Concepts and strategy of functional food science: the European perspective[1–3]

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ABSTRACT Recent knowledge supports the hypothesis that, beyond meeting nutrition needs, diet may modulate various functions in the body and play detrimental or beneficial roles in some diseases. Concepts in nutrition are expanding from emphasis on survival, hunger satisfaction, and preventing adverse effects to emphasizing the use of foods to promote a state of well-being and better health and to help reduce the risk of disease. In many countries, especially Japan and the United States, research on functional foods is addressing the physiologic effects and health benefits of foods and food components, with the aim of authorizing specific health claims. The positive effects of a functional food can be either maintaining a state of well-being and health or reducing the risk of pathologic consequences. Among the most promising targets for functional food science are gastrointestinal functions, redox and antioxidant systems, and metabolism of macronutrients. Ongoing research into functional foods will allow the establishment of health claims that can be translated into messages for consumers that will refer to either enhanced function or reduction of disease risk. Only a rigorous scientific approach that produces highly significant results will guarantee the success of this new discipline of nutrition. This presents a challenge for the scientific community, health authorities, and the food industry. *Am J Clin Nutr* 2000;71(suppl):1660S–4S.

KEY WORDS Functional foods, macronutrient, micronutrient, health claim

INTRODUCTION

The primary role of diet is to provide enough nutrients to meet metabolic requirements while giving the consumer a feeling of satisfaction and well-being. Recent knowledge, however, supports the hypothesis that, beyond meeting nutrition needs, diet may modulate various functions in the body and may play detrimental or beneficial roles in some diseases. We stand today at the threshold of a new frontier in nutrition sciences. Indeed, at least in the Western world, concepts in nutrition are expanding from the past emphasis on survival, hunger satisfaction, and preventing adverse effects to an emphasis on the use of foods to promote a state of well-being and better health and to help reduce the risk of diseases. These concepts are particularly important in light of the increasing cost of health care, the steady increase in life expectancy, and the desire of older people for improved quality of their later years.

These changes of emphasis in nutrition have, over the past 10–12 y, justified the efforts of health authorities in many countries, especially Japan and the United States, to stimulate and support research on physiologic effects and health benefits of foods and food components and to authorize health claims.

In Japan, research on functional foods began in the early 1980s, when 86 specified research programs on "systematic analysis and development of food functions" were funded by a scientific fellowship grant from the Ministry of Education. Later in the 1980s and early in the 1990s, the Ministry of Education sponsored additional focal point studies on "analysis of physiologic regulation of the functions of foods" and "analysis of functional foods and molecular design." In 1991, the Japanese Minister of Health and Welfare established Labeling Regulations for Foods for Specified Health Use (FOSHU). These foods are included as 1 of 4 categories described in Japan's Nutrition Improvement Law as "foods for special dietary use" (ie, foods that are used to improve people's health and for which claims for specific health effects are allowed).

In the United States, the Nutrition Labeling and Education Act (NLEA), which was established in 1990 and first enforced completely in 1994, allows health claims to be made for foods containing ingredients for which the Food and Drug Administration (FDA) has scientific evidence demonstrating a correlation between intake and prevention or cure of certain diseases. As of July 1997, there were 10 foods or ingredients for which the FDA had recognized correlations with risk of disease.

In the European Union, it is already recognized that to improve the competitive position of the European food and drink industry, European research expertise must be at the forefront in understanding the role of food components in modulating body functions, maintaining and improving well-being and health, and reducing the risk of major diseases.

These concepts have begun to become popular with consumers. Although there are still many people who know little about nutrition

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itself, consumer awareness of the subject and its relation to health is growing appreciably. Finally, advances in food science and technology are providing the food industry with increasingly performable techniques to control and improve the physical structure and chemical composition of food products, and industry increasingly realizes that functional foods add value and have a market potential for growth.

