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The development of functional foods: lessons from the gut

Bruce German, Eduardo J. Schiffrin, Roberto Reniero, Beat Mollet, Andrea Pfeifer and Jean-Richard Neeser

Functional foods have resulted from the gradual recognition that healthy diets result from eating nutritious foods and from the identification of the mechanisms by which foods modulate metabolism and health. After initial successes with foods that reduce blood cholesterol level, probiotic bacteria and prebiotic carbohydrates have now also demonstrated added health benefits. As ingredients become more complex, the need to stabilize such ingredients in foods become increasingly important to the success of functional foods. Modern biotechnologies such as genomics, genetic expression and biomarkers of health and performance will be applied to this increasingly visible portion of human diets.

The field of nutritional science has enjoyed great successes this century, defining the essential requirements for specific nutrients during growth, development and reproduction[1]. This knowledge base extends from the molecular and biochemical actions of nutrients within cells to the pathological consequences of nutrient deficiencies within the human population. These advances have been implemented into the food supply as a series of regulations, fortifications and enrichments that has resulted in the virtual elimination of true nutritional deficiences in affluent populations[2].

However, there remains a discernible variation in the epidemiological health outcome among individuals consuming different diets: even when adequate, diet still has a strong influence on health. With this realization came the notion of 'healthy' diets, which are the consequence of the abundance of their unusually nutritious components. The health connotation of diets rich in fruits and vegetables is such a notion. Today, the nutritional principles underlying the benefits of these commodities are being discovered. These advances in nutritional science and the identification of the active ingredients of the most desirable commodities have practical applications in transferring these ingredients to other diets and thus developing 'functional foods'[3].

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What are functional foods?

Functional foods have been broadly defined as 'foods similar in appearance to conventional foods that are consumed as part of a normal diet and have demonstrated physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions'[4]. This definition makes the point that foods can provide a nutritional value beyond the basic nutritional requirements. The concerted action program on functional foods of the International Life Sciences Institute (ILSI) European Branch established six key messages within its consensus document (Box 1)[5].

The basic idea that foods can be functional because of added ingredients is certainly not limited to the newly emphasized 'nutritional' functionality[3,6]. Every time a breakthrough has linked a valuable food attribute to a specific ingredient, the result has been to transfer those ingredients with their performance attributes to other foods. The classical example of such an ingredient transfer is 'sweetness'. Historically, sweetness was a taste attribute of only a very few prized commodities, and

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scientific and chemical breakthroughs that identified sweetness as a technologically extractable ingredient (simple sugars) revolutionized the food supply. Foods became sweet because of added functionality and with this functionality came added value.

Four basic stages can be identified in the successes in developing 'added value' foods: (1) the recognition of a desirable functionality (e.g. sweetness); (2) the discovery, usually by chance, of commodities that provide that functionality (e.g. fruits); (3) the identification of the molecular basis of the functionality (e.g. sugars); and (4) the application of this knowledge and its transfer to foods that would not naturally exhibit it (e.g. baked goods, confections, beverages). More recently, a fifth stage has emerged, in which substitutes for functionality have been developed that further extend its value (e.g. artificial sweeteners).

The recent achievements in understanding the molecular basis of the positive effects of specific nutrients on health are leading to the next logical step: the transfer and commercialization of the nutritional value into functional foods. With regard to improvement of gut health and lipid metabolism, successes in cholesterol reduction were followed by new innovations including: probiotics, which are live bacteria that not only protect the gut from undesirable microbial species but also encourage the effective modulation of the host immune system; fibers, which modify intestinal digestion and absorption rates, and influence rheology and motility; prebiotic oligosaccharides (e.g. bifidogenic carbohydrates), which, via fermentation, both encourage a beneficial microflora and provide products that enhance intestinal-cell differentiation and health; and growth factors that promote the optimal development of intestinal and immune systems (Fig. 1).

As these new ingredients with greater overall nutritional benefits (e.g. improved health and disease-risk reduction) have emerged, the perception of their value to the consumer became an issue. Such health benefits require an extra dimension of visibility over foods whose organoleptic functionalities (texture and flavor) are more easily detected by the consumer. The commercialization of 'nutritional' functional foods can only be successful if the consumer is confident in the scientific validity of the claims. The question is whether this will be achieved through consumer awareness of the nutritional value or through a regulated system of the health claims on which the value is based.

