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Ingredients

White Paper

The Gut-Muscle Axis, an Opportunity for Serious Athletes and Casual Gym-Goers



Solutions for a
good gut feeling



Gut
health

The Gut-Muscle Axis, an Opportunity for Serious Athletes and Casual Gym-Goers

More people are taking serious steps to improve their health and fitness. This presents an opportunity for performance nutrition companies to offer protein “plus” solutions for athletes and sports enthusiasts with gastrointestinal issues. And also for active nutrition companies to tap into the growing demand for protein products from a new demographic - the casual gym-goer who is more interested in their holistic health instead of simply maximising athletic performance.

New research into the interplay between gut health, strength and overall well-being might be key to unlocking these opportunities.

The pursuit of well-rounded healthiness

The desire to live healthier for longer is fuelling growing interest in a proactive approach to health. There is also a growing understanding that our bodily functions are more interconnected than previously thought. It's unsurprising then that a holistic approach that treats the whole person as one, rather than treating symptoms in silos, is gathering momentum. Globally, 6 in 10 consumers worldwide are more conscious about their overall health and well-being because of COVID-19, and 61% are interested in solutions for cognitive, digestive, heart, immune, skin and joint health, even when not suffering from health problems¹.

As part of this, more consumers are turning to exercise to improve their overall health, and demand for high-protein products continues to grow, with 81% of active consumers looking to increase their protein intake as part of a healthy diet¹.



Research has demonstrated a link between the human gut and other areas of health.^{2,3} Recent studies now suggest a correlation between the gut microbiota, muscle function, athletic performance and body composition.⁴ This is known as the gut-muscle axis. Targeting this gut-muscle axis could have significant appeal in applications across the sports and active nutrition market.



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All eyes on the gut-muscle axis

Exercise is regarded as one of the main environmental factors that positively influences the gut microbiota.⁵ In fact, exercise has been shown to lead to improved carbohydrate and amino acid metabolism.^{5,6} However, there is a point when exercise can have adverse effects on the gut. Over-exercising, especially if the individual is unused to strenuous exercise, can cause undesired changes to gut microbiota like dysbiosis⁵.

Research into the gut-muscle axis also suggests that muscle recovery and athletic performance are affected by processes in the gut and may be targeted by gut microbiota intervention.^{4,7,8,11} Recent studies with fermented and nondigestible compounds - prebiotics* - highlight the stimulation of health-promoting bacteria that may positively affect the human body⁴ and muscle health.^{4,9} An athlete could therefore be eating the right foods to support recovery,¹⁴ but if their gut is unbalanced,^{10,11} this will influence the process of nutrient absorption and extraction and may have negative effects on skeletal muscle mass^{4,7} and metabolic health.⁴



Effectively leveraging the gut-muscle axis could support older individuals in maintaining muscle mass,⁶ supporting them in leading independent and active lives for longer.

Indeed, there are suggestions that 86% of athletes suffer from gastrointestinal problems associated with training and competition.¹² An athlete with compromised skeletal muscle mass and function can struggle with their body composition, metabolic health, performance and recovery but regular dietary protein can help mitigate these negative impacts.¹³ This is just as important for the everyday consumer looking to embark on a healthier, more active lifestyle. Furthermore, effectively leveraging the gut-muscle axis could support older individuals in maintaining muscle mass,⁶ supporting them in leading independent and active lives for longer.

What is the gut-muscle axis?

Put simply, the gut-muscle axis is the interaction between the gut microbiome and muscle function.⁴ The gut microbiome has a far-reaching impact on multiple health areas, similar links are often described as the gut-brain axis,¹⁴ gut-skin axis¹⁵ and others.

The gut-muscle axis is particularly important for athletes as diet significantly affects a person's ability to exercise and develop and maintain muscle and the gut microbiome plays a critical role in nutrient absorption.⁴

Combining two power-houses of gut health: dairy and fermentation

Whey protein and muscle health

As consumers' food needs evolve and they endeavour to live a healthier lifestyle, protein-rich products are increasingly in demand. Dairy proteins, and especially whey proteins, are continuing to lead in premium applications and market segments, such as sports nutrition, with the market expected to expand at a compound annual growth rate (CAGR) of 9.8% by 2027.¹⁶

Milk contains both whey and casein proteins which are both high quality proteins that contain relatively high levels of essential amino acids and are well digested and absorbed.¹⁷ It has repeatedly been shown that these proteins stimulate muscle protein synthesis in both young and older adults.^{18,19,20} However, whey protein has a higher leucine content²¹ and is more rapidly digested than (micellar) casein.¹⁴ The faster rise in circulating amino acids (and leucine in particular) is likely responsible for the greater post-exercise muscle protein synthesis rates observed after consuming whey, compared with casein.^{22,14,23}

Consumers have increasingly higher expectations for their functional food and beverages. And while whey protein has enjoyed sustained consumer appeal, fermented whey protein supplements present an exciting opportunity for food manufacturers to unlock new audiences.