Until now, in both Japan and the United States, approaches to developing these new concepts in nutrition have been mainly product driven and likely to be influenced by local, traditional, or cultural characteristics. To be more universal, a science-based, function-driven approach is preferable because the functions and their modulation are universal. Functional food science is a new discipline that is part of the science of nutrition and is aimed at stimulating research and development of these foods by using a function-driven approach (1).

FUNCTIONAL FOODS

As a working definition, a food can be said to be functional if it contains a component (whether or not a nutrient) that benefits one or a limited number of functions in the body in a targeted way that is relevant to either the state of well-being and health or the reduction of the risk of a disease (1), or if it has physiologic or psychologic effect beyond the traditional nutritional effect (2). At a consensus meeting (Madrid, October 1998) that was the last activity of a 3-y action supported by the European Union and coordinated by the International Life Science Institute Europe, a group of European experts adopted the following working definition: "a food can be regarded as functional if it is satisfactorily demonstrated to affect beneficially one or more target functions in the body, beyond adequate nutritional effects in a way which is relevant to either the state of well-being and health or the reduction of the risk of a disease" (3).

A functional food component can be a macronutrient if it has specific physiologic effects (eg, resistant starch or n−3 fatty acids) or an essential micronutrient if its intake is more than the daily recommendations. It can also be a food component that, even though of some nutritive value, is not essential (eg, some oligosaccharides) or is even of no nutritive value (eg, live microorganisms or plant chemicals). Indeed, beyond its nutritional (metabolic requirements) value and function of providing pleasure, a diet provides consumers with components able to both modulate body functions and reduce the risk of some diseases.

PRODUCTION OF FUNCTIONAL FOODS

A food product can be made functional by using any of these 5 approaches:

1) Eliminating a component known to cause or identified as causing a deleterious effect when consumed (eg, an allergenic protein).

2) Increasing the concentration of a component naturally present in food to a point at which it will induce predicted effects [eg, fortification with a micronutrient to reach a daily intake higher than the recommended daily intake but compatible with the dietary guidelines for reducing risk of disease (4)], or increasing the concentration of a nonnutritive component to a level known to produce a beneficial effect.

3) Adding a component that is not normally present in most foods and is not necessarily a macronutrient or a micronutrient but for which beneficial effects have been shown (eg, nonvitamin antioxidant or prebiotic fructans).

4) Replacing a component, usually a macronutrient (eg, fats), whose intake is usually excessive and thus a cause of deleterious effects, by a component for which beneficial effects have been shown [eg, chicory inulin such as Rafticream (ORAFTI, Tienen, Belgium) (5)].

5) Increasing bioavailability or stability of a component known to produce a functional effect or to reduce the disease-risk potential of the food.

The demonstration of such beneficial effects must be based on science, however. Having a science of functional foods will be necessary to guarantee the credibility of any assertion of benefit.

FUNCTIONAL FOOD SCIENCE

The positive effects of a functional food can be either maintenance of a state of well-being and health or reduction of the risk of pathologic consequences. The initial step in research and development of a functional food is the identification of a specific interaction between one or a few components of this food and a function (ie, genomic, cellular, biochemical, or physiologic) in the organism that is potentially beneficial for health. This step is fundamental research and should lead to one or more proposals for hypothetical mechanisms of the identified interactions as well as to the development and validation of relevant biomarkers. With this as background, a functional effect can then be defined that must be demonstrated in relevant models. This experimental part of functional food development concludes with a new hypothesis on the relevance of the functional effect to human health. The hypothesis must be tested in strictly designed nutritional studies involving carefully chosen volunteers, and the demonstration of effects must be accompanied by a safety assessment, an absolute prerequisite for functional food development.

In any case, the health benefit of a functional food will be limited if the food is not part of the diet. In his presentation at the First East West Perspectives Conference on Functional Foods, Pascal (6) stated, "Functional foods must remain foods; they are not pills or capsules but components of a diet or part of a food pattern recognized as being beneficial for well-being and health."

