



# Health benefits of fermented foods: microbiota and beyond

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Fermented foods and beverages were among the first processed food products consumed by humans. The production of foods such as yogurt and cultured milk, wine and beer, sauerkraut and kimchi, and fermented sausage were initially valued because of their improved shelf life, safety, and organoleptic properties. It is increasingly understood that fermented foods can also have enhanced nutritional and functional properties due to transformation of substrates and formation of bioactive or bioavailable end-products. Many fermented foods also contain living microorganisms of which some are genetically similar to strains used as probiotics. Although only a limited number of clinical studies on fermented foods have been performed, there is evidence that these foods provide health benefits well-beyond the starting food materials.

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## Introduction

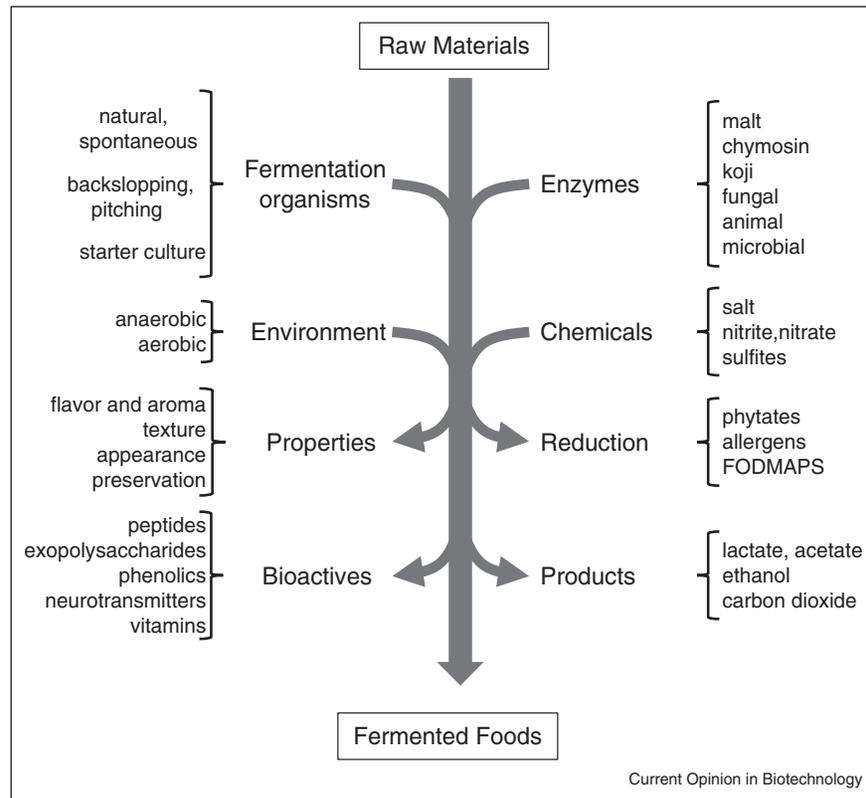
Fermented foods and beverages are staples of the human diet and have been produced and consumed since the development of human civilizations [1]. Fermented foods are generally defined as those foods or beverages made through controlled microbial growth and enzymatic conversions of major and minor food components (Figure 1). Food fermentation processes can be categorized by the primary metabolites and microorganisms involved: alcohol and carbon dioxide (yeast), acetic acid (*Acetobacter*), lactic acid (lactic acid bacteria (LAB) belonging to genera such as *Leuconostoc*, *Lactobacillus*, and *Streptococcus*), propionic acid (*Propionibacterium freudenreichii*), and ammonia and fatty acids (*Bacillus*, molds). Fermentations can also be described based on the food substrates, which include meats and fish, dairy, vegetables, soy beans and other legumes, cereals, starchy roots, and grapes and other fruits. Raw materials that contain high concentrations of monosaccharides and disaccharides, or in some cases starch, are fermented by yeasts or lactic acid bacteria. Molds and *Bacillus* are generally employed for starch saccharification or proteolysis or as secondary ripening microbiota after a primary fermentation.

As a result of the multitude of food-microbe combinations, there are thousands of different types of fermented foods and beverages. At least some form of these products is consumed by nearly every culture world-wide. Despite their long history, popularity, and culinary importance, the acceleration and industrialization of food production over the past century has reduced the diversity of fermented foods, particularly in the West. Recently, however, fermented foods have regained popularity as part of Western diets that emphasize artisanal processes. One reason for this surge in interest is their health-promoting potential. Recently, several groups have suggested that fermented foods should be included as part of national dietary recommendations [2,3]. This review will address what is currently known about how some of those foods support human health and the potential mechanisms underlying those effects.

## Traditional fermented foods are diverse but stable microbial ecosystems

Traditional food fermentations are elegantly simple in that they generally require very few ingredients and minimal

Figure 1



Overview of the transformative nature of fermented foods. Raw materials are fermented in specific conditions to create interesting and desirable foods. Fermentation then creates novel and potentially health promoting compounds in foods, while removing those with negative health potential.

preparation and processing. Although some fermentations contain only a few dominant taxa (Table 1), strain differences and population dynamics during processing can be remarkably complex. In some foods, even minor alterations to species diversity or numbers can result in significantly different food products and variations in quality and

organoleptic properties. Therefore, a microbial composition with temporal and spatial stability and resilience results in consistent fermentations and process conditions that are necessary to produce high quality food. Recent studies have explored the microbial diversity of numerous fermented food types and their associations with

Table 1

Primary source of fermentative organisms for common fermented foods and beverages. Microbial associations shown in the table are stable over time and show remarkable similarity in different regions or countries