A potential game-changer

Alongside growing consumer interest in a more holistic approach to health, scientific research is also exploring how different health areas and bodily functions are connected.

New research exploring the gut microbiome of humans (bacteria, viruses, fungi and other life forms that are collectively known as the microbiome),²⁴ suggests the gut microbiome could be the answer to addressing multiple consumer health concerns, beyond digestive discomfort such as bloating, heartburn and digestive disorders such as constipation and irritable bowel syndrome.^{25,26} This research is highlighting links between the gut microbiota and other areas of health, from obesity and diabetes to heart and liver disease, and even mental health or muscle maintenance.^{27,28}

Fermentation of dairy is one process that has been associated with products that improve gut and digestive health. Studies show that such products can help increase beneficial bacteria and gut microbiome diversity. Because of this, fermented products have piqued both consumer and scientific interest, particularly in regard to digestive

health. But how can fermentation present opportunities for manufacturers to tap into the demand for holistic health solutions and allow them to create a combination of products that address the concerns of an increasingly health conscious and active population?

What is fermentation?

Firstly, we must understand the fermentation process in food, as well as its known associated benefits both for health and taste. Fermentation is a process which requires a natural substrate (e.g. milk, cabbage, etc.) and beneficial microorganisms, such as yeasts, moulds and bacteria. Initially, food fermentations were mainly used as a method for preserving precious raw materials. This was achieved by the generation of antimicrobial metabolites and

conditions which help to reduce the risk of contamination with pathogenic microorganisms.³ During the fermentation process, the beneficial microbes use the present carbohydrates, proteins and fats for growth, which gives rise to a fermented product containing many metabolites that not only reduce the pH but also add texture, flavour and/or provide health benefits.²⁴



Benefits of fermentation

The benefits of fermentation can include food preservation, improved digestive health, stronger immunity and better metabolic health, as demonstrated in studies with yoghurt's effect on heart disease³⁰ and type 2 diabetes.^{31,32,33}

Fermented food and drinks also can increase the availability of beneficial nutrients.^{34,35,36,37,38}

Some of the fermented foods and drinks that have been shown to improve health and digestion are:



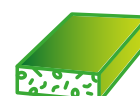
Kefir
cultured dairy product³⁴



Yoghurt
produced by bacterial fermentation of milk³⁴



Kimchi
fermented cabbage⁴¹



Tempeh
made from fermented soybeans³⁹



Kombucha
fermented tea⁴⁰

In recent years, fermented foods have undergone a surge in popularity due to their perceived health benefits. Fermenting foods has evolved beyond a method for food preservation into a tool for creating desirable organoleptic, nutritional, and functional attributes in food products. For instance, kimchi can offer a range of health and digestive effects such as anti-obesity, anticonstipation and reduced cardiovascular risks,⁴¹ whereas kefir and yoghurt have been purported to reduce lactose intolerance symptoms, supports the immune system, and lower cholesterol.⁴³

With increasing interest in the health benefits of fermentation, demand for protein products at an all-time high, and an increased focus on solutions that offer multiple health benefits, fermented protein solutions could present a substantial opportunity. Companies who can capitalise on this currently underdeveloped category will benefit from brand differentiation and also contributing to improved population health. The composition of whey protein makes it an ideal base for fermentation as it has been found to be a suitable growth medium for the production of selected strains of mainly lactic acid bacteria and yeast.⁴⁴

The science supporting fermented whey

We know that dairy and fermented products are popular ingredients for people looking to improve their overall well-being - but where does fermented whey sit in the better-for-you category?