A success in functional-food development: cholesterol reduction

To date, success in nutritional functionality is best exemplified by foods in which the driving force for development, commercialization and increased market share has been reduction of the blood cholesterol level[3]. This success has derived from a century of scientific research and public health education linking blood cholesterol to cardiovascular disease[1]. Important aspects of the commercial success of foods for cholesterol reduction include: (1) the consumer's need to appreciate the functional value; (2) the high incidence of heart disease in the affluent world, which provided the nutritional opportunity; (3) the ability of blood cholesterol levels to predict heart disease accurately and to provide an essential biological marker as a functional-food target; and (4) accurate knowledge of the relationship between blood cholesterol levels and heart disease, acquired over years of observation, epidemiology and intervention.

Box 1. Functional foods: the six key messages[a]

(1) The food industry has the opportunity to improve the health and well-being of its customers and/or to reduce their risk of disease through foods with added activities.
(2) Functional foods are those that can be demonstrated to benefit target functions in the body in a way that improves the state of health and/or reduces the risk of disease. They are foods that are consumed as part of a normal diet rather than pills or supplements.
(3) Foods based on functionality will need to link the scientific basis of such a functionality to the communication of its benefit to the general public.
(4) Both the efficacy and the safety of the food components with health benefits will require evidence based on the measurement of scientific biomarkers relevant to their biological responses and health end points.
(5) Sound evidence from human studies based on intermediate health end points using accepted biomarkers will provide the basis for promotional messages divided into two categories – enhanced function and reduced risk of disease.
(6) Success in solving key scientific and technological challenges will only be achieved by interdisciplinary research programs to exploit the scientific concepts in functional-food science.

[a] Adapted from Ref. 5.

After all of these were in place, functional foods for controlling cholesterol began to emerge as predicted[3]. Commodity foods exhibiting functionality were identified by chance (e.g. oat and barley, and vegetable oils). Next, the β-glucan components from these cereals and the polyunsaturated fatty acids from vegetable oils were shown to be the active ingredients. This led to their transfer into foods that did not naturally contain them but to which the nutritional functionality added new value[7]. In the development of foods for cholesterol reduction, the field has now advanced to a stage in which substitutes with similar cholesterol-lowering properties to fibers and polyunsaturated fatty acids are being developed[8]. One example is the emergence of phytosterol esters as cholesterol-absorption inhibitors[9] and their addition to margarine as a functional food targeted directly at cholesterol reduction[10]. Thus, the ability of food ingredients to influence blood cholesterol levels has provided the means to deliver functionality in cholesterol reduction.

Diseases of the arteries, especially the major coronary vessels, are largely a problem of modern, affluent lifestyles[1]. During the 20th century, diseases of the circulatory system have become one of the major causes of death in both women and men[1]. In the 19th century, cholesterol was identified as the distinguishing constituent of atherosclerotic plaque[11], since when blood cholesterol has been increasingly recognized to be a predictive indicator of heart disease[12]: there is now convincing evidence that blood cholesterol level is a reflection of disease incidence[1]. This association between blood cholesterol and disease was first identified as a dietary issue by the work of Keys[13], in which the relationship between dietary cholesterol and saturated fats (which raise the blood cholesterol level) and polyunsaturated fats (which lower cholesterol levels) was demonstrated.