Food	Source of organisms	Organisms
Yogurt	Starter culture	<i>St. thermophilus</i> , <i>L. delbrueckii</i> ssp. <i>bulgaricus</i>
Cheese, sour cream	Starter culture, backslopping	<i>Lc. lactis</i> , <i>Lu. mesenteroides</i>
Sausage	Backslopping, starter culture, spontaneous	<i>L. sake</i> , <i>L. plantarum</i> , <i>S. carnosus</i> , <i>S. xylosum</i> , <i>P. acidilactici</i>
Wine	Spontaneous, starter culture	<i>Sa. cerevisiae</i> , <i>O. oeni</i>
Beer	Backslopping, starter culture	<i>Sa. cerevisiae</i> ( <i>L. brevis</i> )
Bread	Starter culture	<i>Sa. cerevisiae</i>
Sourdough bread	Backslopping	<i>L. sanfranciscensis</i> , <i>C. humilis</i>
Sauerkraut or kimchi	Spontaneous	<i>Lu. mesenteroides</i> , <i>L. plantarum</i> , <i>L. brevis</i>
Olives	Spontaneous	<i>L. plantarum</i>
Soy sauce, miso	Starter culture, spontaneous	<i>A. soyae</i> , <i>Z. rouxii</i> , <i>T. halophilus</i>
Tempeh	Starter culture, backslopping	<i>R. oligosporus</i>
Natto	Starter culture, backslopping	<i>B. subtilis</i> var. <i>natto</i>

*St.*, *Streptococcus*; *L.*, *Lactobacillus*; *Lc.*, *Lactococcus*; *Lu.*, *Leuconostoc*; *S.*, *Staphylococcus*; *P.*, *Pediococcus*; *Sa.*, *Saccharomyces*; *O.*, *Onococcus*; *C.*, *Candida*; *A.*, *Aspergillus*; *Z.*, *Zygosaccharomyces*; *T.*, *Tetragenococcus*; *R.*, *Rhizopus*; *B.*, *Bacillus*.

metabolite and sensory attributes, such as acidity and texture. Importantly, this research not only informs fermentation management efforts, but also fundamental ecological concepts for improving the nutritional properties and organoleptic quality of fermented foods [4,5<sup>••</sup>,6].

### Benefits of fermented foods

Fermentation can be viewed as a biological method of food preservation. Foods produced in this way have a reduced risk of contamination when enriched in antimicrobial end-products, such as organic acids, ethanol, and bacteriocins. Advantages of fermented foods also include the new and desirable tastes and textures that are completely unlike those present in the starting materials. Other benefits are more specific to the particular food type. Table olives, for example, are inedible without the microbial (or chemical) — induced removal of bitter-tasting phenolic compounds. Another example is the growth of bakers' yeast (*Saccharomyces cerevisiae*), alone or with lactic acid bacteria, that achieves dough leavening during bread manufacture.

Beyond these characteristics, it is increasingly understood that some fermented foods also promote human health in ways not directly attributable to the starting food materials. That is, the outcomes of fermentation, and the contributions of microbes, in particular, can provide additional properties beyond basic nutrition. Recent human clinical studies on fermented foods support this possibility (Table 2). Large cohort investigations have revealed strong associations between consumption of fermented dairy foods and weight maintenance [7]. Likewise, other long-term prospective studies show reductions in risk of cardiovascular disease (CVD), type 2 diabetes (T2D), and overall mortality from frequent yogurt consumption [8<sup>•</sup>,9–11]. These benefits might extend to immediate physiological responses, a possibility recently indicated by the finding that fermented milk consumption improved glucose metabolism and reduced muscle soreness induced by acute resistance exercise [12]. Similarly, evidence is accumulating for anti-diabetic and anti-obesity benefits of kimchi [13]. In inflammatory bowel diseases and other immune-related pathologies such as arthritis and sclerosis, health benefits of fermented foods have also been proposed, although clinical data have not yet been reported [14]. Lastly, although the microbiota-gut-brain axis is a nascent field of research, there is an indication that fermented food consumption can alter mood and brain activity [15–17]. The following sections discuss how fermented foods could lead to these outcomes by modifying the food constituents, synthesizing metabolites and proteins, and providing living microorganisms to the gastrointestinal (GI) tract.

### Transformation of food constituents

During fermentation, the enzymatic activity of the raw material and the metabolic activity of microorganisms can

change the nutritive and bioactive properties of food matrices in a manner that has beneficial consequences for human health. For example, most cheeses are typically well-tolerated by lactose-intolerant individuals because some of the lactose originally in the milk is fermented and the remaining lactose is separated into the whey fraction during cheese production. Yogurt, in particular, is generally well tolerated by lactose-maldigesters due to the *in vivo* release of  $\beta$ -galactosidase by yogurt cultures [18]. The bacterial  $\beta$ -galactosidases survive the acidic conditions of the stomach, apparently being physically protected within the bacterial cells and facilitated by the buffering capacity of yogurt. This mechanistic understanding was instrumental in these yogurt-associated species (*Lactobacillus delbrueckii* subsp. *bulgaricus* and *Streptococcus thermophilus*) becoming the only live microbes for which an EFSA health claim has been approved [19]. Specifically, the EFSA claim states that 'Live yogurt cultures in yogurt improve digestion of yogurt lactose in individuals with lactose maldigestion'.

Another dairy constituent, conjugated linoleic acid, a fatty acid with putative atheroprotective properties, can be enriched by LAB that possess linoleate isomerase. Some LAB also have proteolytic capacities active in milk and other foods that can result in increased concentrations of bioactive peptides and polyamines [20]. It should be noted that biogenic amines, which are generally undesirable, can also be produced in such fermentations [21]. Several peptides and peptide fractions having bioactive properties have been isolated from yogurt, sour milk, kefir, dahi, and other fermented food products. These and other peptides are being investigated for their anti-hypertensive, anti-thrombotic, satiety, opioid, immunomodulatory, osteogenic, and antioxidant effects [22]. Of particular interest are the peptides present in fermented dairy products that have activity as anti-hypertensive angiotensin-converting-enzyme (ACE) inhibitors [23].

In plant and vegetable fermentations, the growth of LAB enhances conversion of phenolic compounds such as flavonoids to biologically active metabolites via expression of glycosyl hydrolase, esterase, decarboxylase, and phenolic acid reductase [24]. The subsequent reaction of these metabolites with anthocyanidins results in formation of pyranoanthocyanidins or 3-desoxy-pyranoanthocyanidins [25]. Some of these alkyl catechols potently activate Nrf2 (NFE2L2), the master regulator of oxidant stress responses in mammals and thereby induce the expression of anti-oxidant and detoxifying enzymes protecting against oxidative and chemical damage [26<sup>••</sup>].