Fermenting whey can have the desired effect of generating health benefiting bioactive peptides resulting from the partial breakdown of the protein during the fermenting process, which may support general health, improve uptake efficiency and nutrient absorption.^{8,45} Studies have also shown how fermented ammoniated condensed whey could provide benefits for individuals that experience slower or more difficult protein digestion and uptake, such as active consumers, athletes, or older adults suffering from gut-related issues.^{6,46,47}



One answer to the challenge

Fermented whey protein is one answer to the many challenges faced by active consumers, supporting with nutrient digestion and absorption,⁸ and the production of functional nutrients like peptides, vitamins and short chain fatty acids (SCFA).⁸ The decreased lactose content of fermented foods also supports consumers with restrictive dietary preferences or intolerances.



Fermented whey can also support muscle recovery – the process of regaining muscle or improving function – and muscle building, both of which are beneficial to active adults who want to reduce the risk of injury and build muscle without a complicated nutrition programme; the elderly, who lose muscle as they age; and athletes, who use nutrition to maximise training and performance. The increased availability of dietary protein-derived amino acids following digestion has additional benefits, particularly for busy adults balancing family, work and social commitments as well as trying to take better care of their own health. Several studies suggest that protein-rich

snacking may boost satiety and facilitate weight loss,^{48,49} as well as help maintain normal blood glucose levels.⁵⁰

Fermented whey improves the ability to ferment lactic acid and propionic acid. There is some evidence that fermentation in the gut can contribute to increased energy, whereby lactic acid (and propionic acid) is efficiently metabolised as an energy source. A 2021 paper, building on the findings above, hypothesizes that 'lactate shuttling' during exercise supports athletes' efforts by fuelling hard-working muscles as opposed to clearing lactate.⁵¹

Formulating for further benefits: the next step up?

Fermented whey formulations can include various complementary ingredients that support overall well-being.

Prebiotics

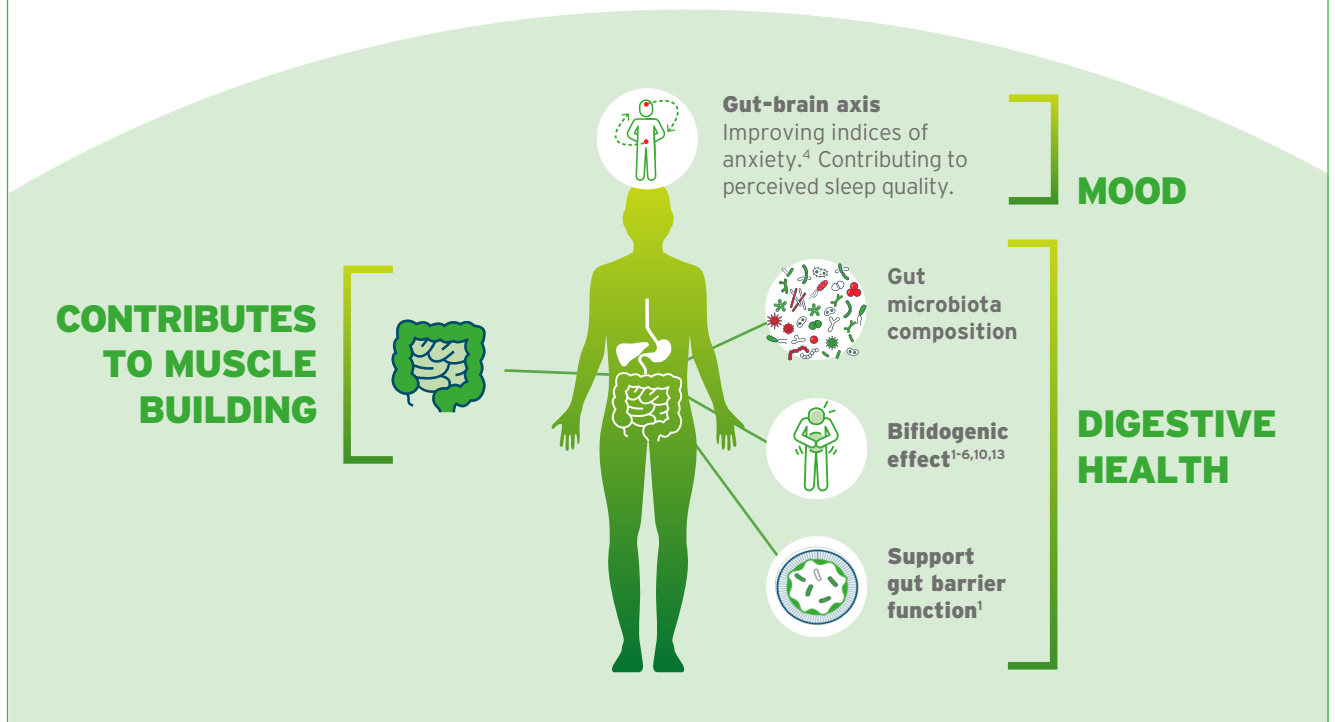
Several studies have explored the effects of fermenting galacto-oligosaccharides (GOS),^{52,53,54,55} a dairy derived prebiotic* which can deliver enhanced benefits via the microbiota, that works alongside fermented whey protein to support consumer demand for products that improve gut microbiota and support nutrient digestion and absorption. This may be especially interesting within sports nutrition, as dietary fibre intake has been reported to be surprisingly low in athletes.^{56,57}

