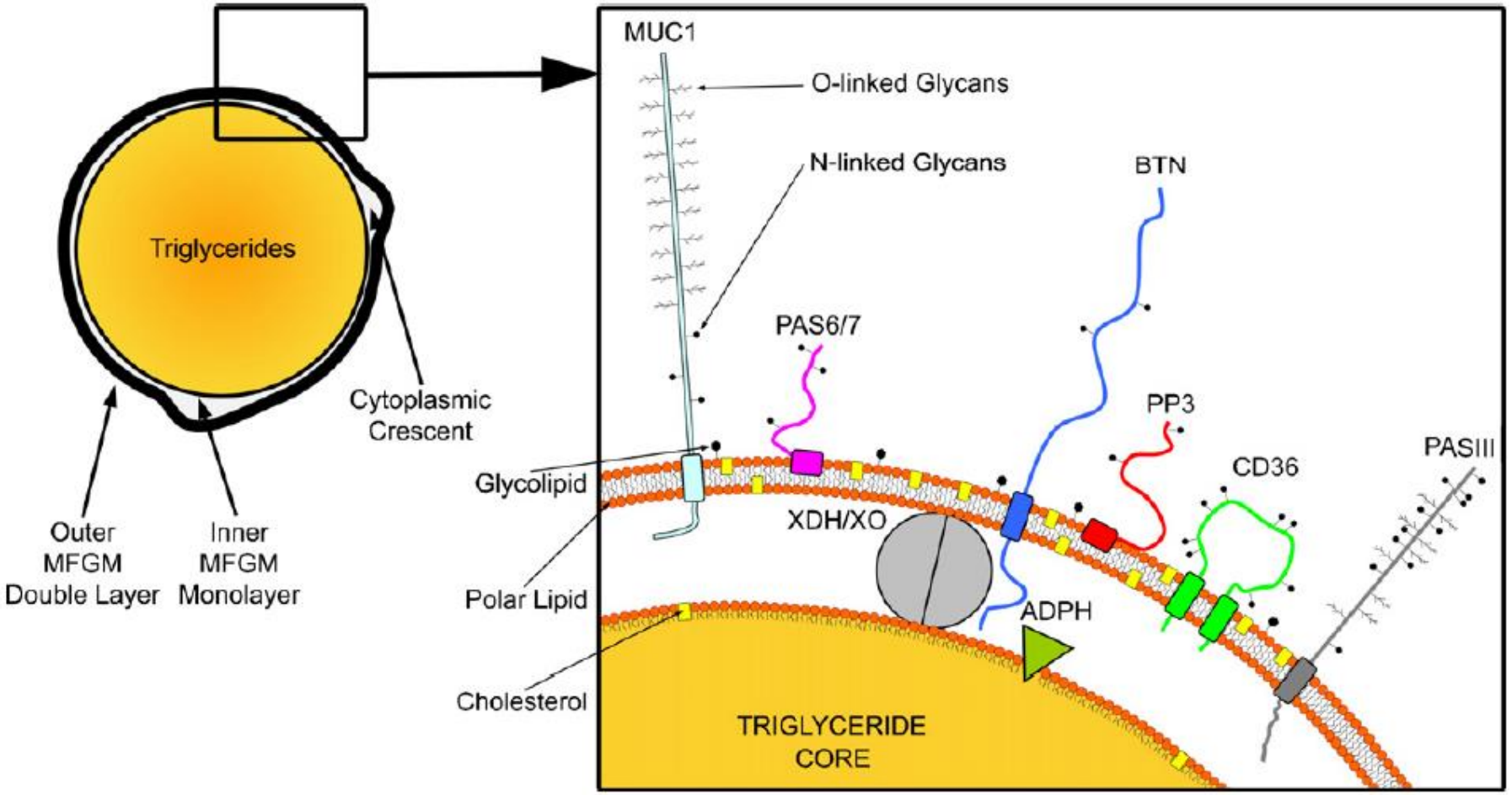


Glycolipids



Aldredge et al. (2013) Glycobiology 23: 664-676

Milk fat globule membrane



Dewettinck et al. (2008) Int. Dairy J. 18: 436–457

The nourishment in milk

- ‘Nourishment’
  - Nutrition…protein quality
  - Health
  - Food

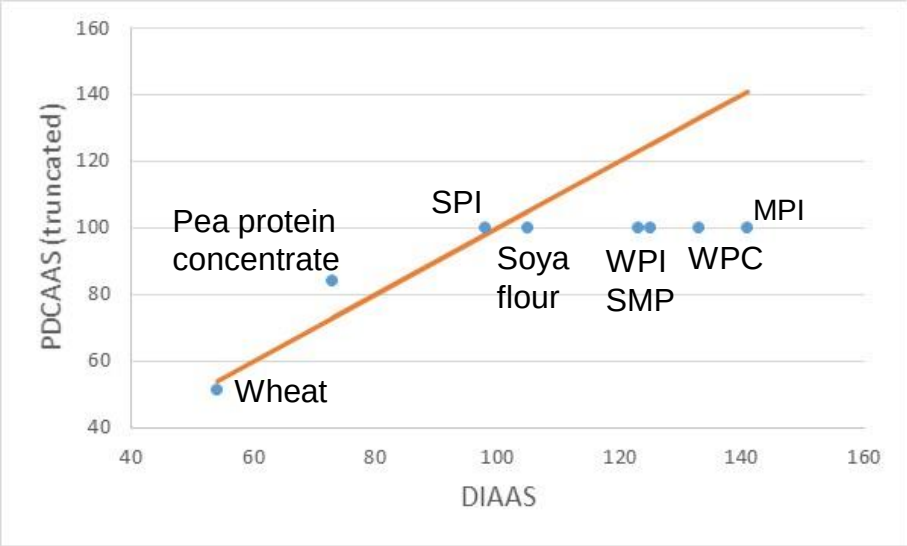
Protein quality of human foods

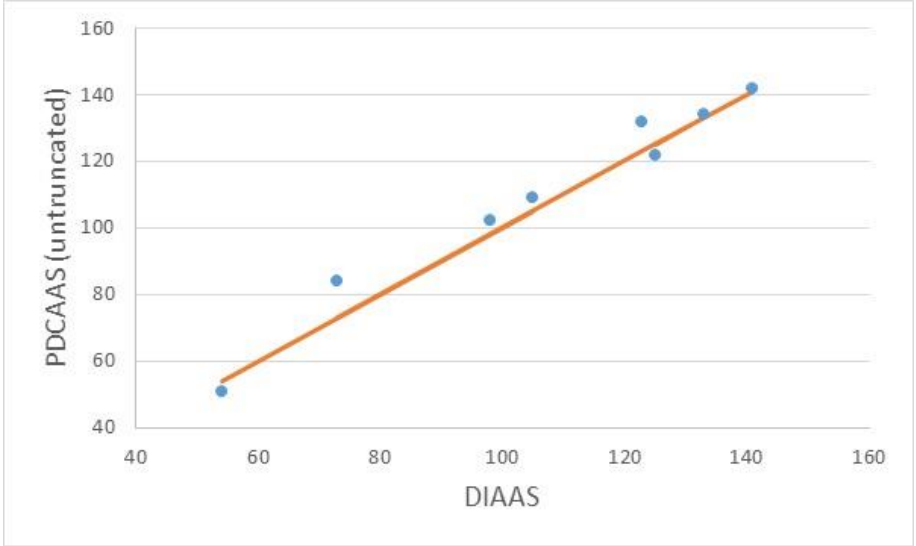
- FAO (2011) Dietary protein quality evaluation in human nutrition
  - recommended replacement of 'Protein Digestibility Corrected Amino Acid Score' (PDCAAS) by 'Digestible Indispensable Amino Acid Score' (DIAAS)

	PDCAAS	DIAAS
Digestibility	Protein	Individual amino acids
	Total tract (rats)	Ileal (pigs, calibrated against human)
Maillard products		Accounts for true ileal digestibility
Truncation	Values > 100% are truncated to 100%. No recognition that high quality proteins (PDCAAS>100) can complement low quality proteins in meals.	No truncation

  - *However*, PDCAAS will continue to be used until a sufficient database of ileal digestibility values are generated for commonly consumed foods

DIAAS versus PDCAAS





Truncation penalises higher-quality proteins

'PDCAAS values do not accurately predict ileal AA digestibility and it appears that specifically for low-quality proteins, values for PDCAAS overestimate the protein quality'

Mathai et al. (2017) Br. J. Nutr. 117: 490-499
PDCAAS-like values and DIAAS both calculated from digestibility measured in pigs