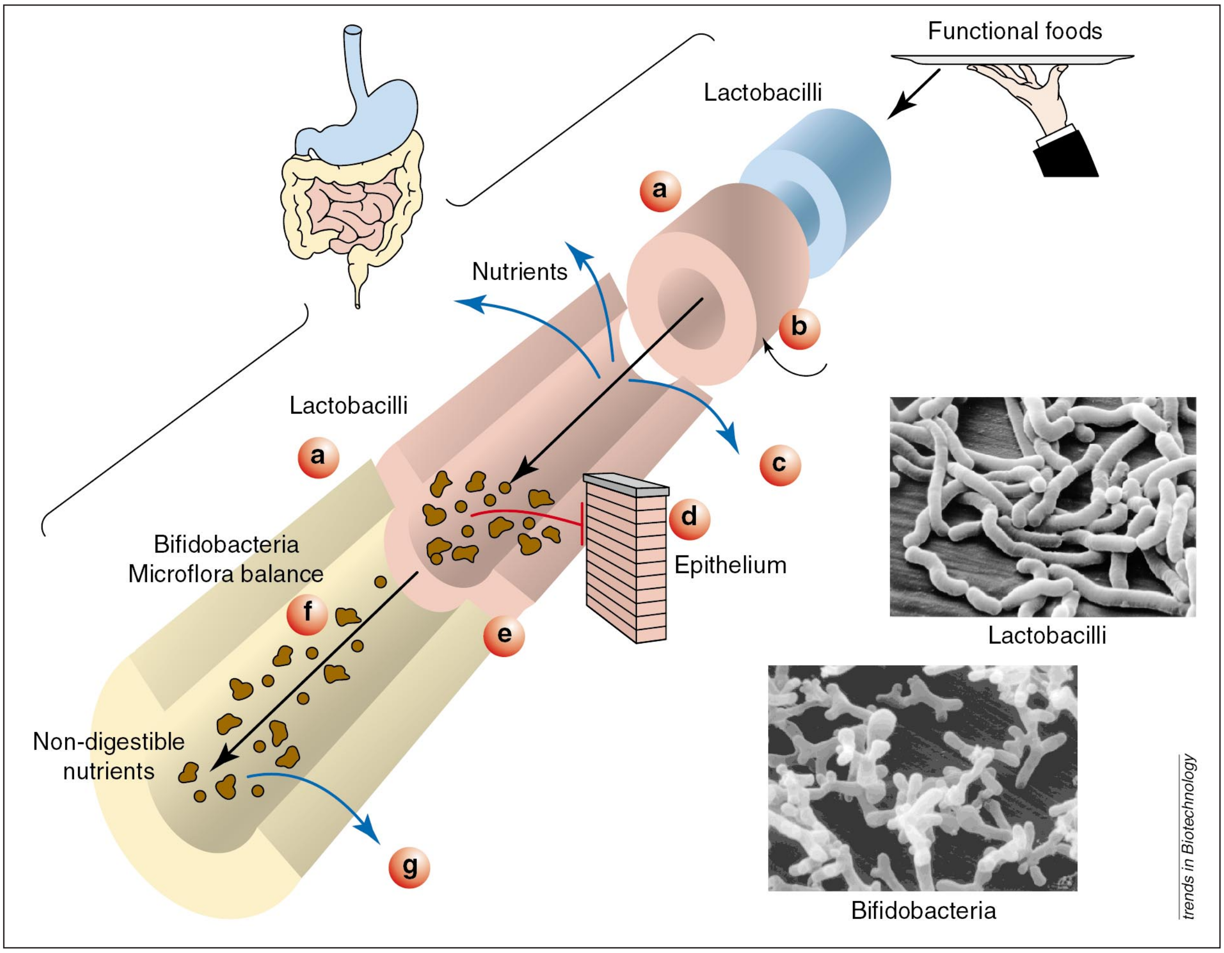

Figure 1

Targets throughout the gastrointestinal tract for functional-food ingredients. (**a**) Pre- and probiotics inhibit pathogenic bacteria at various sites, from *Helicobacteria pylori* in the gastric mucosa to *Salmonella* sp. and *Clostridia* sp. in the intestine. (**b**) Multiple ingredients alter the rate and extent of digestion of nutrients. (**c**) The absorption of nutrients and anti-nutritional factors throughout the stomach and intestine is affected by the presence, form and activity of functional-food components. (**d**) Pre- and probiotics modify the barrier functions of the intestinal epithelium. (**e**) Nutrients, from vitamins and minerals to probiotics, interact with and enhance the functions of gastrointestinal immune cells and, via systemic communication, the entire body's immune system. (**f**) Pre- and probiotics modulate the overall ecology of the gut microflora. (**g**) Fermentation products of fibers or non-digestible oligosaccharides and other components from the microflora not only nourish the intestine but also improve the differentiation, maturation and overall health of colonic cells. Adapted from F. Rochat, unpublished.