In one study, several *bifidobacteria* (*B. catenulatum*, *B. bifidum*, and *B. longum*) and lactobacilli (*L. gasseri* and *L. salivarius*) were fermented and *B. catenulatum*, *B. bifidum* and *L. gasseri* and *L. salivarius* were stimulated, highlighting that GOS was specifically fermented by *bifidobacteria* and *lactobacilli*.⁵⁸ There is an increasing amount of evidence regarding the health benefits of GOS and several studies have shown that Biotis® GOS positively influences the microbiota, and more specifically, increases the relative abundance of *bifidobacteria* in the gut.^{59,60,61,62} Furthermore, Biotis® GOS has also been linked to gastrointestinal health benefits demonstrating increased gut comfort, such as benefitting stool frequency.^{63,64,65,66}

Finally, there is evidence suggesting that GOS' impact on beneficial bacteria abundance correlates with a reduction of stress⁶⁷ and anxiety symptoms.⁶⁸ Many athletes struggle with stress and anxiety on a daily basis, and each athlete reacts to the stress and anxiety differently.⁶⁹ While a certain amount of pressure can be beneficial to athletes,⁷⁰ too much stress can have negative effects on the body.



Benefits of Fermented Whey Protein and Galacto-Oligosaccharides



Source: ¹Krumbeck et al., 2018; ²Walton et al., 2012; ³Canfora et al., 2017; ⁴Johnstone et al., 2021; ⁵Schaafsma et al., 2021; ⁶Wilms et al., 2021; ⁷Wilson et al., 2019; ⁸Teuri & Korpela, 1998; ⁹Sairanen et al., 2007; ¹⁰Schoemaker et al., 2022; ¹¹Ladirat et al., 2014; ¹²Ambrogi et al., 2021; ¹³DarmBoost study, ASN June 2022

Paraprobiotics

Alongside fermented ingredients, paraprobiotics present an emerging opportunity to support gut health. Paraprobiotics, are non-viable microbial cells (either intact or broken), or crude cell extracts⁷¹ and have been associated with several potential health benefits including modulating anti-inflammatory and positive immune responses.⁶⁶ Paraprobiotics can also reduce the risk of sepsis and antibiotic resistance, as well as facilitate a longer shelf life in foods.⁶⁶

Furthermore, paraprobiotics could be of interest to the dairy sector as they are pH and temperature stable, allowing incorporation into foods with high acidity and before thermal processing without loss of functionality. The addition of paraprobiotics does not change the sensory properties of a product, avoiding effects like high acidification after fermentation in yoghurt.⁶⁶

Unlock the opportunity

While demand for increasingly holistic solutions is growing, formulating with other functional ingredients that complement fermented whey protein, such as GOS, may

unlock further opportunities, enabling producers to create integral multifunctional concepts - something particularly important for active, health-conscious consumers pursuing overall 'healthiness'.

Biotis® - The FrieslandCampina Ingredients solution

At FrieslandCampina Ingredients we strive to improve people's health through leading ingredient science. With our Biotis® solutions, we're opening up new opportunities for our customers by tapping into our world-leading experience in infant, performance and medical nutrition to create fresh, innovative Health Benefit Solutions that work with the body's natural processes throughout the human lifecycle. Stay tuned for FrieslandCampina Ingredients innovations in the gut-muscle area.

To learn more about Biotis® solutions, **visit:** www.biotis.com.