Generation of a DIAAS database

- An international project is underway to facilitate the adoption of DIAAS[1]

- "The global dataset [DIAAS]… will be used for assessing nutritional adequacy… planning for food security and sustainability… and for assessing the role of dietary protein in the maintenance of health and fitness of the worldwide population… It will also influence international trade in proteins as well as facilitating the establishment of claims made about protein in foods and beverages."

1. 'Proteos' is a collaboration between Riddet Institute (Massey University), University of Illinois, Wageningen University and AgroParisTech
2. Prof. Paul Moughan, Massey University. https://www.massey.ac.nz/massey/about-massey/news/article.cfm?mnarticle_uuid=8EFD4A9A-BE62-E5B3-C8F9-072E3035B5A0

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food & nutrition research

REVIEW ARTICLE

Milk and dairy products: good or bad for human health? An assessment of the totality of scientific evidence

Tanja Kongerslev Thorning[1], Anne Raben[1], Tine Tholstrup[1], Sabita S. Soedamah-Muthu[2], Ian Givens[3] and Arne Astrup[1]*

[1]Department of Nutrition, Exercise and Sports, Faculty of Science, University of Copenhagen, Copenhagen, Denmark; [2]Division of Human Nutrition, Wageningen University, Wageningen, The Netherlands; [3]Centre for Food, Nutrition and Health, University of Reading, Reading, UK