Additionally, fermentation can result in the removal of toxic or undesirable food constituents such as phytic acid. This plant-associated, anti-nutritional compound chelates divalent metal ions. Fermentation of cereal substrates reduces the pH which optimizes endogenous

Table 2

## Recent human studies involving fermented foods

Target	Food type (organism(s) if referenced)	Study characteristics	Outcome	Reference (citation number)
T2D	Yogurt	Adult, 20-year factor-adjusted prospective, $N = 194\,458$	Consumption of one serving of yogurt per day was inversely correlated with T2D (HR = 0.83, $P < 0.001$ )	Chen <i>et al.</i> [8*]
T2D, CHD, mortality	FMD	Adult, 10-year factor-adjusted prospective, $N = 4526$	Fermented dairy consumption was inversely associated with overall mortality (HR = 0.7, $P < 0.01$ )	Soedamah-Muthu <i>et al.</i> [10]
IGM, T2D	FMD	Adult, extensive phenotyping, $N = 2391$	Fermented dairy consumption was inversely associated with IGM (HR = 0.74, 95% CI 0.54, 0.99)	Eussen <i>et al.</i> [9]
T2D	Yogurt	Elderly, 4.1-year factor-adjusted prospective, $N = 3454$	Total yogurt consumption was associated with a lower T2D risk (HR = 0.60 $P = 0.002$ )	Díaz-López <i>et al.</i> [60]
IGM, T2D	Kimchi	Adult, PC, crossover RCT, $N = 21$ , 8 weeks on diet, 4 week washout, 8 weeks on switched diet	Fermented kimchi decreased insulin resistance, and increased insulin sensitivity ( $P = 0.004$ and $0.028$ , respectively). The percentages of participants who showed improved glucose tolerance were 9.5 and 33.3% in the fresh and fermented kimchi groups, respectively	An <i>et al.</i> [13]
Obesity	Chungkookjang ( <i>Bacillus licheniformis</i> )	Adult, PC, DB, crossover RCT, $N = 120$ , 12 week diet followed by 12 week diet switch	Percentage body fat, lean body mass, waist circumference and waist-to-hip ratio of women in the Chungkookjang group were significantly improved compared with the placebo group	Byun <i>et al.</i> [61]
CVD	Fermented soy product ( <i>Enterococcus faecium</i> CRL 183, <i>Lactobacillus helveticus</i> 416)	Adult, PC, DB, RCT, $N = 49$ , once daily consumption for 42 days	Consumption of fermented soy product led to improved total cholesterol, non-HDL-C and LDL concentrations (reduction of 13.8%, 14.7% and 24.2%, respectively, $P < 0.05$ )	Cavallini <i>et al.</i> [62]
Hyperlipidemia	Kochujang ( <i>Aspergillus oryzae</i> )	Adult, PC, DB, RCT, $N = 30$ , three times daily consumption for 12 weeks	Kochujang-supplemented group, subjects' total cholesterol level significantly decreased (from $215.5 \pm 16.1$ mg/dL to $194.5 \pm 25.4$ mg/dL, $P = 0.001$ )	Lim <i>et al.</i> [63]
Hypertension	Casein-derived lactotripeptides	Adult, meta-analysis of 20 RCTs	Pooled treatment effect for SBP was $-2.95$ mmHg (95% CI: $-4.17$ , $-1.73$ ; $P < 0.001$ ), and for DBP was $-1.51$ mmHg (95% CI: $-2.21$ , $-0.80$ ; $P < 0.001$ )	Fekete <i>et al.</i> [23]
Osteoporosis	Kefir	Adult, PC, DB, RCT, $N = 40$ , once daily consumption for 6 months	Kefir-fermented milk therapy was associated with short-term changes in turnover and greater 6-month increases in hip BMD among osteoporotic patients	Tu <i>et al.</i> [64]
Muscle soreness	FM ( <i>Lactobacillus helveticus</i> )	Adult, PC, DB, RCT, $N = 18$ , 3 doses of FM before and after exercise	Muscle soreness was significantly suppressed by the consumption of FM compared with placebo (placebo, $14.2 \pm 1.2$ score vs. fermented milk, $12.6 \pm 1.1$ score, $P < 0.05$ )	Iwasa <i>et al.</i> [12]
Depression in T2D patients	Coffee	Adult, cross-sectional query based study, $N = 89$	Patients who drank 3 or more cups of coffee per day were more common in the non-depressed group (27/74 = 36.5%) than in depressed group (1/14 = 7.1%) ( $P = 0.032$ )	Omagari <i>et al.</i> [17]
Brain intrinsic activity or emotional attention	Fermented milk ( <i>Bifidobacterium animalis</i> subsp. <i>lactis</i> , <i>Streptococcus thermophilus</i> , <i>Lactobacillus bulgaricus</i> , <i>Lactococcus lactis</i> subsp. <i>lactis</i> )	Adult, PC, RCT, $N = 36$ , daily consumption for 4 weeks	Consumption of the FM by healthy women affected activity of brain regions that control central processing of emotion and sensation	Tillisch <i>et al.</i> [15]

Table 2 (Continued)

Target	Food type (organism(s) if referenced)	Study characteristics	Outcome	Reference (citation number)
Infection control, bowel movement normalcy	FM ( <i>Lactobacillus casei</i> Shirota)	Elderly, PC, DB, RCT, <i>N</i> = 72, once daily consumption for 6 months	Consumption of FM resulted in significantly lower incidence of fever (1.1 days vs. 2.5 days, <i>P</i> < 0.05) and improved bowel movements (constipation 0.6 times vs. 1 time, <i>P</i> < 0.05) (diarrhea 0.3 days vs. 0.7 days, <i>P</i> < 0.05)	Nagata <i>et al.</i> [65]
IBS	Rye bread	Adult, PC, DB, crossover RCT, <i>N</i> = 87, 7–8 pieces per day, 4 week diet, 4 week washout, 4 week switch	Signs of IBS (flatulence, abdominal pain, cramps and stomach rumbling) were milder on the low-FODMAP rye bread ( <i>P</i> values: 0.04; 0.049; 0.01 and 0.001)	Laatikainen <i>et al.</i> [27]