Since these pivotal studies of Keys, the potential of different commodities to influence blood cholesterol and the risk of coronary disease has had a great influence on their perceived value in foods. For example, the consumption of whole hen eggs dropped precipitously when the implications of their high cholesterol content became known[14]. Consumption of polyunsaturated margarines rose at the expense of a decline in butter in the USA once the role of polyunsaturated fats in lowering cholesterol was demonstrated[13]. Similarly, oats as a grain commodity were incorporated into a variety of breakfast products when oat fibers were recognized to lower blood cholesterol levels in humans[15]. The future of functional foods with other health targets will probably revisit these same fundamental steps on the road to success in the marketplace: identify the health opportunities and their mechanisms of action; develop agreed biological markers by scientific research that reflect the health advantage; educate the consumer about the biomarkers and their benefits; and, finally, discover ingredients that provide nutritional benefits when added to foods. Ingredients with health advantages will also need to be delivered within food products that match the consumer's dietary preferences.

Probiotics: from spoiled milk to clinical tool

It is hard to overstate the importance of intestinal health to an individual's overall sense of well being, even though this is evident when it is lost. The disabling effects of intestinal dysfunctions owing to food-borne pathogens remain a constant driving force for food safety. The idea that specific foods provide protective functions has been a long-held belief of populations that eat fermented foods such as yogurt. In essence, functionality (gut health) and the commodity providing it (yogurt) evolved together[16]. Not surprisingly, it has taken until the last decades of the 20th century to convert this observation into scientific understanding. Gut protection as a functionality is not defined by single molecules but by living bacteria and their metabolic products[17].

The next stage in the development of probiotic functional foods requires a very new approach. The benefits of ingesting living bacteria can only result when

Table 1. Comparison between the two best-characterized commercially produced probiotic bacterial strains: *Lactobacillus johnsonii* La1 and *Lactobacillus rhamnosus* GG

	La1	GG
In vitro adhesion to intestinal cells	++	+
Survival in gastrointestinal tract ('colonization')	+	+
In vitro competition with pathogens causing diarrhea	+	Not documented
In vivo anti-diarrheic effects (rotavirus, traveler diarrheas)	Not investigated	+
Anti-*Clostridium difficile* colitis	Not investigated	+
Anti-*Helicobacter pylori* effects (*in vitro*, *in vivo*)	+	Not documented
Enhancement of phagocytosis	+	Not documented
Stimulation of immunoglobulin-A production (rotavirus/GG, *Salmonella typhi* – vaccine/La1, La1 alone)	+	+
Ability to ferment lactose	+	–
Reduction of carcinogenic-enzyme activities (animal models and humans)	+	+

multiple properties are simultaneously expressed by a single bacterial strain or appropriate mixtures of strains[18]. This scientific breakthrough continues to be developed today. Probiotic bacteria must simultaneously survive in the food in high numbers, survive gastric pH, survive intestinal bile acids, adhere to or interact with the intestinal surface, colonize the intestinal environment, displace pathogenic bacterial competitors and prevent immune sensitization by the host[19]. Establishing molecular assays for each of these actions to enable screening of candidate strains was the key to the success of the Nestlé probiotic program[20–22]. Only recently has it been possible to transfer this complex living functionality from yogurt to other foods. The final stage of development, in which additional bacterial action and their health benefits are being discovered and incorporated into new strains, is just beginning but it is already clear that the future for this field is promising[23].

Probiotics have been defined as ingested live bacteria that can improve the host's microbial balance and in doing so, promote health[24,25]. To accomplish such diverse physiological activities[18,26], several probiotic biological actions are considered to be important: (1) increased digestive capacity; (2) improved intestinal defenses; (3) sustained and modulated intestinal and systemic immunity; (4) enhanced mucosal barrier; and (5) reduced inflammation and lowered allergic sensitization to foods (Table 1). With such actions, probiotic bacterial strains are being considered not only as agents with preventive functionality but also as active even in a curative or therapeutic setting[27,28]. Indeed, probiotics now face the challenge to demonstrate their unique role in the more stringent world of clinical nutrition[29].