References

1. FMCG Gurus (2020).
2. Tooley, K.L. Effects of the Human Gut Microbiota on Cognitive Performance, Brain Structure and Function: A Narrative Review. *Nutrients* 2020, 12, 3009. <https://doi.org/10.3390/nu12103009>.
3. Johnstone, N., Milesi, C., Burn, O. et al. Anxiolytic effects of a galacto-oligosaccharides prebiotic in healthy females (18-25 years) with corresponding changes in gut bacterial composition. *Sci Rep* 11, 8302 (2021).
4. Przewiócka, K. et al. Gut-Muscle Axis Exists and May Affect Skeletal Muscle Adaptation to Training. *Nutrients* 12(5):1451, doi:10.3390/nu12051451 (2020).
5. Ticinesi, A. et al. Exercise and immune system as modulators of intestinal microbiome: implications for the gut-muscle axis hypothesis. *Exerc Immunol Rev.* 2019;25:84-95. PMID: 30753131.
6. Petersen LM, Bautista EJ, Nguyen H, Hanson BM, Chen L, Lek SH, Sodergren E, Weinstock GM. Community characteristics of the gut microbiomes of competitive cyclists. *Microbiome* 5: 98, 2017
7. Picca, A. et al. Gut Dysbiosis and Muscle Aging: Searching for Novel Targets against Sarcopenia. *Mediators of Inflammation*, 2018, pp.1-15 (2018).
8. Scheiman, J. et al. Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism. *Nature Medicine*, 25(7), pp.1104-1109 (2019).
9. Widyastuti Y, Febrisiantosa A, Tidona F. Health-Promoting Properties of Lactobacilli in Fermented Dairy Products. *Front Microbiol.* 2021 May 21;12:673890. doi: 10.3389/fmicb.2021.673890. PMID: 34093496; PMCID: PMC8175972.
10. Sohail MU, Yassine HM, Sohail A, Thani AAA, Impact of Physical Exercise on Gut Microbiome, Inflammation, and the Pathobiology of Metabolic Disorders. *Rev Diabet Stud.* 2019; 15(1):35-48.
11. Coleman N. et al. Gastrointestinal Issues in Athletes. *Curr. Sports Med. Rep.* 2019;18:185-187. doi: 10.1249/JSR.0000000000000599.
12. Pugh JN, et al. Gastrointestinal symptoms in elite athletes: time to recognise the problem? *Br J Sports Med.* 2018 Apr;52(8):487-488. doi: 10.1136/bjsports-2017-098376. Epub 2017 Oct 10. PMID: 29018062.
13. Wall BT, Morton JP, van Loon LJ. Strategies to maintain skeletal muscle mass in the injured athlete: nutritional considerations and exercise mimetics. *Eur J Sport Sci.* 2015;15(1):53-62. doi: 10.1080/17461391.2014.936326. Epub 2014 Jul 16. PMID: 25027662.
14. Marilia Carabotti, Annunziata Scirocco, Maria Antonietta Maselli, and Carola Severia. The gut-brain axis: interactions between enteric microbiota, central and enteric nervous systems. 2015, 28(2): 203-209.
15. Iman Salem, Amy Ramser, Nancy Isham, and Mahmoud A. Ghannoum. The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. 2018 doi: 10.3389/fmicb.2018.01459
16. Grandviewresearch.com. 2021. Whey Protein Market Size | Industry Report, 2020-2027. [online] Available at: <https://www.grandviewresearch.com/industry-analysis/whey-protein-market>.
17. Gorissen, S.H.M., Crombag, J.J.R., Senden, J.M.G. et al. Protein content and amino acid composition of commercially available plant-based protein isolates. *Amino Acids* 50, 1685-1695 (2018). <https://doi.org/10.1007/s00726-018-2640-5>
18. Witard OC, et al. Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. *Am J Clin Nutr.* 2014 Jan;99(1):86-95. doi: 10.3945/ajcn.112.055517. Epub 2013 Nov 20. PMID: 24257722.
19. Yang Y, et al. Myofibrillar protein synthesis following ingestion of soy protein isolate at rest and after resistance exercise in elderly men. *Nutr Metab (Lond).* 2012 Jun 14;9(1):57. doi: 10.1186/1743-7075-9-57. PMID: 22698458; PMCID: PMC3478988.
20. Pennings B, et al. Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. *Am J Clin Nutr.* 2011 May;93(5):997-1005. doi: 10.3945/ajcn.110.008102. Epub 2011 Mar 2. PMID: 21367943.