T2D, type 2 diabetes; CHD, coronary heart disease; IGM, impaired glucose metabolism; CVD, cardiovascular disease; IBS, irritable bowel syndrome; PC, placebo controlled; DB, double blinded; RCT, randomized clinical trial; HR, hazard ratio; FDP, fermented dairy products; FM, fermented milk; SBP, systolic blood pressure; Hg, mercury; DBP, diastolic blood pressure; BMD, bone mineral density; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, polyols.

phytase activity thus removing most phytic acid. Additionally, sourdough fermentation and extended fermentation times on other breads can also reduce fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPS). Reductions in FODMAP content of wheat and rye bread can increase the tolerance of these compounds by IBS patients [27,28].

### Synthesis of bioactive and nutritive compounds

Fermentation can also result in new compounds with health-modulating potential. Lactic acid is one such metabolite that is synthesized in amounts often reaching over 1% in LAB fermentations. Lactic acid (or lactate) was recently shown to reduce pro-inflammatory cytokine secretion of TLR-activated, bone-marrow-derived macrophages and dendritic cells in a dose-dependent manner [29]. Lactate also alters redox status by reducing the reactive oxygen species burden in intestinal enterocytes [30]. Therefore, should a fraction of the lactic acid or possibly other organic acids in fermented foods reach the small intestine those cell products might provide a core benefit of those foods.

Other microbial-derived products made during fermentation are typically strain dependent. The B vitamins including folate, riboflavin, and B12 are synthesized from various non-vitamin precursors by certain bacteria in plant and dairy foods [31,32]. Amino acids and derivatives with neurotransmitter (e.g.  $\gamma$ -aminobutyric acid) and immunomodulatory functions are also synthesized during fermentation [33]. Additionally, certain secreted proteins and exopolysaccharides produced during food fermentations might serve as anti-oxidants [34,35], prevent adhesion of pathogens to the intestinal mucosa [36], or confer immune-stimulatory [37] or hypocholesterolemic activities [38,39]. Some polysaccharides also act as prebiotics and are fermented by the intestinal microbiota to short chain fatty acids [40].

### Delivery of commensal microbes to the GI tract

Many fermented food and beverage products are processed such that viable microorganisms are absent at the time of consumption. Nonetheless, some of the most familiar fermented foods, including sauerkraut, kimchi, kefir, dry fermented sausage, yogurt, cheese, kombucha, and miso ordinarily contain viable cells in notable quantities ranging between  $10^6$  and  $10^9$  cells/g or cells/ml. A relatively large fraction of those microbes survives passage through the human digestive tract [41,42]. The ingestion of fermented foods potentially increases the numbers of microbes in the diet by up to 10 000-fold [43], and consuming 'living' fermented foods on a daily basis could be equivalent to introducing new, albeit transient microbes into the indigenous, intestinal microbiota [44]. Such diets contrast with the highly processed and sanitized foods consumed in Western societies that limit microbial exposures. The hygiene (or diversity) hypothesis proposes that such microbial exposures are essential for the normal development of immune system and neural function [45,46]. Therefore, consumption of fermented foods may provide an indirect means of counteracting the hygienic, sanitized Western diet and lifestyle.

The delivery of high numbers of microorganisms to the GI tract is supported by the matrix of some fermented foods which promote the long-term survival of organisms during distribution and storage. Fermented foods show particular potential as a practical vehicle in which to provide established probiotic strains to people in low-income countries [47,48]. The health-modulating potential of some of those strains also might be enhanced by the delivery matrix as indicated by the significantly reduced levels of colitis in mice fed *L. casei* BL23 incubated in milk as opposed to the same strain incubated in non-nutritive buffer [49]. Interestingly, the cell-associated proteome of *L. casei* was modified in response to milk and expressed certain proteins that contributed to

reduced inflammatory responses in the mouse intestine [50\*].

### Probiotic features of fermented food microorganisms

Many of the species found in fermented foods are either identical to or share physiological traits with species relevant to promoting GI tract health (Table 3). The importance of this was recently demonstrated by a study in which cheeses were produced using starter culture strains (*L. delbrueckii* subsp. *lactis* CNRZ327 and *P. freudenreichii* ITG) that had been selected based on their *in vitro*, anti-inflammatory potential [51\*]. When fed to mice, cheese containing those strains, but not the control cheese, protected against colitis and epithelial cell damage.

The concept that live microbes associated with food fermentations can provide beneficial functions in the GI tract is consistent with the emerging view that core health benefits of probiotic cultures can be assigned to a species, rather than to specific strains of a species [52\*]. At least this is the case for some species of LAB for which certain strains have long been applied as probiotics. Therefore, when a fermented food (e.g. sauerkraut, kimchi) contains large numbers of live cells belonging to a species for which health benefits have been demonstrated (e.g. *L. plantarum*), a reasonable argument could be made that these foods should be considered to have similar health benefits as those conferred by probiotic lactobacilli of the same species. It is worth noting that some countries (e.g. Italy and Canada) incorporate a list of species considered as probiotics in their regulatory guidelines. In contrast, in most of Europe, foods are not permitted to use or mention 'probiotics' or 'contain probiotics' on labels.

Ingestion of viable, fermentation-associated microbes could therefore exert influence on intestinal epithelial,

immune, and enteroendocrine cells in a manner similar to existing probiotic strains. Until now, such effects have been largely attributed to individual strains. Recent reports using strains of food-associated bacteria, *L. plantarum* and *L. rhamnosus* [53], *L. reuteri* [54\*\*] and *P. freudenreichii* [55], demonstrate the potential of those bacteria to directly alter host responses in the GI tract. Synthesis of histamine *in vivo* by *L. reuteri* [54\*\*] indicates that such outcomes could be due to metabolites already known to be made by many strains of a particular species.