Presently, the most attractive potential use of probiotics is in the fight against abnormal intestinal microorganisms. This covers a wide range of conditions, such as virulent enteropathogens, *Helicobacter pylorii* with its wide virulence variability[30], rotavirus[27], diarrhea associated with the use of antibiotics[28] and small-bowel bacterial overgrowth[31] (a frequent condition of the elderly or of patients administered with drugs that suppress gastric acid secretion). The last two conditions are most often not associated with an enteropathogen but with a globally disturbed ecology that can alter digestive and absorptive intestinal functions or promote inflammatory gut-barrier damage[32].

Despite this heterogeneity, probiotic benefits have been demonstrated in, or claimed to be responsible for, most of the above-mentioned clinical conditions. Moreover, the same probiotic strain can succeed in different conditions whose pathophysiologies have no common underlying mechanisms. A possible explanation for this is that the mucosal surface of the intestine is the interface on a highly variable intestinal content. A dysfunction at this level could promote a discordance between the luminal signal and the host response, with the result that exaggerated responses could lead to food allergy or chronic inflammation, with harmful consequences; on the other hand, weak responses could impair the host's control of harmful bacteria, leading, for example, to infectious diarrhea.

The fine tuning of such a dynamic interface depends on an intricate cell-to-cell cross talk that will preserve the homeostasis of the intestinal mucosa. How could probiotics help the host to find the right response? The interaction of probiotic strains with the intestinal epithelial cells might be the first event of a cascade of cellular events that will affect tissue homeostasis. Understanding the molecular mechanisms and physiological consequences of this first prokaryote–eukaryote interaction could thus help nutritional intervention to preserve gut homeostasis.

Probiotics protect the mucosal barrier from undesired bacterial colonization through more than one mechanism, which fall into three broad categories: (1) effects on the bacterial populations and their metabolism; (2) effects on the intestinal epithelia and their differentiation; and (3) effects on the immune cells and their activation[19]. Barrier effects of the microflora could include competition with a pathogen for a specific receptor, a nonspecific steric hindrance caused by the bacteria adhering to the gut wall, the production of antibacterial molecules or competition for metabolic substrates[19]; barrier effects at the epithelium could include mucus secretion, receptor expression and intercellular adhesion[33]. In addition, probiotics could improve mucosal health by activating the host's defense mechanisms without stimulating an inflammatory reaction in the intestinal mucosa[34]. The arrival of live, adherent, nonpathogenic bacterial cells in an active immune compartment such as the small-bowel mucosa triggers multiple events, only some of which are now starting to be understood[34].

Box 2. Proposed equivalence tests using *in vitro* assays to compare the probiotic activity of bacterial strains between fresh and processed foods

Determination of bacterial strain viability
Strain sensitivity to different stresses
Probiotic stress-protein expression (mRNA and protein levels)
Physiological activity (length to the lag phase of culture growth)
Adhesion to relevant intestinal cell lines
Competition with enteroadherent and enteroinvasive pathogens (onto intestinal cells)
Expression of immune markers (e.g. human peripheral-blood mononuclear cells)
Resistance of probiotic strain preparations to simulated gastric juice and bile acids[a]

[a] Simple models may be sufficient in some cases, with *in vitro* models simulating gastric transit and duodenal conditions being necessary for others.

Overall, disparate probiotic bacteria antagonize pathogens, establish a protective surface ecosystem, stimulate differentiation and absorption of intestinal cells, and increase the host defenses[17]. These activities are already the basis of successful strain-screening and -selection procedures[21]. The use of probiotics in health strategies from infants to the elderly, and even as part of a therapeutic strategy against undesired microbial colonization of the gut, is the result of screening existing strains over the past two decades[6]. Their potential is very exciting, for the next generation of scientific advances to add further physiological and protective properties to the already-existing spectrum of benefits assembled by screening available bacteria. The rate of these advances will depend on the sciences of bacterial and human physiology, and genetics, and the extent to which the medical community and the health authorities are amenable to a new way of promoting health and preventing disease.

Overcoming new technological challenges in mainstream foods

In the past, most conventional food-processing methods were aimed at reducing or inactivating any form of microbial population found in food products[35]. One of the major breakthroughs of the food industry was the introduction of shelf-stable products, achieved primarily by destroying spoilage microflora by heat inactivation (pasteurization and sterilization)[36]. The new age of functional foods and the introduction of the probiotic concept into the food industry have brought new and unforeseen challenges to the design and application of such 'living' solutions to a new generation of stable but functional foods.