The design and development of functional foods is a scientific challenge that should rely on the stepwise process shown in **Figure 1**. The process begins with basic scientific knowledge relevant to functions that are sensitive to modulation by food components, that are pivotal to maintenance of well-being and health, and that, when altered, may be linked to a change in the risk of a disease. Next is the exploitation of this knowledge in the development of markers that can be shown to be relevant to the key functions. Next is a new generation of hypothesis-driven human intervention studies that will include the use of these validated, relevant markers and allow the establishment of effective and safe intakes. Last is the development of advanced techniques for human studies that, preferably, are minimally invasive and applicable on a large scale.

The most promising targets for functional food science are the following:

1) Gastrointestinal functions. These functions include those that are associated with a balanced colonic microflora, mediated by the endocrine activity of the gastrointestinal tract, dependent on the tract's immune activity, in control of nutrient (minerals in particular) bioavailability, in control of transit time

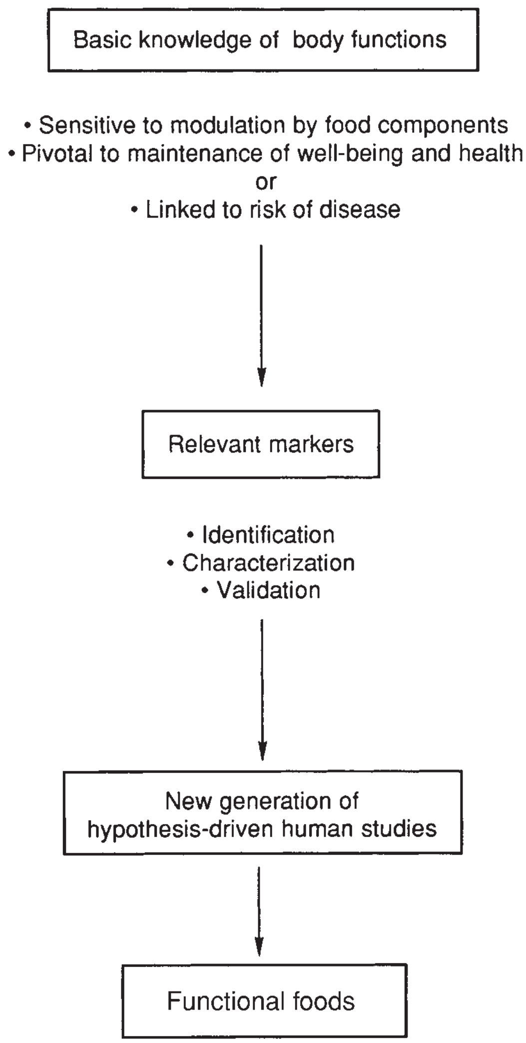

FIGURE 1. Stepwise process of the design and development of functional foods.

and mucosal motility, and modulators of epithelial cell proliferation (7; Roberfroid, unpublished observations, 1997).

2) Redox and antioxidant systems. These systems require a balanced and satisfactory intake of antioxidant (pro-) vitamins as well as nonvitamin food components such as polyphenols and other natural antioxidants of plant origin. Redox activities and antioxidant protection are important for almost every cell and tissue, and their imbalance is associated with miscellaneous pathologies. Although well-founded hypotheses often exist regarding the mechanisms of action of dietary antioxidants, demonstration of their beneficial effects, except when they are consumed as components of fresh fruit and vegetables (8), remains problematic.

3) Metabolism of the macronutrients. This target concerns metabolism of carbohydrates, amino acids, and fatty acids and, in particular, hormonal modulation of their metabolism via insulin and glucagon balance or the production of gastrointestinal peptides. The objective of this process is to reduce the risk of pathologic effects associated with insulin resistance and cardiovascular disease; doing so will require the study of interactions between nutrient intake and regulation of gene expression [eg, the direct role of glucose or some polyunsaturated fatty acids (9) or more indirect interactions such as the reduction of hepatic lipogenesis by chicory fructans (10, 11)].