21. Phillips, S.M. The impact of protein quality on the promotion of resistance exercise-induced changes in muscle mass. *Nutr Metab (Lond)* 13, 64 (2016). <https://doi.org/10.1186/s12986-016-0124-8>.
22. Devries MC, Phillips SM. Supplemental protein in support of muscle mass and health: advantage whey. *J Food Sci.* 2015 Mar;80 Suppl 1:A8-A15. doi: 10.1111/1750-3841.12802. PMID: 25757896. <https://pubmed.ncbi.nlm.nih.gov/25757896/>.
23. Boirie Y, et al. Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proc Natl Acad Sci U S A* 1997;94:14930-5.
24. Brody, H. The gut microbiome. *Nature* 2020. Vol 577. S5
25. Carco et al. Increasing Evidence That Irritable Bowel Syndrome and Functional Gastrointestinal Disorders Have a Microbial Pathogenesis. *Front Cell Infect Microbiol.* 2020 Sept 9;10:468.
26. Carco et al. Increasing Evidence That Irritable Bowel Syndrome and Functional Gastrointestinal Disorders Have a Microbial Pathogenesis. *Front Cell Infect Microbiol.* 2020 Sept 9;10:468.
27. Ghosh ST, et al. Adjusting for age improves identification of gut microbiome alterations in multiple diseases. *eLife* 2020;9:e50240.
28. An R, et al. Age-dependent changes in GI physiology and microbiota: time to reconsider? *Gut.* 2018 Dec;67(12):2213-2222.
29. Stanford Medicine. A fermented-food diet increases microbiome diversity and lowers inflammation, study finds. *ScienceDaily*, www.sciencedaily.com/releases/2021/07/2107212122151.htm (2021).
30. Ivey, K.L., et al. Association between yogurt, milk, and cheese consumption and common carotid artery intima-media thickness and cardiovascular disease risk factors in elderly women. *Am J Clin Nutr.* 2011 Jul;94(1):234-9.
31. Margolis, K.L., et al. A diet high in low-fat dairy products lowers diabetes risk in postmenopausal women. *J Nutr.* 2011 Nov;141(11):1969-74.
32. Chen, Mu, et al. Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis. *BMC medicine*.1 (2014): 215.
33. Gijbbers L, Ding EL, Malik VS, De Goede J, Geleijnse JM, Soedamah-Muthu SS. Consumption of dairy foods and diabetes incidence: a dose-response meta-analysis of observational studies. *The American journal of clinical nutrition.* 2016 Apr 1;103(4):1111-24.
34. Bell, V. et al. One Health, Fermented Foods, and Gut Microbiota. *Foods*, 7(12), p195 (2018).
35. Moon, G. Bifidobacterial Growth Stimulation by Lactobacillus casei via Whey Fermentation. *Preventive Nutrition and Food Science*, 14(3), pp.265-268 (2009).
36. Caputo Oliveira, R. et al. Postpartum supplementation of fermented ammoniated condensed whey improved feed efficiency and plasma metabolite profile. *Journal of Dairy Science*, 102(3), pp.2283-2297 (2019).
37. Lisko, D.J. et al. Effects of Dietary Yogurt on the Healthy Human Gastrointestinal (GI) microbiome. *Microorganisms.* 2017 Feb 15;5(1).
38. Mozaffarian, D., et al. Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men. *N Engl J Med.* 2011; 364:2392-404.
39. Amadeus Driandio Ahnan-Winaro, Lorraine Cordeiro, Florentinus Gregorius Winarno, John Gibbons, Hang Xiao. Tempeh: A semicentennial review on its health benefits, fermentation, safety, processing, sustainability, and affordability. 2021. <https://doi.org/10.1111/1541-4337.12710>
40. Julie M.Kapp, Walton Sumner, Kombucha: a systematic review of the empirical evidence of human health benefit. 2019. <https://doi.org/10.1016/j.annepidem.2018.11.001>
41. Myung-Sunny Kim, PhD, Hye Jeong Yang, PhD, Soon-Hee Kim, PhD, Hye Won Lee, PhD, and Myeong Soo Lee, PhD. Effects of Kimchi on human health. 2018. doi: 10.1097/MD.00000000000010163
42. Kim, E. et al. Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients. *Nutrition Research*, 31(6), pp.436-443 (2011).