Abstract

Background: There is scepticism about health effects of dairy products in the public, which is reflected in an increasing intake of plant-based drinks, for example, from soy, rice, almond, or oat.
Objective: This review aimed to assess the scientific evidence mainly from meta-analyses of observational studies and randomised controlled trials, on dairy intake and risk of obesity, type 2 diabetes, cardiovascular disease, osteoporosis, cancer, and all-cause mortality.
Results: The most recent evidence suggested that intake of milk and dairy products was associated with reduced risk of childhood obesity. In adults, intake of dairy products was shown to improve body composition and facilitate weight loss during energy restriction. In addition, intake of milk and dairy products was associated with a neutral or reduced risk of type 2 diabetes and a reduced risk of cardiovascular disease, particularly stroke. Furthermore, the evidence suggested a beneficial effect of milk and dairy intake on bone mineral density but no association with risk of bone fracture. Among cancers, milk and dairy intake was inversely associated with colorectal cancer, bladder cancer, gastric cancer, and breast cancer, and not associated with risk of pancreatic cancer, ovarian cancer, or lung cancer, while the evidence for prostate cancer risk was inconsistent. Finally, consumption of milk and dairy products was not associated with all-cause mortality. Calcium-fortified plant-based drinks have been included as an alternative to dairy products in the nutrition recommendations in several countries. However, nutritionally, cow's milk and plant-based drinks are completely different foods, and an evidence-based conclusion on the health value of the plant-based drinks requires more studies in humans.
Conclusion: The totality of available scientific evidence supports that intake of milk and dairy products contribute to meet nutrient recommendations, and may protect against the most prevalent chronic diseases, whereas very few adverse effects have been reported.

Keywords: *obesity*; *type 2 diabetes*; *cardiovascular disease*; *osteoporosis*; *cancer*; *mortality*

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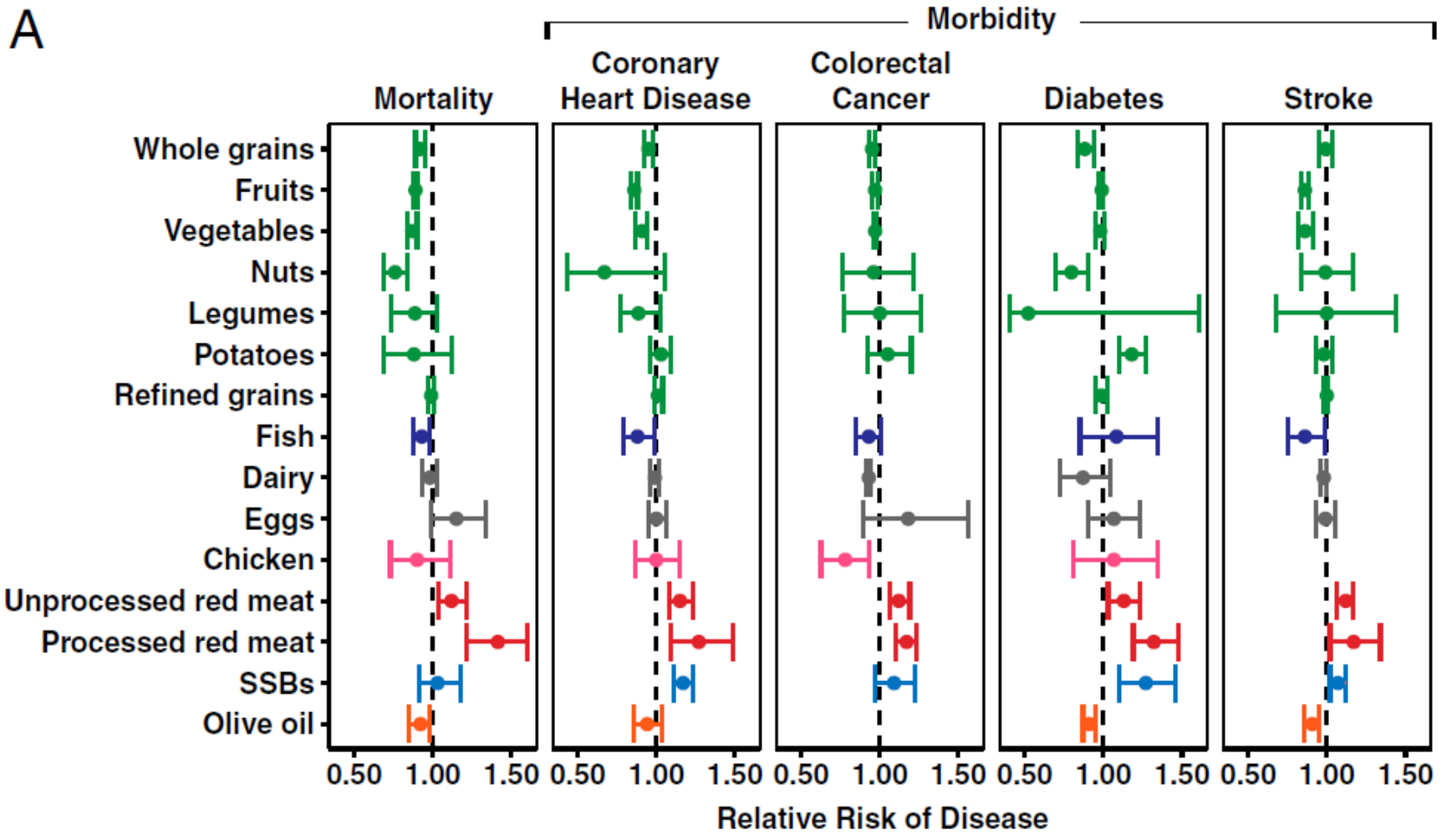
SRUC

Dairy foods associated with:

- Reduced risk of childhood obesity
- Facilitation of weight loss
- Neutral or reduced risk of type-2 diabetes
- Reduced risk of cardiovascular disease
- Higher bone mineral density
- Lower risk of colorectal, bladder cancer, gastric cancer, breast cancer

Dairy foods and health



Clark et al. (2019) Multiple health and environmental impacts of foods. PNAS.