These are true challenges even for companies, such as dairy firms, that are experienced in the handling and industrial management of microorganisms. Selected lactic-acid-bacterial cultures are essential for the production of yogurt, fermented milk and cheeses[37] but, nevertheless, the introduction of probiotic lactic-acid bacteria presents substantial new problems. Dairy-processing parameters are well adapted to dairy bacterial strains, but probiotic bacteria are more accustomed to live and grow in the human bowel[38]. This difference in growth preferences leads to the need to take particular care during industrial handling.

Growth of probiotic bacteria in milk is frequently a problem, so a starter culture must be prepared that is supplemented with key growth factors, frequently specifically designed for an individual strain[39]. The environmental conditions during milk processing (temperature, pH, redox potential, pO_2) are acceptable for dairy bacteria but far from optimal for strains that normally grow in the gut. Relevant corrections must thus be introduced to adapt the technology to the needs of the probiotic microorganism[40]. Moreover, relatively long storage in chilled dairy products may seriously hamper the survival of these strains[41,42]. Survival is, of course, essential for organisms targeted to populate the human gut, one of the most important issues in health-benefit provision by probiotic bacteria.

In some countries, certain dairy products (e.g. yogurts) must contain a defined number of live bacteria to comply with standards of identity legislation[43,44]. In the case of products containing probiotics, the presence of an adequate number of live bacteria at the end of the shelf life is even more important because this is the essence of the health-promoting value. It appears to be more and more evident that bacterial counts alone are not sufficient to assure probiotic activity: other physiological properties of the strain are more important[45]. It is not only necessary to guarantee an adequate number of bacteria but also to provide the consumer with probiotics in their most active condition. The definition of this new end point is mandated by the need for successful clinical trials demonstrating to the consumer the efficacy claimed by the product.

In technological terms, once a strain has demonstrated a specific health effect on the host, it is then useful to define *in vitro* tests that precisely reflect a bacterial culture's physiological state: a 'fingerprint' in its best probiotic condition (Box 2). These data then become important in transferring the bacterial culture from one food to another, such as from a fresh dairy product to a dried food preparation. The physiological state of the strain in a new food matrix will be completely different, owing to the quite different processing, storage and distribution channels to which the product will be subjected. Knowledge of the relevant key physiological traits that underlie and are essential to generate the final probiotic activity must effectively drive the development of new technological processes. This approach would guide the optimal design of processes to produce, for example, bioactive dried preparations whose activity could be tested and confirmed *in vivo*. Such a new perspective opens the field to 'bioequivalence tests', which consist of *in vitro* investigations to establish the biological equivalence of different probiotic preparations (Box 2). Although this approach needs to be intensively developed and exhaustively validated, it should, in the long term, partially replace time-consuming clinical trials.

Functional carbohydrates: from dietary fibers to non-digestible oligosaccharides

Based on epidemiological observations, the health benefits brought by dietary fibers were first formulated in 1975 by Burkitt and Trowell as the 'fiber hypothesis'[46]. Among the physiological effects that have been proposed for dietary fibers are their positive influence on constipation, hyperlipidemias, diabetes, obesity and diverticular disease[47]. Here, the term 'dietary fibers'

Table 2. Functional carbohydrates and their nutritional properties

Functional carbohydrates	Physiological effects
Dietary fibers (general)	Carbohydrate and lipid metabolism modulation
Intermediate type of fibers (e.g. β-glucan from oat and barley brans)	Cholesterol lowering
Resistant starch	Colon nutrition, reduced risk of cancer
Non-digestible oligosaccharides (e.g. inulin and fructo-oligosaccharides)	Prebiotic effect: enrichment of bifidobacteria

refers to 'the remains of plant cells that are resistant to hydrolysis by human enzymes'[48], that is, the lignin and polysaccharides that are not hydrolysed by the endogenous secretions of the human digestive tract[49].