Fermentation-associated microorganisms might alter the intestinal composition or function of the autochthonous microbiota in the GI tract. However the magnitude of these changes and importance to probiotic efficacy is currently a point of contention [56,57]. Three ways in which such changes could occur include trophic interactions (e.g. production of SCFA), direct inhibition or stimulation of competitors, and indirect effects as a result of impacting the host [41]. These effects are generally quite broad and therefore not likely limited to only certain strains. However, consistent with currently applied probiotics, fermentation-associated microbes are likely to be affected by host diet and other gut-associated factors [58] and are not likely to have long-lasting effects on the resident colonic microbiota [59].

### Conclusions

Heightened interest in the human microbiome as a major determinant of human health and behavior underscores the need to understand the functions of microorganisms and their cell products that enter the GI tract through food and beverages. Fermented foods are increasingly understood for their properties that reach well-beyond preservation and sensory attributes. Therefore, there is a critical need for additional fundamental research comparing different fermentation-associated strains for core properties expressed either for food transformations, product synthesis, or survival and host-microbe interactions in the GI tract. Also needed are randomized, controlled, clinical trials to measure the quantitative and repeatable effects of different fermented foods on human health. These studies are implicitly challenging to design because 'blinding' is not possible when whole foods are compared. Such efforts are still needed, however, because the benefits of fermented foods are likely greater than the sum of their individual microbial, nutritive, or bioactive components. This research will clarify the relevance, and potentially the necessity, of certain fermented foods in the human diet and justification for inclusion into national dietary guidelines.

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**Table 3**

#### Traditional or novel food fermentations with probiotic organisms

Species with recognized probiotic activity <sup>a</sup>	Fermented foods that reproducibly contain high cell counts of strains of the species
<i>Lactobacillus acidophilus</i>	NSLAB long ripened cheese
<i>Lactobacillus johnsonii</i>	Kefir
<i>Lactobacillus fermentum</i>	Bushera, ting and other African cereal porridges and beverages
<i>Lactobacillus plantarum</i>	Salami <sup>b</sup> , sauerkraut/kimchi, olives, others
<i>Lactobacillus paracasei</i>	Salami, kvass, NSLAB in long-ripened cheese
<i>Lactobacillus rhamnosus</i>	'Villi', fermented oatmeal
<i>Lactobacillus casei</i>	NSLAB long-ripened cheese

NSLAB, non-starter lactic acid bacteria.

<sup>a</sup> According to Health Canada.

<sup>b</sup> Fermented foods are printed in bold if presence of the probiotic organism depends on its addition as competitive starter culture.