Sarcopenia

- ‘the decline of muscle mass and strength with age’
- Loss of muscle mass = 30-50% decrease between 40 and 80 years of age[1]
- Sarcopenia is a major predictor of frailty, hip fracture, disability and mortality[2]
- Healthcare costs to the UK of more than £2.5 billion/year[3]

1. Faulkner et al. (2007) Clin. Exp. Pharmacol. Physiol. 34: 1091-1096
2. Reginster et al. (2016) Aging Clin. Exp. Res. 28:47–58
3. Pinedo-Villanueva et al. (2019) Calcif. Tissue Int. 104:137–144

Protein for sarcopenia

- Amount
  - Current international RDA = 0.8g/kg BW, regardless of age[1]
  - Recommendation from ESPEN Expert Group = 1.0–1.2g/kg BW > 65 years of age[2]
- Daily distribution
  - 2-3 meals/d each containing 25-30g high-quality protein optimal for 24h muscle protein synthesis[3]
- Protein source
  - 'The addition of nutrient-rich dairy proteins may… attenuate loss of muscle strength, thereby helping to prevent sarcopenia syndrome in the elderly population'[4]
  - Milk and whey proteins support greater increases in muscle protein synthesis than an equivalent amount of soya protein[5]

1. WHO (2007) World Health Organisation Technical Report Series 935
2. Deutz et al. (2014) Clin. Nutr. 33: 929-936
3. Loenneke et al. (2016) Clin, Nutr. 35: 1506-1511
4. Cuesta-Triana et al. (2019) Adv. Nutr. 10: S105–S119
5. Wilkinson et al. (2007) Am. J. Clin. Nutn. 85: 1031-1040

Dairy foods and sarcopenia

SRUC

Supplement Article

Update on protein intake: importance of milk proteins for health status of the elderly

Robert R. Wolfe

International Journal of Dairy Technology SDT SOCIETY OF DAIRY TECHNOLOGY

doi: 10.1111/1471-0307.12078

REVIEW

Towards a Sustainable Dairy Sector: The underappreciated role of dairy protein in the preservation of lean tissue mass in the elderly

CATHERINE NORTON* and PHILIP JAKEMAN

Faculty of Education & Health Sciences, University of Limerick, Limerick, Ireland

Whey protein, amino acids, and vitamin D supplementation with physical activity increases fat-free mass and strength, functionality, and quality of life and decreases inflammation in sarcopenic elderly[1,2]

Mariangela Rondanelli,[3] Catherine Klersy,[6] Gilles Terracol,[7] Jacopo Talluri,[8] Roberto Maugeri,[7] Davide Guido,[4] Milena A Faliva,[3] Bruno S Solerte,[5] Mar*

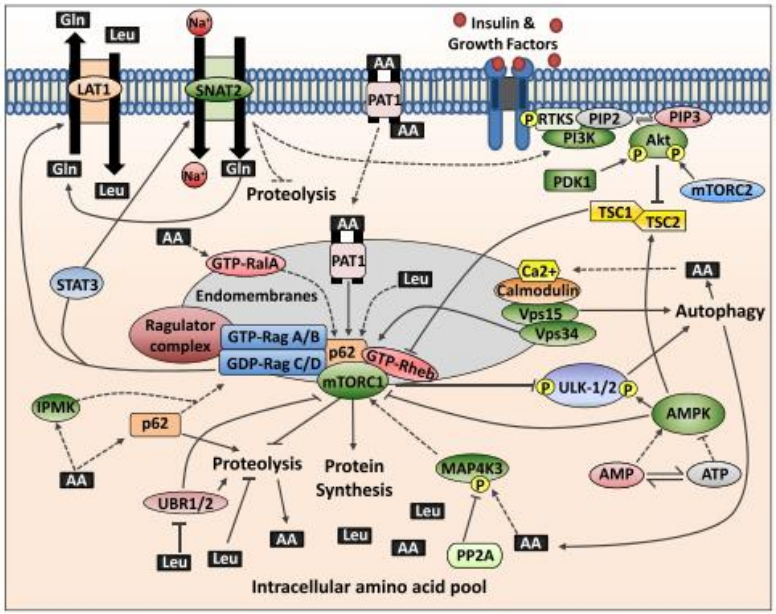
Effects of leucine-enriched essential amino acid and whey protein bolus dosing upon skeletal muscle protein synthesis at rest and after exercise in older women

Daniel J. Wilkinson [a, 1], Syed S.I. Bukhari [a, 1], Bethan E. Phillips [a], Marie C. Limb [a], Jessica Cegielski [a], Matthew S. Brook [a], Debbie Rankin [a], William K. Mitchell [a], Hisamine Kobayashi [b], John P. Williams [a], Jonathan Lund [a], Paul L. Greenhaff [a], Kenneth Smith [a], Philip J. Atherton [a, *]

[a] *MRC/ARUK Centre of Excellence for Musculoskeletal Ageing Research, National Institute for Health Research Nottingham Biomedical Research Centre, University of Nottingham, Derby DE22 3DT, UK*