Attempts to establish the precise effects of fibers on weight regulation, carbohydrate and lipid metabolism, and colon function led to the realization that many different types of fiber exist that have different effects in the gastrointestinal tract[50]. For example, particulate fibers (which are mostly insoluble) have no cholesterol-lowering effect[47], whereas viscous polysaccharides (e.g. pectin, guar gum) lower cholesterol but only in much higher doses than usually consumed[51]. The intermediate type of fibers (those with physical and chemical properties in between those of particulate and viscous fibers, such as β-glucans from oat bran) exhibit a potent cholesterol-lowering effect (Table 2)[47]. In conclusion, the major drawback to using fiber concentrates as functional ingredients lies in the difficulty of incorporating 'pure', well-defined polysaccharide fractions in food products, which would enable a clear structure–activity relationship to substantiate the health claims.

Resistant starch

The colonic fermentability of dietary fibers is also highly dependent on the fiber source[47]. On present evidence, the hypothesis that fiber could reduce the risk of colon cancer would thus focus on fibers that act as substrates for butyrate-producing fermentations because butyrate itself is attributed with cancer-preventing properties[52]. Resistant starch (starch that resists digestion and thus reaches the colon) has been established as one of the main sources of carbohydrate substrates for the colonic microflora and thus as a determinant of human large-bowel function[53].

However, there are various reasons for starch resistance (physical enclosure, ungelatinized starch granules of different types and retrogradation) and the choice of raw materials and processing conditions influence the structure and the site of resistant-starch fermentation in the large bowel and thus their physiological effects. *In vivo* experiments suggest that a high proportion of butyrate produced from resistant-starch fermentation, has an important effect for colonic health, especially against cancer risk[53]. Consequently, the future development of certain types of resistant starch as functional-food ingredients will require the careful selection of raw materials, a combination of innovative food processes and the establishment of a physiological profile based on intervention studies in humans[54].

Non-digestible oligosaccharides

Recently, another group of complex carbohydrates – the non-digestible oligosaccharides (NDOs) – has attracted considerable attention[55,56]. Such oligosaccharides (containing between approximately three and fifteen monomers linked together) can be either extracted from natural sources (then used as is or subjected to partial enzymatic hydrolysis) or synthesized by transferases[57]. Similar to dietary fibers and resistant starch, they are resistant to human intestinal enzymes but can be distinguished from them *in vitro* on the basis of their solubility[58] (which results from their smaller molecules).

Today, the most thoroughly investigated NDOs are inulin and fructo-oligosaccharides (FOS)[58,59]. The nutritional properties of the different NDOs have been analysed in a recent consensus report (funded by the European Commission) and placed in three categories: (1) strong, when based on confirmed human studies; (2) promising, when based on unconfirmed human studies; and (3) preliminary, when based on animal studies[59]. As a result, there is a general consensus that inulin and FOS modify the bowel habit, causing fecal bulking, normalization of stool frequency and a prebiotic effect (a food-induced increase in the numbers and/or activity of bifidobacteria and lactic-acid bacteria, in the human intestine)[59]. Other claims (e.g. increased calcium absorption, modulation of lipid metabolism, preventive effect against colon cancer) will need further studies in order to be substantiated.

Thus, NDOs appear to be extremely attractive for the development of new functional foods. Their physicochemical properties make them more promising for incorporation into various types of food product than polysaccharides (e.g. viscous dietary fibers or insoluble resistant starch), which cannot be added to many types of foods[47,53]. In addition, their well-defined structures allow intervention studies to be conducted in humans, which should yield reproducible results[59]. However, at present, their main confirmed benefit is on the bifidobacteria, which are considered to be a good biomarker of a well-balanced intestinal flora. To date, no information is available to support a more general statement on disease-risk reduction[59].

Genetic modification may lead to new developments

The use of modern gene technology has contributed significantly to human health and welfare over the past 15 years as a result of its adoption by the pharmaceutical industry. However, in the food sector, including the agricultural and food processing industry, the development and implication of modern gene technology has been much slower.