## References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Hutkins RW: *Microbiology and Technology of Fermented Foods*. Wiley-Blackwell; 2008.
2. Ebner S, Smug LN, Kneifel W, Salminen SJ, Sanders ME: **Probiotics in dietary guidelines and clinical recommendations outside the European Union**. *World J Gastroenterol* 2014, **20**:16095-16100.
3. Chilton SN, Burton JP, Reid G: **Inclusion of fermented foods in food guides around the world**. *Nutrients* 2015 <http://dx.doi.org/10.3390/nu7010390>.
4. Wolfe BE, Button JE, Santarelli M, Dutton RJ: **Cheese rind communities provide tractable systems for in situ and in vitro studies of microbial diversity**. *Cell* 2014, **158**:422-433.
5. Walsh AM, Crispie F, Kilcawley K, O'Sullivan O, O'Sullivan MG, •• Claesson MJ, Cotter PD: **Microbial succession and flavor production in the fermented dairy beverage kefir**. *mSystems* 2016 <http://dx.doi.org/10.1128/mSystems.00052-16>.  
In addition to genes encoding for flavor production and other functional properties, this metagenome analysis shows that kefir bacteria also encode genes for probiotic functions, including bile salt transporters, mucus binding proteins, bacteriolysins and exopolysaccharides.
6. Erkus O, De Jager VCL, Spus M, Van Alen-boerrigter IJ, Van Rijswijk IMH, Hazelwood L, Janssen PWM, Van Hijum SAFT, Kleerebezem M, Smid EJ: **Multifactorial diversity sustains microbial community stability**. *Int Soc Microb Ecol* 2013, **7**:2126-2136.
7. Mozaffarian D: **Changes in diet and lifestyle and long-term weight gain in women and men**. *N Engl J Med* 2011, **364**:2392-2404.
8. Chen M, Sun Q, Giovannucci E, Mozaffarian D, Manson JE, • Willett WC, Hu FB: **Dairy consumption and risk of type 2 diabetes: 3 cohorts of US adults and an updated meta-analysis**. *BMC Med* 2014 <http://dx.doi.org/10.1186/s12916-014-0215-1>.  
This paper reports the earliest large cohort study to determine an anti-diabetic effect from routine consumption of yogurt. The authors used data taken from a 4-year study including over 150 000 men and women to determine risk of developing diabetes.
9. Eussen SJPM, van Dongen MCJM, Wijckmans N, den Biggelaar L, Oude Elferink SJWH, Singh-Povel CM, Schram MT, Sep SJS, van der Kallen CJ, Koster A *et al.*: **Consumption of dairy foods in relation to impaired glucose metabolism and type 2 diabetes mellitus: the Maastricht Study**. *Br J Nutr* 2016, **115**:1453-1461.
10. Soedamah-Muthu SS, Masset G, Verberne L, Geleijnse JM, Brunner EJ: **Consumption of dairy products and associations with incident diabetes, CHD and mortality in the Whitehall II study**. *Br J Nutr* 2013, **109**:718-726.
11. Tapsell LC: **Fermented dairy food and CVD risk**. *Br J Nutr* 2015, **113**:131-135.
12. Iwasa M, Aoi W, Mune K, Yamauchi H, Furuta K, Sasaki S, Takeda K, Harada K, Wada S, Nakamura Y *et al.*: **Fermented milk improves glucose metabolism in exercise-induced muscle damage in young healthy men**. *Nutr J* 2013 <http://dx.doi.org/10.1186/1475-2891-12-83>.
13. An SY, Lee MS, Jeon JY, Ha ES, Kim TH, Yoon JY, Ok CO, Lee HK, Hwang WS, Choe SJ *et al.*: **Beneficial effects of fresh and fermented kimchi in prediabetic individuals**. *Ann Nutr Metab* 2013, **63**:111-119.
14. Lorea Baroja M, Kirjavainen PV, Hekmat S, Reid G: **Anti-inflammatory effects of probiotic yogurt in inflammatory bowel disease patients**. *Clin Exp Immunol* 2007, **149**:470-479.
15. Tillisch K, Labus J, Kilpatrick L, Jiang Z, Stains J, Ebrat B, Guyonnet D, Legrain-Raspaud S, Trotin B, Naliboff BME: **Consumption of fermented milk product with probiotics modulates brain activity**. *Gastroenterology* 2014 <http://dx.doi.org/10.1053/j.gastro.2013.02.043>.
16. Hillmire MR, DeVlylder JE, Forestell CA: **Fermented foods, neuroticism, and social anxiety: an interaction model**. *Psychiatry Res* 2015, **228**:203-208.
17. Omagari K, Sakaki M, Tsujimoto Y, Shiogama Y, Iwanaga A, Ishimoto M, Yamaguchi A, Masuzumi M, Kawase M, Ichimura M *et al.*: **Coffee consumption is inversely associated with depressive status in Japanese patients with type 2 diabetes**. *J Clin Biochem Nutr* 2014, **55**:135-142.
18. Savaiano DA: **Lactose digestion from yogurt: mechanism and relevance**. *Am J Clin Nutr* 2014, **99**:1251-1255.
19. EFSA (European Food Safety Authority): **Scientific Opinion on the substantiation of health claims related to live yoghurt cultures and improved lactose digestion (ID 1143, 2976) pursuant to Article 13 (1) of Regulation (EC) No. 1924/2006**. *Eur Food Saf Auth J* 2011 <http://dx.doi.org/10.2903/j.efsa.2010.1763>.
20. Pessione E, Cirrincione S: **Bioactive molecules released in food by lactic acid bacteria: encrypted peptides and biogenic amines**. *Front Microbiol* 2016 <http://dx.doi.org/10.3389/fmicb.2016.00876>.
21. Linares DM, Del Rio B, Redruello B, Ladero V, Martin MC, Fernandez M, Ruas-Madiedo P, Alvarez MA: **Comparative analysis of the in vitro cytotoxicity of the dietary biogenic amines tyramine and histamine**. *Food Chem* 2016, **197**:658-663.
22. Pihlanto A, Korhonen H: *Advances in Fermented Foods and Beverages*. Elsevier Ltd.; 2015.
23. Fekete Á, Givens D, Lovegrove J: **Casein-derived lactotriptides reduce systolic and diastolic blood pressure in a meta-analysis of randomised clinical trials**. *Nutrients* 2015, **7**:659-681.
24. Filannino P, Bai Y, Di Cagno R, Gobbetti M, Gänzle MG: **Metabolism of phenolic compounds by *Lactobacillus* spp. during fermentation of cherry juice and broccoli puree**. *Food Microbiol* 2015, **46**:272-279.
25. Bai Y, Findlay B, Sanchez Maldonado AF, Schieber A, Vederas JC, Gänzle MG: **Novel pyrano and vinylphenol adducts of deoxyanthocyanidins in sorghum sourdough**. *J Agric Food Chem* 2014, **62**:11536-11546.
26. Senger DR, Li D, Jaminet SC, Cao S: **Activation of the Nrf2 cell defense pathway by ancient foods: disease prevention by important molecules and microbes lost from the modern western diet**. *PLOS ONE* 2016 <http://dx.doi.org/10.1371/journal.pone.0148042>.  
The authors observed that species of *Lactobacillus* (*plantarum*, *brevis*, *collinoides*) which are consumed from a diet rich in traditionally fermented foods and beverages, convert common phenolic acids found in fruits and vegetables to alkyl catechols. These compounds were further shown to be potent co-factors for activation of a major eukaryotic damage control pathway (the Nrf2 pathway) both *in vitro* and *in vivo*.
27. Laatikainen R, Koskenpato J, Hongisto SM, Lojonen J, Poussa T, Hillilä M, Korpela R: **Randomised clinical trial: low-FODMAP rye bread vs. regular rye bread to relieve the symptoms of irritable bowel syndrome**. *Aliment Pharmacol Ther* 2016, **44**:460-470.
28. Ziegler JU, Steiner D, Longin CFH, Würschum T, Schweiggert RM, Carle R: **Wheat and the irritable bowel syndrome – FODMAP levels of modern and ancient species and their retention during bread making**. *J Funct Foods* 2016, **25**:257-266.
29. Iraperda C, Errea A, Romanin DE, Cayet D, Pereyra E, Pignataro O, Sirard JC, Garrote GL, Abraham AG, Rumbo M: **Lactate and short chain fatty acids produced by microbial fermentation downregulate proinflammatory responses in intestinal epithelial cells and myeloid cells**. *Immunobiology* 2015, **220**:1161-1169.
30. Kahlert S, Junnikkala S, Renner L, Hynönen U, Hartig R, Nossol C, Barta-Böszörményi A, Dánicse S, Souffrant WB, Palva A *et al.*: **Physiological concentration of exogenous lactate reduces antimycin a triggered oxidative stress in intestinal epithelial cell line IPEC-1 and IPEC-J2 in vitro**. *PLOS ONE* 2016 <http://dx.doi.org/10.1371/journal.pone.0153135>.