[b] *Ajinomoto Co., Inc., Tokyo 104-8315, Japan*

Leucine: substrate and signal

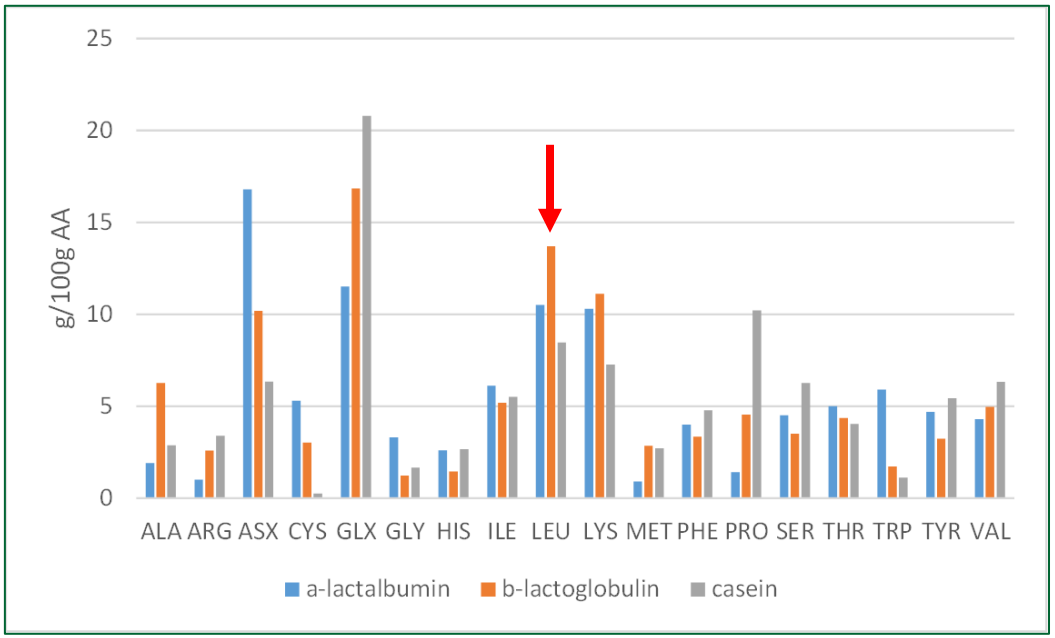


Dodd and Tee (2011) Am. J. Physiol. Endocrinol. Metab. 302: E1329

‘The mTOR pathway detects and integrates nutrient and energy availability before signalling for protein synthesis.

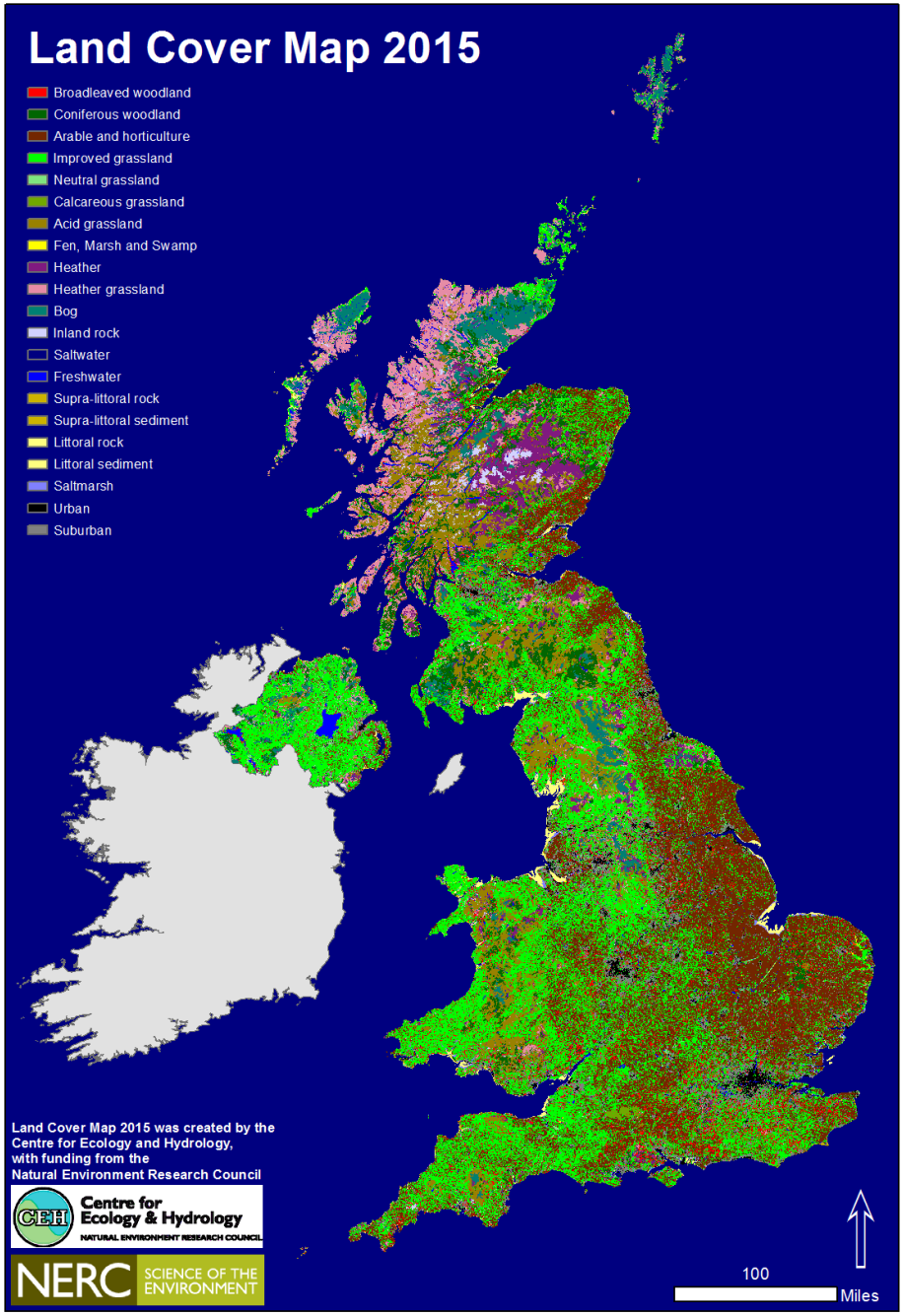
Total amino acid withdrawal, or strictly leucine withdrawal in many cell types, inhibits mTOR signalling.’
Mahoney et al. (2009) Prog. Mol. Biol. Transl. Sci. 90: 53-107