43. Guzel-Seydim, Z.B., et al. Review: functional properties of kefir. *Crit. Rev. Food Sci. Nutr.* 51.
44. ResearchGate. 2021. (PDF) Fermented and Non Fermented Whey Beverages. [online] Available at: https://www.researchgate.net/publication/289326629_Fermented_and_Non_Fermented_Whey_Beverages (2011).
45. Geiker NRW, Mølgaard C, Iuliano S, Rizzoli R, Manios Y, van Loon LJC, Lecerf JM, Moschonis G, Reginger JY, Givens I, Astrup A. Impact of whole dairy matrix on musculoskeletal health and aging-current knowledge and research gaps. *Osteoporos Int.* 2020 Apr;31(4):601-615. doi: 10.1007/s00198-019-05229-7. Epub 2019 Nov 14. Erratum in: *Osteoporos Int.* 2020 Jan 13; PMID: 31728607; PMCID: PMC7075832.
46. Kume H, Okazaki K, Takahashi T, Yamaji T. Protective effect of an immune-modulating diet comprising whey peptides and fermented milk products on indomethacin-induced small-bowel disorders in rats. *Clin Nutr.* 2014 Dec;33(6):1140-6. doi: 10.1016/j.clnu.2013.12.014. Epub 2014 Jan 10. PMID: 24461940.
47. Ano Y, Ayabe T, Kutsukake T, Ohya R, Takaichi Y, Uchida S, Yamada K, Uchida K, Takashima A, Nakayama H. Novel lactopeptides in fermented dairy products improve memory function and cognitive decline. *Neurobiol Aging.* 2018 Dec;72:23-31. doi: 10.1016/j.neurobiolaging.2018.07.016. Epub 2018 Aug 6. PMID: 30176402.
48. Navas-Carretero S, Abete I, Zulet MA, Martinez JA. Chronologically scheduled snacking with high-protein products within the habitual diet in type-2 diabetes patients leads to a fat mass loss: a longitudinal study. *Nutr J.* 10:74 (2011).
49. Ortinau LC, Hoertel HA, Douglas SM, Leidy HJ. Effects of high-protein vs. high-fat snacks on appetite control, satiety, and eating initiation in healthy women. *Nutr J.* 13:97 (2014).
50. El Khoury D, Brown P, Smith G, et al. Increasing the protein to carbohydrate ratio in yogurts consumed as a snack reduces post-consumption glycemia independent of insulin. *Clin Nutr.* 33(1):29-38 (2014).
51. Brooks, G. et al. Lactate in contemporary biology: a phoenix risen. *The Journal of Physiology* (2021).
52. Annet J. H. Maathuis, Ellen G. van den Heuvel, Margriet H. C. Schoterman, Koen Venema, Galacto-Oligosaccharides Have Prebiotic Activity in a Dynamic In Vitro Colon Model Using a 13C-Labeling Technique, *The Journal of Nutrition*, Volume 142, Issue 7, July 2012, Pages 1205-1212, <https://doi.org/10.3945/jn.111.157420>
53. Cruz, M., Basseto, R., Bonfim, T., Brand, D., Chiquetto, N. and Almeida, M., 2017. Production and partial purification of galacto-oligosaccharides by sequential fermentation. *Brazilian Journal of Food Research*, 8(4).
54. Torres, D., Gonçalves, M., Teixeira, J. and Rodrigues, L., 2010. Galacto-Oligosaccharides: Production, Properties, Applications, and Significance as Prebiotics. *Comprehensive Reviews in Food Science and Food Safety*, 9(5).
55. Ladirat, S., Schols, H., Nauta, A., Schoterman, M., Schuren, F. and Gruppen, H., 2014. In vitro fermentation of galacto-oligosaccharides and its specific size-fractions using non-treated and amoxicillin-treated human inoculum. *Bioactive Carbohydrates and Dietary Fibre*, 3(2).
56. Soric M, Misigoj-Durakovic M, Pedisic Z. Dietary intake and body composition of prepubescent female aesthetic athletes. *Int J Sport Nutr Exerc Metab.* (2008) 18:343-54. doi: 10.1123/ijsnem.18.3.343.
57. Collins AC, et al. Comparison of nutritional intake in US adolescent swimmers and nonathletes. *Health.* (2012) 4:873-80. doi: 10.4236/health.2012.410133.
58. Annet J. H. Maathuis et al. Galacto-Oligosaccharides Have Prebiotic Activity in a Dynamic In Vitro Colon Model Using a 13C-Labeling Technique. (2012).