31. Chamlagain B, Edelmann M, Kariluoto S, Ollilainen V, Piironen V: **Ultra-high performance liquid chromatographic and mass spectrometric analysis of active vitamin B12 in cells of *Propionibacterium* and fermented cereal matrices.** *Food Chem* 2015, **166**:630-638.
32. Russo P, Capozzi V, Arena MP, Spadaccino G, Dueñas MT, López P, Fiocco D, Spano G: **Riboflavin-overproducing strains of *Lactobacillus fermentum* for riboflavin-enriched bread.** *Appl Microbiol Biotechnol* 2014, **98**:3691-3700.
33. Becerra-Tomas N, Guasch-Ferre M, Quilez J, Merino J, Ferre R, Diaz-Lopez A, Bullo M, Hernandez-Alonso P, Palau-Galindo A, Salas-Salvado J: **Effect of functional bread rich in potassium, gamma-aminobutyric acid and angiotensin-converting enzyme inhibitors on blood pressure, glucose metabolism and endothelial function: a double-blind randomized crossover clinical trial.** *Medicine (Baltimore)* 2015 <http://dx.doi.org/10.1097/MD.0000000000001807>.
34. Li W, Ji J, Chen X, Jiang M, Rui X, Dong M: **Structural elucidation and antioxidant activities of exopolysaccharides from *Lactobacillus helveticus* MB2-1.** *Carbohydr Polym* 2014, **102**:351-359.
35. Hong YF, Lee H, young, Jung BJ, Jang S, Chung DK, Kim H: **Lipoteichoic acid isolated from *Lactobacillus plantarum* down-regulates UV-induced MMP-1 expression and up-regulates type I procollagen through the inhibition of reactive oxygen species generation.** *Mol Immunol* 2015, **67**:248-255.
36. Chen XY, Woodward A, Zijlstra RT, Gänzle MG: **Exopolysaccharides synthesized by *Lactobacillus reuteri* protect against enterotoxigenic *Escherichia coli* in piglets.** *Appl Environ Microbiol* 2014, **80**:5752-5760.
37. Makino S, Sato A, Goto A, Nakamura M, Ogawa M, Chiba Y, Hemmi J, Kano H, Takeda K, Okumura K *et al.*: **Enhanced natural killer cell activation by exopolysaccharides derived from yogurt fermented with *Lactobacillus delbrueckii* ssp. *bulgaricus* OLL1073R-1.** *J Dairy Sci* 2016, **99**:915-923.
38. Martoni CJ, Labbe A, Ganopolsky JG, Prakash S, Jones ML: **Changes in bile acids, FGF-19 and sterol absorption in response to bile salt hydrolase active *L. reuteri* NCIMB 30242.** *Gut Microbes* 2015 <http://dx.doi.org/10.1080/19490976.2015.1005474>.
39. London LEE, Kumar AHS, Wall R, Casey PG, O'Sullivan O, Shanahan F, Hill C, Cotter PD, Fitzgerald GF, Ross RP *et al.*: **Exopolysaccharide-producing probiotic lactobacilli reduce serum cholesterol and modify enteric microbiota in ApoE deficient mice.** *J Nutr* 2014, **144**:1956-1962.
40. Salazar N, Gueimonde M, De Los Reyes-Gavilán CG, Ruas-Madiedo P: **Exopolysaccharides produced by lactic acid bacteria and bifidobacteria as fermentable substrates by the intestinal microbiota.** *Crit Rev Food Sci Nutr* 2015 <http://dx.doi.org/10.1080/10408398.2013.770728>.
41. Derrien M, van Hylckama Vlieg JET: **Fate, activity, and impact of ingested bacteria within the human gut microbiota.** *Trends Microbiol* 2015, **23**:354-366.
42. Kim JY, Choi EY, Hong YH, Song YO, Han JS, Lee SS, Han ES, Kim TW, Choi IS, Cho KK: **Changes in Korean adult females' intestinal microbiota resulting from kimchi intake.** *J Nutr Food Sci* 2016 <http://dx.doi.org/10.4172/2155-9600.1000486>.
43. Lang JM, Eisen JA, Zivkovic AM: **The microbes we eat: abundance and taxonomy of microbes consumed in a day's worth of meals for three diet types.** *PeerJ* 2014 <http://dx.doi.org/10.7717/peerj.659>.
44. Plé C, Breton J, Daniel C, Foligné B: **Maintaining gut ecosystems for health: are transitory food bugs stowaways or part of the crew?** *Int J Food Microbiol* 2015, **213**:139-143.
45. Stefka AT, Feehley T, Tripathi P, Qiu J, McCoy K, Mazmanian SK, Tjota MY, Seo G-Y, Cao S, Theriault BR *et al.*: **Commensal bacteria protect against food allergen sensitization.** *Proc Natl Acad Sci U S A* 2014, **111**:13145-13150.
46. Campbell B, Raheison C, Lodge CJ, Lowe AJ, Gislason T, Heinrich J, Sunyer J, Gómez Real F, Norbäck D, Matheson MC *et al.*: **The effects of growing up on a farm on adult lung function and allergic phenotypes: an international population-based study.** *Thorax* 2016 <http://dx.doi.org/10.1136/thoraxjnl-2015-208154>.
47. Kort R, Westerik N, Mariela Serrano L, Douillard FP, Gottstein W, Mukisa IM, Tuijn CJ, Basten L, Hafkamp B, Meijer WC *et al.*: **A novel consortium of *Lactobacillus rhamnosus* and *Streptococcus thermophilus* for increased access to functional fermented foods.** *Microb Cell Fact* 2015 <http://dx.doi.org/10.1186/s12934-015-0370-x>.
48. Mpofu A, Linnemann AR, Sybesma W, Kort R, Nout MJR, Smid EJ: **Development of a locally sustainable functional food based on mutandabota, a traditional food in southern Africa.** *J Dairy Sci* 2014, **97**:2591-2599.
49. Lee B, Yin X, Griffey SM, Marco ML: **Attenuation of colitis by *Lactobacillus casei* BL23 is dependent on the dairy delivery matrix.** *Appl Environ Microbiol* 2015, **81**:6425-6435.
50. Lee B, Tachon S, Eigenheer RA, Phinney BS, Marco ML: ***Lactobacillus casei* low-temperature, dairy-associated proteome promotes persistence in the mammalian digestive tract.** *J Proteome Res* 2015, **14**:3136-3147.
- This paper details the changes to the *L. casei* cell-associated proteome which occur as a result of milk incubation. Notably, several bacterially upregulated proteins were identified which were important for alleviation of disease in a mouse model of chemically induced colitis.
51. Plé C, Breton J, Richoux R, Nurdin M, Deutsch SM, Falentin H, Hervé C, Chuat V, Lemée R, Maguin E *et al.*: **Combining selected immunomodulatory *Propionibacterium freudenreichii* and *Lactobacillus delbrueckii* strains: reverse engineering development of an anti-inflammatory cheese.** *Mol Nutr Food Res* 2016, **60**:935-948.
- This study represents an important step in validating controls for fermented foods, in that the control used was the fermented product with health-promoting bacteria removed.
52. Hill C, Guarner F, Reid G, Gibson GR, Merenstein DJ, Pot B, Morelli L, Canani RB, Flint HJ, Salminen S *et al.*: **Expert consensus document: the International Scientific Association for Probiotics and Prebiotics consensus statement on the scope and appropriate use of the term probiotic.** *Nat Rev Gastroenterol Hepatol* 2014, **11**:506-514.
- This scientific consensus statement indicates the current opinion that certain species of LAB and bifidobacteria can be classified as probiotic regardless of strain-level variation. Extending this statement to fermented foods validates some of the health claims associated with fermented foods with viable cells of these species.
53. Wu S, Yoon S, Zhang Y, Lu R, Xia Y, Wan J, Petrof EO, Claud EC, Chen D, Sun J: **Vitamin D receptor pathway is required for probiotic protection in colitis.** *Am J Physiol: Gastrointest Liver Physiol* 2015 <http://dx.doi.org/10.1152/ajpgi.00105.2015>.
54. Gao C, Major A, Rendon D, Lugo M, Jackson V, Shi Z, Mori-Akiyama Y, Versalovic J: **Histamine H2 receptor-mediated suppression of intestinal inflammation by probiotic *Lactobacillus reuteri*.** *MBio* 2015 <http://dx.doi.org/10.1128/mBio.01358-15>.
- This preclinical study demonstrates the crucial contribution of a strain-specific bacterial metabolic pathway, converting a substrate from food into an anti-inflammatory molecule inside the gut, and providing further alleviation of colitis.
55. Kwon G, Lee J, Lim Y: **Dairy *Propionibacterium* extends the mean lifespan of *Caenorhabditis elegans* via activation of the innate immune system.** *Sci Rep* 2016 <http://dx.doi.org/10.1038/srep31713>.
56. Kolmeder CA, Salojärvi J, Ritari J, De Been M, Raes J, Falony G, Vieira-Silva S, Kekkonen RA, Corthals GL, Palva A *et al.*: **Faecal metaproteomic analysis reveals a personalized and stable functional microbiome and limited effects of a probiotic intervention in adults.** *PLOS ONE* 2016 <http://dx.doi.org/10.1371/journal.pone.0153294>.
57. Kato-kataoka A, Nishida K, Takada M, Kawai M, Kikuchi-hayakawa H, Suda K, Ishikawa H, Gondo Y, Shimizu K, Matsuki T *et al.*: **Fermented milk containing *Lactobacillus casei* strain Shirota preserves the diversity of the gut microbiota and relieves abdominal dysfunction in medical students exposed to academic stress.** *Appl Environ Microbiol* 2016, **82**:3649-3658.