Leucine is abundant in milk proteins, particularly in the major whey protein, β-lactoglobulin



It’s not just for athletes and bodybuilders

Dairy is the link between grass and muscle health



https://www.ceh.ac.uk/services/land-cover-map-2015

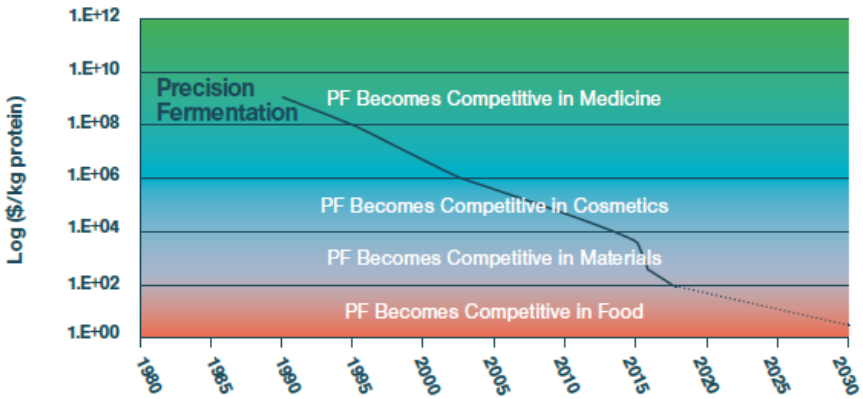
Dairy is the link between grass and muscle health

The elephant in the room

Precision Fermentation:

Fermentation plus precision biology. A process that allows us to program micro-organisms to produce almost any complex organic molecule.

Figure 5. PF Disrupting More Industries as Costs Fall



Source: RethinkX

Tubb and Seba (2019) Rethinking Food and Agriculture 2020-2030. A RethinkX Sector Disruption Report.

The disruptive innovation of precision fermentation milk

FLORA-BASED, COW-FREE

We're doing this by creating milk proteins — casein and whey — that are nutritionally identical to what comes from a cow, but without animals.

Flora-based dairy means dairy produced sustainably using less water, energy, greenhouse gas emissions and land. It means cruelty-free dairy produced without the use of factory farms. It also means dairy free from hormones, lactose, cholesterol, and pathogens that can make our food unsafe.

https://www.perfectdayfoods.com/mission/

Food compositions comprising one or both of recombinant beta-lactoglobulin protein and recombinant alpha-lactalbumin protein

Patent number: 9924728

Abstract: Disclosed herein are methods and compositions including casein, and methods for making these compositions.