4) Development in fetal and early life. Both the mother's and the infant's diet can influence this development; examples are the importance of folic acid in the diet of pregnant women and the role of long-chain polyunsaturated fatty acids in the early stage of brain development.

5) Xenobiotic metabolism and its modulation by nonnutritive dietary components, such as some phytochemicals. Such modulations may have important implications for the control of toxicity or carcinogenicity caused by chemical contaminants present in food or the environment.

6) Mood and behavior or cognition and physical performance. Many questions have been raised about the effect of food components on these functions, but the border between nutritional and pharmacologic effects is not always easy to draw. Moreover, methodologies for studying such effects are generally perceived as inadequate to generate the firm quantitative data required for a reliable statistical analysis. New developments are expected in this field soon, which will make it possible to address these issues.

The present state of scientific knowledge in functional food science has been critically assessed by 6 groups of European experts (1).

COMMUNICATION TO THE PUBLIC

The science base generated by research and development in the field of functional foods will establish health claims that can be translated into messages for consumers. According to Clydesdale (2), a health claim describes "a positive relationship (ie, reduction in risk and/or lessening of an adverse physiologic or psychological condition) between a food substance in a diet and a disease or other health related condition." With reference to the strategy for research and development, these claims will refer either to enhanced functions or reduction of disease risk (**Figure 2**).

A claim of enhanced function describes the positive consequences of interactions between a food component and a specific genomic, biochemical, cellular, or physiologic function without direct reference to any health benefit or reduction in disease risk. Examples include positive modulation of metabolic activities (eg, lipid homeostasis), strengthening immune functions (ie, immunostimulation), reducing the risk of oxidative stress (eg, by using antioxidants), protecting against chemical toxicity (eg, chemically induced steatosis), restoring or stabilizing a balanced colonic microflora (eg, through selective stimulation of bifidobacteria by inulin-type fructans), and improving bioavailability of nutrients [eg, of minerals by adding oligopeptides or inulin-type fructans (Roberfroid, unpublished observations, 1997)].

Research on claims of enhanced function has already led and will continue to lead to new concepts in nutrition. Examples of such new concepts are prebiotics and synbiotics, colonic foods, and bifidogenic factors (12). Reduction in disease risk involves lowering the risk of pathologic effects or diseases by consuming a specific food components or ingredients. Examples are food components that may reduce the risk of cardiovascular disease,

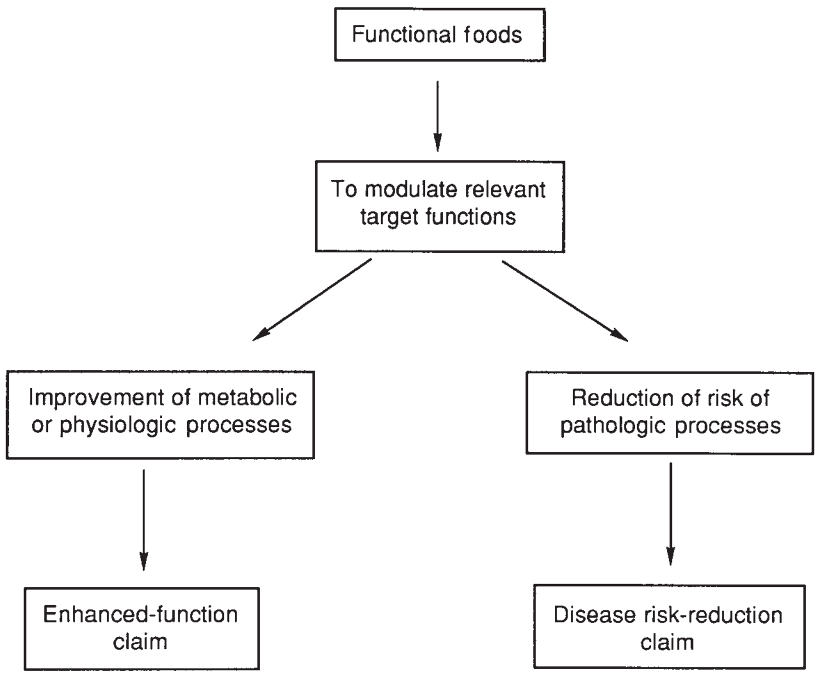

FIGURE 2. Scientific basis for enhanced structure-function or disease risk-reduction claims.