58. Tachon S, Lee B, Marco ML: **Diet alters probiotic *Lactobacillus* persistence and function in the intestine.** *Environ Microbiol* 2013, **16**:2915-2926.
59. Zhang C, Derrien M, Levenez F, Brazeilles R, Ballal SA, Kim J, Degivry M, Quéré G, Garault P, van Hylckama Vlieg JET *et al.*: **Ecological robustness of the gut microbiota in response to ingestion of transient food-borne microbes.** *ISME J* 2016 <http://dx.doi.org/10.1038/ismej.2016.13>.
60. Díaz-López A, Bulló M, Martínez-González MA, Corella D, Estruch R, Fitó M, Gómez-Gracia E, Fiol M, García de la Corte FJ, Ros E *et al.*: **Dairy product consumption and risk of type 2 diabetes in an elderly Spanish Mediterranean population at high cardiovascular risk.** *Eur J Nutr* 2016, **55**:349-360.
61. Byun M-S, Yu O-K, Cha Y-S, Park T-S: **Korean traditional chungkookjang improves body composition, lipid profiles and atherogenic indices in overweight/obese subjects: a double-blind, randomized, crossover, placebo-controlled clinical trial.** *Eur J Clin Nutr* 2016, **70**:1116-1122.
62. Cavallini DCU, Manzoni MSJ, Bedani R, Roselino MN, Celiberto LS, Vendramini RC, de Valdez GF, Abdalla DSP, Pinto RA, Rosetto D *et al.*: **Probiotic soy product supplemented with isoflavones improves the lipid profile of moderately hypercholesterolemic men: a randomized controlled trial.** *Nutrients* 2016 <http://dx.doi.org/10.3390/nu8010052>.
63. Lim JH, Jung ES, Choi EK, Jeong DY, Jo SW, Jin JH, Lee JM, Park BH, Chae SW: **Supplementation with *Aspergillus oryzae*-fermented kochujang lowers serum cholesterol in subjects with hyperlipidemia.** *Clin Nutr* 2015, **34**:383-387.
64. Tu M, Chen H, Tung Y, Kao C, Hu F, Chen C-M: **Short-term effects of kefir-fermented milk consumption on bone mineral density and bone metabolism in a randomized clinical trial of osteoporotic patients.** *PLOS ONE* 2015 <http://dx.doi.org/10.1371/journal.pone.0144231>.
65. Nagata S, Asahara T, Wang C, Suyama Y, Chonan O, Takano K, Daibou M, Takahashi T, Nomoto K, Yamashiro Y: **The effectiveness of *Lactobacillus* beverages in controlling infections among the residents of an aged care facility: a randomized placebo-controlled double-blind trial.** *Ann Nutr Metab* 2016, **68**:51-59.