Type: Grant

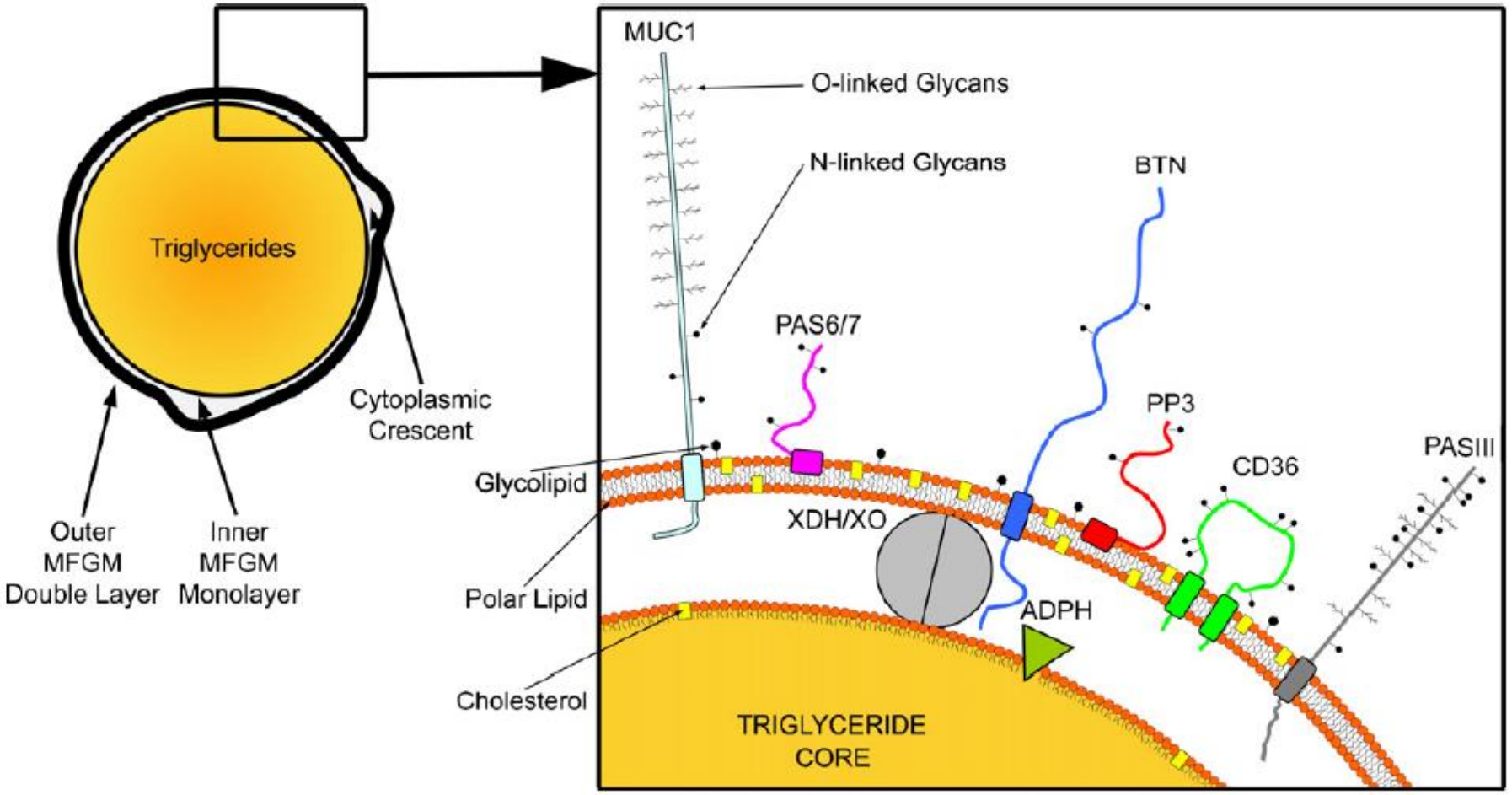
Filed: February 21, 2017

Date of Patent: March 27, 2018

Assignee: Perfect Day, Inc.

Inventors: Ryan Pandya, Perumal Gandhi, Shaowen Ji, Derek Beauchamp, Louis Hom

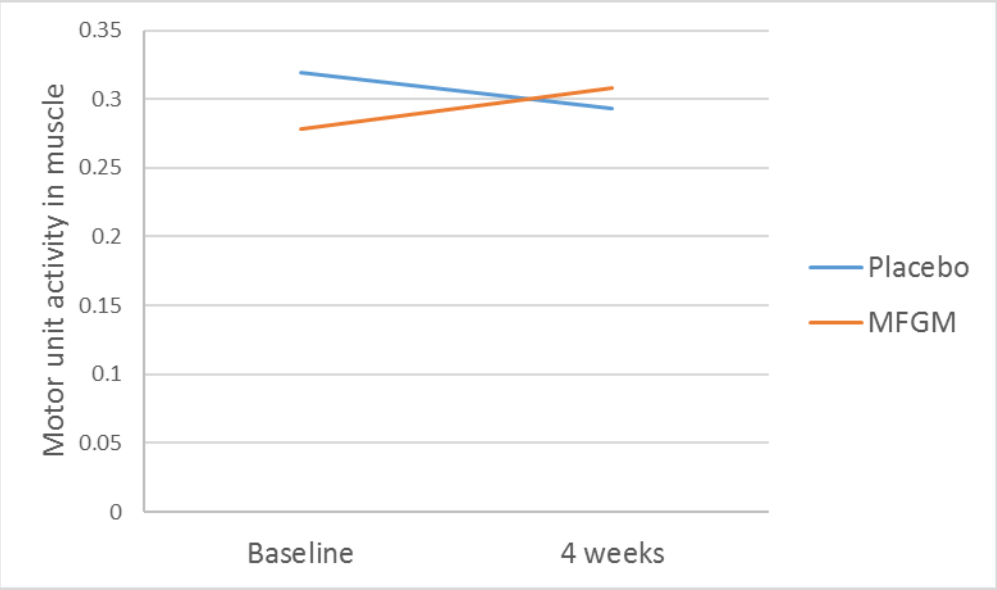
Milk fat globule membrane



Dewettinck et al. (2008) Int. Dairy J. 18: 436–457

MFGM and muscle health

40 year old males supplemented daily with Milk Fat Globule Membrane (in tablet form)