The first genetically modified crops (soybean and corn) appeared on the US market in 1996 and have since been commercialized in many countries. This first wave of genetically engineered food materials consisted of herbicide- and disease-resistant plant varieties and thus focused on agronomic traits, bringing at first increased yields and reduced costs to the farmer. The benefit to consumers will be indirect, arising from the anticipated lower long-term environmental damage. The next wave of genetically modified crops will target the modification of selected quality traits such as appearance, texture, flavor and nutritional and health benefits[60,61]. With these developments under way, the consumer should have the opportunity to experience new food products in the future that bring not only improved organoleptic properties but also health-related benefits. It has yet to be seen to what extent these advantages will counterbalance the current perception by some consumer groups of the risks associated with these new technologies.

Currently, research follows several approaches to bring functional benefits to new food products. The first follows the continued development of the raw materials that are the basis for the preparation of food products. A well-recognized example of this is the modification of the lipid composition of crops used for oil production[62]. Today, high-oleic-acid soybean and high-lauric-acid rapeseed oils are commercially available, and high-stearic-acid oils are close behind[63]; soybean oil free of saturated fat and oils containing γ-linolenic acid are also being developed[64]. It is now becoming possible not only to change the fatty-acid composition of the oils in transgenic plants but also to genetically engineer the biosynthesis of the lipid structure itself. This would enable the design of novel lipids and oils adapted to the specific functional property of a desired food product and allow their economic production on a large scale.

The era of genomics and proteomics will contribute to an improved understanding of the molecular mechanisms underlying the relationships between food components and ingredients, food microorganisms and the human intestinal system, including the gut and immunocompetent cells, and the mechanisms underlying the interactions of the microbial community in the intestinal tract. Thus, in the future, we may see food microorganisms expressing the adhesins of gastrointestinal pathogens so that molecular competition will reduce the risk of infections, or lactic-acid bacteria designed as oral vaccines to protect us against viral infections[65]. Ultimately, it is the consumer who will benefit from these novel developments as a result of changes in their health and well being.

Conclusion

The goal of functional foods is to translate scientific advances in understanding the role of diet in health into effective foods, and to maintain the quality and safety of the modern food supply. Scientifically, three factors will be critical – mechanisms, molecules and markers. It will be necessary to understand the mechanisms by which health performance and disease prevention are supported by diet. Ingredients (whether specific molecules or mixtures of complementary molecules) that have beneficial effects on these mechanisms must continue to be discovered and their activity, stability and delivery within foods assured.

The successes in reducing cholesterol, introducing probiotic bacteria and prebiotic carbohydrates are examples of the successes possible to this approach. The lessons learned in developing foods to improve gut health and lipid metabolism will in the future be extended to targets ranging from bones and teeth to skin and even to mental performance. Finally, markers that accurately reflect the influence of diets on health are crucial to distinguishing truly effective foods and the populations on which they are effective. It is not sufficient to propose that an ingredient might be effective: it is necessary to prove that it is effective.

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The development and applications of thermal biosensors for bioprocess monitoring

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Enzyme thermistors are biosensors that use thermal resistors to measure the heat change caused by an enzymatic reaction. They combine the selectivity of enzymes with the sensitivity of biosensors and allow continuous analysis in a flow-injection mode. They can be used to monitor fermentation systems, biocatalysis, enzyme-catalysed synthesis and clinical and food technology. This article gives an overview of the general principles of enzyme thermistors, the sampling process and the ongoing developments in the field of bioprocess monitoring.

Bioprocess monitoring using biosensors can be defined as the application of a chemical or biochemical principle to monitor an ongoing process[1,2], for example, a fermentation process. However, the main challenge is how to identify a particular metabolite and estimate its concentration in, for example, a fermentation broth containing actively growing microorganisms, or to identify a specific enzyme that is used to detect a particular molecule in a solution such as body fluids. This need has led to the development of biosensors for the monitoring and control of reactions such as in industrial fermentations[3].

In the biotechnology industry, including the pharmaceutical, food, agricultural and chemical industries, there is a large demand for automated monitoring and control of systems during the production process[4–6]. The analysers need to be highly specific and selective, with the ability to deliver the results rapidly and reliably. Nevertheless, all bioprocesses are susceptible to contamination, which causes a major setback in large-scale production plants or even to small-scale clinical monitoring. Consequently, there has been a need to develop analytical techniques that are compatible with a specific bioprocess[7]. Various approaches to the problem can be adopted, such as the development of stable

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