cancers, infections (eg, intestinal infections), atherosclerosis, liver disease, diarrhea, constipation, osteoporosis, or diseases associated with insulin resistance syndrome (eg, type 2 diabetes or obesity). Even though it will depend on the particular disease risk to be reduced, the demonstration of such health effects remains a difficult task that requires long-term experiments, the final results of which are difficult to predict and often hard to interpret.

In the case of some recent long-term studies on effects of antioxidant vitamins on lung cancer, a protective effect was anticipated but the opposite was actually found (13). This finding reinforces the importance of using a careful scientific approach based on a sound hypothesis and reasonable evidence of the mechanism of the health response expected. Both for enhanced function and reduction of disease risk, demonstration of an effect in humans will always be required in nutrition studies, but the protocols and evaluation criteria will not necessarily be those presently used in clinical studies for drug development.

The target population for these nutrition studies is, in most cases, "healthy persons" or "persons supposedly healthy" for whom the usual diet will be modified to demonstrate a significant change (statistically but, perhaps more important, biologically) in variables or biomarkers indicative of a state of good health. In the vast majority of these cases, these variables or biomarkers have yet to be discovered and validated.

PROCEDURES FOR AUTHORIZATION OF CLAIM

If a primary objective of functional food science is to contribute to the improvement, maintenance, and reinforcement of the health of consumers via a better diet, consumers and those who make recommendations to consumers have the right to require guarantees about the reliability of claims and the scientific data supporting them. Health authorities, in collaboration with the food industry and academia, will thus have the responsibility to elaborate procedures for authorizing claims that meet these legitimate requirements. Such an authorization can be given either by reference to a "positive list" or after scientific review of a file containing scientific information. Most of this information will have been published in peer-reviewed journals and will have shown a specific, biologically significant, and beneficial health interaction with one or a few functions in the body, leading either to maintenance (or possibly improvement) of a state of good health or reduction in the risk of a disease.

The establishment of a positive list and the evaluation of the dossiers containing all scientific data available, as well as the elaboration of the scientific requirements, must be made by a multidisciplinary expert committee. This committee should establish a constructive and confidential dialogue with the scientific representative of food industries with the objective of recommending, a priori, the most relevant protocols to demonstrate effects that could support a claim. Authorization for using a claim should also include a clear definition of the context as well as the limits of its communication to consumers. In particular, the dose necessary to cause a particular effect should be clearly identified on the label of each functional food for which the claim is authorized so as to make clear to consumers what portion of this dose they will be taking when consuming a given food product.

CONCLUSION

The development of functional foods provides a unique opportunity to contribute to improvement of the quality of the food offered to consumers who want to benefit their health and well-being. Only a rigorous scientific approach producing highly significant results will guarantee the success of this new discipline of nutrition. It is clearly a challenge for the food industry. However, before being considered an economic challenge, it is and must remain a scientific challenge. It is also a challenge for the health authorities because they need to elaborate new rules and new procedures that will be successful only if they rely on science in a constructive dialogue with all the relevant partners (ie, researchers in basic science, nutritionists and dietitians, and scientists in industry).

The major challenge to all these partners is to give consumers guarantees that these new food products not only are safe and based on research but also are products that will allow consumers to better control their health. It is also a challenge for nutritionists to include most of the new information in basic biological sciences in the development of new products and, at the same time, to develop new guidelines for better nutrition.

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