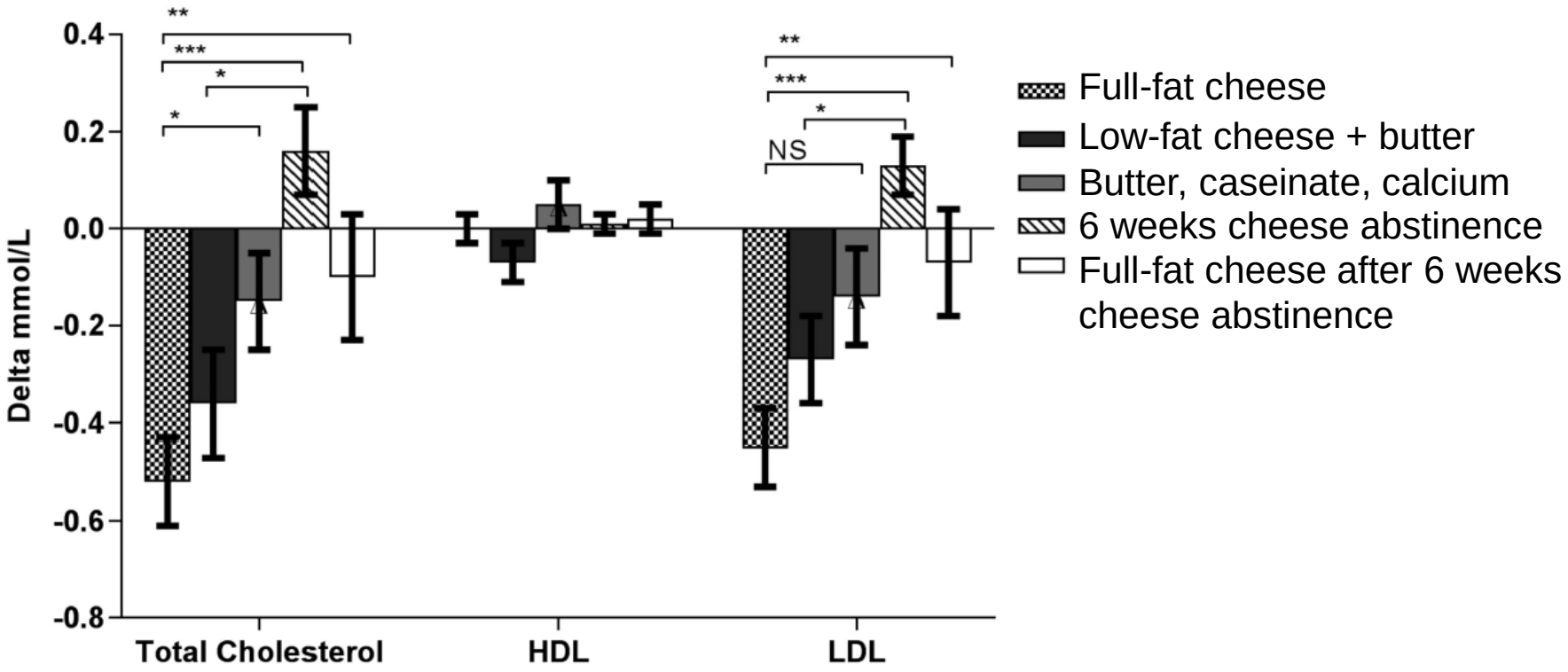


'…results…indicate that dietary MFGM… increases motor unit recruitment and enhances muscle strength, probably owing to neuromuscular mechanisms'

Sato et al. (2015) Nutrition J. 14: 85

Dairy fat as cheese or butter

Subjects > 50y, 6 week intervention, 40g/d dairy fat



Thorning et al. (2017) Am. J. Clin. Nutr. Doi: 10.3945/ajcn.116.151548

The nourishment in milk

- ‘Nourishment’
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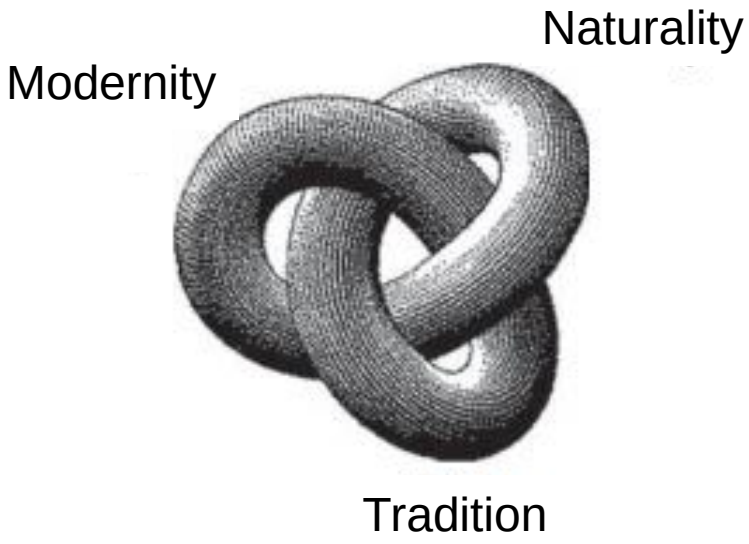
  - Health…sarcopenia
  - Food

Food and the hierarchy of human needs

Maslow (1943) A Theory of Human Motivation

Modernity, tradition, naturality



‘Modernity represents the values of progress, efficiency and prosperity… But modernity also has a negative face, in which modern developments are seen as destructive – a threat to natural and traditional values.

Tradition. This side of livestock farming is often used to depict a situation in which humans and animals live in harmony. But, on the negative side, tradition can be regarded as dull, backward, old-fashioned and static.

Naturality. Agriculture is a prime example of humanity’s success in cultivating nature for human progress. However, the very success of this…puts nature under pressure, giving rise to social concerns about preserving naturality.’

Boorgaard et al. (2011) Animal 5: 1458–1466

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