59. Krumbeck et al. Probiotic Bifidobacterium strains and galacto-oligosaccharides improve intestinal barrier function in obese adults but show no synergism when used together as synbiotics, *Microbiome*, vol.6, p121 (2018).
60. Jeroense et al. Acute Consumption of Prebiotic Galacto-Oligosaccharides Increases Iron Absorption from Ferrous Fumarate, but not from Ferrous Sulfate and Ferric Pyrophosphate: Stable Iron Isotope Studies in Iron-Depleted Young Women, *The Journal of Nutrition* (2020).
61. Ladirat et al. Exploring the effects of galacto-oligosaccharides on the gut microbiota of healthy adults receiving amoxicillin treatment, *Br J Nutr* (2014).
62. Walton et al. A randomised crossover study investigating the effects of galactooligosaccharides on the faecal microbiota in men and women over 50 years of age, *Br J Nutr* 107 (2012).
63. Teuri & Korpela. Galacto-oligosaccharides relieve constipation in elderly people, *Annals of Nutrition & Metabolism* (1998).
64. Sairanen et al. Yoghurt containing galacto-oligosaccharides, prunes and linseed reduces the severity of mild constipation in elderly subjects, *European Journal of Clinical Nutrition* (2007).
65. Prebiotic Galacto-oligosaccharides Impact Stool Frequency and Fecal Microbiota in Self-reported Constipated Adults: A Randomized Clinical Trial, Schoenmaker et al., 2022. Manuscript submitted for publication.
66. Schoemaker et al., Prebiotic Galacto-Oligosaccharides Impact Stool Frequency and Fecal Microbiota in Self-Reported Constipated Adults: A Randomized Clinical Trial. *Nutrients*. 2022 Jan 12;14(2):309 <https://pubmed.ncbi.nlm.nih.gov/35057489/>
67. Thompson, R. et al. Dietary prebiotics alter novel microbial dependent fecal metabolites that improve sleep. *Scientific Reports*, 10(1) (2020).
68. Johnstone, N.; Milesi, C.; Burn, O.; van den Bogert, B.; Nauta, A.; Hart, K.; Sowden, P.; Burnet, P.W.J.; Cohen Kadosh, K. Anxiolytic effects of galacto-oligosaccharides prebiotic in healthy female volunteers are associated with reduced negative bias and the gut bacterial composition. *MedRxiv Prepubl.* doi:10.17605/OSF.IO/NGMSU (2019).
69. Judge LW, Urbina LJ, Hoover DL, et al. The Impact of Competitive Trait Anxiety on Collegiate Powerlifting Performance. *J Strength Cond Res*. 2016;30(9):2399-2405. doi:10.1519/JSC.0000000000001363.
70. Hardy L, Hutchinson A. Effects of performance anxiety on effort and performance in rock climbing: a test of processing efficiency theory. *Anxiety Stress Coping*. 2007;20(2):147-161. doi:10.1080/10615800701217035
71. Siciliano RA, Reale A, Mazzeo MF, Morandi S, Silvetti T, Brasca M. Paraprobiotics: A New Perspective for Functional Foods and Nutraceuticals. *Nutrients*. 2021;13(4):1225. Published 2021 Apr 8. doi:10.3390/nu13041225

*Gibson et al., 2017; Substrates that are selectively utilized by host microorganisms conferring a health benefit



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The Netherlands
Stationsplein 4
3818 LE Amersfoort
The Netherlands
Tel: +31 (0)33 713 33 33

Asia-Pacific
3 Temasek Avenue
#11-01 Centennial Tower
Singapore 039190
Tel: +65 6580 8100

China
2506, West Tower of
Twin Towers
B12 Jianguomenwai Ave,
Chaoyang Dist.
Beijing 100022 China
Tel: +86 10 6566 6099

North America
61 S. Paramus Road,
Suite 535
Paramus, NJ 07652, USA
Tel: +1 551 497 7300

Latin America
Rua Fradique Coutinho
30 - 6° - Cj. 61
Condomínio Edifício WinWork
Pinheiros
05416-000 São Paulo, Brasil
Tel: +55 11 2395 1700